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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/675,614	05/28/2024	Theis TERWEY	P71400	3345

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EXAMINER
LEE, CHIHYI NMN

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
05/05/2025	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 18/675,614	Applicant(s) TERWEY, Theis	
	Examiner Chihyi Lee	Art Unit 1628	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 12/20/2024.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 1-30 is/are pending in the application.

5a) Of the above claim(s) 16-21,23 and 25-30 is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-15,22 and 24 is/are rejected.

8) ☑ Claim(s) 1-2 and 22 is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☑ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☑ Certified copies of the priority documents have been received in Application No. 17/431,626.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Election/Restrictions

Applicant's election without traverse of the following species:

- Claim 3 as the elected patient species shown as follows:

3. The method according to claim 1, wherein the patient suffers from moderate or severe major depressive disorder as indicated by a Montgomery-Åsberg Depression Rating Scale (MADRS) score of 20 or more or by a 17-item Hamilton Depression Rating Scale (HAM-D) score of 17 or more.

- Claim 2 as the elected diagnostic criteria species shown as follows:

2. The method according to claim 1, wherein the disorder is diagnosed in accordance with the Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition (DSM-5) published by the American Psychiatric Association.

- Claim 13 as the elected criteria species to identify the occurrence of a peak psychedelic experience shown as follows:

13. The method according to claim 9, wherein the occurrence of a peak psychedelic experience is identified through achievement of at least 60% of the maximum possible score in each of the four subscales (mystical, positive mood, transcendence of time and space, and ineffability) of the 30-item revised Mystical Experience Questionnaire (MEQ30) or is identified through achievement of at least 60% of the maximum possible score of the Oceanic Boundlessness (OBN) dimension of the Altered States of Consciousness (ASC) questionnaire or is identified through achievement of a Peak Psychedelic Experience Questionnaire (PPEQ) Total Score of at least 75.

- Claim 22 as the elected assessment species for a clinical response shown as follows:

> 22. The method according to claim 1, wherein the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof.

- Claim 24 as the elected assessment species for a remission of depressive symptoms shown as follows:

> 24. The method according to claim 1, wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof.

in the reply filed on December 20, 2024 is acknowledged.

Please note Applicant noted claims 1-30 are encompassing by the elected species; However, Applicant elects claim 22 as the assessment species for a clinical response (“

> 22. The method according to claim 1, wherein the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof.

”), and that is not encompassing by an assessment of a clinical response using CGI or PGI-I score, or a clinical response assessed by MADRS or HAM-D score no later than about 2 hours after the last administration, at least 14 days or 28 days after the last administration, on day 14 or 28 after the last administration.

Please note Applicant elects claim 24 as the assessment species for a remission of depressive symptoms (“

> 24. The method according to claim 1, wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof.

”), and that is not encompassing by an assessment performed no later than about 2 hours, on day 14, or day 28 after the last administration.

Claims 16-21, 23, and 25-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 20, 2024.

Expansion of Election of Species Requirement

A reasonable and comprehensive search of the elected species (see Election/Restrictions section) conducted by the Examiner discover a prior art by Santos et al. that anticipates the claimed invention, wherein the prior art teaches treatment-resistant form of a major depressive disorder as the patient species; and a prior art by Russ et al. that renders obvious the claimed invention, wherein the prior art teaches major depression associated with suicidality. In light of this discovery, the search is expanded to the subject matter of the patient species to include major depressive disorder and major depressive disorder with suicidal ideation in addition to the elected patient species ("wherein the patient suffers from moderate or severe major depressive disorder as indicated by a Montgomery-Asberg Depression Rating Scale (MADRS) score of 20 or more or by a 17-item Hamilton Depression Rating Scale (HAM-D) score of 17 or more"), such that it does not encompass the full scope of the claims.

Status of Claims

Claims 1-30 pending. Claims 16-21, 23, and 25-30 are withdrawn.

Claims 1-15, 22, and 24 are under examination in accordance to the elected species along with the expanded species set forth in the Expansion of Election of Species Requirement section above.

Priority

The instant application 18/675,614 filed on May 28, 2024 is a continuation of U.S. Application No. 17/431,626 filed on August 21, 2021, which is a 371 of PCT/EP2020/054803 filed on February 24, 2020, which claims priority to and the benefits of Foreign Application No. EP19158774.0 filed on February 22, 2019.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119 (a)-(d). The certified copy has been filed in parent Application No. 17/431,626, filed on August 17, 2021.

Receipt is acknowledged of a certified copy of foreign application EP19158774.0, however the present application does not properly claim priority to the submitted foreign application. It is noted that the foreign application fails to discloses "a licensed professional in accordance with accepted medical practice" in the context of diagnosing patient with major depressive disorder, the elected patient species ("the patient suffers from moderate or severe major depressive disorder as indicated by Montgomery-Asberg Depression Rating Scale (MADRS) score of 20 or more or by a 17-item Hamilton Depression Rating Scale (HAM-D) score of 17 or more"), and the Peak Psychedelic Experience Questionnaire as part of the elected criteria species to identify the occurrence of a peak psychedelic experience are not disclosed in said foreign application; therefore, each of these findings demonstrate that claims 1-15, 22, and 24, drawn to a method of treating a patient who is diagnosed with major depressive disorder by a licensed professional, are not entitled to the benefit of the foreign application, and will receive an effective filing date of February 24, 2020, which is the filing date of 371 of PCT/EP2020/054803.

If this copy is being filed to obtain priority to the foreign filing date under 35 U.S.C. 119(a)-(d) or (f), 365(a) or (b), or 386(a), applicant must also file a claim for such priority as required by 35 U.S.C. 119(b) or 365(b), and 37 CFR 1.55. If the application was filed before September 16, 2012, the priority claim must be made in either the oath or declaration or in an application data sheet; if the application

was filed on or after September 16, 2012, the claim for foreign priority must be presented in an application data sheet.

If the application being examined is an original application filed under 35 U.S.C. 111(a) (other than a design application), the claim for priority must be presented during the pendency of the application, and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior foreign application. See 37 CFR 1.55(d)(1). If the application being examined is a national stage application under 35 U.S.C. 371, the claim for priority must be made within the time limit set forth in the PCT and Regulations under the PCT. See 37 CFR 1.55(d)(2). Any claim for priority under 35 U.S.C. 119(a)-(d) or (f), 365(a) or (b), or 386(a) not presented within the time period set forth in 37 CFR 1.55 is considered to have been waived. If a claim for foreign priority is presented after the time period set forth in 37 CFR 1.55, the claim may be accepted if the claim properly identifies the prior foreign application and is accompanied by a grantable petition under 37 CFR 1.55(e) to accept an unintentionally delayed claim for priority and the applicable petition fee under 37 CFR 1.17(m)(1) or (m)(2).

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 6/26/2024, 7/12/2024, 7/23/2024, 08/26/2024, 9/27/2024, 10/28/2024, 11/26/2024, 12/27/2024, 1/31/2025, 2/27/2025, and 3/28/2025 are in compliance with the provisions of 37 CFR 1.97 unless otherwise noted. Accordingly, the information disclosure statements are being considered by the examiner.

Please note the foreign references without an English translation but have an English translation of the abstract will only have the abstract considered by the Examiner; and the foreign references without an English translation but has foreign equivalent written in English as indicated in the IDS will have the foreign equivalent considered by the Examiner.

The IDS submitted on 08/02/2024 does not recite any documents therein. Therefore, while the IDS has been submitted, it has not been considered by the examiner.

Foreign patent documents CL2021002174, CL2021002173 (cited under "Foreign Patent Documents", cited letter e and f in IDS filed on June 26, 2024), and EP 3927337 A1 (cited under "Foreign Patent Documents", cited letter a in IDS filed on June 26, 2024) do not have a legible copy in the application file. Thus, while these references have been cited in the IDS filed on June 26, 2024, the documents have not been considered by the Examiner.

Foreign patent documents EP 19158774.0 and EP19158806.0 (cited under "Foreign Patent Documents", cited letter c and d in IDS filed on June 26, 2024) do not have a legible copy in the application file. Thus, while these references have been cited in the IDS filed on June 26, 2024, the documents have not been considered by the Examiner.

n/a (cited under "Other Documents", cited no. 1 in the IDS filed on August 26, 2024) does not have a proper citation and a legible copy in the application file. Thus, while this reference "n/a" have been cited in the IDS filed on August 26, 2024, it has not been considered by the Examiner.

Foreign patent document EP 3941583 (cited under "Foreign Patent Documents", cited letter a in IDS filed on December 27, 2024) do not have a legible copy in the application file. Thus, while this reference has been cited in the IDS filed on December 27, 2024, the document has not been considered by the Examiner.

Foreign patent documents AU 2020225410, AU2020225766, and CO 2021/0010883 (cited under "Foreign Patent Documents", cited letter c, f, and j in IDS filed on March 28, 2025, respectively) do not have a legible copy in the application file. Thus, while these references have been cited in the IDS filed on March 28, 2025, the documents have not been considered by the Examiner.

In the instant application, it is duly noted that Applicant has submitted an information disclosure statement with a total of over 1,500+ references. While the Examiner has made every effort to thoroughly review these references, one could have very well overlooked a pertinent document.

As noted by the court, Applicant has an obligation to call the most pertinent prior art to the attention of the Patent Office in a proper fashion. Burying one reference amongst a large number of other IDS references is like citing nothing. See *Penn Yan Boats, Inc. v. Sea Lark Boats Inc.,* 359 F. Supp 948, 175 USPQ 260 (S.D. Fla. 1972; *Golden Valley Microwave Foods Inc. v. Weaver Popcorn Co. Inc.*, 24 USPQ2d 1801 (U.S. Dist. N. Dist. IN 1992).

The third-party submissions under 37 CFR 1.290 submitted on 9/26/2024, 9/27/2024, and 10/16/2024 are being considered by the Examiner.

Claim Interpretation

The process steps followed by the phrase of "and then increased, unless the patient has already experienced a peak psychedelic experience," in claim 12 as indicated as follows:

> 12. The method according to claim 1, wherein the 5-MeO-DMT is administered in a dosage from about 2 mg to about 8 mg for a first administration, and then increased, unless the patient has already experienced a peak psychedelic experience, to a dosage from about 8 mg to about 14 mg for a second administration, and then increased, unless the patient has already experienced a peak psychedelic experience, to a dosage from about 14 mg to about 20 mg for a third administration, or wherein equimolar amounts of the pharmaceutically acceptable salt are administered instead of 5-MeO-DMT.

, is reasonably construed to be a conditional step and does not require the dosage of 5-MeO-DMT to be increased if the subject has experienced a peak psychedelic experience.

