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(54) Title: PREVENTION OF DRUG DIVERSION

(57) Abstract: Implantable product(s) and methods for predetermined release of one or more active pharmaceutical ingredients (APIs). More specifically, implantable, subcutaneous product(s) and methods for treating depression and other mental and/or mood disorders and/or for prevention and/or mitigation of abuse of the one or more APIs, which may lead to addiction, intoxication, overdose, and/or death.

# PREVENTION OF DRUG DIVERSION

## FIELD OF THE INVENTION

**[0001]** Implantable, subcutaneous product(s) and methods for predetermined release of one or more active pharmaceutical ingredients (APIs). More specifically, implantable, subcutaneous product(s) and methods for treating depression and other mental and/or mood disorders and/or for prevention and/or mitigation of abuse of one or more APIs, which may lead to addiction, intoxication, overdose, and/or death.

## BACKGROUND OF THE DISCLOSURE

**[0001a]** Controlled substances, including but not limited to psychedelic drugs, have recently become of interest for the treatment of mental health disorders among other medical indications. A problem associated with the dispensing of controlled substances is the risk of the patient self-administering a larger dose than prescribed. This can result in addiction, intoxication, overdose, and possibly death.

## SUMMARY

[0001b] Aspects of the invention are as follows, which are non-limiting:

1. An implantable, subcutaneous product comprising one or more active pharmaceutical ingredient(s) (API(s)).

2. The implantable, subcutaneous product according to claim 1, wherein the implantable, subcutaneous product facilitates a sustained release of the one or more API(s).

3. The implantable, subcutaneous product according to claim 2, wherein the sustained release of the one or more API(s) is at a predetermined release rate and/or for a predetermined amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s).

4. The implantable, subcutaneous product according to claim 2 or 3, wherein the sustained release of the one or more API(s) from the implantable, subcutaneous product may be controlled or tuned before implantation into a subject.

5. The implantable, subcutaneous product according to claim 2 or 3, wherein the sustained release of the one or more API(s) from the implantable, subcutaneous product may be controlled or tuned after implantation into a subject.

6. The implantable, subcutaneous product according to any one of claims 1 to 5, wherein the one or more APIs comprise APIs classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

7. The implantable, subcutaneous product according to any one of claims 1 to 6, wherein the implantable, subcutaneous product is for preventing or mitigating abuse of the one or more API(s), which could lead to addiction, intoxication, overdose, and/or death.

8. The implantable, subcutaneous product according to any one of claims 1 to 7, wherein the implantable, subcutaneous product is for treatment of depression and other mental and/or mood disorders.

9. The implantable, subcutaneous product according to any one of claims 1 to 8, wherein the one or more API(s) are selected from the group consisting of Ergolines, Tryptamines, Phenethylamines and combinations thereof.

10. The implantable, subcutaneous product according to claim 9, wherein the Tryptamines are one or more of: DBT - N,N-Dibutyl-T, DET - N,N-Diethyl-T, DiPT - N,N-Diisopropyl-T, alpha,O-DMS - 5-Methyoxy-alpha-methyl-T, DMT - N,N-Dimethyl-T, 2,alpha-DMT - 2,alpha-Dimethyl-T, alpha,N-DMT - alpha,N-Dimethyl-T, DPT - N,N-Dipropyl-T, EiPT - N-Ethyl-N-isopropyl-T, alpha-ET - alpha-Ethyl-T, Harmaline - 3,4-Dihydro-7-methoxy-1-methyl-C, Harmine - 7-Methyoxy-1-methyl-C, 4-HO-DBT - N,N-Dibutyl-4-hydroxy-T, 4-HO-DET - N,N-Diethyl-4-hydroxy-T, 4-HO-DiPT - N,N-Diisopropyl-4-hydroxy-T, 4-HO-DMT - N,N-Dimethyl-4-hydroxy-T, 5-HO-DMT - N,N-Dimethyl-5-hydroxy-T, 4-HO-DPT - N,N-Dipropyl-4-hydroxy-T, 4-HO-MET - N-Ethyl-4-hydroxy-N-methyl-T, 4-HO-MiPT - 4-Hydroxy-N-isopropyl-N-methyl-T, 4-HO-MPT - 4-Hydroxy-N-methyl-N-propyl-T, 4-HO-pyr-T - 4-Hydroxy-N,N-tetramethylene-T, Ibogaine - A complexly substituted-T, MBT - N-Butyl-N-methyl-T, 4,5-MDO-DiPT - N,N-Diisopropyl-4,5-methylenedioxy-T, 5,6-MDO-DiPT - N,N-Diisopropyl-5,6-methylenedioxy-T, 4,5-MDO-DMT - N,N-Dimethyl-4,5-methylenedioxy-T, 5,6-MDO-DMT - N,N-Dimethyl-5,6-methylenedioxy-T, 5,6-MDO-MiPT - N-Isopropyl-N-methyl-5,6-methylenedioxy-T, 2-Me-DET - N,N-Diethyl-2-methyl-T, 2-Me-DMT - 2,N,N-Trimethyl-T, 5-MeO-DET - N,N-Diethyl-5-methoxy-T, 5-MeO-DiPT - N,N-Diisopropyl-5-

methoxy-T, 5-MeO-DMT - 5-Methoxy-N,N-dimethyl-T, 4-MeO-MiPT - N-Isopropyl-4-methoxy-N-methyl-T, 5-MeO-MiPT - N-Isopropyl-5-methoxy-N-methyl-T, 5,6-MeO-MiPT - 5,6-Dimethoxy-N-isopropyl-N-methyl-T, 5-MeO-NMT - 5-Methoxy-N-methyl-T, 5-MeO-pyr-T - 5-Methoxy-N,N-tetramethylene-T, 6-MeO-THH - 6-Methoxy-1-methyl-1,2,3,4-tetrahydro-C, 5-MeO-TMT - 5-Methoxy-2,N,N-trimethyl-T, 5-MeS-DMT - N,N-Dimethyl-5-methylthio-T, MiPT - N-Isopropyl-N-methyl-T, alpha-MT - alpha-Methyl-T, NET - N-Ethyl-T, NMT - N-Methyl-T, pyr-T - N,N-Tetramethylene-T, T – Tryptamine, Tetrahydroharmine - 7-Methoxy-1-methyl-1,2,3,4-tetrahydro-C, and alpha,N,O-TMS - alpha,N-Dimethyl-5-methoxy-T.

11. The implantable, subcutaneous product according to claim 9, wherein the Ergolines are one or more of: AL-LAD - 6-Allyl-N,N-diethyl-NL, ETH-LAD - 6,N,N-Triethyl-NL, LSD - N,N-Diethyl-Lysergic acid, PRO-LAD - 6-Propyl-NL, and 1P-LSD (1-propionyl-lysergic acid diethylamide).

12. The implantable, subcutaneous product according to any one of claims 1 to 9, wherein the API(s) comprises lysergic acid diethylamide (LSD) or a derivative or salt thereof.

13. The implantable, subcutaneous product according to any one of claims 1 to 9, wherein the API(s) comprises a composition comprising or consisting of lysergic acid diethylamide (LSD) or a derivative or salt thereof.

14. The implantable, subcutaneous product according to claim 9, wherein the Phenethylamines are one or more of: AEM - alpha-Ethyl-3,4,5-trimethoxy-PEA; AL - 4-Allyloxy-3,5-dimethoxy-PEA; ALEPH - 4-Methylthio-2,5-dimethoxy-A; ALEPH-2 - 4-Ethylthio-2,5-dimethoxy-A; ALEPH-4 - 4-Isopropylthio-2,5-dimethoxy-A; ALEPH-6 - 4-Phenylthio-2,5-dimethoxy-A; ALEPH-7 - 4-Propylthio-2,5-dimethoxy-A; ARIADNE - 2,5-Dimethoxy-alpha-ethyl-4-methyl-PEA; ASB - 3,4-Diethoxy-5-methoxy-PEA; B - 4-Butoxy-3,5-dimethoxy-PEA; BEATRICE - 2,5-Dimethoxy-4,N-dimethyl-A; BIS-TOM - 2,5-Bismethylthio-4-methyl-A; BOB - 4-Bromo-2,5,beta-trimethoxy-PEA; BOD - 2,5,beta-Trimethoxy-4-methyl-PEA; BOH - beta-Methoxy-3,4-methylenedioxy-PEA; BOHD - 2,5-Dimethoxy-beta-hydroxy-4-methyl-PEA; BOM - 3,4,5,beta-Tetramethoxy-PEA; 4-Br-3,5-DMA - 4-Bromo-3,5-dimethoxy-A; 2-Br-4,5-MDA - 2-Bromo-4,5-methylenedioxy-A; 2C-B - 4-Bromo-2,5-dimethoxy-PEA; 3C-BZ - 4-Benzyloxy-3,5-dimethoxy-A; 2C-C - 4-Chloro-2,5-dimethoxy-PEA; 2C-D - 4-Methyl-2,5-dimethoxy-PEA; 2C-E - 4-Ethyl-2,5-dimethoxy-PEA; 3C-E - 4-Ethoxy-3,5-dimethoxy-A, 2C-F - 4-Fluoro-2,5-dimethoxy-PEA; 2C-G - 3,4-Dimethyl-2,5-dimethoxy-PEA; 2C-G-3 - 3,4-

Trimethylene-2,5-dimethoxy-PEA; 2C-G-4 - 3,4-Tetramethylene-2,5-dimethoxy-PEA; 2C-G-5 - 3,4-Norbornyl-2,5-dimethoxy-PEA; 2C-G-N - 1,4-Dimethoxynaphthyl-2-ethylamine; 2C-H - 2,5-Dimethoxy-PEA; 2C-I - 4-Iodo-2,5-dimethoxy-PEA; 2C-N - 4-Nitro-2,5-dimethoxy-PEA; 2C-O-4 - 4-Isopropoxy-2,5-dimethoxy-PEA; 2C-P - 4-Propyl-2,5-dimethoxy-PEA; CPM - 4-Cyclopropylmethoxy-3,5-dimethoxy-PEA; 2C-SE - 4-Methylseleno-2,5-dimethoxy-PEA; 2C-T - 4-Methylthio-2,5-dimethoxy-PEA; 2C-T-2 - 4-Ethylthio-2,5-dimethoxy-PEA; 2C-T-4 - 4-Isopropylthio-2,5-dimethoxy-PEA; psi-2C-T-4 - 4-Isopropylthio-2,6-dimethoxy-PEA; 2C-T-7 - 4-Propylthio-2,5-dimethoxy-PEA; 2C-T-8 - 4-Cyclopropylmethylthio-2,5-dimethoxy-PEA; 2C-T-9 - 4-(t)-Butylthio-2,5-dimethoxy-PEA; 2C-T-13 - 4-(2-Methoxyethylthio)-2,5-dimethoxy-PEA; 2C-T-15 - 4-Cyclopropylthio-2,5-dimethoxy-PEA; 2C-T-17 - 4-(s)-Butylthio-2,5-dimethoxy-PEA; 2C-T-21 - 4-(2-Fluoroethylthio)-2,5-dimethoxy-PEA; 4-D - 4-Trideuteromethyl-3,5-dimethoxy-PEA; beta-D - beta,beta-Dideutero-3,4,5-trimethoxy-PEA; DESOXY - 4-Methyl-3,5-Dimethoxy-PEA; 2,4-DMA - 2,4-Dimethoxy-A; 2,5-DMA - 2,5-Dimethoxy-A; 3,4-DMA - 3,4-Dimethoxy-A; DMCPA - 2-(2,5-Dimethoxy-4-methylphenyl)-cyclopropylamine; DME - 3,4-Dimethoxy-beta-hydroxy-PEA; DMMDA - 2,5-Dimethoxy-3,4-methylenedioxy-A; DMMDA-2 - 2,3-Dimethoxy-4,5-methylenedioxy-A, DMPEA - 3,4-Dimethoxy-PEA; DOAM - 4-Amyl-2,5-dimethoxy-A; DOB - 4-Bromo-2,5-dimethoxy-A; DOBU - 4-Butyl-2,5-dimethoxy-A; DOC - 4-Chloro-2,5-dimethoxy-A; DOEF - 4-(2-Fluoroethyl)-2,5-dimethoxy-A; DOET - 4-Ethyl-2,5-dimethoxy-A; DOI - 4-Iodo-2,5-dimethoxy-A; DOM (STP) - 4-Methyl-2,5-dimethoxy-A, psi-DOM - 4-Methyl-2,6-dimethoxy-A; DON - 4-Nitro-2,5-dimethoxy-A; DOPR - 4-Propyl-2,5-dimethoxy-A; E - 4-Ethoxy-3,5-dimethoxy-PEA; EEE - 2,4,5-Triethoxy-A; EEM - 2,4-Diethoxy-5-methoxy-A; EME - 2,5-Diethoxy-4-methoxy-A; EMM - 2-Ethoxy-4,5-dimethoxy-A; ETHYL-J - N,alpha-diethyl-3,4-methylenedioxy-PEA; ETHYL-K - N-Ethyl-alpha-propyl-3,4-methylenedioxy-PEA; F-2 - Benzofuran-2-methyl-5-methoxy-6-(2-aminopropane); F-22 - Benzofuran-2,2-dimethyl-5-methoxy-6-(2-aminopropane); FLEA - N-Hydroxy-N-methyl-3,4-methylenedioxy-A; G-3 - 3,4-Trimethylene-2,5-dimethoxy-A; G-4 - 3,4-Tetramethylene-2,5-dimethoxy-A; G-5 - 3,4-Norbornyl-2,5-dimethoxy-A; GANESHA - 3,4-Dimethyl-2,5-dimethoxy-A; G-N - 1,4-Dimethoxynaphthyl-2-isopropylamine; HOT-2 - 2,5-Dimethoxy-N-hydroxy-4-ethylthio-PEA; HOT-7 - 2,5-Dimethoxy-N-hydroxy-4-(n)-propylthio-PEA; HOT-17 - 2,5-Dimethoxy-N-hydroxy-4-(s)-butylthio-PEA; IDNNA - 2,5-Dimethoxy-N,N-dimethyl-4-iodo-A; IM - 2,3,4-Trimethoxy-PEA; IP - 3,5-Dimethoxy-4-

