

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Lobe Sciences Ltd

Confirmation No.:

Serial No.: 17/916,855

Group No.:

Filing or 371(c) Date: 20 April 2021

Examiner:

Entitled: Methods, Compositions and Devices for Treating Mild Traumatic Brain Injury, Post Traumatic Stress Disorder and Mild Traumatic Brain Injury with Post Traumatic Stress Disorder

**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. EAKIN (2014) "Efficacy of N-Acetyl Cysteine in Traumatic Brain Injury" *PLoS One*. Vol. 9(4): e90617.
2. BACK (2017) "A Double-Blind Randomized Controlled Pilot Trial of N-Acetylcysteine in Veterans with PTSD and Substance Use Disorders" *Journal of Clinical Psychiatry*. Vo. 77(11): e1439–e1446.
3. HOFFER (2013) "Amelioration of Acute Sequelae of Blast Induced Mild Traumatic Brain Injury by N-Acetyl Cysteine: A Double-Blind, Placebo Controlled Study" *PLoS One*. Vol. 8(1): e54163.
4. Intl. Pat. Doc. No. WO2020212952 "TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN" (Published 22 October 2020)
5. CISION (2020) "ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI)" Published 6 January 2020. Retrieved from 3 March 2020. URL: <https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html>
6. NEURONASAL (2017) "Treating Brain Injury" Retrieved from 12 November 2017. URL: <https://web.archive.org/web/20171112165607/http://www.neuronasal.com/deck-link.html>

7. NEURONASAL (2017) “Reduce acute brain injury by novel patented nose-to-brain drug delivery route” Retrieved from 12 November 2017. Linked presentation located in the URL: <https://web.archive.org/web/20171112165607/http://www.neuronasal.com/deck-link.html>
8. MAYO CLINIC (2017) “Post-traumatic stress disorder (PTSD)” Retrieved from 09 October 2017. URL: <https://web.archive.org/web/20171009044608/https://www.mayoclinic.org/diseases-conditions/post-traumatic-stress-disorder/symptoms-causes/syc-20355967>
9. WIKIPEDIA (2019) “Psilocybin” Retrieved from 28 December 2019. URL: <https://web.archive.org/web/20191228184209/https://en.wikipedia.org/wiki/Psilocybin>
10. RAMBOUSEK (2014) “The Effect of Psilocin on Memory Acquisition, Retrieval, and Consolidation in the Rat” *Frontiers in Behavioral Neuroscience*. Vol 8: pages 1-7
11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved from 19 July 2019. URL: <https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595>
12. BIRD (2020) “Smell changes memory processing and could treat trauma” *Medical News Today*. URL: <https://www.medicalnewstoday.com/articles/smell-changes-memory-processing-and-could-treat-trauma#1>
13. WIKIPEDIA (2017) “Psilocybe azurescens” Retrieved from January 2017. URL: [https://web.archive.org/web/20170131223629/https://en.wikipedia.org/wiki/Psilocybe\\_azurescens](https://web.archive.org/web/20170131223629/https://en.wikipedia.org/wiki/Psilocybe_azurescens)
14. BAUER (2019) “What Are Psilocybin Derivatives?” Retrieved from 27 July 2019. URL: <https://web.archive.org/web/20190727145651/https://psychedelicreview.com/what-are-psilocybin-derivatives/>

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. 17/916,855 Pending Claims	References
<b>1. A method for alleviating one or more symptoms of mild traumatic brain injury (mTBI), post-traumatic stress</b>	11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a>

**disorder (PTSD) or mTBI with PTSD, said method comprising administering to a subject suffering from mTBI, PTSD or mTBI with PTSD a psychedelic agent in combination with N-acetylcysteine (NAC).**

From **page 1** “Normally **I consume between 1 and 3.5 grams dried mushrooms**. I scaled back this time to half a gram, just to be safe and see.”

From **page 1** “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. **I do take N-ACETYL CYSTEINE supplements**, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. **All these supplements are taken daily.**”

From **page 1** “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. **I am dealing with a good deal of PTSD**; lately I have loathed myself for failing to see an abusive person in my life for what they were. **The mushrooms facilitated a self-acceptance process**. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”

1. EAKIN (2014) “Efficacy of N-Acetyl Cysteine in Traumatic Brain Injury” *PLoS One*. Vol. 9(4): e90617.

From **Abstract** “In this study, using two different injury models in two different species, we found that early **post-injury treatment with N-Acetyl Cysteine (NAC) reversed the behavioral deficits associated with the TBI.**”

2. BACK (2017) “A Double-Blind Randomized Controlled Pilot Trial of N-Acetylcysteine in Veterans with PTSD and Substance Use Disorders” *Journal of Clinical Psychiatry*. Vo. 77(11): e1439–e1446.

From **Abstract** “**Participants treated with NAC, as compared to placebo, evidenced significant improvements in PTSD symptoms, craving, and depression.**”

3. HOFFER (2013) “Amelioration of Acute Sequelae of Blast Induced Mild Traumatic Brain Injury by N-Acetyl Cysteine: A Double-Blind, Placebo Controlled Study” *PLoS One*. Vol. 8(1): e54163.

From **Abstract** “Secondary analysis revealed **subjects receiving NAC within 24 hours of blast had an 86% chance of symptom resolution** with no reported side effects versus 42% for those seen early who received placebo.”

From **Abstract** “This study, conducted in an active theatre of war, demonstrates that **NAC, a safe pharmaceutical countermeasure, has beneficial effects on the severity and resolution of sequelae of blast induced mTBI**. This is the first demonstration of an effective short term countermeasure for mTBI. Further work on long term outcomes and the potential use of NAC in civilian mTBI is warranted.”

4. Intl. Pat. Doc. No. WO2020212952 “TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN” (Published 22 October 2020)

From **claim 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 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.”