Claim Objections

Claims 1-2 and 22 are objected to because of the following informalities:

With regard to claim 1, the term of "a licensed professional in accordance with accepted medical practice" is recited twice in the phrase of "patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice" noted as follows:

> 1. A method of treating a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice, the method comprising administering to the patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice a therapeutically effective amount of 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) or a pharmaceutically acceptable salt thereof.

. Since the licensed professional who diagnosed the patient is the same as the one properly set forth in the preamble, an article -the- should be use to clarify the licensed professional recited in the second recitation is the licensed professional previously mentioned in the first recitation for clarity.

With regard to claim 2, the recitation of "Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition (DSM-5)" should starts an article –a– , because the article "the" is used to refer to something that is previously mentioned. Since DSM-5 is not mentioned prior to this recitation, an article –a – should be used to for clarity.

With regard to claim 22, the recitation of "MADRS or HAM-D score" should starts with an article –a– , because the article "the" is used to refer to something that is previously mentioned. Since MADRS and HAM-D score are not mentioned prior to this recitation, an article –a – should be used to for clarity.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

> (a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15, 22, and 24 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for applications subject to pre-AIA 35 U.S.C. 112, the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites a 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) or a pharmaceutically acceptable salt thereof. The specification discloses only one salt species of 5-MeO-DMT, which is hydrochloride. The specification does not disclose any other salt species of 5-MeO-DMT as broadly encompassed by the claims.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, Regents of the *University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.I "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5,2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure ..." *Enzo Biochem*,

Inc. v. Gen-Probe Inc., 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting Guidelines, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v G.D. Searle & Co., 249 Supp*. 2d 216, 225 (W.D.N.Y. 2003).

Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties of pharmaceutically acceptable salts of 5-MeO-DMT, aside from a broad recitation that such are contemplated for use in the invention. As such, it is not apparent that Applicant was actually in possession of, and intended to be used within the context of the present invention, any specific pharmaceutically acceptable salts species of 5-MeO-DMT at the time the present invention was made.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claims is a recitation of pharmaceutically acceptable salts of 5-MeO-DMT, and the disclosure only provides a single salt species, hydrochloride (see "definition" section in the specification). Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Therefore, the scope of the claimed inventions contains a pharmaceutically acceptable salt of the compound fails to comply with the written description requirement, because pharmaceutically acceptable salts are not described in the specification in such a way as to reasonably encompassed any pharmaceutically acceptable salts of the compound due to the limited disclosure provided.

Accordingly, claims 2-15, 22, and 24 are rejected based on their dependency on a rejected base claim.

The following is a quotation of 35 U.S.C. 112(b):
(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-12, 22, and 24 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

With regard to claims 9-12, the term “about”, including those recited in the phrase of “about … to about…”, is a relative term which renders the claim indefinite. The term “term” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the present case, the boundaries of said term is unclear because the specification does not provide a standard to determine the numerical boundaries to the specific parameters.

With regard to claim 22,

- the claim recites the limitation "the clinical response" in line 1. There is insufficient antecedent basis for this limitation in the claim, because a clinical response is not mentioned prior to said recitation. It is not clear if Applicant is referring to (i) a clinical response assessed at a specific time after administering 5-MeO-DMT, and said clinical response has to persist at least 6 days after the last administration of 5-MeO-DMT; or (ii) a clinical response assessed 6 days after the last treatment of 5-MeO-DMT has to reach at least 50% improvement of the MADRS or HAM-D

score to demonstrate persistence? If Applicant is referring to the first scenario (i), then it is not clear when the clinical response is being assessed after the administration in order to determine whether the clinical response persists at least 6 days?

- The phrase of "the respective score" and "the last administration" lacks antecedent basis, because these terms are not recited prior to said phrase. As a result, it is not clear what these phrases are referring to.

With regard to claim 24, the phrase of "the last administration" lacks antecedent basis, because the term is not recited prior to said phrase. As a result, it is not clear what said phrase is referring to.

Claim Rejections - 35 USC § 102

In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis (i.e., changing from AIA to pre-AIA) for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.
>
> (a)(2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.

Claims 1, 3-4, 22, and 24 are rejected under 35 U.S.C. 102(a)(1) as being anticipated by **Osório et al.** (Revista brasileira de psiquiatria (Sao Paulo, Brazil : 1999), 2015. Vol. 37(1): 13-20; cited in the IDS

filed on June 26, 2024), as evidenced by Halberstadt et al. (Psychopharmacology, 2008. Vol. 201: 55–66; cited under "other documents", cite no. 143 in the IDS filed on June 26, 2024).

Osório et al. teaches an oral administration of 120-200 mL of ayahuasca (AYA), a natural psychedelic brew prepared from Amazonian plants (see e.g., p. 14, right column, "Drug" section), to a patient diagnosed with recurrent major depressive disorder demonstrates significant acute antidepressant effects (see e.g., p. 17, left column, "Discussion" section, 1st paragraph; p. 14, "Methods" , "Volunteers" section); wherein the patient suffers from severe major depressive disorder as indicated by MADRS score of 39 and HAM-D score of 29 (see e.g., "Table 1", patient 3). ***Please note*** the ayahuasca taught by Osório et al. is a hallucinogenic tea known to contain active components, N,N-dimethyltryptamine (DMT) and 5-methoxy-DMT (5-MeO-DMT), as well as monoamine oxidase inhibitor harmine and harmaline, as evidenced by Halberstadt et al. (see e.g., abstract). ***Please further note*** the 120-200 mL of ayahuasca taught by Osório contains an amount of 5-MeO-DMT as active components, and that is a therapeutically effective amount. Osório et al. further teaches a structured clinical interview for DSM-IV was used to assess whether potential patients met the inclusion and exclusion criteria (see e.g., p. 15, left column, "psychometric instruments" section). Osório et al. further teaches the MADRS scores is 82% below baseline on day 7 after AYA administration as illustrated as follows (see e.g., Figure 1; p. 15, right column, "Results"):

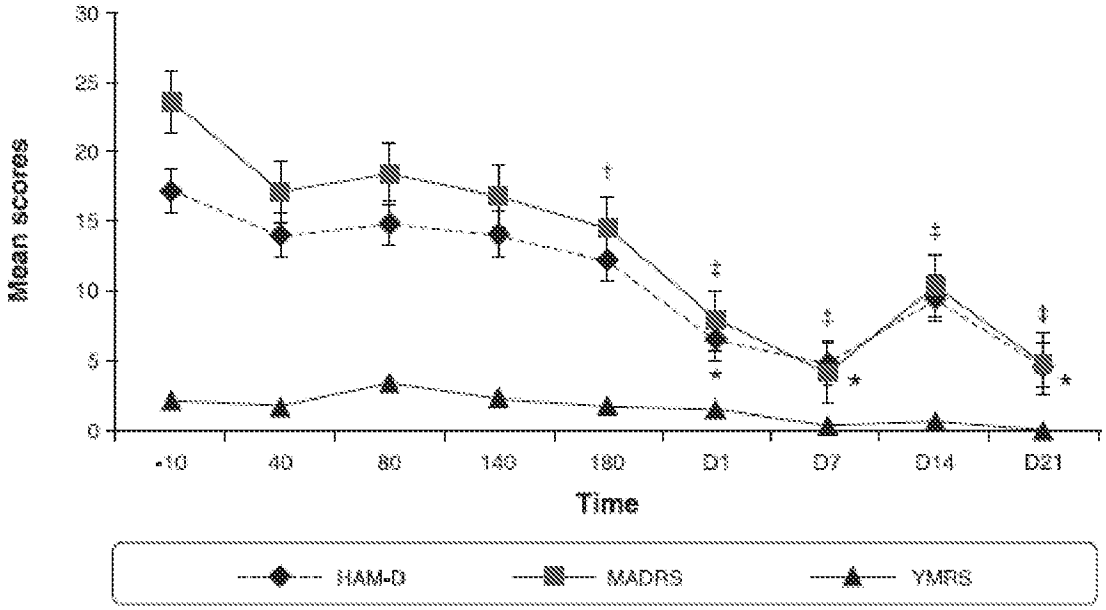

Figure 1 Temporal distribution of scores (means from six volunteers) on the Hamilton Rating Scale for Depression (HAM-D), Montgomery-Åsberg Depression Rating Scale (MADRS), and Young Mania Rating Scale (YMRS). HAM-D: * $p < 0.05$; MADRS: † $p < 0.05$, ‡ $p < 0.01$. Error bars denote one standard error of the mean.

. Osório et al. further teaches the HAM-D and MADRS scales were completed by a psychiatrist with clinical experience and training in the use of these scales (see e.g., p. 15, right column). ***Please note*** the psychiatrist taught by Osório et al. is a licensed professional in accordance with accepted medical practice.

MPEP 2112 I states: "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. IRECO Inc.,* 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best,* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In the present case, Osório et al. is silent regarding "5-methoxy-DMT" in the ayahuasca; However, by practicing the method of Osório et al., one would also be administering to the patient a therapeutically effective amount of 5-MeO-DMT even

though the prior art was not aware of it, because ayahuasca is known to contain 5-MeO-DMT as an active component, as evidenced by Halberstadt et al. (see e.g., "abstract").

With respect to "wherein the patient suffers from moderate or severe major depressive disorder as indicated by a Montgomery-Asberg Depression Rating Scale (MADRS) score of 20 or more or by a 17-item Hamilton Depression Rating Scale (HAM-D) score of 17 or more" in **claim 3**, and "wherein the patient suffers from severe major depressive disorder as indicated by a MADRS score of 35 or more or by a HAM-D score of 25 or more" in **claim 4**, Osório et al. clearly teaches the patient that undergoes ayahuasca treatment includes a patient with severe major depressive disorder with a MADRS score of 39 and a HAM-D score of 29, and that anticipates the claimed limitation.

With respect to "wherein the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" in **claim 22**, Osório et al. clearly teaches the MADRS scores is 82% below baseline on day 7 after ayahuasca administration and that anticipates the claimed limitation.

With respect to "wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" in **claim 24**, Osório et al. clearly teaches the MADRS scores is about 5 on day 7 after ayahuasca administration (see Figure 1) and that anticipates the claimed limitation.

Therefore, the teachings of Osório et al. anticipates the claimed invention.

Claims 1-2, 5, 22 and 24 are rejected under 35 U.S.C. 102(a)(1) as being anticipated by **Santos et al.** (Arc Clin Psychiatr, 2018. Vol. 45 (1):22-24; cited under "Other Documents", cite no. 35 in the IDS

filed on June 26, 2024), as evidenced by Halberstadt et al. (Psychopharmacology, 2008. Vol. 201: 55–66; cited under "other documents", cite no. 143 in the IDS filed on June 26, 2024).

