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

In re Application of: ATAI Life Sciences AG

Serial No.: 17/957,851

Filing or 371(c) Date: 03 September 2022

Entitled: COMPOSITIONS AND METHODS FOR TREATING HEADACHES

Confirmation No.:

Group No.:

Examiner:

**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. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)
2. Priority Doc. of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)
3. Priority Doc. of Pat. Doc. No. WO/2022/235514 "LIPOSOME DELIVERY OF PSYCHEDELICS" (Filing date: 04 May 2021)
4. Priority Doc. of Pat. Doc. No. WO/2023/036473 "COMBINATION DRUG THERAPIES" (Filing date: 08 September 2021)
5. Priority Doc. of Pat. Doc. No. WO/2022/235529 "METHOD OF TITRATING DOSE OF PSYCHEDELICS" (Filing date: 14 May 2021)
6. U.S. Pat. Doc. No. US/2021/0363104 "DEUTERATED TRYPTAMINE DERIVATIVES AND METHODS OF USE" (Publication date 25 November 2021)
7. DAVIS (2018) "The epidemiology of 5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT) use: Benefits, consequences, patterns of use, subjective effects, and reasons for consumption" *Journal of Psychopharmacology*. Vol 32(7):779-792.

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. 17/957,851 Pending Claims | References |
|---|---|
| **1. A method of treating an acute headache in a patient in need thereof comprising administering a therapeutically effective amount of a tryptamine comprising 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), 5-hydroxy-N,N-dimethyltryptamine (5-OH-DMT) or prodrugs or pharmaceutically acceptable salts thereof.** | *From the application of interest 17/957,851, paragraph [0038] "In embodiments, the acute headache is an acute migraine. In embodiments, the acute headache is a cluster headache episode."*<br><br>1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse." |

| | |
|---|---|
| **2. The method of claim 1, wherein the acute headache is an acute migraine.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse."<br><br>6. U.S. Pat. Doc. No. US/2021/0363104 "DEUTERATED TRYPTAMINE DERIVATIVES AND METHODS OF USE" (Publication date 25 November 2021)<br><br>From **paragraph [0001]** "The present disclosure relates generally to chemical compounds and, in some embodiments, to serotonin 5-HT2 receptor agonists and uses in the **treatment of diseases associated with a 5-HT2 receptor.**"<br><br>From **paragraph [0200]** "In some embodiments, **the disease or disorder may include central nervous system (CNS) disorders**, for example, post-traumatic stress disorder (PTSD), major depressive disorder (MDD), treatment-resistant depression (TRD), suicidal ideation, suicidal behavior, major depressive disorder with suicidal ideation or suicidal behavior, |

| | |
|---|---|
| | nonsuicidal self-injury disorder (NSSID), bipolar and related disorders (including but not limited to bipolar I disorder, bipolar II disorder, cyclothymic disorder), obsessive-compulsive disorder (OCD), generalized anxiety disorder (GAD), social anxiety disorder, substance use disorders (including but not limited to alcohol use disorder, opioid use disorder, amphetamine use disorder, nicotine use disorder, and cocaine use disorder), anorexia nervosa, bulimia nervosa, Alzheimer's disease, **cluster headache and migraine**, attention deficit hyperactivity disorder (ADHD), pain and neuropathic pain, aphantasia, childhood-onset fluency disorder, major neurocognitive disorder, mild neurocognitive disorder, sexual dysfunction, and obesity. In some embodiments, the disease or disorder is alcohol use disorder. In some embodiments, the disease or disorder may include conditions of the autonomic nervous system (ANS). In some embodiments, the disease or disorder may include pulmonary disorders (e.g., asthma and chronic obstructive pulmonary disorder (COPD). In some embodiments, the disease or disorder may include cardiovascular disorders (e.g., atherosclerosis)."<br><br>From **paragraph [0202]** "Also disclosed herein is a single-layer orally administered **tablet composition comprising a tryptamine derivative, such as DMT, 5-MeO-DMT**, psilocybin, and psilocin, or any of the compounds described herein, or a pharmaceutically acceptable salt thereof, and a polymer."<br><br>From **paragraph [0320]** "The term "treating" or "treatment" as used herein means the treating or treatment of a disease or medical condition in a patient, such as a mammal (particularly a human) that includes: **ameliorating the disease or medical condition, such as, eliminating or causing regression of the disease or medical condition in a patient**; suppressing the disease or medical condition, for example by, slowing or arresting the development of the disease or medical condition in a patient; or alleviating a symptom of the disease or medical condition in a patient. In an embodiment, prophylactic treatment can result in preventing the disease or medical condition from occurring, in a subject." |
| **3. The method of claim 1, wherein the acute headache is a cluster headache episode.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and |