From **claim 112** “**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: Neurocognitive Disorders due

	<p>to Alzheimer's, Lewy Bodies, <b>Traumatic Brain Injury</b>, 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; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p>
<p><b>2. The method of claim 1 wherein the one or more symptoms is selected from intrusive memories, nightmares, a sense of reliving the trauma, or psychological or physiological distress when reminded of the trauma, active avoidance of thoughts, feelings, or reminders of the trauma, inability to recall some aspect of the trauma, withdrawal from others, or emotional numbing, insomnia, irritability, difficulty concentrating, hypervigilance, or heightened startle response.</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms</b>. I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements</b>, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD</b>; lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process</b>. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p> <p>2. BACK (2017) “A Double-Blind Randomized Controlled Pilot Trial of N-Acetylcysteine in Veterans with PTSD and Substance Use Disorders” <i>Journal of Clinical Psychiatry</i>. Vo. 77(11): e1439–e1446.</p> <p>From <b>Abstract</b> “<b>Participants treated with NAC, as compared to placebo, evidenced significant improvements in PTSD symptoms, craving, and depression.</b>”</p> <p>8. MAYO CLINIC (2017) “Post-traumatic stress disorder (PTSD)” Retrieved from 09 October 2017. URL: <a href="https://web.archive.org/web/20171009044608/https://www.mayoclinic.org/d">https://web.archive.org/web/20171009044608/https://www.mayoclinic.org/d</a></p>

[iseases-conditions/post-traumatic-stress-disorder/symptoms-causes/syc-20355967](https://www.medicines.com.au/medicines-conditions/post-traumatic-stress-disorder/symptoms-causes/syc-20355967)

From **page 1**

“Symptoms

Post-traumatic stress disorder symptoms may start within one month of a traumatic event, but sometimes symptoms may not appear until years after the event. These symptoms cause significant problems in social or work situations and in relationships. They can also interfere with your ability to go about your normal daily tasks.

**PTSD symptoms** are generally grouped into four types: intrusive memories, avoidance, negative changes in thinking and mood, and changes in physical and emotional reactions. Symptoms can vary over time or vary from person to person.

#### **Intrusive memories**

Symptoms of intrusive memories may include:

Recurrent, unwanted distressing memories of the traumatic event  
**Reliving the traumatic event** as if it were happening again (flashbacks)  
Upsetting dreams or **nightmares** about the traumatic event  
**Severe emotional distress or physical reactions to something that reminds you of the traumatic event**

#### **Avoidance**

Symptoms of avoidance may include:

**Trying to avoid thinking or talking about the traumatic event**  
Avoiding places, activities or people that remind you of the traumatic event

Negative changes in thinking and mood

Symptoms of negative changes in thinking and mood may include:

Negative thoughts about yourself, other people or the world  
Hopelessness about the future  
**Memory problems, including not remembering important aspects of the traumatic event**  
**Difficulty maintaining close relationships**  
**Feeling detached from family and friends**

	<p>Lack of interest in activities you once enjoyed          Difficulty experiencing positive emotions  <b>Feeling emotionally numb</b></p> <p>Changes in physical and emotional reactions</p> <p>Symptoms of changes in physical and emotional reactions (also called arousal symptoms) may include:</p> <p><b>Being easily startled or frightened</b>  <b>Always being on guard for danger</b>          Self-destructive behavior, such as drinking too much or driving too fast  <b>Trouble sleeping</b>  <b>Trouble concentrating</b>  <b>Irritability, angry outbursts or aggressive behavior</b>          Overwhelming guilt or shame”</p>
<p><b>3. The method of claim 1 wherein the psychedelic agent and NAC are administered simultaneously.</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms</b>. I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements</b>, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD</b>; lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process</b>. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p> <p>1. EAKIN (2014) “Efficacy of N-Acetyl Cysteine in Traumatic Brain Injury” <i>PLoS One</i>. Vol. 9(4): e90617.</p> <p>From Abstract “In this study, using two different injury models in two different species, we found that early <b>post-injury treatment with N-Acetyl</b></p>

**Cysteine (NAC) reversed the behavioral deficits associated with the TBI.”**

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	<p>Conversion Disorder (Functional Neurological Symptom Disorder), Factitious Disorder, <b>Post-Traumatic Stress Disorder (PTSD)</b>, 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.”</p> <p>From <b>claim 112</b> “<b>A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin</b>, wherein the subject has at least one of the following diseases, disorders, or conditions: Neurocognitive Disorders due to Alzheimer's, Lewy Bodies, <b>Traumatic Brain Injury</b>, 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; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p>
<p><b>4. The method of claim 3 wherein the psychedelic agent and NAC in various concentrations are formulated in a solid dosage form and administered to a patient orally.</b></p>	<p>9. WIKIPEDIA (2019) “Psilocybin” Retrieved from 28 December 2019. URL: <a href="https://web.archive.org/web/20191228184209/https://en.wikipedia.org/wiki/Psilocybin">https://web.archive.org/web/20191228184209/https://en.wikipedia.org/wiki/Psilocybin</a></p> <p>From <b>page 5, Available Forms</b> section “<b>The psilocybin present in certain species of mushrooms can be ingested in several ways: by consuming fresh or dried fruit bodies, by preparing a herbal tea, or by combining with other foods to mask the bitter taste.</b>”</p> <p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p>

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From **page 7 paragraph 4** “In some embodiments the **psilocybin is administered in an oral dosage form**. In some embodiments the psilocybin is administered in a capsule. In some embodiments the psilocybin is administered in a tablet.”

3. HOFFER (2013) “Amelioration of Acute Sequelae of Blast Induced Mild Traumatic Brain Injury by N-Acetyl Cysteine: A Double-Blind, Placebo Controlled Study” *PLoS One*. Vol. 8(1): e54163.

