

**PATENT COOPERATION TREATY**  
**PCT**  
**THIRD PARTY OBSERVATION**  
**(PCT Administrative Instructions Part 8)**

Applicant's or agent's file reference 37427-0122PTWO	
International application number PCT/US2022/044039	International filing date (day/month/year) 19 Sep 2022 (19/09/2022)
Applicant 1242753 ONTARIO INC.	
Third party observation submitted by Sisi LI	Observation submitted on behalf of Porta Sophia
Date of submission(day/month/year) 26 Apr 2023 (26/04/2023)	Language of observation English

**Basis and contents of observation**

1. The observation is made on the basis of the claims in the international application as filed.
2. The observation comprises:  
References to documents: 10  
Uploaded copies of documents: 3
3. Further explanations:  
Uploaded copies of documents: 0

**Citation # 1(Periodical article) (# uploaded documents:1):**

Author: Milne; Thomsen; Mølgaard Knudsen; Rubaszka; Kristensen ; Borodina	Title of article: Metabolic engineering of Saccharomyces cerevisiae for the de novo production of psilocybin and related tryptamine derivatives	Title of Periodical: Metabolic Engineering	Publication Date: Jul 2020 (07/2020)
Issue Number of Periodical: 60	Publisher of Periodical:	Place of publication:	
Page range of article within periodical:	ISBN:	ISSN:	
DOI: 10.1016/j.ymben.2019.12.007			
Most relevant passages or drawings: Pages 25		Relevant to Claims: 1, 2, 3, 4	
Brief explanation of relevance: From page 25 "Psilocybin is a tryptamine-derived psychoactive alkaloid found mainly in the fungal genus Psilocybe, among others, and is the active ingredient in so-called "magic mushrooms".... In this work, we demonstrate the de novo biosynthetic production of psilocybin and related tryptamine derivatives in Saccharomyces cerevisiae by expression of a heterologous biosynthesis pathway sourced from Psilocybe cubensis... Further rational engineering resulted in a final production strain producing 627 ± 140 mg/L of psilocybin and 580 ± 276 mg/L of the dephosphorylated degradation product psilocin in triplicate controlled fed-batch fermentations in minimal synthetic media. Pathway intermediates baeocystin, norbaeocystin as well the dephosphorylated baeocystin degradation product norpsilocin were also detected in strains engineered for psilocybin production."; relevant to WO2023044135 claims 1, 2, 3, 4			

## Citation # 2 (Patent/utility model) (# uploaded documents: 0):

Country code: WO	Publication number: 2018/135943	Document kind code: A1	
Patent Applicant/Patent Owner: PROCARE BEHEER B.V.		Title of invention: PSILOCYBIN AND/OR PSILOCIN IN COMBINATION WITH CANNABINOIDS AND/OR TERPENES	
Link to document:			
Publication Date: 26 Jul 2018 (26/07/2018)	Filing Date: 18 Jan 2018 (18/01/2018)	Priority Date: 18 Jan 2017 (18/01/2017)	
Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:
Most relevant passages or drawings: Claims 5		Relevant to Claims: 5	
Brief explanation of relevance: From claim 5 "5. Psilocybin and/or psilocin in combination with at least one cannabinoid and/or at least one terpene for use according to any of the preceding claims, wherein the at least one cannabinoid is at least one, two or three chosen from the group consisting of cannabidiol (CBD); cannabidiolic acid (CBDA); tetrahydrocannbidivarin (THCV)."; relevant to WO2023044135 claims 5			

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Citation # 3 (Patent/utility model) (# uploaded documents: 0):