| | |
|---|---|
| | memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse." |
| **4. The method of claim 1, comprising administering a therapeutically effective amount of 5-MeO-DMT or a prodrug or a pharmaceutically acceptable salt thereof to the patient.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache** |

| | |
|---|---|
| | **disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse." |
| **5. The method of claim 4, comprising administering between about 0.25 mg to about 50 mg of 5-MeO-DMT.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse."<br><br>From **page 41 paragraph 1** "In particular embodiments, the **specific amount of the psilocybin analogue in the formulation is, e.g., at least about 1 mg, at least about 2 mg, at least about 3 mg, at least about 4 mg, at least about 5 mg, at least about 6 mg, at least about 7 mg, at least about 8 mg, at least about 9 mg, at least about 10 mg, at least about 11 mg, at least about 12 mg, at least about 13 mg, at least about 14 mg, at least about 15 mg, at least about 16 mg, at least about 17 mg, at least about 18 mg, at least about 19 mg, at least about 20 mg, at least about 21 mg, at least about 22 mg, at least about 23 mg, at least about 24 mg,** |

| | |
|---|---|
| | **at least about 25 mg, at least about 26 mg, at least about 27 mg, at least about 28 mg, at least about 29 mg, at least about 30 mg, at least about 31 mg, at least about 32 mg, at least about 33 mg, at least about 34 mg, at least about 35 mg, at least about 36 mg, at least about 37 mg, at least about 38 mg, at least about 39 mg, at least 40 mg, at least 45 mg, at least 50 mg,** at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, or at least 100 mg." |
| **6. The method of claim 4, comprising administering between about 0.25 mg to about 36 mg of 5-MeO-DMT.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse."<br><br>From **page 41 paragraph 1** "In particular embodiments, the **specific amount of the psilocybin analogue in the formulation is, e.g., at least about 1 mg, at least about 2 mg, at least about 3 mg, at least about 4 mg, at least about 5 mg, at least about 6 mg, at least about 7 mg, at least about 8 mg, at least about 9 mg, at least about 10 mg, at least about 11 mg, at least about 12 mg, at least about 13 mg, at least about 14 mg, at** |

| | |
|---|---|
| | **least about 15 mg, at least about 16 mg, at least about 17 mg, at least about 18 mg, at least about 19 mg, at least about 20 mg, at least about 21 mg, at least about 22 mg, at least about 23 mg, at least about 24 mg, at least about 25 mg, at least about 26 mg, at least about 27 mg, at least about 28 mg, at least about 29 mg, at least about 30 mg, at least about 31 mg, at least about 32 mg, at least about 33 mg, at least about 34 mg, at least about 35 mg, at least about 36 mg,** at least about 37 mg, at least about 38 mg, at least about 39 mg, at least 40 mg, at least 45 mg, at least 50 mg, at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, or at least 100 mg." |
| **7. The method of claim 4, comprising administering between about 6 mg to about 30 mg of 5-MeO-DMT.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse."<br><br>From **page 41 paragraph 1** "In particular embodiments, the **specific amount of the psilocybin analogue in the formulation is, e.g.,** at least about 1 mg, at least about 2 mg, at least about 3 mg, at least about 4 mg, at |

| | |
|---|---|
| | least about 5 mg, **at least about 6 mg, at least about 7 mg, at least about 8 mg, at least about 9 mg, at least about 10 mg, at least about 11 mg, at least about 12 mg, at least about 13 mg, at least about 14 mg, at least about 15 mg, at least about 16 mg, at least about 17 mg, at least about 18 mg, at least about 19 mg, at least about 20 mg, at least about 21 mg, at least about 22 mg, at least about 23 mg, at least about 24 mg, at least about 25 mg, at least about 26 mg, at least about 27 mg, at least about 28 mg, at least about 29 mg, at least about 30 mg,** at least about 31 mg, at least about 32 mg, at least about 33 mg, at least about 34 mg, at least about 35 mg, at least about 36 mg, at least about 37 mg, at least about 38 mg, at least about 39 mg, at least 40 mg, at least 45 mg, at least 50 mg, at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, or at least 100 mg." |
| **8. The method of claim 4, comprising administering between about 0.25 mg to about 3 mg of 5-MeO-DMT.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse." |