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From **page 5** “This is the first prospective, double-blinded, placebo-controlled randomized study to focus on the acute treatment of combat blast-related mTBI in a forward war zone. Supplementation of standard therapy

	<p>with oral NAC had a significant impact on neuropsychological test results, number of mTBI symptoms, and complete symptom resolution by day seven of treatment when compared to placebo.”</p>
<p><b>5. The method of claim 3 wherein the psychedelic agent and NAC in various concentrations are formulated as a solution or a suspension with one or more excipients in a nonpressurized dispenser or dispensers and delivered to a patient as a nasal spray containing a metered dose of each ingredient.</b></p>	<p>4. Intl. Pat. Doc. No. WO2020212952 “TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN” (Published 22 October 2020)</p> <p>From <b>claim 111</b> “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 Neurological Symptom Disorder), Factitious Disorder, <b>Post-Traumatic Stress Disorder (PTSD)</b>, 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.”</p> <p>From <b>claim 112</b> “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: Neurocognitive Disorders due to Alzheimer's, Lewy Bodies, <b>Traumatic Brain Injury</b>, 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);</p>

	<p>Social (Pragmatic) Communication Disorder; Tourette's Disorder; Persistent (Chronic) Motor or Vocal Tic Disorder; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p> <p>From <b>page 45 paragraph 4</b> “Exemplary modes for administration of psilocybin include oral, parenteral (e.g. , intravenous, subcutaneous, intradermal, intramuscular [including administration to skeletal, diaphragm and/or cardiac muscle], intradermal, intrapleural, intracerebral, and intra-articular), topical (e.g., to both skin and mucosal surfaces, including airway surfaces, and transdermal administration), <b>inhalation (e.g. , via an aerosol)</b>, rectal (e.g., via a suppository), transmucosal, <b>intranasal</b>, buccal (e.g. , sublingual), vaginal, intrathecal, intraocular, transdermal, in utero (or in ovo), intralymphatic, and direct tissue or organ injection (e.g., to liver, skeletal muscle, cardiac muscle, diaphragm muscle or brain). In some embodiments, psilocybin is administered orally to the subject.”</p> <p>5. CISION (2020) “ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI)” Published 6 January 2020. URL: <a href="https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html">https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html</a></p> <p>From <b>page 2</b> “By contrast, <b>Neuronasal's intranasal approach</b> enables direct nose-to-brain delivery, allowing for significantly lower doses and outpatient treatment. Given its apparent efficacy in disrupting the underlying neurochemical cascade, <b>intranasal NAC</b> has the potential to induce a fundamental shift in the natural course of the condition for hundreds of thousands of people.”</p>
<p><b>6. The method of claim 3 wherein the composition is administered to prevent pathological conversion of STM to LTM and promote disengagement of pathological LTM by a chemical agonist/antagonist shock.</b></p>	<p>10. RAMBOUSEK (2014) “The Effect of Psilocin on Memory Acquisition, Retrieval, and Consolidation in the Rat” <i>Frontiers in Behavioral Neuroscience</i>. Vol 8: pages 1-7</p> <p>From <b>page 4</b> “Our findings indicate that <b>psilocin affects learning and memory acquisition necessary for spatial navigation and that it also has a disruptive effect on memory retrieval</b> in MWM.”</p>
<p><b>7. The method of claim 1 wherein the</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL:</p>

<p>psychedelic agent is administered before NAC.</p>	<p><a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms</b>. I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements</b>, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD</b>; lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process</b>. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p>
<p><b>8. The method of claim 1 wherein the psychedelic agent is administered after NAC.</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms</b>. I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements</b>, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD</b>; lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process</b>. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p>
<p><b>9. The method of claim 1 wherein the psychedelic agent is</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL:</p>

mescaline, lysergic acid diethylamide (LSD), psilocybin or a psilocybin-derived agent, or N,N-Dimethyltryptamine (DMT) .

<https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595>

From **page 1** “Normally **I consume between 1 and 3.5 grams dried mushrooms**. I scaled back this time to half a gram, just to be safe and see.”

From **page 1** “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. **I do take N-ACETYL CYSTEINE supplements**, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. **All these supplements are taken daily.**”

From **page 1** “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. **I am dealing with a good deal of PTSD**; lately I have loathed myself for failing to see an abusive person in my life for what they were. **The mushrooms facilitated a self-acceptance process**. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”

13. WIKIPEDIA (2018) “Psilocybe azurescens” Retrieved from January 2017. URL:

[https://web.archive.org/web/20170131223629/https://en.wikipedia.org/wiki/Psilocybe\\_azurescens](https://web.archive.org/web/20170131223629/https://en.wikipedia.org/wiki/Psilocybe_azurescens)

From **page 2**

Effects [\[ edit \]](#)

See also: *Psilocybin § Effects*

Alkaloid concentration of fresh Psilocybin Mushrooms<sup>[5]</sup>

Name	Psilocybin [% of weight]	Psilocin [% of weight]	Baeocystin [% of weight]	Total [% of weight]
<i>Psilocybe azurescens</i>	1.78	0.38	0.35	2.51
<i>Psilocybe cubensis</i>	0.63	0.60	0.025	1.26

14. BAUER (2019) “What Are Psilocybin Derivatives?” Retrieved from 27 July 2019. URL:

<https://web.archive.org/web/20190727145651/https://psychedelicreview.com/what-are-psilocybin-derivatives/>

From **page 2**

“Other examples of **psilocybin derivatives** include:

- **Psilocin (sometimes spelled psilocyn)**
- [3-(2-trimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate (aka Aeruginascin)
- 4-hydroxy-N,N,N-trimethyltryptamine
- **Baeocystin (aka [3-(2-methylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate)**
- 4-hydroxy-N-methyltryptamine
- Norbaeocystin (aka [3-(aminoethyl)-1H-indol-4-yl] dihydrogen phosphate), and
- 4-hydroxytryptamine (serotonin)”

4. Intl. Pat. Doc. No. WO2020212952 “TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN” (Published 22 October 2020)

From **claim 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 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.”



