IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Deepak Cyril D'Souza	Confirmation No: 8242
Serial No.: 18/308357	Group No.:
Filing or 371(c) Date: 27 April 2023	Examiner:

Entitled: METHOD OF TREATING, AMELIORATING AND/OR PREVENTING DEPRESSION

Examiner:

The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application:

1. U.S. Pat. No. US11,406,619B2 (2021) "INJECTABLE FORMULATIONS" (Filed 27 Aug 2021)

2. EROWID (2020) "Mainlining into Peaceful Transcendence" EROWID. Retrieved from April 27 2020. URL: https://erowid.org/experiences/exp.php?ID=101186

3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020. https://clinicaltrials.gov/study/NCT04673383

4. BIOSPACE (2022) "Small Pharma Inc.: World's First Clinical Trial For DMT-Assisted Therapy in Major Depressive Disorder Shows Consistent Quality of Psychedelic Response in Phase I" BioSpace. Retrieved from 22 February 2022. URL: https://www.biospace.com/article/releases/small-pharma-inc-world-s-first-clinical-trial-for-dmt-assisted-therapy-in-major-depressive-disorder-shows-consistent-quality-of-psychedelic-response-in-phase-i/?s=67

5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021)

6. COZZI (2020) "Synthesis and characterization of high-purity N,N-dimethyltryptamine hemifumarate for human clinical trials" Drug Testing and Analysis. Vol 12(10):1483-1493

7. BARKER (2018) "N, N-Dimethyltryptamine (DMT), an Endogenous Hallucinogen: Past, Present, and Future Research to Determine Its Role and Function" Frontiers in Neuroscience. Vol 12:536

8. ZIMMERMAN (2013) " Severity classification on the Hamilton depression rating scale" Journal of Affective Disorders. Vol 150(2):384-388

9. LEUCHT (2018) "Translating the HAM-D into the MADRS and vice versa with equipercentile linking" Journal of Affective Disorders. Vol 226:326-331

10. NIMH (2009) "Depression" NIMH. Retrieved from May 31 2021. URL: https://web.archive.org/web/20210531222859/https://www.nimh.nih.gov/health/publications/depression/

11. CA Pat. App. No. CA3127854A1 (2020) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 29 Jan 2020)

12. KAPLAN (1974) "Blood and urine levels of N,N-dimethyltryptamine following administration of psychoactive dosages to human subjects" Psychopharmacologia Vol 38(3):239-245

13. PALHANO-FONTEZ (2019) “Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial” Psychological Medicine. Vol. 49:655-663

14. EATON (2008) “Population-Based Study of First Onset and Chronicity in Major Depressive Disorder” Archives of General Psychiatry. Vol 65(5):513-520

15. MALCOLM (2019) “Can Psychedelics Heal Without Psychotherapy?" Federal Register. Retrieved from October 4 1, 2019. URL https://web.archive.org/web/20210925064427/https://www.spiritpharmacist.com/blog/can-psychedelics-heal-without-psychotherapy

16. Federal Register (2006) “Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" Federal Register. Retrieved from May 1, 2017. URL https://web.archive.org/web/20170501143753/https://www.federalregister.gov/documents/2006/01/24/06-545/requirements-on-content-and-format-of-labeling-for-human-prescription-drug-and-biological-products

Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

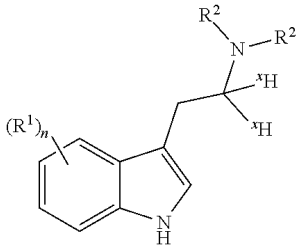
U.S.S.N. 18/308357 Pending Claims	References
1. A method of treating, ameliorating, or preventing depression in a subject in need thereof, the method comprising: administering parenterally to the subject an effective amount of a dimethyltryptamine (DMT) compound, wherein the DMT compound is selected from the group consisting of DMT, a DMT salt, a DMT solvate, an isotopically labelled derivative of DMT, or any mixture thereof.	1. U.S. Pat. No. US11,406,619B2 (2021) “INJECTABLE FORMULATIONS” (Filed 27 Aug 2021) From **Column 3, Line 58** “As used herein **the term ‘depressive disorder’ includes major depressive disorder, persistent depressive disorder, bipolar disorder, bipolar depression, and depression in terminally ill patients.**” From **Column 19, Line 47** “Viewed from a sixth aspect**, the invention provides a formulation** of the first aspect **for use in a method of treating a psychiatric or neurological disorder in a patient**. Often, **the psychiatric or neurological disorder is selected from the group consisting of** (i) an obsessive compulsive disorder, (ii) **a depressive disorder**, (iii) an anxiety disorder, (iv) substance abuse, and (v) an avolition disorder. **Often, the disorder is selected from the group consisting of major depressive disorder, treatment resistant major depressive disorder, post-partum depression,** an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder.” From **Column 5, Line 50** “**The invention provides a pharmaceutical formulation suitable for injection, comprising a salt of a dimethyltryptamine (DMT) compound** optionally substituted with

	deuterium and optionally substituted at position 4 or 5 with acetoxy or methoxy or position 4 with monohydrogen phosphate; a buffer which is separate to the salt; and water, wherein the formulation has a pH of about 3.5 to about 6.5 and an osmolality of about 250 to about 350 mOsm/Kg." From **Column 20, Line 6** "**The formulation is suitable for injection**, thus its administration in therapy typically comprises injection of the formulation. **The formulation may be suitable for bolus injection, in which a discrete amount of an optionally substituted DMT salt is administered** in one injection such that the concentration of DMT in the body quickly increases. **Bolus injections are typically administered intravenously (directly into the vein), intramuscularly (within the muscle), intradermally (beneath the skin) or subcutaneously (within the fat or skin).**"
2. The method of claim 1, wherein the subject is administered the DMT compound intravenously.	1. U.S. Pat. No. US11,406,619B2 (2021) "INJECTABLE FORMULATIONS" (Filed 27 Aug 2021) From **Column 19, Line 47** "Viewed from a sixth aspect**, the invention provides a formulation** of the first aspect **for use in a method of treating a psychiatric or neurological disorder in a patient**. Often, **the psychiatric or neurological disorder is selected from the group consisting of** (i) an obsessive compulsive disorder, (ii) **a depressive disorder**, (iii) an anxiety disorder, (iv) substance abuse, and (v) an avolition disorder. **Often, the disorder is selected from the group consisting of major depressive disorder, treatment resistant major depressive disorder, post-partum depression,** an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder." From **Column 20, Line 6** "**The formulation is suitable for injection**, thus its administration in therapy typically comprises injection of the formulation. **The formulation may be suitable for bolus injection, in which a discrete amount of an optionally substituted DMT salt is administered** in one injection such that the concentration of DMT in the body quickly increases. **Bolus injections are typically administered intravenously (directly into the vein**), intramuscularly (within the muscle), intradermally (beneath the skin) or subcutaneously (within the fat or skin)."
3. The method of claim 1, wherein the amount of the DMT compound administered to the subject ranges from about 0.038 mg/kg to about 0.38 mg/kg in terms of DMT content.	2. EROWID (2020) "Mainlining into Peaceful Transcendence" EROWID. Retrieved from April 27 2020. URL: https://erowid.org/experiences/exp.php?ID=101186

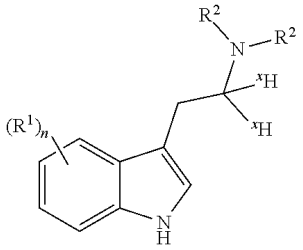
	
4. The method of claim 1, wherein the subject is administered at least a first dose of an independently selected DMT compound and a second dose of an independently selected DMT compound, and wherein the dosage of the second dose in terms of DMT content is higher than the dosage of the first dose	3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020. https://clinicaltrials.gov/study/NCT04673383 From **Brief Summary "SPL026 (N,N-dimethyltryptamine [DMT] fumarate) is a psychedelic tryptamine being developed as a therapy for patients with major depressive disorder (MDD)**." From **Detailed Description** "2-part study. Part A in psychedelic-naïve healthy volunteers**. Part B in patients with MDD** who score moderate-severe on Ham-D. Healthy volunteers will receive a single dose of SPL026 in a **dose-escalation** parallel group study. **Patients will receive up to 2 single doses of SPL026, 2 weeks apart**. Dose 1 will be randomised double-blind with placebo. Dose 2 will be open label, active SPL026. **SPL026 will**

in terms of DMT content, wherein optionally the first dose and the second dose are at least 48 hours apart from each other.	**be administered by IV injection**. Safety and tolerability, PK, PD and efficacy will be measured."
5. The method of claim 4, wherein the dosage of the first dose ranges from 0.038 mg/kg to 0.12 mg/kg in terms of DMT content, and wherein the dosage of the second dose ranges from 0.15 mg/kg to 0.38 mg/kg in terms of DMT content.	4. BIOSPACE (2022) "Small Pharma Inc.: World's First Clinical Trial For DMT-Assisted Therapy in Major Depressive Disorder Shows Consistent Quality of Psychedelic Response in Phase I" BioSpace. Retrieved from 22 February 2022. URL: https://www.biospace.com/article/releases/small-pharma-inc-world-s-first-clinical-trial-for-dmt-assisted-therapy-in-major-depressive-disorder-shows-consistent-quality-of-psychedelic-response-in-phase-i/?s=67 From **Main Text** "Small Pharma Inc., a neuroscience company focused on psychedelic-assisted therapies for mental health, is pleased to share the **analysis of Phase I data from the combined Phase I/IIa clinical trial of SPL026 with psychotherapy for the treatment of Major Depressive Disorder ("MDD")**." From **About Small Pharma** "Small Pharma initiated **a clinical program into DMT-assisted therapy** in February 2021." From **Key Results "IV administration of SPL026** offers a short-lived, well-tolerated psychedelic experience of ~20 minutes, enabling a dosing session to last only ~30 minutes." From **Key Results** "Data show a clear correlation between quality of psychedelic experience and dosing levels, **starting at 9mg and up to 21.5mg**, across all four cohorts. 5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Paragraph [0025**] "The synthesis of **DMT** from auxin (a plant hormone and natural product) has been reported by P. E. Morris and C. Chiao in J. Lab. Comp. Radiopharm., 1993, 33, 6, 455-465 (see bottom synthetic route depicted in FIG. 1… **there is a need in the art for an alternative method for the synthesis of DMT and DMT-type compounds of Formula III,** which avoids the use of problematic oxalyl chloride whilst