isopropoxy-PEA; IRIS - 5-Ethoxy-2-methoxy-4-methyl-A; J - alpha-Ethyl-3,4-methylenedioxy-PEA; LOPHOPHINE - 3-Methoxy-4,5-methylenedioxy-PEA; M - 3,4,5-Trimethoxy-PEA; 4-MA - 4-Methoxy-A; MADAM-6 - 2,N-Dimethyl-4,5-methylenedioxy-A; MAL - 3,5-Dimethoxy-4-methallyloxy-PEA; MDA - 3,4-Methylenedioxy-A; MDAL - N-Allyl-3,4-methylenedioxy-A; MDBU - N-Butyl-3,4-methylenedioxy-A; MDBZ - N-Benzyl-3,4-methylenedioxy-A; MDCPM - N-Cyclopropylmethyl-3,4-methylenedioxy-A; MDDM - N,N-Dimethyl-3,4-methylenedioxy-A; MDE - N-Ethyl-3,4-methylenedioxy-A; MDHOET - N-(2-Hydroxyethyl)-3,4-methylenedioxy-A; MDIP - N-Isopropyl-3,4-methylenedioxy-A; MDMA - N-Methyl-3,4-methylenedioxy-A; MDMC - N-Methyl-3,4-ethylenedioxy-A; MDMEO - N-Methoxy-3,4-methylenedioxy-A; MDMEOET - N-(2-Methoxyethyl)-3,4-methylenedioxy-A; MDMP - alpha,alpha,N-Trimethyl-3,4-methylenedioxy-PEA; MDOH - N-Hydroxy-3,4-methylenedioxy-A; MDPEA - 3,4-Methylenedioxy-PEA; MDPH - alpha,alpha-Dimethyl-3,4-methylenedioxy-PEA; MDPL - N-Propargyl-3,4-methylenedioxy-A; MDPR - N-Propyl-3,4-methylenedioxy-A; ME - 3,4-Dimethoxy-5-ethoxy-PEA; MEDA - 3-methoxy-4,5-Ethylenedioxy-A; MEE - 2-Methoxy-4,5-diethoxy-A; MEM - 2,5-Dimethoxy-4-ethoxy-A; MEPEA - 3-Methoxy-4-ethoxy-PEA; META-DOB - 5-Bromo-2,4-dimethoxy-A; META-DOT - 5-Methylthio-2,4-dimethoxy-A; METHYL-DMA - N-Methyl-2,5-dimethoxy-A; METHYL-DOB - 4-Bromo-2,5-dimethoxy-N-methyl-A; METHYL-J - N-Methyl-alpha-ethyl-3,4-methylenedioxy-PEA; METHYL-K - N-Methyl-alpha-propyl-3,4-methylenedioxy-PEA; METHYL-MA - N-Methyl-4-methoxy-A; METHYL-MMDA-2 - N-Methyl-2-methoxy-4,5-methylenedioxy-A; MMDA - 3-Methoxy-4,5-methylenedioxy-A; MMDA-2 - 2-Methoxy-4,5-methylenedioxy-A; MMDA-3a - 2-Methoxy-3,4-methylenedioxy-A; MMDA-3b - 4-Methoxy-2,3-methylenedioxy-A; MME - 2,4-Dimethoxy-5-ethoxy-A; MP - 3,4-Dimethoxy-5-propoxy-PEA; MPM - 2,5-Dimethoxy-4-propoxy-A; ORTHO-DOT - 2-Methylthio-4,5-dimethoxy-A; P - 3,5-Dimethoxy-4-propoxy-PEA; PE - 3,5-Dimethoxy-4-phenethyloxy-PEA; PEA – PEA; PROPYNYL - 4-Propynyloxy-3,5-dimethoxy-PEA; SB - 3,5-Diethoxy-4-methoxy-PEA; TA - 2,3,4,5-Tetramethoxy-A; 3-TASB - 4-Ethoxy-3-ethylthio-5-methoxy-PEA; 4-TASB - 3-Ethoxy-4-ethylthio-5-methoxy-PEA; 5-TASB - 3,4-Diethoxy-5-methylthio-PEA; TB - 4-Thiobutoxy-3,5-dimethoxy-PEA; 3-TE - 4-Ethoxy-5-methoxy-3-methylthio-PEA; 4-TE - 3,5-Dimethoxy-4-ethylthio-PEA; 2-TIM - 2-Methylthio-3,4-dimethoxy-PEA; 3-TIM - 3-Methylthio-2,4-dimethoxy-PEA; 4-TIM - 4-Methylthio-2,3-dimethoxy-PEA; 3-TM - 3-Methylthio-4,5-

dimethoxy-PEA; 4-TM - 4-Methylthio-3,5-dimethoxy-PEA; TMA - 3,4,5-Trimethoxy-A; TMA-2 - 2,4,5-Trimethoxy-A; TMA-3 - 2,3,4-Trimethoxy-A; TMA-4 - 2,3,5-Trimethoxy-A; TMA-5 - 2,3,6-Trimethoxy-A; TMA-6 - 2,4,6-Trimethoxy-A; 3-TME - 4,5-Dimethoxy-3-ethylthio-PEA; 4-TME - 3-Ethoxy-5-methoxy-4-methylthio-PEA; 5-TME - 3-Ethoxy-4-methoxy-5-methylthio-PEA; 2T-MMDA-3a - 2-Methylthio-3,4-methylenedioxy-A; 4T-MMDA-2 - 4,5-Thiomethyleneoxy-2-methoxy-A; TMPEA - 2,4,5-Trimethoxy-PEA; 2-TOET - 4-Ethyl-5-methoxy-2-methylthio-A; 5-TOET - 4-Ethyl-2-methoxy-5-methylthio-A; 2-TOM - 5-Methoxy-4-methyl-2-methylthio-A; 5-TOM - 2-Methoxy-4-methyl-5-methylthio-A; TOMSO - 2-Methoxy-4-methyl-5-methylsulfinyl-A; TP - 4-Propylthio-3,5-dimethoxy-PEA; TRIS - 3,4,5-Triethoxy-PEA; 3-TSB - 3-Ethoxy-5-ethylthio-4-methoxy-PEA; 4-TSB - 3,5-Diethoxy-4-methylthio-PEA; 3-T-TRIS - 4,5-Diethoxy-3-ethylthio-PEA; and 4-T-TRIS - 3,5-Diethoxy-4-ethylthio-PEA.

15. The implantable, subcutaneous product according to claim 9, wherein the Phenethylamines are substituted beta-keto phenethylamines.

16. The implantable, subcutaneous product according to claim 15, wherein the substituted beta-keto phenethylamines are Methcathinone Cathinone and/or Cathine.

17. The implantable, subcutaneous product according to claim 15, wherein the substituted beta-keto phenethylamines are one or more of: 25B-NBOMe**;** 25B-NAcPip; 25B-NB; 25B-NB23DM; 25B-NB25DM; 25B-NB3OMe; 25B-NB4OMe; 25B-NBF; 25B-NBMD; 25B-NBOH; 25B-NBOMe (NBOMe-2CB); 25B-NMe7BF; 25B-NMe7BT; 25B-NMe7Box; 25B-NMe7DHBF; 25B-NMe7Ind; 25B-NMe7Indz; and 25B-NMePyr.

18. The implantable, subcutaneous product according to claim 9, wherein the API(s) is a substituted benzofurans of one or more of: 2C-B-FLY; 2CBFly-NBOMe (NBOMe-2CB-Fly); 2C-B-AN; 2C-B-BUTTERFLY; 2C-B-DRAGONFLY-NBOH; 2C-B-DragonFLY; 2C-B-FLY-NB2EtO5Cl; 2CB-5-hemifly; 2CB-Ind; βk-2C-B (beta-keto 2C-B); and TCB-2 (2C-BCB).

19. An implantable pellet or tablet comprising one or more active pharmaceutical ingredient(s) (API(s)), wherein the implantable pellet or tablet facilitates a sustained release of the one or more API(s).

20. The implantable implantable pellet or tablet according to claim 19, wherein the sustained release of the one or more API(s) is at a predetermined release rate and/or for a predetermined

amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s).

21. The implantable implantable pellet or tablet according to claim 19 or 20, wherein the sustained release of the one or more API(s) may be controlled or tuned before implantation into a subject.

22. The implantable pellet or tablet according to claim 19 or 20, wherein the sustained release of the one or more API(s) may be controlled or tuned after implantation into a subject.

23. The implantable pellet or tablet according to any one of claims 19 to 22, wherein the one or more APIs comprise APIs classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

24. The implantable pellet or tablet according to claim 23, wherein the one or more API(s) are selected from the group consisting of Ergolines, Tryptamines, Phenethylamines and combinations thereof.

25. The implantable pellet or tablet according to any one of claims 19 to 23, wherein the one or more API(s) is lysergic acid diethylamide (LSD) or a derivative or salt thereof for providing a controlled and/or pulsatile release of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof.

26. The implantable pellet or tablet according to any one of claims 19 to 25, wherein the pellet or tablet comprises (i) coated particles, and (ii) one or more excipients.

27. The implantable pellet or tablet according to claim 26, wherein the coated particles comprise a core coated with one or more release layers, each of the one or more release layers comprises one or more polymers and/or copolymers.

28. The implantable pellet or tablet according to claim 27, wherein an amount of the one or more API(s) included within the core is from about 5% to about 80% by weight of the core.

29. The implantable pellet or tablet according to claim 27, wherein an amount of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof included within the core ranges from about 5% to about 80% by weight of the core.

30. The implantable pellet or tablet according to claim 29, wherein an amount of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof included within the core ranges from about 40% to about 70% by weight of the core.

31. The implantable pellet or tablet according to claim 29, wherein an amount of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof included within the core ranges from about 55% to about 65% by weight of the core.

32. The implantable pellet or tablet according to any one of claims 27 to 31, wherein the core further comprises one or more additives selected from the group consisting of binders, fillers, osmotic agents, diluents, absorbents, colorants, dyes, pigments, disintegrants, dispersants, encapsulants, flow aids, hardeners, permeation enhancers, demulcents, stabilizers, disintegrants, tableting aids, glidants, lubricants, plasticizers and wetting agents.

33. The implantable pellet or tablet according to claim 32, wherein an amount of additives in the core is from about 1% to about 60% by weight of the core.

34. The implantable pellet or tablet according to any one of claims 27 to 33, wherein the one or more polymers or copolymers are selected from water soluble polymers and/or copolymers, water insoluble polymers and/or copolymers, or any mixture thereof.

35. The implantable pellet or tablet according to claim 34, wherein the water soluble polymers comprise ethylcellulose, an aqueous suspension system of ethylcellulose, and/or co-polymers of acrylic and methacrylic acid esters.

36. The implantable pellet or tablet according to claim 34, wherein the water soluble polymers comprise polyvinylpyrrolidone or hypromellose.

37. The implantable pellet or tablet according to claim 34, wherein the polymer is selected from the group consisting of polymethacrylates, cellulose, polymeric derivatives of acetate, polymeric derivatives of citrate, and mixtures thereof.

38. The implantable pellet or tablet according to claim 34, wherein the polymer is selected from the group consisting of ethyl cellulose, cellulose acetate, cellulose acetate butyrate, ethylene vinylacetate copolymer, polyvidone acetate, polyvinyl acetate, ethyl acrylate/methyl methacrylate copolymer, ammonia methacrylate copolymer, methylcellulose, hydroxypropyl cellulose, and combinations thereof.

39. The implantable pellet or tablet according to claim 34, wherein the polymer comprises a mixture of Aquacoat ECD, (30% by weight aqueous dispersion of ethylcelluose polymer) and acetyltributyl citrate (CAS 77-90-7).

40. The implantable pellet or tablet according to any one of claims 27 to 39, wherein the one or more release layers may further comprise one or more additives selected from binders, fillers, diluents, absorbents, colorants, dyes, pigments, disintegrants, dispersants, encapsulants, flow aids, hardeners, permeation enhancers, demulcents, stabilizers, disintegrants, tableting aids, anti-tack agents, glidants, lubricants, wetting agents and combinations thereof.

41. The implantable pellet or tablet according to any one of claims 27 to 40, wherein the one or more release layers are applied/coated onto the core using a coating apparatus including a centrifugal fluidized bed coating apparatus, a pan coating apparatus, or a fluidized bed coating apparatus.

42. The implantable pellet or tablet according to any one of claims 27 to 41, wherein any solvent used to form the one or more release layers onto the core is removed by drying and/or curing.

43. The implantable pellet or tablet according to any one of claims 27 to 42, wherein for the pulsatile release, the core is coated with one or more release layers, followed by removal of a desired percentage of the coated API(s) to form an appropriate release profile from the particles.

44. The implantable pellet or tablet according to any one of claims 19 to 43, wherein the coated particles are blended with an excipient that is pressed into a cylinder or capsule to provide a shaped pellet or tablet.

45. The implantable pellet or tablet according to any one of claims 19 to 44, wherein the pellet or tablet is packaged into a glass vial or blister pack that is terminally sterilized by exposure to gamma radiation or e-beam treatment.

46. The implantable pellet or tablet according to any one of claims 19 to 45 for administration under anesthesia.

47. The implantable pellet or tablet according to claim 46, wherein a trocar is for use with said pellet or tablet for said administration via an incision

48. The implantable pellet or tablet according to any one of claims 19 to 47, further comprising a lipid derivative to further modify the release profile of the API.

49. The implantable pellet or tablet according to claim 48, wherein the lipid derivative is Cholesterol, Stearic Acid, and/or Glyceryl tristearate.

50. The implantable pellet or tablet according to claim 48, wherein the lipid derivative is Dynasan$^{TM}$ 118.

50a. A method for treatment of a subject suffering from depression or other mental and/or mood disorders, the method comprising subcutaneous administration of one or more of the implantable, subcutaneous product according to any one of claims 1 to 18, or one or more of the implantable pellet or tablet according to any one of claims 19 to 50 to the subject.

50b. A method for preventing or mitigating abuse of the one or more API(s), which could lead to addiction, intoxication, overdose, and/or death, the method comprising subcutaneous administration of one or more of the implantable, subcutaneous product according to any one of claims 1 to 18, or one or more of the implantable pellet or tablet according to any one of claims 19 to 50 to the subject.

50c. The method according to claim 50a or 50b, wherein said one or more of the implantable, subcutaneous product according to any one of claims 1 to 18, or the one or more of the implantable pellet or tablet according to any one of claims 19 to 50 can each comprise a different API(s) or combination of API(s).

51. A subcutaneously implantable medical device for sustained or pulsatile release of one or more API(s) at a predetermined release rate and/or for a predetermined amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s), optionally wherein the device comprises a programming interface for control of the release of the one or more API(s).

52. The subcutaneously implantable medical device according to claim 51, wherein the wherein the one or more API(s) are selected from the group consisting of Ergolines, Tryptamines, Phenethylamines and combinations thereof.

53. The subcutaneously implantable medical device according to claim 52, wherein the Ergolines are one or more of: AL-LAD - 6-Allyl-N,N-diethyl-NL, ETH-LAD - 6,N,N-Triethyl-NL, LSD - N,N-Diethyl-Lysergic acid, PRO-LAD - 6-Propyl-NL, and 1P-LSD (1-propionyl-lysergic acid diethylamide).

54. The subcutaneously implantable medical device according to claim 53, wherein the Ergoline comprises lysergic acid diethylamide (LSD) or a derivative or salt thereof.