	<p>From <b>claim 112</b> “A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of <b>psilocybin</b>, wherein the subject has at least one of the following diseases, disorders, or conditions: Neurocognitive Disorders due to Alzheimer's, Lewy Bodies, <b>Traumatic Brain Injury</b>, 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; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p>
<p><b>10. The method of 8 claim 1 wherein the psychedelic agent is psilocybin or a psilocybin-derived agent.</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms</b>. I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements</b>, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD</b>; lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process</b>. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p> <p>13. WIKIPEDIA (2018) “Psilocybe azurescens” Retrieved from January 2017. URL: <a href="https://web.archive.org/web/20170131223629/https://en.wikipedia.org/wiki/Psilocybe_azurescens">https://web.archive.org/web/20170131223629/https://en.wikipedia.org/wiki/Psilocybe_azurescens</a></p> <p>From <b>page 2</b></p>

## Effects [\[ edit \]](#)

See also: *Psilocybin § Effects*

Alkaloid concentration of fresh Psilocybin Mushrooms<sup>[5]</sup>

Name	Psilocybin [% of weight]	Psilocin [% of weight]	Baeocystin [% of weight]	Total [% of weight]
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From **page 2**

“Other examples of **psilocybin derivatives** include:

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- 4-hydroxy-N,N,N-trimethyltryptamine
- **Baeocystin (aka [3-(2-methylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate)**
- 4-hydroxy-N-methyltryptamine
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	<p>Anxiety Disorder, Anxiety Disorder Due to Another Medical Condition, Somatic Symptom Disorder, Illness Anxiety Disorder (hypochondriac), Conversion Disorder (Functional Neurological Symptom Disorder), Factitious Disorder, <b>Post-Traumatic Stress Disorder (PTSD)</b>, 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.”</p> <p>From <b>claim 112</b> “<b>A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin</b>, wherein the subject has at least one of the following diseases, disorders, or conditions: Neurocognitive Disorders due to Alzheimer's, Lewy Bodies, <b>Traumatic Brain Injury</b>, 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; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p>
<p><b>11. The method of claim 1 further comprising imprint pairing one or more symptoms of mTBI, PTSD or mTBI with PTSD in the subject with an odor and eliminating the subject’s ability to smell the odor.</b></p>	<p>12. BIRD (2020) “Smell changes memory processing and could treat trauma” Medical News Today. URL: <a href="https://www.medicalnewstoday.com/articles/smell-changes-memory-processing-and-could-treat-trauma#1">https://www.medicalnewstoday.com/articles/smell-changes-memory-processing-and-could-treat-trauma#1</a></p> <p>From <b>Title</b> “Smell changes memory processing and could treat trauma”</p> <p>From <b>page 1</b> “Research in mice suggests that <b>smell helps consolidate memories and may help people overcome trauma.</b>”</p> <p>From <b>page 4</b> “Beyond the academic interest, these findings could pave the way for <b>new tools to treat mental health conditions caused by traumatic memories, namely PTSD.</b>”</p>

From **page 5** “Most current approaches to treat PTSD try to suppress or dampen the traumatic memory, but — crucially — this only works when a person can recall the memory first. **Using smells to spark memories could, therefore, be a significant pathway to treatment.**”

1. EAKIN (2014) “Efficacy of N-Acetyl Cysteine in Traumatic Brain Injury” *PLoS One*. Vol. 9(4): e90617.

From **Abstract** “In this study, using two different injury models in two different species, we found that early **post-injury treatment with N-Acetyl Cysteine (NAC) reversed the behavioral deficits associated with the TBI.**”

2. BACK (2017) “A Double-Blind Randomized Controlled Pilot Trial of N-Acetylcysteine in Veterans with PTSD and Substance Use Disorders” *Journal of Clinical Psychiatry*. Vo. 77(11): e1439–e1446.

From **Abstract** “**Participants treated with NAC, as compared to placebo, evidenced significant improvements in PTSD symptoms, craving, and depression.**”

3. HOFFER (2013) “Amelioration of Acute Sequelae of Blast Induced Mild Traumatic Brain Injury by N-Acetyl Cysteine: A Double-Blind, Placebo Controlled Study” *PLoS One*. Vol. 8(1): e54163.

From **Abstract** “Secondary analysis revealed **subjects receiving NAC within 24 hours of blast had an 86% chance of symptom resolution** with no reported side effects versus 42% for those seen early who received placebo.”

From **Abstract** “This study, conducted in an active theatre of war, demonstrates that **NAC, a safe pharmaceutical countermeasure, has beneficial effects on the severity and resolution of sequelae of blast induced mTBI.** This is the first demonstration of an effective short term countermeasure for mTBI. Further work on long term outcomes and the potential use of NAC in civilian mTBI is warranted.”

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	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms</b>. I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements</b>, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD</b>; lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process</b>. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p>
<p><b>12. A pharmaceutical composition comprising a psychedelic agent and N-acetylcysteine (NAC) and one or more excipients.</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms</b>. I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements</b>, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD</b>; lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process</b>. The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p>

4. Intl. Pat. Doc. No. WO2020212952 “TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN” (Published 22 October 2020)

From **claim 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 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.”

From **claim 112** “**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: 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; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral

	<p>Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p> <p>From <b>page 38, paragraph 2</b> “In some embodiments, the disclosure provides a <b>pharmaceutical composition comprising crystalline psilocybin and one or more pharmaceutically acceptable carriers or excipients.</b>”</p>
<p><b>13. The pharmaceutical composition of claim 12 formulated in a solid dosage form and administered to a patient orally or in a nasal spray.</b></p>	<p>11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <a href="https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595">https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595</a></p> <p>From <b>page 1</b> “Normally <b>I consume between 1 and 3.5 grams dried mushrooms.</b> I scaled back this time to half a gram, just to be safe and see.”</p> <p>From <b>page 1</b> “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough research. <b>I do take N-ACETYL CYSTEINE supplements,</b> ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. <b>All these supplements are taken daily.</b>”</p> <p>From <b>page 1</b> “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. <b>I am dealing with a good deal of PTSD;</b> lately I have loathed myself for failing to see an abusive person in my life for what they were. <b>The mushrooms facilitated a self-acceptance process.</b> The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”</p> <p>9. WIKIPEDIA (2019) “Psilocybin” Retrieved from 28 December 2019. URL: <a href="https://web.archive.org/web/20191228184209/https://en.wikipedia.org/wiki/Psilocybin">https://web.archive.org/web/20191228184209/https://en.wikipedia.org/wiki/Psilocybin</a></p> <p>From <b>page 5, Available Forms section</b> “The <b>psilocybin present in certain species of mushrooms can be ingested in several ways: by consuming fresh or dried fruit bodies, by preparing a herbal tea, or by combining with other foods to mask the bitter taste.</b>”</p> <p>3. HOFFER (2013) “Amelioration of Acute Sequelae of Blast Induced Mild Traumatic Brain Injury by N-Acetyl Cysteine: A Double-Blind, Placebo Controlled Study” <i>PLoS One</i>. Vol. 8(1): e54163.</p>



From **Abstract** “Secondary analysis revealed **subjects receiving NAC within 24 hours of blast had an 86% chance of symptom resolution** with no reported side effects versus 42% for those seen early who received placebo.”