Country code: US	Publication number: 2021/0251976	Document kind code: A1	
Patent Applicant/Patent Owner: Paul Edward Stamets		Title of invention: TRYPTAMINE COMPOSITIONS FOR ENHANCING NEURITE OUTGROWTH	
Link to document:			
Publication Date: 19 Aug 2021 (19/08/2021)	Filing Date: 05 May 2021 (05/05/2021)	Priority Date: 23 Jul 2016 (23/07/2016)	
Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:
Most relevant passages or drawings: Claims 1, [0007], [0005]		Relevant to Claims: 6	
<p>Brief explanation of relevance:</p> <p>From claim 1 "1. A method of treating or improving a mental health disorder in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a composition comprising from about 1 mg to about 10 mg of one or more of psilocybin, psilocin, esters, or salts thereof; or an equivalent amount of a psilocybin containing mushroom; and one or more pharmaceutically acceptable excipients."; relevant to WO2023044135 claims 6</p> <p>From claim [0007] "One embodiment described herein is a composition comprising norpsilocin or a salt or hydrate thereof or combinations thereof combined with one or more erinacines or hericenones in pure form, extracts or isolates from Hericium mushroom species, or combinations thereof. In one aspect, the erinacines or hericenones comprise...In another aspect, the composition comprises an extract of extracts or isolates from Hericium erinaceus. In another aspect, the composition further comprises baeocystin or a salt or hydrate thereof."; relevant to WO2023044135 claims 6</p> <p>From claim [0005] "Lion's Mane (Hericium erinaceus), Bear's Head (H. coralloides), or Comb Tooth (H. ramosum) mushrooms and mycelium are reported to influence myelin regeneration myelin on the axons of nerves. Two cyanthane terpenes the erinacines and hericenones are thought to promote NGF (nerve growth factor) synthesis."; relevant to WO2023044135 claims 6</p>			

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Citation # 4 (Patent/utility model) (# uploaded documents: 0):

Country code: US	Publication number: 2021/0268046	Document kind code: A1	
Patent Applicant/Patent Owner: SALMONS; Leann, Glick-Mazziotti; Gretchen		Title of invention: CANNABINOID & PROBIOTIC SUPPOSITORIES & METHODS OF USE	
Link to document:			
Publication Date: 02 Sep 2021 (02/09/2021)	Filing Date: 17 Feb 2021 (17/02/2021)	Priority Date: 18 Feb 2020 (18/02/2020)	
Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:
Most relevant passages or drawings: Abstract, [0021], [0049] table 3, [0006], [0031]		Relevant to Claims: 7, 8, 17, 18, 19	
<p>Brief explanation of relevance:</p> <p>From abstract "Cannabinoids and probiotics formulated into a suppository and used to treat urogenital, gastrointestinal or aural infections and/or inflammation by local use of the suppository for a period of time are described"; relevant to WO2023044135 claims 7, 8</p> <p>From [0021] "Preferred probiotics for vaginal use include, Lactobacilli: acidophilus, brevis, bulgaricus, plantarum, rhamnosus, gasseri, casei, salivarius, paracasei, fermentum, salivarius, reuteri, helveticus, lactis, cremoris, kefir, parakefir, faecium, crispatus, delbrueckii, and Lactococcus : lactus"; relevant to WO2023044135 claims 7, 8</p> <p>From [0049] table 3 "Other active ingredients that may advantageously be combined with cannabinoids and probiotics include those in Table 3:</p> <p>TABLE-US-00004 TABLE 3 Additional ingredients Mushrooms Psilocybin (P. azurescens, P. semilanceata, P. cyanescens, P. subaeruginosa, P. bohemica, P. cubensis, P. cyanofibrillosa) 5-10 mg 10-25 mg, 30-45+ mg &amp; root network Cordyceps militaris &amp; sinensis (mycelium) &amp; adaptogens Organic reishi (ganoderma lucidum) Organic lions mane (hericiumerinaceus) ..."; relevant to WO2023044135 claims 7, 8, 19</p> <p>From [0006] "However, millennia before the HMP initiative, women around the world appreciated the value of vaginal flora in maintaining a healthy and comfortable vaginal environment. Thus, women have long treated, e.g., yeast infections, by supplementing with Lactobacillus cultures, both orally and locally."; relevant to WO2023044135 claims 7, 8, 17</p> <p>From [0006] "...In addition, probiotics have been applied rectally to the GI tract to aid in immunological function, digestion, protect against pathogenic bacteria such as Salmonella typhimurium, Helicobacter pylori, and Escherichia coli, improve lactose intolerance, decrease cholesterol levels, treat Crohn's disease, ulcerative colitis, irritable bowel syndrome ("IBS"), and replenish intestinal flora after antibiotic therapy to prevent antibiotic-induced diarrhea. Indeed, the global market for probiotics reached a value of about 49.4 billion U.S. dollars in 2018."; relevant to WO2023044135 claims 17, 18, 19</p> <p>From [0031] "As used herein, "supplement" is a product taken orally that contains one or more ingredients (such as vitamins or amino acids) that are intended to supplement one's diet and are not considered food or drugs under the US regulatory scheme"; relevant to WO2023044135 claims 17, 18, 19</p> <p>From Table 8, Ingredient Psilocybin... Amount F1 Trace to &lt;5 mg; relevant to WO2023044135 claims 18</p>			