	producing high-purity compounds of Formula III without sacrificing yield." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **Paragraph [0246]** "Viewed from a fourth aspect, **a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient. The pharmaceutical composition may comprise one or more pharmaceutically acceptable excipients**…**Compositions include those suitable for** oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including subcutaneous, intravenous and intramuscular)** or rectal **administration**." From **[0004]** "**DMT** has been shown to be safely **administered in humans from a low dose of 0.05 mg/kg to a high dose of 0.4 mg/kg.** Of the 5 studies conducted since 1994, 2 used **single-bolus injections**, one used **repeat-bolus dosing** and two used prolonged **infusions** (over 90 and 20 minutes). DMT was found to be well-tolerated, with only a small number of mild to moderate adverse effects observed, with most being categorised as either a negative psychological effect or a hypertensive response."
6. The method of claim 1, wherein the subject is not administered a monoamine oxidase inhibitor (MAOI).	3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020. https://clinicaltrials.gov/study/NCT04673383 From **Brief Summary "**SPL026 **(N,N-dimethyltryptamine [DMT] fumarate) is a psychedelic tryptamine being developed as a therapy for patients with major depressive disorder (MDD)**." From **Detailed Description** "2-part study. Part A in psychedelic-naïve healthy volunteers**. Part B in patients with** MDD who score moderate-severe on Ham-D. Healthy volunteers will receive a single dose of SPL026 in a dose-escalation parallel group study. **Patients will receive up to 2 single doses of SPL026, 2 weeks apart**. Dose 1 will be randomised double-blind with placebo. Dose 2 will be open label, active SPL026. **SPL026 will be administered by IV injection**. Safety and tolerability, PK, PD and efficacy will be measured." From **Inclusion Criteria** "Inclusion Criteria: Part B only: **MDD diagnosis** (as per DSM-V**); not on antidepressant medication or willing to discontinue antidepressant medication (eg selective serotonin reuptake**

	inhibitor [SSRI] treatment) for a sufficient time before and during the study…" From **Exclusion Criteria** "Exclusion Criteria: ...antidepressant medication must have ceased for at least 14 days**; 28 days for MOAIs**) before first dose of trial medication…"
7. The method of claim 1, wherein the DMT compound is administered as a pharmaceutical composition further comprising at least one pharmaceutically acceptable carrier.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Paragraph [0025**] "The synthesis of **DMT** from auxin (a plant hormone and natural product) has been reported by P. E. Morris and C. Chiao in J. Lab. Comp. Radiopharm., 1993, 33, 6, 455-465 (see bottom synthetic route depicted in FIG. 1… **there is a need in the art for an alternative method for the synthesis of DMT and DMT-type compounds of Formula III,** which avoids the use of problematic oxalyl chloride whilst **producing high-purity compounds of Formula III** without sacrificing yield." From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder."

	From **Paragraph [0246]** "Viewed from a fourth aspect, **a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient. The pharmaceutical composition may comprise one or more pharmaceutically acceptable excipients**…**Compositions include those suitable for** oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including subcutaneous, intravenous and intramuscular)** or rectal **administration**." From **Paragraph [0248]** "**Suitable fillers with which the pharmaceutical compositions can be prepared and administered include lactose, starch, cellulose and derivatives thereof, and the like, or mixtures thereof used in suitable amounts. For parenteral administration, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agent**s and/or wetting agents, such as propylene glycol or butylene glycol."
8. The method of claim 7, wherein the pharmaceutical composition does not comprise any other hallucinogenic or psychedelic agent besides the DMT compound.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Paragraph [0296]** "The compositions described above **for use in treating a psychiatric** or psychocognitive **disorder selected from** (i) an obsessive compulsive disorder, **(ii) a depressive disorder**, (iii) a schizophrenia disorder, (iv) a schizotypal disorder, (v) an anxiety disorder, (vi) substance abuse, and (vii) an avolition disorder." From **Paragraph [0297]** "**The compositions described above wherein the compound of Formula III is DMT** or 5-MeO-DMT." From **Paragraph [0298]** "The compositions described above wherein **the pharmaceutically acceptable salt of the compound of Formula III is DMT fumarate**, and is preferably crystalline having a pattern A polymorphic form." From **Paragraph [0246]** "Viewed from a fourth aspect, **a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient. The pharmaceutical composition may comprise one or more pharmaceutically acceptable excipients**…**Compositions include those suitable for** oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including subcutaneous, intravenous and intramuscular)** or rectal **administration**."
9. The method of claim 7, wherein the pharmaceutical composition does not comprise any other	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021)

hallucinogenic or psychedelic agent besides the DMT compound in an amount sufficient to cause a measurable antidepressive, hallucinogenic, or psychedelic effect in the subject.	From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **Paragraph [0246]** "Viewed from a fourth aspect, **a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient. The pharmaceutical composition may comprise one or more pharmaceutically acceptable excipients**…**Compositions include those suitable for** oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including subcutaneous, intravenous and intramuscular)** or rectal **administration**." From **Paragraph [0248]** "**Suitable fillers with which the pharmaceutical compositions can be prepared and administered include lactose, starch, cellulose and derivatives thereof, and the like, or mixtures thereof used in suitable amounts. For parenteral administration, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agent**s and/or wetting agents, such as propylene glycol or butylene glycol."
10. The method of claim 1, wherein the pharmaceutical	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021)

composition consists essentially of the DMT compound and at least one pharmaceutically acceptable carrier.	From **Paragraph [0296]** "The compositions described above **for use in treating a psychiatric** or psychocognitive **disorder selected from** (i) an obsessive compulsive disorder, **(ii) a depressive disorder**, (iii) a schizophrenia disorder, (iv) a schizotypal disorder, (v) an anxiety disorder, (vi) substance abuse, and (vii) an avolition disorder." From **Paragraph [0297]** "**The compositions described above wherein the compound of Formula III is DMT** or 5-MeO-DMT." From **Paragraph [0298]** "The compositions described above wherein **the pharmaceutically acceptable salt of the compound of Formula III is DMT fumarate**, and is preferably crystalline having a pattern A polymorphic form." From **Paragraph [0246]** "Viewed from a fourth aspect, **a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient. The pharmaceutical composition may comprise one or more pharmaceutically acceptable excipients**…**Compositions include those suitable for** oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including subcutaneous, intravenous and intramuscular)** or rectal **administration**."
11. The method of claim 1, wherein the DMT compound (or DMT salt) is N,N-dimethyltryptamine hemifumarate.	6. COZZI (2020) "Synthesis and characterization of high-purity N,N-dimethyltryptamine hemifumarate for human clinical trials" Drug Testing and Analysis. Vol 12(10):1483-1493 From **Abstract** "Newly planned clinical trials to assess the safety and efficacy of DMT in humans with **major depressive disorders require high-purity water-soluble DMT for intravenous administration**. **Accordingly, we synthesized and characterized DMT hemifumarate for these upcoming studies**. The synthetic approach of Speeter and Anthony was slightly modified to gain some efficiency in time. In particular, this is the first known report to use aluminum hydride, generated in situ from lithium aluminum hydride, to reduce the intermediate 2-(1H-indol-3-yl)-N,N-dimethyl-2-oxoacetamide to DMT. **A quench protocol was developed to produce a good yield of exceptionally pure free base DMT upon workup, which was then converted to the hemifumarate salt.** Analysis of the final product included differential scanning calorimetry, thermogravimetric analysis, gas chromatography–mass spectrometry (GC–MS), 1H and 13C nuclear magnetic resonance spectroscopy, high-performance liquid chromatography, residual solvent analysis by GC headspace sampling, X-ray powder diffraction analysis, and residual lithium analysis by inductively coupled plasma-mass spectrometry. **The DMT hemifumarate was minimally 99.9% pure, with no significant impurities or residual solvents, thus meeting regulatory standards for administration to humans.**"

12. The method of claim 1, wherein psychedelic effects experienced by the subject after the administration last for 60 minutes or less.	1. U.S. Pat. No. US11,406,619B2 (2021) "INJECTABLE FORMULATIONS" (Filed 27 Aug 2021) From **Column 3, Line 58** "As used herein **the term 'depressive disorder' includes major depressive disorder, persistent depressive disorder, bipolar disorder, bipolar depression, and depression in terminally ill patients.**" From **Column 19, Line 47** "Viewed from a sixth aspect**, the invention provides a formulation** of the first aspect **for use in a method of treating a psychiatric or neurological disorder in a patient**. Often, **the psychiatric or neurological disorder is selected from the group consisting of** (i) an obsessive compulsive disorder, (ii) **a depressive disorder**, (iii) an anxiety disorder, (iv) substance abuse, and (v) an avolition disorder. **Often, the disorder is selected from the group consisting of major depressive disorder, treatment resistant major depressive disorder, post-partum depression,** an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder." From **Column 5, Line 50** "**The invention provides a pharmaceutical formulation suitable for injection, comprising a salt of a dimethyltryptamine (DMT) compound** optionally substituted with deuterium and optionally substituted at position 4 or 5 with acetoxy or methoxy or position 4 with monohydrogen phosphate; a buffer which is separate to the salt; and water, wherein the formulation has a pH of about 3.5 to about 6.5 and an osmolality of about 250 to about 350 mOsm/Kg." From **Column 20, Line 6** "**The formulation is suitable for injection**, thus its administration in therapy typically comprises injection of the formulation. **The formulation may be suitable for bolus injection, in which a discrete amount of an optionally substituted DMT salt is administered** in one injection such that the concentration of DMT in the body quickly increases. **Bolus injections are typically administered intravenously (directly into the vein), intramuscularly (within the muscle), intradermally (beneath the skin) or subcutaneously (within the fat or skin).**" 7. BARKER (2018) "N, N-Dimethyltryptamine (DMT), an Endogenous Hallucinogen: Past, Present, and Future Research to Determine Its Role and Function" Frontiers in Neuroscience. Vol 12:536 From **p. 5** "**All of the in vivo metabolism studies have shown that exogenously administered (IV, IM**, smoking, etc.) **DMT is rapidly metabolized and cleared**… **DMT administered in this manner reached a peak concentration in blood within 10–15 min and was below the limits of detection within 1 h…**DMT is pharmacologically active following **administration by injection (intravenous or intramuscular routes)** or smoking (vaporization and inhalation), pathways which can avoid first-pass metabolism by the liver to some degree (Riba et al., 2015). **The time to**