From **Abstract** “This study, conducted in an active theatre of war, demonstrates that **NAC, a safe pharmaceutical countermeasure, has beneficial effects on the severity and resolution of sequelae of blast induced mTBI**. This is the first demonstration of an effective short term countermeasure for mTBI. Further work on long term outcomes and the potential use of NAC in civilian mTBI is warranted.”

From **page 5** “This is the first prospective, double-blinded, placebo-controlled randomized study to focus on the acute treatment of combat blast-related mTBI in a forward war zone. Supplementation of standard therapy with **oral NAC had a significant impact on neuropsychological test results, number of mTBI symptoms, and complete symptom resolution by day seven of treatment when compared to placebo.**”

4. Intl. Pat. Doc. No. WO2020212952 “TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN” (Published 22 October 2020)

From **claim 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 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-,

	<p>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.”</p> <p>From <b>claim 112</b> “<b>A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of psilocybin</b>, wherein the subject has at least one of the following diseases, disorders, or conditions: Neurocognitive Disorders due to Alzheimer's, Lewy Bodies, <b>Traumatic Brain Injury</b>, 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; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p> <p>From <b>page 7 paragraph 4</b> “In some embodiments the <b>psilocybin is administered in an oral dosage form</b>. In some embodiments the psilocybin is administered in a capsule. In some embodiments the psilocybin is administered in a tablet.”</p>
14. Cancelled	
15. Cancelled	
16. Cancelled	
17. Cancelled	
18. Cancelled	
<p><b>19. A nasal mist transducer (NMT) for administration of one or more pharmaceutically active ingredients as fine mist particles at preselected dosages and times, said NMT comprising:</b></p> <p><b>a nasal funnel capable of fitting into a</b></p>	<p><i>From paragraph [0062] of the application of interest, U.S. App. No. 17/916,855, “In one nonlimiting embodiment, the psychedelic agent and NAC are administered sequentially in a <b>nasal spray or mist transducer (NMT) programmed time release administration.</b>”</i></p> <p>5. CISION (2020) “ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI)” Published 6 January 2020. URL: <a href="https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html">https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html</a></p>

vestibular anatomy of a human:

a mist generator with a top and bottom which produces a fine mist at the top which is propelled toward the nasal funnel;

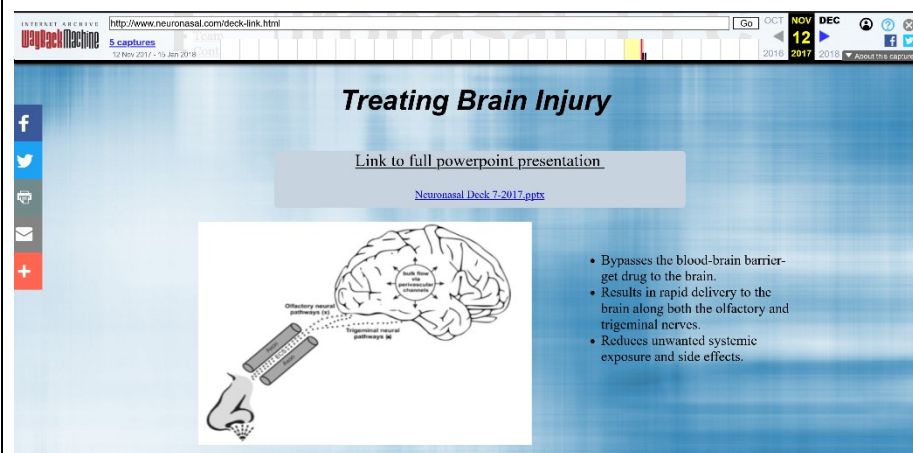
a syringe loading apparatus capable of holding one or more micro syringes attached at the bottom of the mist generator;

and a means for applying pressure to a plunger of a microsyringe loaded into the syringe loading apparatus.

From page 2 “By contrast, **Neuronasal's intranasal approach** enables direct nose-to-brain delivery, allowing for significantly lower doses and outpatient treatment. Given its apparent efficacy in disrupting the underlying neurochemical cascade, intranasal NAC has the potential to induce a fundamental shift in the natural course of the condition for hundreds of thousands of people.”

6. NEURONASAL (2017) “Treating Brain Injury” Retrieved from 12 November 2017. URL:

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7. NEURONASAL (2017) “Reduce acute brain injury by novel patented nose-to-brain drug delivery route” Retrieved from 12 November 2017.

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From slide 8



## Neuronasal

### Neuronasal approach – approved device



#### Aptar UDS device

- Used in Flonase (marketed drug).
- FDA master file (access granted).
- Manufacturing is well understood
- Patient use is well understood
- Similar to device used in animal experiments.
- Gets appropriately formulated drugs to upper third of nasal cavity for nose-to-brain delivery.**