55. The subcutaneously implantable medical device according to claim 53, wherein the Ergolines comprises a composition comprising or consisting of lysergic acid diethylamide (LSD) or a derivative or salt thereof.

56. The subcutaneously implantable medical device according to any one of claims 51 to 55, wherein the device is for preventing or mitigating abuse of the one or more API(s), which could lead to addiction, intoxication, overdose, and/or death.

57. The subcutaneously implantable medical device according to any one of claims 51 to 56, wherein the device is for treatment of depression and other mental and/or mood disorders.

58. The subcutaneously implantable medical device according to any one of claims 51 to 57, manufactured on a 3D printer or by Fused Deposition Modelling (FDM).

59. A method of treating a subject suffering from depression or other mental and/or mood disorders, the method comprising:

implanting a subcutaneous product comprising one or more active pharmaceutical ingredient(s) (API(s)) into the subject, wherein the subcutaneous product is configured for a sustained release of the one or more API(s), and wherein the sustained release is a predetermined release rate and/or a predetermined amount of time.

60. The method of claim 59, wherein the implantable, subcutaneous product, after implantation facilitates the release of the one or more API(s) for a predetermined amount of time for achieving a predetermined blood plasma concentration(s) of the one or more APIs.

61. The method of claim 59 or 60, wherein the product is configured for adjusting the release of the one or more API(s) after implantation.

62. The method of any one of claims 59 to 61, wherein the one or more API(s) comprise one or more API(s) classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

63. A method for preventing or mitigating abuse of one or more API(s) by a subject, which may lead to addiction, intoxication, overdose, and/or death of the subject, the method comprising:

implanting a subcutaneous product comprising one or more active pharmaceutical ingredients (API(s)) into the subject, wherein the subcutaneous product is configured for a sustained release of the one or more API(s), and wherein the sustained release is a predetermined release rate and/or a predetermined amount of time.

64. The method of claim 63, wherein the implantable, subcutaneous product, after implantation facilitates the release of the one or more API(s) for a predetermined amount of time for achieving a predetermined blood plasma concentration(s) of the one or more API(s).

65. The method of claim 63 or 64, wherein the product is configured for adjusting the release of the one or more API(s) after implantation.

66. The method of any one of claims 63 to 65, wherein the one or more API(s) comprise API(s) classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

67. The method of any one of claims 59 to 66, wherein the one or more API(s) comprises lysergic acid diethylamide (LSD) or a derivative or salt thereof.

68. The implantable pellet or tablet according to any one of claims 19 to 31, wherein the one or more API(s) is blended with a solvent and optionally a surfactant.

69. The implantable pellet or tablet according to claim 68, wherein the solvent comprises a water-soluble organic solvent selected from the group consisting of: polyethylene glycol 300, polyethylene glycol 400, ethanol, propylene glycol, glycerin, N-methyl-2-pyrrolidone, dimethylacetamide, and dimethylsulfoxide.

70. The implantable pellet or tablet according to claim 68, wherein the surfactant comprises a non-ionic surfactant selected from the group consisting of non-ionic surfactants Cremophor EL, Cremophor RH 40, Cremophor RH 60, d--tocopherol, polyethylene glycol 1000 succinate, polysorbate 20, polysorbate 80, Solutol HS 15, sorbitan monooleate, poloxamer 407, Labrafil M-1944CS, Labrafil M-2125CS, Labrasol, Gellucire 44/14, Softigen 767, and mono- and di-fatty acid esters of PEG 300, 400, or 1750), water-insoluble lipids (castor oil, corn oil, cottonseed oil, olive oil, peanut oil, peppermint oil, safflower oil, sesame oil, soybean oil, hydrogenated vegetable oils, hydrogenated soybean oil, and medium-chain triglycerides of coconut oil and palm seed oil), organic liquids/semi-solids (beeswax, d--tocopherol, oleic acid, medium-chain mono- and diglycerides), various cyclodextrins (-cyclodextrin, -cyclodextrin, hydroxypropyl--cyclodextrin, and sulfobutylether-cyclodextrin), and phospholipids (hydrogenated soy phosphatidylcholine, distearoylphosphatidylglycerol, L-dimyristoylphosphatidylcholine, L-dimyristoylphosphatidylglycerol.

71. The implantable pellet or tablet according to any one of claims 68 to 70, wherein water-insoluble API(s) are solubilized by pH adjustment, cosolvents, complexation, microemulsions, self-emulsifying drug delivery systems, micelles, liposomes, and emulsions.

72. The implantable pellet or tablet according to any one of claims 68 to 71, formulated with one or more of Poly(D, L-lactide) (PDLLA) and Poly(D, L-lactide-co-glycolide) (PLGA) polymers and sterile filtered into a sterile vial for administration.

73. The implantable pellet or tablet according to any one of claims 68 to 72, wherein the solvent is absorbed by the body of the subject leaving the one or more API(s) in a polymer that has a controlled release based on the length and substitution of the polymer.

74. The implantable pellet or tablet according to claim 73, wherein the administered bioabsorbable polymer allows for a pulsatile controlled release of the one or more API(s) from hours to over a year.

75. A subcutaneously implantable product for sustained or pulsatile release of one or more API(s) at a predetermined release rate and/or for a predetermined amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s),

wherein the one or more API(s) is blended with a polymer for providing a desired release duration, the polymer selected from one or more of: urethane; PGA, PGLA, Hydralese(tm) (PGSU) (poly(glycerol sebacate) urethane), Polyvinyl alcohol (PVA); Poly(vinylpyrrolidone) (PVP); (MW 7000–11,000) Kollidon® 17 PF, (MW 2000–3000) Kollidon® 12 PF, Poly(vinylpyrrolidone)/vinyl acetate; (PVP/VA) (MW 45,000–70,000) Kollidon® VA64; Poly(vinyl caprolactam-covinylacetate-ethylene glycol, (MW 90,000–140,000) Soluplus®; Hydroxypropyl cellulose (HPC); (MW 95,000) Klucel® LF; Hydroxypropylmethyl cellulose (HPMC); (MW 25,000) Methocel™ K100LV; (MW 150,000) Methocel™ K100M; Hydroxypropyl methyl cellulose acetate succinate (HPMCAS) Affinisol™; Poly ethylene oxide (PEO); Poly(butyl methacrylate-co-(2-demethylamino ethyl) methacrylate-co-methyl methacrylate) 1:2:1 Eudragit E PO®; Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonio ethyl methacrylate chloride) 1:2:0.2 Eudragit RL®; Poly(methacrylic acid-co-methyl methacrylate) 1:1 Eudragit L®; Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethylmethacrylate chloride) 1:2:0.1 Eudragit RS®; Poly(e-caprolactone) (PCLa); Ethylene vinyl acetate (EVA); Ethylcellulose; (4 cPs) Ethocel® 4P; (7 cPs) Ethocel® 7P; (10 cPs) Ethocel® 10P; Polyvinyl alcohol; polyethylene glycol graft copolymer (PVA:PEG) Kollicoat® IR; LSD tartrate (melting point 80°F to 85°C (176°F to 185°F); and (poly(glycerol sebacate) urethane), and

wherein the subcutaneously implantable product is for treatment of a subject suffering from depression or other mental and/or mood disorders, and/or

wherein the subcutaneously implantable product is for preventing or mitigating abuse of the one or more API(s) by the subject, which could lead to addiction, intoxication, overdose, and/or death.

76. The subcutaneously implantable product according to claim 75, wherein the one or more polymer(s)s are selected compatible with Hot Melt Extrusion (HME).

## DETAILED DESCRIPTION

**[0002]** It should also be understood that, unless clearly indicated to the contrary, in any methods claimed herein that include more than one step or act, the order of the steps or acts of the method is not necessarily limited to the order in which the steps or acts of the method are recited.

**[0003]** References in the specification to "one embodiment," "an embodiment," "an illustrative embodiment," etc., indicate that the embodiment described may include a particular feature, structure, or characteristic, but every embodiment may or may not necessarily include that particular feature, structure, or characteristic. Moreover, such phrases are not necessarily referring to the same embodiment. Further, when a particular feature, structure, or characteristic is described in connection with an embodiment, it is submitted that it is within the knowledge of one skilled in the art to affect such feature, structure, or characteristic in connection with other embodiments whether or not explicitly described.

**[0004]** As used herein, the singular terms "a," "an," and "the" include plural referents unless context clearly indicates otherwise. Similarly, the word "or" is intended to include "and" unless the context clearly indicates otherwise. The term "includes" is defined inclusively, such that "includes A or B" means including A, B, or A and B.

**[0005]** As used herein in the specification and in the claims, "or" should be understood to have the same meaning as "and/or" as defined above. For example, when separating items in a list, "or" or "and/or" shall be interpreted as being inclusive, e.g., the inclusion of at least one, but also including more than one, of a number or list of elements, and, optionally, additional unlisted items. Only terms clearly indicated to the contrary, such as "only one of" or "exactly one of," or, when used in the claims, "consisting of," will refer to the inclusion of exactly one element of a number or list of elements. In general, the term "or" as used herein shall only be interpreted as indicating exclusive alternatives (e.g. "one or the other but not both") when preceded by terms of

exclusivity, such as "either" "one of," "only one of" or "exactly one of." "Consisting essentially of," when used in the claims, shall have its ordinary meaning as used in the field of patent law.

**[0006]** As used herein, the terms "comprising," "including," "having," and the like are used interchangeably and have the same meaning. Similarly, "comprises," "includes," "has," and the like are used interchangeably and have the same meaning. Specifically, each of the terms is defined consistent with the common United States patent law definition of "comprising" and is therefore interpreted to be an open term meaning "at least the following," and is also interpreted not to exclude additional features, limitations, aspects, etc. Thus, for example, "a device having components a, b, and c" means that the device includes at least components a, b, and c. Similarly, the phrase: "a method involving steps a, b, and c" means that the method includes at least steps a, b, and c. Moreover, while the steps and processes may be outlined herein in a particular order, the skilled artisan will recognize that the ordering steps and processes may vary.

**[0007]** As used herein in the specification and in the claims, the phrase "at least one," in reference to a list of one or more elements, should be understood to mean at least one element selected from any one or more of the elements in the list of elements, but not necessarily including at least one of each and every element specifically listed within the list of elements and not excluding any combinations of elements in the list of elements. This definition also allows that elements may optionally be present other than the elements specifically identified within the list of elements to which the phrase "at least one" refers, whether related or unrelated to those elements specifically identified. Thus, as a non-limiting example, "at least one of A and B" (or, equivalently, "at least one of A or B," or, equivalently "at least one of A and/or B") can refer, in one embodiment, to at least one, optionally including more than one, A, with no B present (and optionally including elements other than B); in another embodiment, to at least one, optionally including more than one, B, with no A present (and optionally including elements other than A); in yet another embodiment, to at least one, optionally including more than one, A, and at least one, optionally including more than one, B (and optionally including other elements); etc.

**[0008]** As used herein, the term "subject" refers to any animal subject including laboratory animals (e.g., primates, rats, mice), livestock (e.g., cows, sheep, goats, pigs, turkeys, chickens), household pets (e.g., dogs, cats, rodents, etc.), and humans. Typically, the mammal is a human (homo sapiens).

**[0009]** As used herein, the terms "treatment," "treating," or "treat," with respect to a specific condition (e.g. major depressive disorder), refer to obtaining a desired pharmacologic and/or physiologic effect. The effect can be prophylactic in terms of completely or partially preventing a disease or symptom thereof and/or can be therapeutic in terms of a partial or complete cure for a disease and/or adverse effect attributable to the disease. "Treatment", as used herein, covers any treatment of a disease or disorder in a subject, particularly in a human, and includes: (a) preventing the disease or disorder from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it; (b) inhibiting the disease or disorder, i.e., arresting its development; and (c) relieving or alleviating the disease or disorder, i.e., causing regression of the disease or disorder and/or relieving one or more disease or disorder symptoms. "Treatment" can also encompass delivery of an agent or administration of a therapy in order to provide for a pharmacologic effect, even in the absence of a disease, disorder or condition. The term "treatment" is used in some embodiments to refer to administration of a compound of the present disclosure to mitigate a disease or a disorder in a host, preferably in a mammalian subject, more preferably in humans. Thus, the term "treatment" can include preventing a disorder from occurring in a host, particularly when the host is predisposed to acquiring the disease but has not yet been diagnosed with the disease; inhibiting the disorder; and/or alleviating or reversing the disorder. As far as the methods of the present disclosure are directed to preventing disorders, it is understood that the term "prevent" does not require that the disease state be completely thwarted. Rather, as used herein, the term preventing refers to the ability of the skilled artisan to identify a population that is susceptible to disorders, such that administration of the compounds of the present disclosure can occur prior to onset of a disease. The term does not mean that the disease state must be completely avoided.

**[0009a]** As recited herein, any recited feature can be excluded from any aspect using a negative limitation.

**[0010]** **Overview**

**[0011]** It would be desirable to treat subjects suffering from depression and other mental and/or mood disorders with an implantable, subcutaneous product including one or more active pharmaceutical ingredients (APIs). In some embodiments, the implantable, subcutaneous product facilitates a sustained release of the one or more APIs, such as at a predetermined release rate

and/or for a predetermined amount of time. In some embodiments, the implantable, subcutaneous product, after implantation to a subject in need of treatment thereof, facilitates the release of the one or more APIs for a predetermined amount of time to achieve predetermined blood plasma concentrations of the one or more APIs. In some embodiments, the release of the one or more APIs from the implantable, subcutaneous product may be controlled or tuned after implantation into a subject in need of treatment thereof. In those embodiments where the one or more APIs include one or more APIs classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances, the implantable, subcutaneous product of the present disclosure may prevent or mitigate abuse of the one or more APIs, which could lead to addiction, intoxication, overdose, and/or death.