Santos et al. teaches the administration of a single oral dose of ayahuasca (dose: 2.2 mL/kg) in an open-label trial to 17 patients with treatment-resistant major depressive disorder was associated with significant decreases in depression symptoms assessed with the HAM-D and the MADRS from 80 minutes to day 21 (see e.g., p. 22, "Introduction" section, 3rd paragraph). Santos et al. further teaches the average baseline score in the HAM-D scale was 19.24 (SD = 5.52), and at day 21 the average score was 7.56 (SD = 4.7) shown as follows (see e.g., Table 1):

	Age at the time of the experiment	Time since the experiment (months)	HAM-D / MADRS (baseline)	HAM-D / MADRS (D1)	HAM-D / MADRS (D7)	HAM-D / MADRS (D14)	HAM-D / MADRS (D21)
Patient 1	31	76	20 / 27	14 / 12	3 / 6	3 / 3	2 / 1
Patient 2	36	67	20 / 32	9 / 17	11 / 7	4 / 2	2 / 3
Patient 3	38	52	20 / 32	3 / 1	7 / 11	2 / 2	4 / 2
Patient 4	46	55	17 / 21	10 / 12	8 / 15	10 / 15	13 / 15
Patient 5	39	51	20 / 28	17 / 20	18 / 22	15 / 18	15 / 19
Patient 6	54	51	19 / 23	6 / 3	10 / 9	16 / 14	5 / 8
Patient 7	28	50	23 / 25	5 / 7	5 / 5	6 / 6	5 / 5
Patient 8	47	49	24 / 29	13 / 17	20 / 23	16 / 19	10 / 17

(see e.g., p. 22, "Introduction" section, 3rd paragraph). Santos et al. further teaches compared to placebo, HAM-D scores at day 7 were significantly lower in patients treated with ayahuasca (Cohen's d = 0.98), and MADRS scores were significantly reduced in the ayahuasca group at days 1, 2 and 7 (see e.g., p. 22, "Introduction" section, 3rd paragraph).

MPEP 2112 I states: "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. IRECO Inc.,* 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best,*

562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In the present case, Santos et al. is silent regarding "5-methoxy-DMT" in the ayahuasca; However, by practicing the method of Santos et al., one would also be administering to the patient a therapeutically effective amount of 5-MeO-DMT even though the prior art was not aware of it, because ayahuasca is known to contain 5-MeO-DMT as an active component, as evidenced by Halberstadt et al. (see e.g., "abstract").

With respect to "wherein the patient suffers from moderate or severe major depressive disorder as indicated by a Montgomery-Asberg Depression Rating Scale (MADRS) score of 20 or more or by a 17-item Hamilton Depression Rating Scale (HAM-D) score of 17 or more" in **claim 3**, Santos et al. clearly teaches the patient that undergoes ayahuasca treatment includes patient 1 who has a HAM-D score of 20, and that anticipates the claimed limitation of "a 17-item Hamilton Depression Rating Scale (HAM-D) score of 17 or more".

With respect to "wherein the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" in **claim 22**, Santos et al. clearly teaches the method includes patient 1 with a baseline HAM-D score of 20, and the HAM-D score is 3 on day 7. ***Please note*** the percentage improvement can be calculated using the HAM-D score on day 7 and the baseline HAM-D score, which when calculated by

$$100\% - \left(\frac{3}{20} \times 100\%\right) = 85\%$$

, gives an 85% improvement of the HAM-D score on day 6, and that anticipates a clinical response that persist until at least 6 day after the last administration of 5-MeO-DMT.

With respect to "wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" in **claim 24**, Santos et al.

clearly teaches the method includes patient 1 with a baseline HAM-D score of 20, and the HAM-D score is 3 on day 7, and that anticipates the claimed limitation.

Therefore, the teachings of Santos et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis (i.e., changing from AIA to pre-AIA) for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries for establishing a background for determining obviousness under 35 U.S.C. 103 are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims the examiner presumes that the subject matter of the various claims was commonly owned as of the

effective filing date of the claimed invention(s) absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and effective filing dates of each claim that was not commonly owned as of the effective filing date of the later invention in order for the examiner to consider the applicability of 35 U.S.C. 102(b)(2)(C) for any potential 35 U.S.C. 102(a)(2) prior art against the later invention.

Claims 1-2, 6-11, 13, 15, 22, and 24 are rejected under 35 U.S.C. 103 as being unpatentable over **Russ et al.** (WO2018/195455A1; cited under "foreign patent documents", cited letter a in the IDS filed on June 26, 2024), in view of **Davis et al.** (J Psychopharmacol, 2018. Vol. 32(7): 779-792; cited under "other documents", cite no. 69 in the IDS filed on June 26, 2024), as evidenced by Nestler et al. (Elsevier Science, 2012: 53-57) and APA Dictionary of Psychology ([online]. Published on April 14, 2018).

Russ et al. teaches a method of improving mental or physical well-being of a subject, the method comprising: (i) providing a subject, wherein based on a score of one or more predictors in the subject, the subject has been identified as likely to have a positive therapeutic response to a psychedelic agent; and (ii) following step (i), administering to the subject the psychedelic agent (see e.g., p. 2, line 1-11; claim 1); wherein the method is for treating a depressive disorder that is, *inter alia*, major depression (see e.g., p. 8, line 23-26; claims 126-127); wherein the psychedelic agent is a 5-HT_{2A} agonist, for example, ayahuasca or 5-methoxy-N,N-dimethyltryptamine (5-Meo-DMT)(see e.g., p. 9, line 4-12). Russ et al. further teaches diagnostic guidance for psychological disorders can be found, for example, in the DSM-V by citing the fifth edition of Diagnostic and Statistical Manual of Mental Disorders published by American Psychiatric Association (see e.g., p. 13, line 30-34). Russ et al. further teaches the methods are performed in the context of an authorized treatment facility (e.g., a specialized treatment facility) that features a staff that has training and expertise in administering and overseeing psychedelic therapy (see e.g., p. 24, line 31 to p. 25, line2). Russ et al. further teaches the depressive disorder may be associated with one or more prodromal symptoms selected from the group consisting of, *inter alia*,

suicidality (see e.g., p. 8, line 26-30). Russ et al. further teaches the term "administering" refers to a method of giving a dosage of pharmaceutical composition to a subject, where the method is, e.g., by inhalation (see e.g., p. 18, line 5-7). Russ et al. further teaches a positive therapeutic response is a long-term response, such as remission (see e.g., p. 14, line1-4). Russ et al. further teaches a subject may have a psychedelic-induced mystical experience, and the occurrence of an mystical experience in a subject suggests that the subject may be more likely to have a positive therapeutic response to the psychedelic treatment, e.g., remission (see e.g., p. 2, line 38-41). Russ et al. further teaches characteristics of mystical experience can be self-reported, e.g., using MEQ-30 (see e.g., p. 15, line 11-14).

Russ et al. does not specifically teach administering a therapeutically effective amount of 5-MeO-DMT for treating major depressive disorder.

Davis et al. teaches 5-MeO-DMT is a potent, fast acting, psychedelic substance that acts as an non-selective 5-HT agonist, active at both the 5-HT_{1A} and 5-HT_{2A} receptors, but with a higher affinity for the 5-HT1A receptor subtype and also inhibits the reuptake of 5-HT (see e.g., p. 780, left column, 2nd paragraph). Davis et al. further teaches in a 5-MeO-DMT survey study, which includes respondents that used 5-MeO-DMT at least once in their lifetime (see e.g., p. 780, "procedure" section), 81% of survey respondents had consumed 5-MeO-DMT through a smoking/vaporizing route of administration (see e.g., p. 783, left column, 1st paragraph under Table 2; Table 3); 57% of survey respondents had a 'complete mystical experience' characterized by endorsement of ≥ 60% of the total possible score across all four subscales of the MEQ30 (see e.g., p. 784, left column, 1st paragraph under "Subjective effects of 5-MeO-DMT" section). Davis et al. further teaches the incidence of self-reported lifetime psychiatric disorders in this sample included depression (61%), wherein 77% of the survey respondents with depression reported improvement of their psychiatric conditions (see e.g., p. 784, right column, 1st paragraph; Table 6). Davis et al. further teaches the typical dose of 5-MeO-DMT used by the survey respondents shown as follows (see e.g., Table 3):

Table 3. (Continued) **(Modified)**

Characteristic	Total sample	Synthetic	Toad	Plant Extract/Yopo	χ^2	Post hoc
	n=515[a]	n=284[b]	n=148[c]	n=83[d]		
	M(SD) or %	M(SD) or %	M(SD) or %	M(SD) or %		
	Total Sample	**Synthetic**	**Toad**	**Plant/Other/Unsure**	***F* or χ^2**	**Post hoc**
Milligrams typically used (based on type of 5-MeO-DMT they have the most experience with)					84.20***	
Unknown	38%	25%	56%	48%		S<T=P
0–10	25	34	10	22		T<P=S
11–50	29	37	16	23		S>T
51+	9	5	18	7		S<T

.

Regarding claim 1, even though Russ et al. does not specifically teach administering a therapeutically effective amount of 5-Meo-DMT for treating major depression, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to particularly select 5-MeO-DMT as the psychedelic agent for the method of treating major depression. ***Please note*** the major depression taught by Russ et al. is major depressive disorder, as evidenced by Nestler et al. (see e.g., p. 55, "Depression" section). One would have motivated to do so, because the fact that Davis et al. teaches 5-MeO-DMT is a potent, fast acting, psychedelic substance and a non-selective 5-HT agonist, and the fact that the 5-MeO-DMT survey respondents with depression reported improvement of their psychiatric conditions after the administration of 5-MeO-DMT. One of ordinary skill in the art would have a reasonable expectation of success to arrive the claimed invention, because one would have reasonably expected that the administration of a therapeutically effective amount of 5-Meo-DMT as the psychedelic agent successfully treats major depressive disorder diagnosed by a licensed professional in accordance with accepted medical practice.

With regard to "wherein the disorder is diagnosed in accordance with the Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition (DSM-5) published by the American Psychiatric

Association" in **claim 2**, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the method of treating major depressive disorder as set forth above by incorporating patient who is diagnosed with major depressive disorder in accordance with the DSM-5 published by the American Psychiatric Association. One would have been motivated to do so, because Russ et al. further teaches the diagnostic guidance for psychological disorders, including major depression, can be found in the DSM-V published by American Psychiatric Association. One would have reasonable expectation of success, because one would have reasonably expected that the patient who is diagnosed with major depressive disorder in accordance to the diagnostic guidance DSM-V as suggested by Russ et al. would successfully be treated by 5-Meo-DMT.

