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Acknowledgement of receipt

We hereby acknowledge receipt of the Notice of Opposition:

Submission number	13222100
Application number	EP20710059.5
Patent number	EP3927337
Date of receipt	22 May 2024
Your reference	E18450EP00
Opponent	Porta Sophia
Title	5-METHOXY-N,N-DIMETHYLTRYPTAMINE (5-MEO-DMT) FOR TREATING MAJOR DEPRESSION

Documents submitted	
package-data.xml	ep-opposition-data.xml
ep-oppo.pdf (4 p.)	FACTS_ARGMTS.pdf\Notice_Opposition-E18450EP00.pdf (17 p.)
Published-Evidence-Article-1.pdf (14 p.)	Published-Evidence-Article-2.pdf (20 p.)
Published-Evidence-Article-3.pdf (11 p.)	Published-Evidence-Article-4.pdf (3 p.)
Published-Evidence-Article-5.pdf (6 p.)	Published-Evidence-Article-6.pdf (10 p.)
Published-Evidence-Database-1.pdf (4 p.)	

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/European Patent Office/

Europäisches Patentamt
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Notice of opposition to a European patent

Date of receipt: (for internal use only)

I. Patent opposed

European patent No.	EP3927337
European application No.	EP20710059.5
Date of mention of the grant in the European Patent Bulletin (Art. 97(3), Art. 99(1) EPC)	14 February 2024
Title of the invention	5-METHOXY-N,N-DIMETHYLTRYPTAMINE (5-MEO-DMT) FOR TREATING MAJOR DEPRESSION

II. Proprietor of the patent

First named in the patent specification	GH Research Ireland Limited
Opponent's or representative's reference	E18450EP00

III. Opponent

Organisation name:	Porta Sophia
Department:	
Address:	Psychedelic Prior Art Library / 2800 Woods Hollow Rd 53711 Wisconsin Madison United States of America
Country/territory of principal place of business	United States of America

IV. Authorisation

1. Representative

Representative:	Fleuchaus & Gallo Partnerschaft mbB
Association No.:	1218
Address:	Steinerstr. 15/A 81369 München Germany
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General authorisation number (Art. 133(3) EPC):

is/are enclosed ☐

has/have been registered under No. ☐

V. Opposition is filed against

5.1 The patent as a whole ☒

5.2 Claim(s) No(s).

VI. Grounds for opposition:

6.1 Opposition is based on the following grounds:

(a) The subject matter of the European patent opposed is not patentable (Art. 100(a) EPC) because:

• it is not new (Art. 52(1); Art. 54 EPC) ☒

• it does not involve an inventive step (Art. 52(1); 56 EPC) ☒

• patentability is excluded on other grounds, namely articles ☐

(b) The patent opposed does not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Art. 100(b) EPC; see Art.83 EPC) ☒

(c) The subject-matter of the patent opposed extends beyond the content of the application / of the earlier application as filed (Art. 100(c) EPC; see Art.123(2) EPC) ☐

VII. Facts (Rule 76(2)(c) EPC)

7.1 Presented in support of the opposition are submitted herewith on an attached document ☒

VIII. Other requests:

• Oral proceedings are hereby requested.

IX. Evidence presented

E1	Non-patent literature - article	Davis et al, "The epidemiology of 5-methoxy-N, N-dimethyltryptamine (5-MeO-DMT) use: Benefits, consequences, patterns of use, subjective effects, and reasons for consumption" Journal of Psychopharmacology, 30 April 2018 attached as: Published-Evidence-Article-1.pdf
E2	Non-patent literature - article	Greer Ewing, Christopher, "Ground to Sourceexperiencing the Divine within" The practical tripper, 15 April 2017 attached as: Published-Evidence-Article-2.pdf
E3	Non-patent literature - database	The American Psychiatric Association (APA), "What Is Depression?" Host: American Psychiatric Association website page 17.01.2019 attached as: Published-Evidence-Database-1.pdf
E4	Non-patent literature - article	Jaffe et al, "The humanistic and economic burden of treatment-resistant depression in Europe: a cross-sectional study" BMC Psychiatry, 07 August 2019 attached as: Published-Evidence-Article-3.pdf
E5	Non-patent literature - article	Malhi et al, "Treatment-resistant depression: problematic illness or a problem in our approach?" The British Journal of Psychiatry (2019), January 2019 attached as: Published-Evidence-Article-4.pdf
E6	Non-patent literature - article	Barsuglia et al, "Intensity of Mystical Experiences Occasioned by 5-MeO-DMT and Comparison With a Prior Psilocybin Study" frontiers in Psychology, 06 December 2018 attached as: Published-Evidence-Article-5.pdf
E7	Non-patent literature - article	Quilty et al, "The structure of the Montgomery–Åsberg depression rating scale over the course of treatment for depression" International Journal of Methods in Psychiatric Research, 19 August 2013 attached as: Published-Evidence-Article-6.pdf

X. Payment

Mode of payment	Debit from deposit account

The European Patent Office is hereby authorised, to debit from the deposit account with the EPO any fees and costs indicated on the fees section below.