**[0012]** In some embodiments, the one or more APIs are selected from the group consisting of Ergolines, Tryptamines, and Phenethylamines. Examples of Tryptamines include, but are not limited, to the following:

**[0013]** DBT - N,N-Dibutyl-T (di-**n**-butyltin)

**[0014]** DET - N, N -diethyltryptamine

**[0015]** DiPT - N,N-Diisopropyl-T

**[0016]** alpha,O-DMS - 5-Methyoxy-alpha-methyl-T

**[0017]** DMT - N,N-Dimethyl-T

**[0018]** 2,alpha-DMT - 2,alpha-Dimethyl-T

**[0019]** alpha,N-DMT - alpha,N-Dimethyl-T

**[0020]** DPT - N,N-Dipropyl-T

**[0021]** EiPT - N-Ethyl-N-isopropyl-T

**[0022]** alpha-ET - alpha-Ethyl-T

**[0023]** Harmaline - 3,4-Dihydro-7-methoxy-1-methyl-C

**[0024]** Harmine - 7-Methyoxy-1-methyl-C

**[0025]** 4-HO-DBT - N,N-Dibutyl-4-hydroxy-T

**[0026]** 4-HO-DET - N,N-Diethyl-4-hydroxy-T

**[0027]** 4-HO-DiPT - N,N-Diisopropyl-4-hydroxy-T

**[0028]** 4-HO-DMT - N,N-Dimethyl-4-hydroxy-T

**[0029]** 5-HO-DMT - N,N-Dimethyl-5-hydroxy-T

**[0030]** 4-HO-DPT - N,N-Dipropyl-4-hydroxy-T

[0031] 4-HO-MET - N-Ethyl-4-hydroxy-N-methyl-T

[0032] 4-HO-MiPT - 4-Hydroxy-N-isopropyl-N-methyl-T

[0033] 4-HO-MPT - 4-Hydroxy-N-methyl-N-propyl-T

[0034] 4-HO-pyr-T - 4-Hydroxy-N,N-tetramethylene-T

[0035] Ibogaine

[0036] MBT - N-Butyl-N-methyl-Tryptamine

[0037] 4,5-MDO-DiPT - N,N-Diisopropyl-4,5-methylenedioxy-T

[0038] 5,6-MDO-DiPT - N,N-Diisopropyl-5,6-methylenedioxy-T

[0039] 4,5-MDO-DMT - N,N-Dimethyl-4,5-methylenedioxy-T

[0040] 5,6-MDO-DMT - N,N-Dimethyl-5,6-methylenedioxy-T

[0041] 5,6-MDO-MiPT - N-Isopropyl-N-methyl-5,6-methylenedioxy-T

[0042] 2-Me-DET - N,N-Diethyl-2-methyl-T

[0043] 2-Me-DMT - 2,N,N-Trimethyl-T

[0044] 5-MeO-DET - N,N-Diethyl-5-methoxy-T

[0045] 5-MeO-DiPT - N,N-Diisopropyl-5-methoxy-T

[0046] 5-MeO-DMT - 5-Methoxy-N,N-dimethyl-T

[0047] 4-MeO-MiPT - N-Isopropyl-4-methoxy-N-methyl-T

[0048] 5-MeO-MiPT - N-Isopropyl-5-methoxy-N-methyl-T

[0049] 5,6-MeO-MiPT - 5,6-Dimethoxy-N-isopropyl-N-methyl-T

[0050] 5-MeO-NMT - 5-Methoxy-N-methyl-T

[0051] 5-MeO-pyr-T - 5-Methoxy-N,N-tetramethylene-T

[0052] 6-MeO-THH - 6-Methoxy-1-methyl-1,2,3,4-tetrahydro-C

[0053] 5-MeO-TMT - 5-Methoxy-2,N,N-trimethyl-T

[0054] 5-MeS-DMT - N,N-Dimethyl-5-methylthio-T

[0055] MiPT - N-Isopropyl-N-methyl-T

[0056] alpha-MT - alpha-Methyl-T

[0057] NET - N-Ethyl-T

[0058] NMT - N-Methyl-T

[0059] pyr-T - N,N-Tetramethylene-T

[0060] T - Tryptamine

[0061] Tetrahydroharmine - 7-Methoxy-1-methyl-1,2,3,4-tetrahydro-C

**[0062]** alpha,N,O-TMS - alpha,N-Dimethyl-5-methoxy-T

**[0063]** Examples of Ergolines include, but are not limited, to the following:

**[0064]** AL-LAD - 6-Allyl-N,N-diethyl-NL

**[0065]** ETH-LAD - 6,N,N-Triethyl-NL

**[0066]** LSD - N,N-Diethyl-Lysergic acid

**[0067]** PRO-LAD - 6-Propyl-NL

**[0068]** 1P-LSD (1-propionyl-lysergic acid diethylamide)

**[0069]** Examples of Phenethylamines include, but are not limited to, the following:

**[0070]** AEM - alpha-Ethyl-3,4,5-trimethoxy-PEA

**[0071]** AL - 4-Allyloxy-3,5-dimethoxy-PEA

**[0072]** ALEPH - 4-Methylthio-2,5-dimethoxy-A

**[0073]** ALEPH-2 - 4-Ethylthio-2,5-dimethoxy-A

**[0074]** ALEPH-4 - 4-Isopropylthio-2,5-dimethoxy-A

**[0075]** ALEPH-6 - 4-Phenylthio-2,5-dimethoxy-A

**[0076]** ALEPH-7 - 4-Propylthio-2,5-dimethoxy-A

**[0077]** ARIADNE - 2,5-Dimethoxy-alpha-ethyl-4-methyl-PEA

**[0078]** ASB - 3,4-Diethoxy-5-methoxy-PEA

**[0079]** B - 4-Butoxy-3,5-dimethoxy-PEA

**[0080]** BEATRICE - 2,5-Dimethoxy-4,N-dimethyl-A

**[0081]** BIS-TOM - 2,5-Bismethylthio-4-methyl-A

**[0082]** BOB - 4-Bromo-2,5,beta-trimethoxy-PEA

**[0083]** BOD - 2,5,beta-Trimethoxy-4-methyl-PEA

**[0084]** BOH - beta-Methoxy-3,4-methylenedioxy-PEA

**[0085]** BOHD - 2,5-Dimethoxy-beta-hydroxy-4-methyl-PEA

**[0086]** BOM - 3,4,5,beta-Tetramethoxy-PEA

**[0087]** 4-Br-3,5-DMA - 4-Bromo-3,5-dimethoxy-A

**[0088]** 2-Br-4,5-MDA - 2-Bromo-4,5-methylenedioxy-A

**[0089]** 2C-B - 4-Bromo-2,5-dimethoxy-PEA

**[0090]** 3C-BZ - 4-Benzyloxy-3,5-dimethoxy-A

**[0091]** 2C-C - 4-Chloro-2,5-dimethoxy-PEA

**[0092]** 2C-D - 4-Methyl-2,5-dimethoxy-PEA

**[0093]** 2C-E - 4-Ethyl-2,5-dimethoxy-PEA

**[0094]** 3C-E - 4-Ethoxy-3,5-dimethoxy-A

**[0095]** 2C-F - 4-Fluoro-2,5-dimethoxy-PEA

**[0096]** 2C-G - 3,4-Dimethyl-2,5-dimethoxy-PEA

**[0097]** 2C-G-3 - 3,4-Trimethylene-2,5-dimethoxy-PEA

**[0098]** 2C-G-4 - 3,4-Tetramethylene-2,5-dimethoxy-PEA

**[0099]** 2C-G-5 - 3,4-Norbornyl-2,5-dimethoxy-PEA

**[00100]** 2C-G-N - 1,4-Dimethoxynaphthyl-2-ethylamine

**[00101]** 2C-H - 2,5-Dimethoxy-PEA

**[00102]** 2C-I - 4-Iodo-2,5-dimethoxy-PEA

**[00103]** 2C-N - 4-Nitro-2,5-dimethoxy-PEA

**[00104]** 2C-O-4 - 4-Isopropoxy-2,5-dimethoxy-PEA

**[00105]** 2C-P - 4-Propyl-2,5-dimethoxy-PEA

**[00106]** CPM - 4-Cyclopropylmethoxy-3,5-dimethoxy-PEA

**[00107]** 2C-SE - 4-Methylseleno-2,5-dimethoxy-PEA

**[00108]** 2C-T - 4-Methylthio-2,5-dimethoxy-PEA

**[00109]** 2C-T-2 - 4-Ethylthio-2,5-dimethoxy-PEA

**[00110]** 2C-T-4 - 4-Isopropylthio-2,5-dimethoxy-PEA

**[00111]** psi-2C-T-4 - 4-Isopropylthio-2,6-dimethoxy-PEA

**[00112]** 2C-T-7 - 4-Propylthio-2,5-dimethoxy-PEA

**[00113]** 2C-T-8 - 4-Cyclopropylmethylthio-2,5-dimethoxy-PEA

**[00114]** 2C-T-9 - 4-(t)-Butylthio-2,5-dimethoxy-PEA

**[00115]** 2C-T-13 - 4-(2-Methoxyethylthio)-2,5-dimethoxy-PEA

**[00116]** 2C-T-15 - 4-Cyclopropylthio-2,5-dimethoxy-PEA

**[00117]** 2C-T-17 - 4-(s)-Butylthio-2,5-dimethoxy-PEA

**[00118]** 2C-T-21 - 4-(2-Fluoroethylthio)-2,5-dimethoxy-PEA

**[00119]** 4-D - 4-Trideuteromethyl-3,5-dimethoxy-PEA

**[00120]** beta-D - beta,beta-Dideutero-3,4,5-trimethoxy-PEA

**[00121]** DESOXY - 4-Methyl-3,5-Dimethoxy-PEA

**[00122]** 2,4-DMA - 2,4-Dimethoxy-A

**[00123]** 2,5-DMA - 2,5-Dimethoxy-A

**[00124]** 3,4-DMA - 3,4-Dimethoxy-A

**[00125]** DMCPA - 2-(2,5-Dimethoxy-4-methylphenyl)-cyclopropylamine

**[00126]** DME - 3,4-Dimethoxy-beta-hydroxy-PEA

**[00127]** DMMDA - 2,5-Dimethoxy-3,4-methylenedioxy-A

**[00128]** DMMDA-2 - 2,3-Dimethoxy-4,5-methylenedioxy-A

**[00129]** DMPEA - 3,4-Dimethoxy-PEA

**[00130]** DOAM - 4-Amyl-2,5-dimethoxy-A

**[00131]** DOB - 4-Bromo-2,5-dimethoxy-A

**[00132]** DOBU - 4-Butyl-2,5-dimethoxy-A

**[00133]** DOC - 4-Chloro-2,5-dimethoxy-A

**[00134]** DOEF - 4-(2-Fluoroethyl)-2,5-dimethoxy-A

**[00135]** DOET - 4-Ethyl-2,5-dimethoxy-A

**[00136]** DOI - 4-Iodo-2,5-dimethoxy-A

**[00137]** DOM (STP) - 4-Methyl-2,5-dimethoxy-A

**[00138]** psi-DOM - 4-Methyl-2,6-dimethoxy-A

**[00139]** DON - 4-Nitro-2,5-dimethoxy-A

**[00140]** DOPR - 4-Propyl-2,5-dimethoxy-A

**[00141]** E - 4-Ethoxy-3,5-dimethoxy-PEA

**[00142]** EEE - 2,4,5-Triethoxy-A

**[00143]** EEM - 2,4-Diethoxy-5-methoxy-A

**[00144]** EME - 2,5-Diethoxy-4-methoxy-A

**[00145]** EMM - 2-Ethoxy-4,5-dimethoxy-A

**[00146]** ETHYL-J - N,alpha-diethyl-3,4-methylenedioxy-PEA

**[00147]** ETHYL-K - N-Ethyl-alpha-propyl-3,4-methylenedioxy-PEA

**[00148]** F-2 - Benzofuran-2-methyl-5-methoxy-6-(2-aminopropane)

**[00149]** F-22 - Benzofuran-2,2-dimethyl-5-methoxy-6-(2-aminopropane)

**[00150]** FLEA - N-Hydroxy-N-methyl-3,4-methylenedioxy-A

**[00151]** G-3 - 3,4-Trimethylene-2,5-dimethoxy-A

**[00152]** G-4 - 3,4-Tetramethylene-2,5-dimethoxy-A

**[00153]** G-5 - 3,4-Norbornyl-2,5-dimethoxy-A

**[00154]** GANESHA - 3,4-Dimethyl-2,5-dimethoxy-A

**[00155]** G-N - 1,4-Dimethoxynaphthyl-2-isopropylamine

**[00156]** HOT-2 - 2,5-Dimethoxy-N-hydroxy-4-ethylthio-PEA

**[00157]** HOT-7 - 2,5-Dimethoxy-N-hydroxy-4-(n)-propylthio-PEA

**[00158]** HOT-17 - 2,5-Dimethoxy-N-hydroxy-4-(s)-butylthio-PEA

**[00159]** IDNNA - 2,5-Dimethoxy-N,N-dimethyl-4-iodo-A

**[00160]** IM - 2,3,4-Trimethoxy-PEA

**[00161]** IP - 3,5-Dimethoxy-4-isopropoxy-PEA

**[00162]** IRIS - 5-Ethoxy-2-methoxy-4-methyl-A

**[00163]** J - alpha-Ethyl-3,4-methylenedioxy-PEA

**[00164]** LOPHOPHINE - 3-Methoxy-4,5-methylenedioxy-PEA

**[00165]** M - 3,4,5-Trimethoxy-PEA

**[00166]** 4-MA - 4-Methoxy-A

**[00167]** MADAM-6 - 2,N-Dimethyl-4,5-methylenedioxy-A

**[00168]** MAL - 3,5-Dimethoxy-4-methallyloxy-PEA

**[00169]** MDA - 3,4-Methylenedioxy-A

**[00170]** MDAL - N-Allyl-3,4-methylenedioxy-A

**[00171]** MDBU - N-Butyl-3,4-methylenedioxy-A

**[00172]** MDBZ - N-Benzyl-3,4-methylenedioxy-A

**[00173]** MDCPM - N-Cyclopropylmethyl-3,4-methylenedioxy-A

**[00174]** MDDM - N,N-Dimethyl-3,4-methylenedioxy-A

**[00175]** MDE - N-Ethyl-3,4-methylenedioxy-A

**[00176]** MDHOET - N-(2-Hydroxyethyl)-3,4-methylenedioxy-A

**[00177]** MDIP - N-Isopropyl-3,4-methylenedioxy-A

**[00178]** MDMA - N-Methyl-3,4-methylenedioxy-A

**[00179]** MDMC - N-Methyl-3,4-ethylenedioxy-A

**[00180]** MDMEO - N-Methoxy-3,4-methylenedioxy-A

**[00181]** MDMEOET - N-(2-Methoxyethyl)-3,4-methylenedioxy-A

**[00182]** MDMP - alpha,alpha,N-Trimethyl-3,4-methylenedioxy-PEA

**[00183]** MDOH - N-Hydroxy-3,4-methylenedioxy-A

**[00184]** MDPEA - 3,4-Methylenedioxy-PEA

**[00185]** MDPH - alpha,alpha-Dimethyl-3,4-methylenedioxy-PEA

**[00186]** MDPL - N-Propargyl-3,4-methylenedioxy-A

**[00187]** MDPR - N-Propyl-3,4-methylenedioxy-A

**[00188]** ME - 3,4-Dimethoxy-5-ethoxy-PEA

**[00189]** MEDA - 3-methoxy-4,5-Ethylenedioxy-A

**[00190]** MEE - 2-Methoxy-4,5-diethoxy-A

**[00191]** MEM - 2,5-Dimethoxy-4-ethoxy-A

**[00192]** MEPEA - 3-Methoxy-4-ethoxy-PEA

**[00193]** META-DOB - 5-Bromo-2,4-dimethoxy-A

**[00194]** META-DOT - 5-Methylthio-2,4-dimethoxy-A

**[00195]** METHYL-DMA - N-Methyl-2,5-dimethoxy-A

**[00196]** METHYL-DOB - 4-Bromo-2,5-dimethoxy-N-methyl-A

**[00197]** METHYL-J - N-Methyl-alpha-ethyl-3,4-methylenedioxy-PEA

**[00198]** METHYL-K - N-Methyl-alpha-propyl-3,4-methylenedioxy-PEA

**[00199]** METHYL-MA - N-Methyl-4-methoxy-A

**[00200]** METHYL-MMDA-2 - N-Methyl-2-methoxy-4,5-methylenedioxy-A

**[00201]** MMDA - 3-Methoxy-4,5-methylenedioxy-A

**[00202]** MMDA-2 - 2-Methoxy-4,5-methylenedioxy-A

**[00203]** MMDA-3a - 2-Methoxy-3,4-methylenedioxy-A

**[00204]** MMDA-3b - 4-Methoxy-2,3-methylenedioxy-A

**[00205]** MME - 2,4-Dimethoxy-5-ethoxy-A

**[00206]** MP - 3,4-Dimethoxy-5-propoxy-PEA

**[00207]** MPM - 2,5-Dimethoxy-4-propoxy-A

**[00208]** ORTHO-DOT - 2-Methylthio-4,5-dimethoxy-A

**[00209]** P - 3,5-Dimethoxy-4-propoxy-PEA

**[00210]** PE - 3,5-Dimethoxy-4-phenethyloxy-PEA

**[00211]** PEA - PEA

**[00212]** PROPYNYL - 4-Propynyloxy-3,5-dimethoxy-PEA

**[00213]** SB - 3,5-Diethoxy-4-methoxy-PEA

**[00214]** TA - 2,3,4,5-Tetramethoxy-A

**[00215]** 3-TASB - 4-Ethoxy-3-ethylthio-5-methoxy-PEA

**[00216]** 4-TASB - 3-Ethoxy-4-ethylthio-5-methoxy-PEA

**[00217]** 5-TASB - 3,4-Diethoxy-5-methylthio-PEA

**[00218]** TB - 4-Thiobutoxy-3,5-dimethoxy-PEA

**[00219]** 3-TE - 4-Ethoxy-5-methoxy-3-methylthio-PEA

**[00220]** 4-TE - 3,5-Dimethoxy-4-ethylthio-PEA

**[00221]** 2-TIM - 2-Methylthio-3,4-dimethoxy-PEA

**[00222]** 3-TIM - 3-Methylthio-2,4-dimethoxy-PEA

**[00223]** 4-TIM - 4-Methylthio-2,3-dimethoxy-PEA

**[00224]** 3-TM - 3-Methylthio-4,5-dimethoxy-PEA

**[00225]** 4-TM - 4-Methylthio-3,5-dimethoxy-PEA

**[00226]** TMA - 3,4,5-Trimethoxy-A

**[00227]** TMA-2 - 2,4,5-Trimethoxy-A

**[00228]** TMA-3 - 2,3,4-Trimethoxy-A

**[00229]** TMA-4 - 2,3,5-Trimethoxy-A

**[00230]** TMA-5 - 2,3,6-Trimethoxy-A

**[00231]** TMA-6 - 2,4,6-Trimethoxy-A

**[00232]** 3-TME - 4,5-Dimethoxy-3-ethylthio-PEA

**[00233]** 4-TME - 3-Ethoxy-5-methoxy-4-methylthio-PEA

**[00234]** 5-TME - 3-Ethoxy-4-methoxy-5-methylthio-PEA

**[00235]** 2T-MMDA-3a - 2-Methylthio-3,4-methylenedioxy-A

**[00236]** 4T-MMDA-2 - 4,5-Thiomethyleneoxy-2-methoxy-A

**[00237]** TMPEA - 2,4,5-Trimethoxy-PEA

**[00238]** 2-TOET - 4-Ethyl-5-methoxy-2-methylthio-A

**[00239]** 5-TOET - 4-Ethyl-2-methoxy-5-methylthio-A

**[00240]** 2-TOM - 5-Methoxy-4-methyl-2-methylthio-A

**[00241]** 5-TOM - 2-Methoxy-4-methyl-5-methylthio-A

**[00242]** TOMSO - 2-Methoxy-4-methyl-5-methylsulfinyl-A

**[00243]** TP - 4-Propylthio-3,5-dimethoxy-PEA

**[00244]** TRIS - 3,4,5-Triethoxy-PEA

**[00245]** 3-TSB - 3-Ethoxy-5-ethylthio-4-methoxy-PEA

**[00246]** 4-TSB - 3,5-Diethoxy-4-methylthio-PEA

**[00247]** 3-T-TRIS - 4,5-Diethoxy-3-ethylthio-PEA

**[00248]** 4-T-TRIS - 3,5-Diethoxy-4-ethylthio-PEA

**[00249]** Similarly substituted beta-keto phenethylamines, such as Methcathinone Cathinone, and Cathine.