| | |
|---|---|
| | From **page 41 paragraph 1** "In particular embodiments, the **specific amount of the psilocybin analogue in the formulation is, e.g., at least about 1 mg, at least about 2 mg, at least about 3 mg,** at least about 4 mg, at least about 5 mg, at least about 6 mg, at least about 7 mg, at least about 8 mg, at least about 9 mg, at least about 10 mg, at least about 11 mg, at least about 12 mg, at least about 13 mg, at least about 14 mg, at least about 15 mg, at least about 16 mg, at least about 17 mg, at least about 18 mg, at least about 19 mg, at least about 20 mg, at least about 21 mg, at least about 22 mg, at least about 23 mg, at least about 24 mg, at least about 25 mg, at least about 26 mg, at least about 27 mg, at least about 28 mg, at least about 29 mg, at least about 30 mg, at least about 31 mg, at least about 32 mg, at least about 33 mg, at least about 34 mg, at least about 35 mg, at least about 36 mg, at least about 37 mg, at least about 38 mg, at least about 39 mg, at least 40 mg, at least 45 mg, at least 50 mg, at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, or at least 100 mg." |
| **9. The method of claim 4, comprising administering about 10 mg of 5-MeO-DMT.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic |

| | |
|---|---|
| | Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse."<br><br>From **page 41 paragraph 1** "In particular embodiments, the **specific amount of the psilocybin analogue in the formulation is,** e.g., at least about 1 mg, at least about 2 mg, at least about 3 mg, at least about 4 mg, at least about 5 mg, at least about 6 mg, at least about 7 mg, at least about 8 mg, at least about 9 mg, **at least about 10 mg,** at least about 11 mg, at least about 12 mg, at least about 13 mg, at least about 14 mg, at least about 15 mg, at least about 16 mg, at least about 17 mg, at least about 18 mg, at least about 19 mg, at least about 20 mg, at least about 21 mg, at least about 22 mg, at least about 23 mg, at least about 24 mg, at least about 25 mg, at least about 26 mg, at least about 27 mg, at least about 28 mg, at least about 29 mg, at least about 30 mg, at least about 31 mg, at least about 32 mg, at least about 33 mg, at least about 34 mg, at least about 35 mg, at least about 36 mg, at least about 37 mg, at least about 38 mg, at least about 39 mg, at least 40 mg, at least 45 mg, at least 50 mg, at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, or at least 100 mg."<br><br>1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache** |
| **10. The method of any claim 1, comprising administering a therapeutically effective amount of 5-OH-DMT or a prodrug or a pharmaceutically acceptable salt thereof to the patient.** | |

| | |
|---|---|
| | **disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse." |
| **11. The method of claim 10, comprising administering between about 0.25 mg to about 50 mg of 5-OH-DMT.** | 1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse."<br><br>From **page 41 paragraph 1** "In particular embodiments, the **specific amount of the psilocybin analogue in the formulation is, e.g., at least about 1 mg, at least about 2 mg, at least about 3 mg, at least about 4 mg, at least about 5 mg, at least about 6 mg, at least about 7 mg, at least about 8 mg, at least about 9 mg, at least about 10 mg, at least about 11 mg, at least about 12 mg, at least about 13 mg, at least about 14 mg, at least about 15 mg, at least about 16 mg, at least about 17 mg, at least about 18 mg, at least about 19 mg, at least about 20 mg, at least about 21 mg, at least about 22 mg, at least about 23 mg, at least about 24 mg,** |

