IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Judith Blumstock, Guy Andrew Higgins, Edward Moncrieff Sellers

Confirmation No:

Serial No.: 18/102,268 Group No.:

Filing or 371(c) Date: 27 January 2023 Examiner:

Entitled: EXTENDED RELEASE 5-HT RECEPTOR AGONISTS FOR NEUROLOGICAL CONDITIONS

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. FADIMAN & KORB (2019) "Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration" Journal of Psychoactive Drugs. 51(2):118-122.

2. HUTTEN (2019) "Self-Rated Effectiveness of Microdosing With Psychedelics for Mental and Physical Health Problems Among Microdosers" Frontiers in Psychiatry. 10:1-9.

3. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44:1328-1334.

4. MERTENS (2020) "Therapeutic mechanisms of psilocybin: Changes in amygdala and prefrontal functional connectivity during emotional processing after psilocybin for treatment-resistant depression" Journal of Psychopharmacology. 34(2):167-180.

5. LEA (2020) "Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders" Psychopharmacology. 237:1521-1532.

6. VOINESKOS (2020) "Management of Treatment-Resistant Depression: Challenges and Strategies" Neuropsychiatric Disease and Treatment. 16: 221-234.

7. USONA INSTITUTE (2019) "A Randomized, Double-Blind, Support-of-Concept Phase 2 Study of Single-Dose Psilocybin for Major Depressive Disorder (MDD)". Study record first posted 5 March 2019. https://clinicaltrials.gov/study/NCT03866174

8. HUTTEN (2019) "Motives and Side-Effects of Microdosing With Psychedelics Among Users" International Journal of Neuropsychopharmacology. 22(7):426-434.

9. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study" Lancet Psychiatry. 3:619-27.

10. Intl. Pat. App. No. WO2020181194 (2020) "COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS

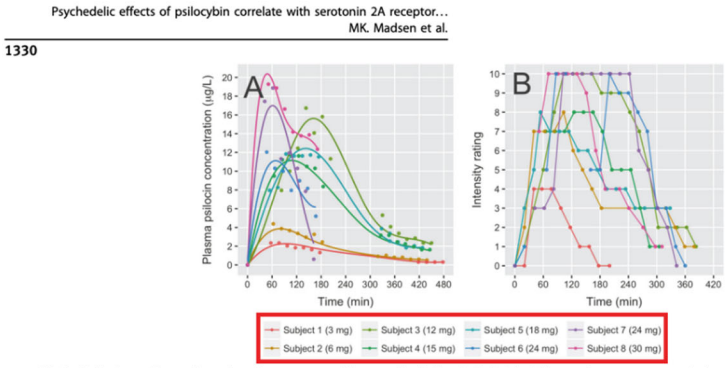
ADMINISTERED AT NON-PSYCHEDELIC/PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS" (Filed 6 March 2020)

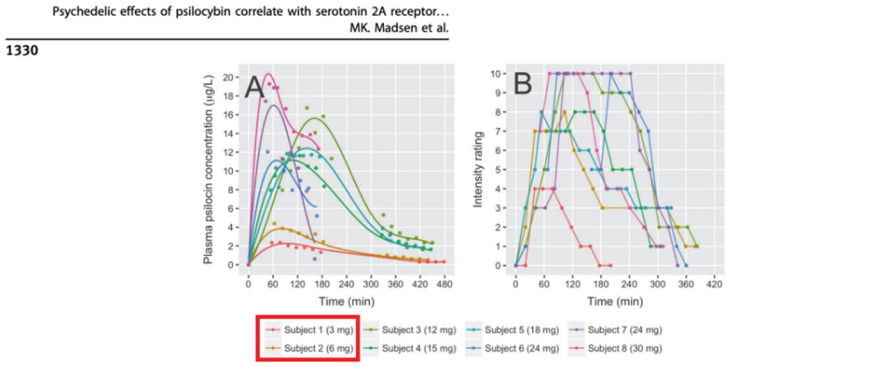
11. US Pat. App. No. 16/947003 (2020) "ORAL SOFT GEL CAPSULE CONTAINING PSYCHEDELIC COMPOUND" (Filed 14 July 2020)

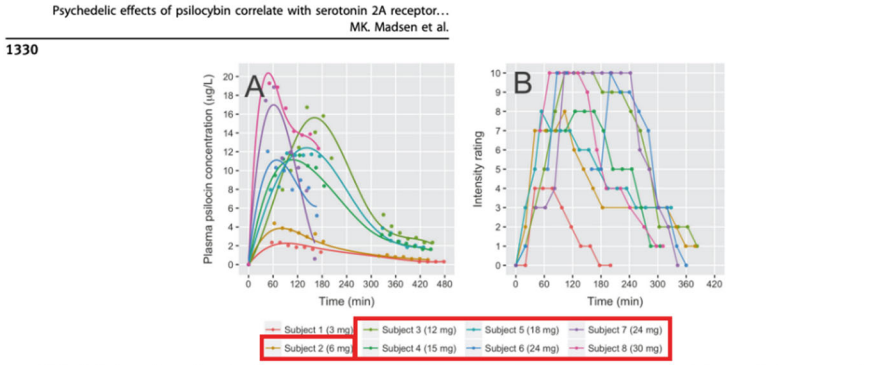
Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

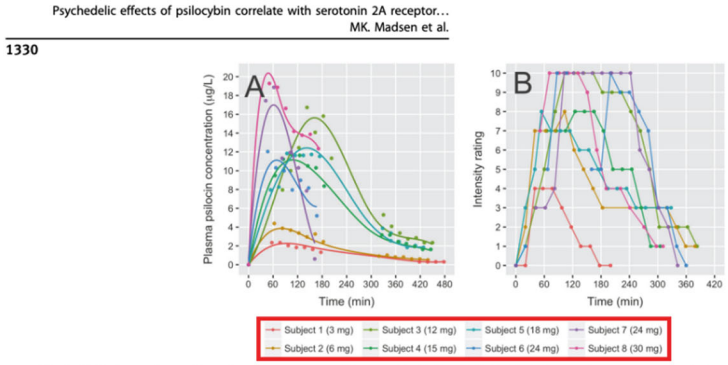
U.S.S.N.18/102,268 Pending Claims	References
1-39. (Canceled)	
40. A method for improving symptoms of a cognitive or neuropsychiatric disorder, in an individual in need thereof, comprising: **a.** administering to the individual a therapeutically effective amount of psilocybin or psilocin, or a pharmaceutically acceptable salt thereof, and **b.** maintaining a plasma concentration of an active form of psilocybin or psilocin (i) at or above a minimum therapeutically effective threshold in the individual and (ii) below a hallucinogenic threshold in the individual for more than or equal to two hours.	*From application of interest 18/102,268 paragraph [0043] "In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 0.001 ng/mL or more (e.g., 0.01 ng/mL or more, 0.1 ng/mL or more, 1 ng/mL or more, 10 ng/mL or more, 20 ng/mL or more, or 50 ng/mL or more). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 100 ng/mL or less (e.g., 50 ng/mL or less, 25 ng/mL or less, 15 ng/mL or less, 5 ng/mL or less, or 0.5 ng/mL or less). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of about 0.001 ng/mL to about 100 ng/mL."* *Paragraph [0045] "In some embodiments, the level (e.g., Cmax) of the active 5-HT receptor agonist (e.g., psilocin) is measured after a dose of at least 1 mg or more (e.g., 5 mg or more, 10 mg or more, 15 mg or more, or 20 mg or more) of the 5-HT receptor agonist (e.g., psilocybin) is administered to the individual."* 1. FADIMAN & KORB (2019) "Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration" Journal of Psychoactive Drugs. 51(2):118-122. From **pg. 118** "In our initial exploration of microdosing and its effects, in which we simply corresponded with people about microdosing**, we defined microdosing as being a "subperceptual dose."** This created some misunderstandings as, almost always, one can tell that one has taken a microdose. **The intention was to say that microdosing did not cause visual or perceptual changes usually associated with psychedelics**. A microdose of a psychedelic is between 1/10 and 1/20 of a "recreational dose." For LSD, that is between 7–13 micrograms; for dried psilocybin mushrooms, 0.1–0.4 grams. (For other substances, see microdosingpsychedelics.com). A correct microdose produces no classic psychedelic effects (e.g., visual distortions, internal visions). "