With regard to "wherein the patient suffers in addition from suicidal ideation" in **claim 6**, "wherein the patient suffers from suicidal ideation with intent to act" in **claim 7**, and "wherein the patient is at imminent risk for suicide" in **claim 8**, these claimed limitations are drawn to suicidal ideation in the mind of the patient diagnosed with major depressive disorder. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method of treating major depressive disorder as set forth above by incorporating patient diagnosed with major depressive disorder that suffers from suicidal ideation, suicidal ideation with intent to act, or at immediate risk for suicide. One would have been motivated to do so, because Russ et al. teaches the depressive disorder, such as major depression, may be associated with suicidality. ***Please note*** the term "suicidality" is defines as the risk of suicide, usually indicated by suicidal ideation or intent, especially as evident in the presence of a well-elaborated suicidal plan, as evidenced by the Dictionary of Psychology Published by American Psychological Association. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the patients diagnosed with major depressive disorder associated with suicidality, including those indicated by

suicidal intent, is at imminent risk for suicide, and said patient would successfully be treated by 5-Meo-DMT.

With regard to "wherein the 5-MeO-DMT or salt thereof is administered at a dose or in a dosage regimen that causes the patient to experience a peak psychedelic experience" in **claim 9**, the claimed limitation is drawn to the dosage of 5-MeO-DMT being administered to the patient, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method of treating major depressive disorder as set forth above to incorporate the dose of 5-Meo-DMT taught by Davis et al. to arrive the claimed invention. One would have been motivated to do so, because Davis et al. teaches 57% of 5-MeO-DMT survey respondents had a 'complete mystical experience', characterized by endorsement of ≥ 60% of the total possible score across all four subscales of the MEQ30; and 25% of respondents used 0-10 mg of 5-MeO-DMT, 29% of respondents used 11-50 mg of 5-MeO-DMT, and 9% used 51+ mg of 5-MeO-DMT. ***Please note*** the 'complete mystical experience' taught by Davis et al. is the peak psychedelic experience when construed in light of the instant specification (see claim interpretation section as set forth above). One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the administration of 5-MeO-DMT in the dose reported by the survey respondents of Davis et al., including those who had a complete mystical experience, would successfully treat major depressive disorder by causing complete mystical experience.

With regard to "wherein a dosage of about 4 mg to about 20 mg 5-MeO-DMT is administered, or wherein equimolar amounts of the pharmaceutically acceptable salt are administered instead of 5-MeO-DMT" in **claim 10**, and "wherein a dosage of about 6 mg; or of about 12 mg; or of about 18 mg is administered, or wherein equimolar amounts of the pharmaceutically acceptable salt are administered instead of 5-MeO-DMT in **claim 11**, the claimed limitations are drawn to the dosage of 5-MeO-DMT. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie*

case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976*); In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). In the present case, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method of treating major depressive disorder as set forth above to incorporate the dose of 5-Meo-DMT taught by Davis et al. to arrive the claimed invention. One would have been motivated to do so, because Davis et al. teaches 25% of survey respondents who used 5-MeO-DMT at least once in their lifetime, including those with depression, use 5-MeO-DMT in the dosage range of 0-10 mg. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that by administering 5-MeO-DMT in the dosage range of 0-10 mg taught by Davis et al. would successfully treat major depressive disorder; and that meets the claimed limitations.

With respect to "wherein the occurrence of a peak psychedelic experience is identified through achievement of at least 60% of the maximum possible score in each of the four subscales (mystical, positive mood, transcendence of time and space, and ineffability)" in **claim 13**, the claimed limitation is drawn to the survey used to identified the peak psychedelic experience in the patient diagnosed with major depressive disorder. It would have *been prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method of treating major depressive disorder as set forth above to specifically incorporate MEQ-30 to report the occurrence of a complete mystical experience. One would have been motivated to do so, because Russ et al. teaches MEQ30 enables patient to self-report mystical experience, which indicate that the subject is likely to have a positive therapeutic response to said treatment; and the fact that Davis et al. teaches 57% of survey respondents who used a dose of 5-MeO-DMT once in their lifetime had a 'complete mystical experience' characterized by endorsement of ≥ 60% of the total possible score across all four subscales of the MEQ30. ***Please note*** complete mystical experience taught by Davis et al. is a peak psychedelic experience. One would have reasonably expected that the incorporation of MEQ-30 would have

successfully identified the patients that experience complete mystical experience after administering the dose of 5-MeO-DMT.

With respect to "wherein the 5-MeO-DMT or a pharmaceutically acceptable salt thereof is administered via inhalation" in **claim 15**, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method of treating major depressive disorder as set forth above to specifically administer the 5-MeO-DMT via inhalation. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent, including 5-MeO-DMT, can be administer via inhalation for treating major depression, and Davis et al. teaches 81% of 5-MeO-DMT survey respondents had consumed 5-MeO-DMT through a smoking/vaporizing route of administration. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the administration of 5-MeO-DMT via inhalation would have successfully deliver said psychedelic agent for treating major depressive disorder.

With respect to "wherein the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" in **claim 22**, the claimed limitation is reasonably interpreted by the Examiner as being drawn to an intended outcome ("clinical response") of the active step positively recited in the method of treating major depressive disorder. Even though the prior art does not specifically teach the clinical response as claimed; However, the limitation of "the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" will naturally flow from the method made obvious by Russ et al. and Davis et al. as set forth above. Since the same compound (5-MeO-DMT) is being administered to the same subject (subject diagnosed with major depressive disorder), products of identical or similar composition cannot exert mutually exclusive

properties when administered under the same or similar circumstances. Therefore, by practicing the method of treating major depressive disorder as set forth above, one will also be achieving the claimed outcome even though the prior art does not specifically measure the clinical response using the MADRS or HAM-D score. "The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

With respect to "wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" in **claim 24**, the claimed limitation is reasonably interpreted by the Examiner as being drawn to an intended outcome ("clinical response") of the active step positively recited in the method of treating major depressive disorder. Even though the prior art does not specifically teach the patient is in remission of depressive symptoms as assessed by the score instantly claimed, Russ et al. teaches the subject's response to the psychedelic agent, including 5-MeO-DMT, is a positive therapeutic response (e.g., remission). Since the same compound (5-MeO-DMT) is being administered to the same subject (subject diagnosed with major depressive disorder), products of identical or similar composition cannot exert mutually exclusive properties when administered under the same or similar circumstances. Therefore, by practicing the method of treating major depressive disorder as set forth above, one will also be achieving the claimed outcome even though the prior art does not specifically measure the remission of depressive symptoms using the MADRS or HAM-D score. "The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Therefore, the claimed invention is *prima facie* obvious to one of ordinary skill in the art at the time the application was filed, absent factual evidence to the contrary.

Claims 1-4, 6-11, 13, 15, 22, and 24 are rejected under 35 U.S.C. 103 as being unpatentable over Russ et al. (WO2018/195455A1), in view of Davis et al. (J Psychopharmacol, 2018. Vol. 32(7): 779-792) as applied to claims 1-2, 6-11, 13, 15, 22, and 24 above, and further in view of **Osório et al.** (Revista brasileira de psiquiatria (Sao Paulo, Brazil : 1999), 2015. Vol. 37(1): 13-20; cited in the IDS filed on June 26, 2024).

The teachings of Russ et al. and Davis et al. are set forth above and applied as before.

Russ et al. and Davis et al. does not specifically teach the patient suffers from moderate or severe major depressive disorder as indicated by a MADRS score of 20 or more or by a 17-item HAM-D score of 17 or more as claimed in **claim 3**. Russ et al. and Davis also does not teach the patient suffers from severe major depressive disorder as indicated by a MADRS score of 35 or more or by a HAM-D score of 25 or more as claimed in **claim 4**.

Osório et al. teaches an oral administration of 120-200 mL of ayahuasca (AYA), a natural psychedelic brew prepared from Amazonian plants (see e.g., p. 14, right column, “Drug” section), to a patient diagnosed with recurrent major depressive disorder demonstrates significant acute antidepressant effects (see e.g., p. 17, left column, “Discussion” section, 1st paragraph; p. 14, “Methods” , “Volunteers” section); wherein the patient suffers from severe major depressive disorder as indicated by MADRS score of 39 and HAM-D score of 29 (see e.g., “Table 1”, patient 3).

Even though Russ et al. and Davis et al. does not specifically teach the patient as claimed in claim 3, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application as file to modify the method of treating major depressive disorder as set forth above to specifically incorporate the patient suffers from severe major depressive disorder. One would have been

motivated to do so, because Russ et al. teaches a list of psychedelic agents that are 5-HT2A agonist, including ayahuasca or 5-MeO-DMT, that can be used interchangeably for treating major depressive disorder; and the fact that Osório et al. teaches the administration of 120-200 mL of ayahuasca to patients suffers from severe major depressive disorder as indicated by MADRS score of 39 and HAM-D score of 29 demonstrates significant acute antidepressant effects. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that 5-MeO-DMT would have exerts 5-HT2A agonist affect as ayahuasca of Osório et al., and therefore by administering 5-MeO-DMT in a therapeutically effective amount to patients with severe major depressive disorder, including those with a MDRS score of 39, would have successfully exerts antidepressant effects.

Therefore, the claimed invention is *prima facie* obvious to one of ordinary skill in the art at the time the application was filed, absent factual evidence to the contrary.

Claims 1-2, 5-11, 13, 15, 22, and 24 are rejected under 35 U.S.C. 103 as being unpatentable over Russ et al. (WO2018/195455A1), in view of Davis et al. (J Psychopharmacol, 2018. Vol. 32(7): 779-792) as applied to claims 1-2, 6-11, 13, 15, 22, and 24 above, and further in view of **Santos et al.** (Arc Clin Psychiatr, 2018. Vol. 45 (1):22-24; cited under "Other Documents", cite no. 35 in the IDS filed on June 26, 2024).

The teachings of Russ et al. and Davis et al. are set forth above and applied as before.

Russ et al. and Davis et al. does not specifically teach the patient is diagnosed with a treatment-resistant form of major depressive disorder as claimed in **claim 5**.

Santos et al. teaches the administration of a single oral dose of ayahuasca (dose: 2.2 mL/kg) in an open-label trial to 17 patients with treatment-resistant major depressive disorder was associated with significant decreases in depression symptoms assessed with the HAM-D and the MADRS from 80

minutes to day 21 (see e.g., p. 22, "Introduction" section, 3rd paragraph). Santos et al. further teaches the average baseline score in the HAM-D scale was 19.24 (SD = 5.52), and at day 21 the average score was 7.56 (SD = 4.7) (see e.g., p. 22, "Introduction" section, 3rd paragraph). Santos et al. further teaches compared to placebo, HAM-D scores at day 7 were significantly lower in patients treated with ayahuasca (Cohen's d = 0.98), and MADRS scores were significantly reduced in the ayahuasca group at days 1, 2 and 7 (see e.g., p. 22, "Introduction" section, 3rd paragraph).

