IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	LONDESBROUGH; Derek John.	Confirmation No.: 9614
Serial No.:	17/604,610	Group No.:
Filing or 371(c) Date:		Examiner:

Entitled: Treatment of depression and other various disorders with psilocybin

THIRD-PARTY PRE-ISSUANCE SUBMISSION

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. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408.
2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627.
3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197.
4. JOHNSON (2008) "Human hallucinogen research: guidelines for safety" Journal of Psychopharmacology. 22(6)603-620.
5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283.
6. MORENO (2006) "Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients With Obsessive-Compulsive Disorder" The Journal of Clinical Psychiatry. 67(11)1735-1740
7. U.S. Pat. App. Pub. No. 2021/0267966 "Method of Inducing Dendritic and Synaptic Genesis in Neurodegenerative Chronic Diseases" (Published September 2, 2021)
8. U.S. Pat. App. Pub. No. 2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012)

9. U.S. Pat. App. Pub. No. 2020/0375967 “Compositions of psilocybin and analogs” (Published December 3, 2020)
10. KATALYST, “Microdosing for Seasonal Depression: An Experience with Mushrooms exp110358)” 2017; retrieved from Erowid. https://erowid.org/experiences/exp.php?ID=110358, retrieved May 18, 2017
11. CARHART-HARRIS (2017) “Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms” Scientific Reports. 7: 13187
12. BARRETT (2018) “Serotonin 2A Receptor Signaling Underlies LSD induced Alteration of the Neural Response to Dynamic Changes in Music” Cerebral Cortex. 28: 3939–3950
13. AGIN-LEIBES (2020) “Long-term follow-up of psilocybin-assisted psychotherapy for psychiatric and existential distress in patients with life-threatening cancer” Journal of Psychopharmacology. 34(2) 155–166
14. DRUGS.COM, “VenlafaxinePronunciation” 2014; retrieved from Web.Archives, Drugs.com. http://web.archive.org/web/20140502180823/https://www.drugs.com/venlafaxine.html, retrieved May 02, 2014
15. SHERWOOD (2021) “Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples” Acta Crystallographica. 78(1) 1-20
16. U.S. Pat. App. Pub. No. 2016/0331725 “Use of compounds that are able to increase the serum igf-1 level for the preparation of a therapeutical composition for treatment of various disease states associated with a reduced igf-1 serum level in humans and animals” (Published November 17, 2016)
17. W.I.P.O. Pat. App. No. 2018/195455 “Assessing and treating psychedelic-responsive subjects” (Published October 25, 2018)
18. U.S. Pat. App. Pub. No. 2018/0021326 “Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin” (Published January 25, 2018)
19. U.S. Pat. App. Pub. No. 2019/0105313 “PSILOCYBIN COMPOSITIONS” (Published April 11, 2019)
20. W.I.P.O. Pat. App. No. 2019/161050 “Cognitive platform including computerized elements coupled with a therapy for mood disorder” (Published August 22, 2019)
21. GROB (2013) Use of the Classic Hallucinogen Psilocybin for Treatment of Existential Distress Associated with Cancer. Springer ISBN 978-1-4614-4865-5
22. W.I.P.O. Pat. App. No. 2005/039546 “USE OF INDOLEACETIC ACID DERIVATIVES WHICH INCREASE THE SERUM IGF-1 LEVEL FOR THE PREPARATION OF A THERAPEUTICAL COMPOSITION FOR TREATMENT OF VARIOUS DISEASES” (Published May 6, 2005)

23. U.S. Pat. App. Pub. No. 2009/0259039 “Salts of physiologically active and psychoactive alkaloids and amines simultaneously exhibiting bioavailability and abuse resistance” (Published October 15, 2009)
24. LYONS (2018) “Increased nature relatedness and decreased authoritarian political views after psilocybin for treatment-resistant depression” Journal of Psychopharmacology. 32(7) 811-819
25. WAHLBERG (2015) “UW-Madison tunes in to 'magic mushroom' medicine” October 11, 2015; retrieved from Web Archive, Reset https://web.archive.org/web/20181214181711/https://madison.com/wsj/news/local/health-med-fit/uw-madison-tunes-in-to-magic-mushroom-medicine/article_5c229322-1132-5328-90c1-017e917f0696.html, retrieved December 14, 2018
26. FADIMAN (2019) “Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration” Journal of Psychoactive Drugs. 51(2) 118-122.
27. TUMOLO (2018) “Uncovering the Therapeutic Potential of Psychedelics” Retrieved from Psychiatry & Behavioral Health Learning Network. https://www.hmpgloballearningnetwork.com/site/pcn/article/uncovering-therapeutic-potential-psychedelics, retrieved September 19th 2018
28. AARON (2017) “Open Your Mind: Merging Psychedelic Therapy with Sex Therapy” Retrieved from Psychology Today. https://www.psychologytoday.com/us/blog/standard-deviations/201710/open-your-mind-merging-psychedelic-therapy-sex-therapy, retrieved October 24th, 2017
29. W.I.P.O. Pat. App. No. 2003/047551 “AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE” (Published June 12, 2003)
30. PARK (2021) “Characterization of Psilocybin” Retrieved from Triclinic Labs Report. Report Number: R2021638.01, Retrieved December 2, 2021
31. W.I.P.O. Pat. App. No. 2018/135943 “Psilocybin and/or psilocin in combination with cannabinoids and/or terpenes” (Published July 26, 2018)
32. KUHNERT (1976) “Polymorphe Modifikationen und Solvate von Psilocin und Psilocybin” Aus dem Institut fur Pharmakognosie der Universitiit Innsbruck. 309(76): 625-631
33. ICH (2017) “Q3C — Tables and List Guidance for Industry” U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER) Revision 3. Retrieved June 2017
34. FMC Product Overview (2017) Avicel® SMCC HD 90 Silicified Microcrystalline cellulose NF. Product Specifications. Retrieved 2011.
35. FMC Product Overview (2017) Avicel® SMCC HD 50 Silicified Microcrystalline cellulose NF. Product Specifications. Retrieved 2011.
36. DEBOTTON (2017) “Applications of Polymers as Pharmaceutical Excipients in Solid Oral Dosage Forms” Med Res Rev. 37(1):52-97
37. W.I.P.O. Pat. App. No. 2018/184206 “Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same” (Published October 11, 2018)
38. U.S. Pat. App. Pub. No. 2016/0051476 “Novel Dispersible Tablet Composition” (Published February 25, 2016)

39. PROSOLV® SMCC. Retrieved from Web Archive, Reset https://web.archive.org/web/20160318071326/http://www.jrspharma.com/pharma_en/products-services/excipients/hfe/prosolv-smcc.php Retrieved March 18th, 2016.

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. # 17/604,610 Pending Claims	References
1. A method of treating depression in a subject in need thereof, the method comprising administering an effective amount of psilocybin or an active metabolite thereof to the subject.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "Objectives Here, we report on safety and efficacy outcomes for up to 6 months in an open-label trial of **psilocybin for treatment resistant depression**…**Psilocybin represents a promising paradigm for unresponsive depression** that warrants further research in double-blind randomised control trials."
2. The method of claim 1, wherein the subject has major depressive disorder, atypical depression, bipolar disorder, catatonic depression, a depressive disorder due to a medical condition, postpartum depression, premenstrual dysphoric disorder, or seasonal affective disorder.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 405** "Recent studies (Griffiths et al. 2016; Ross et al. 2016; Carhart-Harris et al. 2016), including the present one, help demonstrate the feasibility of **treating patients with major depressive disorder** with **psilocybin** plus psychological support." From **p. 405** "Two recent double-blind randomised control trials (RCTs) of **psilocybin for depression and anxiety symptoms in a combined sample of 80 patients with life-threatening cancer found consistent safety and efficacy outcomes** with those reported here (Griffiths et al. 2016; Ross et al. 2016)."
3. The method of claim 2, wherein the subject has major depressive disorder.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 405** "Recent studies (Griffiths et al. 2016; Ross et al. 2016; Carhart-Harris et al. 2016), including the present one, help demonstrate the feasibility of **treating patients with major depressive disorder** with **psilocybin** plus psychological support."
4. The method of claim 2, wherein the subject has bipolar disorder.	10. KATALYST, "Microdosing for Seasonal Depression: An Experience with Mushrooms exp110358)" 2017; retrieved from Erowid. https://erowid.org/experiences/exp.php?ID=110358, retrieved May 18, 2017 "There are a few resources on the internet about **microdosing with psilocybin**, but none that provide guidance on how to approach it if you have bipolar disorder. Now that I've run this experiment on myself, I decided I would add my anecdote into the mix, hoping that it will help someone out in a similar situation…For context: I have a diagnosis of **Bipolar II and PTSD**… The sweet spot for me

	was 0.15g, every 2 weeks… At the dose I found to be best for me (0.15g), I sometimes felt mild euphoria in the mornings when I took it, but did not experience any of the other side effects noted above. Overall I would consider this a huge success."
5. The method of claim 4, wherein the subject has bipolar disorder I.	8. U.S. Pat. App. Pub. No. 2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012) From **claim 1** "A method of improving the efficacy of psychotherapeutic treatment comprising administering a pharmaceutical composition comprising an oxytocin releasing agent to a subject diagnosed with a psychiatric or behavioral disorder." From **claim 3** "The method of claim 1, wherein the psychiatric disorder is selected from the group consisting of depression, **bi-polar disorders**, anxiety disorders, panic attacks, agoraphobia, attention deficit syndrome, mid-cycle dysphoria, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS), addiction, obsessive-compulsive disorder, Tourette's Syndrome, post-traumatic stress disorder (PTSD), and schizophrenia." From **claim 13** "The method of claim 1, wherein the oxytocin releasing agent is buspirone, gepirone, tandospirone serotonin, ergine, ergotamine, lysergic acid, lysergic acid diethylamide, **psilocybin**, 4-hydroxy-dimethyltryptamine, N,N-dimethyltryptamine, 5-methoxy-dimethyltryptamine, mescaline, 4-bromo-2,5-dimethoxyphenethylamine, 3,4-methylenedioxymethamphetamine, methylenedioxyethylamphetamine, tenamfetamine, lorcaserin or salts thereof." 26. FADIMAN (2019) "Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration" Journal of Psychoactive Drugs. 51(2) 118-122. From **p. 120** "Studies are starting in which participants are to be given measured doses of LSD, **psilocybin**, or a placebo in a structured setting, measuring physical parameters, and answering questions related to self-observations of mental and physical changes during and after microdosing." From **p. 120** "Participants diagnosed with bipolar disorder present one special group for inquiry. **People with bipolar disorder, diagnosed with both type I and II, reported that microdosing was helpful** for their depressive periods but not for their manic or hypomanic ones."

	31. W.I.P.O. Pat. App. No. 2018/135943 "Psilocybin and/or psilocin in combination with cannabinoids and/or terpenes" (Published July 26, 2018) From **claim 1** "**Psilocybin and/or psilocin** in combination with at least one cannabinoid and/or at least one terpene for use in the prevention or **treatment of a psychological disorder**, wherein the at least one cannabinoid and/or at least one terpene is administered separately, sequentially or simultaneously to the psilocybin and/or psilocin." From **claim 2** "**Psilocybin and/or psilocin** in combination with at least one cannabinoid and/or at least one terpene for use according to claim 1 , wherein the psychological disorder is chosen from depression, psychotic disorder, schizophrenia, schizophreniform disorder (acute schizophrenic episode); schizoaffective disorder; **bipolar I disorder** (mania, manic disorder, manic-depressive psychosis); bipolar II disorder; major depressive disorder with psychotic feature (psychotic depression); delusional disorders (paranoia); Shared Psychotic Disorder (Shared paranoia disorder); Brief Psychotic disorder (Other and Unspecified Reactive Psychosis); Psychotic disorder not otherwise specified (Unspecified Psychosis); paranoid personality disorder; schizoid personality disorder; schizotypal personality disorder, anxiety disorder, panic disorder, panic attacks, agoraphobia, attention deficit syndrome, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS)."
6. The method of claim 4, wherein the subject has bipolar disorder II.	10. KATALYST, "Microdosing for Seasonal Depression: An Experience with Mushrooms exp110358)" 2017; retrieved from Erowid. https://erowid.org/experiences/exp.php?ID=110358, retrieved May 18, 2017 "There are a few resources on the internet about **microdosing with psilocybin**, but none that provide guidance on how to approach it if you have bipolar disorder. Now that I've run this experiment on myself, I decided I would add my anecdote into the mix, hoping that it will help someone out in a similar situation…For context: I have a diagnosis of **Bipolar II and PTSD**… The sweet spot for me was 0.15g, every 2 weeks… At the dose I found to be best for me (0.15g), I sometimes felt mild euphoria in the mornings when I took it, but did not experience any of the other side effects noted above. Overall I would consider this a huge success."

7. The method of any one of claims 1 -6, wherein the depression is resistant to treatment.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "Objectives Here, we report on safety and efficacy outcomes for up to 6 months in an open-label trial of **psilocybin for treatment resistant depression.** Methods Twenty patients (six females) with (mostly) severe, unipolar, **treatment-resistant major depression received two oral doses of psilocybin (10 and 25 mg, 7 days apart)** in a supportive setting…**Psilocybin represents a promising paradigm for unresponsive depression** that warrants further research in double-blind randomised control trials." From **p. 401** "The main inclusion criteria were as follows: unipolar major **depression** of at least moderate severity (16+ on the 21-item HAM-D) and **no improvement despite two courses of pharmacologically distinct antidepressant medications for an adequate duration (6 weeks minimum) within the current episode.**"
8. The method of any one of claims 1 -7, wherein at least one sign or symptom of depression is reduced.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "Relative to baseline, **marked reductions in depressive symptoms were observed for the first 5 weeks post-treatment** (Cohen's $d = 2.2$ at week 1 and 2.3 at week 5, both $p < 0.001$)"
9. The method of claim 8, wherein the sign or symptom of depression is depressed mood, diminished interest in activities, weight loss or gain, decrease or increase in appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, diminished ability to concentrate or indecisiveness, or suicidal ideation or behavior.	17. W.I.P.O. Pat. App. No. 2018/195455 "Assessing and treating psychedelic-responsive subjects" (Published October 25, 2018) From **claim 41** "The method of claim 39 or 40, wherein the depressive disorder is associated with one or more prodromal symptoms selected from the group consisting of **depressed mood**, **decreased appetite**, **weight loss, increased appetite, weight gain, initial insomnia, middle insomnia**, early waking, hypersomnia, decreased energy, decreased interest or pleasure, self-blame, **decreased concentration**, **indecision**, **suicidality**, psychomotor agitation, **psychomotor retardation**, crying more frequently, inability to cry, hopelessness, worrying/brooding, decreased self-esteem, irritability, dependency, self-pity, somatic complaints, decreased effectiveness, helplessness, and decreased initiation of voluntary responses."

	From **claim 53** "The method of any one of claims 1 -52, wherein the psychedelic agent is selected from lysergic acid diethylamide, **psilocybin**, and pharmaceutically acceptable salts thereof." 1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 404** "**Suicidality scores on the QIDS-SR16 were significantly reduced 1 and 2 weeks post-treatment** (mean reductions at week 1 = − 0.9, 95% CI = − 0.4 to − 1.4, $p < 0.002$; mean reduction at week 2 = − 0.85, 95% CI = − 0.4 to − 1.3, $p = 0.004$), with trend decreases at 3 (mean reduction = − 0.8, 95% CI = − 0.25 to − 1.3, $p = 0.01$) and 5 weeks (mean reduction = − 0.7, 95% CI = − 0.22 to − 1.2, $p = 0.01$). **Scores on the suicide item of the HAM-D were significantly decreased 1-week post-treatment** (mean reduction = − 0.95, 95% CI = − 0.58 to − 1.3, $p < 0.001$), with 16 of 19 patients scoring 0 at this time point and none showing an increase from baseline nor scoring the maximum on this measure."
10. The method of claim 9, wherein the sign or symptom of depression is measured according to a diary assessment, an assessment by clinician or caregiver, a clinical rating scale, or by functional MRI.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 401** "SHAPS (anhedonia) was collected at 1 week and 3 months and **HAM-D (depression, clinician-administered) and GAF (global functioning, clinician administered**) ratings were collected at 1 week only." From **p. 401** "This comprised of informed consent, documenting mental and physical health backgrounds, **a psychiatric interview (MINI- 5) to confirm diagnosis**, physical examination, routine blood tests, ECG, urine test for drugs of abuse and pregnancy where relevant, a breathalyser and the completion of baseline assessments." From **p. 401** "Eligible patients attended a **pretreatment MRI scan** and psychological preparation visit, followed by two dosing sessions, separated by 1 week. In the first session, **patients received 10 mg psilocybin and in the second, 25 mg.** Patients were seen the following day for debriefing and a post-treatment MRI scan, and for one final time 1 week after the 25-mg session."
11. The method of claim 10, wherein the clinical depression rating scale is a Quick Inventory	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408.

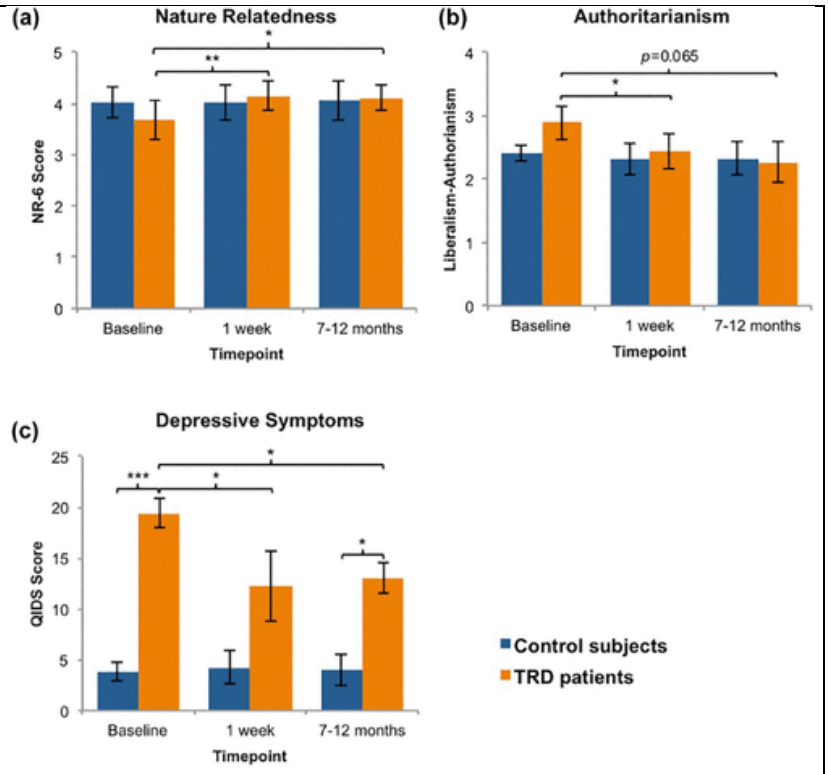
of Depressive Symptomatology (QIDS)-16 scale, a QIDS-16 daily scale, a Hamilton Depression Rating scale, a Beck Depression Inventory scale, a Montgomery-Asberg Depression Rating Scale, a Clinical Global Impression Scale, a Zung Self-Rating Depression Scale, a Raskin Depression Rating Scale, and/or Young Mania Rating Scale.	From **p. 400-401** "The primary outcome was mean change in the severity of self-reported (SR) depressive symptoms (**measured primarily with the 16-item Quick Inventory of Depressive Symptoms, QIDS-SR16**) from baseline to specific time points after the high-dose psilocybin session (henceforth referred to as 'post-treatment'). QIDS-SR16 ratings were collected 1–3 and 5 weeks and 3 and 6 months post-treatment, with 5 weeks post-treatment regarded as the primary endpoint. **BDI (depression)** and STAI (anxiety) ratings were collected at 1 week and 3 and 6 months. SHAPS (anhedonia) was collected at 1 week and 3 months and **HAM-D (depression, clinician-administered)** and GAF (global functioning, clinician administered) ratings were collected at 1 week only." From **p. 403** "Relative to baseline, **QIDS-SR16 scores were significantly reduced at all six post-treatment time points** ($p < 0.001$), with the maximum effect size at 5 weeks (− 9.2, 95%CI = − 11.8 to − 6.6, $t = -7.2$, $p < 0.001$, Cohen's $d = 2.3$) (see Fig. 1). Of the 19 patients who completed all assessments, all showed some reduction in depression severity at 1 week and these were sustained in the majority for 3–5 weeks. **Changes in HAM-D ratings from baseline to 1-week posttreatment showed a reasonable correspondence with changes in QIDS-SR16 data across the same period** ($r = 0.61$, $p < 0.001$) and the relationship between the QIDS-SR16 and BDI at 1 week was very strong ($r = 0.81$, $p < 0.001$)."
12. The method of claim 10, wherein the sign or symptom of depression is measured using a Spielberger's Trait and Anxiety Inventory, a Generalized Anxiety Disorder 7-Item Scale, a Warwick-Edinburgh Mental Wellbeing Scale, a Flourishing Scale, a Snaith Hamilton Anhedonia Pleasure Scale, a Life Orientation Test, a Meaning in Life Questionnaire, a Brief Resilience Scale, a Dysfunctional Attitudes Scale, a 44-item Big Five Inventory, a Peters 21 -item Delusional Inventory, an Examination of Anomalous Self- Experience, a Ruminative	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400-401** "The primary outcome was mean change in the severity of self-reported (SR) depressive symptoms (measured primarily with the 16-item Quick Inventory of Depressive Symptoms, QIDS-SR16) from baseline to specific time points after the high-dose psilocybin session (henceforth referred to as 'post-treatment'). QIDS-SR16 ratings were collected 1–3 and 5 weeks and 3 and 6 months post-treatment, with 5 weeks post-treatment regarded as the primary endpoint. BDI (depression) and **STAI (anxiety)** ratings were collected at 1 week and 3 and 6 months. **SHAPS (anhedonia)** was collected at 1 week and 3 months and HAM-D (depression, clinician-administered) and GAF (global functioning, clinician administered) ratings were collected at 1 week only."