Currency:	EUR
Deposit account number:	28001053
Account holder:	Fleuchaus & Gallo Partnerschaft mbB

Fees	Factor applied	Fee schedule	Amount to be paid
010 Opposition fee	1	880.00	880.00
Total:		**EUR**	**880.00**

	A **Forms**	Details:	System file name:
A-1	Form for notice of opposition		ep-oppo.pdf

	B **Attached document files**	Original file name:	System file name:
B-1	1. Facts and arguments	Notice_Opposition-E18450EP00.pdf	FACTS_ARGMTS.pdf

	C **Attached evidence files**	Original file name:	System file name:

Signature(s)

Signature(s)

Place:	**Munich**
Date:	**22 May 2024**
Signed by:	**/Dr. Andrea Fleuchaus/**
Association:	**Fleuchaus & Gallo Partnerschaft mbB**
Representative name:	**Dr. Andrea Fleuchaus**
Capacity:	**Representative**
Function of person signing:	**Representative**

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Europäisches Patentamt
80298 München

per eOLF

Munich, May 21, 2024 AF/YL

Opposition against European Patent No. 3 927 337 (EP 20710059.5)
Proprietor: GH Research Ireland Limited
Opponent: Porta Sophia | Psychedelic Prior Art Library
Our ref.: E18450EP00-HN7FQ

In the name and by authorization of **Porta Sophia | Psychedelic Prior Art Library**, 2800 Woods Hollow Rd Madison, Wisconsin 53711, US, (hereinafter the Opponent), we file notice of

O P P O S I T I O N

against European Patent No. 3 927 337 B1 of GH Research Ireland Limited (hereafter Proprietor) according to Article 99 EPC.

Please find enclosed a Notice of Opposition to the above European patent together with a statement of Facts and Arguments and an electronic copy of evidence arguments E1 to E7.

The Opposition fee in the amount of EUR 880,00 is paid by debit order.

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Notice of Opposition to

European Patent No 3 927 337 B1
European Patent application EP 20 710 059.5
Statement of Facts and Arguments

1. Grounds of opposition

1.1. The Opponent request that the European Patent No. 3927337 B1 be revoked on the grounds that subject-matter of claims 1 to 5 is not patentable within the terms of Articles 52 to 57 EPC (Article 100(a) EPC).

1.2. In particular the subject matter of claims 1 to 5 as granted is not new over prior art of E1-E5 and E7 nor does it involve an inventive step in the light of the prior art of E2 and E6.

1.3. Furthermore, the European Patent does not disclose the invention of claims 1 to 5 in a manner sufficiently clear and complete for it to be carried out by a person skilled in the Art (Art. 100(b) EPC).

2. Short summary of the opposed patent and its examination proceeding

It is assumed that the opposed patent intents to relate to 5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT) or pharmaceutically acceptable salt thereof for use in treating major depressive disorder, comprising administrating to a patient in need thereof a therapeutically effective amount of 5-MeO-DMT. However, the granted claim wording is obscure and actually allows for the suspicion that the EPO specific quality standard was not applied. This introduction starts with “It is assumed” that the independent claim is meant to be worded as a second medical use claim, i.e. a proper use-limited product claim; however it is not, as we show and explain below:

2.1. Independent claim 1

5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT) or pharmaceutically acceptable salt thereof for use in treating a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice.

2.2. Dependent claims 2-5

Claims 2-5 are dependent on claim 1 and introduce embodiments relating to the allegedly specific patient subgroups. The dependent claim 2 adds nothing to the subject-matter of claim 1. Claims 3 and 4 tries to select a subgroup of patients with moderate or severe major depressive disorder as indicated by MADRS or HAM-D values. Claim 5 tries to select a subgroup of patients with a treatment-resistant form of major depressive disorder.

3. Case history

EPO	Applicant	Third parties
• 02.07.2021 Entry into Euroepan phase before EPO	• 24.02.2020 PCT priority	• 22.08.2021 third party observations (TIPA)
• 15.07.2021 Notification of entry of change	• 24.06.2020 ISA	• 28.06.2022 TIPA-2
• 26.08.2021 Notification of TIPA to Applicant	• 27.08.2020 International publication	• 03.04.2023 TIPA-3
• 15.10.2021 Communication putsuant R. 161(1) and 162 EPC	• 12.07.2021 Request of change of applicant name	• 20.10.2023 TIPA-4
• 01.12.2021 Communication Art. 67(3) EPC	• 20.09.2021 Request for examination **(examination of claims 1-5)**	• 15.01.2024 TIPA-5
• 12.07.2022 Notification of TIPA-2 to Applicant	• 25.04. 2022 Amendment received before substantive examination	
• 02.08.2022 Communication R. 143(1)(f) EPC	• 27.07.2022 Submission concerning change of name of the applicant	
• 06.04.2023 Notification of TIPA-3 to Applicant		
• 27.07.2023 Start of examiniation		
• 18.10.2023 Intention to grant		
• 20.10.2023 **Communication dated 16.12.2022 (claims lacking clarity and inventive step)**		
• 26.10.2023 Notification of TIPA-4 to Applicant		
• 04.01.2024 Intention to grant		
• 18.01.2024 Decision to grant		
• 19.01.2024 Notification of TIPA-5 to Applicant		
	• 11.12.2023 Request of correction **(no amendment of claims 1 to 5; no reasoning)**	

As shown in the timeline, there was **no appropriate examination** following EPO quality standard or properly following EPO Guidelines for Examination, particularly from the start of examination to the first intention to grant as marked in the case history. Even with the severe problems of lacking clarity and inventive step documented by the Examiner and issued in OA dated Oct. 20, 2023, the application was immediately granted without any reasoning from the applicant, without any clarifying claim amendment or any attempt to overcome the objections raised by the examiner.