8

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	<p>Defiant Disorder, Intermittent Explosive Disorder, Conduct Disorder, Antisocial Personality Disorder, Psychopathy, Pyromania, or Kleptomania.”</p> <p>From <b>claim 112</b> “A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically-effective dose of <b>psilocybin</b>, wherein the subject has at least one of the following diseases, disorders, or conditions: Neurocognitive Disorders due to Alzheimer's, Lewy Bodies, <b>Traumatic Brain Injury</b>, 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; Amnesic Disorder Due to Known Physiological Condition; Transient Cerebral Ischemic Attack, Cerebral Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p> <p>From <b>page 45 paragraph 4</b> “Exemplary modes for administration of psilocybin include oral, parenteral (e.g. , intravenous, subcutaneous, intradermal, intramuscular [including administration to skeletal, diaphragm and/or cardiac muscle], intradermal, intrapleural, intracerebral, and intra-articular), topical (e.g., to both skin and mucosal surfaces, including airway surfaces, and transdermal administration), <b>inhalation (e.g. , via an aerosol)</b>, rectal (e.g., via a suppository), transmucosal, <b>intranasal</b>, buccal (e.g. , sublingual), vaginal, intrathecal, intraocular, transdermal, in utero (or in ovo), intralymphatic, and direct tissue or organ injection (e.g., to liver, skeletal muscle, cardiac muscle, diaphragm muscle or brain). In some embodiments, psilocybin is administered orally to the subject.”</p>
20. Cancelled	
21. Cancelled	
22. Cancelled	
23. Cancelled	
<p><b>24. The NMT device of claim 19 further comprising one or more preloaded micro syringes comprising selected dosages of one or more pharmaceutical ingredients positioned in the syringe loading apparatus.</b></p>	<p><i>From paragraph [0062] of the application of interest, U.S. App. No. 17/916,855, “In one nonlimiting embodiment, the psychedelic agent and NAC are administered sequentially in a <b>nasal spray or mist transducer (NMT)</b> programmed time release administration.”</i></p> <p>5. CISION (2020) “ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI)” Published 6 January 2020. URL: <a href="https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html">https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html</a></p>

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The screenshot shows a web browser window with the URL <http://www.neuronasal.com/deck-link.html>. The page content includes a slide titled "Treating Brain Injury". On the left side of the slide, there are social media sharing icons for Facebook, Twitter, and a plus sign for more options. The main content of the slide features a diagram of a human brain with a nasal spray nozzle positioned at the bottom left. Dotted lines represent the drug delivery path from the nose, through the olfactory and trigeminal nerves, to the brain. A central box in the brain is labeled "Bypass the blood-brain barrier". To the right of the diagram, there is a list of three bullet points:

- Bypasses the blood-brain barrier-get drug to the brain.
- Results in rapid delivery to the brain along both the olfactory and trigeminal nerves.
- Reduces unwanted systemic exposure and side effects.

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From **slide 8**



## Neuronasal

### Neuronasal approach – approved device



#### Aptar UDS device

- Used in Flonase (marketed drug).
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<p><b>25. The NMT device of claim 24 wherein the preloaded micro syringes comprising a psychedelic agent and NAC</b></p>	<p><i>From paragraph [0062] of the application of interest, U.S. App. No. 17/916,855, “In one nonlimiting embodiment, the psychedelic agent and NAC are administered sequentially in a <b>nasal spray or mist transducer (NMT)</b> programmed time release administration.”</i></p> <p>5. CISION (2020) “ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI)” Published 6 January 2020. URL: <a href="https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html">https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html</a></p> <p>From <b>page 2</b> “By contrast, <b>Neuronasal's intranasal approach</b> enables direct nose-to-brain delivery, allowing for significantly lower doses and outpatient treatment. Given its apparent efficacy in disrupting the underlying neurochemical cascade, intranasal NAC has the potential to induce a</p>



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- Treating Brain Injury**
- Link to full powerpoint presentation: [Neuronasal Deck 7-2017.pptx](#)
- Diagram of the brain showing the olfactory and trigeminal neural pathways.
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7. NEURONASAL (2017) “Reduce acute brain injury by novel patented nose-to-brain drug delivery route” Retrieved from 12 November 2017.

Linked presentation located in the URL:

<https://web.archive.org/web/20171112165607/http://www.neuronasal.com/deck-link.html>

From **slide 8**

The slide features the Neuronasal logo (a head profile with a brain) and the text:

- Neuronasal**
- Neuronasal approach – approved device**
- Aptomar UDS device**
- Bullet points:
  - Used in Flonase (marketed drug).
  - FDA master file (access granted).
  - Manufacturing is well understood
  - Patient use is well understood
  - Similar to device used in animal experiments.
  - Gets appropriately formulated drugs to upper third of nasal cavity for nose-to-brain delivery.

The slide number 8 is located in the bottom right corner.

4. Intl. Pat. Doc. No. WO2020212952 “TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN” (Published 22 October 2020)

From **claim 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 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.”

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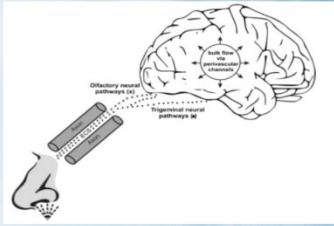
	<p>Infarction, Cerebral Bleeding, Progressive Supranuclear Ophthalmoplegia, or Retrograde Amnesia.”</p> <p>From <b>page 45 paragraph 4</b> “Exemplary modes for administration of psilocybin include oral, parenteral (e.g. , intravenous, subcutaneous, intradermal, intramuscular [including administration to skeletal, diaphragm and/or cardiac muscle], intradermal, intrapleural, intracerebral, and intra-articular), topical (e.g., to both skin and mucosal surfaces, including airway surfaces, and transdermal administration), <b>inhalation (e.g. , via an aerosol)</b>, rectal (e.g., via a suppository), transmucosal, <b>intranasal</b>, buccal (e.g. , sublingual), vaginal, intrathecal, intraocular, transdermal, in utero (or in ovo), intralymphatic, and direct tissue or organ injection (e.g., to liver, skeletal muscle, cardiac muscle, diaphragm muscle or brain). In some embodiments, psilocybin is administered orally to the subject.”</p>
<p><b>26. Cancelled</b></p>	
<p><b>27. Cancelled</b></p>	
<p><b>28. Cancelled</b></p>	
<p><b>29. A method for administering one or more pharmaceutical ingredients to the circulatory system of the brain, said method comprising administering the one or more pharmaceutical ingredients via the NMT of claim 19.</b></p>	<p><i>From paragraph [0062] of the application of interest, U.S. App. No. 17/916,855, “In one nonlimiting embodiment, the psychedelic agent and NAC are administered sequentially in a <b>nasal spray or mist transducer (NMT)</b> programmed time release administration. ”</i></p> <p>5. CISION (2020) “ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI)” Published 6 January 2020. URL: <a href="https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html">https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html</a></p> <p>From <b>page 2</b> “By contrast, <b>Neuronasal's intranasal approach</b> enables <b>direct nose-to-brain delivery</b>, allowing for significantly lower doses and outpatient treatment. Given its apparent efficacy in disrupting the underlying neurochemical cascade, <b>intranasal NAC</b> has the potential to induce a fundamental shift in the natural course of the condition for hundreds of thousands of people.”</p> <p>6. NEURONASAL (2017) “Treating Brain Injury” Retrieved from 12 November 2017. URL: <a href="https://web.archive.org/web/20171112165607/http://www.neuronasal.com/dck-link.html">https://web.archive.org/web/20171112165607/http://www.neuronasal.com/dck-link.html</a></p>