Responses Scale, a White Bear Suppression Inventory, a Barrett Impulsivity Scale, a Brief Experiential Avoidance Questionnaire, a Modified Tellegen Absorption Questionnaire, a Scale to Assess Therapeutic Relationship, Credibility/Expectancy Questionnaire, a Connectedness to Nature Scale, a Political Perspective Questionnaire, a Social Connectedness Scale, a Bech-Rafaelsen Mania Rating Scale, a Revised Santa Clara brief compassion scale, a Gratitude Questionnaire, a Short Suggestibility Scale, a Rosenberg Self-Esteem Scale, a Universality Subscale of the Spiritual Transcendence Scale, an Oxford Questionnaire on the Emotional Side-effects of Antidepressants, a Lauks Emotional Intensity Scale, Sexual Dysfunction Questionnaire, a Brief Index of Sexual Functioning for Women, a Sexual Perceptions Questionnaire, a Barnes Akathisia Rating Scale, a Work Productivity and Activity Impairment Questionnaire, a Work and Social Adjustment Scale, a Connectedness Questionnaire, a Standard Assessment of Personality, a Positive and Negative Syndrome Scale, a Mastery Insight Scale, a Self-Reflection and Insight Scale, a Psychological Insight Scale, a Metaphysical Beliefs Questionnaire, a Spiritual Bypassing Scale, an Adverse Childhood Experience Questionnaire, a Therapeutic	

Music Experience Questionnaire, a Setting Questionnaire, an Absorption in Music Scale, a Psychedelic Predictor Scale, a Surrender Scale, a EuroQOL-5 Dimension-3 Level Scale, a Columbia-Suicide Severity Rating Scale, a Suicidal Ideation Attributes Scale, or any combinations thereof.	
13. The method of claim 10, wherein the functional MRI measures the amygdala blood oxygen level-dependent (BOLD) response.	11. CARHART-HARRIS (2017) "Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms" Scientific Reports. 7: 13187 From **p. 1** "Here, cerebral blood flow (CBF) and **blood oxygen-level dependent (BOLD)** resting-state functional connectivity (RSFC) were measured with **functional magnetic resonance imaging (fMRI) before and after treatment with psilocybin (serotonin agonist) for treatment resistant depression (TRD).** From **p. 2** "Based on previous findings of **increased amygdala blood flow** and metabolism in **depression**[25], reductions in amygdala CBF were compared with the **reductions in depressive symptoms** between scan 1 and 2 (i.e. decreased depressed mood at the time of scanning), and a significant relationship was found (r=0.59; p=0.01)."
14. The method of claim 13, wherein the BOLD response is measured at resting state, in response to emotional faces, and/or music as a hedonic stimulus.	12. BARRETT (2018) "Serotonin 2A Receptor Signaling Underlies LSD induced Alteration of the Neural Response to Dynamic Changes in Music" Cerebral Cortex. 28: 3939–3950 From **p. 3939** "In the current report, **blood oxygen level-dependent (BOLD) signal was collected during music listening** in 25 healthy adults after administration of placebo, **lysergic acid diethylamide (LSD),** and LSD pretreated with the 5HT2A antagonist ketanserin, to investigate the role of 5HT2A receptor signaling in the neural response to the time-varying tonal structure of music." From **p. 3945** "This might explain the increased salience of **music** that is anecdotally reported after the administration of **classic psychedelics, including LSD and psilocybin**"
15. The method of any one of claims 1 -14, wherein at least one sign or symptom of depression is alleviated within	3. GRIFFITHS (2011) "Psilocybin occasioned mystical-type experiences: Immediate and persisting dose-related effects" Psychopharmacology (Berl). 218(4): 649–665

24 hours of administration of the psilocybin.	From **p.3** "At about **7 hours after drug ingestion (when the primary drug effects had subsided), participants completed several questionnaires** designed to assess various aspects of hallucinogen experience (described below)." From **p.18** "Fig 1. Within session time-course of psilocybin. Systolic and diastolic blood pressure and monitor ratings of overall drug effect, and **joy/intense happiness as a function of time since capsule ingestion** (time 0 = before drug administration). Data points are means; filled data points indicate a significant difference from 0 mg/70 kg at the indicated time point (Planned Comparisons)." 
16. The method of any one of claims 1 -14, wherein at least one symptom of depression is alleviated within 1 week of administration of the psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 403** "Of the 19 patients who completed all assessments, **all showed some reduction in depression severity at 1 week and these were sustained in the majority for 3–5 weeks**."
17. The method of any one of claims 1-14, wherein at least one symptom of depression is alleviated for a period of at least 1 month after administration of the psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 403** "Of the 19 patients who completed all assessments, **all showed some reduction in depression severity** at 1 week and these were **sustained in the majority for 3–5 weeks**." From **p. 403** "**BDI scores were significantly reduced at** 1 week (mean reduction = − 22.7, 95% CI = − 17.6 to − 27.8, $p < 0.001$), **3 months** (mean reduction = − 15.3, 95% CI = − 8.7 to − 21.9, $p < 0.001$) and **6 months post-treatment** (mean reduction = − 14.9, 95% CI = − 8.7 to − 21.1, $p < 0.001$)"

18. The method of any one of claims 1 -14, wherein the at least one symptom of depression is alleviated for a period of at least 3 months after administration of the psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 403** "**BDI scores were significantly reduced at** 1 week (mean reduction = − 22.7, 95% CI = − 17.6 to − 27.8, p < 0.001), **3 months** (mean reduction = − 15.3, 95% CI = − 8.7 to − 21.9, p < 0.001) and **6 months post-treatment** (mean reduction = − 14.9, 95% CI = − 8.7 to − 21.1, p < 0.001)"
19. The method of any one of claims 1 -14, wherein the at least one symptom of depression is alleviated for a period of at least 12 months after administration of the psilocybin.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 619** "Here, we aimed to investigate the feasibility, safety, and efficacy of **psilocybin** in patients with unipolar **treatment-resistant depression.**" From **p.619** "Relative to baseline, **depressive symptoms were markedly reduced 1 week** (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, =0·002, Hedges' g=3·1) and **3 months** (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) after high-dose treatment." 13. AGIN-LEIBES (2020) "Long-term follow-up of psilocybin-assisted psychotherapy for psychiatric and existential distress in patients with life-threatening cancer" Journal of Psychopharmacology. 34(2) 155–166 From **p. 155** "Results: **Reductions in anxiety, depression**, hopelessness, demoralization, and death anxiety **were sustained at the first and second follow-ups**. Within-group effect sizes were large. **At the second (4.5 year) follow-up approximately 60–80% of participants met criteria for clinically significant antidepressant or anxiolytic responses**. Participants overwhelmingly (71–100%) attributed positive life changes to the **psilocybin**-assisted therapy experience and rated it among the most personally meaningful and spiritually significant experiences of their lives." 24. LYONS (2018) "Increased nature relatedness and decreased authoritarian political views after psilocybin for treatment-resistant depression" Journal of Psychopharmacology. 32(7) 811-819



From **p. 814** "Figure 1 (a) Nature relatedness. Patients reported being significantly more connected to nature 1 week ($t(6)=-4.242$, $p=0.003$) and 7–12 months ($t(5)=-2.707$, $p=0.021$) after psilocybin treatment compared with baseline. No significant difference was found for the controls at the first ($t(6)=0.008$, $p=0.994$) or second follow-ups ($t(5)=-1.228$, $p=0.274$). (b) Political perspective. Patients were significantly less authoritarian 1 week after psilocybin treatment ($t(6)=2.120$, $p=0.039$) and a trend-level decrease was found at 7–12 months ($t(5)=-1.811$, $p=0.065$) compared with baseline. No significant differences were found for the controls at the first ($t(6)=0.642$, $p=0.544$) or second follow-up ($t(5)=0.515$, $p=0.629$). **(c) Depressive symptoms.** Patients had significantly more depressive symptoms than controls at baseline ($U=0.0E0$, $p=0.001$). One week after psilocybin treatment, depressive symptoms were significantly reduced to levels more comparable with controls ($Z=-2.040$, $p=0.025$) as no significant between-groups differences were found ($U=10.000$, $p=0.062$). **The patients' depressive symptoms remained significantly reduced at the 7–12-months follow-up** ($Z=-1.782$, $p=0.038$); however, a between-groups difference was found ($U=3.500$, $p=0.020$). No significant differences were found for the control subjects at the first ($Z=-0.422$, $p=0.673$) or second ($Z=-0.137$, $p=0.891$) follow-ups compared with baseline. Data expressed as mean ± SEM [$p<0.05$*; $p\leq0.01$**; $p\leq0.001$***]"

20. The method of any one of claims 1 -19, wherein no other treatment is administered to the subject to reduce the sign or symptom of depression after administration of the psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "**No patients sought conventional antidepressant treatment within 5 weeks of psilocybin**." From **p. 401 "**With the exception of patient 2 (Table 1), **eligible patients medicated with an antidepressant were advised to stop this for the trial, to avoid suspected attenuation of psilocybin's effects (Bonson et al. 1996).** This was done in a tapered manner under careful supervision from the study psychiatrist. Washout occurred over at least 2 weeks prior to study entry, with the exception of patient 6, who stopped tramadol use only after the first psilocybin session (when the tramadol use was discovered)." From **p. 404** "With the exception of patient 2 (who remained on venlafaxine throughout the trial and also received CBT shortly afterwards), **no patients received additional treatments within 5 weeks of the 25-mg psilocybin dose**."
21. The method of any one of claims 1 -19, wherein the method further comprises administering to the subject at least one additional therapeutic to reduce the sign or symptom of depression.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 404** "With the exception of **patient 2 (who remained on venlafaxine throughout the trial and also received CBT shortly afterwards**), no patients received additional treatments within 5 weeks of the **25-mg psilocybin dose**."
22. The method of claim 21, wherein the at least one additional therapeutic is a selective serotonin reuptake inhibitor, a serotonin and norepinephrine reuptake inhibitor, a tricyclic antidepressant, a tetracyclic antidepressant, a dopamine reuptake inhibitor, a 5-HT|| receptor antagonist, a 5-HT| receptor antagonist, a 5-HT1 receptor antagonist, a monoamine oxidase inhibitor, or a noradrenergic antagonist.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 404** "With the exception of **patient 2 (who remained on venlafaxine throughout the trial** and also received CBT shortly afterwards), no patients received additional treatments within 5 weeks of the **25-mg psilocybin dose**." 14. DRUGS.COM, "VenlafaxinePronunciation" 2014; retrieved from Web.Archives, Drugs.com. http://web.archive.org/web/20140502180823/https://www.drugs.com/venlafaxine.html, retrieved May 02, 2014 "**Venlafaxine is an antidepressant** in a group of drugs called selective **serotonin and norepinephrine reuptake inhibitors (SSNRIs)**."

23. The method of claim 21 or 22, wherein the at least one additional therapeutic is administered prior to administration of psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 402** Employment status / Illness duration (years) / QIDS-16 / BDI / HAM-D / STAI / Past meds / Past psychotherapy Employed / 30 / 19 / 36 / 19 / 72 / SSRI (two), SNRI (two), NDRI, NSSRI, MAOI / None Unemployed / 25 / 20 / 33 / 28 / 76 / SSRI (two), SNRI, NDRI, NSSRI, Na + channel blocker (two), ketamine, TCA / CNT Employed / 17 / 22 / 22 / 18 / 63 / SSRI (two), SNRI / CBT, GT Studying / 10 / 14 / 26 / 18 / 67 / NDRI, NSSRI / CBT Unemployed / 12 / 19 / 38 / 25 / 71 / SSRI (three), TCA / CBT, MBT Unemployed / 29 / 19 / 39 / 23 / 78 / SSRI (four), SNRI, SARI / CS Unemployed / 27 / 18 / 33 / 22 / 57 / TCA, SARI / CS, MBT Employed / 17 / 19 / 39 / 17 / 71 / SSRI (two), TCA / CS Unemployed / 15 / 20 / 32 / 26 / 71 / SSRI (three), SNRI / CS, CBT Unemployed / 8 / 21 / 47 / 28 / 75 / SSRI (two), NSSRI / CS Employed / 15 / 18 / 24 / 16 / 72 / SSRI (four), SNRI (two), NDRI, MAOI, Na + channel blocker, SARI, DRI / CBT Employed / 8 / 21 / 35 / 17 / 68 / SSRI, TCA / CBT Employed / 7 / 18 / 29 / 26 / 55 / SSRI, TCA, SARI, NDRI / CBT Unemployed / 30 / 23 / 36 / 29 / 70 / SSRI (four), SNRI, TCA, NDRI / JA, GT Unemployed / 30 / 25 / 44 / 36 / 66 / SSRI, SARI / CBT Unemployed / 22 / 17 / 45 / 29 / 69 / SSRI (three), SARI (two), TCA / None Unemployed / 6 / 19 / 44 / 20 / 66 / SSRI, SNRI / None Part retired / 10 / 16 / 28 / 28 / 61 / SSRI (two), SARI / JA Retired / 15 / 17 / 42 / 24 / 74 / SSRI (two), TCA, pregabalin / JA Unemployed / 20 / 14 / 27 / 28 / 68 / SSRI (three), SARI, SNRI, Na + channel blocker, TCA, MAOI / CBT, MBT 11 Unemployed / 17.7 (8.5) / 19 (2.-7) / 35 (-7--4) / 23.9 (5.-4) / 68.5 (6.-0) / 4.6 (2.6) / 17 psychotherapy
24. The method of claim 21 or 22, wherein the at least one additional therapeutic is administered after administration of psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 404-405 "Six began new courses of antidepressant medication after the 3-month time point. Five received psychotherapy (CBT, psychodynamic, counselling and group therapy × 2) shortly before or after the 3-month period**"
25. The method of claim 21 or 22, wherein the at least one additional therapeutic is administered on the same day as the psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 404** "With the exception of **patient 2 (who remained on venlafaxine throughout the trial** and also received CBT shortly afterwards), no patients received additional treatments within 5 weeks of the **25-mg psilocybin dose**."

	14. DRUGS.COM, "VenlafaxinePronunciation" 2014; retrieved from Web.Archives, Drugs.com. http://web.archive.org/web/20140502180823/https://www.drugs.com/venlafaxine.html, retrieved May 02, 2014 "Venlafaxine should be taken with food. **Try to take venlafaxine at the same time each day.**"
26. The method of any one of claims 1 -25, wherein the subject has no prior psilocybin exposure.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 402** Employment status | Illness duration (years) | QIDS-16 | BDI | HAM-D | STAI | Past meds | Past psychotherapy Employed | 30 | 19 | 36 | 19 | 72 | SSRI (two), SNRI (two), NDRI, NSSRI, MAOI | None Unemployed | 25 | 20 | 33 | 28 | 76 | SSRI (two), SNRI, NDRI, NSSRI, Na + channel blocker (two), ketamine, TCA | CNT Employed | 17 | 22 | 22 | 18 | 63 | SSRI (two), SNRI | CBT, GT Studying | 10 | 14 | 26 | 18 | 67 | NDRI, NSSRI | CBT Unemployed | 12 | 19 | 38 | 25 | 71 | SSRI (three), TCA | CBT, MBT Unemployed | 29 | 19 | 39 | 23 | 78 | SSRI (four), SNRI, SARI | CS Unemployed | 27 | 18 | 33 | 22 | 57 | TCA, SARI | CS, MBT Employed | 17 | 19 | 39 | 17 | 71 | SSRI (two), TCA | CS Unemployed | 15 | 20 | 32 | 26 | 71 | SSRI (three), SNRI | CS, CBT Unemployed | 8 | 21 | 47 | 28 | 75 | SSRI (two), NSSRI | CS Employed | 15 | 18 | 24 | 16 | 72 | SSRI (four), SNRI (two), NDRI, MAOI, Na + channel blocker, SARI, DRI | CBT Employed | 8 | 21 | 35 | 17 | 68 | SSRI, TCA | CBT Employed | 7 | 18 | 29 | 26 | 55 | SSRI, TCA, SARI, NDRI | CBT Unemployed | 30 | 23 | 36 | 29 | 70 | SSRI (four), SNRI, TCA, NDRI | JA, GT Unemployed | 30 | 25 | 44 | 36 | 66 | SSRI, SARI | CBT Unemployed | 22 | 17 | 45 | 29 | 69 | SSRI (three), SARI (two), TCA | None Unemployed | 6 | 19 | 44 | 20 | 66 | SSRI, SNRI | None Part retired | 10 | 16 | 28 | 28 | 61 | SSRI (two), SARI | JA Retired | 15 | 17 | 42 | 24 | 74 | SSRI (two), TCA, pregabalin | JA Unemployed | 20 | 14 | 27 | 28 | 68 | SSRI (three), SARI, SNRI, Na + channel blocker, TCA, MAOI | CBT, MBT 11 Unemployed | 17.7 (8.5) | 19 (2.-7) | 35 (-7--4) | 23.9 (5.-4) | 68.5 (6.-0) | 4.6 (2.6) | 17 psychotherapy
27. The method of any one of claims 1 -25, wherein the subject has prior psilocybin exposure.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 402**

	Employment status | Illness duration (years) | QIDS-16 | BDI | HAM-D | STAI | Past meds | Past psychotherapy Employed | 30 | 19 | 36 | 19 | 72 | SSRI (two), SNRI (two), NDRI, NSSRI, MAOI | None Unemployed | 25 | 20 | 33 | 28 | 76 | SSRI (two), SNRI, NDRI, NSSRI, Na + channel blocker (two), ketamine, TCA | CNT Employed | 17 | 22 | 22 | 18 | 63 | SSRI (two), SNRI | CBT, GT Studying | 10 | 14 | 26 | 18 | 67 | NDRI, NSSRI | CBT Unemployed | 12 | 19 | 38 | 25 | 71 | SSRI (three), TCA | CBT, MBT Unemployed | 29 | 19 | 39 | 23 | 78 | SSRI (four), SNRI, SARI | CS Unemployed | 27 | 18 | 33 | 22 | 57 | TCA, SARI | CS, MBT Employed | 17 | 19 | 39 | 17 | 71 | SSRI (two), TCA | CS Unemployed | 15 | 20 | 32 | 26 | 71 | SSRI (three), SNRI | CS, CBT Unemployed | 8 | 21 | 47 | 28 | 75 | SSRI (two), NSSRI | CS Employed | 15 | 18 | 24 | 16 | 72 | SSRI (four), SNRI (two), NDRI, MAOI, Na + channel blocker, SARI, DRI | CBT Employed | 8 | 21 | 35 | 17 | 68 | SSRI, TCA | CBT Employed | 7 | 18 | 29 | 26 | 55 | SSRI, TCA, SARI, NDRI | CBT Unemployed | 30 | 23 | 36 | 29 | 70 | SSRI (four), SNRI, TCA, NDRI | JA, GT Unemployed | 30 | 25 | 44 | 36 | 66 | SSRI, SARI | CBT Unemployed | 22 | 17 | 45 | 29 | 69 | SSRI (three), SARI (two), TCA | None Unemployed | 6 | 19 | 44 | 20 | 66 | SSRI, SNRI | None Part retired | 10 | 16 | 28 | 28 | 61 | SSRI (two), SARI | JA Retired | 15 | 17 | 42 | 24 | 74 | SSRI (two), TCA, pregabalin | JA Unemployed | 20 | 14 | 27 | 28 | 68 | SSRI (three), SARI, SNRI, Na + channel blocker, TCA, MAOI | CBT, MBT 11 Unemployed | 17.7 (8.5) | 19 (2.-7) | 35 (-7-.-4) | 23.9 (5.-4) | 68.5 (6.-0) | 4.6 (2.6) | 17 psychotherapy
28. The method of any one of claims 1 -27, wherein the subject has an additional comorbidity or disorder.	10. KATALYST, "Microdosing for Seasonal Depression: An Experience with Mushrooms exp110358)" 2017; retrieved from Erowid. https://erowid.org/experiences/exp.php?ID=110358, retrieved May 18, 2017 "There are a few resources on the internet about **microdosing with psilocybin**, but none that provide guidance on how to approach it if you have bipolar disorder. Now that I've run this experiment on myself, I decided I would add my anecdote into the mix, hoping that it will help someone out in a similar situation…For context: I have a diagnosis of **Bipolar II and PTSD**… I have gotten **seasonal depression every year** of my life from around November until April, without exception…The sweet spot for me was 0.15g, every 2 weeks… At the dose I found to be best for me (0.15g), I sometimes felt mild euphoria in the mornings when I took it, but did not experience any of the other side effects noted above. Overall I would consider this a huge success."
29. The method of claim 28, wherein the subject has an anxiety disorder, an obsessive-compulsive disorder, alcoholism, a personality disorder, a cardiovascular	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "Psilocybin has shown promise in the treatment of **obsessive compulsive disorder** (Moreno et al. 2006), **alcohol** (Bogenschutz et al. 2015) and tobacco addiction (Johnson et al.