**Citation # 5 (Patent/utility model) (# uploaded documents: 0):**

Country code: US	Publication number: 20220280482	Document kind code: A1	
Patent Applicant/Patent Owner: Mind Medicine, Inc.		Title of invention: FORMULATIONS OF PSILOCIN THAT HAVE ENHANCED STABILITY	
Link to document:			
Publication Date: 08 Sep 2022 (08/09/2022)	Filing Date: 04 Mar 2022 (04/03/2022)	Priority Date: 06 Mar 2021 (06/03/2021)	
Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:
Most relevant passages or drawings: Claims 1, [0056]		Relevant to Claims: 9	
<p>Brief explanation of relevance:</p> <p>From claim 1 “A composition of psilocin that is stable including at least one agent that provides enhanced stability in combination with psilocin”; relevant to WO2023044135 claims 9</p> <p>From claim [0056] “Any of the photostabilizing or antioxidant agents can also work synergistically with the psilocin or provide additional beneficial effects. For example, prebiotics such as lactulose provide antioxidant effects as well as other advantageous effects in pain treatment.”; relevant to WO2023044135 claims 9</p>			

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Citation # 6 (Patent/utility model) (# uploaded documents: 0):

Country code: US	Publication number: 20220313713	Document kind code: A1	
Patent Applicant/Patent Owner: MOSS; Ryan, LIGHTBURN; Benjamin, RANKEN; Lisa		Title of invention: VAPORIZABLE PSYCHOACTIVE ALKALOID COMPOSITION AND PREPARATION THEREOF	
Link to document:			
Publication Date: 06 Oct 2022 (06/10/2022)	Filing Date: 14 Jun 2022 (14/06/2022)	Priority Date: 20 Jan 2021 (20/01/2021)	
Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:
Most relevant passages or drawings: Claims 1, 3, 13, [0006]		Relevant to Claims: 11, 12	
<p>Brief explanation of relevance:</p> <p>From claim 1 "A liquid, vaporizable psychoactive alkaloid composition made by mixing, by weight: 0.1-15% of a psychoactive alkaloid component; 5-71.9% of alcohol, polyol, or an alcohol and polyol mixture; 2-78.1% of fatty acid; 5-40% of fatty alcohol; 0-10% of antioxidant; and 0-10% of flavorant"; relevant to WO2023044135 claims 11, 12</p> <p>From claim 3 "The composition of claim 2, wherein: the phosphorylated psychoactive alkaloid is psilocybin, baeocystin, norbaeocystin, aeruginascin, or any combination selected therefrom; and the dephosphorylated psychoactive alkaloid is psilocin, bufotenine, bufotenidine, norpsilocin, 4-hydroxytryptamine, N,N,N-trimethyl-4-hydroxytryptamine, or any combination selected therefrom"; relevant to WO2023044135 claims 11, 12</p> <p>From claim 13 "The composition of claim 1, wherein the fatty acid is palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, arachidonic acid, eicosapentaenoic acid, docosahexaenoic acid, ascorbyl palmitate, cetyl palmitate, colfosceril palmitate, ehtylhexyl palmitate, isopropyl palmitate, palmitoyl-CoA, retinyl palmitate, sucrose monopalmitate or any combination selected therefrom"; relevant to WO2023044135 claims 11</p> <p>From claim [0006] "Oral administration of phosphorylated psychoactive alkaloid compositions via the human gastrointestinal tract allows the conversion of the phosphorylated form to the corresponding biological effective dephosphorylated form..."; relevant to WO2023044135 claims 11, 12</p>			

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Citation # 7(Periodical article) (# uploaded documents:1):

Author: Denise S, Lin	Title of article: Case Report: Resolution of Rheumatoid Arthritis in a Patient Consuming Psilocybin Mushrooms	Title of Periodical: Journal of healthcare	Publication Date: 19 Aug 2020 (19/08/ 2020)
Issue Number of Periodical: Volume 3 Issue 1	Publisher of Periodical:	Place of publication:	
Page range of article within periodical:	ISBN:	ISSN:	
DOI: 10.36959/569/456			
Most relevant passages or drawings: Pages 25, 26		Relevant to Claims: 13	
<p>Brief explanation of relevance:</p> <p>From page 25 “Shortly after that he consumed some psilocybin mushrooms and was surprised to observe that his joint pain and swelling completely resolved for about 24 hours. In addition, his seasonal allergy symptoms also completely resolved. When he had another flare of joint pain several years later, he took four doses of psilocybin mushrooms of 2 grams each over a two-week period and again had complete resolution of his symptoms. That was one year prior to the writing of this paper. Subsequently he has been using psilocybin mushrooms periodically and he has not experienced any signs or symptoms of rheumatoid arthritis since then.”; relevant to WO2023044135 claims 13</p> <p>From page 26 “Psilocybin and its active metabolite psilocin are tryptamines [28] found in more than a hundred species of mushroom, many of which belong to the Psilocybe genus”; relevant to WO2023044135 claims 13</p>			