	onset of effects is rapid (seconds to minutes) by these routes and short lived (15–60 min depending on dose and route)."
13. The method of claim 1, wherein the depression is a major depressive disorder (MDD).	1. U.S. Pat. No. US11,406,619B2 (2021) "INJECTABLE FORMULATIONS" (Filed 27 Aug 2021) From **Column 3, Line 58** "As used herein **the term 'depressive disorder' includes major depressive disorder,** persistent depressive disorder, bipolar disorder, bipolar depression, and depression in terminally ill patients." From **Column 19, Line 47** "Viewed from a sixth aspect**, the invention provides a formulation** of the first aspect **for use in a method of treating a psychiatric or neurological disorder in a patient**. Often, **the psychiatric or neurological disorder is selected from the group consisting of** (i) an obsessive compulsive disorder, (ii) **a depressive disorder**, (iii) an anxiety disorder, (iv) substance abuse, and (v) an avolition disorder. **Often, the disorder is selected from the group consisting of major depressive disorder**, treatment resistant major depressive disorder, post-partum depression**,** an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder." From **Column 5, Line 50** "**The invention provides a pharmaceutical formulation suitable for injection, comprising a salt of a dimethyltryptamine (DMT) compound** optionally substituted with deuterium and optionally substituted at position 4 or 5 with acetoxy or methoxy or position 4 with monohydrogen phosphate; a buffer which is separate to the salt; and water, wherein the formulation has a pH of about 3.5 to about 6.5 and an osmolality of about 250 to about 350 mOsm/Kg." From **Column 20, Line 6** "**The formulation is suitable for injection**, thus its administration in therapy typically comprises injection of the formulation. **The formulation may be suitable for bolus injection, in which a discrete amount of an optionally substituted DMT salt is administered** in one injection such that the concentration of DMT in the body quickly increases. **Bolus injections are typically administered intravenously (directly into the vein), intramuscularly (within the muscle), intradermally (beneath the skin) or subcutaneously (within the fat or skin).**"
14. The method of claim 1, wherein the Hamilton Rating Scale for Depression (HAMD-17) of the subject prior to the administration of the DMT or the salt, solvate, or isotopically labelled derivative thereof, or any mixture thereof, is 17 or higher.	3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020. https://clinicaltrials.gov/study/NCT04673383 From **Brief Summary "**SPL026 **(N,N-dimethyltryptamine [DMT] fumarate) is a psychedelic tryptamine being developed as a therapy for patients with major depressive disorder (MDD)**." From **Detailed Description** "2-part study. Part A in psychedelic-naïve healthy volunteers**. Part B in patients with MDD who score moderate-severe on Ham-D**. Healthy volunteers will receive a single dose of SPL026 in a dose-escalation parallel group study. **Patients will receive up to 2 single doses of SPL026, 2 weeks apart**. Dose 1 will be randomised double-

<table>
<tr><td></td><td>blind with placebo. Dose 2 will be open label, active SPL026. SPL026 will be administered by IV injection. Safety and tolerability, PK, PD and efficacy will be measured."

8. ZIMMERMAN (2013) "Severity classification on the Hamilton depression rating scale" Journal of Affective Disorders. Vol 150(2):384-388

From Abstract "Based on this large study of psychiatric outpatients with major depressive disorder we recommend the following severity ranges for the HAMD: no depression (0–7); mild depression (8–16); moderate depression (17–23); and severe depression (≥24)."</td></tr>
<tr><td>15. The method of claim 1, wherein the reduction of the HAMD-17 score of the subject is 3.0 points or more the day after the administration of the DMT compound.</td><td>3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020. https://clinicaltrials.gov/study/NCT04673383

From Brief Summary "SPL026 (N,N-dimethyltryptamine [DMT] fumarate) is a psychedelic tryptamine being developed as a therapy for patients with major depressive disorder (MDD)."

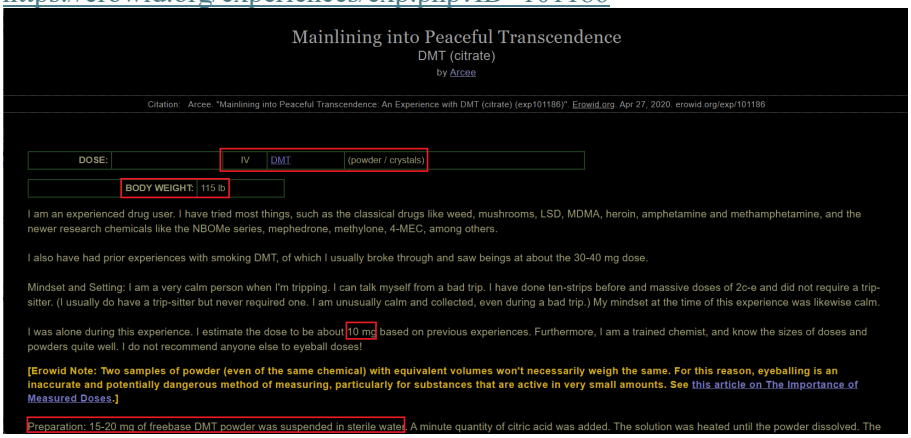
From Detailed Description "2-part study. Part A in psychedelic-naïve healthy volunteers. Part B in patients with MDD who score moderate-severe on Ham-D. Healthy volunteers will receive a single dose of SPL026 in a dose-escalation parallel group study. Patients will receive up to 2 single doses of SPL026, 2 weeks apart. Dose 1 will be randomised double-blind with placebo. Dose 2 will be open label, active SPL026. SPL026 will be administered by IV injection. Safety and tolerability, PK, PD and efficacy will be measured."

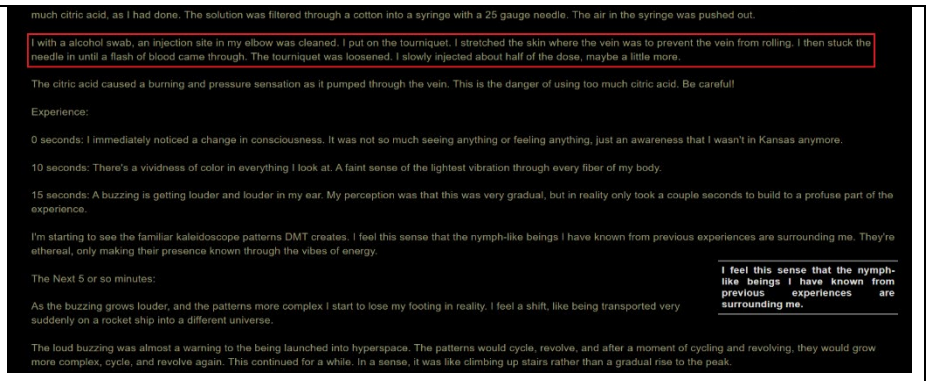
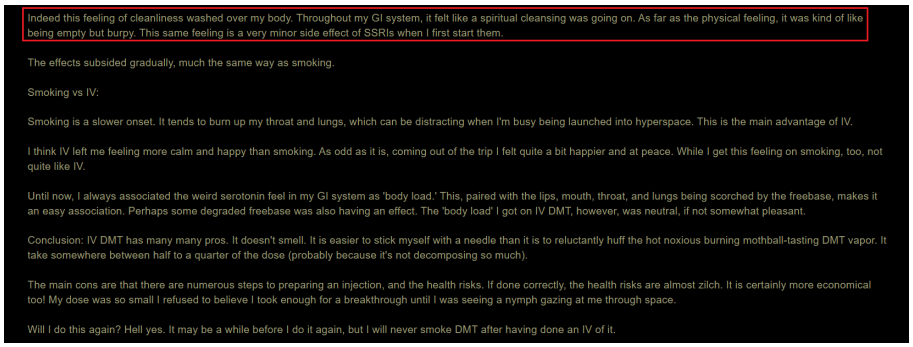
From What Is The Study Measuring?; Primary Outcome Measures
<table><tr><td>Efficacy of SPL026 in MDD patients with moderate to severe depression</td><td>Montgomery-Åsberg Depression Rating Scale (MADRS) score (where 7 - 19 is mild depression, 20 - 34 is moderate depression, and >34 is severe depression) change from baseline at 2 weeks after the first dose (± 2 days)</td><td>2 weeks after a single dose</td></tr></table>
9. LEUCHT (2018) "Translating the HAM-D into the MADRS and vice versa with equipercentile linking" Journal of Affective Disorders. Vol 226:326-331
From Abstract "The Hamilton Depression Rating Scale (HAM-D) and the Montgomery Asberg Depression Rating Scale (MADRS) are scales used frequently to rate the symptoms of depression. There are many situations in which it is important to know what a given total score or a percent reduction from baseline score of one scale means in relation to the other scale."