disease, a neurological disease, or cancer.	2014) and **anxiety related to terminal diagnoses** (Griffiths et al. 2016; Ross et al. 2016; Grob et al. 2011)." From **p. 405** "Two recent double-blind randomised control trials (RCTs) of **psilocybin for depression and anxiety symptoms in a combined sample of 80 patients with life-threatening cancer found consistent safety and efficacy outcomes** with those reported here (Griffiths et al. 2016; Ross et al. 2016)." 2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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." From **p. 619** "Relative to baseline, **depressive symptoms were markedly reduced 1 week** (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**. Marked and sustained **improvements in anxiety and anhedonia** were also noted."
30. The method of claim 29, wherein the neurological disease is dementia, Alzheimer's Disease, or Parkinson's Disease.	7. U.S. Pat. App. Pub. No. 2021/0267966A1 "Method of Inducing Dendritic and Synaptic Genesis in Neurodegenerative Chronic Diseases" (Published September 2, 2021) From **claim 1** "A method of inducing neuron dendritic and synaptic genesis in neurodegenerative diseases by administering one or more tryptamine molecules or pharmaceutically acceptable salts thereof, to a patient in suffering from a neurodegenerative disease. From **claim 2** "The method according to claim 1, wherein said one or more tryptamine molecules is selected from the group consisting of lysergic acid diethylamide, N, N-dimethyltryptamine, 5-methoxy-N, N-dimethyltryptamine, mescaline, psilocin, 3,4-methylenedioxymethamphetamine, and **psilocybin**, pharmaceutically acceptable salts thereof and combinations thereof. From **claim 4** "The method according to claim 1, wherein said neurodegenerative disease is a chronic condition." From **claim 5** "The method according to claim 4, wherein said chronic neurodegenerative disease is selected from the group consisting of dementia, **Alzheimer's disease, Parkinson's disease,**

	frontal temporal **dementia**, Huntington's disease and multiple Sclerosis." 16. U.S. Pat. App. Pub. No. 2016/0331725 "Use of compounds that are able to increase the serum igf-1 level for the preparation of a therapeutical composition for treatment of various disease states associated with a reduced igf-1 serum level in humans and animals" (Published November 17, 2016) From **claim 1** "A method comprising: using one or more compounds that are capable of activating the hypothalamus in an individual to increase the serum level of Growth Hormone Releasing Hormone (GHRH), which, in turn, leads to an increase in the secretion of growth hormone (GH) and the subsequent rise of the serum level of insulin-like growth factor 1 (IGF-1) for the preparation of a therapeutical composition for the treatment of serious fatigue and exhaustion symptoms, burn-out, chronic fatigue syndrome, depression, **Alzheimer disease**, irritated bowel syndrome, osteoporosis, type 2 diabetes, or for anti-aging therapy, immune therapy and for stimulating recovery after physical exercise in humans or for stimulating growth and the immune system in animals. From **claim 5** "The method as claimed in claim 1, wherein the compound is a precursor of indole acetic acid selected from the group consisting of tryptophan, 4-hydroxytryptophan, 4-methoxytryptophan, 5-hydroxytryptophan, 5-methoxytryptophan, 6-hydroxytryptophan, 6-methoxytryptophan, 7-hydroxytryptophan, 7-methoxytryptophan, hypaphorine, tryptamine, 4-hydroxytryptamine, 4-methoxytryptamine, psilocin (4-hydroxy, dimethyl tryptamine), **psilocybin** (4-phosphate, dimethyl-tryptamine), baeocystin, serotonin (5-hydroxytryptamine), 5-methoxytryptamine, bufotenine (dimethylserotonine), O-methylbufotenine, melatonin, 6-hydroxytryptamine, 6-methoxytryptamine, 7-hydroxytryptamine, 7-methoxytryptamine, indole butyric acid and indole-3-pyruvate."
31. The method of any one of claims 28-30, wherein reducing at least one sign or symptom of depression in the subject treats or prevents one or more comorbidities or disorders in the subject.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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."

	From **p. 619** "Relative to baseline, **depressive symptoms were markedly reduced** 1 week (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**. Marked and sustained **improvements in anxiety and anhedonia** were also noted." 1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 405** "Two recent double-blind randomised control trials (RCTs) of **psilocybin for depression and anxiety symptoms in a combined sample of 80 patients with life-threatening cancer found consistent safety and efficacy outcomes** with those reported here (Griffiths et al. 2016; Ross et al. 2016)."
32. The method of any one of claims 1 -31, wherein the subject is a mammal.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "Methods **Twenty patients (six females)** with (mostly) severe, unipolar, treatment-resistant major **depression** received two oral doses of **psilocybin** (10 and 25 mg, 7 days apart) in a supportive setting.
33. The method of claim 32, wherein the subject is human.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "Methods **Twenty patients (six females)** with (mostly) severe, unipolar, treatment-resistant major **depression** received two oral doses of **psilocybin** (10 and 25 mg, 7 days apart) in a supportive setting.
34. The method of any of claims 1 -33, wherein the psilocybin is administered in a dosage form comprising a therapeutically effective amount of highly pure crystalline psilocybin in the form of Polymorph A, wherein the crystalline psilocybin comprises at least 90% by weight of Polymorph A.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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." From **p. 619** "Relative to baseline, **depressive symptoms were markedly reduced** 1 week (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2,

	95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**." 15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "**Sample 10415-25 (4) was provided by the Johns Hopkins University School of Medicine clinical pharmacy**. The psilocybin was **originally synthesized by Dr David Nichols** (Purdue University, Lafayette, IN, USA) and distributed to Johns Hopkins University and the University of New Mexico for use in human clinical trials… **This lot of psilocybin supported several clinical trials (Bogenschutz et al., 2015; Barrett et al., 2018; Griffiths et al., 2006, 2016).**" From **p. 12**

	Table 8 Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Code | Sample name | Hydrate A (%) | Polymorph A (%) | Polymorph B (%) 1 | RTI-1823-17-15 | 100 | – | 2 | Folen | 4.5 (4) | 85.9 (54) | 9.6 (30) 3 | USP 0274-F | 100 | – | – 4[a] | 10415-25 | 0.3 (1) | 99.7 (6) | – 4[b] | 10415-25 | 0.2 (1) | 99.8 (19) | – 5 | Ψ-67-2 | 6.5 (1) | 80.9 (22) | 12.5 (10) 6 | Ψ-81-1 | 100 | – | – 7 | Ψ-97-1 | 0.2 (1) | 99.8 (17) | – 8 | *Polymorph A* | – | 80.9 (6) | 19.1 (7) 9 | *Polymorph A′* | – | 99.7 (8) | 0.3 (3) 10 | Hydrate A | 100 | 11 | Polymorph B | – | – | 100 12 | SPS5107/20/1 | 0.1 (1) | 99.9 (10) | – 13 | 17/44/136G | 0.1 (1) | 99.1 (13) | – 14 | 17/44/132E | – | 100.0 (11) | – 15 | 17/44/116*Z* | 0.1 (1) | 99.1 (12) | – 16 | 17/44/123*L* | 0.2 (1) | 99.8 (11) | – 17 | 800325750 | 0.2 (1) | 99.8 (25) | – 18 | 800326600 | 0.2 (1) | 99.8 (10) | – 19 | ARN-19-002654 | – | 100 | – 20 | CG002E-035-04 | 100 | – | – 21 | CG-0019E-038-03 | – | – | 100 22 | PL005E-004-40C | – | 100 | – 23 | PL005E-004-45C | – | 91.7 (7) | 8.3 (4) 24 | PL005E-004-55C | – | 77.4 (8) | 22.6 (5) Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry. 3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197. From **p. 1195** "Acknowledgements The authors thank **David Nichols PhD for synthesizing the psilocybin**, Una McCann MD for support in protocol development and initiation, Michael Bogenschutz MD, John Rotrosen MD, Charles Raison MD, Darrick May MD and Fred Barrett PhD for helpful comments on the manuscript. We thank Linda Felch MA for statistical analysis."
35. The method of claim 34, wherein the crystalline	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20

<table>
<tr>
<td>psilocybin comprises at least 95% by weight of Polymorph A.</td>
<td>From p. 7 “2.3.6. Polymorph A, Polymorph A’, Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for Compass Pathways’ Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019) [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin).”

From p. 12
Table 8
Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA.

The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.
<table>
<tr><th>Code</th><th>Sample name</th><th>Hydrate A (%)</th><th>Polymorph A (%)</th><th>Polymorph B (%)</th></tr>
<tr><td>1</td><td>RTI-1823-17-15</td><td>100</td><td>–</td><td></td></tr>
<tr><td>2</td><td>Folen</td><td>4.5 (4)</td><td>85.9 (54)</td><td>9.6 (30)</td></tr>
<tr><td>3</td><td>USP 0274-F</td><td>100</td><td>–</td><td>–</td></tr>
<tr><td>4[a]</td><td>10415-25</td><td>0.3 (1)</td><td>99.7 (6)</td><td>–</td></tr>
<tr><td>4[b]</td><td>10415-25</td><td>0.2 (1)</td><td>99.8 (19)</td><td>–</td></tr>
<tr><td>5</td><td>Ψ-67-2</td><td>6.5 (1)</td><td>80.9 (22)</td><td>12.5 (10)</td></tr>
<tr><td>6</td><td>Ψ-81-1</td><td>100</td><td>–</td><td>–</td></tr>
<tr><td>7</td><td>Ψ-97-1</td><td>0.2 (1)</td><td>99.8 (17)</td><td>–</td></tr>
<tr><td>8</td><td>Polymorph A</td><td>–</td><td>80.9 (6)</td><td>19.1 (7)</td></tr>
<tr><td>9</td><td>Polymorph A′</td><td>–</td><td>99.7 (8)</td><td>0.3 (3)</td></tr>
<tr><td>10</td><td>Hydrate A</td><td>100</td><td></td><td></td></tr>
<tr><td>11</td><td>Polymorph B</td><td>–</td><td>–</td><td>100</td></tr>
<tr><td>12</td><td>SPS5107/20/1</td><td>0.1 (1)</td><td>99.9 (10)</td><td>–</td></tr>
<tr><td>13</td><td>17/44/136G</td><td>0.1 (1)</td><td>99.1 (13)</td><td>–</td></tr>
<tr><td>14</td><td>17/44/132E</td><td>–</td><td>100.0 (11)</td><td>–</td></tr>
<tr><td>15</td><td>17/44/116Z</td><td>0.1 (1)</td><td>99.1 (12)</td><td>–</td></tr>
<tr><td>16</td><td>17/44/123L</td><td>0.2 (1)</td><td>99.8 (11)</td><td>–</td></tr>
<tr><td>17</td><td>800325750</td><td>0.2 (1)</td><td>99.8 (25)</td><td>–</td></tr>
<tr><td>18</td><td>800326600</td><td>0.2 (1)</td><td>99.8 (10)</td><td>–</td></tr>
<tr><td>19</td><td>ARN-19-002654</td><td>–</td><td>100</td><td>–</td></tr>
<tr><td>20</td><td>CG002E-035-04</td><td>100</td><td>–</td><td>–</td></tr>
<tr><td>21</td><td>CG-0019E-038-03</td><td>–</td><td>–</td><td>100</td></tr>
<tr><td>22</td><td>PL005E-004-40C</td><td>–</td><td>100</td><td>–</td></tr>
<tr><td>23</td><td>PL005E-004-45C</td><td>–</td><td>91.7 (7)</td><td>8.3 (4)</td></tr>
<tr><td>24</td><td>PL005E-004-55C</td><td>–</td><td>77.4 (8)</td><td>22.6 (5)</td></tr>
</table>
Notes: (a) Sample analyzed by PXRD with transmission geometry. (b) Sample analyzed by PXRD with reflection geometry.</td>
</tr>
<tr>
<td>36. The method of claim 34 or 35, wherein the crystalline psilocybin has a chemical purity of greater than 97% by HPLC,</td>
<td>15. SHERWOOD (2021) “Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples” Acta Crystallographica. 78(1) 1-20</td>
</tr>
</table>

and no single impurity of greater than 1 %.	From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for **Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019)** [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)**." From **p. 18** "The QPA by RM also shed light on what was described as an unexpected result in the same patent application by providing compelling evidence that **a phase impurity, Polymorph B**, was responsible for the minor PXRD reflection at 17.5° 2θ observed from psilocybin produced in large-scale batches." From **p. 12**

	Table 8 Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Code | Sample name | Hydrate A (%) | Polymorph A (%) | Polymorph B (%) 1 | RTI-1823-17-15 | 100 | – | 2 | Folen | 4.5 (4) | 85.9 (54) | 9.6 (30) 3 | USP 0274-F | 100 | – | – 4[a] | 10415-25 | 0.3 (1) | 99.7 (6) | – 4[b] | 10415-25 | 0.2 (1) | 99.8 (19) | – 5 | Ψ-67-2 | 6.5 (1) | 80.9 (22) | 12.5 (10) 6 | Ψ-81-1 | 100 | – | – 7 | Ψ-97-1 | 0.2 (1) | 99.8 (17) | – 8 | *Polymorph A* | – | 80.9 (6) | 19.1 (7) 9 | *Polymorph A′* | – | 99.7 (8) | 0.3 (3) 10 | Hydrate A | 100 | 11 | Polymorph B | – | – | 100 12 | SPS5107/20/1 | 0.1 (1) | 99.9 (10) | – 13 | 17/44/136G | 0.1 (1) | 99.1 (13) | – 14 | 17/44/132E | – | 100.0 (11) | – 15 | 17/44/116Z | 0.1 (1) | 99.1 (12) | – 16 | 17/44/123L | 0.2 (1) | 99.8 (11) | – 17 | 800325750 | 0.2 (1) | 99.8 (25) | – 18 | 800326600 | 0.2 (1) | 99.8 (10) | – 19 | ARN-19-002654 | – | 100 | – 20 | CG002E-035-04 | 100 | – | – 21 | CG-0019E-038-03 | – | – | 100 22 | PL005E-004-40C | – | 100 | – 23 | PL005E-004-45C | – | 91.7 (7) | 8.3 (4) 24 | PL005E-004-55C | – | 77.4 (8) | 22.6 (5) Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.
37. The method of any one of claims 1 -33, wherein the psilocybin is administered in a dosage form comprising a therapeutically effective amount of highly pure crystalline psilocybin in the form of Polymorph A, wherein the crystalline psilocybin has a chemical purity of greater than 97% by HPLC, and no single impurity of greater than 1 %.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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." From **p. 619** "Relative to baseline, **depressive symptoms were markedly reduced** 1 week (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**."

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	Table 8 Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

Code	Sample name	Hydrate A (%)	Polymorph A (%)	Polymorph B (%)
1	RTI-1823-17-15	100	–	
2	Folen	4.5 (4)	85.9 (54)	9.6 (30)
3	USP 0274-F	100	–	–
4[a]	10415-25	0.3 (1)	99.7 (6)	–
4[b]	10415-25	0.2 (1)	99.8 (19)	–
5	Ψ-67-2	6.5 (1)	80.9 (22)	12.5 (10)
6	Ψ-81-1	100	–	–
7	Ψ-97-1	0.2 (1)	99.8 (17)	–
8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116Z	0.1 (1)	99.1 (12)	–
16	17/44/123L	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

38. The method of claim 37, wherein the highly pure crystalline psilocybin comprises at least 90% by weight of Polymorph A.	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for **Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019)** [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)**." From **p. 8** "**Samples 12–18 were provided by Usona Institute and were obtained from batches of psilocybin produced during**

	chemistry process development. Samples were recrystallized from aqueous acetone or pure water as reported in Sherwood et al. (2020)" From **p. 12** **Table 8** Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Code | Sample name | Hydrate A (%) | Polymorph A (%) | Polymorph B (%) 1 | RTI-1823-17-15 | 100 | – | 2 | Folen | 4.5 (4) | 85.9 (54) | 9.6 (30) 3 | USP 0274-F | 100 | – | – 4[a] | 10415-25 | 0.3 (1) | 99.7 (6) | – 4[b] | 10415-25 | 0.2 (1) | 99.8 (19) | – 5 | Ψ-67-2 | 6.5 (1) | 80.9 (22) | 12.5 (10) 6 | Ψ-81-1 | 100 | – | – 7 | Ψ-97-1 | 0.2 (1) | 99.8 (17) | – 8 | *Polymorph A* | – | 80.9 (6) | 19.1 (7) 9 | *Polymorph A′* | – | 99.7 (8) | 0.3 (3) 10 | Hydrate A | 100 | 11 | Polymorph B | – | – | 100 12 | SPS5107/20/1 | 0.1 (1) | 99.9 (10) | – 13 | 17/44/136G | 0.1 (1) | 99.1 (13) | – 14 | 17/44/132E | – | 100.0 (11) | – 15 | 17/44/116*Z* | 0.1 (1) | 99.1 (12) | – 16 | 17/44/123*L* | 0.2 (1) | 99.8 (11) | – 17 | 800325750 | 0.2 (1) | 99.8 (25) | – 18 | 800326600 | 0.2 (1) | 99.8 (10) | – 19 | ARN-19-002654 | – | 100 | – 20 | CG002E-035-04 | 100 | – | – 21 | CG-0019E-038-03 | – | – | 100 22 | PL005E-004-40C | – | 100 | – 23 | PL005E-004-45C | – | 91.7 (7) | 8.3 (4) 24 | PL005E-004-55C | – | 77.4 (8) | 22.6 (5) Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.
39. The method of claim 38, wherein the highly pure crystalline psilocybin comprises at least 95% by weight of Polymorph A.	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for **Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019)** [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing**

	crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)." From **p. 8** "**Samples 12–18 were provided by Usona Institute and were obtained from batches of psilocybin produced during chemistry process development**. Samples were recrystallized from aqueous acetone or pure water as reported in Sherwood et al. (2020)" From **p. 12** **Table 8** Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.

Code	Sample name	Hydrate A (%)	Polymorph A (%)	Polymorph B (%)
1	RTI-1823-17-15	100	–	
2	Folen	4.5 (4)	85.9 (54)	9.6 (30)
3	USP 0274-F	100	–	–
4[a]	10415-25	0.3 (1)	99.7 (6)	–
4[b]	10415-25	0.2 (1)	99.8 (19)	–
5	Ψ-67-2	6.5 (1)	80.9 (22)	12.5 (10)
6	Ψ-81-1	100	–	–
7	Ψ-97-1	0.2 (1)	99.8 (17)	–
8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116*Z*	0.1 (1)	99.1 (12)	–
16	17/44/123*L*	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

40. The method of any one of claims 34-39, wherein the highly pure crystalline psilocybin is further characterized having either: (i) a water content of <0.5% w/w; or	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 2** "Kuhnert-Brandsta¨ tter & Heindl (1976), using IR spectroscopy and differential scanning calorimetry (DSC), showed

(ii) <0.5% w/w loss in the TGA thermogram between 25° C and 200° C.	that both dehydration of a psilocybin hydrate and desolvation of the methanol solvate gave rise to the same anhydrous form rather than two different polymorphs. In the same report, the authors noted that the commercial drug provided by Sandoz was received as the common desolvated/anhydrous form. In addition, the authors described the preparation of the hydrated form by crystallization from water or from organic solvents with a **low water content**, which resulted in thin needle-shaped crystals" From **p. 12** **Table 8** Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.

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8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116*Z*	0.1 (1)	99.1 (12)	–
16	17/44/123*L*	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

32. KUHNERT (1976) "Polymorphe Modifikationen und Solvate von Psilocin und Psilocybin" Aus dem Institut fur Pharmakognosie der Universitiit Innsbruck. 309(76): 625-631

<table>
<tr>
<td></td>
<td>From p. 628 “Preparation of the solvates. The preferred form is the hydrate. It crystallizes from water as well as from organic solvents with a low water content.”

30. PARK (2021) “Characterization of Psilocybin” Retrieved from Triclinic Labs Report. Report Number: R2021638.01, Retrieved December 2, 2021

From p. 2
This report summarizes testing of psilocybin by X-ray powder diffraction (XRPD) and thermogravimetry analysis (TGA). The sample received and filenames of associated analytical testing are listed in Table 1. The sample was analyzed as received. The test results showed that psilocybin was anhydrous crystalline material.

Table 1. Sample, filenames of associated testing and results.
<table>
<tr><th>Sample Name</th><th>Lot Number</th><th>Triclinic Sample Number</th><th>Analytical Test[a]</th><th>Filename</th><th>Results</th></tr>
<tr><td rowspan="3">Psilocybin</td><td rowspan="3">10415-25 (Johns Hopkins; protocol number 1909)</td><td rowspan="3">TCL15312</td><td rowspan="2">XRPD</td><td>RX3-11622 (reflection)</td><td rowspan="2">crystalline</td></tr>
<tr><td>RX1-28949 (transmission)</td></tr>
<tr><td>TGA</td><td>TG3.1712</td><td>0.1% weight loss between 25-200°C</td></tr>
</table>
a. XRPD = X-ray powder diffraction, TGA = thermogravimetric analysis.</td>
</tr>
<tr>
<td>41. The method of any one of claims 34-40, wherein the highly pure crystalline psilocybin is further characterized by an endothermic event in a DSC thermogram having a first onset temperature of between 145°C and 155°C and a second onset temperature of between 205 and 220°C.</td>
<td>15. SHERWOOD (2021) “Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples” Acta Crystallographica. 78(1) 1-20

From p. 3 “More recently, synthetic process development efforts (Kargbo et al., 2020; Londesbrough et al., 2019) provided additional systematic characterization of Hydrate A and the corresponding anhydrate Polymorph A by PXRD (Fig. 1). These hydrate and anhydrate forms are expected to have been originally observed by Kuhnert-Brandstätter and Heindl, given the consistent DSC thermograms and analogous preparation conditions using aqueous crystallization to give the hydrate followed by vacuum drying to the anhydrous form (Fig. 2).”