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Citation # 8 (Patent/utility model) (# uploaded documents: 0):

Country code: US	Publication number: 20220331344	Document kind code: A1	
Patent Applicant/Patent Owner: GREENBAUM; Eric, BUENO; Justin		Title of invention: ORAL FORMULATIONS OF PSYCHOTROPIC MACROFUNGUS BOTANICAL EXTRACTS WITH MOUTHFEEL EXPERIENCE ENHANCERS	
Link to document:			
Publication Date: 20 Oct 2022 (20/10/2022)	Filing Date: 23 Mar 2022 (23/03/2022)	Priority Date: 15 Apr 2021 (15/04/2021)	
Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:
Most relevant passages or drawings: Claims 1, 3 [0056], [0060]		Relevant to Claims: 14, 15, 16	
<p>Brief explanation of relevance:</p> <p>From claim [0056] "The oral formulations of the present disclosure can be configured to deliver a heroic dose of psychoactive compound(s) in one or more unit dosage forms, or a microdose of psychoactive compound(s). For example, a heroic dose can be the quantity of psychoactive compounds in 5 grams of whole, dry Psilocybe Cubensis mushrooms, whereas a microdose is a sub-hallucinogenic quantity associated with enhanced creativity and meta-creative processes, such as perspective-shifting/divergent thinking and openness/curiosity. The concentration of botanical extract in the formulation can be based upon the amount needed to provide about 1-25 mg psilocybin per 70 kg body weight. For example, a single dosage unit can include about 0.5 mg-40 mg, such as 0.75 mg, 1 mg, 5 mg, 10 mg, 15 mg, 20 mg, 22 mg, 25 mg, 27 mg, 30 mg, 35 mg, or 40 mg, depending on the desired psychophysiological effect."; relevant to WO2023044135 claims 14, 15, 16</p> <p>From claim 1 "An oral formulation comprising at least one botanical extract of a psychotropic macrofungus and at least one mouthfeel experience enhancer"; relevant to WO2023044135 claims 14, 15, 16</p> <p>From claim 3 "The oral formulation of claim 1, wherein the at least one botanical extract comprises at least one psychoactive compound selected from the group consisting of psilocybin, psilocin, norpsilocin, baeocystin, norbaeocystin, aeruginascin, serotonin, bufotenin, <math>\beta</math>-carboline alkaloids, muscarine, muscimol, muscazone, and ibotenic acid, or a combination thereof"; relevant to WO2023044135 claims 14</p> <p>From claim [0060] "Formulations further comprising one or more cannabinoids can be used to address a variety of diseases and/or medical conditions. In some embodiments, the diseases include, but are not limited to, Acquired Hypothyroidism, Acute Gastritis, Acute Pain, Adrenal Disease, Agoraphobia, AIDS Related Illness, Alcohol Abuse, Alcoholism, Alopecia Areata, Alzheimer's Disease, Amphetamine Dependency, Amyloidosis, Amyotrophic Lateral Sclerosis (ALS), Angina Pectoris, Ankylosis, Anorexia, Anorexia Nervosa, Anxiety Disorders, any Chronic Medical Symptom that Limits Major Life Activities, Arteriosclerotic Heart Disease, Arthritis, Arthritis (Rheumatoid)..."; relevant to WO2023044135 claims 14, 15, 16</p>			



Citation # 9(Web page) (# uploaded documents:1):