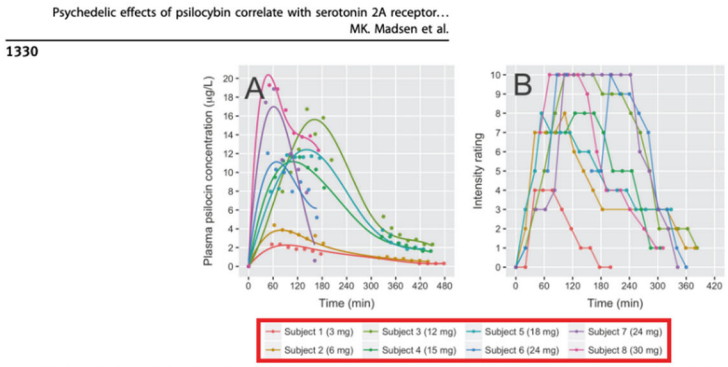
	2. HUTTEN (2019) "Self-Rated Effectiveness of Microdosing With Psychedelics for Mental and Physical Health Problems Among Microdosers" Frontiers in Psychiatry. 10:1-9. From **p. 2 "**There is a growing interest in the **use of psychedelic substances** for health related purposes, including s**ymptom relief for disorders like anxiety, depression, and pain**...**anecdotal evidence suggests that low** (micro) **doses are also effective**, and may be more suitable for certain conditions." From **p. 2** "**Recent clinical studies have suggested that** LSD (13), **psilocybin** (14), ayahuasca (15), and methylenedioxymethamphetamine (MDMA) (16, 17), in combination with psychological support, **can provide therapeutic relief for those suffering from post-traumatic stress disorder (PTSD), anxiety, and depression."** From **p. 2** "While the primary motivation to microdose is indeed to enhance performance, including creativity and mental concentration (10), **it is also reported to be used to alleviate psychological and physical symptoms, such as anxiety and headache** (10–12)." From **p. 2 "**Respondents were asked whether a **medical doctor or therapist diagnosed them with a psychiatric, neurological**, or physical disorder. When affirmed, they were asked **which of the pre-set disorders** applied: **depression, anxiety/panic disorder, attention deficit hyperactivity disorder (ADHD)** or **attention deficit disorder (ADD), bipolar disorder, schizophrenia, obsessive compulsive disorder (OCD), autism/Asperger syndrome, antisocial behavior disorder, borderline personality disorder, substance abuse disorder, Tourette's, Parkinson's, epilepsy, migraine, cluster headache, multiple sclerosis (MS)**, and/or **chronic pain**. Furthermore, they had the option to enter free text in a text box when the disorder was not listed. **Disorders were clustered** afterwards into main categories according to the classification system of the two leading diagnostic manuals, **the DSM-5 for mental disorders** and the **ICD-10 for physiological disorders** which resulted in 1**4 sub-categories for mental disorders** and **11 sub-categories for physiological disorders** (Table 1)." From **p. 5 "**The most reported **psychedelics used to self-medicate for mental disorders** in descending order are: **psilocybin** (N = 297; 57.1%), LSD (N = 248; 47.7%), and 1P-LSD (N = 68; 13.1**%) in microdoses**…"." 3. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44:1328-1334. From **p. 1328** "Recent clinical trials have shown that **psilocybin may be an effective treatment for neuropsychiatric disorders**, including **treatment-resistant major depressive disorder (MDD)** [3], cancer related **anxiety and depression** [4, 5], and for **addiction** to nicotine [6] and alcohol [7]. Thus**, psilocybin is an emerging and promising**

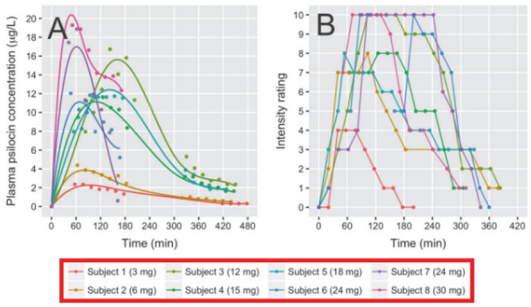
	drug for a range of mental disorders where existing drugs have shown shortcomings."  **Fig. 1** Psilocin and intensity rating time course. **a** Plasma psilocin levels. Individual data points are measured plasma psilocin concentrations, fitted with spline fits. **b** Time course of subjective intensity ratings. Time = 0 indicates time of psilocybin ingestion
41. The method of claim 40, wherein the active form of the psilocybin or psilocin is maintained below a plasma concentration in the individual of about 10 ng/mL.	*From application of interest 18/102,268 paragraph [0043] "In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 0.001 ng/mL or more (e.g., 0.01 ng/mL or more, 0.1 ng/mL or more, 1 ng/mL or more, 10 ng/mL or more, 20 ng/mL or more, or 50 ng/mL or more). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 100 ng/mL or less (e.g., 50 ng/mL or less, 25 ng/mL or less, 15 ng/mL or less, 5 ng/mL or less, or 0.5 ng/mL or less). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of about 0.001 ng/mL to about 100 ng/mL."* *Paragraph [0045] "In some embodiments, the level (e.g., Cmax) of the active 5-HT receptor agonist (e.g., psilocin) is measured after a dose of at least 1 mg or more (e.g., 5 mg or more, 10 mg or more, 15 mg or more, or 20 mg or more) of the 5-HT receptor agonist (e.g., psilocybin) is administered to the individual."* 3. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44:1328-1334. From **p. 1328** "Recent clinical trials have shown that **psilocybin may be an effective treatment for neuropsychiatric disorders**, including **treatment-resistant major depressive disorder (MDD)** [3], cancer related **anxiety and depression** [4, 5], and for **addiction** to nicotine [6] and alcohol [7]. Thus**, psilocybin is an emerging and promising drug for a range of mental disorder**s where existing drugs have shown shortcomings." From **p. 1329** "On the intervention day, **participants ingested between 3 and 30 mg psilocybin (3 mg capsules)** … For assessment **of plasma psilocin levels**, **venous blood samples** were **taken** simultaneously with the [11C] Cimbi-36 injection and **at 20-min intervals throughout** each scan

	session. Subjective psychedelic intensity ratings (0–10 Likert scale, 0 = not intense at all, 10 = very intense) were assessed at 20-min intervals throughout the day until effects had waned." From **p. 1330**  **Fig. 1** Psilocin and intensity rating time course. **a** Plasma psilocin levels. Individual data points are measured plasma psilocin concentrations, fitted with spline fits. **b** Time course of subjective intensity ratings. Time = 0 indicates time of psilocybin ingestion
42. The method of claim 40, wherein the active form of the psilocybin or psilocin is maintained above a plasma concentration of about 2 ng/mL in the individual for 2 hours or more.	*From application of interest 18/102,268 paragraph [0043] "In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 0.001 ng/mL or more (e.g., 0.01 ng/mL or more, 0.1 ng/mL or more, 1 ng/mL or more, 10 ng/mL or more, 20 ng/mL or more, or 50 ng/mL or more). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 100 ng/mL or less (e.g., 50 ng/mL or less, 25 ng/mL or less, 15 ng/mL or less, 5 ng/mL or less, or 0.5 ng/mL or less). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of about 0.001 ng/mL to about 100 ng/mL."* *Paragraph [0045] "In some embodiments, the level (e.g., Cmax) of the active 5-HT receptor agonist (e.g., psilocin) is measured after a dose of at least 1 mg or more (e.g., 5 mg or more, 10 mg or more, 15 mg or more, or 20 mg or more) of the 5-HT receptor agonist (e.g., psilocybin) is administered to the individual."* 3. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44:1328-1334. From **p. 1328** "Recent clinical trials have shown that **psilocybin may be an effective treatment for neuropsychiatric disorders**, including **treatment-resistant major depressive disorder (MDD)** [3], cancer related **anxiety and depression** [4, 5], and for **addiction** to nicotine [6] and alcohol [7]. Thus**, psilocybin is an emerging and promising drug for a range of mental disorder**s where existing drugs have shown shortcomings."

	From **p. 1329** "On the intervention day, **participants ingested between 3 and 30 mg psilocybin (3 mg capsules)** … For assessment **of plasma psilocin levels**, **venous blood samples** were **taken** simultaneously with the [11C] Cimbi-36 injection and **at 20-min intervals throughout** each scan session. Subjective psychedelic intensity ratings (0–10 Likert scale, 0 = not intense at all, 10 = very intense) were assessed at 20-min intervals throughout the day until effects had waned." From **p. 1330**  **Fig. 1** Psilocin and intensity rating time course. **a** Plasma psilocin levels. Individual data points are measured plasma psilocin concentrations, fitted with spline fits. **b** Time course of subjective intensity ratings. Time = 0 indicates time of psilocybin ingestion
43. The method of claim 40, wherein the active form of the psilocybin or psilocin is maintained above a plasma concentration of about 1 ng/mL in the individual for 2 hours or more.	*From application of interest 18/102,268 paragraph [0043] "In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 0.001 ng/mL or more (e.g., 0.01 ng/mL or more, 0.1 ng/mL or more, 1 ng/mL or more, 10 ng/mL or more, 20 ng/mL or more, or 50 ng/mL or more). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 100 ng/mL or less (e.g., 50 ng/mL or less, 25 ng/mL or less, 15 ng/mL or less, 5 ng/mL or less, or 0.5 ng/mL or less). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of about 0.001 ng/mL to about 100 ng/mL."* *Paragraph [0045] "In some embodiments, the level (e.g., Cmax) of the active 5-HT receptor agonist (e.g., psilocin) is measured after a dose of at least 1 mg or more (e.g., 5 mg or more, 10 mg or more, 15 mg or more, or 20 mg or more) of the 5-HT receptor agonist (e.g., psilocybin) is administered to the individual."* 3. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44:1328-1334. From **p. 1328** "Recent clinical trials have shown that **psilocybin may be an effective treatment for neuropsychiatric disorders**, including

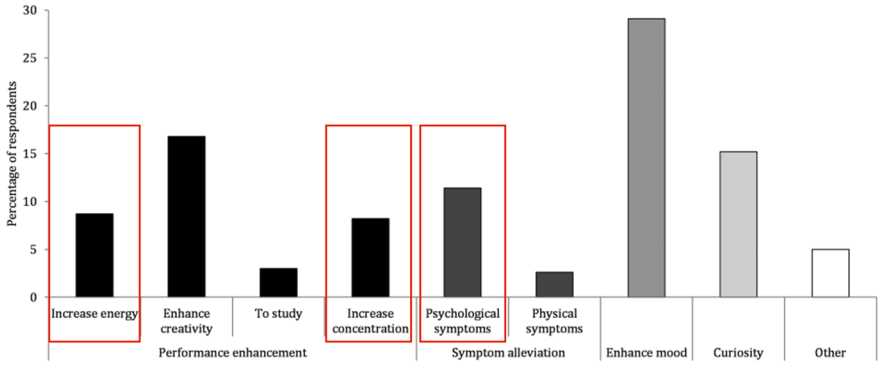
	treatment-resistant major depressive disorder (MDD) [3], cancer related **anxiety and depression** [4, 5], and for **addiction** to nicotine [6] and alcohol [7]. Thus**, psilocybin is an emerging and promising drug for a range of mental disorder**s where existing drugs have shown shortcomings." From **p. 1329** "On the intervention day, **participants ingested between 3 and 30 mg psilocybin (3 mg capsules)** … For assessment **of plasma psilocin levels**, **venous blood samples** were **taken** simultaneously with the [11C] Cimbi-36 injection and **at 20-min intervals throughout** each scan session. Subjective psychedelic intensity ratings (0–10 Likert scale, 0 = not intense at all, 10 = very intense) were assessed at 20-min intervals throughout the day until effects had waned." From **p. 1330**  **Fig. 1** Psilocin and intensity rating time course. **a** Plasma psilocin levels. Individual data points are measured plasma psilocin concentrations, fitted with spline fits. **b** Time course of subjective intensity ratings. Time = 0 indicates time of psilocybin ingestion
44. The method of claim 40, wherein the active form of the psilocybin or psilocin is maintained above a plasma concentration of about 0.1 ng/mL in the individual for 6 hours or more.	*From application of interest 18/102,268 paragraph [0043] "In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 0.001 ng/mL or more (e.g., 0.01 ng/mL or more, 0.1 ng/mL or more, 1 ng/mL or more, 10 ng/mL or more, 20 ng/mL or more, or 50 ng/mL or more). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 100 ng/mL or less (e.g., 50 ng/mL or less, 25 ng/mL or less, 15 ng/mL or less, 5 ng/mL or less, or 0.5 ng/mL or less). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of about 0.001 ng/mL to about 100 ng/mL."* *Paragraph [0045] "In some embodiments, the level (e.g., Cmax) of the active 5-HT receptor agonist (e.g., psilocin) is measured after a dose of at least 1 mg or more (e.g., 5 mg or more, 10 mg or more, 15 mg or more, or 20 mg or more) of the 5-HT receptor agonist (e.g., psilocybin) is administered to the individual."*