32. KUHNERT (1976) “Polymorphe Modifikationen und Solvate von Psilocin und Psilocybin” Aus dem Institut fur Pharmakognosie der Universitiit Innsbruck. 309(76): 625-631

From p. 629</td>
</tr>
</table>

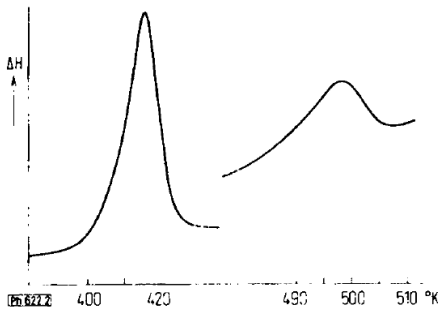

Abb. 2: DSC-Thermogramm: Psilocybin-Methanolsolvat

42. The method of any one of claims 34-41 , wherein the highly pure crystalline psilocybin is further characterized by one or more of the following: (a) ~~a loss on drying of no more than 2% w/w;~~ (b) residue on ignition of no more than 0.5% w/w; (c) assay (on a dry basis) of 95-103% by weight as measured by HPLC; (d) residual solvent content of no more than ~~3000 ppm methanol;~~ 5000 ppm ethanol, 720 ppm THF, and 890 ppm toluene, as measured by HRGC; (e) phosphoric acid content of no more than 1 % w/w as measured by 31 P NMR; and (f) Inductively Coupled Plasma Mass Spectrometry (ICP-MS) elemental analysis of: (i) no more than 1.5ppm Cd; (ii) no more than 1.5ppm Pb; (iii) no more than 4.5ppm As; (iv) no more than 9.0ppm Hg; (v) no more than 15ppm Co; (vi) no more than 30ppm V; (vii) no more than 60ppm Ni; (viii) no more than 165ppm Li; and (ix) no more than 30ppm Pd.

15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20

From **p. 12**

Table 8

Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA.

The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.

Code	Sample name	Hydrate A (%)	Polymorph A (%)	Polymorph B (%)
1	RTI-1823-17-15	100	–	
2	Folen	4.5 (4)	85.9 (54)	9.6 (30)
3	USP 0274-F	100	–	–
4[a]	10415-25	0.3 (1)	99.7 (6)	–
4[b]	10415-25	0.2 (1)	99.8 (19)	–
5	Ψ-67-2	6.5 (1)	80.9 (22)	12.5 (10)
6	Ψ-81-1	100	–	–
7	Ψ-97-1	0.2 (1)	99.8 (17)	–
8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116*Z*	0.1 (1)	99.1 (12)	–
16	17/44/123*L*	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
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Sample Name	Lot Number	Triclinic Sample Number	Analytical Test[a]	Filename	Results
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				RX1-28949 (transmission)	
			TGA	TG3.1712	0.1% weight loss between 25-200°C

a. XRPD = X-ray powder diffraction, TGA = thermogravimetric analysis.

33. ICH (2017) “Q3C — Tables and List Guidance for Industry” U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER) Revision 3. Retrieved June 2017

From **p. 6**

	Contains Nonbinding Recommendations Solvents in Class 2 (Table 2) should be limited in pharmaceutical products because of their inherent toxicity. PDEs are given to the nearest 0.1 mg/day, and concentrations are given to the nearest 10 ppm. The stated values do not reflect the necessary analytical precision of determination. Precision should be determined as part of the validation of the method. **Table 2. – Class 2 Solvents in Pharmaceutical Products** **Solvent** / **PDE (mg/day)** / **Concentration Limit (ppm)** Acetonitrile 4.1 410 Chlorobenzene 3.6 360 Chloroform 0.6 60 Cyclohexane 38.8 3,880 Cumene 0.7 70 1,2-Dichloroethene 18.7 1,870 Dichloromethane 6.0 600 1,2-Dimethoxyethane 1.0 100 N,N-Dimethylacetamide 10.9 1,090 N,N-Dimethylformamide 8.8 880 1,4-Dioxane 3.8 380 2-Ethoxyethanol 1.6 160 Ethyleneglycol 6.2 620 Formamide 2.2 220 Hexane 2.9 290 Methanol 30.0 3,000 2-Methoxyethanol 0.5 50 Methylbutylketone 0.5 50 Methylcyclohexane 11.8 1,180 Methylisobutylketone[2] 45 4,500 N-Methylpyrrolidone 5.3 530 Nitromethane 0.5 50 Pyridine 2.0 200 Sulfolane 1.6 160 Tetrahydrofuran 7.2 720 Tetralin 1.0 100 [2] The information included for Methylisobutylketone reflects that included in the *Revision of PDE Information for Methylisobutylketone*, which reached *Step 4* in November 2016 and was subsequently incorporated into the core guidance. 6
43. The method of any one of claims 34-42, wherein the highly pure crystalline psilocybin has no single impurity of greater than 0.5%.	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 18** "The QPA by RM also shed light on what was described as an unexpected result in the same patent application by providing compelling evidence that **a phase impurity, Polymorph B**, was responsible for the minor PXRD reflection at 17.5° 2θ observed from psilocybin produced in large-scale batches." From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for **Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in**

Londesbrough et al. (2019) [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)**."

From **p. 8** "**Samples 12–18 were provided by Usona Institute and were obtained from batches of psilocybin produced during chemistry process development**. Samples were recrystallized from aqueous acetone or pure water as reported in Sherwood et al. (2020)"

From **p. 12**

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Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA.

The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.

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13	17/44/136G	0.1 (1)	99.1 (13)	–
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17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

44. The method of any of claims 34-43, wherein the dosage form further comprises about 5 to 40 mg of the highly pure crystalline psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 401** "In the first session, **patients received 10 mg psilocybin and in the second, 25 mg**."
45. The method of claim 44, wherein the dosage form comprises 5 mg of highly pure crystalline psilocybin.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1184** "The **low dose of psilocybin** was decreased from 3 to 1 mg/70 kg after 12 participants because data from the same dose-effect study showed **significant psilocybin effects at 5 mg/70 kg**, which raised concern that 3 mg/70 kg might not serve as an inactive placebo."
46. The method of claim 44, wherein the dosage form comprises about 10 mg of highly pure crystalline psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 401** "In the first session, **patients received 10 mg psilocybin and in the second, 25 mg**."
47. The method of claim 44, wherein the dosage form comprises about 35 mg of highly pure crystalline psilocybin.	22. W.I.P.O. Pat. App. No. 2005/039546 "USE OF INDOLEACETIC ACID DERIVATIVES WHICH INCREASE THE SERUM IGF-1 LEVEL FOR THE PREPARATION OF A THERAPEUTICAL COMPOSITION FOR TREATMENT OF VARIOUS DISEASES" (Published May 6, 2005) From **claim 1** "Use of one or more compounds that are capable of activating the hypothalamus in an individual to increase the serum level of Growth Hormone Releasing Hormone (GHRH) which in turn leads to an increase in the secretion of growth hormone (GH) and the subsequent rise of the serum level of insulin-like growth factor 1 (IGF-1) for the preparation of a therapeutical composition for the treatment of serious fatigue and exhaustion symptoms, burn-out, chronic fatigue syndrome, **depression**, Alzheimer disease, irritated bowel syndrome, osteoporosis, type 2 diabetes, or for anti-aging therapy, immune therapy and for stimulating recovery after physical exercise in humans or for stimulating growth and the immune system in animals."

	From **claim 5**: "Use as claimed in claim 1, wherein the compound is a precursor of indole acetic acid selected from the group consisting of tryptophan, 4-hydroxytryptophan, 4-methoxy-tryptophan, 5-hydroxytryptophan, 5-methoxytryptophan, 6-hydroxytryptophan, 6-methoxytryptophan, 7-hydroxytryptophan, 7-methoxytryptophan, hypaphorine, tryptamine, 4-hydroxytryptamine, 4-methoxytryptamine, psilocin (4-hydroxy, dimethyl tryptamine) , **psilocybin** (4-phosphate, dimethyl-tryptamine) , baeocystin, serotonin (5 hydroxytryptamine) , 5-methoxytryptamine, bufotenine (dimethylserotonine) , O-methylbufotenine, melatonin, 6-hydroxytryptamine, 6-methoxy-tryptamine, 7-hydroxytryptamine, 7-methoxytryptamine, indole butyric acid and indole-3-pyruvate." From **claim 14** "Use as claimed in any one of the claims 1-13, wherein the composition comprises **1 to 100 mg, preferably 10 to 90 mg, more preferably 40 mg of the active ingredient**."
48. The method of any one of claims 34-47, wherein the dosage form comprises silicified microcrystalline cellulose.	29. W.I.P.O. Pat. App. No. 2003/047551 "AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE" (Published June 12, 2003) From **claim 1** "A solid dosage form comprising an **active agent and silicified microcrystalline cellulose**" From **claim 147** "The dosage form of claim 1, wherein said active agent is selected from the group consisting of water soluble or insoluble drugs." From **claim 148** "The dosage form of claim 147, wherein said active agent is selected from the group consisting of antihistamines, analgesics, non-steroidal anti-inflammatory agents, anti-emetics, anti-epileptics, vasodilators, anti-tussive agents and expectorants, anti-asthmatics, antacids, anti-spasmodics, antidiabetics, diuretics, anti-hypotensives, antihypertensives, bronchodilators, steroids, antibiotics, antihemorrhoidals, hypnotics, **psychotropics**, antidiarrheals, mucolytics, sedatives, decongestants, laxatives, vitamins, stimulants, anti-fungal agents, anti-viral agents, breath fresheners, anti-carcinogenic compounds, local anesthetics, oral antiseptics, hormonal agents, antiplaque agents, acidity reducing agents, and tooth desensitizers."
49. The method of claim 48, wherein the silicified microcrystalline cellulose has a	29. W.I.P.O. Pat. App. No. 2003/047551 "AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE" (Published June 12, 2003)

particle size range from about 45 to 150 microns.	From **claim 73** "Agglomerated particles of an **active agent and silicified microcrystalline cellulose**, the agglomerated particles being formed by combining a wetted active agent and dried silicified microcrystalline cellulose in a dryer to form agglomerated particles, the agglomerated particles having an average particle size from about **10 µm to about 500 µm.**"
50. The method of any one of claims 34-49, further comprising a mixture of two silicified microcrystalline cellulose variants wherein the first variant has a particle size from about 45 to 80 microns and the second variant has a particle size of about 90 to 150 microns.	29. W.I.P.O. Pat. App. No. 2003/047551 "AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE" (Published June 12, 2003) From **claim 73** "Agglomerated particles of an **active agent and silicified microcrystalline cellulose**, the agglomerated particles being formed by combining a wetted active agent and dried silicified microcrystalline cellulose in a dryer to form agglomerated particles, the agglomerated particles having an **average particle size from about 10 µm to about 500 µm.**" 34. FMC Product Overview (2017) Avicel® SMCC HD 90 Silicified Microcrystalline cellulose NF. Product Specifications. Retrieved 2011. Additional FMC Specifications Particle size distribution — D10 20-70 — D50 90-160 — D90 160-320 Particle size (Air Jet): wt. % + 60 mesh (250 microns) — NMT 8.0 wt. % + 200 mesh (75 microns) — 45.0 - 80.0 35. FMC Product Overview (2017) Avicel® SMCC HD 50 Silicified Microcrystalline cellulose NF. Product Specifications. Retrieved 2011. Additional FMC Specifications Particle size distribution — D10 15-30 — D50 45-80 — D90 100-180 Particle size (Air Jet): wt. % + 60 mesh (250 microns) — NMT 1.0 wt. % + 200 mesh (75 microns) — 10.0 - 30.0 37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018)

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<tr>
<td></td>
<td>From claim 26 “ The pharmaceutical composition of any of claims 1-25, which comprises at least two different kinds of silicified microcrystalline cellulose.”

From claim 27 “The pharmaceutical composition of claim 26, which comprises Prosolv@ SMCC 50 and Prosolv@ SMCC 90.”

From claim 28 “The pharmaceutical composition of claim 27, which comprises from about 15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90.”

39. PROSOLV® SMCC. Retrieved from Web Archive, Reset https://web.archive.org/web/20160318071326/http://www.jrspharma.com/pharma_en/products-services/excipients/hfe/prosolv-smcc.php Retrieved March 18th, 2016

<table>
<tr><th colspan="4">Silicified Microcrystalline Cellulose, NF
(Microcrystalline Cellulose, Ph.Eur., NF, JP, E 460(i) and Silica, Colloidal Anhydrous, Ph.Eur., E 551)</th></tr>
<tr><th>Grade</th><th>Average Particle Size by Laser Diffraction (µm)</th><th>Bulk Density (g/mL)</th><th>Main Application</th></tr>
<tr><td>PROSOLV® SMCC 50</td><td>65</td><td>0.25 – 0.37</td><td>Formulas in which optimal compaction and decent flow is required.</td></tr>
<tr><td>PROSOLV® SMCC 50 LD</td><td>50</td><td>0.20 – 0.30</td><td>Best in class binders.</td></tr>
<tr><td>PROSOLV® SMCC 90</td><td>125</td><td>0.25 – 0.37</td><td>Formulas in which a balance of flow and compaction is required.</td></tr>
<tr><td>PROSOLV® SMCC HD 90</td><td>125</td><td>0.38 – 0.50</td><td>Formulas in which optimal flow and consolidation is required. This grade shows the best disintegration times.
*Low moisture grade available on request.</td></tr>
<tr><td>PROSOLV® SMCC 90 LM</td><td>125</td><td>0.27 – 0.39</td><td>Equivalent to quality of PROSOLV® SMCC 90, but with lower moisture content (< 3%)</td></tr>
</table>
</td>
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<td>51. The method of claim 50, wherein about 30% or less of the microcrystalline cellulose is the first variant having a particle size from about 45 to 80 microns and about 70% or more of the microcrystalline cellulose is the second variant having a particle size of about 90 to 150 microns.</td>
<td>29. W.I.P.O. Pat. App. No. 2003/047551 “AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE” (Published June 12, 2003)

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<td>52. The method of claim 50, wherein about 20% or less of the microcrystalline cellulose is the first variant having a particle size from about 45 to 80 microns and about 80% or more of the microcrystalline cellulose is the second variant having a</td>
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(Microcrystalline Cellulose, Ph.Eur., NF, JP, E 460(i) and Silica, Colloidal Anhydrous, Ph.Eur., E 551)</th></tr>
<tr><th>Grade</th><th>Average Particle Size by Laser Diffraction (µm)</th><th>Bulk Density (g/mL)</th><th>Main Application</th></tr>
<tr><td>PROSOLV® SMCC 50</td><td>65</td><td>0.25 – 0.37</td><td>Formulas in which optimal compaction and decent flow is required.</td></tr>
<tr><td>PROSOLV® SMCC 50 LD</td><td>50</td><td>0.20 – 0.30</td><td>Best in class binders.</td></tr>
<tr><td>PROSOLV® SMCC 90</td><td>125</td><td>0.25 – 0.37</td><td>Formulas in which a balance of flow and compaction is required.</td></tr>
<tr><td>PROSOLV® SMCC HD 90</td><td>125</td><td>0.38 – 0.50</td><td>Formulas in which optimal flow and consolidation is required. This grade shows the best disintegration times.
*Low moisture grade available on request.</td></tr>
<tr><td>PROSOLV® SMCC 90 LM</td><td>125</td><td>0.27 – 0.39</td><td>Equivalent to quality of PROSOLV® SMCC 90, but with lower moisture content (< 3%)</td></tr>
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<tr>
<td>53. The method of claim 50, wherein about 15% or less of the microcrystalline cellulose is the first variant having a particle size from about 45 to 80 microns and about 85% or more</td>
<td>29. W.I.P.O. Pat. App. No. 2003/047551 “AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE” (Published June 12, 2003)</td>
</tr>
</table>

<table>
<tr>
<td>of the microcrystalline cellulose is the second variant having a particle size of about 90 to 150 microns.</td>
<td>From claim 73 “Agglomerated particles of an active agent and silicified microcrystalline cellulose, the agglomerated particles being formed by combining a wetted active agent and dried silicified microcrystalline cellulose in a dryer to form agglomerated particles, the agglomerated particles having an average particle size from about 10 µm to about 500 µm.”

37. W.I.P.O. Pat. App. No. 2018/184206 “Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same” (Published October 11, 2018)

From claim 26 “ The pharmaceutical composition of any of claims 1-25, which comprises at least two different kinds of silicified microcrystalline cellulose.”

From claim 27 “The pharmaceutical composition of claim 26, which comprises Prosolv@ SMCC 50 and Prosolv@ SMCC 90.”

From claim 28 “The pharmaceutical composition of claim 27, which comprises from about 15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90.”

39. PROSOLV® SMCC. Retrieved from Web Archive, Reset https://web.archive.org/web/20160318071326/http://www.jrspharma.com/pharma_en/products-services/excipients/hfe/prosolv-smcc.php Retrieved March 18th, 2016

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<tr>
<td>54. The method of claim 53, wherein the dosage form</td>
<td>3. GRIFFITHS (2016) “Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-</td>
</tr>
</table>

comprises 5 mg of crystalline psilocybin in the form of Polymorph A, 12.5 mg of SMCC 50, 79.5 mg of SMCC 90, 1 mg sodium starch glycolate, 1 mg colloidal silicon dioxide and 1 mg sodium stearyl fumarate.	threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1184** "The **low dose of psilocybin** was decreased from 3 to 1 mg/70 kg after 12 participants because data from the same dose-effect study showed **significant psilocybin effects at 5 mg/70 kg**, which raised concern that 3 mg/70 kg might not serve as an inactive placebo." 36. DEBOTTON (2017) "Applications of Polymers as Pharmaceutical Excipients in Solid Oral Dosage Forms" Med Res Rev. 37(1):52-97 From **p. 54** "For instance, continuous line production of tablets by means of fluid bed granulation and drying production method was reproducible when the APIs were wet granulated with a certain blend of **common polymeric excipients**: powdered cellulose, maize starch, pregelatinized starch, and **sodium starch glycolate**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs,

	erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 6** "The dispersible tablet composition of claim 1 wherein the hydrophilic polymer is polyethylene oxide, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, sodium carboxymethylcellulose, **microcrystalline cellulose**, guar gum, xanthan gum, alginates and combinations thereof." From **claim 7** "The dispersible tablet composition of claim 1 wherein the hydrophilic polymer is present in an amount from about **2% to about 75%** by weight of the total composition." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
55. The method of claim 53, wherein the dosage form comprises 1 mg of crystalline psilocybin in the form of Polymorph A, 20.5 mg of SMCC 50, 75.5 mg of SMCC 90, 1 mg sodium starch glycolate, 1 mg colloidal silicon dioxide, and 1 mg sodium stearyl fumarate.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1184** "The **low dose of psilocybin** was decreased from 3 to **1 mg/70 kg** after 12 participants because data from the same dose-effect study showed significant psilocybin effects at 5 mg/70 kg, which raised concern that 3 mg/70 kg might not serve as an inactive placebo."

	36. DEBOTTON (2017) "Applications of Polymers as Pharmaceutical Excipients in Solid Oral Dosage Forms" Med Res Rev. 37(1):52-97 From **p. 54** "For instance, continuous line production of tablets by means of fluid bed granulation and drying production method was reproducible when the APIs were wet granulated with a certain blend of **common polymeric excipients**: powdered cellulose, maize starch, pregelatinized starch, and **sodium starch glycolate**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 6** "The dispersible tablet composition of claim 1 wherein the hydrophilic polymer is polyethylene oxide, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, sodium carboxymethylcellulose,

	microcrystalline cellulose, guar gum, xanthan gum, alginates and combinations thereof." From **claim 7** "The dispersible tablet composition of claim 1 wherein the hydrophilic polymer is present in an amount from about **2% to about 75%** by weight of the total composition." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
56. The method any one of claims 34-55, wherein the dosage form is an oral dosage form.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
57. The method claim 56, wherein the dosage form is a capsule.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Drug sessions were conducted in an aesthetic living-room-like environment with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the research unit. A urine sample was taken to verify abstinence from common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. **Psilocybin doses were administered in identically**

	appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler. For most of the time during the session, participants were encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a music program was played."
58. The method claim 56, wherein the dosage form is a tablet.	23. U.S. Pat. App. Pub. No. 2009/0259039 "Salts of physiologically active and psychoactive alkaloids and amines simultaneously exhibiting bioavailability and abuse resistance" (Published October 15, 2009) From **claim 75** "The prescribing of a drug product containing at least one drug substance as an organic acid addition salt of an amine containing pharmaceutically active compound to a patient by a defined method of administration wherein said drug substance is a prophylactic in a different method of administration." From **claim 82** "The prescribing of a drug product of claim 75 wherein said amine containing pharmaceutically active compound comprises a material selected from acetaminophen, caffeine, acetorphine, acetylmethadol, allylprodine, alphacetylmethadol, bufotenine, dextromoramide, diethyltryptamine, etorphine, heroin, ibogaine, ketobemidone, lysergic acid diethylamide, mescaline, methaqualone, 3,4-methylenedioxyamphetamine, 3,4-methylenedioxymethamphetamine, N-ethyl-1-phenylcyclohexylamine, peyote, 1-(1-phenylcyclohexyl)pyrrolidine, **psilocybin**, psilocin, 1-{1-(2-thienyl)-cyclohexyl}-piperidine, alphaprodine, anileridine, cocaine, dextropropoxyphene, diphenoxylate, ethylmorphine, glutethimide, hydrocodone, hydromorphone, levo-alphaacetylmethadol, levorphanol, meperidine, methadone, morphine, opium, oxycodone, oxymorphone, poppy straw, thebaine, amphetamine, methamphetamine, methylphenidate, phencyclidine, codeine, benzphetamine, ketamine, alprazolam, chlorodiazepoxide, clorazepate, diethylpropion, fenfluramine, flurazepam, halaze" From **claim 94** "The prescribing of a drug product of claim 75 in a form selected from the group consisting of **a tablet**, a capsule, a caplet, and an oral suspension."
59. The method of any one of claims 1 -58, wherein at least one dose of psilocybin is administered to the subject.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."