INTERNET ARCHIVE <http://www.neuronasal.com/deck-link.html> GO NOV 12 DEC 2017 2018 About this capture

Wapack Machine 8 captures 12 Nov 2017 19:58:20

## Treating Brain Injury

[Link to full powerpoint presentation](#)  
Neuronasal Deck 7-2017.pptx




- Bypasses the blood-brain barrier-get drug to the brain.
- Results in rapid delivery to the brain along both the olfactory and trigeminal nerves.
- Reduces unwanted systemic exposure and side effects.

7. NEURONASAL (2017) “Reduce acute brain injury by novel patented nose-to-brain drug delivery route” Retrieved from 12 November 2017.


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From **slide 8**

 **Neuronasal**

### Neuronasal approach – approved device



Aptar UDS device

- Used in Flonase (marketed drug).
- FDA master file (access granted).
- Manufacturing is well understood
- Patient use is well understood
- Similar to device used in animal experiments.
- Gets appropriately formulated drugs to upper third of nasal cavity for nose-to-brain delivery.**

8

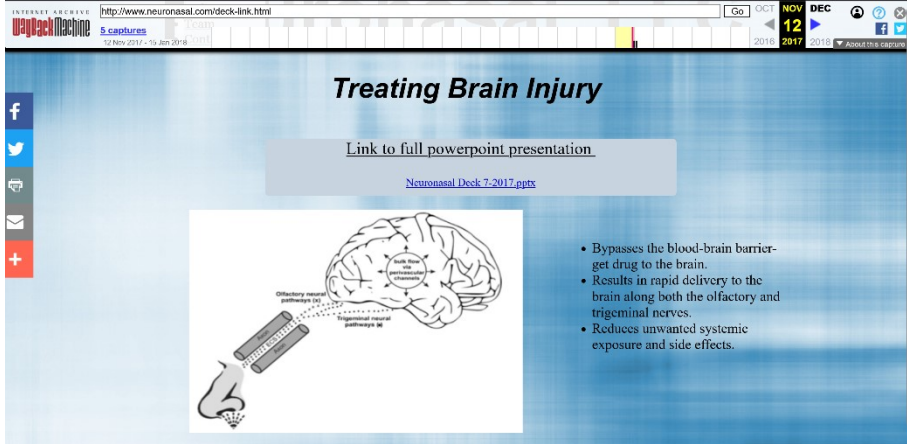
4. Intl. Pat. Doc. No. WO2020212952 “TREATMENT OF DEPRESSION AND OTHER VARIOUS DISORDERS WITH PSILOCYBIN” (Published 22 October 2020)

From **claim 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 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.”

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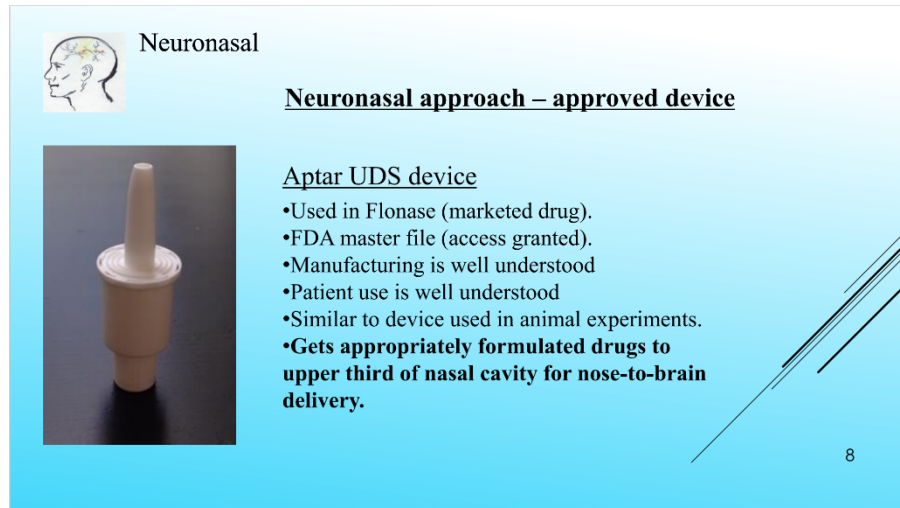
From **page 45 paragraph 4** “Exemplary modes for administration of psilocybin include oral, parenteral (e.g. , intravenous, subcutaneous, intradermal, intramuscular [including administration to skeletal, diaphragm and/or cardiac muscle], intradermal, intrapleural, intracerebral, and intra-articular), topical (e.g., to both skin and mucosal surfaces, including airway surfaces, and transdermal administration), **inhalation (e.g. , via an aerosol)**, rectal (e.g., via a suppository), transmucosal, **intranasal**, buccal (e.g. , sublingual), vaginal, intrathecal, intraocular, transdermal, in utero (or in ovo), intralymphatic, and direct tissue or organ injection (e.g., to liver,