Author:		Title of Page Or Article: Psilocybin helped heal my Irritable Bowel Disease	
URL: <a href="https://www.shroomery.org/forums/showflat.php/Number/24137933">https://www.shroomery.org/forums/showflat.php/Number/24137933</a>			
DOI:			
Name of Website:	Publication Date: 05 Mar 2017 (05/03/2017)	Retrieval Date: 26 Apr 2023 (26/04/2023)	
Most relevant passages or drawings: Quotes from post		Relevant to Claims: 17, 18, 20	
<p>Brief explanation of relevance:</p> <p>From #24137933 "While also in a flare up, I decided to go on a liquid diet prior to consuming 2-3g of psilocybin in the form of ginger tea. It was the most pleasant trip I've had since being dx'd with IBD.</p> <p>I was also taking horrible medication(prednisone) with crazy side effects, but during the trip I felt "normal". My adrenal glands were not their usual agony. The next morning I awoke with energy and great digestion.</p> <p>Thus began my first real remission of the "disease".</p> <p>As this forum is likely aware of, there's an unfortunate amount of scientific literature on psilocybin, but we know there is psilocin that targets proteins typically responsible for IBD inflammation. It is suppressed by activating hormonal receptors. Some claim it can work better than pharmaceuticals.</p> <p>I also experimented with micro-dosing for a month and found the results to be beneficial with both digestion, energy and motivation"; relevant to WO2023044135 claims 17, 18, 20</p>			

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## Citation # 10 (Patent/utility model) (# uploaded documents: 0):

Country code: WO	Publication number: WO2021101926	Document kind code: A1	
Patent Applicant/Patent Owner: Paul Edward Stamets		Title of invention: TRYPTAMINE COMPOSITIONS FOR ENHANCING NEURITE OUTGROWTH	
Link to document:			
Publication Date: 27 May 2021 (27/05/2021)	Filing Date: 18 Nov 2020 (18/11/2020)	Priority Date: 19 Nov 2019 (19/11/2019)	
Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:
Most relevant passages or drawings: Claims 28, page 4 line 24-34		Relevant to Claims: 1, 2, 3, 4, 10	
Brief explanation of relevance:			
<p>From claim 28 "28. A method of treating or preventing serotonin (5-hydroxytryptamine, 5-HT) receptor disorders, neuronal injuries, neurodegeneration, neurological diseases, congenital or organic cognitive impairment, learning disabilities, autism spectrum disorder, psychiatric and mood disorders, cognitive enhancement, physical or motor neuron enhancement, or general improvement of mental health in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a composition comprising norpsilocin, norbaeocystin, baeocystin, or psilocybin, combined with one or more erinacines or hericenones in pure form or pharmaceutically acceptable salts, hydrates, solvates, prodrugs, stereoisomers, or tautomer thereof, or combinations thereof, extracts or isolates from <i>Herichium</i> mushroom species, combinations thereof and one or more pharmaceutically acceptable excipients."; relevant to WO2023044135 claims 1, 2, 3, 4</p> <p>From page 4 line 24-34 "In another aspect, the composition further comprises one or more extracts or pure chemicals from other fungi comprising one or more of, <i>Antrodia</i>, <i>Beauveria</i>, <i>Copelandia</i>, <i>Cordyceps</i>, <i>Fomitopsis</i>, <i>Ganoderma</i>, <i>Grifola</i>, <i>Herichium</i>, <i>Hypsizygus</i>, <i>Inonotus</i>, <i>Isaria</i>, <i>Panaeolus</i>, <i>Phellinus</i>, <i>Piptoporus</i>, <i>Pleurotus</i>, <i>Polyporus</i> or <i>Trametes</i> species or combinations thereof; a mycelium extract of <i>Antrodia</i>, <i>Beauveria</i>, <i>Copelandia</i>, <i>Cordyceps</i>, <i>Fomitopsis</i>, <i>Ganoderma</i>, <i>Grifola</i>, <i>Herichium</i>, <i>Hypsizygus</i>, <i>Inonotus</i>, <i>Isaria</i>, <i>Panaeolus</i>, <i>Phellinus</i>, <i>Piptoporus</i>, <i>Pleurotus</i>, <i>Polyporus</i> or <i>Trametes</i> species or combinations thereof; or a fruiting body extract of <i>Antrodia</i>, <i>Beauveria</i>, <i>Copelandia</i>, <i>Cordyceps</i>, <i>Fomitopsis</i>, <i>Ganoderma</i>, <i>Grifola</i>, <i>Herichium</i>, <i>Hypsizygus</i>, <i>Inonotus</i>, <i>Isaria</i>, <i>Panaeolus</i>, <i>Phellinus</i>, <i>Piptoporus</i>, <i>Pleurotus</i>, <i>Polyporus</i> or <i>Trametes</i> species or combinations thereof, or combinations thereof"; relevant to WO2023044135 claims 10</p>			