Even though Russ et al. and Davis et al. does not specifically teach the patient is diagnosed with a treatment-resistant form of major depressive disorder, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application as file to modify the method of treating major depressive disorder as set forth above to specifically incorporate the patient diagnosed with a treatment-resistant form of major depressive disorder. One would have been motivated to do so, because Russ et al. teaches a list of psychedelic agents that are 5-HT2A agonist, including ayahuasca or 5-MeO-DMT, that can be used interchangeably for treating major depressive disorder; and the fact that Santos et al. teaches a single oral dose of ayahuasca significantly lower HAM-D score. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that 5-MeO-DMT would have exerts 5-HT2A agonist affect as ayahuasca of Santos et al., and therefore by administering 5-MeO-DMT in a therapeutically effective amount to patients with treatment-resistant form of major depressive disorder, would have successfully treat major depressive disorder by reducing the HAM-D score.

Therefore, the claimed invention is *prima facie* obvious to one of ordinary skill in the art at the time the application was filed, absent factual evidence to the contrary.

Claims 1-2, 6-13, 15, 22, and 24 are rejected under 35 U.S.C. 103 as being unpatentable over Russ et al. (WO2018/195455A1), in view of Davis et al. (J Psychopharmacol, 2018. Vol. 32(7): 779-792) as

applied to claims 1-2, 6-11, 13, 15, 22, and 24 above, and further in view of **McCormack et al.** (CMAJ., 2011. Vol. 183(1): 65-69) and **Erowid** (5-MEO-DMT dosage. The Vaults of Erowid [online]; cited under "other documents", cite no. 90 in the IDS filed on June 26, 2024).

The teachings of Russ et al. and Davis et al. are set forth above and applied as before.

Russ et al. and Davis et al. does not specifically teach the 5-MeO-DMT is administered in a dosage from about 2mg to about 8 mg for a first administration as claimed in **claim 12**.

McCormack et al. teaches the use of a very low dose when starting a new medication if the condition is not life-threatening or producing severe symptoms (see e.g., p. 65, left column, 1st paragraph). McCormack further teaches the approach of using a very low starting dose has several important advantages, including further decrease the risk of adverse effects and engage patients in determining the best dose for them (see e.g., p. 65, left column, 3rd paragraph). McCormack further teaches dose titration will likely improve tolerability, may improve adherence if side effects are reduced, and will reduce drug costs if a low or very low dose is found to be effective (see e.g., p. 68, right column, "discussion" section).

McCormack et al. does not teach the low starting dose of 5-MeO-DMT.

Erowid teaches the dosage of smoked/vaporized 5-MeO-DMT shown as follows:

Smoked/Vaporized 5-MeO-DMT Dosages	
Threshold	1 - 2 mg
Light	2 - 5 mg
Common	5 - 10 mg
Strong	10 - 20 mg

Onset : **0 - 30 seconds**
Peak : **1 - 15 minutes**
Duration : **30 minutes**
After Effects : **1 hour**

(see e.g., "Smoked/Vaporized 5-MeO-DMT Dosages" Table)

Even though Russ et al. and Davis et al. does not specifically teach the 5-MeO-DMT is administered in a dosage from about 2 mg to about 8 mg for a first administration, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application as file to modify the method of treating major depressive disorder as set forth above by incorporating the threshold dosage of 5-MeO-DMT taught by Erowid for the first administration, and the optimize said dosage through routine experimentation. One would have been motivated to do so, because McCormack recommend starting a new medication from a very low dose followed by upward titration can reduce side effects; and the fact that Erowid teaches the threshold dose of 5-MeO-DMT is 1-2 mg. One would have a reasonable expectation of success to arrive at the claimed invention through routine experimentation, because one would have reasonably expected that by optimizing the dosage of 5-MeO-DMT, starting from the threshold dose of 5-MeO-DMT taught by Erowid et al., would successfully incorporate the benefit of reducing side effects for the treatment of major depressive disorder, and that meets the limitation of "a dosage from about 2 mg to about 8 mg for a first administration".

Therefore, the claimed invention is *prima facie* obvious to one of ordinary skill in the art at the time the application was filed, absent factual evidence to the contrary.

Claims 1-2, 6-11, 13-15, 22, and 24 are rejected under 35 U.S.C. 103 as being unpatentable over Russ et al. (WO2018/195455A1), in view of Davis et al. (J Psychopharmacol, 2018. Vol. 32(7): 779-792) as applied to claims 1-2, 6-11, 13, 15, 22, and 24 above, and further in view of **Barrett et al.** (Frontiers in psychology, 2017. Vol. 8, 1238).

The teachings of Russ et al. and Davis et al. are set forth above and applied as before.

Russ et al. and Davis et al. does not specifically teach the occurrence of a peak psychedelic experience is identified through achievement of a Peak Psychedelic Experience Questionnaire (PPEQ) Total Score of at least 75 as claimed in **claim 14**.

Barrett et al. teaches mystical experiences are described as non-dual experiences that include a deeply felt positive mood, difficulty putting the experience into words, and an experience where traditional notions of time and space do not have meaning, and they are operationally defined and investigated in psychedelic research through the use of instruments such as the Mystical Experience Questionnaire (see e.g., p.2, left column, 1st paragraph). Barrett et al. further teaches peak psychedelic experiences is measured using questionnaires that assess subjective experiences during psychedelic drug effect, for example, the Mystical Experience Questionnaire or MEQ30 (see e.g., p. 9, left column).

Even though Russ et al. and Davis et al. does not specifically teach the occurrence of a peak psychedelic experience is identified through achievement of a Peak Psychedelic Experience Questionnaire (PPEQ) Total Score of at least 75 as claimed, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method of treating major depressive disorder as set forth above to specifically incorporate a Peak Psychedelic Experience Questionnaire to identify the occurrence of the complete mystical experience taught by Davis et al. One would have been motivated to do so, because Barrett et al. teaches peak psychedelic experiences are subjective experiences that relies on the use of instrument such as Mystical Experience Questionnaire for assessment. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that by incorporation a Peak Psychedelic Experience Questionnaire can successfully identified the patients that experience complete mystical experience taught by Davis et al. after administering the dose of 5-MeO-DMT.

Therefore, the claimed invention is *prima facie* obvious to one of ordinary skill in the art at the time the application was filed, absent factual evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The filing of a terminal disclaimer by itself is not a complete reply to a nonstatutory double patenting (NSDP) rejection. A complete reply requires that the terminal disclaimer be accompanied by a reply requesting reconsideration of the prior Office action. Even where the NSDP rejection is provisional the reply must be complete. See MPEP § 804, subsection I.B.1. For a reply to a non-final Office action, see 37 CFR 1.111(a). For a reply to final Office action, see 37 CFR 1.113(c). A request for reconsideration

while not provided for in 37 CFR 1.113(c) may be filed after final for consideration. See MPEP §§ 706.07(e) and 714.13.

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The actual filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/apply/applying-online/eterminal-disclaimer.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 34-41, 43, and 46-47 of **copending Application No. 18/679,917** (reference application), in view of **Russ et al.** (WO2018/195455A1; cited under "foreign patent documents", cited letter a in the IDS filed on June 26, 2024), as evidenced by APA Dictionary of Psychology ([online]. Published on April 14, 2018).

Although the claims at issue are not identical, they are not patentably distinct from each other because the claims of the reference application is also drawn to a method of treating a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice, the method comprising administering to the patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice a therapeutically effective amount of 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) or a pharmaceutically acceptable salt thereof, wherein the 5-MeO-DMT is administered via the intravenous, intramuscular or subcutaneous route. The claims of the reference application also teaches the patient suffers from moderate or severe major depressive disorder, and the patient diagnosed with treatment-resistant form of major depressive disorder. The claims of reference application also teaches the dose

and the dosage regimen that causes a peak psychedelic experience; the instruments used to identify the peak psychedelic experience; the route of administration, in this case, via inhalation; the clinical response; and remission of depressive disorders (see reference claims 34-41, 43, and 46-47).

The claims of reference application does not teach the 5-MeO-DMT is administered via inhalation as claimed in claim 15. The claims of reference application also does not teach patient suffers in addition from suicidal ideation as claimed in claims 6-8.

Russ et al. teaches a method of treating major depression, the method comprising: administering to the subject a psychedelic agent, wherein the psychedelic agent is selected from psilocybin or 5-MeO-DMT (see e.g., p. 2, line 1-11; p. 8, line 23-26; p. 9, line 4-12; claims 1, 126-127). Russ et al. further teaches the depressive disorder may be associated with one or more prodromal symptoms selected from the group consisting of, *inter alia*, suicidality (see e.g., p. 8, line 26-30). Russ et al. further teaches the term "administering" refers to a method of giving a dosage of pharmaceutical composition to a subject, where the method is, e.g., by inhalation (see e.g., p. 18, line 5-7).

Regarding claim 6-8, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient that suffers from suicidal ideation, suicidal ideation with intent to act, or at immediate risk for suicide. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent such as 5-MeO-DMT can treat major depression associated with suicidality. ***Please note*** the term "suicidality" is defines as the risk of suicide, usually indicated by suicidal ideation or intent, especially as evident in the presence of a well-elaborated suicidal plan, as evidenced by the Dictionary of Psychology Published by American Psychological Association. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the patients associated with suicidality, including those indicated by suicidal intent, is at imminent risk for suicide, and said patient would successfully be treated by 5-Meo-DMT.

Regarding claim 15, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to administer the 5-MeO-DMT via inhalation. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent, including 5-MeO-DMT, can administered by inhalation for treating major depression. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that by administering the 5-MeO-DMT via inhalation would have successfully deliver said compound for treating major depression.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-5, 9, 19-23, 29, 32-33 and 36-37 of **copending Application No. 18/373,904** (reference application), in view of Russ et al. (WO2018/195455A1; cited under "foreign patent documents", cited letter a in the IDS filed on June 26, 2024) and Carhart-Harris (The Lancet Psychiatry, 2016. Vol. 3(7): 619-627; cited under "other documents", cited no. 45 in the IDS filed on June 26, 2024), as evidenced by APA Dictionary of Psychology ([online]. Published on April 14, 2018).