**[00250]** Examples of Benzodifuran include, but are not limited to, the following analogs and/or derivatives:

**[00251]** 25B-N1POMe

**[00252]** 25B-NAcPip

**[00253]** 25B-NB

**[00254]** 25B-NB23DM

**[00255]** 25B-NB25DM

**[00256]** 25B-NB3OMe

**[00257]** 25B-NB4OMe

**[00258]** 25B-NBF

**[00259]** 25B-NBMD

**[00260]** 25B-NBOH

**[00261]** 25B-NBOMe (NBOMe-2CB)

**[00262]** 25B-NMe7BF

**[00263]** 25B-NMe7BT

**[00264]** 25B-NMe7Box

**[00265]** 25B-NMe7DHBF

**[00266]** 25B-NMe7Ind

**[00267]** 25B-NMe7Indz

**[00268]** 25B-NMePyr

**[00269]** Examples of substituted benzofurans include, but are not limited to, the following:

**[00270]** 2C-B-FLY

**[00271]** 2CBFly-NBOMe (NBOMe-2CB-Fly)

**[00272]** 2C-B-AN

**[00273]** 2C-B-BUTTERFLY

**[00274]** 2C-B-DRAGONFLY-NBOH

**[00275]** 2C-B-DragonFLY

**[00276]** 2C-B-FLY-NB2EtO5Cl

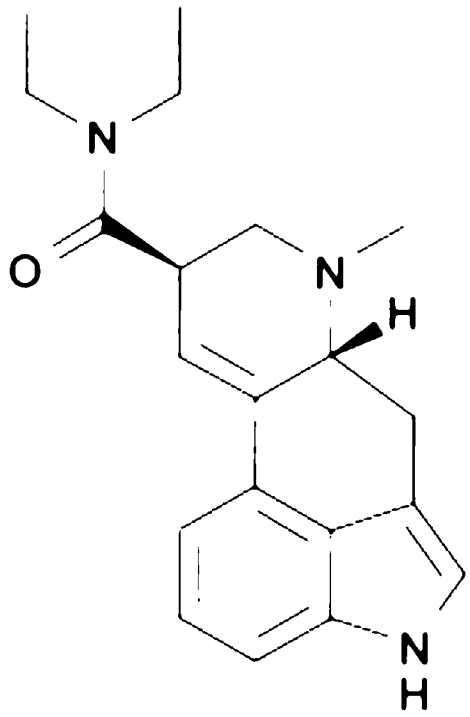
**[00277]** 2CB-5-hemifly

**[00278]** 2CB-Ind

**[00279]** βk-2C-B (beta-keto 2C-B)

**[00280]** TCB-2 (2C-BCB)

**[00281]** In other embodiments, the API includes lysergic acid diethylamide (hereinafter "LSD") or a derivative or salt thereof, or a pharmaceutical composition comprising LSD or a derivative or salt thereof. LSD is depicted below:




**[00282]** Another aspect of the present disclosure is a pellet or tablet capable of providing a controlled and/or pulsatile release of one or more APIs. In some embodiments, the pellet or tablet comprises (i) coated particles, and (ii) one or more excipients. In some embodiments, the coated particles comprise a core coated with one or more release layers. In some embodiments, the core comprises one or more APIs. In some embodiments, each of the one or more release layers comprises one or more polymers and/or copolymers.

**[00283]** The amount of the one or more APIs included within the core may vary depending on the API or APIs included therein. In some embodiments, an amount of the one or more APIs present in the core ranges from about 5% to about 80% by weight of the core, preferably ranging

from about 40% to about 70% by weight of the core, and most preferably ranging from about 55% to about 65% by weight of the core.

**[00284]** In some embodiments, the core may contain one or more additives selected from the group consisting of binders, fillers, osmotic agents, diluents, absorbents, colorants, dyes, pigments, disintegrants, dispersants, encapsulants, flow aids, hardeners, permeation enhancers, demulcents, stabilizers, disintegrants, tableting aids, glidants, lubricants, plasticizers and wetting agents. Any additive utilized must be pharmaceutically acceptable and compatible with the API(s) and/or other additive(s). Moreover, any combination of additives may be utilized in the core of the present disclosure. For example, an amount of additives in the core may range from about 1% to about 60% by weight of the core.

**[00285]** In some embodiments, the one or more polymers or copolymers included within the one or more release layers are selected from water soluble polymers and/or copolymers, water insoluble polymers and/or copolymers, or any mixture thereof. Water insoluble polymers may include various compositions, for example, ethylcellulose or its aqueous suspension system such as Aquacoat ECD and co-polymers of acrylic and methacrylic acid esters (Eudragit® RS or RL). Water soluble polymers may include various compositions, for example, polyvinylpyrrolidone or hypromellose. In one exemplary embodiment, the polymer may be selected from the group consisting of polymethacrylates, cellulose, polymeric derivatives of acetate, polymeric derivatives of citrate, and mixtures thereof. In further exemplary embodiments, the polymer may comprise ethyl cellulose, cellulose acetate, cellulose acetate butyrate, ethylene vinylacetate copolymer, polyvidone acetate, polyvinyl acetate, ethyl acrylate/methyl methacrylate copolymer, ammonia methacrylate copolymer, methylcellulose, hydroxypropyl cellulose, or combinations thereof. In an exemplary embodiment, the polymer comprises a mixture of Aquacoat ECD, (a 30% by weight aqueous dispersion of ethylcelluose polymer commercially available from FMC Biopolymer) and acetyltributyl citrate (CAS 77-90-7 sold as a carrier or plasticizer).

**[00286]** In some embodiments, the one or more release layers may further comprise one or more additives including binders, fillers, diluents, absorbents, colorants, dyes, pigments, disintegrants, dispersants, encapsulants, flow aids, hardeners, permeation enhancers, demulcents, stabilizers, disintegrants, tableting aids, anti-tack agents, glidants, lubricants, and wetting agents.

**[00287]** The one or more release layers are added to (coated onto) the core by methods known in the art. In some embodiments, one or more coating compositions may be applied to the

core in a fluidized bed or pan. In other embodiments, the one or more coating compositions may be applied by spraying or painting the coating compositions onto the core. In yet other embodiments, the coating compositions are applied in a fluid bed bottom spray or top spray coater by having the core fluidized in an air stream, and an aqueous dispersion of the coating is sprayed thereon. Various conventional coating apparatuses may be employed to facilitate these methods including a centrifugal fluidized bed coating apparatus, a pan coating apparatus, or a fluidized bed coating apparatus. In the processes described herein, it is to be understood that any solvent used in the preparations is removed by techniques known to one of ordinary skill in the art such as by drying or curing. In a preferred embodiment, the coating layers are applied to the core via a Wurster bottom spray coater. The method for applying each of the one or more release layers may be the same or different. Apparatus which have been used for coating and/or making core particles or sustained release particles are described in U.S. Pat. No. 4,895,733 and in U.S. Pat. No. 5,132,142, each of which are incorporated by reference.

**[00288]** For a pulsatile release, the core is coated with one or more release layers, followed by removal of a desired percentage of the coated API. The remaining coated API will have an additional layer of one or more polymers and/or copolymers applied followed by removal of a desired percentage to form the appropriate release profile. This process is continued until the desired volume and variety of coatings have been applied to the API particles.

**[00289]** In some embodiments, the coated particles are then blended with an excipient that is pressed into a cylinder or capsule (rounded ends) shaped pellet or tablet. This process is performed in a sterile clean room. The final pellets or tablets are packaged into a glass vial or blister pack that is terminally sterilized by exposure to gamma radiation or e-beam treatment. The pellets or tablets are administered by a trained physician that anesthetizes the area of administration. A small incision is performed, and a trocar inserted along with the pellets or tablets. The trocar may include a plunger or have a retractable sterile tube of administration. The incision is closed with a suture. The tablets or pellets may include a modified release profile by use of lipid derivatives, such as Cholesterol, Stearic Acid, and/or Glyceryl tristearate under the product name Dynasan 118.

**[00290]** Another aspect of the present disclosure is an API is blended with a solvent and optionally a surfactant. Examples of solvents include water-soluble organic solvents including, but not limited to, polyethylene glycol 300, polyethylene glycol 400, ethanol, propylene glycol,

glycerin, N-methyl-2-pyrrolidone, dimethylacetamide, and dimethylsulfoxide. Examples of surfactants include non-ionic surfactants including, but not limited to, non-ionic surfactants Cremophor EL, Cremophor RH 40, Cremophor RH 60, d--tocopherol, polyethylene glycol 1000 succinate, polysorbate 20, polysorbate 80, Solutol HS 15, sorbitan monooleate, poloxamer 407, Labrafil M-1944CS, Labrafil M-2125CS, Labrasol, Gellucire 44/14, Softigen 767, and mono- and di-fatty acid esters of PEG 300, 400, or 1750), water-insoluble lipids (castor oil, corn oil, cottonseed oil, olive oil, peanut oil, peppermint oil, safflower oil, sesame oil, soybean oil, hydrogenated vegetable oils, hydrogenated soybean oil, and medium-chain triglycerides of coconut oil and palm seed oil), organic liquids/semi-solids (beeswax, d--tocopherol, oleic acid, medium-chain mono- and diglycerides), various cyclodextrins (-cyclodextrin, -cyclodextrin, hydroxypropyl--cyclodextrin, and sulfobutylether-cyclodextrin), and phospholipids (hydrogenated soy phosphatidylcholine, distearoylphosphatidylglycerol, L--dimyristoylphosphatidylcholine, L—dimyristoylphosphatidylglycerol.

**[00291]** The chemical techniques to solubilize water-insoluble drugs for oral and injection administration include pH adjustment, cosolvents, complexation, microemulsions, self-emulsifying drug delivery systems, micelles, liposomes, and emulsions.