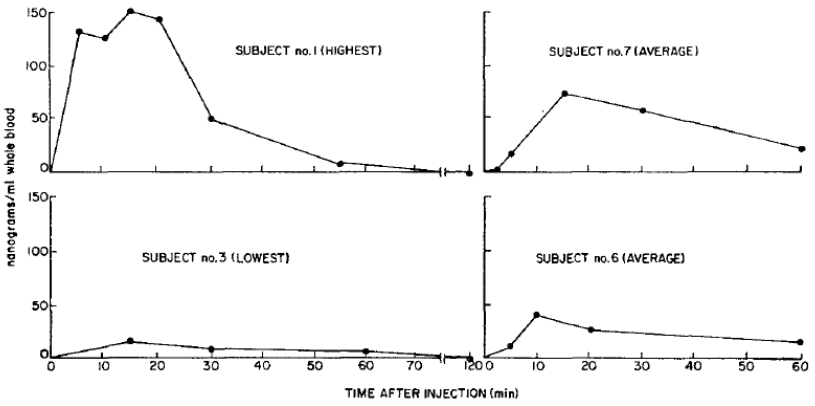
From Abstract "HAM-D scores of 10, 20, 30 and 40 roughly corresponded to MADRS scores of 13, 26, 39 and 52–53, respectively. An absolute HAM-D improvement of 10, 20, 25 points corresponded to a MADRS improvement of 12, 26, and 34. A percentage improvement from</td></tr>
</table>

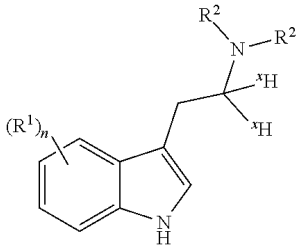
	baseline of the HAM-D was approximately the same as a percentage improvement on the MADRS."
16. The method of claim 1, wherein the depression is treatment resistant or partially responsive.	1. U.S. Pat. No. US11,406,619B2 (2021) "INJECTABLE FORMULATIONS" (Filed 27 Aug 2021) From **Column 3, Line 58** "As used herein **the term 'depressive disorder' includes major depressive disorder, persistent depressive disorder, bipolar disorder, bipolar depression, and depression in terminally ill patients.**" From **Column 19, Line 47** "Viewed from a sixth aspect**, the invention provides a formulation of the first aspect for use in a method of treating a psychiatric or neurological disorder in a patient.** Often**, the psychiatric or neurological disorder is selected from the group consisting of** (i) an obsessive compulsive disorder, (ii) **a depressive disorder**, (iii) an anxiety disorder, (iv) substance abuse, and (v) an avolition disorder. **Often, the disorder is selected from the group consisting of** major depressive disorder, **treatment resistant major depressive disorder**, post-partum depression, an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder." From **Column 5, Line 50** "**The invention provides a pharmaceutical formulation suitable for injection, comprising a salt of a dimethyltryptamine (DMT) compound** optionally substituted with deuterium and optionally substituted at position 4 or 5 with acetoxy or methoxy or position 4 with monohydrogen phosphate; a buffer which is separate to the salt; and water, wherein the formulation has a pH of about 3.5 to about 6.5 and an osmolality of about 250 to about 350 mOsm/Kg." From **Column 20, Line 6** "**The formulation is suitable for injection**, thus its administration in therapy typically comprises injection of the formulation. **The formulation may be suitable for bolus injection, in which a discrete amount of an optionally substituted DMT salt is administered** in one injection such that the concentration of DMT in the body quickly increases. **Bolus injections are typically administered intravenously (directly into the vein), intramuscularly (within the muscle), intradermally (beneath the skin) or subcutaneously (within the fat or skin).**"
17. The method of claim 1, wherein the subject has suffered from the depression for 10 years or more prior to the administration of the DMT compound.	3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020. https://clinicaltrials.gov/study/NCT04673383 From **Brief Summary "SPL026 (N,N-dimethyltryptamine [DMT] fumarate) is a psychedelic tryptamine being developed as a therapy for patients with major depressive disorder (MDD)**." From **Detailed Description** "2-part study. Part A in psychedelic-naïve healthy volunteers**. Part B in patients with MDD** who score moderate-severe on Ham-D. Healthy volunteers will receive a single dose of SPL026 in a **dose-escalation** parallel group study. **Patients will receive up to 2**

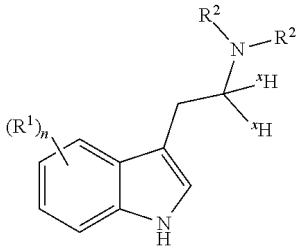
	single doses of SPL026, 2 weeks apart. Dose 1 will be randomised double-blind with placebo. Dose 2 will be open label, active SPL026. **SPL026 will be administered by IV injection**. Safety and tolerability, PK, PD and efficacy will be measured." 10. NIMH (2009) "Depression" NIMH. Retrieved from May 31 2021. URL: https://web.archive.org/web/20210531222859/https://www.nimh.nih.gov/health/publications/depression/ From **What are the different types of depression?** "**Major depression, which includes symptoms of depression most of the time for at least 2 weeks** that typically interfere with one's ability to work, sleep, study, and eat.**"**
18. The method of claim 1, wherein the subject is further administered a psychological distress medication or a hypertension medication.	1. U.S. Pat. No. US11,406,619B2 (2021) "INJECTABLE FORMULATIONS" (Filed 27 Aug 2021) From **Column 3, Line 58** "As used herein **the term 'depressive disorder' includes major depressive disorder, persistent depressive disorder, bipolar disorder, bipolar depression, and depression in terminally ill patients.**" From **Column 19, Line 47** "Viewed from a sixth aspect**, the invention provides a formulation** of the first aspect **for use in a method of treating a psychiatric or neurological disorder in a patient**. Often, **the psychiatric or neurological disorder is selected from the group consisting of** (i) an obsessive compulsive disorder, (ii) **a depressive disorder**, (iii) an anxiety disorder, (iv) substance abuse, and (v) an avolition disorder. **Often, the disorder is selected from the group consisting of major depressive disorder, treatment resistant major depressive disorder, post-partum depression,** an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder." From **Column 5, Line 50** "**The invention provides a pharmaceutical formulation suitable for injection, comprising a salt of a dimethyltryptamine (DMT) compound** optionally substituted with deuterium and optionally substituted at position 4 or 5 with acetoxy or methoxy or position 4 with monohydrogen phosphate; a buffer which is separate to the salt; and water, wherein the formulation has a pH of about 3.5 to about 6.5 and an osmolality of about 250 to about 350 mOsm/Kg." From **Column 20, Line 6** "**The formulation is suitable for injection**, thus its administration in therapy typically comprises injection of the formulation. **The formulation may be suitable for bolus injection, in which a discrete amount of an optionally substituted DMT salt is administered** in one injection such that the concentration of DMT in the body quickly increases. **Bolus injections are typically administered intravenously (directly into the vein), intramuscularly (within the muscle), intradermally (beneath the skin) or subcutaneously (within the fat or skin).**"

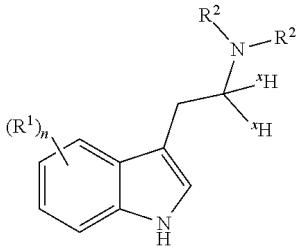
	11. CA Pat. App. No. CA3127854A1 (2020) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 29 Jan 2020) From **[47]** "Substituted tryptamines are substituted with any suitable group, such as being modified on the indole ring (RI, R2), the ethylene chain (R3) and/or on the amino group (R4, R5) as illustrated below, and are collectively referred to herein as tryptarnines. **Examples of tryptamines include** serotonin, melatonin, psilocybin and **N,N-dimethyltryptamine**…" From **Claim 1** "A method of **managing a neurological condition** or one or more symptoms thereof **in a subject in need thereof**, comprising **administering to the subject a pharmaceutical composition comprising:** a) **a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof**…" From **Claim 18** "The method of any one of the preceding claims, wherein **the pharmaceutical composition further comprises an effective amount of a second agent**." From **Claim 23** "The method of claim 18, wherein **the second agent is an anti-psychotic agent**." From **[138]** "**For injection, the pharmaceutical compositions disclosed herein are optionally formulated in aqueous solutions**…" From **[52]** "In certain embodiments, a composition or formulation described herein comprises an antidepressant. Similarly**, in some embodiments, a therapeutic method provided herein comprises the administration of an antidepressant**, such as utilizing a formulation or composition described herein. In certain instances, **antidepressants are classified into three families: monoamine oxidase inhibitors (MAOIs), tricyclics and selective serotonin reuptake inhibitors (SSRIs).**"
19. The method of claim 1, wherein the subject is not provided psychotherapy at the time of the administration of the DMT compound.	2. EROWID (2020) "Mainlining into Peaceful Transcendence" EROWID. Retrieved from April 27 2020. URL: https://erowid.org/experiences/exp.php?ID=101186  Mainlining into Peaceful Transcendence DMT (citrate) by Arcee Citation: Arcee "Mainlining into Peaceful Transcendence: An Experience with DMT (citrate) (exp101186)" Erowid.org Apr 27, 2020 erowid.org/exp/101186 DOSE: IV DMT (powder / crystals) BODY WEIGHT: 115 lb I am an experienced drug user. I have tried most things, such as the classical drugs like weed, mushrooms, LSD, MDMA, heroin, amphetamine and methamphetamine, and the newer research chemicals like the NBOMe series, mephedrone, methylone, 4-MEC, among others. I also have had prior experiences with smoking DMT, of which I usually broke through and saw beings at about the 30-40 mg dose. Mindset and Setting: I am a very calm person when I'm tripping. I can talk myself from a bad trip. I have done ten-strips before and massive doses of 2c-e and did not require a trip-sitter. (I usually do have a trip-sitter but never required one. I am unusually calm and collected, even during a bad trip.) My mindset at the time of this experience was likewise calm. I was alone during this experience. I estimate the dose to be about 10 mg based on previous experiences. Furthermore, I am a trained chemist, and know the sizes of doses and powders quite well. I do not recommend anyone else to eyeball doses! [Erowid Note: Two samples of powder (even of the same chemical) with equivalent volumes won't necessarily weigh the same. For this reason, eyeballing is an inaccurate and potentially dangerous method of measuring, particularly for substances that are active in very small amounts. See this article on The Importance of Measured Doses.] Preparation: 15-20 mg of freebase DMT powder was suspended in sterile water. A minute quantity of citric acid was added. The solution was heated until the powder dissolved. The