| | |
|---|---|
| | **at least about 25 mg, at least about 26 mg, at least about 27 mg, at least about 28 mg, at least about 29 mg, at least about 30 mg, at least about 31 mg, at least about 32 mg, at least about 33 mg, at least about 34 mg, at least about 35 mg, at least about 36 mg, at least about 37 mg, at least about 38 mg, at least about 39 mg, at least 40 mg, at least 45 mg, at least 50 mg,** at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, or at least 100 mg." |
| **12. The method of claim 1, comprising administering the tryptamine by insufflation.** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)<br><br>From **paragraph [0098]** "in some embodiments, the one or more psychedelics are selevted from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…"<br><br>From **paragraph [00121]** "The **one or more hallucinogens**....are administered to a subject or are used in a variety of forms depending on the selected route of administration, as will be understood by those skilled in the art...the hallucinogens...**are administered by** oral, inhalation, parenteral, buccal, sublingual, **insufflation**, epidurally, nasal, rectal, vaginal, patch, pump, minipump, topical or transdermal administration, and the pharmaceutical compositions formulated accordingly."<br><br>From **paragraph [0141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, **cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof." |
| **13. The method of claim 1, comprising administering the tryptamine intranasally.** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)<br><br>From **paragraph [0098]** "in some embodiments, the one or more psychedelics are selected from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…"<br><br>From **paragraph [00121]** "The **one or more hallucinogens**....are administered to a subject or are used in a variety of forms depending on the selected route of administration, as will be understood by those skilled in the art...the hallucinogens...**are administered by** oral, inhalation, parenteral, buccal, sublingual, insufflation, epidurally, **nasal**, rectal, vaginal, patch, pump, minipump, topical or transdermal administration, and the |

| | |
|---|---|
| | pharmaceutical compositions formulated accordingly."<br><br>From **paragraph [00141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, **cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof." |
| **14. The method of claim 1, comprising administering the tryptamine orally.** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)<br><br>From **paragraph [0098]** "in some embodiments, the one or more psychedelics are selected from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…"<br><br>From **paragraph [00121]** "The **one or more hallucinogens**....are administered to a subject or are used in a variety of forms depending on the selected route of administration, as will be understood by those skilled in the art...the hallucinogens...**are administered by oral**, inhalation, parenteral, buccal, sublingual, insufflation, epidurally, nasal, rectal, vaginal, patch, pump, minipump, topical or transdermal administration, and the pharmaceutical compositions formulated accordingly."<br><br>From **paragraph [00141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, **cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof." |
| **15. The method of claim 1, comprising administering the tryptamine subcutaneously.** | 3. Priority Doc. Of Pat. Doc. No. WO/2022/235514 "LIPOSOME DELIVERY OF PSYCHEDELICS" (Filing date: 04 May 2021)<br><br>From **paragraph [00012]** "The **present invention provides for a composition of a psychedelic** in a liposome formulation. The composition can be used in methods of preferentially distributing psychedelics at the CNS."<br><br>From **paragraph [00013]** "The **psychedelics in the present invention can be**, but are not limited to, ibogaine, noribogaine, lysergic acid diethylamide |

| | |
|---|---|
| | (LSD), psilocybin, psilocin, mescaline, **5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**,…"<br><br>From **paragraph [00018]** "The **compounds can be administered** orally, transcutaneously, **subcutaneously**, or parenterally including intravenous, intramuscular, and intranasal administration."<br><br>From **paragraph [00025]** "The **condition or disease being treated can include**, but is not limited to, anxiety disorders (including anxiety in advanced stage illness e.g. cancer, as well as generalized anxiety disorder), depression (including post partum depression, major depressive disorder, and treatment-resistant depression), **headache disorder (including cluster headaches and migraine headaches)**,…" |
| **16. The method of claim 1, comprising administering the tryptamine sublingually.** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)<br><br>From **paragraph [0098]** "in some embodiments, the one or more psychedelics are selected from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…"<br><br>From **paragraph [00121]** "The **one or more hallucinogens**....are administered to a subject or are used in a variety of forms depending on the selected route of administration, as will be understood by those skilled in the art...the hallucinogens...**are administered** by oral, inhalation, parenteral, buccal, **sublingual**, insufflation, epidurally, nasal, rectal, vaginal, patch, pump, minipump, topical or transdermal administration, and the pharmaceutical compositions formulated accordingly."<br><br>From **paragraph [00141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, **cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof." |
| **17. The method of claim 1, comprising administering the tryptamine buccally.** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)<br><br>From **paragraph [0098]** "in some embodiments, the one or more psychedelics are selected from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…" |