	3. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44:1328-1334. From **p. 1328** "Recent clinical trials have shown that **psilocybin may be an effective treatment for neuropsychiatric disorders**, including **treatment-resistant major depressive disorder (MDD)** [3], cancer related **anxiety and depression** [4, 5], and for **addiction** to nicotine [6] and alcohol [7]. Thus**, psilocybin is an emerging and promising drug for a range of mental disorder**s where existing drugs have shown shortcomings." From **p. 1329** "On the intervention day, **participants ingested between 3 and 30 mg psilocybin (3 mg capsules)** … For assessment **of plasma psilocin levels**, **venous blood samples** were **taken** simultaneously with the [11C] Cimbi-36 injection and **at 20-min intervals throughout** each scan session. Subjective psychedelic intensity ratings (0–10 Likert scale, 0 = not intense at all, 10 = very intense) were assessed at 20-min intervals throughout the day until effects had waned." From **p. 1330**  **Fig. 1** Psilocin and intensity rating time course. **a** Plasma psilocin levels. Individual data points are measured plasma psilocin concentrations, fitted with spline fits. **b** Time course of subjective intensity ratings. Time = 0 indicates time of psilocybin ingestion
45. The method of claim 40, wherein the active form of the psilocybin or psilocin is maintained above a plasma concentration of about 0.5 ng/mL in the individual for 6 hours or more.	*From application of interest 18/102,268 paragraph [0043] "In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 0.001 ng/mL or more (e.g., 0.01 ng/mL or more, 0.1 ng/mL or more, 1 ng/mL or more, 10 ng/mL or more, 20 ng/mL or more, or 50 ng/mL or more). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 100 ng/mL or less (e.g., 50 ng/mL or less, 25 ng/mL or less, 15 ng/mL or less, 5 ng/mL or less, or 0.5 ng/mL or less). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of about 0.001 ng/mL to about 100 ng/mL."* *Paragraph [0045] "In some embodiments, the level (e.g., Cmax) of the active 5-HT receptor agonist (e.g., psilocin) is measured after a dose of at least 1 mg or more (e.g., 5 mg or more, 10 mg or more, 15 mg or more, or 20 mg or more) of the 5-HT receptor agonist (e.g., psilocybin) is*

	administered to the individual." 3. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44:1328-1334. From **p. 1328** "Recent clinical trials have shown that **psilocybin may be an effective treatment for neuropsychiatric disorders**, including **treatment-resistant major depressive disorder (MDD)** [3], cancer related **anxiety and depression** [4, 5], and for **addiction** to nicotine [6] and alcohol [7]. Thus**, psilocybin is an emerging and promising drug for a range of mental disorder**s where existing drugs have shown shortcomings." From **p. 1329** "On the intervention day, **participants ingested between 3 and 30 mg psilocybin (3 mg capsules)** … For assessment **of plasma psilocin levels**, **venous blood samples** were **taken** simultaneously with the [11C] Cimbi-36 injection and **at 20-min intervals throughout** each scan session. Subjective psychedelic intensity ratings (0–10 Likert scale, 0 = not intense at all, 10 = very intense) were assessed at 20-min intervals throughout the day until effects had waned." From **p. 1330** Psychedelic effects of psilocybin correlate with serotonin 2A receptor… MK. Madsen et al. 1330  **Fig. 1** Psilocin and intensity rating time course. **a** Plasma psilocin levels. Individual data points are measured plasma psilocin concentrations, fitted with spline fits. **b** Time course of subjective intensity ratings. Time = 0 indicates time of psilocybin ingestion
46. The method of claim 40, wherein the cognitive or neuropsychiatric disorder is an anxiety, attention, or depression disorder.	4. MERTENS (2020) "Therapeutic mechanisms of psilocybin: Changes in amygdala and prefrontal functional connectivity during emotional processing after psilocybin for treatment-resistant depression" Journal of Psychopharmacology. 34(2):167-180. From **p. 2** "Inclusion criteria were (a) **a diagnosis of moderate to severe major depression**, as defined by a score of 16+ on the 21-item Mertens et al. 3 Hamilton Depression Rating Scale..." From **p. 2 "**From **p. 2 "**The present study focused on changes in brain FC after **psilocybin in 19 patients with TRD** who underwent two psilocybin-assisted therapy sessions a week apart, first **10 mg p.o**. (test dose), then **25 mg, p.o. (therapeutic dose)**."

	From **pg. 8** "As already reported previously (Carhart-Harris et al., 2018a; 2016a), BDI scores were significantly reduced at one week (mean reduction=22.26, SD=11.37, p<0.001); 63.2% of patients showed a treatment response (50% drop in BDI score) at this time-point, with 57.9% meeting criteria for remission (BDI⩽9)." 5. LEA (2020) "Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders" Psychopharmacology. 237:1521-1532. From **p. 1522 "**Microdosing refers to the **ingestion of low to very low doses of psychedelic drugs** (typically between 5 and 10% of a standard dose) on a routine schedule (e.g., every third day) **without the intention of experiencing effects** typically **experienced at higher psychedelic doses** (e.g., visual distortions, mystical experiences) (Fadiman 2011; Kuypers et al. 2019; Liechti 2019)." From **p. 1524 "**Over half of **respondents** (56.7%) had ever been **diagnosed with a mental disorder** (excluding substance use disorders), including **depression (41.2%), anxiety disorders (32.0%; generalised anxiety disorder, 25.4%; social anxiety disorder, 14.5%; panic disorder/panic attacks, 12.5%), ADHD (19.5%)**, PTSD (15.6%), bipolar disorder (7.4%), personality disorder (5.1%), eating disorder (4.8%), obsessive compulsive disorder (4.7%) and schizophrenia (1.0%)." From **p. 1524 "**Thirty-nine percent of **respondents reported that they primarily microdosed as mental health** or substance use **therapies**, including **for depression (21.3%), anxiety (6.9%)**, other mental health conditions including PTSD and **ADHD (8.9%)**…"
47. The method of claim 46, wherein the depression disorder is major depressive disorder.	6. VOINESKOS (2020) "Management of Treatment-Resistant Depression: Challenges and Strategies" Neuropsychiatric Disease and Treatment. 16: 221-234. From **p. 221** "**Major Depressive Disorder (MDD)** and associated mood syndromes are among the most common psychiatric disorders in specialist and general medical practice. These syndromes span life stages and present with varying combinations of symptoms. While depressive symptoms are at times part of normal human behavior, MDD can be debilitating and at its worst, life threatening. MDD can present at any age across the life span, differences in biological vulnerability, age of onset, risk factors, symptomatic presentation and comorbidities are present among people with the same diagnosis. **MDD is, therefore, a very heterogeneous disorder, and approximately 30% of people with this illness are resistant to conventional treatments.**" From **p. 222** "Once 2 adequate antidepressant trials have been unsuccessful, **the illness is termed treatment-resistant depression (TRD)**." 4. MERTENS (2020) "Therapeutic mechanisms of psilocybin: Changes in amygdala and prefrontal functional connectivity during emotional

	processing after psilocybin for treatment-resistant depression" Journal of Psychopharmacology. 34(2):167-180. From **p. 2** "Inclusion criteria were (a) **a diagnosis of moderate to severe major depression**, as defined by a score of 16+ on the 21-item Mertens et al. 3 Hamilton Depression Rating Scale..." From **p. 2 "**The present study focused on changes in brain FC after **psilocybin in 19 patients with TRD** who underwent **two psilocybin**-assisted therapy **sessions** a week apart, first **10 mg p.o**. (test dose), then **25 mg, p.o. (therapeutic dose)**." 7. USONA INSTITUTE (2019) "A Randomized, Double-Blind, Support-of-Concept Phase 2 Study of Single-Dose Psilocybin for **Major Depressive Disorder (MDD)**". Study record version first posted 5 March 2019. https://clinicaltrials.gov/study/NCT03866174 From **Study Overview** "The purpose of this study is to evaluate the potential efficacy of a single **25 mg oral dose of psilocybin for MDD** compared to the active placebo in otherwise medically-healthy participants, assessed as the difference between groups in changes in depressive symptoms from Baseline to Day 43 post-dose." From **Design Details, Intervention/Treatment** "The … Protocol prescribes 6-8 hours of preparatory meetings with two facilitators prior to dosing, **a 7-10 hour dosing session** in a comfortable room under the supervision of the same two facilitators, and 4 hours of post-dose integration sessions with facilitators."
48. The method of claim 46, wherein the anxiety disorder is generalized anxiety disorder.	5. LEA (2020) "Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders" Psychopharmacology. 237:1521-1532. From **p. 1522 "**Microdosing refers to the **ingestion of low to very low doses of psychedelic drugs** (typically between 5 and 10% of a standard dose) on a routine schedule (e.g., every third day) **without the intention of experiencing effects** typically **experienced at higher psychedelic doses** (e.g., visual distortions, mystical experiences) (Fadiman 2011; Kuypers et al. 2019; Liechti 2019)." From **p. 1524 "**Over half of **respondents** (56.7%) had ever been **diagnosed with a mental disorder** (excluding substance use disorders), including depression (41.2%), anxiety disorders (32.0%; **generalised anxiety disorder, 25.4%**; social anxiety disorder, 14.5%; panic disorder/panic attacks, 12.5%), ADHD (19.5%), PTSD (15.6%), bipolar disorder (7.4%), personality disorder (5.1%), eating disorder (4.8%), obsessive compulsive disorder (4.7%) and schizophrenia (1.0%)." From **p. 1524 "**Thirty-nine percent of **respondents reported that they primarily microdosed as mental health** or substance use **therapies**, including for depression (21.3%), **anxiety (6.9%)**, other mental health conditions including PTSD and ADHD (8.9%)."