	 
20. The method of claim 1, wherein the peak serum level of the DMT compound in the subject after the administration is 300 µg/dl or lower in terms of DMT content.	1. U.S. Pat. No. US11,406,619B2 (2021) "INJECTABLE FORMULATIONS" (Filed 27 Aug 2021) From **Column 3, Line 58** "As used herein **the term 'depressive disorder' includes major depressive disorder, persistent depressive disorder, bipolar disorder, bipolar depression, and depression in terminally ill patients.**" From **Column 19, Line 47** "Viewed from a sixth aspect**, the invention provides a formulation** of the first aspect **for use in a method of treating a psychiatric or neurological disorder in a patient**. Often, **the psychiatric or neurological disorder is selected from the group consisting of** (i) an obsessive compulsive disorder, (ii) **a depressive disorder**, (iii) an anxiety disorder, (iv) substance abuse, and (v) an avolition disorder. **Often, the disorder is selected from the group consisting of major depressive disorder, treatment resistant major depressive disorder, post-partum depression,** an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder." From **Column 5, Line 50** "**The invention provides a pharmaceutical formulation suitable for injection, comprising a salt of a dimethyltryptamine (DMT) compound** optionally substituted with deuterium and optionally substituted at position 4 or 5 with acetoxy or methoxy or position 4 with monohydrogen phosphate; a buffer which is separate to the salt; and water, wherein the formulation has a pH of about 3.5 to about 6.5 and an osmolality of about 250 to about 350 mOsm/Kg."

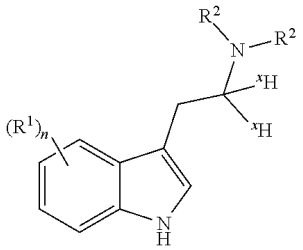
	From **Column 20, Line 6** "**The formulation is suitable for injection**, thus its administration in therapy typically comprises injection of the formulation. **The formulation may be suitable for bolus injection, in which a discrete amount of an optionally substituted DMT salt is administered** in one injection such that the concentration of DMT in the body quickly increases. **Bolus injections are typically administered intravenously (directly into the vein), intramuscularly (within the muscle), intradermally (beneath the skin) or subcutaneously (within the fat or skin).**" 12. KAPLAN (1974) "Blood and urine levels of N,N-dimethyltryptamine following administration of psychoactive dosages to human subjects" Psychopharmacologia Vol 38(3):239-245 From **p. 240** "Wyatt, Mandel, Ahn, Walker, and VandenHeuvel (1973) were **unable to demonstrate any difference in DMT plasma levels between groups of normals**, chronic schizophrenics, acute schizophrenics, **and** psychotic **depressives**…" From **p. 240** "**DMT was administered intramuscularly at a dosage of 0.7 mg/kg body weight.**" From **p. 241**  Fig. 1. Individual DMT blood levels
21. A kit for treating, ameliorating, or preventing depression in a subject in need thereof, the kit comprising: a dimethyltryptamine (DMT) compound selected from the group consisting of DMT, a DMT salt, a DMT solvate, an isotopically	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**"

labelled derivative of DMT, or any mixture thereof; and a manual instructing that the DMT compound is to be administered parenterally to the subject in an effective amount.	From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**:  III From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration."

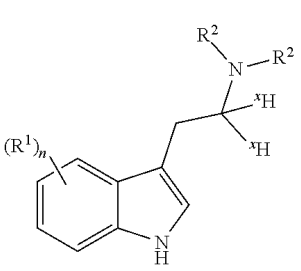
22. The kit of claim 21, wherein the manual instructs that the subject is to be administered with the DMT compound intravenously.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**"

	From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration."
23. The kit of claim 21, wherein the manual instructs that the amount of the DMT compound to be administered to the subject ranges from about 0.038 mg/kg to about 0.38 mg/kg in terms of DMT content.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder."

	From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration." 4. BIOSPACE (2022) "Small Pharma Inc.: World's First Clinical Trial For DMT-Assisted Therapy in Major Depressive Disorder Shows Consistent Quality of Psychedelic Response in Phase I" BioSpace. Retrieved from 22 February 2022. URL: https://www.biospace.com/article/releases/small-pharma-inc-world-s-first-clinical-trial-for-dmt-assisted-therapy-in-major-depressive-disorder-shows-consistent-quality-of-psychedelic-response-in-phase-i/?s=67 From **Main Text** "Small Pharma Inc., a neuroscience company focused on psychedelic-assisted therapies for mental health, is pleased to share the **analysis of Phase I data from the combined Phase I/IIa clinical trial of SPL026 with psychotherapy for the treatment of Major Depressive Disorder ("MDD")**." From **Main Text** "This study will assess the efficacy of one dose of SPL026 versus a placebo, **and one versus two doses of SPL026** in combination with psychotherapy **in patients with MDD** while bolstering existing safety and tolerability data. From **About Small Pharma** "Small Pharma initiated **a clinical program into DMT-assisted therapy** in February 2021." From **Key Results "IV administration of SPL026** offers a short-lived, well-tolerated psychedelic experience of ~20 minutes, enabling a dosing session to last only ~30 minutes." From **Key Results** "Data show a clear correlation between quality of psychedelic experience and dosing levels, **starting at 9mg and up to 21.5mg**, across all four cohorts." From **Key Results** "**Participant-reported scores**, using a 0 to 100 scale, **on** the richness of **the psychedelic experience** demonstrated increasing values

	of 48 (**9mg**), 79, 79, 88 (**21.5mg**) across the **four increasing doses**. A dose correlation was seen across most patient-reported scores.
24. The kit of claim 21, wherein the manual instructs that the subject is to be administered with at least a first dose of an independently selected DMT compound and a second dose of an independently selected DMT compound, and wherein the dosage of the second dose in terms of DMT content is higher than the dosage of the first dose in terms of DMT content, wherein optionally the first dose and the second dose are at least 48 hours apart.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol."

	From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration." 4. BIOSPACE (2022) "Small Pharma Inc.: World's First Clinical Trial For DMT-Assisted Therapy in Major Depressive Disorder Shows Consistent Quality of Psychedelic Response in Phase I" BioSpace. Retrieved from 22 February 2022. URL: https://www.biospace.com/article/releases/small-pharma-inc-world-s-first-clinical-trial-for-dmt-assisted-therapy-in-major-depressive-disorder-shows-consistent-quality-of-psychedelic-response-in-phase-i/?s=67 From **Main Text** "Small Pharma Inc., a neuroscience company focused on psychedelic-assisted therapies for mental health, is pleased to share the **analysis of Phase I data from the combined Phase I/IIa clinical trial of SPL026 with psychotherapy for the treatment of Major Depressive Disorder ("MDD")**." From **Main Text** "This study will assess the efficacy of one dose of SPL026 versus a placebo, **and one versus two doses of SPL026** in combination with psychotherapy **in patients with MDD** while bolstering existing safety and tolerability data. From **About Small Pharma** "Small Pharma initiated **a clinical program into DMT-assisted therapy** in February 2021." From **Key Results "IV administration of SPL026** offers a short-lived, well-tolerated psychedelic experience of ~20 minutes, enabling a dosing session to last only ~30 minutes." From **Key Results** "Data show a clear correlation between quality of psychedelic experience and dosing levels, **starting at 9mg and up to 21.5mg**, across all four cohorts." From **Key Results** "**Participant-reported scores**, using a 0 to 100 scale, **on** the richness of **the psychedelic experience** demonstrated increasing values of 48 (**9mg**), 79, 79, 88 (**21.5mg**) across the **four increasing doses**. A dose correlation was seen across most patient-reported scores.

25. The kit of claim 24, wherein the dosage of the first dose ranges from 0.038 mg/kg to 0.12 mg/kg, and the dosage of the second dose ranges from 0.15 mg/kg to 0.38 mg/kg in terms of DMT content.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**"

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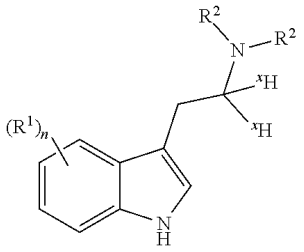
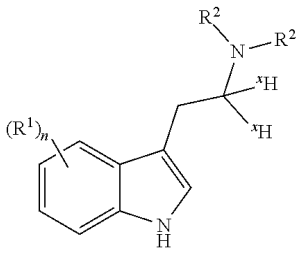
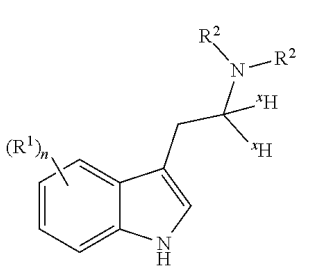
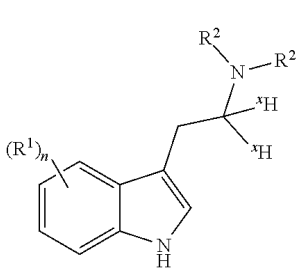
26. The kit of claim 21, wherein the DMT compound is not mixed with a monoamine oxidase inhibitor (MAOI).	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as

	particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and

	transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration.”
27. The kit of claim 21, wherein the DMT compound is formulated as a pharmaceutical composition further comprising at least one pharmaceutically acceptable carrier.	5. U.S. Pat. No. US2021/0395201A1 (2021) “SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES” (Filed 26 Aug 2021) From **Abstract** “Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**” From **Claim 1** “A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** “**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III.” From **Claim 17** “**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1.” From **Claim 18** “The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder.” From **[0248]** “**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, **containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol.**”

	From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, **in combination with a pharmaceutically acceptable excipient**…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration."
28. The kit of claim 27, wherein the pharmaceutical composition does not comprise any other hallucinogenic or psychedelic agent besides the DMT compound.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1."