**[00292]** A variety of soluble Poly(D, L-lactide) (PDLLA) and Poly(D, L-lactide-co-glycolide) (PLGA) polymers and sterile filtered into a sterile vial prepared for injection. In this embodiment, the solvent is absorbed by the body leaving the API in a polymer that has a controlled release based on the length and substitution of the polymer. The deposited bioabsorbable polymer allows for a pulsatile controlled release of the API from hours to over a year.

**[00293]** Yet another aspect of the present disclosure is an API is blended into polymers compatible with Hot Melt Extrusion (HME). The polymer selection is associated with the release duration and multiple implants can be inserted simultaneously for a pulsatile release effect. HME polymers may include:

**[00294]** urethane

**[00295]** PGA

**[00296]** PGLA

**[00297]** Hydralese(tm) (PGSU) (poly(glycerol sebacate) urethane)

**[00298]** Polyvinyl alcohol (PVA)

**[00299]** Poly(vinylpyrrolidone) (PVP)

**[00300]** (MW 7000–11,000) Kollidon® 17 PF

**[00301]** (MW 2000–3000) Kollidon® 12 PF

**[00302]** Poly(vinylpyrrolidone)/vinyl acetate

**[00303]** (PVP/VA) (MW 45,000–70,000) Kollidon® VA64

**[00304]** Poly(vinyl caprolactam-covinylacetate-ethylene glycol

**[00305]** (MW 90,000–140,000) Soluplus®

**[00306]** Hydroxypropyl cellulose (HPC)

**[00307]** (MW 95,000) Klucel® LF

**[00308]** Hydroxypropylmethyl cellulose (HPMC)

**[00309]** (MW 25,000) Methocel™ K100LV

**[00310]** (MW 150,000) Methocel™ K100M

**[00311]** Hydroxypropyl methyl cellulose acetate succinate (HPMCAS) Affinisol™

**[00312]** Poly ethylene oxide (PEO) ---

**[00313]** Poly(butyl methacrylate-co-(2-demethylamino ethyl) methacrylate-co-methyl methacrylate) 1:2:1 Eudragit E PO®

**[00314]** Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonio ethyl methacrylate chloride) 1:2:0.2 Eudragit RL®

**[00315]** Poly(methacrylic acid-co-methyl methacrylate) 1:1 Eudragit L®

**[00316]** Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethylmethacrylate chloride) 1:2:0.1 Eudragit RS®

**[00317]** Poly(e-caprolactone) (PCLa)

**[00318]** Ethylene vinyl acetate (EVA)

**[00319]** Ethylcellulose

**[00320]** (4 cPs) Ethocel® 4P

**[00321]** (7 cPs) Ethocel® 7P

**[00322]** (10 cPs) Ethocel® 10P

**[00323]** Polyvinyl alcohol;polyethylene glycol graft copolymer (PVA:PEG) Kollicoat® IR

**[00324]** LSD tartrate has a melting point 80°F to 85°C (176°F to 185°F) (poly(glycerol sebacate) urethane) has a lower melting point and glass transition temperature.

**[00325]** In some embodiments, the addition of a plasticizer may allow for HME formulations to be manufactured on a 3D printer or used in a process called Fused Deposition Modelling (FDM).

**[00326]** In yet a further embodiment of the present disclosure is a subcutaneous release medical device which can be administered to deliver the API over a programmed time. The access to the programming interface can provide a deterrent to diversion of the API.

**[00327]** All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet are incorporated herein by reference, in their entirety. Aspects of the embodiments can be modified, if necessary, to employ concepts of the various patents, applications and publications to provide yet further embodiments.

**[00328]** Although the present disclosure has been described with reference to a number of illustrative embodiments, it should be understood that numerous other modifications and embodiments can be devised by those skilled in the art that will fall within the spirit and scope of the principles of this disclosure. More particularly, reasonable variations and modifications are possible in the component parts and/or arrangements of the subject combination arrangement within the scope of the foregoing disclosure, the drawings, and the appended claims without departing from the spirit of the disclosure. In addition to variations and modifications in the component parts and/or arrangements, alternative uses will also be apparent to those skilled in the art.

CLAIMS:

1. An implantable, subcutaneous product comprising one or more active pharmaceutical ingredient(s) (API(s)).

2. The implantable, subcutaneous product according to claim 1, wherein the implantable, subcutaneous product facilitates a sustained release of the one or more API(s).

3. The implantable, subcutaneous product according to claim 2, wherein the sustained release of the one or more API(s) is at a predetermined release rate and/or for a predetermined amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s).

4. The implantable, subcutaneous product according to claim 2 or 3, wherein the sustained release of the one or more API(s) from the implantable, subcutaneous product may be controlled or tuned before implantation into a subject.

5. The implantable, subcutaneous product according to claim 2 or 3, wherein the sustained release of the one or more API(s) from the implantable, subcutaneous product may be controlled or tuned after implantation into a subject.

6. The implantable, subcutaneous product according to any one of claims 1 to 5, wherein the one or more APIs comprise APIs classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

7. The implantable, subcutaneous product according to any one of claims 1 to 6, wherein the implantable, subcutaneous product is for preventing or mitigating abuse of the one or more API(s), which could lead to addiction, intoxication, overdose, and/or death.

8. The implantable, subcutaneous product according to any one of claims 1 to 7, wherein the implantable, subcutaneous product is for treatment of depression and other mental and/or mood disorders.

9. The implantable, subcutaneous product according to any one of claims 1 to 8, wherein the one or more API(s) are selected from the group consisting of Ergolines, Tryptamines, Phenethylamines and combinations thereof.

10. The implantable, subcutaneous product according to claim 9, wherein the Tryptamines are one or more of: DBT - N,N-Dibutyl-T, DET - N,N-Diethyl-T, DiPT - N,N-Diisopropyl-T, alpha,O-DMS - 5-Methyoxy-alpha-methyl-T, DMT - N,N-Dimethyl-T, 2,alpha-DMT - 2,alpha-Dimethyl-T, alpha,N-DMT - alpha,N-Dimethyl-T, DPT - N,N-Dipropyl-T, EiPT - N-Ethyl-N-isopropyl-T, alpha-ET - alpha-Ethyl-T, Harmaline - 3,4-Dihydro-7-methoxy-1-methyl-C, Harmine - 7-Methyoxy-1-methyl-C, 4-HO-DBT - N,N-Dibutyl-4-hydroxy-T, 4-HO-DET - N,N-Diethyl-4-hydroxy-T, 4-HO-DiPT - N,N-Diisopropyl-4-hydroxy-T, 4-HO-DMT - N,N-Dimethyl-4-hydroxy-T, 5-HO-DMT - N,N-Dimethyl-5-hydroxy-T, 4-HO-DPT - N,N-Dipropyl-4-hydroxy-T, 4-HO-MET - N-Ethyl-4-hydroxy-N-methyl-T, 4-HO-MiPT - 4-Hydroxy-N-isopropyl-N-methyl-T, 4-HO-MPT - 4-Hydroxy-N-methyl-N-propyl-T, 4-HO-pyr-T - 4-Hydroxy-N,N-tetramethylene-T, Ibogaine - A complexly substituted-T, MBT - N-Butyl-N-methyl-T, 4,5-MDO-DiPT - N,N-Diisopropyl-4,5-methylenedioxy-T, 5,6-MDO-DiPT - N,N-Diisopropyl-5,6-methylenedioxy-T, 4,5-MDO-DMT - N,N-Dimethyl-4,5-methylenedioxy-T, 5,6-MDO-DMT - N,N-Dimethyl-5,6-methylenedioxy-T, 5,6-MDO-MiPT - N-Isopropyl-N-methyl-5,6-methylenedioxy-T, 2-Me-DET - N,N-Diethyl-2-methyl-T, 2-Me-DMT - 2,N,N-Trimethyl-T, 5-MeO-DET - N,N-Diethyl-5-methoxy-T, 5-MeO-DiPT - N,N-Diisopropyl-5-methoxy-T, 5-MeO-DMT - 5-Methoxy-N,N-dimethyl-T, 4-MeO-MiPT - N-Isopropyl-4-methoxy-N-methyl-T, 5-MeO-MiPT - N-Isopropyl-5-methoxy-N-methyl-T, 5,6-MeO-MiPT - 5,6-Dimethoxy-N-isopropyl-N-methyl-T, 5-MeO-NMT - 5-Methoxy-N-methyl-T, 5-MeO-pyr-T - 5-Methoxy-N,N-tetramethylene-T, 6-MeO-THH - 6-Methoxy-1-methyl-1,2,3,4-tetrahydro-C, 5-MeO-TMT - 5-Methoxy-2,N,N-trimethyl-T, 5-MeS-DMT - N,N-Dimethyl-5-methylthio-T, MiPT - N-Isopropyl-N-methyl-T, alpha-MT - alpha-Methyl-T, NET - N-Ethyl-T, NMT - N-Methyl-T, pyr-T - N,N-Tetramethylene-T, T – Tryptamine, Tetrahydroharmine - 7-Methoxy-1-methyl-1,2,3,4-tetrahydro-C, and alpha,N,O-TMS - alpha,N-Dimethyl-5-methoxy-T.

11. The implantable, subcutaneous product according to claim 9, wherein the Ergolines are one or more of: AL-LAD - 6-Allyl-N,N-diethyl-NL, ETH-LAD - 6,N,N-Triethyl-NL, LSD - N,N-Diethyl-Lysergic acid, PRO-LAD - 6-Propyl-NL, and 1P-LSD (1-propionyl-lysergic acid diethylamide).

12. The implantable, subcutaneous product according to any one of claims 1 to 9, wherein the API(s) comprises lysergic acid diethylamide (LSD) or a derivative or salt thereof.

13. The implantable, subcutaneous product according to any one of claims 1 to 9, wherein the API(s) comprises a composition comprising or consisting of lysergic acid diethylamide (LSD) or a derivative or salt thereof.

14. The implantable, subcutaneous product according to claim 9, wherein the Phenethylamines are one or more of: AEM - alpha-Ethyl-3,4,5-trimethoxy-PEA; AL - 4-Allyloxy-3,5-dimethoxy-PEA; ALEPH - 4-Methylthio-2,5-dimethoxy-A; ALEPH-2 - 4-Ethylthio-2,5-dimethoxy-A; ALEPH-4 - 4-Isopropylthio-2,5-dimethoxy-A; ALEPH-6 - 4-Phenylthio-2,5-dimethoxy-A; ALEPH-7 - 4-Propylthio-2,5-dimethoxy-A; ARIADNE - 2,5-Dimethoxy-alpha-ethyl-4-methyl-PEA; ASB - 3,4-Diethoxy-5-methoxy-PEA; B - 4-Butoxy-3,5-dimethoxy-PEA; BEATRICE - 2,5-Dimethoxy-4,N-dimethyl-A; BIS-TOM - 2,5-Bismethylthio-4-methyl-A; BOB - 4-Bromo-2,5,beta-trimethoxy-PEA; BOD - 2,5,beta-Trimethoxy-4-methyl-PEA; BOH - beta-Methoxy-3,4-methylenedioxy-PEA; BOHD - 2,5-Dimethoxy-beta-hydroxy-4-methyl-PEA; BOM - 3,4,5,beta-Tetramethoxy-PEA; 4-Br-3,5-DMA - 4-Bromo-3,5-dimethoxy-A; 2-Br-4,5-MDA - 2-Bromo-4,5-methylenedioxy-A; 2C-B - 4-Bromo-2,5-dimethoxy-PEA; 3C-BZ - 4-Benzyloxy-3,5-dimethoxy-A; 2C-C - 4-Chloro-2,5-dimethoxy-PEA; 2C-D - 4-Methyl-2,5-dimethoxy-PEA; 2C-E - 4-Ethyl-2,5-dimethoxy-PEA; 3C-E - 4-Ethoxy-3,5-dimethoxy-A, 2C-F - 4-Fluoro-2,5-dimethoxy-PEA; 2C-G - 3,4-Dimethyl-2,5-dimethoxy-PEA; 2C-G-3 - 3,4-Trimethylene-2,5-dimethoxy-PEA; 2C-G-4 - 3,4-Tetramethylene-2,5-dimethoxy-PEA; 2C-G-5 - 3,4-Norbornyl-2,5-dimethoxy-PEA; 2C-G-N - 1,4-Dimethoxynaphthyl-2-ethylamine; 2C-H - 2,5-Dimethoxy-PEA; 2C-I - 4-Iodo-2,5-dimethoxy-PEA; 2C-N - 4-Nitro-2,5-dimethoxy-PEA; 2C-O-4 - 4-Isopropoxy-2,5-dimethoxy-PEA; 2C-P - 4-Propyl-2,5-dimethoxy-PEA; CPM - 4-Cyclopropylmethoxy-3,5-dimethoxy-PEA; 2C-SE - 4-Methylseleno-2,5-dimethoxy-PEA; 2C-T -