49. The method of claim 40, wherein the improvement of the symptoms of the cognitive or neuropsychiatric disorder ameliorates low motivation and cognitive engagement.	1. FADIMAN & KORB (2019) "Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration" Journal of Psychoactive Drugs. 51(2):118-122. From **p. 121 "Many participants reported** that **they** wanted to **microdose for their diagnosed ADHD**, or for their self-diagnosed attention issues..." *From application of interest 18/102,268 paragraph [0272] "Provided in some instances herein is **a method for increasing motivation in an individual** (e.g., in an individual suffering from or susceptible to low motivation (e.g., **as a symptom of a neurocognitive or neurodevelopmental disorder**..."* 7. HUTTEN (2019) "Motives and Side-Effects of Microdosing With Psychedelics Among Users" International Journal of Neuropsychopharmacology. 22(7):426-434. From **p. 427 "**Another commonly reported motivation and subsequent outcome is the **alleviation of psychological symptom**s including depressive mood and anxiety and/or physiological symptoms such as pain (Smith, 2017; Wong, 2017; Johnstad, 2018; Waldman, 2018)…" From **p. 427 "**Respondents were asked to indicate the main reason they microdosed ... answers were clustered afterwards into 5 main categories: **performance enhancement (increase energy, to study, increase concentration, enhance creativity)**, **symptom alleviation (psychiatric symptom alleviation** ..." From **p. 433 "**With regard to microdosing motives, **the majority of the respondents (37%) indicated they microdosed** for performance enhancement, such as **to increase energy, creativity, and concentration**." From **p. 432. Figure 1** **432** | *International Journal of Neuropsychopharmacology*, 2019  **Figure 1.** Percentage of respondents who indicated their main motivation to microdose, presented per category (performance enhancement: black bars; symptom alleviation: dark grey bars; mood enhancement: grey bar; curiosity: light grey bar; and other: white bar).
50. The method of claim 40, wherein the method comprises	2. HUTTEN (2019) "Self-Rated Effectiveness of Microdosing With Psychedelics for Mental and Physical Health Problems Among Microdosers" Frontiers in Psychiatry. 10:1-9.

administering a therapeutically effective amount of psilocybin or psilocin, or a pharmaceutically acceptable salt thereof, at a first time.	From **p. 2 "**There is a growing interest in the **use of psychedelic substances** for health related purposes, including s**ymptom relief for disorders like anxiety, depression, and pain**...**anecdotal evidence suggests that low** (micro) **doses are also effective**, and may be more suitable for certain conditions." From **p. 5 "**The most reported **psychedelics used to self-medicate for mental disorders** in descending order are: **psilocybin** (N = 297; 57.1%), … in regular doses."
51. The method of claim 50, wherein the method comprises administering to the individual a therapeutically effective amount of psilocybin or psilocin, or a pharmaceutically acceptable salt thereof, at a second time.	9. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study" Lancet Psychiatry. 3:619-27. From **p. 619** "In this open-label feasibility trial, **12 patients** (six men, six women) **with moderate-to-severe, unipolar, treatment-resistant major depression received two oral doses of psilocybin (10 mg and 25 mg, 7 days apart)** in a supportive setting. There was no control group…**Depressive symptoms were assessed** with standard assessments **from 1 week to 3 months after treatment**, with the 16-item Quick Inventory of Depressive Symptoms (QIDS) serving as the primary efficacy outcome. This trial is registered with ISRCTN, number ISRCTN14426797." 2. HUTTEN (2019) "Self-Rated Effectiveness of Microdosing With Psychedelics for Mental and Physical Health Problems Among Microdosers" Frontiers in Psychiatry. 10:1-9. From **p. 7** "Additionally, compared to traditionally offered medications which are taken daily or even several times a day**, microdosers do not usually consume the substance daily** (2, 10), thus reducing potential costs and side effects, and even potentially reducing the number of reminders to the patient of being ill." 8. HUTTEN (2019) "Motives and Side-Effects of Microdosing With Psychedelics Among Users" International Journal of Neuropsychopharmacology. 22(7):426-434. **Table 4.** Number (percentage) of respondents who indicated to (have) use(d) the listed psychedelic substance to microdose via the listed route of administration[a] and the corresponding frequency of use (Mean (SD), range Route of administration, n (%) — Frequency of microdosing per week | Substance | Number of respondents who answered, n (%) | Oral | Sublingual | Inspiration | Intranasal | Ocular | Cutaneous | Rectal | Other | Number of respondents who answered N (%) | Frequency of dosing per week M (SD) | Range of dosing per week (min–max) | |---|---|---|---|---|---|---|---|---|---|---|---|---| | 1P-LSD | 120 (77.5) | 71 (55.0) | 28 (21.7) | – | – | – | – | 1 (0.8) | – | 76 (58.9) | 2.13 (2.23) | 0.001–14 | | 2Cs | 13 (59.1) | 11 (50.0) | – | – | 1 (4.5) | – | – | 1 (4.5) | – | 10 (45.5) | 2.89 (4.11) | 0.2–14 | | 5-MeO-DMT | 2 (30.0) | 1 (20.0) | – | – | – | – | – | 1 (20.0) | – | 2 (40.0) | 7.5 (9.19) | 1–14 | | ALD-52/ 1A-LSD | 28 (68.3) | 18 (43.9) | 9 (22.0) | – | – | – | – | 1 (2.4) | – | 22 (53.7) | 2.23 (2.82) | 0.005–14 | | Ayahuasca | 7 (46.7) | 5 (33.3) | – | 1 (6.7) | – | – | – | 1 (6.7) | – | 6 (40.0) | 4.37 (5.16) | 0.25–14 | | DMT | 35 (54.7) | 2 (3.1) | – | 32 (50.0) | – | – | – | 1 (1.6) | – | 25 (39.1) | 2.26 (3.17) | 0.002–14 | | LSD | 491 (73.7) | 387 (58.1) | 99 (14.9) | – | 1 (0.2) | 1 (0.2) | – | 1 (0.2) | 2 (0.3) | 384 (57.7) | 2.02 (1.89) | 0.0001–15 | | MDMA/ ecstasy | 34 (47.9) | 24 (33.8) | 2 (2.8) | – | 7 (9.9) | – | – | 1 (1.4) | – | 19 (26.8) | 2.08 (3.46) | 0.005–14 | | Mescaline | 12 (46.2) | 11 (42.3) | – | – | – | – | – | 1 (3.8) | – | 6 (23.1) | 3.46 (5.26) | 0.25–14 | | NBOMes | 3 (33.3) | – | 2 (22.2) | – | – | – | – | 1 (11.1) | – | 3 (33.3) | 5.67 (7.23) | 1–14 | | Other | 26 (43.3) | 16 (26.7) | – | 6 (10.0) | 2 (3.3) | – | 1 (1.7) | 1 (1.7) | – | 21 (35.0) | 6.78 (6.98) | 0.5–30 | | Psilocybin | 416 (64.5) | 415 (64.3) | – | – | – | – | – | 1 (0.2) | – | 325 (78.3) | 3.74 (3.35) | 0.001–30 | | Salvinorin A | 15 (45.4) | 3 (9.7) | 2 (6.5) | 8 (25.8) | – | – | – | 1 (3.2) | 1 (3.2) | 8 (25.8) | 2.63 (4.65) | 0.01–14 | Abbreviations: 1P-LSD, 1-propionyl-lysergic acid diethylamide; 2C, 2-ethylamine; 5-MeO-DMT, 5-methoxy-N,N-dimethyltryptamine; ALD-52/1A-LSD, 1-Acetyl-N,N-diethyllysergamide; DMT, N,N-dimethyltryptamine; LSD, lysergic acid diethylamide; MDMA, 3,4,-methylenedioxymethamphetamine; NBOMe, N-benzyl Methoxy. aRoute of administration: "injection" is not shown, as no respondent reported injection as route of administration.