	From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder is an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, **containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol.**" From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, **in combination with a pharmaceutically acceptable excipient**…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (includin**g subcutaneous, **intravenous** and intramuscular) or rectal administration."
29. The kit of claim 27, wherein the pharmaceutical composition does not comprise any other hallucinogenic or psychedelic agent besides the DMT compound in an amount sufficient to cause a measurable antidepressive, hallucinogenic, or psychedelic effect in the subject.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and

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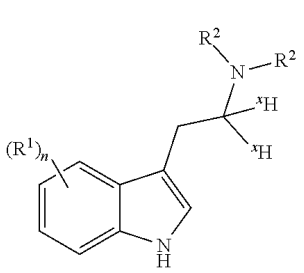
30. The kit of claim 27, wherein the pharmaceutical composition consists essentially of the DMT compound and at least one pharmaceutically acceptable carrier.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder."

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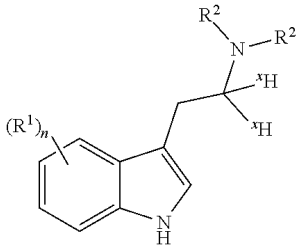
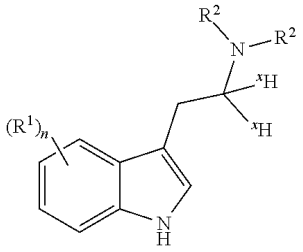
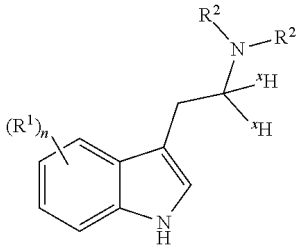
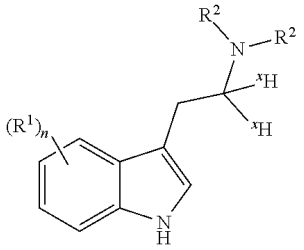
31. The kit of claim 21, wherein the DMT compound is N,N-dimethyltryptamine hemifumarate.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient**

	an effective amount of the fumarate salt of the compound of Formula III prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration." 6. COZZI (2020) "Synthesis and characterization of high-purity N,N-dimethyltryptamine hemifumarate for human clinical trials" Drug Testing and Analysis. Vol 12(10):1483-1493 From **Abstract** "Newly planned clinical trials to assess the safety and efficacy of DMT in humans with **major depressive disorders require high-purity water-soluble DMT for intravenous administration**. **Accordingly, we synthesized and characterized DMT hemifumarate for these upcoming studies**. The synthetic approach of Speeter and Anthony was slightly modified to gain some efficiency in time. In particular, this is the first known report to use aluminum hydride, generated in situ from lithium aluminum hydride, to reduce the intermediate 2-(1H-indol-3-yl)-N,N-dimethyl-2-oxoacetamide to DMT. **A quench protocol was developed to produce a good yield of exceptionally pure free base DMT upon workup, which was then converted to the hemifumarate salt.** Analysis of the final product included differential scanning calorimetry, thermogravimetric analysis, gas chromatography–mass spectrometry (GC–MS), 1H and 13C nuclear magnetic resonance spectroscopy, high-performance liquid chromatography, residual solvent analysis by GC headspace sampling, X-ray powder diffraction analysis, and residual lithium analysis by inductively coupled plasma-mass spectrometry. **The DMT hemifumarate was minimally 99.9% pure, with no significant impurities or residual solvents, thus meeting regulatory standards for administration to humans.**"

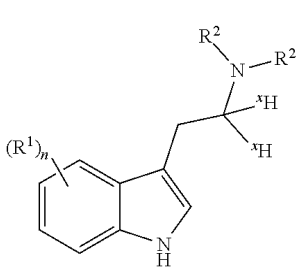
32. The kit of claim 21, wherein, when the DMT compound is to be administered to the subject according to the instruction of the manual, psychedelic effects experienced by the subject after the administration last for 60 minutes or less.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, **containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol.**" From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**"

	From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, **in combination with a pharmaceutically acceptable excipient**…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration." 7. BARKER (2018) "N, N-Dimethyltryptamine (DMT), an Endogenous Hallucinogen: Past, Present, and Future Research to Determine Its Role and Function" Frontiers in Neuroscience. Vol 12:536 From **p. 5** "**All of the in vivo metabolism studies have shown that exogenously administered (IV, IM**, smoking, etc.) **DMT is rapidly metabolized and cleared**… **DMT administered in this manner reached a peak concentration in blood within 10–15 min and was below the limits of detection within 1 h…**DMT is pharmacologically active following **administration by injection (intravenous or intramuscular routes)** or smoking (vaporization and inhalation), pathways which can avoid first-pass metabolism by the liver to some degree (Riba et al., 2015). **The time to onset of effects is rapid (seconds to minutes) by these routes and short lived (15–60 min depending on dose and route).**"
33. The kit of claim 21, wherein the depression is a major depressive disorder (MDD).	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III 

	From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0253]** "In some embodiments, **the disorder is selected from the group consisting of major depressive disorder**, treatment resistant major depressive disorder, post-partum depression, an obsessive compulsive disorder and an eating disorder such as a compulsive eating disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, **containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol.**" From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, **in combination with a pharmaceutically acceptable excipient**…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (includin**g subcutaneous, **intravenous** and intramuscular) or rectal administration."
34. The kit of claim 21, wherein the Hamilton Rating Scale for Depression (HAMD-17) of the subject prior to the administration of the DMT or the salt, solvate, or isotopically labelled derivative thereof, or any mixture thereof is 17 or higher.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**"

	From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration." 3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020.

	https://clinicaltrials.gov/study/NCT04673383 From **Brief Summary "**SPL026 **(N,N-dimethyltryptamine [DMT] fumarate) is a psychedelic tryptamine being developed as a therapy for patients with major depressive disorder (MDD)**." From **Detailed Description** "2-part study. Part A in psychedelic-naïve healthy volunteers**. Part B in patients with MDD who score moderate-severe on Ham-D**. Healthy volunteers will receive a single dose of SPL026 in a dose-escalation parallel group study. Patients will receive up to 2 single doses of SPL026, 2 weeks apart. Dose 1 will be randomised double-blind with placebo. Dose 2 will be open label, active SPL026**. SPL026 will be administered by IV injection.** Safety and tolerability, PK, PD and efficacy will be measured." 8. ZIMMERMAN (2013) " Severity classification on the Hamilton depression rating scale" Journal of Affective Disorders. Vol 150(2):384-388 From **Abstract** "Based on this large study of psychiatric outpatients with major depressive disorder we recommend the following severity ranges for the **HAMD**: no depression (0–7); mild depression (8–16); **moderate depression (17–23);** and severe depression (≥24)." 13. PALHANO-FONTEZ (2019) "Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial" Psychological Medicine. Vol. 49:655-663 From **p. 656** "Ayahuasca is most often prepared by decoction of two plants (McKenna et al., 1984**): Psychotria viridis that contains the psychedelic N, N-dimethyltryptamine (N,N-DMT)**, a serotonin and sigma-1 receptors agonist (Carbonaro and Gatch, 2016), and Banisteriopsis caapi, rich in reversible monoamine oxidase inhibitors (MAOi) such as harmine, harmaline, and tetrahydroharmine (Riba et al., 2003)." From **p. 656** "In a recent open-label trial, **17 patients with major depressive disorder** attended a single dosing session with ayahuasca. **Depression severity was assessed before, during and after dosing, using the Hamilton Depression Rating scale (HAM-D) and the Montgomery–Åsberg Depression Rating Scale (MADRS)** (Sanches et al., 2016). **Significant reduction in depression severity was found already in the first hours after dosing, an effect that remained significant for 21 days** (Osório et al., 2015; Sanches et al., 2016)." From **p. 656** "**We used the MADRS and the HAM-D** (Carneiro et al., 2015) **to access depression severi**ty. MADRS assessments were at baseline (one day before dosing), and at 1 (D1), 2 (D2), and 7 (D7) days after dosing. **HAM-D was applied only at baseline and D7, as it was designed to access depression symptoms present in the last week** (Hamilton, 1960)."

35. The kit of claim 21, wherein, when the DMT compound is administered to the subject according to the instruction of the manual, the HAMD-17 score of the subject is reduced by 3.0 points or more the day after the administration.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**"

	From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration." 3. SMALL PHARMA LTD (2020) "SPL026 (DMT Fumarate) in Healthy Subjects and MDD Patients". Study record first posted 17 December 2020. https://clinicaltrials.gov/study/NCT04673383 From **Brief Summary "**SPL026 **(N,N-dimethyltryptamine [DMT] fumarate) is a psychedelic tryptamine being developed as a therapy for patients with major depressive disorder (MDD)**." From **Detailed Description** "2-part study. Part A in psychedelic-naïve healthy volunteers**. Part B in patients with MDD who score moderate-severe on Ham-D**. Healthy volunteers will receive a single dose of SPL026 in a dose-escalation parallel group study. Patients will receive up to 2 single doses of SPL026, 2 weeks apart. Dose 1 will be randomised double-blind with placebo. Dose 2 will be open label, active SPL026**. SPL026 will be administered by IV injection.** Safety and tolerability, PK, PD and efficacy will be measured." 8. ZIMMERMAN (2013) "Severity classification on the Hamilton depression rating scale" Journal of Affective Disorders. Vol 150(2):384-388 From **Abstract** "Based on this large study of psychiatric outpatients with major depressive disorder we recommend the following severity ranges for the **HAMD**: no depression (0–7); mild depression (8–16); **moderate depression (17–23);** and severe depression (≥24)." 13. PALHANO-FONTEZ (2019) "Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial" Psychological Medicine. Vol. 49:655-663 From **p. 656** "Ayahuasca is most often prepared by decoction of two plants (McKenna et al., 1984**): Psychotria viridis that contains the psychedelic N, N-dimethyltryptamine (N,N-DMT)**, a serotonin and sigma-1 receptors agonist (Carbonaro and Gatch, 2016), and Banisteriopsis caapi, rich in reversible monoamine oxidase inhibitors (MAOi) such as harmine, harmaline, and tetrahydroharmine (Riba et al., 2003)." From **p. 656** "In a recent open-label trial, **17 patients with major depressive disorder** attended a single dosing session with ayahuasca. **Depression severity was assessed before, during and after dosing, using**