4-Methylthio-2,5-dimethoxy-PEA; 2C-T-2 - 4-Ethylthio-2,5-dimethoxy-PEA; 2C-T-4 - 4-Isopropylthio-2,5-dimethoxy-PEA; psi-2C-T-4 - 4-Isopropylthio-2,6-dimethoxy-PEA; 2C-T-7 - 4-Propylthio-2,5-dimethoxy-PEA; 2C-T-8 - 4-Cyclopropylmethylthio-2,5-dimethoxy-PEA; 2C-T-9 - 4-(t)-Butylthio-2,5-dimethoxy-PEA; 2C-T-13 - 4-(2-Methoxyethylthio)-2,5-dimethoxy-PEA; 2C-T-15 - 4-Cyclopropylthio-2,5-dimethoxy-PEA; 2C-T-17 - 4-(s)-Butylthio-2,5-dimethoxy-PEA; 2C-T-21 - 4-(2-Fluoroethylthio)-2,5-dimethoxy-PEA; 4-D - 4-Trideuteromethyl-3,5-dimethoxy-PEA; beta-D - beta,beta-Dideutero-3,4,5-trimethoxy-PEA; DESOXY - 4-Methyl-3,5-Dimethoxy-PEA; 2,4-DMA - 2,4-Dimethoxy-A; 2,5-DMA - 2,5-Dimethoxy-A; 3,4-DMA - 3,4-Dimethoxy-A; DMCPA - 2-(2,5-Dimethoxy-4-methylphenyl)-cyclopropylamine; DME - 3,4-Dimethoxy-beta-hydroxy-PEA; DMMDA - 2,5-Dimethoxy-3,4-methylenedioxy-A; DMMDA-2 - 2,3-Dimethoxy-4,5-methylenedioxy-A, DMPEA - 3,4-Dimethoxy-PEA; DOAM - 4-Amyl-2,5-dimethoxy-A; DOB - 4-Bromo-2,5-dimethoxy-A; DOBU - 4-Butyl-2,5-dimethoxy-A; DOC - 4-Chloro-2,5-dimethoxy-A; DOEF - 4-(2-Fluoroethyl)-2,5-dimethoxy-A; DOET - 4-Ethyl-2,5-dimethoxy-A; DOI - 4-Iodo-2,5-dimethoxy-A; DOM (STP) - 4-Methyl-2,5-dimethoxy-A, psi-DOM - 4-Methyl-2,6-dimethoxy-A; DON - 4-Nitro-2,5-dimethoxy-A; DOPR - 4-Propyl-2,5-dimethoxy-A; E - 4-Ethoxy-3,5-dimethoxy-PEA; EEE - 2,4,5-Triethoxy-A; EEM - 2,4-Diethoxy-5-methoxy-A; EME - 2,5-Diethoxy-4-methoxy-A; EMM - 2-Ethoxy-4,5-dimethoxy-A; ETHYL-J - N,alpha-diethyl-3,4-methylenedioxy-PEA; ETHYL-K - N-Ethyl-alpha-propyl-3,4-methylenedioxy-PEA; F-2 - Benzofuran-2-methyl-5-methoxy-6-(2-aminopropane); F-22 - Benzofuran-2,2-dimethyl-5-methoxy-6-(2-aminopropane); FLEA - N-Hydroxy-N-methyl-3,4-methylenedioxy-A; G-3 - 3,4-Trimethylene-2,5-dimethoxy-A; G-4 - 3,4-Tetramethylene-2,5-dimethoxy-A; G-5 - 3,4-Norbornyl-2,5-dimethoxy-A; GANESHA - 3,4-Dimethyl-2,5-dimethoxy-A; G-N - 1,4-Dimethoxynaphthyl-2-isopropylamine; HOT-2 - 2,5-Dimethoxy-N-hydroxy-4-ethylthio-PEA; HOT-7 - 2,5-Dimethoxy-N-hydroxy-4-(n)-propylthio-PEA; HOT-17 - 2,5-Dimethoxy-N-hydroxy-4-(s)-butylthio-PEA; IDNNA - 2,5-Dimethoxy-N,N-dimethyl-4-iodo-A; IM - 2,3,4-Trimethoxy-PEA; IP - 3,5-Dimethoxy-4-isopropoxy-PEA; IRIS - 5-Ethoxy-2-methoxy-4-methyl-A; J - alpha-Ethyl-3,4-methylenedioxy-PEA; LOPHOPHINE - 3-Methoxy-4,5-methylenedioxy-PEA; M - 3,4,5-Trimethoxy-PEA; 4-MA - 4-Methoxy-A; MADAM-6 - 2,N-Dimethyl-4,5-methylenedioxy-A; MAL - 3,5-Dimethoxy-4-methallyloxy-PEA; MDA - 3,4-Methylenedioxy-A; MDAL - N-Allyl-3,4-methylenedioxy-A; MDBU - N-Butyl-3,4-methylenedioxy-A; MDBZ - N-Benzyl-3,4-

methylenedioxy-A; MDCPM - N-Cyclopropylmethyl-3,4-methylenedioxy-A; MDDM - N,N-Dimethyl-3,4-methylenedioxy-A; MDE - N-Ethyl-3,4-methylenedioxy-A; MDHOET - N-(2-Hydroxyethyl)-3,4-methylenedioxy-A; MDIP - N-Isopropyl-3,4-methylenedioxy-A; MDMA - N-Methyl-3,4-methylenedioxy-A; MDMC - N-Methyl-3,4-ethylenedioxy-A; MDMEO - N-Methoxy-3,4-methylenedioxy-A; MDMEOET - N-(2-Methoxyethyl)-3,4-methylenedioxy-A; MDMP - alpha,alpha,N-Trimethyl-3,4-methylenedioxy-PEA; MDOH - N-Hydroxy-3,4-methylenedioxy-A; MDPEA - 3,4-Methylenedioxy-PEA; MDPH - alpha,alpha-Dimethyl-3,4-methylenedioxy-PEA; MDPL - N-Propargyl-3,4-methylenedioxy-A; MDPR - N-Propyl-3,4-methylenedioxy-A; ME - 3,4-Dimethoxy-5-ethoxy-PEA; MEDA - 3-methoxy-4,5-Ethylenedioxy-A; MEE - 2-Methoxy-4,5-diethoxy-A; MEM - 2,5-Dimethoxy-4-ethoxy-A; MEPEA - 3-Methoxy-4-ethoxy-PEA; META-DOB - 5-Bromo-2,4-dimethoxy-A; META-DOT - 5-Methylthio-2,4-dimethoxy-A; METHYL-DMA - N-Methyl-2,5-dimethoxy-A; METHYL-DOB - 4-Bromo-2,5-dimethoxy-N-methyl-A; METHYL-J - N-Methyl-alpha-ethyl-3,4-methylenedioxy-PEA; METHYL-K - N-Methyl-alpha-propyl-3,4-methylenedioxy-PEA; METHYL-MA - N-Methyl-4-methoxy-A; METHYL-MMDA-2 - N-Methyl-2-methoxy-4,5-methylenedioxy-A; MMDA - 3-Methoxy-4,5-methylenedioxy-A; MMDA-2 - 2-Methoxy-4,5-methylenedioxy-A; MMDA-3a - 2-Methoxy-3,4-methylenedioxy-A; MMDA-3b - 4-Methoxy-2,3-methylenedioxy-A; MME - 2,4-Dimethoxy-5-ethoxy-A; MP - 3,4-Dimethoxy-5-propoxy-PEA; MPM - 2,5-Dimethoxy-4-propoxy-A; ORTHO-DOT - 2-Methylthio-4,5-dimethoxy-A; P - 3,5-Dimethoxy-4-propoxy-PEA; PE - 3,5-Dimethoxy-4-phenethyloxy-PEA; PEA – PEA; PROPYNYL - 4-Propynyloxy-3,5-dimethoxy-PEA; SB - 3,5-Diethoxy-4-methoxy-PEA; TA - 2,3,4,5-Tetramethoxy-A; 3-TASB - 4-Ethoxy-3-ethylthio-5-methoxy-PEA; 4-TASB - 3-Ethoxy-4-ethylthio-5-methoxy-PEA; 5-TASB - 3,4-Diethoxy-5-methylthio-PEA; TB - 4-Thiobutoxy-3,5-dimethoxy-PEA; 3-TE - 4-Ethoxy-5-methoxy-3-methylthio-PEA; 4-TE - 3,5-Dimethoxy-4-ethylthio-PEA; 2-TIM - 2-Methylthio-3,4-dimethoxy-PEA; 3-TIM - 3-Methylthio-2,4-dimethoxy-PEA; 4-TIM - 4-Methylthio-2,3-dimethoxy-PEA; 3-TM - 3-Methylthio-4,5-dimethoxy-PEA; 4-TM - 4-Methylthio-3,5-dimethoxy-PEA; TMA - 3,4,5-Trimethoxy-A; TMA-2 - 2,4,5-Trimethoxy-A; TMA-3 - 2,3,4-Trimethoxy-A; TMA-4 - 2,3,5-Trimethoxy-A; TMA-5 - 2,3,6-Trimethoxy-A; TMA-6 - 2,4,6-Trimethoxy-A; 3-TME - 4,5-Dimethoxy-3-ethylthio-PEA; 4-TME - 3-Ethoxy-5-methoxy-4-methylthio-PEA; 5-TME - 3-Ethoxy-4-methoxy-5-methylthio-PEA; 2T-MMDA-3a - 2-Methylthio-3,4-methylenedioxy-A; 4T-MMDA-2 - 4,5-

Thiomethyleneoxy-2-methoxy-A; TMPEA - 2,4,5-Trimethoxy-PEA; 2-TOET - 4-Ethyl-5-methoxy-2-methylthio-A; 5-TOET - 4-Ethyl-2-methoxy-5-methylthio-A; 2-TOM - 5-Methoxy-4-methyl-2-methylthio-A; 5-TOM - 2-Methoxy-4-methyl-5-methylthio-A; TOMSO - 2-Methoxy-4-methyl-5-methylsulfinyl-A; TP - 4-Propylthio-3,5-dimethoxy-PEA; TRIS - 3,4,5-Triethoxy-PEA; 3-TSB - 3-Ethoxy-5-ethylthio-4-methoxy-PEA; 4-TSB - 3,5-Diethoxy-4-methylthio-PEA; 3-T-TRIS - 4,5-Diethoxy-3-ethylthio-PEA; and 4-T-TRIS - 3,5-Diethoxy-4-ethylthio-PEA.

15. The implantable, subcutaneous product according to claim 9, wherein the Phenethylamines are substituted beta-keto phenethylamines.

16. The implantable, subcutaneous product according to claim 15, wherein the substituted beta-keto phenethylamines are Methcathinone Cathinone and/or Cathine.

17. The implantable, subcutaneous product according to claim 15, wherein the substituted beta-keto phenethylamines are one or more of: 25B-NBOMe**;** 25B-NAcPip; 25B-NB; 25B-NB23DM; 25B-NB25DM; 25B-NB3OMe; 25B-NB4OMe; 25B-NBF; 25B-NBMD; 25B-NBOH; 25B-NBOMe (NBOMe-2CB); 25B-NMe7BF; 25B-NMe7BT; 25B-NMe7Box; 25B-NMe7DHBF; 25B-NMe7Ind; 25B-NMe7Indz; and 25B-NMePyr.

18. The implantable, subcutaneous product according to claim 9, wherein the API(s) is a substituted benzofurans of one or more of: 2C-B-FLY; 2CBFly-NBOMe (NBOMe-2CB-Fly); 2C-B-AN; 2C-B-BUTTERFLY; 2C-B-DRAGONFLY-NBOH; 2C-B-DragonFLY; 2C-B-FLY-NB2EtO5Cl; 2CB-5-hemifly; 2CB-Ind; βk-2C-B (beta-keto 2C-B); and TCB-2 (2C-BCB).

19. An implantable pellet or tablet comprising one or more active pharmaceutical ingredient(s) (API(s)), wherein the implantable pellet or tablet facilitates a sustained release of the one or more API(s).

20. The implantable implantable pellet or tablet according to claim 19, wherein the sustained release of the one or more API(s) is at a predetermined release rate and/or for a predetermined

amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s).

21. The implantable implantable pellet or tablet according to claim 19 or 20, wherein the sustained release of the one or more API(s) may be controlled or tuned before implantation into a subject.

22. The implantable pellet or tablet according to claim 19 or 20, wherein the sustained release of the one or more API(s) may be controlled or tuned after implantation into a subject.

23. The implantable pellet or tablet according to any one of claims 19 to 22, wherein the one or more APIs comprise APIs classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

24. The implantable pellet or tablet according to claim 23, wherein the one or more API(s) are selected from the group consisting of Ergolines, Tryptamines, Phenethylamines and combinations thereof.

25. The implantable pellet or tablet according to any one of claims 19 to 23, wherein the one or more API(s) is lysergic acid diethylamide (LSD) or a derivative or salt thereof for providing a controlled and/or pulsatile release of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof.

26. The implantable pellet or tablet according to any one of claims 19 to 25, wherein the pellet or tablet comprises (i) coated particles, and (ii) one or more excipients.

27. The implantable pellet or tablet according to claim 26, wherein the coated particles comprise a core coated with one or more release layers, each of the one or more release layers comprises one or more polymers and/or copolymers.

28. The implantable pellet or tablet according to claim 27, wherein an amount of the one or more API(s) included within the core is from about 5% to about 80% by weight of the core.

29. The implantable pellet or tablet according to claim 27, wherein an amount of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof included within the core ranges from about 5% to about 80% by weight of the core.

30. The implantable pellet or tablet according to claim 29, wherein an amount of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof included within the core ranges from about 40% to about 70% by weight of the core.

31. The implantable pellet or tablet according to claim 29, wherein an amount of the lysergic acid diethylamide (LSD) or the derivative or the salt thereof included within the core ranges from about 55% to about 65% by weight of the core.

32. The implantable pellet or tablet according to any one of claims 27 to 31, wherein the core further comprises one or more additives selected from the group consisting of binders, fillers, osmotic agents, diluents, absorbents, colorants, dyes, pigments, disintegrants, dispersants, encapsulants, flow aids, hardeners, permeation enhancers, demulcents, stabilizers, disintegrants, tableting aids, glidants, lubricants, plasticizers and wetting agents.

33. The implantable pellet or tablet according to claim 32, wherein an amount of additives in the core is from about 1% to about 60% by weight of the core.

34. The implantable pellet or tablet according to any one of claims 27 to 33, wherein the one or more polymers or copolymers are selected from water soluble polymers and/or copolymers, water insoluble polymers and/or copolymers, or any mixture thereof.

35. The implantable pellet or tablet according to claim 34, wherein the water soluble polymers comprise ethylcellulose, an aqueous suspension system of ethylcellulose, and/or co-polymers of acrylic and methacrylic acid esters.

36. The implantable pellet or tablet according to claim 34, wherein the water soluble polymers comprise polyvinylpyrrolidone or hypromellose.

37. The implantable pellet or tablet according to claim 34, wherein the polymer is selected from the group consisting of polymethacrylates, cellulose, polymeric derivatives of acetate, polymeric derivatives of citrate, and mixtures thereof.

38. The implantable pellet or tablet according to claim 34, wherein the polymer is selected from the group consisting of ethyl cellulose, cellulose acetate, cellulose acetate butyrate, ethylene vinylacetate copolymer, polyvidone acetate, polyvinyl acetate, ethyl acrylate/methyl methacrylate copolymer, ammonia methacrylate copolymer, methylcellulose, hydroxypropyl cellulose, and combinations thereof.

39. The implantable pellet or tablet according to claim 34, wherein the polymer comprises a mixture of Aquacoat ECD, (30% by weight aqueous dispersion of ethylcelluose polymer) and acetyltributyl citrate (CAS 77-90-7).

40. The implantable pellet or tablet according to any one of claims 27 to 39, wherein the one or more release layers may further comprise one or more additives selected from binders, fillers, diluents, absorbents, colorants, dyes, pigments, disintegrants, dispersants, encapsulants, flow aids, hardeners, permeation enhancers, demulcents, stabilizers, disintegrants, tableting aids, anti-tack agents, glidants, lubricants, wetting agents and combinations thereof.

41. The implantable pellet or tablet according to any one of claims 27 to 40, wherein the one or more release layers are applied/coated onto the core using a coating apparatus including a centrifugal fluidized bed coating apparatus, a pan coating apparatus, or a fluidized bed coating apparatus.

42. The implantable pellet or tablet according to any one of claims 27 to 41, wherein any solvent used to form the one or more release layers onto the core is removed by drying and/or curing.

43. The implantable pellet or tablet according to any one of claims 27 to 42, wherein for the pulsatile release, the core is coated with one or more release layers, followed by removal of a desired percentage of the coated API(s) to form an appropriate release profile from the particles.

44. The implantable pellet or tablet according to any one of claims 19 to 43, wherein the coated particles are blended with an excipient that is pressed into a cylinder or capsule to provide a shaped pellet or tablet.