52. The method of claim 51, wherein the second time is more than or equal to 24 hours after the first time.	5. LEA (2020) "Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders" Psychopharmacology. 237:1521-1532. From **p. 1522 "**Microdosing refers to the **ingestion of low to very low doses of psychedelic drugs** (typically between 5 and 10% of a standard dose) on a routine schedule (e.g., every third day) **without the intention of experiencing effects** typically **experienced at higher psychedelic doses** (e.g., visual distortions, mystical experiences) (Fadiman 2011; Kuypers et al. 2019; Liechti 2019)." From **p. 1532** "**Fourteen percent** of respondents **microdosed every day**…" From **p. 1524 "**Over half of **respondents** (56.7%) had ever been **diagnosed with a mental disorder** (excluding substance use disorders), including **depression** (41.2%), **anxiety disorders** (32.0%; **generalised anxiety disorder, 25.4%**; **social anxiety disorder**, 14.5**%; panic disorder/panic attacks**, 12.5%), **ADHD** (19.5%), **PTSD** (15.6%), **bipolar disorder** (7.4%), **personality disorder** (5.1%), **eating disorder** (4.8%), **obsessive compulsive disorder** (4.7%) and **schizophrenia** (1.0%)." From **p. 1524 "**Thirty-nine percent of **respondents reported that they primarily microdosed as mental health** or substance use **therapies**, including for **depression** (21.3%), **anxiety (6.9%)**, **other mental health conditions including PTSD and ADHD** (8.9%)." 2. HUTTEN (2019) "Self-Rated Effectiveness of Microdosing With Psychedelics for Mental and Physical Health Problems Among Microdosers" Frontiers in Psychiatry. 10:1-9. From **p. 7** "Additionally, compared to traditionally offered medications which are taken daily or even several times a day**, microdosers do not usually consume the substance daily** (2, 10), thus reducing potential costs and side effects, and even potentially reducing the number of reminders to the patient of being ill." 9. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study" Lancet Psychiatry. 3:619-27. From **p. 619** "In this open-label feasibility trial, **12 patients** (six men, six women) **with moderate-to-severe, unipolar, treatment-resistant major depression received two oral doses of psilocybin (10 mg and 25 mg, 7 days apart)** in a supportive setting. There was no control group…**Depressive symptoms were assessed** with standard assessments **from 1 week to 3 months after treatment**, with the 16-item Quick Inventory of Depressive Symptoms (QIDS) serving as the primary efficacy outcome. This trial is registered with ISRCTN, number ISRCTN14426797."

53. The method of claim 51, wherein the second time is more than or equal to 48 hours after the first time.	1. FADIMAN & KORB (2019) "Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration" Journal of Psychoactive Drugs. 51(2):118-122. From **p. 120 "...**many **participants informed us** that they found **microdosing to be an effective antidepressant**, or replacement for their antidepressants." From **p. 120 "**We offered **a protocol** to people who wanted to do their own microdose self-study. The protocol was: **microdose on day 1, no dose on days 2 and 3. Repeat this cycle for a month."**
54. The method of claim 40, wherein the plasma concentration of the active form of psilocybin or psilocin is maintained (i) at or above a minimum therapeutically effective threshold in the individual and (ii) below a hallucinogenic threshold in the individual for more than or equal to 12 hours.	10. Intl. Pat. App. No. WO2020181194 (2020) "COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON-PSYCHEDELIC/PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS" (filed 6 March 2020) From **Claim 16** "**A method for preventing or treating diseases and conditions or improving functions in patients or subjects, the method comprising:** **administration of a 5-HT2A agonist substance at doses,** dosages, posology, or formulations **devoid of clinically meaningful psychedelic or psychotomimetic actions or effects**, and having clinical effects comparable to those exerted by human plasma psilocin Cmax of 4 ng/ml or less, or human 5-HT2A CNS receptor occupancy of 50% or less, or PD effects comparable to those exerted by human plasma psilocin Tmax in excess of 60 minutes." From **Claim 40** "The **method in claim 16** where **the substance is a modified release formulation of psilocybin, psilocin,** norpsilocin, baeocystin, nor-baeocystin or a mixture thereof." From **Paragraph [00180]** ""**Modified release, long acting and or slow release formulation** of a neuroplastogen drug **will allow for administration of a relatively higher amount of drug while still avoiding the psychedelic and or psychotomimetic side effects caused by a peak in blood levels of the drug (the psychedelic effects caused by a high Cmax and short Tmax)**. The present inventors therefore also disclose modified release long-acting and or slow-release formulations of neuroplastogens, including long-acting oral or transdermal formulations and **or slow-release formulations of psilocybin and or baeocystin at doses up to 30 mg per 24 hours** (or a dose of other 5-HT2A agonists and NMDAR antagonists with equivalent psychedelic / psychotomimetic potency, and thus also devoid of these effects). **The modified release long acting / slow release formulation is designed to maintain plasma levels of psilocin below the 4-6 ng/ml window that causes psychedelic /psychotomimetic effects for psilocin** (or a psychedelic-potency-equivalent plasma level of other 5-HT2A agonists and or NMDAR antagonists) **so they will not determine plasma levels sufficient for psychedelic effects**."

55. The method of claim 40, wherein the plasma concentration of the active form of psilocybin or psilocin is maintained (i) at or above a minimum therapeutically effective threshold in the individual and (ii) below a hallucinogenic threshold in the individual for more than or equal to 24 hours.	10. Intl. Pat. App. No. WO2020181194 (2020) "COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON-PSYCHEDELIC/PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS" (filed 6 March 2020) From **Claim 16 "A method for preventing or treating diseases and conditions or improving functions in patients or subjects, the method comprising:** **administration of a 5-HT2A agonist substance at doses,** dosages, posology, or formulations **devoid of clinically meaningful psychedelic or psychotomimetic actions or effects**, and having clinical effects comparable to those exerted by human plasma psilocin Cmax of 4 ng/ml or less, or human 5-HT2A CNS receptor occupancy of 50% or less, or PD effects comparable to those exerted by human plasma psilocin Tmax in excess of 60 minutes." From **Claim 40** "The **method in claim 16** where **the substance is a modified release formulation of psilocybin, psilocin,** norpsilocin, baeocystin, nor-baeocystin or a mixture thereof." From **Paragraph [00180]** ""**Modified release, long acting and or slow release formulation** of a neuroplastogen drug **will allow for administration of a relatively higher amount of drug while still avoiding the psychedelic and or psychotomimetic side effects caused by a peak in blood levels of the drug (the psychedelic effects caused by a high Cmax and short Tmax)**. The present inventors therefore also disclose modified release long-acting and or slow-release formulations of neuroplastogens, including long-acting oral or transdermal formulations and **or slow-release formulations of psilocybin and or baeocystin at doses up to 30 mg per 24 hours** (or a dose of other 5-HT2A agonists and NMDAR antagonists with equivalent psychedelic / psychotomimetic potency, and thus also devoid of these effects). **The modified release long acting / slow release formulation is designed to maintain plasma levels of psilocin below the 4-6 ng/ml window that causes psychedelic /psychotomimetic effects for psilocin** (or a psychedelic-potency-equivalent plasma level of other 5-HT2A agonists and or NMDAR antagonists) **so they will not determine plasma levels sufficient for psychedelic effects**."
56. The method of claim 40, wherein the therapeutically effective amount of the psilocybin or psilocin, or a pharmaceutically acceptable salt thereof, is administered to the individual in need thereof as a controlled release formulation.	10. Intl. Pat. App. No. WO2020181194 (2020) "COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON-PSYCHEDELIC/PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS" (filed 6 March 2020) From **Claim 16 "A method for preventing or treating diseases and conditions or improving functions in patients or subjects, the method comprising:** **administration of a 5-HT2A agonist substance at doses,** dosages, posology, or formulations **devoid of clinically meaningful psychedelic or psychotomimetic actions or effects**, and having clinical effects comparable to those exerted by human plasma psilocin Cmax of 4 ng/ml or less, or

	human 5-HT2A CNS receptor occupancy of 50% or less, or PD effects comparable to those exerted by human plasma psilocin Tmax in excess of 60 minutes." From **Claim 40** "The **method in claim 16** where **the substance is a modified release formulation of psilocybin, psilocin,** norpsilocin, baeocystin, nor-baeocystin or a mixture thereof." From **Paragraph [00180]** ""**Modified release, long acting and or slow release formulation** of a neuroplastogen drug **will allow for administration of a relatively higher amount of drug while still avoiding the psychedelic and or psychotomimetic side effects caused by a peak in blood levels of the drug (the psychedelic effects caused by a high Cmax and short Tmax)**. The present inventors therefore also disclose modified release long-acting and or slow-release formulations of neuroplastogens, including long-acting oral or transdermal formulations and **or slow-release formulations of psilocybin and or baeocystin at doses up to 30 mg per 24 hours** (or a dose of other 5-HT2A agonists and NMDAR antagonists with equivalent psychedelic / psychotomimetic potency, and thus also devoid of these effects). **The modified release long acting / slow release formulation is designed to maintain plasma levels of psilocin below the 4-6 ng/ml window that causes psychedelic /psychotomimetic effects for psilocin** (or a psychedelic-potency-equivalent plasma level of other 5-HT2A agonists and or NMDAR antagonists) **so they will not determine plasma levels sufficient for psychedelic effects**." 11. US Pat. App. No. 16/947003 (2020) "ORAL SOFT GEL CAPSULE CONTAINING PSYCHEDELIC COMPOUND" (Filed 14 July 2020) From **Summary, Column 1** "The present invention also provides for a method of **treating in a subject a psychological or neurological disorder.** The method includes orally administering to the subject **an oral soft gel capsule** described herein, in an amount and **for a period of time sufficient to effectively treat the psychological or neurological disorder**… The present invention also provides for **a method of administering to a subject a low dose or microdose of a psychedelic compound**. The method includes **orally administering an oral soft gel capsule** described herein, **wherein the oral soft gel capsule includes a low dose or microdose of the psychedelic compound.**" From **Line 31, Column 4** "In some embodiments, **the softgel shells include a layer or coating**. The coating may include a film coating or an enteric resistant **coating that allows for controlled release**, **delayed release or sustained release of the contents of the capsule upon administration**. In certain embodiments, the softgel shells are coated with cellulose acetate phthalate (CAP)." From **Claim 1** "A method of treating anxiety in a subject**, the method comprising orally administering to a subject in need or at risk thereof an oral soft gel capsule** comprising:

	(i) a capsule shell formed from gelatin and at least one of vegetable starch, tapioca starch, carrageenan, potato starch, cassava starch, cornstarch, and arrowroot; (ii) **a psychedelic compound comprising at least one of psilocybin, psilocin**, and baeocystin; and (iii) liquid vehicle comprising at least one of glycerin, beeswax, tocopherols, polyoxyethylene-polyoxypropylene copolymers, and Caprylic/Capric Triglyceride; **wherein, the psilocybin, psilocin baeocystin, or combination thereof is present in a combined amount of 0.01 to 5 mg**…" From **Claim 5** "The method of claim 1, wherein the **psilocybin, psilocin**, baeocystin, or combination thereof **is present in a combined amount of 0.05 to 2.5 mg."** From **Claim 6** "The method of claim 1, wherein the **psilocybin, baeocystin**, or combination thereof **is present in a combined amount of 0.05 to 1 mg."** From **Claim 7** "The method of claim 1, wherein the **psilocybin, baeocystin**, or combination thereof **is present in a combined amount of 0.1 to 1 mg."**
57. The method of claim 56, wherein the controlled release formulation comprises an extended release component that releases the active form of the psilocybin or psilocin at an amount below the hallucinogenic effective threshold and an amount of at least the therapeutically effective threshold in the individual.	10. Intl. Pat. App. No. WO2020181194 (2020) "COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON-PSYCHEDELIC/PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS" (filed 6 March 2020) From **Claim 16 "A method for preventing or treating diseases and conditions or improving functions in patients or subjects, the method comprising:** **administration of a 5-HT2A agonist substance at doses,** dosages, posology, or formulations **devoid of clinically meaningful psychedelic or psychotomimetic actions or effects**, and having clinical effects comparable to those exerted by human plasma psilocin Cmax of 4 ng/ml or less, or human 5-HT2A CNS receptor occupancy of 50% or less, or PD effects comparable to those exerted by human plasma psilocin Tmax in excess of 60 minutes." From **Claim 40** "The **method in claim 16** where **the substance is a modified release formulation of psilocybin, psilocin,** norpsilocin, baeocystin, nor-baeocystin or a mixture thereof." From **Paragraph [00180]** ""**Modified release, long acting and or slow release formulation** of a neuroplastogen drug **will allow for administration of a relatively higher amount of drug while still avoiding the psychedelic and or psychotomimetic side effects caused by a peak in blood levels of the drug (the psychedelic effects caused by a high Cmax and short Tmax)**. The present inventors therefore also disclose modified release long-acting and or slow-release formulations of neuroplastogens, including long-acting oral or transdermal formulations and **or slow-release formulations of psilocybin and or baeocystin at doses up to 30 mg per 24 hours** (or a dose of other 5-HT2A agonists and NMDAR antagonists with

	equivalent psychedelic / psychotomimetic potency, and thus also devoid of these effects). **The modified release long acting / slow release formulation is designed to maintain plasma levels of psilocin below the 4-6 ng/ml window that causes psychedelic /psychotomimetic effects for psilocin** (or a psychedelic-potency-equivalent plasma level of other 5-HT2A agonists and or NMDAR antagonists) **so they will not determine plasma levels sufficient for psychedelic effects**." 11. US Pat. App. No. 16/947,003 (2020) "ORAL SOFT GEL CAPSULE CONTAINING PSYCHEDELIC COMPOUND" (Filed 14 July 2020) From **Summary, Column 1** "The present invention also provides for a method of **treating in a subject a psychological or neurological disorder.** The method includes orally administering to the subject **an oral soft gel capsule** described herein, in an amount and **for a period of time sufficient to effectively treat the psychological or neurological disorder**… The present invention also provides for **a method of administering to a subject a low dose or microdose of a psychedelic compound**. The method includes **orally administering an oral soft gel capsule** described herein, **wherein the oral soft gel capsule includes a low dose or microdose of the psychedelic compound.**" From **Line 31, Column 4** "In some embodiments, **the softgel shells include a layer or coating**. The coating may include a film coating or an enteric resistant **coating that allows for controlled release**, **delayed release or sustained release of the contents of the capsule upon administration**. In certain embodiments, the softgel shells are coated with cellulose acetate phthalate (CAP)." From **Claim 1** "A method of treating anxiety in a subject**, the method comprising orally administering to a subject in need or at risk thereof an oral soft gel capsule** comprising: (i) a capsule shell formed from gelatin and at least one of vegetable starch, tapioca starch, carrageenan, potato starch, cassava starch, cornstarch, and arrowroot; (ii) **a psychedelic compound comprising at least one of psilocybin, psilocin**, and baeocystin; and (iii) liquid vehicle comprising at least one of glycerin, beeswax, tocopherols, polyoxyethylene-polyoxypropylene copolymers, and Caprylic/Capric Triglyceride; **wherein, the psilocybin, psilocin baeocystin, or combination thereof is present in a combined amount of 0.01 to 5 mg**…" From **Claim 3** "The method of claim 1, wherein **1-5 oral soft gel capsules are orally administered a day."** From **Claim 5** "The method of claim 1, wherein the **psilocybin, psilocin**, baeocystin, or combination thereof **is present in a combined amount of 0.05 to 2.5 mg."**

	From **Claim 6** "The method of claim 1, wherein the **psilocybin, baeocystin**, or combination thereof **is present in a combined amount of 0.05 to 1 mg."** From **Claim 7** "The method of claim 1, wherein the **psilocybin, baeocystin**, or combination thereof **is present in a combined amount of 0.1 to 1 mg."**
58. The method of claim 57, wherein the controlled release formulation comprises an immediate release component that releases the active form of the psilocybin or psilocin at an amount below the hallucinogenic effective threshold and an amount of at least the therapeutically effective threshold in the individual.	11. US Pat. App. No. 16/947,003 (2020) "ORAL SOFT GEL CAPSULE CONTAINING PSYCHEDELIC COMPOUND" (Filed 14 July 2020) From **Summary, Column 1** "The present invention also provides for a method of **treating in a subject a psychological or neurological disorder.** The method includes orally administering to the subject **an oral soft gel capsule** described herein, in an amount and **for a period of time sufficient to effectively treat the psychological or neurological disorder**… The present invention also provides for **a method of administering to a subject a low dose or microdose of a psychedelic compound**. The method includes **orally administering an oral soft gel capsule** described herein, **wherein the oral soft gel capsule includes a low dose or microdose of the psychedelic compound.**" From **Line 31, Column 4** "In some embodiments, **the softgel shells include a layer or coating**. The coating may include a film coating or an enteric resistant **coating that allows for controlled release**, **delayed release or sustained release of the contents of the capsule upon administration**. In certain embodiments, the softgel shells are coated with cellulose acetate phthalate (CAP)." From **Line 62, Column 6** "In specific embodiments, **the oral soft gel capsule contains a liquid vehicle which has softgel(s), granules, tablet(s), and/or pellet(s) suspended therein**. In this dosage form, tablets, granules, pellets and/or capsules can be placed inside a large, soft gelatin capsule. **The dosage form allows for different configurations for fixed-dose combinations, such as a softgel within a softgel, one or two tablets within a softgel, granules within a softgel, or any combination of these to address challenges of multi-active formulations**. **This delivery system allows for single or multiple active ingredients with different release profiles**, multiple active ingredients where at least one is a liquid or semi-solid, offering unique options for nutraceutical products. From **Claim 1** "A method of treating anxiety in a subject**, the method comprising orally administering to a subject in need or at risk thereof an oral soft gel capsule** comprising: (i) a capsule shell formed from gelatin and at least one of vegetable starch, tapioca starch, carrageenan, potato starch, cassava starch, cornstarch, and arrowroot; (ii) **a psychedelic compound comprising at least one of psilocybin, psilocin**, and baeocystin; and (iii) liquid vehicle comprising at least one of glycerin, beeswax, tocopherols, polyoxyethylene-polyoxypropylene copolymers, and Caprylic/Capric Triglyceride; **wherein, the psilocybin, psilocin baeocystin, or combination thereof is present in a combined amount of 0.01 to 5 mg**…"

59. The method of claim 40, wherein the therapeutically effective amount of psilocybin or psilocin, or a pharmaceutically acceptable salt thereof is administered orally.	*From application of interest 18/102,268 paragraph [0043] "In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 0.001 ng/mL or more (e.g., 0.01 ng/mL or more, 0.1 ng/mL or more, 1 ng/mL or more, 10 ng/mL or more, 20 ng/mL or more, or 50 ng/mL or more). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of at least about 100 ng/mL or less (e.g., 50 ng/mL or less, 25 ng/mL or less, 15 ng/mL or less, 5 ng/mL or less, or 0.5 ng/mL or less). In some embodiments, the level (e.g., C max) of the active 5-HT receptor agonist (e.g., psilocin) in the individual is (maintained) at a level of about 0.001 ng/mL to about 100 ng/mL."* *Paragraph [0045] "In some embodiments, the level (e.g., Cmax) of the active 5-HT receptor agonist (e.g., psilocin) is measured after a dose of at least 1 mg or more (e.g., 5 mg or more, 10 mg or more, 15 mg or more, or 20 mg or more) of the 5-HT receptor agonist (e.g., psilocybin) is administered to the individual."* 11. US Pat. App. No. 16/947,003 (2020) "ORAL SOFT GEL CAPSULE CONTAINING PSYCHEDELIC COMPOUND" (Filed 14 July 2020) From **Summary, Column 1** "The present invention also provides for a method of **treating in a subject a psychological or neurological disorder.** The method includes orally administering to the subject **an oral soft gel capsule** described herein, in an amount and **for a period of time sufficient to effectively treat the psychological or neurological disorder**… The present invention also provides for **a method of administering to a subject a low dose or microdose of a psychedelic compound**. The method includes **orally administering an oral soft gel capsule** described herein, **wherein the oral soft gel capsule includes a low dose or microdose of the psychedelic compound.**" From **Claim 1** "A method of treating anxiety in a subject**, the method comprising orally administering to a subject in need or at risk thereof an oral soft gel capsule** comprising: (i) a capsule shell formed from gelatin and at least one of vegetable starch, tapioca starch, carrageenan, potato starch, cassava starch, cornstarch, and arrowroot; (ii) **a psychedelic compound comprising at least one of psilocybin, psilocin**, and baeocystin; and (iii) liquid vehicle comprising at least one of glycerin, beeswax, tocopherols, polyoxyethylene-polyoxypropylene copolymers, and Caprylic/Capric Triglyceride; **wherein, the psilocybin, psilocin baeocystin, or combination thereof is present in a combined amount of 0.01 to 5 mg**…" From **Claim 2** "The method of claim 1, wherein **the anxiety is associated with at least one of obsessive compulsive disorder (OCD), pain, irritability, fibromyalgia, post-traumatic stress disorder (PTSD), cluster**

headaches, paranoia, psychosis, anxiety, panic attacks, flashbacks, smoking addiction, alcohol addiction, and cocaine addiction."