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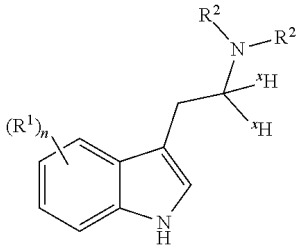
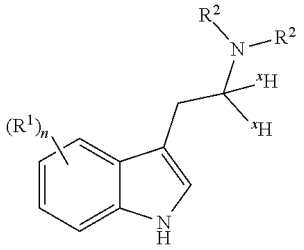
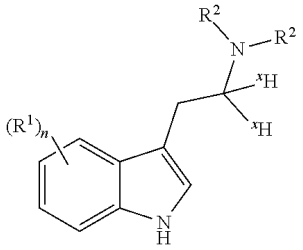
36. The kit of claim 21, wherein the depression is treatment resistant or partially-responsive.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0235]** "**In some embodiments, the disorder is** selected from the group consisting of major depressive disorder, **treatment resistant major depressive disorder**…"

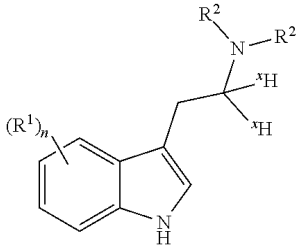
	From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (includin**g subcutaneous, **intravenous** and intramuscular) or rectal administration."
37. The kit of claim 21, wherein the subject has suffered from the depression for 10 years or more.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient**

	an effective amount of the fumarate salt of the compound of Formula III prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" 10. NIMH (2009) "Depression" NIMH. Retrieved from May 31 2021. URL: https://web.archive.org/web/20210531222859/https://www.nimh.nih.gov/health/publications/depression/ From **What are the different types of depression?** "**Major depression, which includes symptoms of depression most of the time for at least 2 weeks** that typically interfere with one's ability to work, sleep, study, and eat.**"** 14. EATON (2008) "Population-Based Study of First Onset and Chronicity in Major Depressive Disorder" Archives of General Psychiatry. Vol 65(5):513-520 From **Abstract** "**Participants**—Probability sample of **3481 adult household residents** in 1981, including 92 with first **lifetime onset of major depressive disorder** during the course of the follow-up, and 1739 other participants followed up for at least 13 years." From **Abstract** "**Results**— … The median episode length was 12 weeks. **About 15% of 92 individuals with first episodes did not have a year free of episodes, even after 23 years**."
38. The kit of claim 21, wherein the kit further comprises a psychological distress medication or a hypertension medication.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of**

	Formula III have uses in the treatment of psychiatric or neurological disorders." From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1." From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (includin**g subcutaneous, **intravenous** and intramuscular) or rectal administration."

	11. CA Pat. App. No. CA3127854A1 (2020) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 29 Jan 2020) From **[47]** "Substituted tryptamines are substituted with any suitable group, such as being modified on the indole ring (RI, R2), the ethylene chain (R3) and/or on the amino group (R4, R5) as illustrated below, and are collectively referred to herein as tryptarnines. **Examples of tryptamines include** serotonin, melatonin, psilocybin and **N,N-dimethyltryptamine**…" From **Claim 1** "A method of **managing a neurological condition** or one or more symptoms thereof **in a subject in need thereof**, comprising **administering to the subject a pharmaceutical composition comprising:** a) **a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof**…" From **Claim 18** "The method of any one of the preceding claims, wherein **the pharmaceutical composition further comprises an effective amount of a second agent**." From **Claim 23** "The method of claim 18, wherein **the second agent is an anti-psychotic agent**." From **[138]** "**For injection, the pharmaceutical compositions disclosed herein are optionally formulated in aqueous solutions**…" From **[52]** "In certain embodiments, a composition or formulation described herein comprises an antidepressant. Similarly**, in some embodiments, a therapeutic method provided herein comprises the administration of an antidepressant**, such as utilizing a formulation or composition described herein. In certain instances, **antidepressants are classified into three families: monoamine oxidase inhibitors (MAOIs), tricyclics and selective serotonin reuptake inhibitors (SSRIs)."**
39. The kit of claim 21, wherein the manual instructs that the subject does not need to be provided psychotherapy at the time of the administration of the DMT compound.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**:

III



From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III."

From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1."

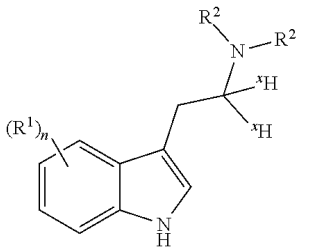
From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder."

From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol."

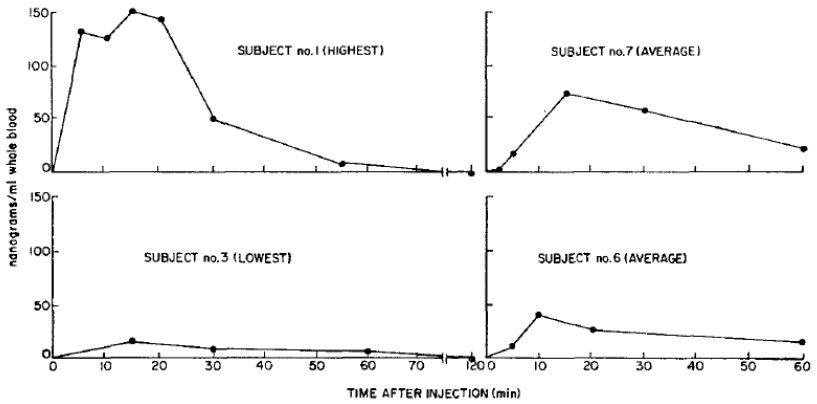
From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**"

From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (includin**g subcutaneous, **intravenous** and intramuscular) or rectal administration."

15. MALCOLM (2019) "Can Psychedelics Heal Without Psychotherapy?" Federal Register. Retrieved from October 4 1, 2019. URL https://web.archive.org/web/20210925064427/https://www.spiritpharmacist.com/blog/can-psychedelics-heal-without-psychotherapy

	From **Ritual Use of Ayahuasca** "**Ayahuasca** has also been studied in medical contexts with positive results and seems to **act as a potent and rapid-onset antidepressant in persons with treatment resistant depression**. **Studies** to date are small, although **do not mention the presence of therapist or formalized psychotherapy sessions before or after as part of the process, yet results persist for weeks after use** [13-15]. In fact, one study mentions that **ayahuasca was deliberately used without therapist oversight,** a musical playlist, or post-use psychological intervention because they wanted to understand what the intrinsic antidepressant effects of ayahuasca were [15]. **Rapid antidepressant effects were observed with remote supervision of users and absence of psychotherapy that persisted at least two weeks later.**"
40. The kit of claim 21, wherein the manual instructs that a peak serum level of the DMT compound in the subject after the administration is 300 µg/dl or lower in terms of DMT content.	5. U.S. Pat. No. US2021/0395201A1 (2021) "SYNTHESIS OF N,N-DIMETHYLTRYPTAMINE-TYPE COMPOUNDS, METHODS, AND USES" (Filed 26 Aug 2021) From **Abstract** "Syntheses of compounds of Formula III from compounds of Formula I via compounds of Formula II are described, as well as **particular compounds of Formula III, or pharmaceutically acceptable salts thereof, compositions comprising such compounds**, and uses thereof. For example, **certain of these compounds and compositions of Formula III have uses in the treatment of psychiatric or neurological disorders.**" From **Claim 1** "A method of synthesizing a fumarate salt of a compound of **Formula III**: III  From **Claim 16** "**A kit** for **preparing the fumarate salt of the compound of Formula III prepared according to the method of claim 1**, wherein the kit comprises: a compound of Formula I; a coupling agent and an additive; an amine having the formula (R2)2NH; LiAlH4 and/or LiAlD4; and an acidic reagent suitable for the production of a pharmaceutically acceptable fumarate salt of the compound of Formula III." From **Claim 17** "**A method treatment of a psychiatric** or neurological **disorder in a patient**, the method comprising: **administering to the patient an effective amount of the fumarate salt of the compound of Formula III** prepared according to the method of claim 1."