45. The implantable pellet or tablet according to any one of claims 19 to 44, wherein the pellet or tablet is packaged into a glass vial or blister pack that is terminally sterilized by exposure to gamma radiation or e-beam treatment.

46. The implantable pellet or tablet according to any one of claims 19 to 45 for administration under anesthesia.

47. The implantable pellet or tablet according to claim 46, wherein a trocar is for use with said pellet or tablet for said administration via an incision

48. The implantable pellet or tablet according to any one of claims 19 to 47, further comprising a lipid derivative to further modify the release profile of the API.

49. The implantable pellet or tablet according to claim 48, wherein the lipid derivative is Cholesterol, Stearic Acid, and/or Glyceryl tristearate.

50. The implantable pellet or tablet according to claim 48, wherein the lipid derivative is Dynasan$^{TM}$ 118.

50a. A method for treatment of a subject suffering from depression or other mental and/or mood disorders, the method comprising subcutaneous administration of one or more of the implantable, subcutaneous product according to any one of claims 1 to 18, or one or more of the implantable pellet or tablet according to any one of claims 19 to 50 to the subject.

50b. A method for preventing or mitigating abuse of the one or more API(s), which could lead to addiction, intoxication, overdose, and/or death, the method comprising subcutaneous administration of one or more of the implantable, subcutaneous product according to any one of claims 1 to 18, or one or more of the implantable pellet or tablet according to any one of claims 19 to 50 to the subject.

50c. The method according to claim 50a or 50b, wherein said one or more of the implantable, subcutaneous product according to any one of claims 1 to 18, or the one or more of the implantable pellet or tablet according to any one of claims 19 to 50 can each comprise a different API(s) or combination of API(s).

51. A subcutaneously implantable medical device for sustained or pulsatile release of one or more API(s) at a predetermined release rate and/or for a predetermined amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s), optionally wherein the device comprises a programming interface for control of the release of the one or more API(s).

52. The subcutaneously implantable medical device according to claim 51, wherein the wherein the one or more API(s) are selected from the group consisting of Ergolines, Tryptamines, Phenethylamines and combinations thereof.

53. The subcutaneously implantable medical device according to claim 52, wherein the Ergolines are one or more of: AL-LAD - 6-Allyl-N,N-diethyl-NL, ETH-LAD - 6,N,N-Triethyl-NL, LSD - N,N-Diethyl-Lysergic acid, PRO-LAD - 6-Propyl-NL, and 1P-LSD (1-propionyl-lysergic acid diethylamide).

54. The subcutaneously implantable medical device according to claim 53, wherein the Ergoline comprises lysergic acid diethylamide (LSD) or a derivative or salt thereof.

55. The subcutaneously implantable medical device according to claim 53, wherein the Ergolines comprises a composition comprising or consisting of lysergic acid diethylamide (LSD) or a derivative or salt thereof.

56. The subcutaneously implantable medical device according to any one of claims 51 to 55, wherein the device is for preventing or mitigating abuse of the one or more API(s), which could lead to addiction, intoxication, overdose, and/or death.

57. The subcutaneously implantable medical device according to any one of claims 51 to 56, wherein the device is for treatment of depression and other mental and/or mood disorders.

58. The subcutaneously implantable medical device according to any one of claims 51 to 57, manufactured on a 3D printer or by Fused Deposition Modelling (FDM).

59. A method of treating a subject suffering from depression or other mental and/or mood disorders, the method comprising:

implanting a subcutaneous product comprising one or more active pharmaceutical ingredient(s) (API(s)) into the subject, wherein the subcutaneous product is configured for a sustained release of the one or more API(s), and wherein the sustained release is a predetermined release rate and/or a predetermined amount of time.

60. The method of claim 59, wherein the implantable, subcutaneous product, after implantation facilitates the release of the one or more API(s) for a predetermined amount of time for achieving a predetermined blood plasma concentration(s) of the one or more APIs.

61. The method of claim 59 or 60, wherein the product is configured for adjusting the release of the one or more API(s) after implantation.

62. The method of any one of claims 59 to 61, wherein the one or more API(s) comprise one or more API(s) classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

63. A method for preventing or mitigating abuse of one or more API(s) by a subject, which may lead to addiction, intoxication, overdose, and/or death of the subject, the method comprising:

implanting a subcutaneous product comprising one or more active pharmaceutical ingredients (API(s)) into the subject, wherein the subcutaneous product is configured for a sustained release of the one or more API(s), and wherein the sustained release is a predetermined release rate and/or a predetermined amount of time.

64. The method of claim 63, wherein the implantable, subcutaneous product, after implantation facilitates the release of the one or more API(s) for a predetermined amount of time for achieving a predetermined blood plasma concentration(s) of the one or more API(s).

65. The method of claim 63 or 64, wherein the product is configured for adjusting the release of the one or more API(s) after implantation.

66. The method of any one of claims 63 to 65, wherein the one or more API(s) comprise API(s) classified as Schedule I Controlled Substances or Schedule II/IIN Controlled Substances.

67. The method of any one of claims 59 to 66, wherein the one or more API(s) comprises lysergic acid diethylamide (LSD) or a derivative or salt thereof.

68. The implantable pellet or tablet according to any one of claims 19 to 31, wherein the one or more API(s) is blended with a solvent and optionally a surfactant.

69. The implantable pellet or tablet according to claim 68, wherein the solvent comprises a water-soluble organic solvent selected from the group consisting of: polyethylene glycol 300, polyethylene glycol 400, ethanol, propylene glycol, glycerin, N-methyl-2-pyrrolidone, dimethylacetamide, and dimethylsulfoxide.

70. The implantable pellet or tablet according to claim 68, wherein the surfactant comprises a non-ionic surfactant selected from the group consisting of non-ionic surfactants Cremophor EL, Cremophor RH 40, Cremophor RH 60, d--tocopherol, polyethylene glycol 1000 succinate, polysorbate 20, polysorbate 80, Solutol HS 15, sorbitan monooleate, poloxamer 407, Labrafil M-1944CS, Labrafil M-2125CS, Labrasol, Gellucire 44/14, Softigen 767, and mono- and di-fatty acid esters of PEG 300, 400, or 1750), water-insoluble lipids (castor oil, corn oil, cottonseed oil, olive oil, peanut oil, peppermint oil, safflower oil, sesame oil, soybean oil, hydrogenated vegetable oils, hydrogenated soybean oil, and medium-chain triglycerides of coconut oil and palm seed oil), organic liquids/semi-solids (beeswax, d--tocopherol, oleic acid, medium-chain mono- and diglycerides), various cyclodextrins (-cyclodextrin, -cyclodextrin, hydroxypropyl--cyclodextrin, and sulfobutylether-cyclodextrin), and phospholipids (hydrogenated soy phosphatidylcholine, distearoylphosphatidylglycerol, L--dimyristoylphosphatidylcholine, L—dimyristoylphosphatidylglycerol.

71. The implantable pellet or tablet according to any one of claims 68 to 70, wherein water-insoluble API(s) are solubilized by pH adjustment, cosolvents, complexation, microemulsions, self-emulsifying drug delivery systems, micelles, liposomes, and emulsions.

72. The implantable pellet or tablet according to any one of claims 68 to 71, formulated with one or more of Poly(D, L-lactide) (PDLLA) and Poly(D, L-lactide-co-glycolide) (PLGA) polymers and sterile filtered into a sterile vial for administration.

73. The implantable pellet or tablet according to any one of claims 68 to 72, wherein the solvent is absorbed by the body of the subject leaving the one or more API(s) in a polymer that has a controlled release based on the length and substitution of the polymer.

74. The implantable pellet or tablet according to claim 73, wherein the administered bioabsorbable polymer allows for a pulsatile controlled release of the one or more API(s) from hours to over a year.

75. A subcutaneously implantable product for sustained or pulsatile release of one or more API(s) at a predetermined release rate and/or for a predetermined amount of time for achieving a predetermined blood plasma concentrations of the one or more API(s),

wherein the one or more API(s) is blended with a polymer for providing a desired release duration, the polymer selected from one or more of: urethane; PGA, PGLA, Hydralese(tm) (PGSU) (poly(glycerol sebacate) urethane), Polyvinyl alcohol (PVA); Poly(vinylpyrrolidone) (PVP); (MW 7000–11,000) Kollidon® 17 PF, (MW 2000–3000) Kollidon® 12 PF, Poly(vinylpyrrolidone)/vinyl acetate; (PVP/VA) (MW 45,000–70,000) Kollidon® VA64; Poly(vinyl caprolactam-covinylacetate-ethylene glycol, (MW 90,000–140,000) Soluplus®; Hydroxypropyl cellulose (HPC); (MW 95,000) Klucel® LF; Hydroxypropylmethyl cellulose (HPMC); (MW 25,000) Methocel™ K100LV; (MW 150,000) Methocel™ K100M; Hydroxypropyl methyl cellulose acetate succinate (HPMCAS) Affinisol™; Poly ethylene oxide (PEO); Poly(butyl methacrylate-co-(2-demethylamino ethyl) methacrylate-co-methyl methacrylate) 1:2:1 Eudragit E PO®; Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonio ethyl methacrylate chloride) 1:2:0.2 Eudragit RL®; Poly(methacrylic acid-co-methyl methacrylate) 1:1 Eudragit L®; Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethylmethacrylate chloride) 1:2:0.1 Eudragit RS®; Poly(e-caprolactone) (PCLa); Ethylene vinyl acetate (EVA); Ethylcellulose; (4 cPs) Ethocel® 4P; (7 cPs) Ethocel® 7P; (10 cPs) Ethocel® 10P; Polyvinyl alcohol; polyethylene glycol graft copolymer (PVA:PEG) Kollicoat® IR; LSD tartrate (melting point 80°F to 85°C (176°F to 185°F); and (poly(glycerol sebacate) urethane), and

wherein the subcutaneously implantable product is for treatment of a subject suffering from depression or other mental and/or mood disorders, and/or

wherein the subcutaneously implantable product is for preventing or mitigating abuse of the one or more API(s) by the subject, which could lead to addiction, intoxication, overdose, and/or death.

76. The subcutaneously implantable product according to claim 75, wherein the one or more polymer(s)s are selected compatible with Hot Melt Extrusion (HME).

**INTERNATIONAL SEARCH REPORT**

International application No.
**PCT/CA2022/050595**

A. CLASSIFICATION OF SUBJECT MATTER

IPC: ***A61K 9/00*** (2006.01) , ***A61K 31/48*** (2006.01) , ***A61K 31/137*** (2006.01) , ***A61K 47/30*** (2006.01) , ***A61K 47/34*** (2017.01) , ***A61L 27/54*** (2006.01) (more IPCs on the last page)

CPC: **A61K 9/0024** (2020.01) , A61K 31/48 (2020.01) , A61K 31/137 (2020.01) , A61K 47/30 (2020.01) , A61K 47/34 (2020.01) , A61L 27/54 (2020.01) (more CPCs on the last page)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC: A61K 9/00 (2006.01) , A61K 31/48 (2006.01) , A61K 31/137 (2006.01) , A61K 47/30 (2006.01) , A61K 47/34 (2017.01) , A61L 27/54 (2006.01), A61P 25/00 (2006.01) , A61P 25/24 (2006.01) (Continued on extra sheet)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Databases: Questel Orbit, Scopus
Keywords: implant, controlled release, tablet, pellet, polymer, controlled substance, addiction, intoxication, overdose, death, abuse, depression, mental, mood, lysergic acid diethylamide, ergoline, tryptamine, phenethylamine

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | CA 3127854 A1 (BLUMSTOCK et al.) 6 August 2020 (06-08-2020)<br>*Entire document* | 1-50, 51-58, 68-76 |

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

| | | | |
|---|---|---|---|
| * | Special categories of cited documents: | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| "A" | document defining the general state of the art which is not considered to be of particular relevance | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| "D" | document cited by the applicant in the international application | "Y" | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "E" | earlier application or patent but published on or after the international filing date | "&" | document member of the same patent family |
| "L" | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | | |
| "O" | document referring to an oral disclosure, use, exhibition or other means | | |
| "P" | document published prior to the international filing date but later than the priority date claimed | | |

| | |
|---|---|
| Date of the actual completion of the international search<br>21 June 2022 (21-06-2022) | Date of mailing of the international search report<br>11 July 2022 (11-07-2022) |
| Name and mailing address of the ISA/CA<br>Canadian Intellectual Property Office<br>Place du Portage I, C114 - 1st Floor, Box PCT<br>50 Victoria Street<br>Gatineau, Quebec K1A 0C9<br>Facsimile No.: 819-953-2476 | Authorized officer<br>Erin Mulrooney |

**INTERNATIONAL SEARCH REPORT**

International application No.
**PCT/CA2022/050595**

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claim Nos.: 50a-50c, 59-67
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 50a-50c and 59-67 are directed to a method of medical treatment that includes a surgical step, which the International Searching Authority is not required to search under PCT Rule 39.1(iv).

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos.:

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**
Information on patent family members

International application No.
**PCT/CA2022/050595**

| Patent Document Cited in Search Report | Publication Date | Patent Family Member(s) | Publication Date |
|---|---|---|---|
| CA3127854A1 | 06 August 2020 (06-08-2020) | AU2020215150A1 | 09 September 2021 (09-09-2021) |
| | | CN114040767A | 11 February 2022 (11-02-2022) |
| | | EP3917537A1 | 08 December 2021 (08-12-2021) |
| | | IL285186D0 | 30 September 2021 (30-09-2021) |
| | | JP2022523700A | 26 April 2022 (26-04-2022) |
| | | KR20210134313A | 09 November 2021 (09-11-2021) |
| | | US2022096504A1 | 31 March 2022 (31-03-2022) |
| | | WO2020157569A1 | 06 August 2020 (06-08-2020) |

Continuation of: Box No. V

Minimum documentation searched (classification system followed by classification symbols)

IPC: C07C 215/30 (2006.01) , C07C 225/16 (2006.01) , C07D 457/06 (2006.01)

CPC: A61K 9/0024 (2020.01) , A61K 31/48 (2020.01) , A61K 31/137 (2020.01) , A61K 47/30 (2020.01) , A61K 47/34 (2020.01) , A61L 27/54 (2020.01), A61P 25/00 (2020.01) , A61P 25/24 (2020.01) , C07C 215/30 (2020.01) , C07C 225/16 (2020.01) , C07D 457/06 (2020.01)

IPC:
***A61P 25/00*** (2006.01) , ***A61P 25/24*** (2006.01) , ***C07C 215/30*** (2006.01) , ***C07C 225/16*** (2006.01) , ***C07D 457/06*** (2006.01)

CPC:
A61P 25/00 (2020.01) , A61P 25/24 (2020.01) , C07C 215/30 (2020.01) , C07C 225/16 (2020.01) , C07D 457/06 (2020.01)