| | |
|---|---|
| | From **paragraph [00121]** "The **one or more hallucinogens**....are administered to a subject or are used in a variety of forms depending on the selected route of administration, as will be understood by those skilled in the art...the hallucinogens...**are administered** by oral, inhalation, parenteral, **buccal**, sublingual, insufflation, epidurally, nasal, rectal, vaginal, patch, pump, minipump, topical or transdermal administration, and the pharmaceutical compositions formulated accordingly."<br><br>From **paragraph [00141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, **cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof." |
| **18. The method of claim 1, comprising administering the tryptamine by inhalation.** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)<br><br>From **paragraph [0098]** "in some embodiments, the one or more psychedelics are selected from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…"<br><br>From **paragraph [00121]** "The **one or more hallucinogens**....are administered to a subject or are used in a variety of forms depending on the selected route of administration, as will be understood by those skilled in the art...the hallucinogens...**are administered by** oral, **inhalation**, parenteral, buccal, sublingual, insufflation, epidurally, nasal, rectal, vaginal, patch, pump, minipump, topical or transdermal administration, and the pharmaceutical compositions formulated accordingly."<br><br>From **paragraph [00141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, **cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof." |
| **19. The method of claim 1, comprising administering a single** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021) |

| | |
|---|---|
| **dose of the tryptamine to the patient.** | From **paragraph [0098]** "In some embodiments, the one or more psychedelics are selected from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…"<br><br>From **paragraph [00141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, **cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof."<br><br>From **paragraph [00155]** "**Treatment methods comprise administering to a subject the one or more hallucinogens**, or a salt, prodrug and/or solvate thereof, and the one or more fatty acids, or a salt, prodrug and/or solvate thereof, and optionally consists of **a single administration**, or alternatively comprises a series of administrations." |
| **20. The method of claim 19, further comprising administering a second dose of tryptamine to the patient about 30 minutes after a first administration if the first dose is not therapeutically effective.** | 5. Priority Doc. of Pat. Doc. No. WO/2022/235529 "METHOD OF TITRATING DOSE OF PSYCHEDELICS" (Filing date: 14 May 2021)<br><br>From **paragraph [00012]** "More specifically, the titrating **dosage regimen can include administering a starting dose to the individual, and at a set amount of time, increasing the dose a set amount and administering the increased dose to the individual**, and repeating these steps over a period of time that the individual is being treated and until a maximum desired dose is achieved."<br><br>From **paragraph [00014]** "**The time period can be hours**, days, weeks, months, or years."<br><br>From **paragraph [00018]** "The **psychedelics in the present invention can be**, but are not limited to, lysergic acid diethylamide (LSD), psilocybin, mescaline, **5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)…**"<br><br>From **paragraph [00029]** "The condition or disease being treated with the methods of the present invention can include, but is not limited to, anxiety disorders (including anxiety in advanced stage illness e.g. cancer, as well as generalized anxiety disorder), depression (including post partum depression, major depressive disorder and treatment resistant depression), **headache disorder (including cluster headaches and migraine headaches)**…"<br><br>7. DAVIS (2018) "The epidemiology of 5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT) use: Benefits, consequences, patterns of |

| | |
|---|---|
| | use, subjective effects, and reasons for consumption" Journal of Psychopharmacology. Vol 32(7):779-792.<br><br>From **page 781** "Published studies of human self-experiments describe a range of subjective **effects of 5-MeO-DMT** that vary depending on the dose and route of administration (Ott, 2001; Shulgin & Shulgin, 1997). Such effects include auditory, visual, and time perception distortions, emotional experiences, as well as memory impairment, with **peak effects between 35–40 minutes after insufflation or within seconds-to-minutes when smoked** (Ott, 2001; Shulgin & Shulgin, 1997)." |
| **21. The method of claim 1, comprising administering the tryptamine at the onset of the acute headache.** | *From the application of interest 17/957,851, paragraph [0038] "In embodiments, the acute headache is an acute migraine. In embodiments, the acute headache is a cluster headache episode."*<br><br>1. Int'l Pat. Doc. No. WO/2021/226416 "NOVEL COMPOSITIONS OF MATTER AND PHARMACEUTICAL COMPOSITIONS" (Publication date: 11 November 2021)<br><br>From **page 52 paragraph 1** "**Provided herein are methods of preventing, managing, and treating neurological, mood or addictive disorders** including post-treatment Lyme disease syndrome, dementias, Alzheimer's disease, post-traumatic stress disorder, anorexia nervosa, depression, anxiety, addiction, substance abuse including but not limited to opioid addiction, alcohol addiction, nicotine addiction, cannabinoid addiction, **headache,** central nervous system inflammation, dementia, cognition and memory **by administering psilocybin analogues transdermally, intranasally, or orally**."<br><br>From **page 28 paragraph 1** "In certain embodiments, the **psilocybin analogue is 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**. In certain embodiments, **the psilocybin analogue is bufotenin (5-OH-DMT)**."<br><br>From **page 21 paragraph 3** "**As used herein, and unless otherwise specified, the term "Neurological Disorder" refers to** diseases of the central and peripheral nervous system e.g., the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. These disorders include epilepsy, Alzheimer's disease and other dementias, cerebrovascular diseases including stroke, **migraine, cluster headaches and other headache disorders**, multiple sclerosis, Parkinson's disease, neuroinfections, brain tumors, traumatic disorders of the nervous system due to head trauma, and traumatic disorders due to traumatic or terrifying experiences (Posttraumatic Stress Disorder e.g. PTSD) and neurological disorders as a result of malnutrition and substance abuse." |