	From **Claim 18** "The method of claim 17, wherein **the psychiatric** or neurological disorder **is** an obsessive compulsive disorder, **a depressive disorder**, a schizophrenia disorder, a schizotypal disorder, an anxiety disorder, substance abuse, or an avolition disorder." From **[0248]** "**For parenteral administration**, aqueous suspensions, isotonic saline solutions and sterile injectable solutions may be used, containing pharmaceutically acceptable dispersing agents and/or wetting agents, such as propylene glycol or butylene glycol." From **[0249]** "A pharmaceutical composition, in combination with packaging material suitable for the composition is provided, **the packaging material including instructions for the use of the pharmaceutical composition.**" From **[0246]** "Viewed from a fourth aspect**, a pharmaceutical composition is provided comprising the compound defined in the second or third aspect, or a pharmaceutically acceptable salt thereof**, in combination with a pharmaceutically acceptable excipient…**Compositions include those suitable** for oral, nasal, topical (including buccal, sublingual and transdermal), **parenteral (including** subcutaneous, **intravenous** and intramuscular) or rectal administration." 16. Federal Register (2006) "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" Federal Register. Retrieved from May 1, 2017. URL https://web.archive.org/web/20170501143753/https://www.federalregister.gov/documents/2006/01/24/06-545/requirements-on-content-and-format-of-labeling-for-human-prescription-drug-and-biological-products From **A. FDA-Approved Prescription Drug Labeling** "**A prescription drug product's FDA-approved labeling (also known as "professional labeling," "package insert," "direction circular," or "package circular**") is a compilation of information about the product, approved by FDA, based on the agency's thorough analysis of the new drug application (NDA) or biologics license application (BLA) submitted by the applicant. **This labeling contains information necessary for safe and effective use. It is written for the health care practitioner audience, because prescription drugs require "professional supervision of a practitioner licensed by law to administer such drug"** (section 503(b) of the act (21 U.S.C. 353(b))). FDA-approved labeling is defined in section 201(m) of the act (21 U.S.C. 321(m)) and is subject to all applicable provisions of section 502 of the act (21 U.S.C. 352)." From **(C) 12.3 Pharmacokinetics** "**This subsection must describe the clinically significant pharmacokinetics of a drug or active metabolites**, (i.e., **pertinent absorption, distribution, metabolism, and excretion parameters**). **Information regarding** bioavailability, the effect of food, **minimum concentration (Cmin), maximum concentration (Cmax), time**

	to maximum concentration (Tmax), area under the curve (AUC), pertinent half-lives (t1/2), time to reach steady state, extent of accumulation, route(s) of elimination, clearance (renal, hepatic, total), mechanisms of clearance (e.g., specific enzyme systems), drug/drug and drug/food (e.g., dietary supplements, grapefruit juice) pharmacokinetic interactions (including inhibition, induction, and genetic characteristics), **and volume of distribution (Vd) must be presented** if clinically significant." 12. KAPLAN (1974) "Blood and urine levels of N,N-dimethyltryptamine following administration of psychoactive dosages to human subjects" Psychopharmacologia Vol 38(3):239-245 From **p. 240** "Wyatt, Mandel, Ahn, Walker, and VandenHeuvel (1973) were **unable to demonstrate any difference in DMT plasma levels between groups of normals**, chronic schizophrenics, acute schizophrenics, **and** psychotic **depressives**…" From **p. 240** "**DMT was administered intramuscularly at a dosage of 0.7 mg/kg body weight.**" From **p. 241**  Fig. 1. Individual DMT blood levels

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/308,357	**04/16/2024 11:57:58 AM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	65110180	FILING DATE	04/27/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 21

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
third-party-preissuance-submission.pdf		3	Third-Party Submission Under 37 CFR 1.290	75 KB
Concise-description-generated.pdf		2	Concise Description of Relevance	40 KB
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	14 KB
Claims Chart Yale University 20230346718.pdf		50	-	796 KB
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB

Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB
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Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
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by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/308,357	**04/16/2024 11:57:58 AM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	65110180	AUTHORIZED BY	-
CUSTOMER #	–	FILING DATE	04/27/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 0837	**E20244FB58456105**	**Juliet Meccia**

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2818	DOCUMENT FEE FOR THIRD-PARTY SUBMISSIONS (SEE 37 CFR 1.290(F))	72.00	1	72.00
			TOTAL AMOUNT:	**$72.00**

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C.

371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/308,357	**04/16/2024 12:06:25 PM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	65110446	FILING DATE	04/27/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 15

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
third-party-preissuance-submission.pdf		2	Third-Party Submission Under 37 CFR 1.290	64 KB
Concise-description-generated.pdf		2	Concise Description of Relevance	34 KB
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	14 KB
Claims Chart Yale University 20230346718.pdf		50	-	796 KB
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB

Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	(1-50)	50	Concise Description of Relevance	782 KB
11_CA3127854A1.pdf		137	-	8038 KB
11_CA3127854A1-FOR.pdf	(1-137)	137	Foreign Reference	8010 KB
12_KAPLAN_1974_Embedded.pdf		7	-	3977 KB
12_KAPLAN_1974_Embedded-NPL.pdf	(1-7)	7	Non Patent Literature	3972 KB
13_PALHANO_FONTES_2019.pdf		9	-	348 KB
13_PALHANO_FONTES_2019-NPL.pdf	(1-9)	9	Non Patent Literature	330 KB
14_EATON_Embedded.pdf		16	-	693 KB
14_EATON_Embedded-NPL.pdf	(1-16)	16	Non Patent Literature	693 KB

15_MALCOLM.pdf		10	-	6620 KB
15_MALCOLM-NPL.pdf	(1-10)	10	Non Patent Literature	6482 KB
16_FEDERALREGISTER.pdf		128	-	2143 KB
16_FEDERALREGISTER-NPL.pdf	(1-128)	128	Non Patent Literature	785 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
third-party-preissuance-submission.pdf	76CE11A12BCA004C126555FF5E37A90C2EBE713546AB3CE1ED5E3F8D1BCC3DB0A6DEDF93DA481C27472575B5FA06ECCFECFCFD56E5FE67C0A22ED89B4D9C3943
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Third-party-notification-request.pdf	B90CE66639CC228B241AAD643F049A88CB51A397B303B4F69BFD9198BE9DA7076675A0893A61117DB91F2EB01C95CD48F6593BBE58BFC5AF36FE684282365945
Claims Chart Yale University 20230346718.pdf	FCA3DF3297D611F8B548BA4F8D214DF629F565117F15C1ABBB74711BE4E1377917E550265CF37F29FF6CF2FB12F2632F7805C0B590B030FCF7D83A054E770413
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	CF15088CA99F289A5E98F8FA61428A56D1C82F4CE8DA506EFEC1FF4FFE567C844D421CDE993D4365C71DC8CC04093C048A2C8E4AD8A3F36CF5E5524D90B83EBC
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	AC0113AB7B218A0207A3E48406206DD60CD18165572A56094493EECE741B4EC2F93DA26CBF3DFAC3C1A8630AE30D7211F850D4C13E3395738185BD3470360BFC
Claims Chart Yale University	6D223F97E36E28F7D0931966FFAB68B5B7E680804EAFDA3BE

20230346718-3P.RELEVANCE.pdf	2D7693D92BFE6F0D44F91130BAD885CAF7F4EAB4E7A2578ED726BCD68A3B6A70D9325F0C6B24879
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	66094DE42D3657A4C1F9F4FA4F8E88C85905CE9DB278F4AFAC7E07E2324812BEEED1ED8BD903BCED7E458070AAC6D7C45DF42EF4DB0C093F4D479C45B2A9DC06
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	DD629A120087259F1E30D43842782BC18F6CA6C0AA36C4D67E684D8C4E05A8209AEB47658226C45F30A930B20E3949DA44A77F8B9321B2108D8B5525B90F513F
Claims Chart Yale University 20230346718-3P.RELEVANCE.pdf	A738FE50B7C70068FCBC5B5FE6A4FE27E52C0BF82C586461E607113492E19C2929BF27CE9D580DA10E3BF71239CAA88B8BC4A8DD6CF8E608930D99264AA1AC8E
11_CA3127854A1.pdf	380A0817089768B23B8BA3726F8C3BD1C3E17FE8437F4710FC62F9FDD9F08C52C4A43EA13F5356E0EDE404B785C6E6CDC210442F5A279C6B29FEB261DC06E439
11_CA3127854A1-FOR.pdf	1D5286EC6D5DC26926475C40E8374F4E8302F3437C447954748695747CD4C1B3F928195EF93F0BDFAFE821E694567B3B49A6AC6A59CCC82A8575E0C6CE1EF9B3
12_KAPLAN_1974_Embedded.pdf	EE04C98ADB689CB30C9FD8EEBF384B27615015C7A2EB451CF1F19EFD87FCCC30B2C6B1C0C727E60FC92593D1D3C494E353FB16BACD00B1B98E4C3129C490C296
12_KAPLAN_1974_Embedded-NPL.pdf	62619CEEE8AE786B3CCE6255DC3B9702E888C1425F174545AC458A3F92DE08719C0A3E10C1CE2B91AC457B8EB1332BB0A7AC7A16BE0AFC67AA5212379677C7CD
13_PALHANO_FONTES_2019.pdf	EC45F34362E77C2EAD5F198991559C3D1C22FBD5D3106590FCAB6E4369159567DA5955AE619A84460CB73B205829E5FEC96190B5DC100EE0E16D8C41826511B9
13_PALHANO_FONTES_2019-NPL.pdf	F9C411508E2741C1D74F6C708CAB6696F9D0A5E502DC745280A3DA6800BEFD5046A91FEA6A17CCDB13F21A4229C071FD2F1BD1A112CFBD2A5845F4EF8544CF6F
14_EATON_Embedded.pdf	37201E5B400063F0291207A037352A33D57CC698CBDD96C9B2

	23BDAB5C31077C0BFCC723B28C8B43FD022DBBF2ADAA8A52865C5A2CA2F26B3B78C61E7C007016
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15_MALCOLM.pdf	34276B1C742F09A361CFF9170154CE397606F2C58EB5B6856DC1CA9CA19FB93348B8C8158F1657DFFE44294615A98E0DEB5322505838BD2544079CDC0C8A034E
15_MALCOLM-NPL.pdf	2CCABFA676E593C01186FE0B2D0AA7002A4E3F62C8380A63216852245595A43A922FFEC4E9EE95D8254BF4C617CD8169E7E2A9CE51B1B5E0EF70DB391AB07036
16_FEDERALREGISTER.pdf	F3A890AC49F43E49D66F2F04C8D9E89AA368F76136B197BE34A97934723446398C8BC49CAB5D998E044A0B0795891040A6903C2C857C6FCEF4CC45964322CCF1
16_FEDERALREGISTER-NPL.pdf	A6C5E2973A308F31B5F5FD6B49F93D8B912989401E7BB095E0F4A6E9D8AE2F410DB37D2460833507427212FEFE0CA57B488B1C41254641F8D807FA2D4E5AC5E8

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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/308,357	**04/16/2024 12:06:25 PM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	65110446	AUTHORIZED BY	-
CUSTOMER #	–	FILING DATE	04/27/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	

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CARD / 0837	**E20244FC07056658**	**Juliet Meccia**

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