Although the claims at issue are not identical, they are not patentably distinct from each other because the conflicting claims of the reference application are directed to a method of treating a patient suffers from postpartum depression (PPD) and moderate or severe depression comprising administering an effective amount of 5-MeO-DMT or a pharmaceutically acceptable salt thereof via intravenous, intramuscular, or subcutaneous route (see claims 1-5, 9, 19-23, 29, 32-33 and 36-37). ***Please note*** the claimed term "postpartum depression (PPD)" refers to a major depressive disorder with peripartum onset according to the definition set forth in the reference application; therefore, the patient of the

reference application is a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice. Furthermore, the claims of reference application also teaches the dose and the dosage regimen that causes the patient to experience a peak psychedelic experience; the scale used to identify the occurrence of the peak psychedelic experience, including 60% of the maximum possible score in each of the four subscales (mystical, positive mood, transcendence of time and space, and ineffability) of the MEQ30 and the Peak Experience Scale (PES) Total Score of at least 75; the administration route, in this case, via inhalation (see references claims as indicated above).

Regarding claim 22 and 24, even though the claims of reference application does not specifically teach "the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" and "wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof", the same compound (5-MeO-DMT) cannot exert mutually exclusive properties when administered to the same subjects (a patient who is diagnosed with major depressive disorder). Therefore, by practicing the method taught by the reference claims, one would also be achieving the same outcome even though the reference application is not aware of it.

The claims of reference application does not teach the 5-MeO-DMT is administered via inhalation as claimed in claim 15. The claims of reference application does not teach the patient is diagnosed in accordance with DSM-5 as claimed in claim 2. The claims of reference application also does not teach the patient is with a treatment-resistant form of major depressive disorder as claimed in claim 5. The claims of reference application also does not teach patient suffers in addition from suicidal ideation as claimed in claims 6-8.

Russ et al. teaches a method of treating major depression, the method comprising: administering to the subject a psychedelic agent, wherein the psychedelic agent is selected from psilocybin or 5-MeO-DMT (see e.g., p. 2, line 1-11; p. 8, line 23-26; p. 9, line 4-12; claims 1, 126-127). Russ et al. further teaches diagnostic guidance for psychological disorders can be found, for example, in the DSM-V by citing the fifth edition of Diagnostic and Statistical Manual of Mental Disorders published by American Psychiatric Association (see e.g., p. 13, line 30-34). Russ et al. further teaches the depressive disorder may be associated with one or more prodromal symptoms selected from the group consisting of, *inter alia,* suicidality (see e.g., p. 8, line 26-30). Russ et al. further teaches the term "administering" refers to a method of giving a dosage of pharmaceutical composition to a subject, where the method is, e.g., by inhalation (see e.g., p. 18, line 5-7).

Carhart-Harris teaches moderate to severe, unipolar, treatment-resistant major depression received two high dose of oral psilocybin (25 mg, 7 days apart) markedly reduced depressive symptoms after 1 week and 3 months (see e.g., abstract). Carhart-Harris further teaches the inclusion criteria were major depression of a moderate to severe degree (17+ on the 21-item Hamilton Depression Rating scale [HAM-D]), and no improvement despite two adequate courses of antidepressant treatment of different pharmacological classes lasting at least 6 weeks within the current depressive episode (see e.g., p. 620, "methods – study design and participants").

Regarding claim 2, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient diagnosed in accordance with DSM-5. One would have been motivated by the fact that Russ et al. teaches DSM-V is the diagnostic guidance for psychological disorders, including major depression. One would have a reasonable expectation of success because one would have expected that by practicing the method of the reference application in the patient diagnosed by DSM-5 would successfully treat major depressive disorder.

Regarding claim 5, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient with treatment-resistant major depression. One would have been motivated to do so, because Russ et al. teaches a list of psychedelic agents, including psilocybin or 5-MeO-DMT, that are interchangeable for treating major depression; and Carhart-Harris teaches psilocybin reduces depressive symptoms in patients with moderate to severe and treatment-resistant major depression. One would have a reasonable expectation of success, because one would have reasonably expected that 5-MeO-DMT would have exerts same psychedelic effect as psilocybin of Carhart-Harris for treating treatment-resistant major depression.

Regarding claim 6-8, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient that suffers from suicidal ideation, suicidal ideation with intent to act, or at immediate risk for suicide. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent such as 5-MeO-DMT can treat major depression associated with suicidality. ***Please note*** the term "suicidality" is defines as the risk of suicide, usually indicated by suicidal ideation or intent, especially as evident in the presence of a well-elaborated suicidal plan, as evidenced by the Dictionary of Psychology Published by American Psychological Association. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the patients associated with suicidality, including those indicated by suicidal intent, is at imminent risk for suicide, and said patient would successfully be treated by 5-Meo-DMT.

Regarding claim 15, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to administer the 5-MeO-DMT via inhalation. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent, including 5-MeO-DMT, can administered by

inhalation for treating major depression. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that by administering the 5-MeO-DMT via inhalation would have successfully deliver said compound for treating major depression.

This is a provisional nonstatutory double patenting rejection.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-5, 9, 19-23, 26-27, and 30-35 of **copending Application No. 18/373,903** (reference application), in view of Russ et al. (WO2018/195455A1; cited under "foreign patent documents", cited letter a in the IDS filed on June 26, 2024) and Carhart-Harris (The Lancet Psychiatry, 2016. Vol. 3(7): 619-627; cited under "other documents", cited no. 45 in the IDS filed on June 26, 2024), as evidenced by APA Dictionary of Psychology ([online]. Published on April 14, 2018).

Although the claims at issue are not identical, they are not patentably distinct from each other because the conflicting claims of the reference application are directed to a method of treating a patient suffers from postpartum depression (PPD) and moderate or severe depression comprising administering an effective amount of 5-MeO-DMT or a pharmaceutically acceptable salt thereof (see claims 1-5, 9, 19-23, 26-27, and 30-35). ***Please note*** the claimed term "postpartum depression (PPD)" refers to a major depressive disorder with peripartum onset according to the definition set forth in the reference application; therefore, the patient of the reference application is a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice. Furthermore, the claims of reference application also teaches the dose and the dosage regimen that causes the patient to experience a peak psychedelic experience; the scale used to identify the occurrence of the peak psychedelic experience, including 60% of the maximum possible score in each of the four subscales (mystical, positive mood, transcendence of time and space, and ineffability) of the

MEQ30 and the Peak Experience Scale (PES) Total Score of at least 75; the administration route, in this case, via inhalation (see references claims as indicated above).

Regarding claim 22 and 24, even though the claims of reference application does not specifically teach "the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" and "wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof", the same compound (5-MeO-DMT) cannot exert mutually exclusive properties when administered to the same subjects (a patient who is diagnosed with major depressive disorder). Therefore, by practicing the method taught by the reference claims, one would also be achieving the same outcome even though the reference application is not aware of it.

The claims of reference application does not teach the patient is diagnosed in accordance with DSM-5 as claimed in claim 2. The claims of reference application also does not teach the patient is with a treatment-resistant form of major depressive disorder as claimed in claim 5. The claims of reference application also does not teach patient suffers in addition from suicidal ideation as claimed in claims 6-8.

Russ et al. teaches a method of treating major depression, the method comprising: administering to the subject a psychedelic agent, wherein the psychedelic agent is selected from psilocybin or 5-MeO-DMT (see e.g., p. 2, line 1-11; p. 8, line 23-26; p. 9, line 4-12; claims 1, 126-127). Russ et al. further teaches diagnostic guidance for psychological disorders can be found, for example, in the DSM-V by citing the fifth edition of Diagnostic and Statistical Manual of Mental Disorders published by American Psychiatric Association (see e.g., p. 13, line 30-34). Russ et al. further teaches the depressive disorder may be associated with one or more prodromal symptoms selected from the group consisting of, inter alia, suicidality (see e.g., p. 8, line 26-30).

Carhart-Harris teaches moderate to severe, unipolar, treatment-resistant major depression received two high dose of oral psilocybin (25 mg, 7 days apart) markedly reduced depressive symptoms after 1 week and 3 months (see e.g., abstract). Carhart-Harris further teaches the inclusion criteria were major depression of a moderate to severe degree (17+ on the 21-item Hamilton Depression Rating scale [HAM-D]), and no improvement despite two adequate courses of antidepressant treatment of different pharmacological classes lasting at least 6 weeks within the current depressive episode (see e.g., p. 620, "methods – study design and participants").

Regarding claim 2, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient diagnosed in accordance with DSM-5. One would have been motivated by the fact that Russ et al. teaches DSM-V is the diagnostic guidance for psychological disorders, including major depression. One would have a reasonable expectation of success because one would have expected that by practicing the method of the reference application in the patient diagnosed by DSM-5 would successfully treat major depressive disorder.

Regarding claim 5, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient with treatment-resistant major depression. One would have been motivated to do so, because Russ et al. teaches a list of psychedelic agents, including psilocybin or 5-MeO-DMT, that are interchangeable for treating major depression; and Carhart-Harris teaches psilocybin reduces depressive symptoms in patients with moderate to severe and treatment-resistant major depression. One would have a reasonable expectation of success, because one would have reasonably expected that 5-MeO-DMT would have exerts same psychedelic effect as psilocybin of Carhart-Harris for treating treatment-resistant major depression.

Regarding claim 6-8, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient that suffers from suicidal ideation, suicidal ideation with intent to act, or at immediate risk for suicide. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent such as 5-MeO-DMT can treat major depression associated with suicidality. Please note the term "suicidality" is defines as the risk of suicide, usually indicated by suicidal ideation or intent, especially as evident in the presence of a well-elaborated suicidal plan, as evidenced by the Dictionary of Psychology Published by American Psychological Association. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the patients associated with suicidality, including those indicated by suicidal intent, is at imminent risk for suicide, and said patient would successfully be treated by 5-Meo-DMT.

This is a provisional nonstatutory double patenting rejection.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 49, 50-51, 69-70, 72, 79-80 and 81-82 of **copending Application No. 18/373,906 (reference application),** in view of Russ et al. (WO2018/195455A1; cited under "foreign patent documents", cited letter a in the IDS filed on June 26, 2024) and Carhart-Harris (The Lancet Psychiatry, 2016. Vol. 3(7): 619-627; cited under "other documents", cited no. 45 in the IDS filed on June 26, 2024) , as evidenced by APA Dictionary of Psychology ([online]. Published on April 14, 2018).

Although the claims at issue are not identical, they are not patentably distinct from each other because the conflicting claims of the reference application are directed to a method of treating a breastfeeding mother suffers from postpartum depression (PPD), comprising administering to said mother an effective amount of 5-MeO-DMT or a pharmaceutically acceptable salt thereof (see reference

claims 1, 49, 50-51, 69-70, 72, 79-80 and 81-82). ***Please note*** the claimed term "postpartum depression (PPD)" refers to a major depressive disorder with peripartum onset according to the definition set forth in the reference application; therefore, the patient of the reference application is a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice. Furthermore, the claims of reference application also teaches the dose and the dosage regimen that causes the patient to experience a peak psychedelic experience; the scale used to identify the occurrence of the peak psychedelic experience, including 60% of the maximum possible score in each of the four subscales (mystical, positive mood, transcendence of time and space, and ineffability) of the MEQ30 and the Peak Experience Scale (PES) Total Score of at least 75; the administration route, in this case, via inhalation (see references claims as indicated above).