60. The method of claim 59, wherein the at least dose of psilocybin is in the range of about 0.1 mg to about 100 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
61 . The method of claim 60, wherein the dose of psilocybin is about 1 mg.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1184** "The **low dose of psilocybin** was decreased from 3 to **1 mg/70 kg** after 12 participants because data from the same dose-effect study showed significant psilocybin effects at 5 mg/70 kg, which raised concern that 3 mg/70 kg might not serve as an inactive placebo."
62. The method of claim 60, wherein the dose of psilocybin is about 10 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
63. The method of claim 60, wherein the dose of psilocybin is about 25 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
64. The method of any one of claims 1 -58, wherein more than one dose of psilocybin is administered to the subject.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
65. The method of claim 65, wherein at least two doses of	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408.

psilocybin are administered to the subject.	From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
66. The method of any one of claims 64-65, wherein the psilocybin is administered once per day.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg), 7 days apart."**
67. The method of any one of claims 64-65, wherein the psilocybin is administered at least once per week.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg), 7 days apart**." 10. KATALYST, "Microdosing for Seasonal Depression: An Experience with Mushrooms exp110358)" 2017; retrieved from Erowid. https://erowid.org/experiences/exp.php?ID=110358, retrieved May 18, 2017 "There are a few resources on the internet about **microdosing with psilocybin**, but none that provide guidance on how to approach it if you have bipolar disorder. Now that I've run this experiment on myself, I decided I would add my anecdote into the mix, hoping that it will help someone out in a similar situation…For context: I have a diagnosis of Bipolar II and PTSD… I have gotten **seasonal depression every year** of my life from around November until April, without exception…**The sweet spot for me was 0.15g, every 2 weeks**… At the dose I found to be best for me (0.15g), I sometimes felt mild euphoria in the mornings when I took it, but did not experience any of the other side effects noted above. Overall I would consider this a huge success. **This was the first winter I've ever had where I wasn't depressed**"
68. The method of any one of claims 64-65, wherein the psilocybin is administered at least twice per week.	10. KATALYST, "Microdosing for Seasonal Depression: An Experience with Mushrooms exp110358)" 2017; retrieved from Erowid. https://erowid.org/experiences/exp.php?ID=110358, retrieved May 18, 2017 "There are a few resources on the internet about **microdosing with psilocybin**, but none that provide guidance on how to approach it if

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69. The method of any one of claims 64-65, wherein the psilocybin is administered at least once per month.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg), 7 days apart."**
70. The method of any one of claims 64-65, wherein the psilocybin is administered at least twice per month.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg), 7 days apart**."
71 . The method of any one of claims 64-65, wherein the psilocybin is administered at least once every three months.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg), 7 days apart**."
72. The method of any one of claims 64-65, wherein the psilocybin is administered at least once every six months.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg), 7 days apart**."

73. The method of any one of claims 64-65, wherein the psilocybin is administered at least once every 12 months.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg), 7 days apart**."
74. The method of any one of claims 64-73, wherein each dose of psilocybin administered is in the range of about 0.1 mg to about 100 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
75. The method of claim 74, wherein each dose of psilocybin administered is about 1 mg.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1184** "The **low dose of psilocybin** was decreased from 3 to **1 mg/70 kg** after 12 participants because data from the same dose-effect study showed significant psilocybin effects at 5 mg/70 kg, which raised concern that 3 mg/70 kg might not serve as an inactive placebo."
76. The method of claim 74, wherein each dose of psilocybin administered is about 10 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
77. The method of claim 74, wherein each dose of psilocybin administered is about 25 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
78. The method of any one of claims 59-77, wherein the psilocybin is administered by one of the following routes:	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408.

~~oral~~, intravenous, intramuscular, parenteral, topical, inhalation, rectal, transmucosal, intranasal, buccal, vaginal, intrathecal, intraocular, transdermal, in utero, intralymphatic, or by direct tissue or organ injection.	From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
79. The method of claim 78, wherein the psilocybin is administered orally.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
80. The method of any one of claims 1 -79, wherein the subject participates in at least one psychological support session before administration of the psilocybin.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "Treatment procedures typically involve **psychological preparation prior to one or two therapist-supported drug sessions** followed by psychological integration. Using a consistent model (i.e. **involving appropriate psychological support**), sustained improvements in well-being in healthy individuals were observed after a single dose of psilocybin in a doubleblind design incorporating an active placebo (Griffiths et al. 2008)."
81. The method of claim 80, wherein the subject participates in at least three psychological support sessions before administration of the psilocybin.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "A description of session monitor roles and the content and rationale for meetings between participants and monitors is provided elsewhere (Johnson et al., 2008). Briefly, **preparation meetings before the first session**, which included discussion of meaningful aspects of the participant's life, served to establish rapport and prepare the participant for the psilocybin sessions. During sessions, monitors were nondirective and supportive, and they encouraged participants to "trust, let go and be open" to the experience." 4. JOHNSON (2008) "Human hallucinogen research: guidelines for safety" Journal of Psychopharmacology. 22(6)603-620.

	From **p. 611** "The next step in volunteer preparation is to conduct a series of meetings between the monitors and volunteer to build rapport and trust. The relationship between the monitors and the volunteers should be well established by the time of the first session (Masters and Houston, 1966). In the Johns Hopkins studies, there are at least eight contact hours over the course of **at least four meetings**, usually over a 1-month period."
82. The method of any one of claims 80-81, wherein the at least one therapeutic intention is discussed during the psychological support session.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The preparation of participants by the monitors explicitly **included the monitor's expectation that the drug session experiences could increase personal awareness and insight**, however, avoided even mention of the criteria used to assess mystical experiences."
83. The method of any one of claims 80-82, wherein self-directed inquiry and experiential processing are practiced during the psychological support session.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Briefly, preparation meetings before the first session, which **included discussion of meaningful aspects of the participant's life**, served to establish rapport and prepare the participant for the psilocybin sessions. During sessions, monitors were nondirective and supportive, and they encouraged participants to "trust, let go and be open" to the experience."
84. The method of any one of claims 80-83, wherein the subject participates in at least one psychological support session after administration of the psilocybin.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 622** "Patients attended one further study visit to the research facility 1 week **after their high-dose session**, during which all baseline questionnaires and assessments were repeated and an opportunity was provided for **further psychological debriefing (the 1 week follow-up visit)**."
85. The method of claim 84, wherein the subject participates in at least three psychological support sessions after administration of the psilocybin.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 622** "P**atients were contacted via telephone 1 day after** their low-dose session to check on their wellbeing and monitor for any adverse events. Patients returned to the research facility 1 day

	after their high-dose session for a post-treatment fMRI scan lasting 60 min. After the fMRI scan, patients completed interim questionnaires (QIDS, STAI-T, and HAM-D), and were **invited back to the research facility where they were met by their psychiatrists** to discuss their experience the previous day. **Patients attended one further study visit** to the research facility 1 week after their high-dose session, during which all baseline questionnaires and assessments were repeated and an opportunity was provided **for further psychological debriefing** (the 1 week follow-up visit)."
86. The method of any one of claims 80-85, wherein the psilocybin is administered to the subject in a room with a substantially non-clinical appearance.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Drug sessions were conducted in an **aesthetic living-room-like environment** with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the research unit. A urine sample was taken to verify abstinence from common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. Psilocybin doses were administered in identically appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler. For most of the time during the session, participants were encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a music program was played."
87. The method of claim 86, wherein the room comprises soft furniture.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627 From **p. 621** "They were then taken to a dosing room that was pre-decorated (e.g., with low lighting). Patients were invited to **relax on a ward bed** in a supine or reclined position and music was played through high-quality stereo speakers and earphones. The two psychiatrists sat on either side of the bed. Patients were supervised at all times by at least two staff members." 3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197

	From **p. 1182** "Drug sessions were conducted in an aesthetic living-room-like environment with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the research unit. A urine sample was taken to verify abstinence from common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. Psilocybin doses were administered in identically appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler. For most of the time during the session, participants were encouraged to **lie down on the couch**, use an eye mask to block external visual distraction, and use headphones through which a music program was played."
88. The method of claim 86, wherein the room is decorated using muted colors.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Drug sessions were conducted in an **aesthetic living-room-like environment** with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the research unit. A urine sample was taken to verify abstinence from common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. Psilocybin doses were administered in identically appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler. For most of the time during the session, participants were encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a music program was played." 21. GROB (2013) Use of the Classic Hallucinogen Psilocybin for Treatment of Existential Distress Associated with Cancer. Springer ISBN 978-1-4614-4865-5 From **p.301**

	 **Fig. 17.1** The living room-like session room used in the Johns Hopkins psilocybin research studies. Comfortable, aesthetic environments free of unnecessary medical or research equipment, in combination with careful volunteer screening, volunteer preparation, and interpersonal support from two or more trained monitors, help to minimize the probability of acute psychological distress during sessions. The use of eyeshades and headphones (through which supportive music is played) may contribute to safety by reducing distractions as well as social pressure to verbally interact with research personnel (reprinted from [47]) 25. WAHLBERG (2015) "UW-Madison tunes in to 'magic mushroom' medicine" October 11, 2015; retrieved from Web Archive, Reset https://web.archive.org/web/20181214181711/https://madison.com/wsj/news/local/health-med-fit/uw-madison-tunes-in-to-magic-mushroom-medicine/article_5c229322-1132-5328-90c1-017e917f0696.html, retrieved December 14, 2018  Karen M. Cooper, the lead guide in a 2015 UW-Madison study of psilocybin, the psychedelic drug in "magic mushrooms," shows the treatment room at the School of Pharmacy building where volunteers experienced the effects of the drug.
89. The method of claim 86, wherein the room comprises a high-resolution sound system.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627

	From **p. 621** "They were then taken to a dosing room that was pre-decorated (e.g., with low lighting). Patients were invited to relax on a ward bed in a supine or reclined position and music was played through **high-quality stereo speakers and earphones.** The two psychiatrists sat on either side of the bed. Patients were supervised at all times by at least two staff members."
90. The method of any one of claims 86-89, wherein the room comprises a bed or a couch.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627 From **p. 621** "They were then taken to a dosing room that was pre-decorated (e.g., with low lighting). Patients were invited to **relax on a ward bed** in a supine or reclined position and music was played through high-quality stereo speakers and earphones. The two psychiatrists sat on either side of the bed. Patients were supervised at all times by at least two staff members." 3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Drug sessions were conducted in an aesthetic living-room-like environment with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the research unit. A urine sample was taken to verify abstinence from common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. Psilocybin doses were administered in identically appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler. For most of the time during the session, participants were encouraged to **lie down on the couch**, use an eye mask to block external visual distraction, and use headphones through which a music program was played."
91. The method of claim 90, wherein the subject lies in the bed or on the couch for approximately 4-8 hours, or a substantial fraction thereof, after administration of the psilocybin.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627 "They were then taken to a dosing room that was pre-decorated (e.g., with low lighting). Patients were invited to **relax on a ward bed** in a supine or reclined position and music was played through high-quality stereo speakers and earphones. The two psychiatrists sat on either side of the bed. Patients were supervised at all times by at least two staff members.

	Dosing commenced at 1030 h in every case. Patients received a low oral dose of **psilocybin** 10 mg (two 5 mg capsules) on a first dosing day and a high oral dose of psilocybin 25 mg (five 5 mg capsules) on a second dosing day, separated by 1 week. Blood pressure, heart rate, and observer ratings of the intensity of psilocybin's acute psychoactive effects (0–4, with 0 signifying no effects and 4 signifying extreme effects8) were measured at baseline (typically 5 min before dosing) and 30, 60, 120, 180, 240, 300, and 360 min after dosing. Subjective ratings of the acute altered state of consciousness using the revised 11 dimension altered states of consciousness questionnaire (11D ASC)24 were completed **6–7 h after dosing**."
92. The method of any one of claims 86-91, wherein the subject listens to music for approximately 4-8 hours, or a substantial fraction thereof, after administration of the psilocybin.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627 "They were then taken to a dosing room that was pre-decorated (e.g., with low lighting). Patients were invited to relax on a ward bed in a supine or reclined position and **music was played through high-quality stereo speakers** and earphones. The two psychiatrists sat on either side of the bed. Patients were supervised at all times by at least two staff members. Dosing commenced at 1030 h in every case. Patients received a low oral dose of **psilocybin** 10 mg (two 5 mg capsules) on a first dosing day and a high oral dose of psilocybin 25 mg (five 5 mg capsules) on a second dosing day, separated by 1 week. Blood pressure, heart rate, and observer ratings of the intensity of psilocybin's acute psychoactive effects (0–4, with 0 signifying no effects and 4 signifying extreme effects8) were measured at baseline (typically 5 min before dosing) and 30, 60, 120, 180, 240, 300, and 360 min after dosing. Subjective ratings of the acute altered state of consciousness using the revised 11 dimension altered states of consciousness questionnaire (11D ASC)24 were completed **6–7 h after dosing**."
93. The method of any one of claims 86-92, wherein the subject wears an eye mask for approximately 4-8 hours, or a substantial fraction thereof, after administration of the psilocybin.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Drug sessions were conducted in an aesthetic living-room-like environment with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the research unit. A urine sample was taken to verify abstinence from

	common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. **Psilocybin** doses were administered in identically appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler. For most of the time during the session, participants were encouraged to lie down on the couch, use an **eye mask** to block external visual distraction, and use headphones through which a music program was played."
94. The method of any one of claims 87-93, wherein a therapist provides psychological support to the subject for approximately 4-8 hours after administration of the psilocybin.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The **8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. If a participant reported significant fear or anxiety, the **monitors provided reassurance verbally or physically** (e.g., with a supportive touch to the hand or shoulder). The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures."
95. The method of claim 94, wherein the therapist uses guided imagery and/or breathing exercises to calm the subject and/or focus the subject's attention.	4. JOHNSON (2008) "Human hallucinogen research: guidelines for safety" Journal of Psychopharmacology. 22(6)603-620. From **p. 610** "Personal experience with techniques such as meditation, yoga or **breathing exercises** may also prove to be helpful in facilitating empathy for volunteers who experience altered states of consciousness **during hallucinogen action**."
96. The method of claim 94, wherein the therapist provides reassuring physical contact with the subject.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The **8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a

	classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. If a participant reported significant fear or anxiety, the **monitors provided reassurance verbally or physically (e.g., with a supportive touch to the hand or shoulder).** The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures."
97. The method of claim 96, wherein the therapist holds the hand, arm, or shoulder of the subject.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The **8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. If a participant reported significant fear or anxiety, the **monitors provided reassurance verbally or physically (e.g., with a supportive touch to the hand or shoulder).** The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures."
98. The method of claim 94, wherein the therapist encourages the subject to perform self- directed inquiry and experiential processing.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "**The 8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to **focus their attention on their inner experiences** throughout the session. If a participant reported significant fear or anxiety, the monitors provided reassurance verbally or physically (e.g., with a supportive touch to the hand or shoulder). The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures."

99. The method of claim 94, wherein the therapist reminds the subject of at least one therapeutic intention.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. "Dosing commenced at 1030 h in every case. Patients received a low oral dose of psilocybin 10 mg (two 5 mg capsules) on a first dosing day and a high oral dose of psilocybin 25 mg (five 5 mg capsules) on a second dosing day, separated by 1 week. Blood pressure, heart rate, and observer ratings of the intensity of psilocybin's acute psychoactive effects (0–4, with 0 signifying no effects and 4 signifying extreme effects8) were measured at baseline (typically 5 min before dosing) and 30, 60, 120, 180, 240, 300, and 360 min after dosing. Subjective ratings of the acute altered state of consciousness using the revised 11 dimension **altered states of consciousness questionnaire (11D ASC)24 were completed 6–7 h after dosing**." 27. TUMOLO (2018) "Uncovering the Therapeutic Potential of Psychedelics" Retrieved from Psychiatry & Behavioral Health Learning Network. https://www.hmpgloballearningnetwork.com/site/pcn/article/uncovering-therapeutic-potential-psychedelics, retrieved September 19th, 2018 "These findings reflect what we see in the lab with controlled studies of healthy individuals and patients with psychiatric disorders such as treatment-resistant depression. They also mirror what we have seen when sampling people using **psychedelics** in a naturalistic way, such as web-based questionnaires with a prospective design. It is important to emphasize we have found evidence that context is important for determining response. **People who have a therapeutic intention experience greater improvement in well-being post-use**. But we have also seen that people can report benefits even if they are not using these compounds for a specific psychiatric purpose, such as if they report using them for self-exploration."
100. The method of claim 94, wherein the therapist counsels the subject to do one or more of the following: (1) to accept feelings of anxiety, (2) to allow the experience to unfold naturally, (3) to avoid psychologically resisting the experience, (4) to relax, and/or	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The **8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a

(5) to explore the subject's own mental space.	classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. If a participant reported significant fear or anxiety, the **monitors provided reassurance verbally** or physically (e.g., with a supportive touch to the hand or shoulder). The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures." 4. JOHNSON (2008) "Human hallucinogen research: guidelines for safety" Journal of Psychopharmacology. 22(6)603-620. From **p. 614** "**If participants become anxious** during the course of hallucinogen action, it is now widely recognized that the appropriate first response is to provide strong personal support and reassurance (O'Brien, 2006). This primarily includes interacting with the volunteer in a comforting and reassuring manner. If the volunteer is behaving anxiously and a negative psychological reaction seems to be escalating, the monitors should convey a solid sense of security and calm, while empathizing with what may be an incredibly intense and unpleasant experience. Attempts to 'talk down' the participant (i.e. the use of reality-defining techniques to distract the participant from or attenuate the altered state of consciousness) may be counter-productive and aggravate a difficult reaction (McCabe, 1977). Instead, **participants should be reminded to surrender to the experience**."
101. The method of claim 94, wherein the therapist does not initiate conversation with the subject.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The **8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. **If a participant reported significant fear or anxiety, the monitors provided reassurance verbally** or physically (e.g., with a supportive touch to the hand or shoulder). The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures."

102. The method of claim 94, wherein the therapist responds to the subject if the subject initiates conversation.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The **8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. **If a participant reported significant fear or anxiety, the monitors provided reassurance verbally** or physically (e.g., with a supportive touch to the hand or shoulder). The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures."
103. The method of any one of claims 80-102, wherein the psychological support is provided remotely to the subject.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 622** "**Patients were contacted via telephone 1 day after** their low-dose session to check on their wellbeing and monitor for any adverse events. Patients returned to the research facility 1 day after their high-dose session for a post-treatment fMRI scan lasting 60 min. After the fMRI scan, patients completed interim questionnaires (QIDS, STAI-T, and HAM-D), and were invited back to the research facility where they were met by their psychiatrists to discuss their experience the previous day."
104. The method of claim 103, wherein the psychological support is provided via a digital or electronic system.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 622** "**Patients were contacted via telephone** 1 day after their low-dose session to check on their wellbeing and monitor for any adverse events. Patients returned to the research facility 1 day after their high-dose session for a post-treatment fMRI scan lasting 60 min. After the fMRI scan, patients completed interim questionnaires (QIDS, STAI-T, and HAM-D), and were invited back to the research facility where they were met by their psychiatrists to discuss their experience the previous day."

105. The method of claim 104, wherein the digital or electronic system is a mobile phone app.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 622** "**Patients were contacted via telephone** 1 day after their low-dose session to check on their wellbeing and monitor for any adverse events. Patients returned to the research facility 1 day after their high-dose session for a post-treatment fMRI scan lasting 60 min. After the fMRI scan, patients completed interim questionnaires (QIDS, STAI-T, and HAM-D), and were invited back to the research facility where they were met by their psychiatrists to discuss their experience the previous day."
106. The method of claim 105, wherein the digital or electronic system is a website.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 622** "**Patients were contacted via telephone** 1 day after their low-dose session to check on their wellbeing and monitor for any adverse events. Patients returned to the research facility 1 day after their high-dose session for a post-treatment fMRI scan lasting 60 min. After the fMRI scan, patients completed interim questionnaires (QIDS, STAI-T, and HAM-D), and were invited back to the research facility where they were met by their psychiatrists to discuss their experience the previous day."
107. A method as described herein.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "Objectives Here, we report on safety and efficacy outcomes for up to 6 months in an open-label trial of **psilocybin for treatment resistant depression**…**Psilocybin represents a promising paradigm for unresponsive depression** that warrants further research in double-blind randomised control trials."
108. A formulation as described herein.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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." From p. 619 "Relative to baseline, **depressive symptoms were markedly reduced** 1 week (mean QIDS difference –11·8, 95% CI

	–9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**." 15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "**Sample 10415-25 (4) was provided by the Johns Hopkins University School of Medicine clinical pharmacy**. The psilocybin was **originally synthesized by Dr David Nichols** (Purdue University, Lafayette, IN, USA) and distributed to Johns Hopkins University and the University of New Mexico for use in human clinical trials… **This lot of psilocybin supported several clinical trials (Bogenschutz et al., 2015; Barrett et al., 2018; Griffiths et al., 2006, 2016).**" From **p. 12**

Table 8
Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA.

The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.

Code	Sample name	Hydrate A (%)	Polymorph A (%)	Polymorph B (%)
1	RTI-1823-17-15	100	–	
2	Folen	4.5 (4)	85.9 (54)	9.6 (30)
3	USP 0274-F	100	–	–
4[a]	10415-25	0.3 (1)	99.7 (6)	–
4[b]	10415-25	0.2 (1)	99.8 (19)	–
5	Ψ-67-2	6.5 (1)	80.9 (22)	12.5 (10)
6	Ψ-81-1	100	–	–
7	Ψ-97-1	0.2 (1)	99.8 (17)	–
8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116*Z*	0.1 (1)	99.1 (12)	–
16	17/44/123*L*	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197.