From **Claim 3** "The method of claim 1, wherein **1-5 oral soft gel capsules are orally administered a day."**

From **Claim 5** "The method of claim 1, wherein the **psilocybin, psilocin**, baeocystin, or combination thereof **is present in a combined amount of 0.05 to 2.5 mg."**

From **Claim 6** "The method of claim 1, wherein the **psilocybin, baeocystin**, or combination thereof **is present in a combined amount of 0.05 to 1 mg."**

From **Claim 7** "The method of claim 1, wherein the **psilocybin, baeocystin**, or combination thereof **is present in a combined amount of 0.1 to 1 mg."**

8. HUTTEN (2019) "Motives and Side-Effects of Microdosing With Psychedelics Among Users" International Journal of Neuropsychopharmacology. 22(7):426-434.

From **p. 427 "**Another commonly reported motivation and subsequent outcome is the **alleviation of psychological symptom**s including **depressive mood and anxiety** and/or physiological symptoms such as pain (Smith, 2017; Wong, 2017; Johnstad, 2018; Waldman, 2018)…"

From **p 429, Table 2**

Table 3. Number (percentage) of respondents who indicated use of one of the listed substances as a microdose, with the self-reported dose in mode and the percentage of respondents who did not know the dose or failed to complete this item

	Psychedelic users per substance	Microdose details		Users who do not know the dose or did not fill out this question	
Substance	n (%)	Amount, mg	Dose range, mg (min–max)	Do not know, n (%)	Missing, n (%)
1P-LSD	129 (11.6)	0.01	0.0005–75	9 (7.0)	9 (7.0)
2Cs	22 (2.0)	3–4	0.75–25	3 (13.6)	3 (13.6)
5-MeO-DMT	5 (0.4)	0.005	0.005–7	–	2 (40.0)
ALD-52/1A-LSD	41 (3.7)	0.01	0.0005–75	3 (7.3)	6 (14.6)
Ayahuasca	15 (1.3)	14	14–500	10 (66.7)	2 (13.3)
DMT	64 (5.7)	10	00.5–25	19 (29.7)	15 (23.4)
LSD	666 (59.7)	0.01	0.00001–500	113 (17.0)	60 (9.0)
MDMA/ecstasy	71 (6.4)	50	0.02–100	18 (25.4)	21 (29.6)
Mescaline	26 (2.3)	50	0.3–1000	14 (53.8)	4 (15.4)
NBOMes	9 (0.8)	0.5–50	0.5–50	3 (33.3)	4 (44.4)
Other	60 (5.4)	5	0.01–1000	15 (25.0)	24 (40.0)
Psilocybin	645 (57.8)	500	0.025–8000	146 (22.6)	93 (14.4)
Salvinorin A	31 (2.8)	0.2	0.2–200	16 (51.6)	10 (32.3)

From **p 431, Table 4**

Table 4. Number (percentage) of respondents who indicated to (have) use(d) the listed psychedelic substance to microdose via the listed route of administration[a] and the corresponding frequency of use (Mean (SD), range

	Route of administration, n (%)									Frequency of microdosing per week		
Substance	Number of respondents who answered, n (%)	Oral	Sublingual	Inspiration	Intranasal	Ocular	Cutaneous	Rectal	Other	Number of respondents who answered N (%)	Frequency of dosing per week M (SD)	Range of dosing per week (min–max)
1P-LSD	120 (77.5)	71 (55.0)	28 (21.7)	–	–	–	–	1 (0.8)	–	76 (58.9)	2.13 (2.23)	0.001–14
2Cs	13 (59.1)	11 (50.0)	–	–	1 (4.5)	–	–	1 (4.5)	–	10 (45.5)	2.89 (4.11)	0.2–14
5-MeO-DMT	2 (30.0)	1 (20.0)	–	–	–	–	–	1 (20.0)	–	2 (40.0)	7.5 (9.19)	1–14
ALD-52/ 1A-LSD	28 (68.3)	18 (43.9)	9 (22.0)	–	–	–	–	1 (2.4)	–	22 (53.7)	2.23 (2.82)	0.005–14
Ayahuasca	7 (46.7)	5 (33.3)	–	1 (6.7)	–	–	–	1 (6.7)	–	6 (40.0)	4.37 (5.16)	0.25–14
DMT	35 (54.7)	2 (3.1)	–	32 (50.0)	–	–	–	1 (1.6)	–	25 (39.1)	2.26 (3.17)	0.002–14
LSD	491 (73.7)	387 (58.1)	99 (14.9)	–	1 (0.2)	1 (0.2)	–	1 (0.2)	2 (0.3)	384 (57.7)	2.02 (1.89)	0.0001–15
MDMA/ ecstasy	34 (47.9)	24 (33.8)	2 (2.8)	–	7 (9.9)	–	–	1 (1.4)	–	19 (26.8)	2.08 (3.46)	0.005–14
Mescaline	12 (46.2)	11 (42.3)	–	–	–	–	–	1 (3.8)	–	6 (23.1)	3.46 (5.26)	0.25–14
NBOMes	3 (33.3)	–	2 (22.2)	–	–	–	–	1 (11.1)	–	3 (33.3)	5.67 (7.23)	1–14
Other	26 (43.3)	16 (26.7)	–	6 (10.0)	2 (3.3)	–	1 (1.7)	1 (1.7)	–	21 (35.0)	6.78 (6.98)	0.5–30
Psilocybin	416 (64.5)	415 (64.3)	–	–	–	–	–	1 (0.2)	–	325 (78.3)	3.74 (3.35)	0.001–30
Salvinorin A	15 (45.4)	3 (9.7)	2 (6.5)	8 (25.8)	–	–	–	1 (3.2)	1 (3.2)	8 (25.8)	2.63 (4.65)	0.01–14

Abbreviations: 1P-LSD, 1-propionyl-lysergic acid diethylamide; 2C, 2-ethylamine; 5-MeO-DMT, 5-methoxy-N,N-dimethyltryptamine; ALD-52/1A-LSD, 1-Acetyl-N,N-diethyllysergamide; DMT, N,N-dimethyltryptamine; LSD, lysergic acid diethylamide; MDMA, 3,4,-methylenedioxymethamphetamine; NBOMe, N-benzyl Methoxy.
aRoute of administration: "injection" is not shown, as no respondent reported injection as route of administration.

UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/102,268	**01/10/2024 05:05:46 PM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	63908696	FILING DATE	01/27/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 23

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
Concise-description-generated.pdf		2	Concise Description of Relevance	40 KB
third-party-preissuance-submission.pdf		3	Third-Party Submission Under 37 CFR 1.290	79 KB
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	14 KB
Claims Chart.pdf		23	-	1792 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-	(1-23)	23	Concise Description of	1790 KB

3P.RELEVANCE.pdf			Relevance	
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB
1_FADIMAN.pdf		5	-	426 KB
1_FADIMAN-NPL.pdf	(1-5)	5	Non Patent Literature	432 KB
2_HUTTEN.pdf		9	-	958 KB
2_HUTTEN-NPL.pdf	(1-9)	9	Non Patent Literature	881 KB
3_MADSEN.pdf		7	-	1161 KB
3_MADSEN-NPL.pdf	(1-7)	7	Non Patent Literature	1119 KB
4_MERTENS.pdf		14	-	1186 KB

4_MERTENS-NPL.pdf	(1-14)	14	Non Patent Literature	869 KB
5_LEA.pdf		12	-	401 KB
5_LEA-NPL.pdf	(1-12)	12	Non Patent Literature	362 KB
6_VOINESKOS.pdf		14	-	460 KB
6_VOINESKOS-NPL.pdf	(1-14)	14	Non Patent Literature	409 KB
7_USONAINSTITUTE.pdf		11	-	495 KB
7_USONAINSTITUTE-NPL.pdf	(1-11)	11	Non Patent Literature	396 KB
8_HUTTEN.pdf		9	-	1327 KB
8_HUTTEN-NPL.pdf	(1-9)	9	Non Patent Literature	1305 KB
9_CARHARTHARRIS.pdf		9	-	473 KB
9_CARHARTHARRIS-NPL.pdf	(1-9)	9	Non Patent Literature	461 KB
10_WO2020181194A1.pdf		7	-	708 KB
10_WO2020181194A1-FOR.pdf	(1-7)	7	Foreign Reference	703 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
Concise-description-generated.pdf	C96FFCA731AA7A2D752A8574CBDF1DC483FB8E7F6FD44E3E75A6E53D06E8F404ED2F682C29EB5C86C5F5583164F97B857E563742376BDC97FF23B1294F33FB14