Regarding claim 22 and 24, even though the claims of reference application does not specifically teach "the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" and "wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof", the same compound (5-MeO-DMT) cannot exert mutually exclusive properties when administered to the same subjects (a patient who is diagnosed with major depressive disorder). Therefore, by practicing the method taught by the reference claims, one would also be achieving the same outcome even though the reference application is not aware of it.

The claims of reference application does not teach the patient is diagnosed in accordance with DSM-5 as claimed in claim 2. The claims of reference application also does not teach the patient is suffer from the disorder as claimed in claims 3-5. The claims of reference application also does not teach patient suffers in addition from suicidal ideation as claimed in claims 6-8.

Russ et al. teaches a method of treating major depression, the method comprising: administering to the subject a psychedelic agent, wherein the psychedelic agent is selected from psilocybin or 5-MeO-DMT (see e.g., p. 2, line 1-11; p. 8, line 23-26; p. 9, line 4-12; claims 1, 126-127). Russ et al. further teaches diagnostic guidance for psychological disorders can be found, for example, in the DSM-V by citing the fifth edition of Diagnostic and Statistical Manual of Mental Disorders published by American Psychiatric Association (see e.g., p. 13, line 30-34). Russ et al. further teaches the depressive disorder may be associated with one or more prodromal symptoms selected from the group consisting of*, inter alia*, suicidality (see e.g., p. 8, line 26-30).

Carhart-Harris teaches moderate to severe, unipolar, treatment-resistant major depression received two high dose of oral psilocybin (25 mg, 7 days apart) markedly reduced depressive symptoms after 1 week and 3 months (see e.g., abstract). Carhart-Harris further teaches the inclusion criteria were major depression of a moderate to severe degree (17+ on the 21-item Hamilton Depression Rating scale [HAM-D]), and no improvement despite two adequate courses of antidepressant treatment of different pharmacological classes lasting at least 6 weeks within the current depressive episode (see e.g., p. 620, "methods – study design and participants").

Regarding claim 2, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient diagnosed in accordance with DSM-5. One would have been motivated by the fact that Russ et al. teaches DSM-V is the diagnostic guidance for psychological disorders, including major depression. One would have a reasonable expectation of success because one would have expected that by practicing the method of the reference application in the patient diagnosed by DSM-5 would successfully treat major depressive disorder.

Regarding claim 3-5, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference

application to incorporate the patient with moderate or severe major depressive disorder, or treatment-resistant major depression. One would have been motivated to do so, because Russ et al. teaches a list of psychedelic agents, including psilocybin or 5-MeO-DMT, that are interchangeable for treating major depression; and Carhart-Harris teaches psilocybin reduces depressive symptoms in patients with moderate to severe and treatment-resistant major depression. One would have a reasonable expectation of success, because one would have reasonably expected that 5-MeO-DMT would have exerts same psychedelic effect as psilocybin of Carhart-Harris would successfully treat major depressive disorder by reducing depressive symptoms.

Regarding claim 6-8, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient that suffers from suicidal ideation, suicidal ideation with intent to act, or at immediate risk for suicide. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent such as 5-MeO-DMT can treat major depression associated with suicidality. ***Please note*** the term "suicidality" is defines as the risk of suicide, usually indicated by suicidal ideation or intent, especially as evident in the presence of a well-elaborated suicidal plan, as evidenced by the Dictionary of Psychology Published by American Psychological Association. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the patients associated with suicidality, including those indicated by suicidal intent, is at imminent risk for suicide, and said patient would successfully be treated by 5-Meo-DMT.

This is a provisional nonstatutory double patenting rejection.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 49, 50-51, 69-72, 78, 82 and 85-86 of **copending Application No. 18/373,914** (reference application), in view of Russ et al. (WO2018/195455A1; cited

under "foreign patent documents", cited letter a in the IDS filed on June 26, 2024) and Carhart-Harris (The Lancet Psychiatry, 2016. Vol. 3(7): 619-627; cited under "other documents", cited no. 45 in the IDS filed on June 26, 2024), as evidenced by APA Dictionary of Psychology ([online]. Published on April 14, 2018).

Although the claims at issue are not identical, they are not patentably distinct from each other because the conflicting claims of the reference application are directed to a method of treating a breastfeeding mother suffers from postpartum depression (PPD), comprising administering to said mother an effective amount of 5-MeO-DMT or a pharmaceutically acceptable salt thereof (see reference claims 1, 49, 50-51, 69-72, 78, 82 and 85-86). ***Please note*** the claimed term "postpartum depression (PPD)" refers to a major depressive disorder with peripartum onset according to the definition set forth in the reference application; therefore, the patient of the reference application is a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice. Furthermore, the claims of reference application also teaches the dose and the dosage regimen that causes the patient to experience a peak psychedelic experience; the scale used to identify the occurrence of the peak psychedelic experience, including 60% of the maximum possible score in each of the four subscales (mystical, positive mood, transcendence of time and space, and ineffability) of the MEQ30 and the Peak Experience Scale (PES) Total Score of at least 75; and the administration route, in this case, via inhalation (see references claims as indicated above).

Regarding claim 22 and 24, even though the claims of reference application does not specifically teach "the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" and "wherein the patient is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a

pharmaceutically acceptable salt thereof", the same compound (5-MeO-DMT) cannot exert mutually exclusive properties when administered to the same subjects (a patient who is diagnosed with major depressive disorder). Therefore, by practicing the method taught by the reference claims, one would also be achieving the same outcome even though the reference application is not aware of it.

The claims of reference application does not teach the 5-MeO-DMT is administered via inhalation as claimed in claim 15. The claims of reference application does not teach the patient is diagnosed in accordance with DSM-5 as claimed in claim 2. The claims of reference application also does not teach the patient is suffer from the disorder as claimed in claims 3-5. The claims of reference application also does not teach patient suffers in addition from suicidal ideation as claimed in claims 6-8.

Russ et al. teaches a method of treating major depression, the method comprising: administering to the subject a psychedelic agent, wherein the psychedelic agent is selected from psilocybin or 5-MeO-DMT (see e.g., p. 2, line 1-11; p. 8, line 23-26; p. 9, line 4-12; claims 1, 126-127). Russ et al. further teaches diagnostic guidance for psychological disorders can be found, for example, in the DSM-V by citing the fifth edition of Diagnostic and Statistical Manual of Mental Disorders published by American Psychiatric Association (see e.g., p. 13, line 30-34). Russ et al. further teaches the depressive disorder may be associated with one or more prodromal symptoms selected from the group consisting of, inter alia, suicidality (see e.g., p. 8, line 26-30). Russ et al. further teaches the term "administering" refers to a method of giving a dosage of pharmaceutical composition to a subject, where the method is, e.g., by inhalation (see e.g., p. 18, line 5-7).

Carhart-Harris teaches moderate to severe, unipolar, treatment-resistant major depression received two high dose of oral psilocybin (25 mg, 7 days apart) markedly reduced depressive symptoms after 1 week and 3 months (see e.g., abstract). Carhart-Harris further teaches the inclusion criteria were major depression of a moderate to severe degree (17+ on the 21-item Hamilton Depression Rating scale [HAM-D]), and no improvement despite two adequate courses of antidepressant treatment of different

pharmacological classes lasting at least 6 weeks within the current depressive episode (see e.g., p. 620, "methods – study design and participants").

Regarding claim 2, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient diagnosed in accordance with DSM-5. One would have been motivated by the fact that Russ et al. teaches DSM-V is the diagnostic guidance for psychological disorders, including major depression. One would have a reasonable expectation of success because one would have expected that by practicing the method of the reference application in the patient diagnosed by DSM-5 would successfully treat major depressive disorder.

Regarding claim 3-5, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient with moderate or severe major depressive disorder, or treatment-resistant major depression. One would have been motivated to do so, because Russ et al. teaches a list of psychedelic agents, including psilocybin or 5-MeO-DMT, that are interchangeable for treating major depression; and Carhart-Harris teaches psilocybin reduces depressive symptoms in patients with moderate to severe and treatment-resistant major depression. One would have a reasonable expectation of success, because one would have reasonably expected that 5-MeO-DMT would have exerts same psychedelic effect as psilocybin of Carhart-Harris would successfully treat major depressive disorder by reducing depressive symptoms.

Regarding claim 6-8, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient that suffers from suicidal ideation, suicidal ideation with intent to act, or at immediate risk for suicide. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent such as 5-MeO-DMT can treat major depression associated with

suicidality. Please note the term "suicidality" is defines as the risk of suicide, usually indicated by suicidal ideation or intent, especially as evident in the presence of a well-elaborated suicidal plan, as evidenced by the Dictionary of Psychology Published by American Psychological Association. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the patients associated with suicidality, including those indicated by suicidal intent, is at imminent risk for suicide, and said patient would successfully be treated by 5-Meo-DMT.

Regarding claim 15, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to administer the 5-MeO-DMT via inhalation. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent, including 5-MeO-DMT, can administered by inhalation for treating major depression. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that by administering the 5-MeO-DMT via inhalation would have successfully deliver said compound for treating major depression.

This is a provisional nonstatutory double patenting rejection.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 49, 50-51, 69-70, 72, 79-80 and 81-82 of **copending Application No. 18/604,747** (reference application).

Even though the conflicting claims of the reference application recites a salt of 5-MeO-DMT and a pharmaceutical composition comprising said salt (see claims 1-24), the specification of the reference applications disclose the utility of the recited compounds as covered by the instant methods of using the compounds, see *Sun Pharmaceutical Industries, Ltd., v. Eli Lilly and Co.* where the district court ruled that the claims of the '826 patent were invalid in light of the '614 patent which disclosed gemcitabine's use in cancer treatment, but did not claim it. In making this ruling, the district court relied on the Federal

Circuit's earlier rulings on double patenting of compound claims, mainly *Geneva Pharmaceuticals, Inc, v. GlaxoSmithKline PLC, 349 F. 3d 1373 (Fed. Cir. 2003),* and *Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc., 518 F.3d 1353 (Fed. Cir. 2008)*. In both of these cases, the Federal Circuit found claims of a later patent invalid for obviousness-type double patenting where an earlier patent claimed a compound, disclosing its utility in the specification, and a later patent claimed a method of using the compound for a use described in the specification of the earlier patent. The cases also established that in determining the scope of compound claims for a double patenting rejection one must look to the specification to interpret the utility of the compound.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-19 of **copending Application No. 17/801,389** (reference application).