	<p>skeletal muscle, cardiac muscle, diaphragm muscle or brain). In some embodiments, psilocybin is administered orally to the subject.”</p>
<p><b>30. A method for treating or alleviating symptoms associated with mTBI, PTSD or mTBI with PTSD, said method comprising administering to a subject suffering from mTBI, PTSD or mTBI with PTSD a psychedelic agent and NAC via the NMT of claim 25.</b></p>	<p><i>From paragraph [0062] of the application of interest, U.S. App. No. 17/916,855, “In one nonlimiting embodiment, the psychedelic agent and NAC are administered sequentially in a <b>nasal spray or mist transducer (NMT)</b> programmed time release administration.”</i></p> <p>5. CISION (2020) “ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI)” Published 6 January 2020. URL: <a href="https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html">https://web.archive.org/web/20200303215829/https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html</a></p> <p>From <b>Title</b> “ATAI Life Sciences Partners with Neuronasal Inc. to Develop <b>Novel Treatment for mild Traumatic Brain Injury (mTBI)</b>”</p> <p>From <b>page 2</b> “By contrast, <b>Neuronasal's intranasal approach</b> enables <b>direct nose-to-brain delivery</b>, allowing for significantly lower doses and outpatient treatment. Given its apparent efficacy in disrupting the underlying neurochemical cascade, <b>intranasal NAC</b> has the potential to induce a fundamental shift in the natural course of the condition for hundreds of thousands of people.”</p> <p>6. NEURONASAL (2017) “Treating Brain Injury” Retrieved from 12 November 2017. URL: <a href="https://web.archive.org/web/20171112165607/http://www.neuronasal.com/deck-link.html">https://web.archive.org/web/20171112165607/http://www.neuronasal.com/deck-link.html</a></p> 

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From **slide 8**



**Neuronasal**

**Neuronasal approach – approved device**

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11. EROWID USER LifeIsIntense (2019) “I Was Slowly on the Crawl Out of Depression” Retrieved 19 July 2019. URL: <https://web.archive.org/web/20190719201116/https://erowid.org/experiences/exp.php?ID=110595>

From **page 1** “Normally **I consume between 1 and 3.5 grams dried mushrooms**. I scaled back this time to half a gram, just to be safe and see.”

From **page 1** “Medication/Supplements: I take no lithium or anti-psychotics for my bipolar. I have decided that medication is not for me after thorough



research. **I do take N-ACETYL CYSTEINE supplements**, ashwaganda supplements, omega-3 supplements, B12 supplements, and folic acid. **All these supplements are taken daily.**”

From **page 1** “Mental Effects: Noticeable at about the half hour mark. Change in thought process first. Flight of thoughts, beautiful but unable to hold on to, quite like the flight of thoughts in mania, but less frustrating. The thought of motion is discretized. A general feeling of self-acceptance. **I am dealing with a good deal of PTSD**; lately I have loathed myself for failing to see an abusive person in my life for what they were. **The mushrooms facilitated a self-acceptance process.** The denial was a survival strategy. I was surviving. I need for forgive myself I decided.”

## Electronic Acknowledgement Receipt

<b>EFS ID:</b>	48370775
<b>Application Number:</b>	17916855
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	6545
<b>Title of Invention:</b>	Methods, Compositions and Devices for Treating Mild Traumatic Brain Injury, Post Traumatic Stress Disorder and Mild Traumatic Brain Injury with Post Traumatic Stress Disorder
<b>First Named Inventor/Applicant Name:</b>	Maghsoud DARIANI
<b>Customer Number:</b>	26259
<b>Filer:</b>	Shahin Shams
<b>Filer Authorized By:</b>	
<b>Attorney Docket Number:</b>	LOB0002US.NP
<b>Receipt Date:</b>	31-JUL-2023
<b>Filing Date:</b>	04-OCT-2022
<b>Time Stamp:</b>	12:35:08
<b>Application Type:</b>	

### Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$72
RAM confirmation Number	E20237UC35067901
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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**Warnings:**

**Information:**

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**Warnings:**

**Information:**

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**Warnings:**

**Information:**

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**Warnings:**

**Information:**

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**Warnings:**

**Information:**

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**Warnings:**

**Information:**

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<b>Information:</b>					
12	Evidence of Publication	7- NEURONASALPRESENTATION. pdf	2608021	no	16
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<b>Information:</b>					
13	Evidence of Publication	8-MayoClinic.pdf	260903	no	6
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<b>Warnings:</b>					
<b>Information:</b>					

14	Evidence of Publication	9-PsilocybinWikipedia.pdf	2389963	no	23
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**Information:**

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**Warnings:**

**Information:**

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**Information:**

<b>Total Files Size (in bytes):</b>	23148686
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**New Applications Under 35 U.S.C. 111**

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

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

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

**New International Application Filed with the USPTO as a Receiving Office**

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

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<b>Filer Authorized By:</b>	
<b>Attorney Docket Number:</b>	LOB0002US.NP
<b>Receipt Date:</b>	31-JUL-2023
<b>Filing Date:</b>	04-OCT-2022
<b>Time Stamp:</b>	12:43:50
<b>Application Type:</b>	

### Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$72
RAM confirmation Number	E20237UC43488101
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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**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	39971 ed508daa7c431a51fcee11fe993489454ab0dc5	no	5

**Warnings:**

**Information:**

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**Warnings:**

**Information:**

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**Warnings:**

**Information:**

4	Concise Description of Relevance	US20230157981ClaimChartComp.pdf	316837 56bd22866616a90c1c5fc8dbb8947266f66dbd14	no	41
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**Warnings:**

**Information:**

5	Evidence of Publication	11-ErowidMushroomsNACWayBack.pdf	305477 d8616e063f5e0660ba7617746970a48cddf6ff06	no	2
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**Warnings:**

**Information:**

6	Evidence of Publication	12-BIRD.pdf	1284687 e241fa7a6248461cf26912b08f02fc65a3abe7cc	no	7
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**Warnings:**

**Information:**

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7	Evidence of Publication	13- PsilocybeAzurescensWikipedia. pdf	738748	no	2
			937da3b60ed791835b9ba789a7c130aef081d3d0		

**Warnings:**

**Information:**

8	Evidence of Publication	14-BAUR.pdf	3624229	no	6
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**Warnings:**

**Information:**

9	Fee Worksheet (SB06)	fee-info.pdf	37893	no	2
			31e0011160b867366d2e54c1e3137c1436d45ec9		

**Warnings:**

**Information:**

<b>Total Files Size (in bytes):</b>	6432432
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