third-party-preissuance-submission.pdf	9A6F7599C751FABB0C4192B3DF0D10BEA61319DD432381B7A3CA460D6E36D57AA79D5DAB0A3696395F14410E4966DBA1817686767825CD8019A869C7A75D4D81
Third-party-notification-request.pdf	B936FFD02C4EBCBE97C188A0F5FB52B065C8695F7C8D589515392564E47EC28DFBD8B31A4748298C9EC47A364CD1480C8F394E4580C683F65C92C9B6EA670369
Claims Chart.pdf	740766E8A99E0A5FC4AE6255595A14A91DDB4FBD366C6C194DFB086266010DFF89480BD80FC2F07AC3433F0501FDB22911E61242EEE6CD30F19AB2B98BBDB0D6
Claims Chart-3P.RELEVANCE.pdf	FFAA3A88FD88B6275BF5F372821C4D87DDA5C71EC1D30129DA63D3BA8C5B91DE782FCE3B4A650E2B0946AD4881562A377BCB1B73182293CFFED77E616D68504B
Claims Chart-3P.RELEVANCE.pdf	97686472C1D2CA9ADD1407640E776792963E2F989EBBA0B7CB5FA6A4DD585CF087B3223F77350660B8A4A313D68CE3387C605F2F880D2C7576AB05E5514E86C3
Claims Chart-3P.RELEVANCE.pdf	6812EC40254C37C7283626B1D6CC916D993F85A1FF9EA34EFFE5FC536FA9763C582E40DB7B8DBBAC56009AFB5D5EEAEFA19FF04AE00602DBA4102B4966FF737B
Claims Chart-3P.RELEVANCE.pdf	0DC280482215988E0C6DA535684517CE70F8DE0916ACE45B51D1B39C217F9051D16F01DFD63FDF4FAB66646575D2A481B609A39BFEA4767BC060E903DDB70D90
Claims Chart-3P.RELEVANCE.pdf	F270EB3F724829E2C1FFD702DDE2BC5A8EF093DB0B2FFC753132665650909174C3D1A0A6B727F9EFFAAB1AB3EECF8A0D0693B95D6CAE64B132D2FECE8FA22755
Claims Chart-3P.RELEVANCE.pdf	C78A462382D6D896FE7F80710D4F0B058DCEE32CCC969B90E9A5542CFE3676C8EC84E28A9A9F9CD0499358EE9DE8945397CDC1836A18F8122FA7920F5A2DE51C
Claims Chart-3P.RELEVANCE.pdf	DE1939BC6D3A7C0D5A1EEC700B34A0049B61EFF4829974B2C4255F751455FB0524E8905E0E39D4A853C1BFB3A66C5F3AC03168B65D820CA25B63FE1F5AD7F852

Claims Chart-3P.RELEVANCE.pdf	045D10A812BD112B536FF0F5679C6700E028E70C7775843A4073A620B00E24C33B1D5FB1DDE49C74F6EF014A600D86546680F321719E1976545CDFE11B7A64FA
Claims Chart-3P.RELEVANCE.pdf	5EE86B33F1234CFE7360092DA4F2CEC3ADCF842E782E2463286AD9E27B51BC32E075234F0AFE1E69610D26C6E855097879A66A1419271E3F7C08900FEAC7C1E6
Claims Chart-3P.RELEVANCE.pdf	FAFAA8AE93410F12FD150E95CB7896D7F1103BF1FA6EB09E587AEA1F4F28FDEB4EE8F83970CF48EEAE267EE715F0367BF5CB47FBAE1DB35C7A3ED122063F3948
1_FADIMAN.pdf	8402B649650DF5F887E50A0677FCF28380F9D45EF7339303378B5DE3B9C391A1A00AD6875347888B1434D8610C1D6EFF0BE10AD7A976B26F72B7BF46E9942D2A
1_FADIMAN-NPL.pdf	DAF44D9C8F2331B191D94238B75AD9A9D9B6E24BA60D2E5958E102C4A0D53358032A6BE7BB4801D89480D04955CAAF3AC3643BD354F16AB3F6FE76F7DF1B6135
2_HUTTEN.pdf	925E25691DFBA622E818721F1F93FD369A4E0BB37BBD8127D698C7E041F44676EB327BDCDB0D6421ABB11410D5C10149F074D8FFFFE07DF02897A9F84DEC6366
2_HUTTEN-NPL.pdf	DF9804EF3F70E3FA0C4CDD18088A01B9BD228105252B62880F9CE3EFBF98D9D8F3C805F4ADA43B50A83F5F33B22E12927D21AD24481B82A8D01A83BCE8AA307F
3_MADSEN.pdf	360AE117D2DB50652F5CE58B37CD87B45E72092C4713D9A1E0D183E70851E0FD47D0284E74F99034B06B2EAA5844C0C5F9BEC857036220AEB30156A8C241FBC0
3_MADSEN-NPL.pdf	6D987A33F8DDCEAB7F2A063888AE6E8CB1F5B946B82EFD399FDD9431E795D90245E6FBCC555316CCD21A3F6194299DE22FA55DBEBC62037FCA4EB0AA8FC80FD4
4_MERTENS.pdf	A242B858C7D78C89A605D15406994D2BDCCBD9BE68955A7A8C998941EAB6563141EB4385D52F5B025085C97E75E15752EEAFDD7089EBFAC5B888D0D8CCBC1C7F

4_MERTENS-NPL.pdf	CDE7EB9EA3BB257FD18FB9DDF85A0A8C2F1192C1D7FE0DFFDEA92D24B4204CA0A7A54B2D6CE6CECC43315BF79951734A978079FA286B2A2F0D958AE0E0AD75E4
5_LEA.pdf	24393F512AFA74D30A9A3A0432B7A8C0B9DA4E779BE479C719BDC2880AE5B74E27DC79E27DA1E30EAA305ED4E4FEBFC0E1C114687E4DD929138BA6AE53BED555
5_LEA-NPL.pdf	0E8FECA8462170A0C537FB0EB24549717EF34AC93CE0892058F8A38D640E84C5A677A5ED8A8A753C96636DCF8EB7CE2691324A5FE3928E67C92734D945158BA4
6_VOINESKOS.pdf	4B583FCD1073206CE3AA2F325E88A5B420681F83F10C857FCE6BA7BA75433CC54B424EB61CD50576C791023644605F871501FAAC523DCA9E91C343A86D8FA169
6_VOINESKOS-NPL.pdf	7D06DE723045651388279FE3DA28384DB26BB686B4F794DD430188BF6EE9015F430F4BF91D6C7AC71C0147E5998322BE987FFF0DD7590D4520EB003EE1B5FED9
7_USONAINSTITUTE.pdf	7F01C4A5AB1CEA9E7F9BE0587BCB047204569612C0C2428476B4B4BBA46C94F0E981A388CDC96AC3C43B2F4689EC40591DA39370C387A59F7C84989CCFCB183E
7_USONAINSTITUTE-NPL.pdf	AFAA79A306FC222291A90E577A3012F0E5B9E4EEA7288670286505AE53C69678AF130CA73DB05C59502C6F8431113480CF2BF74DD83C31F884C24D3E66DBF924
8_HUTTEN.pdf	32B90AD90E2BDFB886B5BF6A86422DF977EADF16D84B213A076F79699DF55C4E3C58E39DEB613539FA097C511D11C9DA10DA24C269C44065135A785E3F90BFD5
8_HUTTEN-NPL.pdf	19290336B93392D9289C349287C256B27739569809044B8C9E96865542370C331365D233CF385D8F8354042F1EDEE2B9B9417FA6BB142BC02A906ED31F3185EE
9_CARHARTHARRIS.pdf	C9ACD101AD76F7BA49ABC5DEB86959CC2D0DA2A3A1E8DDC5342689B0F87F4A0EBC732E41DBD98A0C2A89650A87BBFFBCE8618C4CC0BABF2C0B490D9B9F5093E8

9_CARHARTHARRIS-NPL.pdf	2C239CC9B47FC60CFC5B8A23D639B108B57A85B55A483760E4FD840C980ACBE38E07A82AF1D5DC5890B42729BF5555E92DA5C4CF8729B2DFB9D183B5D77FDE66
10_WO2020181194A1.pdf	CBD312C4C9E838C1E856263FA30C4CCE1AA390E9686C9681AA5FBD4D25AAA7342A4F1869DF67B83B6C4ABF940293D76496A6C3468017DD57A55B961B04BA7DDB
10_WO2020181194A1-FOR.pdf	1BE07763B89D08ED9CC6DD3C1AB3BDB03405E0AD7B9D562ADD283C906A28D554E5C1426C0EDFE1961E5F4F1A333E12C53ED336816A77A8238245AA58720AF320

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized 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.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/102,268	**01/10/2024 05:05:46 PM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	63908696	AUTHORIZED BY	-
CUSTOMER #	–	FILING DATE	01/27/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 0837	**E202410H07295201**	**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**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized 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.

UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/102,268	**01/10/2024 05:12:37 PM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	63909100	FILING DATE	01/27/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 4

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
third-party-preissuance-submission.pdf		2	Third-Party Submission Under 37 CFR 1.290	44 KB
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	14 KB
Concise-description-generated.pdf		1	Concise Description of Relevance	25 KB
Claims Chart.pdf		23	-	1792 KB
Claims Chart-3P.RELEVANCE.pdf	(1-23)	23	Concise Description of Relevance	1790 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
third-party-preissuance-submission.pdf	9EAEF1922384EF37843885785279038 20D6337C16C9658F9A665DAF2ACC653E5B3045CCBC7D6DACB2658D849EB6FFB9ABFB6D0BB1C0CEBE4692AC0CBB08DD613
Third-party-notification-request.pdf	4EA90C4CEED6C0D672441CED4F37DDE50664825CDD68B84CC6C0893DBA4CD53A199AD8B0B6D06ADBB42329AF55927338E7F2EC2CB0EB6529B143FB426F63558C
Concise-description-generated.pdf	F0EC8408D75E2263E5ED36EB492E310CABCA6A7818674E5C0955743D4B8CB7FCA04888F4703E112EC822FAB3C52A527EC9B0C7A33A7CE647A2B66E1A9504472D
Claims Chart.pdf	740766E8A99E0A5FC4AE6255595A14A91DDB4FBD366C6C194DFB086266010DFF89480BD80FC2F07AC3433F0501FDB22911E61242EEE6CD30F19AB2B98BBDB0D6
Claims Chart-3P.RELEVANCE.pdf	8F21D3BAC8E21DA1F395FC3D76E52A531F844356280CCD2BD6F5AEDB938297A2790F6161F5B052C753E7EABE68BC5835CEE459C9BAD96F2C404D305934BB8E1B

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized 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.

UNITED STATES PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/102,268	**01/10/2024 05:12:37 PM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Juliet Meccia
PATENT CENTER #	63909100	AUTHORIZED BY	-
CUSTOMER #	–	FILING DATE	01/27/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 0837	**E202410H13306204**	**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**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized 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.