From **p. 1195** "Acknowledgements The authors thank **David Nichols PhD for synthesizing the psilocybin**, Una McCann MD for support in protocol development and initiation, Michael Bogenschutz MD, John Rotrosen MD, Charles Raison MD, Darrick May MD and Fred Barrett PhD for helpful comments on the manuscript. We thank Linda Felch MA for statistical analysis."

37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018)

	From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**."
109. Crystalline psilocybin as described herein.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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." From p. 619 "Relative to baseline, **depressive symptoms were markedly reduced** 1 week (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**." 15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "**Sample 10415-25 (4) was provided by the Johns Hopkins University School of Medicine clinical pharmacy**. The psilocybin was **originally synthesized by Dr David Nichols** (Purdue University, Lafayette, IN, USA) and distributed to Johns Hopkins University and the University of New Mexico for use in human clinical trials… **This lot of psilocybin supported several clinical trials (Bogenschutz et al., 2015; Barrett et al., 2018; Griffiths et al., 2006, 2016).**" From **p. 12**

Table 8
Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA.

The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.

Code	Sample name	Hydrate A (%)	Polymorph A (%)	Polymorph B (%)
1	RTI-1823-17-15	100	–	
2	Folen	4.5 (4)	85.9 (54)	9.6 (30)
3	USP 0274-F	100	–	–
4[a]	10415-25	0.3 (1)	99.7 (6)	–
4[b]	10415-25	0.2 (1)	99.8 (19)	–
5	Ψ-67-2	6.5 (1)	80.9 (22)	12.5 (10)
6	Ψ-81-1	100	–	–
7	Ψ-97-1	0.2 (1)	99.8 (17)	–
8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116Z	0.1 (1)	99.1 (12)	–
16	17/44/123L	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197.

From **p. 1195** "Acknowledgements The authors thank **David Nichols PhD for synthesizing the psilocybin**, Una McCann MD for support in protocol development and initiation, Michael Bogenschutz MD, John Rotrosen MD, Charles Raison MD, Darrick May MD and Fred Barrett PhD for helpful comments on the manuscript. We thank Linda Felch MA for statistical analysis."

37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018)

	From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**."
110. A pharmaceutical dosage form comprising crystalline psilocybin as described herein as described herein.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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." From p. 619 "Relative to baseline, **depressive symptoms were markedly reduced** 1 week (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**." 15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "**Sample 10415-25 (4) was provided by the Johns Hopkins University School of Medicine clinical pharmacy**. The psilocybin was **originally synthesized by Dr David Nichols** (Purdue University, Lafayette, IN, USA) and distributed to Johns Hopkins University and the University of New Mexico for use in human clinical trials… **This lot of psilocybin supported several clinical trials (Bogenschutz et al., 2015; Barrett et al., 2018; Griffiths et al., 2006, 2016).**" From **p. 12**

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7	Ψ-97-1	0.2 (1)	99.8 (17)	–
8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116*Z*	0.1 (1)	99.1 (12)	–
16	17/44/123*L*	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

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37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018)

	From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**."
111. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Disruptive Mood Dysregulation Disorder, Major Depressive Disorder (MDD), Treatment Resistant Depression, Persistent Depressive Disorder (Dysthymia), Premenstrual Dysphoric Disorder, Substance/Medication-Induced Depressive Disorder, Post-Partum depression, or Depressive Disorder due to Another Medical Condition, Separation Anxiety Disorder, Selective Mutism, Specific Phobia, Social Anxiety Disorder (Social Phobia), Panic Disorder, Panic Attack, Agoraphobia, Generalized Anxiety Disorder, Substance- Medication-Induced Anxiety Disorder, Anxiety Disorder Due to Another Medical Condition, Somatic Symptom Disorder, Illness Anxiety Disorder (hypochondriac), Conversion Disorder (Functional	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 619** "Here, we aimed to investigate the feasibility, safety, and efficacy of **psilocybin** in patients with unipolar **treatment-resistant depression**."

Neurological Symptom Disorder), Factitious Disorder, Post-Traumatic Stress Disorder (PTSD), Adjustment Disorders, Acute Distress Disorder, Obsessive-Compulsive Disorder, Body Dysmorphic Disorder, Hoarding Disorder, Trichotillomania (Hair-Pulling) Disorder, Excoriation (Skin-Picking) Disorder, Substance/Medication-Induced Obsessive-Compulsive and Related Disorder, Obsessive-Compulsive and Related Disorder due to Another Medical Condition, Substance-Related Disorders, Alcohol-Related Disorders, Cannabis-Related Disorders, Hallucinogen-Related Disorders, Inhalant-Related Disorders, Cocaine-Related Disorders, Opioid- Related Disorders, Sedative-, Hypnotic-, or Anxiolytic-Related Disorders, Stimulant-Related Disorders, Tobacco-Related Disorders, Non-Substance-Related Disorders (Gambling or Gaming Disorder), Migraines, Cluster Headaches such as Chronic Cluster Headaches, Cyclical Vomiting, Tension-Type Headache, Dysphasia, Pica, Anorexia Nervosa, Bulimia Nervosa, Binge-Eating Disorder, Oppositional Defiant Disorder, Intermittent Explosive Disorder, Conduct Disorder, Antisocial Personality Disorder, Psychopathy, Pyromania, or Kleptomania.	
112. A method of treating a subject in need thereof, the method comprising administering to the subject a	7. U.S. Pat. App. Pub. No. 2021/0267966A1 “Method of Inducing Dendritic and Synaptic Genesis in Neurodegenerative Chronic Diseases” (Published September 2, 2021)

therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Neurocognitive Disorders due to Alzheimer's, Lewy Bodies, Traumatic Brain Injury, Prion Disease, HIV Infection, Parkinson's, or Huntington's; concussion; chronic traumatic encephalopathy (CTE); Language Disorder, Speech Sound Disorder (Phonological Disorder); Childhood-Onset Fluency Disorder (Stuttering); Social (Pragmatic) Communication Disorder; Tourette's Disorder; Persistent (Chronic) Motor or Vocal Tic Disorder; Amnestic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.	From **claim 1** "A method of inducing neuron dendritic and synaptic genesis in **neurodegenerative diseases** by administering one or more tryptamine molecules or pharmaceutically acceptable salts thereof, to a patient in suffering from a neurodegenerative disease. From **claim 2** "The method according to claim 1, wherein said one or more tryptamine molecules is selected from the group consisting of lysergic acid diethylamide, N, N-dimethyltryptamine, 5-methoxy-N, N-dimethyltryptamine, mescaline, psilocin, 3,4-methylenedioxymethamphetamine, and **psilocybin**, pharmaceutically acceptable salts thereof and combinations thereof. From **claim 4** "The method according to claim 1, wherein said neurodegenerative disease is a chronic condition." From **claim 5** "The method according to claim 4, wherein said chronic neurodegenerative disease is selected from the group consisting of dementia, **Alzheimer's disease, Parkinson's disease,** frontal temporal dementia, Huntington's disease and multiple Sclerosis." 16. U.S. Pat. App. Pub. No. 2016/0331725 "Use of compounds that are able to increase the serum igf-1 level for the preparation of a therapeutical composition for treatment of various disease states associated with a reduced igf-1 serum level in humans and animals" (Published November 17, 2016) From **claim 1** "A method comprising: using one or more compounds that are capable of activating the hypothalamus in an individual to increase the serum level of Growth Hormone Releasing Hormone (GHRH), which, in turn, leads to an increase in the secretion of growth hormone (GH) and the subsequent rise of the serum level of insulin-like growth factor 1 (IGF-1) for the preparation of a therapeutical composition for the treatment of serious fatigue and exhaustion symptoms, burn-out, chronic fatigue syndrome, depression, **Alzheimer disease**, irritated bowel syndrome, osteoporosis, type 2 diabetes, or for anti-aging therapy, immune therapy and for stimulating recovery after physical exercise in humans or for stimulating growth and the immune system in animals. From **claim 5** "The method as claimed in claim 1, wherein the compound is a precursor of indole acetic acid selected from the group consisting of tryptophan, 4-hydroxytryptophan, 4-methoxytryptophan, 5-hydroxytryptophan, 5-methoxytryptophan, 6-hydroxytryptophan, 6-methoxytryptophan, 7-hydroxytryptophan, 7-methoxytryptophan, hypaphorine, tryptamine, 4-

	hydroxytryptamine, 4-methoxytryptamine, psilocin (4-hydroxy, dimethyl tryptamine), **psilocybin** (4-phosphate, dimethyl-tryptamine), baeocystin, serotonin (5-hydroxytryptamine), 5-methoxytryptamine, bufotenine (dimethylserotonine), O-methylbufotenine, melatonin, 6-hydroxytryptamine, 6-methoxytryptamine, 7-hydroxytryptamine, 7-methoxytryptamine, indole butyric acid and indole-3-pyruvate."
113. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Autism Spectrum Disorder, or Antisocial Personality Disorder.	8. U.S. Pat. App. Pub. No. 2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012) From **claim 1** "A method of improving the efficacy of psychotherapeutic treatment comprising administering a pharmaceutical composition comprising an oxytocin releasing agent to a subject diagnosed with a psychiatric or behavioral disorder." From **claim 4** "The method of claim 1, wherein the psychiatric disorder is autism, asperger syndrome, or an **autistic spectrum disorder**." From **claim 13** "The method of claim 1, wherein the oxytocin releasing agent is buspirone, gepirone, tandospirone serotonin, ergine, ergotamine, lysergic acid, lysergic acid diethylamide, **psilocybin**, 4-hydroxy-dimethyltryptamine, N,N-dimethyltryptamine, 5-methoxy-dimethyltryptamine, mescaline, 4-bromo-2,5-dimethoxyphenethylamine, 3,4-methylenedioxymethamphetamine, methylenedioxyethylamphetamine, tenamfetamine, lorcaserin or salts thereof."
114. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Attention-Deficit/Hyperactivity Disorder, Other Specified Attention-Deficit/Hyperactivity Disorder; or Unspecified Attention-Deficit/Hyperactivity Disorder.	8. U.S. Pat. App. Pub. No. 2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012) From **claim 1** "A method of improving the efficacy of psychotherapeutic treatment comprising administering a pharmaceutical composition comprising an oxytocin releasing agent to a subject diagnosed with a psychiatric or behavioral disorder." From **claim 3** "The method of claim 1, wherein the psychiatric disorder is selected from the group consisting of depression, bi-polar disorders, anxiety disorders, panic attacks, agoraphobia, **attention deficit syndrome**, mid-cycle dysphoria, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS), addiction, obsessive-compulsive disorder, Tourette's Syndrome, post-traumatic stress disorder (PTSD), and schizophrenia."

	From **claim 13** "The method of claim 1, wherein the oxytocin releasing agent is buspirone, gepirone, tandospirone serotonin, ergine, ergotamine, lysergic acid, lysergic acid diethylamide, **psilocybin**, 4-hydroxy-dimethyltryptamine, N,N-dimethyltryptamine, 5-methoxy-dimethyltryptamine, mescaline, 4-bromo-2,5-dimethoxyphenethylamine, 3,4-methylenedioxymethamphetamine, methylenedioxyethylamphetamine, tenamfetamine, lorcaserin or salts thereof."
115. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Schizotypal (Personality) Disorder, Delusional Disorder, Schizophrenia, or Schizoaffective Disorder	8. U.S. Pat. App. Pub. No. 2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012) From **claim 1** "A method of improving the efficacy of psychotherapeutic treatment comprising administering a pharmaceutical composition comprising an oxytocin releasing agent to a subject diagnosed with a psychiatric or behavioral disorder." From **claim 3** "The method of claim 1, wherein the psychiatric disorder is selected from the group consisting of depression, bi-polar disorders, anxiety disorders, panic attacks, agoraphobia, attention deficit syndrome, mid-cycle dysphoria, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS), addiction, obsessive-compulsive disorder, Tourette's Syndrome, post-traumatic stress disorder (PTSD), and **schizophrenia**." From **claim 13** "The method of claim 1, wherein the oxytocin releasing agent is buspirone, gepirone, tandospirone serotonin, ergine, ergotamine, lysergic acid, lysergic acid diethylamide, **psilocybin**, 4-hydroxy-dimethyltryptamine, N,N-dimethyltryptamine, 5-methoxy-dimethyltryptamine, mescaline, 4-bromo-2,5-dimethoxyphenethylamine, 3,4-methylenedioxymethamphetamine, methylenedioxyethylamphetamine, tenamfetamine, lorcaserin or salts thereof."
116. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Female Sexual Interest/Arousal Disorder, Male Hypoactive Sexual Desire	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. "Scores on the genital/sexual dysfunction item of the HAM-D were also significantly reduced **1-week post-treatment** (mean reduction = − 0.58, 95% CI = − 0.18 to − 0.98, p = 0.002) and **no one scored the maximum nor showed an increase in sexual dysfunction** from baseline."

Disorder, or Excessive Sexual Drive.	28. AARON (2017) "Open Your Mind: Merging Psychedelic Therapy with Sex Therapy" Retrieved from Psychology Today. https://www.psychologytoday.com/us/blog/standard-deviations/201710/open-your-mind-merging-psychedelic-therapy-sex-therapy, retrieved October 24th, 2017 "Last year she presented a workshop for NYC's Sexuality Speaker Series on "**The Therapeutic Use of Psychedelics in Treating Sexual Dysfunction and Trauma**,"" "Q: You propose that **psilocybin could also be used for sex therapy**. How so and what is the mechanism through which psilocybin could prove therapeutic for sexual concerns? A: The current research on psilocybin is so promising. **While there are no studies that look directly at the possible impact psilocybin might have on sexuality, research suggests to me that there might be several applications in sex therapy.** Psilocybin has been shown to reduce or eliminate entirely existential anxiety and distress and increase openness (defined as an increased capacity for fantasy, appreciation of aesthetics, feelings and increased tolerance). My friend and colleague Dr. Katherine MacLean, a research scientist who has studied psilocybin extensively, was able to show that even a single session with psilocybin that occasioned a mystical experience in the user could change personality traits instantly and more profoundly than occurs over a decade of time in an average adult. **Given my knowledge of this research and my own sex therapy work, I believe psilocybin can assist with body image issues, sexual performance-related anxiety, and feelings of shame. Clients may experience a sense of entitlement to pleasure and experience an increased ability to be present with pleasure.**"
117. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Bipolar I Disorder, Bipolar II Disorder, or Cyclothymic Disorder.	8. U.S. Pat. App. Pub. No. 2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012) From **claim 1** "A method of improving the efficacy of psychotherapeutic treatment comprising administering a pharmaceutical composition comprising an oxytocin releasing agent to a subject diagnosed with a psychiatric or behavioral disorder." From **claim 3** "The method of claim 1, wherein the psychiatric disorder is selected from the group consisting of depression, **bi-polar disorders**, anxiety disorders, panic attacks, agoraphobia, attention deficit syndrome, mid-cycle dysphoria, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS), addiction, obsessive-compulsive disorder, Tourette's Syndrome, post-traumatic stress disorder (PTSD), and schizophrenia."

	From **claim 13** "The method of claim 1, wherein the oxytocin releasing agent is buspirone, gepirone, tandospirone serotonin, ergine, ergotamine, lysergic acid, lysergic acid diethylamide, **psilocybin**, 4-hydroxy-dimethyltryptamine, N,N-dimethyltryptamine, 5-methoxy-dimethyltryptamine, mescaline, 4-bromo-2,5-dimethoxyphenethylamine, 3,4-methylenedioxymethamphetamine, methylenedioxyethylamphetamine, tenamfetamine, lorcaserin or salts thereof." 10. KATALYST, "Microdosing for Seasonal Depression: An Experience with Mushrooms exp110358)" 2017; retrieved from Erowid. https://erowid.org/experiences/exp.php?ID=110358, retrieved May 18, 2017 "There are a few resources on the internet about **microdosing with psilocybin**, but none that provide guidance on how to approach it if you have bipolar disorder. Now that I've run this experiment on myself, I decided I would add my anecdote into the mix, hoping that it will help someone out in a similar situation…For context: I have a diagnosis of **Bipolar II and PTSD**… The sweet spot for me was 0.15g, every 2 weeks… At the dose I found to be best for me (0.15g), I sometimes felt mild euphoria in the mornings when I took it, but did not experience any of the other side effects noted above. Overall I would consider this a huge success." 31. W.I.P.O. Pat. App. No. 2018/135943 "Psilocybin and/or psilocin in combination with cannabinoids and/or terpenes" (Published July 26, 2018) From **claim 1** "**Psilocybin and/or psilocin** in combination with at least one cannabinoid and/or at least one terpene for use in the prevention or **treatment of a psychological disorder**, wherein the at least one cannabinoid and/or at least one terpene is administered separately, sequentially or simultaneously to the psilocybin and/or psilocin." From **claim 2** "**Psilocybin and/or psilocin** in combination with at least one cannabinoid and/or at least one terpene for use according to claim 1 , wherein the psychological disorder is chosen from depression, psychotic disorder, schizophrenia, schizophreniform disorder (acute schizophrenic episode); schizoaffective disorder; **bipolar I disorder** (mania, manic disorder, manic-depressive psychosis); bipolar II disorder; major depressive disorder with psychotic feature (psychotic depression); delusional disorders

	(paranoia); Shared Psychotic Disorder (Shared paranoia disorder); Brief Psychotic disorder (Other and Unspecified Reactive Psychosis); Psychotic disorder not otherwise specified (Unspecified Psychosis); paranoid personality disorder; schizoid personality disorder; schizotypal personality disorder, anxiety disorder, panic disorder, panic attacks, agoraphobia, attention deficit syndrome, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS)."
118. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Insomnia Disorder, Hypersomnolence Disorder, Narcolepsy, or Primary Central Sleep Apnea.	17. W.I.P.O. Pat. App. No. 2018/195455 "Assessing and treating psychedelic-responsive subjects" (Published October 25, 2018) From **claim 41** "The method of claim 39 or 40, wherein the depressive disorder is associated with one or more prodromal symptoms selected from the group consisting of depressed mood, decreased appetite, weight loss, increased appetite, weight gain, **initial insomnia, middle insomnia**, early waking, hypersomnia, decreased energy, decreased interest or pleasure, self-blame, decreased concentration, indecision, suicidality, psychomotor agitation, psychomotor retardation, crying more frequently, inability to cry, hopelessness, worrying/brooding, decreased self-esteem, irritability, dependency, self-pity, somatic complaints, decreased effectiveness, helplessness, and decreased initiation of voluntary responses." From **claim 53** "The method of any one of claims 1 -52, wherein the psychedelic agent is selected from lysergic acid diethylamide, **psilocybin**, and pharmaceutically acceptable salts thereof."
119. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Schizoid Personality Disorder, Schizotypal Personality Disorder, Antisocial Personality Disorder, Borderline Personality Disorder, or Obsessive-Compulsive Personality Disorder.	6. MORENO (2006) "Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients With Obsessive-Compulsive Disorder" The Journal of Clinical Psychiatry. 67(11)1735-1740. From **p. 1735** "This modified double-blind study investigated the safety, tolerability, and clinical **effects of psilocybin,** a potent 5-HT1A and 5-HT2A/2C agonist, **in patients with OCD**."
120. A method of treating a subject in need thereof, the	9. U.S. Pat. App. Pub. No. 2020/0375967 "Compositions of psilocybin and analogs" (Published December 3, 2020)

method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: age-related hearing loss or tinnitus.	From **claim 1** "A composition comprising: **psilocybin**, psilocin, baeocystin, norbaeocystin, salts thereof, or combinations thereof; an erinacine, a hericenone, or a combination thereof." From **claim 6** "A method for treating or improving neurological functioning or mental health in a subject in need thereof comprising administration of an effective amount of the composition of claim 1 to the subject in need thereof." From **claim 7** "The method of claim 6, where the neurological or mental health conditions comprise depression, memory loss, dementia, cognitive dysfunction, **hearing loss,** vision loss, neurologic pain, or combinations thereof." 18. U.S. Pat. App. Pub. No. 2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published January 25, 2018) From **claim 1** "A method for improving neurological health of an animal comprising: administering a therapeutically effective amount of a composition to an animal, wherein the composition comprises one or more of **psilocybin**, psilocin, baeocystin, norbaeocystin, salts thereof, or combinations thereof, one or more of erinacines, hericenones or combinations thereof, and niacin." From **claim 6** "The method of claim 1, wherein the composition additionally **improves hearing**."
121. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Multiple Sclerosis, Cranial Nerve Disorder, Neuromyelitis Optica, Bell's Palsy, Guillain Barre Syndrome, Demyelinating Disease of Central Nervous System, or Chronic Inflammatory Demyelinating Polyneuritis.	7. U.S. Pat. App. Pub. No. 2021/0267966A1 "Method of Inducing Dendritic and Synaptic Genesis in Neurodegenerative Chronic Diseases" (Published September 2, 2021) From **claim 1** "A method of inducing neuron dendritic and synaptic genesis in neurodegenerative diseases by administering one or more tryptamine molecules or pharmaceutically acceptable salts thereof, to a patient in suffering from a neurodegenerative disease. From **claim 2** "The method according to claim 1, wherein said one or more tryptamine molecules is selected from the group consisting of lysergic acid diethylamide, N, N-dimethyltryptamine, 5-methoxy-N, N-dimethyltryptamine, mescaline, psilocin, 3,4-methylenedioxymethamphetamine, and **psilocybin**, pharmaceutically acceptable salts thereof and combinations thereof.