| | |
|---|---|
| | From **page 22, paragraph 2** "As used herein, and unless otherwise specified, the terms **"prevent," "preventing" and "prevention" refer to the prevention of the onset, recurrence or spread of a disease or disorder or of one or more symptoms thereof.**"<br><br>6. U.S. Pat. Doc. No. US/2021/0363104 "DEUTERATED TRYPTAMINE DERIVATIVES AND METHODS OF USE" (Publication date 25 November 2021)<br><br>From **paragraph [0001]** "The present disclosure relates generally to chemical compounds and, in some embodiments, to serotonin 5-HT2 receptor agonists and uses in the **treatment of diseases associated with a 5-HT2 receptor.**"<br><br>From **paragraph [0200]** "In some embodiments, **the disease or disorder may include central nervous system (CNS) disorders**, for example, post-traumatic stress disorder (PTSD), major depressive disorder (MDD), treatment-resistant depression (TRD), suicidal ideation, suicidal behavior, major depressive disorder with suicidal ideation or suicidal behavior, nonsuicidal self-injury disorder (NSSID), bipolar and related disorders (including but not limited to bipolar I disorder, bipolar II disorder, cyclothymic disorder), obsessive-compulsive disorder (OCD), generalized anxiety disorder (GAD), social anxiety disorder, substance use disorders (including but not limited to alcohol use disorder, opioid use disorder, amphetamine use disorder, nicotine use disorder, and cocaine use disorder), anorexia nervosa, bulimia nervosa, Alzheimer's disease, **cluster headache and migraine**, attention deficit hyperactivity disorder (ADHD), pain and neuropathic pain, aphantasia, childhood-onset fluency disorder, major neurocognitive disorder, mild neurocognitive disorder, sexual dysfunction, and obesity. In some embodiments, the disease or disorder is alcohol use disorder. In some embodiments, the disease or disorder may include conditions of the autonomic nervous system (ANS). In some embodiments, the disease or disorder may include pulmonary disorders (e.g., asthma and chronic obstructive pulmonary disorder (COPD). In some embodiments, the disease or disorder may include cardiovascular disorders (e.g., atherosclerosis)."<br><br>From paragraph [0202] "Also disclosed herein is a single-layer orally administered **tablet composition comprising a tryptamine derivative, such as DMT, 5-MeO-DMT**, psilocybin, and psilocin, or any of the compounds described herein, or a pharmaceutically acceptable salt thereof, and a polymer."<br><br>From **paragraph [0320]** "The term "treating" or "treatment" as used herein means the treating or treatment of a disease or medical condition in a |

| | |
|---|---|
| | patient, such as a mammal (particularly a human) that includes: ameliorating the disease or medical condition, such as, eliminating or causing regression of the disease or medical condition in a patient; suppressing the disease or medical condition, for example by, slowing or arresting the development of the disease or medical condition in a patient; or alleviating a symptom of the disease or medical condition in a patient. In an embodiment, **prophylactic treatment can result in preventing the disease or medical condition from occurring, in a subject.**"<br><br>From **paragraph [0322]** "As used herein, and unless otherwise specified, the terms "**prevent," "preventing" and "prevention" refer to the prevention of the onset, recurrence or spread of a disease, disorder, or condition, or of one or more symptoms thereof**. The terms encompass the inhibition or reduction of a symptom of the particular disease, disorder, or condition. Subjects with familial history of a disease, disorder, or condition, in particular, are candidates for preventive regimens in certain embodiments. In addition, subjects who have a history of recurring symptoms are also potential candidates for the prevention. In this regard, the term "prevention" may be interchangeably used with the term "prophylactic treatment.""" |
| **22. The method of claim 1, wherein the administration reduces the patient's pain associated with the acute headache.** | 2. Priority Doc. Of Pat. Doc. No. WO/2022/246572 "HALLUCINOGEN-FATTY ACID COMBINATION" (Filing date: 26 May 2021)<br><br>From **paragraph [0098]** "In some embodiments, the one or more psychedelics are selected from psilocybin, psilocin, dimethyltryptamine (DMT), **5-methoxy-dimethyltryptamine (5-MeO-DMT)**…"<br><br>From **paragraph [00141]** "**In some embodiments, the disease, disorder, or condition that is treated by activation of a serotonin receptor comprises** cognitive impairment; ischemia including stroke; neurodegeneration; refractory substance use disorder; sleep disorders; **pain, such as social pain, acute pain, cancer pain, chronic pain, breakthrough pain, bone pain, soft tissue pain, nerve pain, referred pain, phantom pain, neuropathic pain, cluster headaches or migraine**; obesity or eating disorders; epilepsies or seizure disorders; neuronal cell death; excitotoxic cell death; or a combination thereof." |