Even though the conflicting claims of the reference application recites an aerosol comprising aerosol particles of 5-MeO-DMT or a pharmaceutically acceptable salt thereof useful in therapy (see claims 1-19), the specification of the reference applications disclose the utility of the recited compounds as covered by the instant methods of using the compounds, see Sun Pharmaceutical Industries, Ltd., v. Eli Lilly and Co. where the district court ruled that the claims of the '826 patent were invalid in light of the '614 patent which disclosed gemcitabine's use in cancer treatment, but did not claim it. In making this ruling, the district court relied on the Federal Circuit's earlier rulings on double patenting of compound claims, mainly Geneva Pharmaceuticals, Inc, v. GlaxoSmithKline PLC, 349 F. 3d 1373 (Fed. Cir. 2003), and Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc., 518 F.3d 1353 (Fed. Cir. 2008). In both of these cases, the Federal Circuit found claims of a later patent invalid for obviousness-type double patenting

where an earlier patent claimed a compound, disclosing its utility in the specification, and a later patent claimed a method of using the compound for a use described in the specification of the earlier patent. The cases also established that in determining the scope of compound claims for a double patenting rejection one must look to the specification to interpret the utility of the compound.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 13, 106-108, and 110-118 of **copending Application No. 18/850,376**; claims 1, 9-10, 50, 56-58, 60-61, 63-68 of **copending Application No. 18/850,362**; claims 1, 3, 12-14, 16, and 19-26 of **copending Application No. 18/850,394**; claims 1, 8-11, 96, 99-103, 105, and 108-113 of **copending Application No. 18/850,348**; claims 1, 9-16, 100-102, 104-105, and 107-112 of **copending Application No. 18/851,346**; claims 1, 8-11, 100-106, and 111-112 of **copending Application No. 18/851,294**; claims 1, 10-14, 84-87, 89, and 94-96 of **copending Application No. 18/851,301**; claims 1, 9-12, 56-59, 61, 62, and 66-67 of **copending Application No. 18/851,311**; claims 1, 10-13, 77-80, 82, 87-89 of **copending Application No. 18/851,316**; claims 1-6, 9-17, 19-21, 31, 33 of **copending Application No. 18/851,322**; claims 1, 10-13, 77-79, 81-82, and 84-89 of **copending Application No. 18/850,383**; claims 1, 10-14, 84-86, 88-89, and 91-96 of **copending Application No. 18/850,370**; claims 1, 13-16, 106-109, 111, and 116-117 of **copending Application No. 18/85,1362**; claims 1-6, 9-11, 13-14, 16-21, 32 and 34 of **copending Application No. 18/851,356**; and claims 1, 13-16, 100-103, 105, and 110-111 **of copending Application No. 18/851,349.**

Please note the claim language of "5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) or a pharmaceutically acceptable salt thereof for use" in the claims of each reference application is

interpreted by the Examiner as being drawn to a compound that is 5-MeO-DMT or a pharmaceutically acceptable salt thereof with an intended use.

The claims of each reference application teaches 5-MeO-DMT or a pharmaceutically acceptable salt thereof is useful for patient suffering from major depressive disorder (MDD) or treatment resistant form of MDD. Furthermore, the claims of each reference applications also teaches the dose and the dosage regimen that causes a peak psychedelic experience; the instruments used to identify the peak psychedelic experience; and the route of administration, in this case, via inhalation (see reference claims for each reference application as indicated above).

Moreover, the conflicting claims of each reference applications are drawn to a compound ("5-MeO-DMT or a pharmaceutically acceptable salt thereof"), the claims and the specification of these reference applications also disclose the utility of the recited compounds as covered by the instant methods of using the compounds, see *Sun Pharmaceutical Industries, Ltd., v. Eli Lilly and Co.* where the district court ruled that the claims of the '826 patent were invalid in light of the '614 patent which disclosed gemcitabine's use in cancer treatment, but did not claim it. In making this ruling, the district court relied on the Federal Circuit's earlier rulings on double patenting of compound claims, mainly *Geneva Pharmaceuticals, Inc, v. GlaxoSmithKline PLC, 349 F. 3d 1373 (Fed. Cir. 2003),* and *Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc., 518 F.3d 1353 (Fed. Cir. 2008)*. In both of these cases, the Federal Circuit found claims of a later patent invalid for obviousness-type double patenting where an earlier patent claimed a compound, disclosing its utility in the specification, and a later patent claimed a method of using the compound for a use described in the specification of the earlier patent. The cases also established that in determining the scope of compound claims for a double patenting rejection one must look to the specification to interpret the utility of the compound.

Please note "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition

patentably new to the discoverer." *Atlas Powder Co. v. IRECO Inc.,* 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best,* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Claims 1-15, 22, and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 3, 12-15, 17, 22-23, 25 of **copending Application No. 18/851,329** (reference application), in view of Russ et al. (WO2018/195455A1; cited under "foreign patent documents", cited letter a in the IDS filed on June 26, 2024) and Carhart-Harris (The Lancet Psychiatry, 2016. Vol. 3(7): 619-627; cited under "other documents", cited no. 45 in the IDS filed on June 26, 2024), as evidenced by APA Dictionary of Psychology ([online]. Published on April 14, 2018).

Although the claims at issue are not identical, they are not patentably distinct from each other because the conflicting claims of the reference application are directed to a method of treating a mental or nervous system disorder in a mother having a child of age 18 months or below, comprising administering an effective amount of 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) or a pharmaceutically acceptable salt thereof; wherein the disorder is major depressive disorder; wherein the mother suffers from a treatment resistant form of the disorder. Furthermore, the claims of reference application also teaches the dose and the dosage regimen that causes the patient to experience a peak psychedelic experience; the scale used to identify the occurrence of the peak psychedelic experience, including 60% of the maximum possible score in each of the four subscales (mystical, positive mood, transcendence of time and space, and ineffability) of the MEQ30 and the Peak Experience Scale (PES) Total Score of at least 75 (see reference claims 1, 3, 12-15, 17, 22-23, 25).

The claims of reference application does not teach the 5-MeO-DMT is administered via inhalation as claimed in claim 15. The claims of reference application does not teach the patient is diagnosed in accordance with DSM-5 as claimed in claim 2. The claims of reference application also does not teach patient suffers in addition from suicidal ideation as claimed in claims 6-8.

Russ et al. teaches a method of treating major depression, the method comprising: administering to the subject a psychedelic agent, wherein the psychedelic agent is selected from psilocybin or 5-MeO-DMT (see e.g., p. 2, line 1-11; p. 8, line 23-26; p. 9, line 4-12; claims 1, 126-127). Russ et al. further teaches diagnostic guidance for psychological disorders can be found, for example, in the DSM-V by citing the fifth edition of Diagnostic and Statistical Manual of Mental Disorders published by American Psychiatric Association (see e.g., p. 13, line 30-34). Russ et al. further teaches the depressive disorder may be associated with one or more prodromal symptoms selected from the group consisting of, inter alia, suicidality (see e.g., p. 8, line 26-30). Russ et al. further teaches the term "administering" refers to a method of giving a dosage of pharmaceutical composition to a subject, where the method is, e.g., by inhalation (see e.g., p. 18, line 5-7).

Carhart-Harris teaches moderate to severe, unipolar, treatment-resistant major depression received two high dose of oral psilocybin (25 mg, 7 days apart) markedly reduced depressive symptoms after 1 week and 3 months (see e.g., abstract). Carhart-Harris further teaches the inclusion criteria were major depression of a moderate to severe degree (17+ on the 21-item Hamilton Depression Rating scale [HAM-D]), and no improvement despite two adequate courses of antidepressant treatment of different pharmacological classes lasting at least 6 weeks within the current depressive episode (see e.g., p. 620, "methods – study design and participants").

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to selectively choose to incorporate the patient diagnosed with major depressive disorder in accordance

with DSM-5. One would have been motivated by the fact that Russ et al. teaches DSM-V is the diagnostic guidance for psychological disorders, including major depression, that can be treated by administering a list of psychedelic agents, including psilocybin and 5-MeO-DMT, and the fact Carhart-Harris teaches psilocybin significantly reduce depressive symptoms in patient with moderate to severe and treatment-resistant major depression. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have expected that 5-MeO-DMT would have exerts same psychedelic effect as psilocybin of Carhart-Harris for treating patients diagnosed with moderate or severe major depressive disorder in accordance to DSM-V, including the treatment-resistant form of major depressive disorder.

Regarding claim 6-8, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to incorporate the patient that suffers from suicidal ideation, suicidal ideation with intent to act, or at immediate risk for suicide. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent such as 5-MeO-DMT can treat major depression associated with suicidality. Please note the term "suicidality" is defines as the risk of suicide, usually indicated by suicidal ideation or intent, especially as evident in the presence of a well-elaborated suicidal plan, as evidenced by the Dictionary of Psychology Published by American Psychological Association. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that the patients associated with suicidality, including those indicated by suicidal intent, is at imminent risk for suicide, and said patient would successfully be treated by 5-Meo-DMT.

Regarding claim 22 and 24, even though the claims of reference application does not specifically teach "the clinical response, as assessed by at least 50% improvement of the MADRS or HAM-D score, compared to the respective score prior to treatment, persists until at least 6 days after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof" and "wherein the patient

is in remission of depressive symptoms, as assessed by a MADRS score equal to or less than 10, or a HAM-D score equal to or less than 7, on day 7 after the last administration of 5-MeO-DMT or a pharmaceutically acceptable salt thereof", the same compound (5-MeO-DMT) cannot exert mutually exclusive properties when administered to the same subjects (a patient with major depressive disorder). Therefore, by practicing the method taught by the reference claims, one would also be achieving the same outcome even though the reference application is not aware of it.

Regarding claim 15, it would have been prima facie obvious to one of ordinary skill in the art at the time the application was filed to modify the method as set forth in the claims of the reference application to administer the 5-MeO-DMT via inhalation. One would have been motivated to do so, because Russ et al. teaches the psychedelic agent, including 5-MeO-DMT, can administered by inhalation for treating major depression. One would have a reasonable expectation of success to arrive at the claimed invention, because one would have reasonably expected that by administering the 5-MeO-DMT via inhalation would have successfully deliver said compound for treating major depression.

This is a provisional nonstatutory double patenting rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chihyi Lee whose telephone number is (571)270-0663. The examiner can normally be reached Monday - Friday 8:30 am - 5:00 pm EST.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy L. Clark can be reached on (571) 272-1310. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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