	From **claim 4** "The method according to claim 1, wherein said neurodegenerative disease is a chronic condition." From **claim 5** "The method according to claim 4, wherein said chronic neurodegenerative disease is selected from the group consisting of dementia, Alzheimer's disease, Parkinson's disease, frontal temporal dementia, Huntington's disease and **multiple Sclerosis**." 20. W.I.P.O. Pat. App. No. 2019/161050 "Cognitive platform including computerized elements coupled with a therapy for mood disorder" (Published August 22, 2019) From **claim 17** "A computer-implemented method for quantifying cognitive skills in an individual undergoing therapy for a mood disorder, the method comprising: using one or more processors to execute instructions stored in one or more memory storage devices comprising computer executable instructions to perform operations including: present via a user interface a first instance of a task with an interference at the user interface, requiring a first response from the individual to the first instance of the task in the presence of the interference, wherein the individual at least one of (i) preparing to undergo a therapy for a mood disorder comprising at least one of **ingesting or injecting at least one of a psychedelic or a dissociative drug for treatment of the mood disorder** or (ii) has undergone the therapy; present via the user interface the first instance of the task, requiring a second response from the individual to the first instance of the task in the absence of the interference; wherein: at least one of the first instance of the task and the interference comprises a computerized element; measure substantially simultaneously the first response from the individual to the first instance of the task and the response from the individual to the interference; receive data indicative of the first response and the second response; and analyze the data indicative of the first response and the second response to compute at least one performance metric comprising at least one quantified indicator of cognitive abilities of the individual." From **claim 22** "The method of claim 17 wherein the mood disorder is due to a condition selected from the group consisting of a neuropsychological condition, a neurodegenerative condition, and an executive function disorder." From **claim 23** "The method of claim 22, wherein the condition is selected from the group consisting of social anxiety, depression,

	bipolar disorder, major depressive disorder, post-traumatic stress disorder, schizophrenia, autism spectrum disorder, attention deficit hyperactivity disorder, dementia, Parkinson's disease, Huntington's disease, Alzheimer's disease, and **multiple-sclerosis**." From **claim 30** "The method of claim 17, wherein the at least one psychedelic or dissociative drug is one or more of lysergic acid diethylamide, **psilocybin**, ketamine, methylenedioxy-n-methylamphetamine. mescaline, or N,N-Dimethyltryptamine."
122. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject suffers from pain.	9. U.S. Pat. App. Pub. No. 2020/0375967 "Compositions of psilocybin and analogs" (Published December 3, 2020) From **claim 1** "A composition comprising: **psilocybin**, psilocin, baeocystin, norbaeocystin, salts thereof, or combinations thereof; an erinacine, a hericenone, or a combination thereof." From **claim 6** "A method for treating or improving neurological functioning or mental health in a subject in need thereof comprising administration of an effective amount of the composition of claim 1 to the subject in need thereof." From **claim 7** "The method of claim 6, where the neurological or mental health conditions comprise depression, memory loss, dementia, cognitive dysfunction, hearing loss, vision loss, neurologic **pain**, or combinations thereof." 19. U.S. Pat. App. Pub. No. 2019/0105313 "PSILOCYBIN COMPOSITIONS" (Published April 11, 2019) From **claim 6** "A composition comprising: **psilocybin**, psilocin, baeocystin, norbaeocystin, or salts thereof, psilocybin mushrooms or extracts thereof, or combinations thereof; Cannabis extracts comprising cannabidiol, tetrahydrocannabinol, or combinations thereof; and niacin. " From **claim 9**: "A method for treating or improving neurological or mental health conditions comprising administration of an effective amount of the composition of claim 6 to a subject in need thereof." From **claim 10** "The method of claim 9 where the neurological or mental health conditions comprise depression, memory loss, dementia, cognitive dysfunction, hearing loss, vision loss, **neurologic pain**, or combinations thereof."

123. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has at least one of the following diseases, disorders, or conditions: Myelopathy, Traumatic Brain Injury, Intellectual Disabilities, Mania, Neurodegeneration, Paraphilic disorders, Suicidal Behavior Disorder, Nonsuicidal Self-Injury, Persistent Complex Bereavement Disorder, Gl Tract Related Diseases, Epilepsy, Sickle Cell Disease, locked-in syndrome, restless leg syndrome, stroke, or Amyotrophic Lateral Sclerosis (ALS).	7. U.S. Pat. App. Pub. No. 2021/0267966A1 "Method of Inducing Dendritic and Synaptic Genesis in Neurodegenerative Chronic Diseases" (Published September 2, 2021) From **claim 1** "A method of inducing neuron dendritic and synaptic genesis in neurodegenerative diseases by administering one or more tryptamine molecules or pharmaceutically acceptable salts thereof, to a patient in suffering from a **neurodegenerative disease**." From **claim 2** "The method according to claim 1, wherein said one or more tryptamine molecules is selected from the group consisting of lysergic acid diethylamide, N, N-dimethyltryptamine, 5-methoxy-N, N-dimethyltryptamine, mescaline, psilocin, 3,4-methylenedioxymethamphetamine, and **psilocybin**, pharmaceutically acceptable salts thereof and combinations thereof. 20. W.I.P.O. Pat. App. No. 2019/161050 "Cognitive platform including computerized elements coupled with a therapy for mood disorder" (Published August 22, 2019) From **claim 17** "A computer-implemented method for quantifying cognitive skills in an individual undergoing therapy for a mood disorder, the method comprising: using one or more processors to execute instructions stored in one or more memory storage devices comprising computer executable instructions to perform operations including: present via a user interface a first instance of a task with an interference at the user interface, requiring a first response from the individual to the first instance of the task in the presence of the interference, wherein the individual at least one of (i) preparing to undergo a therapy for a mood disorder comprising at least one of **ingesting or injecting at least one of a psychedelic or a dissociative drug for treatment of the mood disorder** or (ii) has undergone the therapy; present via the user interface the first instance of the task, requiring a second response from the individual to the first instance of the task in the absence of the interference; wherein: at least one of the first instance of the task and the interference comprises a computerized element; measure substantially simultaneously the first response from the individual to the first instance of the task and the response from the individual to the interference; receive data indicative of the first response and the second response; and analyze the data indicative of the first response and the second response to compute at least one performance metric comprising at least one quantified indicator of cognitive abilities of the individual."

	From **claim 22** "The method of claim 17 wherein the mood disorder is due to a condition selected from the group consisting of a neuropsychological condition, a **neurodegenerative condition**, and an executive function disorder." From **claim 30** "The method of claim 17, wherein the at least one psychedelic or dissociative drug is one or more of lysergic acid diethylamide, **psilocybin**, ketamine, methylenedioxy-n-methylamphetamine. mescaline, or N,N-Dimethyltryptamine."
124. A method of treating a subject, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein after administration the subject exhibits an improvement in cognition.	9. U.S. Pat. App. Pub. No. 2020/0375967 "Compositions of psilocybin and analogs" (Published December 3, 2020) From **claim 1** "A composition comprising: **psilocybin**, psilocin, baeocystin, norbaeocystin, salts thereof, or combinations thereof; an erinacine, a hericenone, or a combination thereof." From **claim 6** "A method for treating or **improving neurological functioning** or mental health in a subject in need thereof comprising administration of an effective amount of the composition of claim 1 to the subject in need thereof." From **claim 7** "The method of claim 6, where the neurological or mental health conditions comprise depression, memory loss, dementia, **cognitive dysfunction**, hearing loss, vision loss, neurologic pain, or combinations thereof." 18. U.S. Pat. App. Pub. No. 2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published January 25, 2018) From **claim 1** "A method for improving neurological health of an animal comprising: administering a therapeutically effective amount of a composition to an animal, wherein the composition comprises one or more of **psilocybin**, psilocin, baeocystin, norbaeocystin, salts thereof, or combinations thereof, one or more of erinacines, hericenones or combinations thereof, and niacin." From **claim 3** "The method of claim 1, wherein the composition additionally **improves memory and cognition**."
125. The method of embodiment 124 wherein the improvement in cognition is an improvement in attention,	9. U.S. Pat. App. Pub. No. 2020/0375967 "Compositions of psilocybin and analogs" (Published December 3, 2020)

episodic memory, working memory, spatial memory, social cognition, executive function, and/or cognitive flexibility.	From **claim 1** "A composition comprising: **psilocybin**, psilocin, baeocystin, norbaeocystin, salts thereof, or combinations thereof; an erinacine, a hericenone, or a combination thereof." From **claim 6** "A method for treating or **improving neurological functioning** or mental health in a subject in need thereof comprising administration of an effective amount of the composition of claim 1 to the subject in need thereof." From **claim 7** "The method of claim 6, where the neurological or mental health conditions comprise depression, **memory loss**, dementia, cognitive dysfunction, hearing loss, vision loss, neurologic pain, or combinations thereof." 18. U.S. Pat. App. Pub. No. 2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published January 25, 2018) From **claim 1** "A method for improving neurological health of an animal comprising: administering a therapeutically effective amount of a composition to an animal, wherein the composition comprises one or more of **psilocybin**, psilocin, baeocystin, norbaeocystin, salts thereof, or combinations thereof, one or more of erinacines, hericenones or combinations thereof, and niacin." From **claim 3** "The method of claim 1, wherein the composition additionally **improves memory and cognition**."
126. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has Treatment Resistant Depression (TRD).	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 619** "Here, we aimed to investigate the feasibility, safety, and efficacy of psilocybin in patients with unipolar **treatment-resistant depression**."
127. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin, wherein the subject has Major Depressive Disorder (MDD).	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "Twenty patients (six females) with (mostly) severe, unipolar, treatment-resistant **major depression** received two oral doses of psilocybin (10 and 25 mg, 7 days apart) in a supportive setting. Depressive symptoms were assessed from 1 week to 6

	months post-treatment, with the self-rated QIDS-SR16 as the primary outcome measure."
128. The method of any one of claims 1 1 1 -127 wherein the subject is a mammal.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 619** "Here, we aimed to investigate the feasibility, safety, and efficacy of psilocybin **in patients** with unipolar treatment-resistant depression."
129. The method of claims 18, wherein the subject is a human.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 619** "Here, we aimed to investigate the feasibility, safety, and efficacy of psilocybin **in patients** with unipolar treatment-resistant depression."
130. The method of any of claims 111 -129, wherein the psilocybin is administered in a dosage form comprising a therapeutically effective amount of highly pure crystalline psilocybin in the form of Polymorph A, wherein the crystalline psilocybin comprises at least 90% by weight of Polymorph A.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "Objectives Here, we report on safety and efficacy outcomes for up to 6 months in an open-label trial of **psilocybin for treatment resistant depression**…**Psilocybin represents a promising paradigm for unresponsive depression** that warrants further research in double-blind randomised control trials." 15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 1** "Furthermore, **revision is recommended on characterizations in recently granted patents that include descriptions of crystalline psilocybin** inappropriately reported as a single-phase 'isostructural variant.' Rietveld refinement demonstrated that the **claimed material was composed of approximately 81% Polymorph A and 19% Polymorph B, both of which have been identified in historical samples.** In this article, we show conclusively that all published data can be explained in terms of three well-defined forms of psilocybin and that no additional forms are needed to explain the diffraction patterns." From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for

Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019) [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)**."

From **p. 8** "**Samples 12–18 were provided by Usona Institute and were obtained from batches of psilocybin produced during chemistry process development**. Samples were recrystallized from aqueous acetone or pure water as reported in Sherwood et al. (2020)"

From **p. 12**

Table 8

Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA.

The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24.

Code	Sample name	Hydrate A (%)	Polymorph A (%)	Polymorph B (%)
1	RTI-1823-17-15	100	–	
2	Folen	4.5 (4)	85.9 (54)	9.6 (30)
3	USP 0274-F	100	–	–
4[a]	10415-25	0.3 (1)	99.7 (6)	–
4[b]	10415-25	0.2 (1)	99.8 (19)	–
5	Ψ-67-2	6.5 (1)	80.9 (22)	12.5 (10)
6	Ψ-81-1	100	–	–
7	Ψ-97-1	0.2 (1)	99.8 (17)	–
8	*Polymorph A*	–	80.9 (6)	19.1 (7)
9	*Polymorph A′*	–	99.7 (8)	0.3 (3)
10	Hydrate A	100		
11	Polymorph B	–	–	100
12	SPS5107/20/1	0.1 (1)	99.9 (10)	–
13	17/44/136G	0.1 (1)	99.1 (13)	–
14	17/44/132E	–	100.0 (11)	–
15	17/44/116*Z*	0.1 (1)	99.1 (12)	–
16	17/44/123*L*	0.2 (1)	99.8 (11)	–
17	800325750	0.2 (1)	99.8 (25)	–
18	800326600	0.2 (1)	99.8 (10)	–
19	ARN-19-002654	–	100	–
20	CG002E-035-04	100	–	–
21	CG-0019E-038-03	–	–	100
22	PL005E-004-40C	–	100	–
23	PL005E-004-45C	–	91.7 (7)	8.3 (4)
24	PL005E-004-55C	–	77.4 (8)	22.6 (5)

Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

131. The method of claim 130, wherein the crystalline psilocybin comprises at least 95% by weight of Polymorph A.	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for **Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019)** [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)**." From **p. 12** **Table 8** Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Code | Sample name | Hydrate A (%) | Polymorph A (%) | Polymorph B (%) 1 | RTI-1823-17-15 | 100 | – | 2 | Folen | 4.5 (4) | 85.9 (54) | 9.6 (30) 3 | USP 0274-F | 100 | – | – 4[a] | 10415-25 | 0.3 (1) | 99.7 (6) | – 4[b] | 10415-25 | 0.2 (1) | 99.8 (19) | – 5 | Ψ-67-2 | 6.5 (1) | 80.9 (22) | 12.5 (10) 6 | Ψ-81-1 | 100 | – | – 7 | Ψ-97-1 | 0.2 (1) | 99.8 (17) | – 8 | *Polymorph A* | – | 80.9 (6) | 19.1 (7) 9 | *Polymorph A′* | – | 99.7 (8) | 0.3 (3) 10 | Hydrate A | 100 | | 11 | Polymorph B | – | – | 100 12 | SPS5107/20/1 | 0.1 (1) | 99.9 (10) | – 13 | 17/44/136G | 0.1 (1) | 99.1 (13) | – 14 | 17/44/132E | – | 100.0 (11) | – 15 | 17/44/116*Z* | 0.1 (1) | 99.1 (12) | – 16 | 17/44/123*L* | 0.2 (1) | 99.8 (11) | – 17 | 800325750 | 0.2 (1) | 99.8 (25) | – 18 | 800326600 | 0.2 (1) | 99.8 (10) | – 19 | ARN-19-002654 | – | 100 | – 20 | CG002E-035-04 | 100 | – | – 21 | CG-0019E-038-03 | – | – | 100 22 | PL005E-004-40C | – | 100 | – 23 | PL005E-004-45C | – | 91.7 (7) | 8.3 (4) 24 | PL005E-004-55C | – | 77.4 (8) | 22.6 (5) Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.

132. The method of claim 130 or 131, wherein the crystalline psilocybin has a chemical purity of greater than 97% by HPLC, and no single impurity of greater than 1 %.	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for **Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019)** [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)**." From **p. 18** "The QPA by RM also shed light on what was described as an unexpected result in the same patent application by providing compelling evidence that **a phase impurity, Polymorph B**, was responsible for the minor PXRD reflection at 17.5° 2θ observed from psilocybin produced in large-scale batches." From **p. 12**

	Table 8 Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Code | Sample name | Hydrate A (%) | Polymorph A (%) | Polymorph B (%) 1 | RTI-1823-17-15 | 100 | – | 2 | Folen | 4.5 (4) | 85.9 (54) | 9.6 (30) 3 | USP 0274-F | 100 | – | – 4[a] | 10415-25 | 0.3 (1) | 99.7 (6) | – 4[b] | 10415-25 | 0.2 (1) | 99.8 (19) | – 5 | Ψ-67-2 | 6.5 (1) | 80.9 (22) | 12.5 (10) 6 | Ψ-81-1 | 100 | – | – 7 | Ψ-97-1 | 0.2 (1) | 99.8 (17) | – 8 | *Polymorph A* | – | 80.9 (6) | 19.1 (7) 9 | *Polymorph A′* | – | 99.7 (8) | 0.3 (3) 10 | Hydrate A | 100 | 11 | Polymorph B | – | – | 100 12 | SPS5107/20/1 | 0.1 (1) | 99.9 (10) | – 13 | 17/44/136G | 0.1 (1) | 99.1 (13) | – 14 | 17/44/132E | – | 100.0 (11) | – 15 | 17/44/116Z | 0.1 (1) | 99.1 (12) | – 16 | 17/44/123L | 0.2 (1) | 99.8 (11) | – 17 | 800325750 | 0.2 (1) | 99.8 (25) | – 18 | 800326600 | 0.2 (1) | 99.8 (10) | – 19 | ARN-19-002654 | – | 100 | – 20 | CG002E-035-04 | 100 | – | – 21 | CG-0019E-038-03 | – | – | 100 22 | PL005E-004-40C | – | 100 | – 23 | PL005E-004-45C | – | 91.7 (7) | 8.3 (4) 24 | PL005E-004-55C | – | 77.4 (8) | 22.6 (5) Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.
133. The method of any of claims 111 -132, wherein the psilocybin is administered in a dosage form comprising a therapeutically effective amount of highly pure crystalline psilocybin in the form of Polymorph A, wherein the crystalline psilocybin has a chemical purity of greater than 97% by HPLC, and no single impurity of greater than 1 %.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. 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." From **p. 619** "Relative to baseline, **depressive symptoms were markedly reduced** 1 week (mean QIDS difference –11·8, 95% CI –9·15 to –14·35, p=0·002, Hedges' g=3·1) and 3 months (–9·2, 95% CI –5·69 to –12·71, p=0·003, Hedges' g=2) **after high-dose treatment**."

	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographicas. 78(1) 1-20 From **p. 18** "The QPA by RM also shed light on what was described as an unexpected result in the same patent application by providing compelling evidence that **a phase impurity, Polymorph B**, was responsible for the minor PXRD reflection at 17.5° 2θ observed from psilocybin produced in large-scale batches." From **p. 12** **Table 8** Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Code | Sample name | Hydrate A (%) | Polymorph A (%) | Polymorph B (%) 1 | RTI-1823-17-15 | 100 | – | 2 | Folen | 4.5 (4) | 85.9 (54) | 9.6 (30) 3 | USP 0274-F | 100 | – | – 4[a] | 10415-25 | 0.3 (1) | 99.7 (6) | – 4[b] | 10415-25 | 0.2 (1) | 99.8 (19) | – 5 | Ψ-67-2 | 6.5 (1) | 80.9 (22) | 12.5 (10) 6 | Ψ-81-1 | 100 | – | – 7 | Ψ-97-1 | 0.2 (1) | 99.8 (17) | – 8 | *Polymorph A* | – | 80.9 (6) | 19.1 (7) 9 | *Polymorph A′* | – | 99.7 (8) | 0.3 (3) 10 | Hydrate A | 100 | | 11 | Polymorph B | – | – | 100 12 | SPS5107/20/1 | 0.1 (1) | 99.9 (10) | – 13 | 17/44/136G | 0.1 (1) | 99.1 (13) | – 14 | 17/44/132E | – | 100.0 (11) | – 15 | 17/44/116*Z* | 0.1 (1) | 99.1 (12) | – 16 | 17/44/123*L* | 0.2 (1) | 99.8 (11) | – 17 | 800325750 | 0.2 (1) | 99.8 (25) | – 18 | 800326600 | 0.2 (1) | 99.8 (10) | – 19 | ARN-19-002654 | – | 100 | – 20 | CG002E-035-04 | 100 | – | – 21 | CG-0019E-038-03 | – | – | 100 22 | PL005E-004-40C | – | 100 | – 23 | PL005E-004-45C | – | 91.7 (7) | 8.3 (4) 24 | PL005E-004-55C | – | 77.4 (8) | 22.6 (5) Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.
134. The method of any of claim 130-133, further comprising a mixture of two silicified microcrystalline cellulose variants wherein the	29. W.I.P.O. Pat. App. No. 2003/047551 "AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE" (Published June 12, 2003)

first variant has a particle size from about 45 to 80 microns and the second variant has a particle size of about 90 to 150 microns.	From **claim 73** "Agglomerated particles of an **active agent and silicified microcrystalline cellulose**, the agglomerated particles being formed by combining a wetted active agent and dried silicified microcrystalline cellulose in a dryer to form agglomerated particles, the agglomerated particles having an **average particle size from about 10 µm to about 500 µm.**" 37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** " The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**."
135. The method of claim 24, wherein about 30% or less of the microcrystalline cellulose is the first variant having a particle size from about 45 to 80 microns and about 70% or more of the microcrystalline cellulose is the second variant having a particle size of about 90 to 150 microns.	29. W.I.P.O. Pat. App. No. 2003/047551 "AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE" (Published June 12, 2003) From **claim 73** "Agglomerated particles of an **active agent and silicified microcrystalline cellulose**, the agglomerated particles being formed by combining a wetted active agent and dried silicified microcrystalline cellulose in a dryer to form agglomerated particles, the agglomerated particles having an **average particle size from about 10 µm to about 500 µm.**" 37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**."