# Electronic Acknowledgement Receipt

| | |
|---|---|
| **EFS ID:** | 48033977 |
| **Application Number:** | 17957851 |
| **International Application Number:** | |
| **Confirmation Number:** | 6488 |
| **Title of Invention:** | COMPOSITIONS AND METHODS FOR TREATING HEADACHES |
| **First Named Inventor/Applicant Name:** | Srinivas G. RAO |
| **Customer Number:** | 58249 |
| **Filer:** | Shahin Shams |
| **Filer Authorized By:** | |
| **Attorney Docket Number:** | ATAI-018/01US 338067-2313 |
| **Receipt Date:** | 21-MAY-2023 |
| **Filing Date:** | 30-SEP-2022 |
| **Time Stamp:** | 16:00:55 |
| **Application Type:** | |

## Payment information:

| | |
|---|---|
| Submitted with Payment | yes |
| Payment Type | CARD |
| Payment was successfully received in RAM | $72 |
| RAM confirmation Number | E20235KG00505001 |
| Deposit Account | |
| Authorized User | |

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

## 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 | 41918<br>713d106d76f9ec7303253ac60d7bdbfebaf4fe84 | no | 6 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 2 | Third-Party Submission Under 37 CFR 1.290 | Third-party-preissuance-submission.pdf | 64948<br>378c3a4fac580a5069b50205d4a4f7ccc544c1cc | no | 4 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 3 | Request for Notification of Non-compliant Third-Party Submission | Third-party-notification-request.pdf | 23720<br>46c76d37ba707c90bac35c985517bfedfd81a27e | no | 1 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 4 | Evidence of Publication | 1-WO2021226416A1.pdf | 4927223<br>e42a87529e250b860e30b13e3773a75105bd5788 | no | 76 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 5 | Evidence of Publication | 2-WO2022246572PriorityDoc.pdf | 4885116<br>766001915fe91d697b76f568112a6841b1bd75e4 | no | 128 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 6 | Evidence of Publication | 3-WO2022235514PriorityDoc.pdf | 1121012<br>75ee6f62949df8c62b43a1950d555d686f224c5e | no | 25 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 7 | Evidence of Publication | 4-WO2023036473PriorityDoc.pdf | 4154730<br>3d59e8552dd05ce93bac332f8059159448c3ae9b | no | 111 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 8 | Evidence of Publication | 5-WO2022235529PriorityDoc.pdf | 1086013<br>643037b30d244b3328d825c7435cd398c4264f03 | no | 25 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 9 | Evidence of Publication | 6-US20210363104A1.pdf | 7536321<br>ba248949370a85db579f91df33e0c8d97346225f | no | 62 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 10 | Evidence of Publication | 7-DAVIS.pdf | 132893<br>41b1564b5538f5cfd726afd7006fbb84e74106a5 | no | 14 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 11 | Concise Description of Relevance | US20230099972ClaimChartComp.pdf | 166673<br>59291ac63aac20631041519d46f00b9348d1b422 | no | 20 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| 12 | Fee Worksheet (SB06) | fee-info.pdf | 37347<br>403b867925402bb2b7eab2f1d5240cce995923fc | no | 2 |
| **Warnings:** | | | | | |
| **Information:** | | | | | |
| | | **Total Files Size (in bytes):** | 24177914 | | |

**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**New Applications Under 35 U.S.C. 111**

**If a new application is being filed and the application includes the necessary components for 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.**