	From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**."
136. The method of any one of claims 130-135, wherein the dosage form is an oral dosage form.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
137. The method of claim 136, wherein the dosage form is a capsule.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Drug sessions were conducted in an aesthetic living-room-like environment with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the research unit. A urine sample was taken to verify abstinence from common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. **Psilocybin doses were administered in identically appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler**. For most of the time during the session, participants were encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a music program was played."
138. The method of claim 136, wherein the dosage form is a tablet.	23. U.S. Pat. App. Pub. No. 2009/0259039 "Salts of physiologically active and psychoactive alkaloids and amines simultaneously exhibiting bioavailability and abuse resistance" (Published October 15, 2009) From **claim 75** "The prescribing of a drug product containing at least one drug substance as an organic acid addition salt of an amine containing pharmaceutically active compound to a patient by a defined method of administration wherein said drug substance is a prophylactic in a different method of administration." From **claim 82** "The prescribing of a drug product of claim 75 wherein said amine containing pharmaceutically active compound comprises a material selected from acetaminophen, caffeine,

	acetorphine, acetylmethadol, allylprodine, alphacetylmethadol, bufotenine, dextromoramide, diethyltryptamine, etorphine, heroin, ibogaine, ketobemidone, lysergic acid diethylamide, mescaline, methaqualone, 3,4-methylenedioxyamphetamine, 3,4-methylenedioxymethamphetamine, N-ethyl-1-phenylcyclohexylamine, peyote, 1-(1-phenylcyclohexyl)pyrrolidine, **psilocybin**, psilocin, 1-{1-(2-thienyl)-cyclohexyl}-piperidine, alphaprodine, anileridine, cocaine, dextropropoxyphene, diphenoxylate, ethylmorphine, glutethimide, hydrocodone, hydromorphone, levo-alphaacetylmethadol, levorphanol, meperidine, methadone, morphine, opium, oxycodone, oxymorphone, poppy straw, thebaine, amphetamine, methamphetamine, methylphenidate, phencyclidine, codeine, benzphetamine, ketamine, alprazolam, chlorodiazepoxide, clorazepate, diethylpropion, fenfluramine, flurazepam, halaze" From **claim 94** "The prescribing of a drug product of claim 75 in a form selected from the group consisting of **a tablet**, a capsule, a caplet, and an oral suspension."
139. The method of any one of claims 111 -138, wherein at least one dose of psilocybin is administered to the subject.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
140. The method of claim 139, wherein at least dose of psilocybin is in the range of about 0.1 mg to about 100 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
141. The method of claim 140, wherein the dose of psilocybin is about 25 mg.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
142. The method of any one of claims 111 -141, wherein the subject participates in at least	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408.

one psychological support session before administration of the psilocybin.	From **p. 400** "Treatment procedures typically involve **psychological preparation prior to one or two therapist-supported drug sessions** followed by psychological integration. Using a consistent model (i.e. **involving appropriate psychological support**), sustained improvements in well-being in healthy individuals were observed after a single dose of psilocybin in a doubleblind design incorporating an active placebo (Griffiths et al. 2008)."
143. The method of claim 142, wherein the subject participates in at least one psychological support session after administration of the psilocybin.	2. CARHART-HARRIS (2016) "Psilocybin with psychological support for treatment-resistant depression: an open label feasibility study" The Lancet Psychiatry. 3(7):619-627. From **p. 622** "Patients attended one further study visit to the research facility 1 week **after their high-dose session**, during which all baseline questionnaires and assessments were repeated and an opportunity was provided for **further psychological debriefing (the 1 week follow-up visit)**."
144. The method of claim 142 or 143, wherein a therapist provides psychological support to the subject for approximately 4-8 hours after administration of the psilocybin.	5. GRIFFITHS (2006) "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Psychopharmacology. 187, 268-283. From **p. 270** "The **8-h drug sessions** were conducted in an aesthetic living-room-like environment designed specifically for the study. Two monitors were present with a single participant throughout the session. For most of the time during the session, the participant was encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a classical music program was played. The same music program was played for all participants in all sessions. The participants were encouraged to focus their attention on their inner experiences throughout the session. If a participant reported significant fear or anxiety, the **monitors provided reassurance verbally or physically** (e.g., with a supportive touch to the hand or shoulder). The sessions were videotaped and about 25% were reviewed by the first author to verify session procedures."
145. A dosage form comprising a therapeutically effective amount of highly pure crystalline psilocybin in the form of Polymorph A, wherein the crystalline psilocybin comprises at least 90% by weight of Polymorph A, further	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**."

comprising a mixture of two silicified microcrystalline cellulose variants wherein the first variant has a particle size from about 45 to 80 microns (SMCC 50), and the second variant has a particle size of about 90 to 150 microns (SMCC 90), wherein the ratio of SMCC 50 to SMCC 90 is 1 :5 to 1 :8 wt%.	From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**."
146. The dosage form of claim 145, further comprising a disintegrant, glidant, or lubricant.	29. W.I.P.O. Pat. App. No. 2003/047551 "AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE" (Published June 12, 2003) From **claim 1** "A solid dosage form comprising an **active agent and silicified microcrystalline cellulose**" From **claim 41** "A method of manufacturing a tablet containing an herbal extract comprising: a) providing an extract composition comprising an herbal extract suitable for spray drying; b) combining the herbal extract with a dry silicified microcrystalline cellulose in a dryer to form agglomerated particles; and c) compressing the agglomerated particles into tablets." From **claim 43** "The method of claim 41, wherein tableting agents are added to the agglomerated particles before they are compressed into tablets, said tableting agents being selected from the group consisting of **lubricants, disintegrants**, inert pharmaceutical fillers, bulkingagents, glidants, surfactants, flavorants, sweeteners and mixtures thereof." From **claim 148** "The dosage form of claim 147, wherein said active agent is selected from the group consisting of antihistamines, analgesics, non-steroidal anti-inflammatory agents, anti-emetics, anti-epileptics, vasodilators, anti-tussive agents and expectorants, anti-asthmatics, antacids, anti-spasmodics, antidiabetics, diuretics, anti-hypotensives, antihypertensives, bronchodilators, steroids, antibiotics, antihemorrhoidals, hypnotics, **psychotropics**, antidiarrheals, mucolytics, sedatives, decongestants, laxatives, vitamins, stimulants, anti-fungal agents, anti-viral agents, breath fresheners, anti-carcinogenic compounds, local anesthetics, oral antiseptics, hormonal agents, antiplaque agents, acidity reducing agents, and tooth desensitizers."

147. The dosage form of claim 147, comprising a disintegrant, wherein the disintegrant is sodium starch glycolate at less than 3% (by wt), less than 2%, or 1 % or less.	38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof."

	From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
148. The dosage form of any one of claims 145-147 wherein the ratio of SMCC 50 to SMCC 90 is 1 :5-1 :7; 1 :6-1 :7; 1 :6-1 :8; 1 .7-1.8, 1 :6; 1 :6.1 ; 1 :6.2; 1 :6.3; 1 :6.4; 1 :6.5; 1 :6.6; 1 .6.7; 1 :6.8; 1.6.9; or 1 :7.	29. W.I.P.O. Pat. App. No. 2003/047551 "AGGLOMERATED PARTICLES INCLUDING AN ACTIVE AGENT COPROCESSED WITH SILICIFIED MICROCRYSTALLINE CELLULOSE" (Published June 12, 2003) From claim 73 "Agglomerated particles of an **active agent and silicified microcrystalline cellulose**, the agglomerated particles being formed by combining a wetted active agent and dried silicified microcrystalline cellulose in a dryer to form agglomerated particles, the agglomerated particles having an **average particle size from about 10 µm to about 500 µm.**" 37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**."
149. The dosage form of any one of claims 145-147, comprising 5-40 mg of psilocybin	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 399** "Objectives Here, we report on safety and efficacy outcomes for up to 6 months in an open-label trial of **psilocybin for treatment resistant depression.** Methods Twenty patients (six females) with (mostly) severe, unipolar, **treatment-resistant major depression received two oral doses of psilocybin (10 and 25 mg, 7 days apart)** in a supportive setting"
150. The dosage form of claim 145, comprising 5 mg of psilocybin and SMCC 50 and	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase

SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 0.5% to 1 .0%.	inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof."

	From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
151. The dosage form of claim 145, comprising 5 mg of psilocybin and SMCC 50 and SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 0.5%.	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from

	canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
152. The dosage form of claim 145, comprising 10 mg of psilocybin and SMCC 50 and SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 1 %.	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**."

	From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange

	resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
153. The dosage form of claim 145, comprising 10 mg of psilocybin and SMCC 50 and SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 0.5% to 1 .0%.	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators,

	cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
154. The dosage form of claim 145, comprising comprises 10 mg of psilocybin and SMCC 50 and SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 0.5%.	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of**

	Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**,

	cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
155. The dosage form of claim 145, comprising 25 mg of psilocybin and SMCC 50 and SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 1 %.	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor

	drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
156. The dosage form of claim 145, comprising 25 mg of psilocybin and SMCC 50 and SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 0.5% to 1 .0%.	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016)

	From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."

157. The dosage form of claim 145, comprising 25 mg of psilocybin and SMCC 50 and SMCC 90, wherein the ratio of SMCC 50 to SMCC 90 is 1 :6.4 and sodium starch glycolate at about 0.5%.	37. W.I.P.O. Pat. App. No. 2018/184206 "Pharmaceutical salts, physical forms, and compositions of pyrrolopyrimidine kinase inhibitors, and methods of making same" (Published October 11, 2018) From **claim 26** "The pharmaceutical composition of any of claims 1-25, which comprises **at least two different kinds of silicified microcrystalline cellulose**." From **claim 27** "The pharmaceutical composition of claim 26, which comprises **Prosolv@ SMCC 50 and Prosolv@ SMCC 90**." From **claim 28** "The pharmaceutical composition of claim 27, which comprises from about **15% (w/w) to about 20% (w/w) of Prosolv@ SMCC 50, and from about 45% (w/w) to about 65% (w/w) of Prosolv@ SMCC 90**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising (a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants,

	mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof." From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
158. The dosage form of claim 145, comprising 5 mg of crystalline psilocybin A, 12.5 mg of SMCC 50, 79.5 mg of SMCC 90, 1 mg sodium starch glycolate, 1 mg colloidal silicon dioxide and 1 mg sodium stearyl fumarate.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1184** "The **low dose of psilocybin** was decreased from 3 to 1 mg/70 kg after 12 participants because data from the same dose-effect study showed **significant psilocybin effects at 5 mg/70 kg**, which raised concern that 3 mg/70 kg might not serve as an inactive placebo." 36. DEBOTTON (2017) "Applications of Polymers as Pharmaceutical Excipients in Solid Oral Dosage Forms" Med Res Rev. 37(1):52-97 From **p. 54** "For instance, continuous line production of tablets by means of fluid bed granulation and drying production method was reproducible when the APIs were wet granulated with a certain blend of **common polymeric excipients**: powdered cellulose, maize starch, pregelatinized starch, and **sodium starch glycolate**." 38. U.S. Pat. App. Pub. No. 2016/0051476 "Novel Dispersible Tablet Composition" (Published February 25, 2016) From **claim 1** "A dispersible tablet composition comprising

	(a) at least **one pharmacologically active ingredient;** (b) at least one hydrophilic polymer that reduces the sedimentation rate of the pharmacologically active ingredient; and (c) at least one disintegrant." From **claim 2** "The dispersible tablet composition of claim 1, wherein the pharmacologically active ingredient is selected from canti-cancer agents, antitussives, antihistamines, decongestants, alkaloids, mineral supplements, laxatives, vitamins, antacids, anti-cholesterolemic, anti-lipid agents, antiarrhythmics, antipyretics, analgesics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, anti-infectives, **psychotropic**, antimanics, stimulants, gastrointestinal agents, sedatives, antidiarrheal preparations, anti-anginal drugs, vasodilators, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, antitumor drugs, anticoagulants, antithrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypoglycemic agents, thyroid and antithyroid preparation, diuretics, antispasmodics, uterine relaxants, mineral and nutritional additives, antiobesity drugs, anabolic drugs, erythropoietic drugs, antiasthmatics, cough suppressants, mucolytics, anti-uricemic drugs, anti-viral drugs and mixtures thereof." From **claim 6** "The dispersible tablet composition of claim 1 wherein the hydrophilic polymer is polyethylene oxide, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, sodium carboxymethylcellulose, **microcrystalline cellulose**, guar gum, xanthan gum, alginates and combinations thereof." From **claim 7** "The dispersible tablet composition of claim 1 wherein the hydrophilic polymer is present in an amount from about **2% to about 75%** by weight of the total composition." From **claim 10** "The dispersible tablet composition of claim 1 wherein the disintegrant is selected from **sodium starch glycolate**, pregelatinised starch, crosslinked polyvinyl pyrrolidone, cross linked calcium or sodium carboxymethyl cellulose, low-substituted hydroxypropyl cellulose, microcrystalline cellulose, ion exchange resin, cross-linked polyacrylic acid, alginates, colloidal magnesium-aluminum silicate, calcium silicate and combinations thereof."

	From **claim 11** "The dispersible tablet composition of claim 10 wherein the disintegrant is selected from **sodium starch glycolate**, cross linked polyvinyl pyrrolidone, calcium silicate, croscarmellose sodium and combinations thereof." From **claim 12** "The dispersible tablet composition of claim 1 wherein the disintegrant is present in an amount from about **0.25% to about 50%** by weight of the total composition."
159. The dosage form of any one of claims 145-158, wherein the crystalline psilocybin comprises at least 95% by weight of Polymorph A.	15. SHERWOOD (2021) "Psilocybin: crystal structure solutions enable phase analysis of prior art and recently patented examples" Acta Crystallographica. 78(1) 1-20 From **p. 7** "2.3.6. Polymorph A, Polymorph A', Polymorph B, and Hydrate A (8–11). Diffractograms and analysis parameters for **Compass Pathways' Polymorph A (8) and Polymorph A0 (9), Polymorph B (10), and Hydrate A (11) were reported in Londesbrough et al. (2019)** [patent Figs. 7(a), 7(b), 7(c), and 7(d), respectively], and the corresponding crystallization conditions were described. Briefly, **Samples 8 and 11 (Polymorph A and Hydrate A as denoted in the patent) were produced by recrystallizing crude psilocybin (94 g) from water (9.6 ml per gram of psilocybin)**." From **p. 12**

	Table 8 Relative abundances of crystalline psilocybin phases in each of the samples listed in Table 2, as obtained by Rietveld-based QPA. The estimates are approximate for several samples, as the PXRD data were obtained from several different diffractometers and geometries. Rietveld plots for the refinements of Samples 1, 4[a], 4[b], 5, 8, 9, and 22–24 are included as Figs. 19–24. Code | Sample name | Hydrate A (%) | Polymorph A (%) | Polymorph B (%) 1 | RTI-1823-17-15 | 100 | – | 2 | Folen | 4.5 (4) | 85.9 (54) | 9.6 (30) 3 | USP 0274-F | 100 | – | – 4[a] | 10415-25 | 0.3 (1) | 99.7 (6) | – 4[b] | 10415-25 | 0.2 (1) | 99.8 (19) | – 5 | Ψ-67-2 | 6.5 (1) | 80.9 (22) | 12.5 (10) 6 | Ψ-81-1 | 100 | – | – 7 | Ψ-97-1 | 0.2 (1) | 99.8 (17) | – 8 | *Polymorph A* | – | 80.9 (6) | 19.1 (7) 9 | *Polymorph A′* | – | 99.7 (8) | 0.3 (3) 10 | Hydrate A | 100 | | 11 | Polymorph B | – | – | 100 12 | SPS5107/20/1 | 0.1 (1) | 99.9 (10) | – 13 | 17/44/136G | 0.1 (1) | 99.1 (13) | – 14 | 17/44/132E | – | 100.0 (11) | – 15 | 17/44/116Z | 0.1 (1) | 99.1 (12) | – 16 | 17/44/123L | 0.2 (1) | 99.8 (11) | – 17 | 800325750 | 0.2 (1) | 99.8 (25) | – 18 | 800326600 | 0.2 (1) | 99.8 (10) | – 19 | ARN-19-002654 | – | 100 | – 20 | CG002E-035-04 | 100 | – | – 21 | CG-0019E-038-03 | – | – | 100 22 | PL005E-004-40C | – | 100 | – 23 | PL005E-004-45C | – | 91.7 (7) | 8.3 (4) 24 | PL005E-004-55C | – | 77.4 (8) | 22.6 (5) Notes: (*a*) Sample analyzed by PXRD with transmission geometry. (*b*) Sample analyzed by PXRD with reflection geometry.
160. The dosage form of any one of claims 145-158, wherein the dosage form is an oral dosage form.	1. CARHART-HARRIS (2018) "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up" Psychopharmacology (Berl). 235(2):399-408. From **p. 400** "This was an open-label feasibility study in 20 patients with treatment-resistant depression. Treatment involved **two oral doses of psilocybin (10 and 25 mg),** 7 days apart."
161. The dosage form of any one of claims 145-158, wherein the dosage form is a capsule.	3. GRIFFITHS (2016) "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial" Journal of Psychopharmacology. 30(12)1181-197 From **p. 1182** "Drug sessions were conducted in an aesthetic living-room-like environment with two monitors present. Participants were instructed to consume a low-fat breakfast before coming to the

	research unit. A urine sample was taken to verify abstinence from common drugs of abuse (cocaine, benzodiazepines, and opioids including methadone). Participants who reported use of cannabis or dronabinol were instructed not to use for at least 24 h before sessions. **Psilocybin doses were administered in identically appearing opaque, size 0 gelatin capsules, with lactose as the inactive capsule filler**. For most of the time during the session, participants were encouraged to lie down on the couch, use an eye mask to block external visual distraction, and use headphones through which a music program was played."
162. The dosage form of any one of claims 145-158, wherein the dosage form is a tablet.	23. U.S. Pat. App. Pub. No. 2009/0259039 "Salts of physiologically active and psychoactive alkaloids and amines simultaneously exhibiting bioavailability and abuse resistance" (Published October 15, 2009) From **claim 75** "The prescribing of a drug product containing at least one drug substance as an organic acid addition salt of an amine containing pharmaceutically active compound to a patient by a defined method of administration wherein said drug substance is a prophylactic in a different method of administration." From **claim 82** "The prescribing of a drug product of claim 75 wherein said amine containing pharmaceutically active compound comprises a material selected from acetaminophen, caffeine, acetorphine, acetylmethadol, allylprodine, alphacetylmethadol, bufotenine, dextromoramide, diethyltryptamine, etorphine, heroin, ibogaine, ketobemidone, lysergic acid diethylamide, mescaline, methaqualone, 3,4-methylenedioxyamphetamine, 3,4-methylenedioxymethamphetamine, N-ethyl-1-phenylcyclohexylamine, peyote, 1-(1-phenylcyclohexyl)pyrrolidine, **psilocybin**, psilocin, 1-{1-(2-thienyl)-cyclohexyl}-piperidine, alphaprodine, anileridine, cocaine, dextropropoxyphene, diphenoxylate, ethylmorphine, glutethimide, hydrocodone, hydromorphone, levo-alphaacetylmethadol, levorphanol, meperidine, methadone, morphine, opium, oxycodone, oxymorphone, poppy straw, thebaine, amphetamine, methamphetamine, methylphenidate, phencyclidine, codeine, benzphetamine, ketamine, alprazolam, chlorodiazepoxide, clorazepate, diethylpropion, fenfluramine, flurazepam, halaze" From **claim 94** "The prescribing of a drug product of claim 75 in a form selected from the group consisting of **a tablet**, a capsule, a caplet, and an oral suspension."

Electronic Acknowledgement Receipt

EFS ID:	45190319
Application Number:	17604610
International Application Number:	
Confirmation Number:	9614
Title of Invention:	TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN
First Named Inventor/Applicant Name:	Derek John LONDESBROUGH
Customer Number:	161862
Filer:	Shahin Shams
Filer Authorized By:	
Attorney Docket Number:	COPA-016/01US 337248-2112
Receipt Date:	09-MAR-2022
Filing Date:	
Time Stamp:	21:25:06
Application Type:	

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Concise Description of Relevance	Concise-description-generated.pdf	45832 28f31bfcbd48e97f2f48cb7368222577d6348c55	no	8

Warnings:

Information:					
2	Third-Party Submission Under 37 CFR 1.290	Third-party-preissuance-submission.pdf	70113 9bfe3117eb9c2d78da3711f17c9a41071ebc6933	no	4
Warnings:					
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3	Request for Notification of Non-compliant Third-Party Submission	Third-party-notification-request.pdf	23721 a04b4cb9ecced0efe047dd90e1e1476224a832d6	no	1
Warnings:					
Information:					
4	Concise Description of Relevance	ClaimsChart.pdf	2268638 8e54ffdc1d5dd547efefc94e12dd9ea2df0297ad	no	115
Warnings:					
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5	Foreign Reference	31-WOPatAppPubNo2018135943.pdf	16208745 20d1156659ff486a1e2a097594326396add53d2c	no	26
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6	Foreign Reference	32-KUHNERT.pdf	612285 161969ff8cd3c9ad6a85005932179607506dadc8	no	7
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7	Translation of Non-Patent Publication	32-KUHNERTEnglishTranslation.pdf	123129 0a0831a32e23728038bc9fd6b5c2b3c450e154d3	no	8
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8	Evidence of Publication	33-ICH.pdf	708984 cd8a39f2c9f5703f556e385ecec02f7db43aedb2	no	10
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9	Evidence of Publication	34-FMCHD90.pdf	193212 2a8250c0f28eb93ef4bbbd3225fe4d9163708d7e	no	2
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10	Evidence of Publication	35-FMCHD50.pdf	192751 de71958ed48a654568d36907bae39377180ad5bd	no	2
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11	Non Patent Literature	36-DEBOTTON.pdf	1751230 bdd48746393677773328ba5e1ff747cb5c75ce74	no	46
Warnings:					
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12	Foreign Reference	37-WOPatAppPubNo2018184206.pdf	22524726 098d63ff8f64197291f816e0d1997e3a7a4edba4	no	182
Warnings:					
Information:					
13	Evidence of Publication	39-PROSOLV.pdf	471168 392646d4f59c74ec44b4bfeac7d73f3c9aad83cd	no	2
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