4. Case law summary: Second Medical Use

As generally known, claims to a second medical use are drafted as product claims relating to a specific second or further medical use (see T 1599/06). According to Art. 54(5), it can be any specific use in a method related to Art. 53(c), provided that such use is not comprised in the state of the art.

A claim directed to the further therapeutic use of a substance/composition must indicate the illness/disease to be treated, the nature of the therapeutic compound used for that purpose and, if relevant for establishing novelty and inventive step, the subject to be treated.

If the further therapeutic use relates to a different therapy of the same disease using the same substance/composition, the claim must also define all technical features of the therapy giving rise to the desired technical effect (G 2/08).

4.1. Known drug / new disease

To claim a second medical use with the use of a known drug to treat a new disease. An independent claim directed to a further therapeutic use of a substance/composition which is based on the use of said product in the treatment of a different disease must be formulated in a way suggested by EPO Guidelines for Examination (G VI 7.1.2), “Product X for use in the treatment of [disease Y]”.

In other words, the **new** disease to be treated and the plausible therapeutic effect must be mentioned.

4.2. Known drug / known disease / new therapeutic use

Not limited to a new disease, it is also possible to claim a second medical use with the use of a known drug to treat a known disease using a new therapeutic method, e.g., a new dosage regime, a new administration mode or a new patient group.

4.3. Known drug / known disease / new patient group

According to the established case law of the Boards of Appeal, the use of the same compound in the treatment of the same disease for a particular group of subjects, can nevertheless constitute a novel therapeutic application, provided that it is carried out on a new group of subjects which is **distinguished** from the former **by its physiological or pathological status** (see T 19/86, OJ 1989, 25; T 893/90, T 233/96, T 1399/04, T 734/12).

This does not apply, however if the group chosen overlapped with the group previously treated, or the choice of the novel group was arbitrary which meant that no functional relationship existed between the particular physiological or pathological status of this group of subjects and the therapeutic or pharmacological effect achieved.

If the further therapeutic use is based on the use of the same product in a different treatment of the same disease, the independent claim must be formulated in a way suggested by EPO Guidelines for Examination (G VI 7.1.2), “Product X for use in the treatment of [disease Y], characterized in that / wherein [other features]”.

5. Examination proceedings of the opposed patent

5.1 Unallowable claim language for second medical use

The opposed patent allegedly relates to 5-MeO-DMT or a pharmaceutical acceptable salt or thereof for use in treating major depressive disorder. However, from the state of the art, 5-MeO-DMT, a known compound for its anti-anxiety and anti-depressant effects, has been used to treat depression. Thus, the first medical use of known products is not applicable to the opposed patent.

The opposed patent tries to formulate the claims for second medical use, but with unacceptable claim terms and claim format.

In claim 1, the term “for use in treating a patient **who is diagnosed with major depressive**

disorder by a licensed professional in accordance with accepted medical practice" does not have any limiting character. It has been objected for lack of clarity and cannot be used to delimit the claims from the prior art (see Communication from EPO dated 16.12.2023, Paragraph 5, Article 84EPC).

Furthermore, the claims fail to convey the teaching that "Product X for use in the treatment of [disease Y]" as is required by the second medical use claim, shown in the above sections 4.1. and 4.2..

Firstly, the therapeutic effect for using 5-MeO-DMT or a pharmaceutically acceptable salt thereof are not clear. It can be interpreted as healing from trauma, treatment for addiction, treatment for depression and or it can be interpretated as inducing illusions to forget symptoms of a disease.

Secondly, a patient's medical disease to be treated cannot be referred to as only "diagnosed by a practitioner", because this does not limit the claim to treat his disease but only such patient. For example, a patient who is diagnosed with major depressive disorder may actually be suffering from headache and could under the present claim wording end up being treated for his headache with 5-MeO-DMT.

Therefore, the claims are not properly worded for a second medical use that "5-MeO-DMT or a pharmaceutically acceptable salt thereof for use in treating depression". In the contrast, they include each and every treatment of the selected "depressive" patient groups.

This is unacceptable.

5.2. Failed second medical use claims with known drug / new disease

Even if the claims have been interpreted as "5-MeO-DMT or a pharmaceutically acceptable salt thereof for use in treating major depressive disorder", they should not been accepted as second medical use claims, because in the technical field "depression" is often interchangeably used as "major depressive disorder" (explained on Communication from EPO dated 16.12.2024, Paragraph 8.2.2). In other words, there is no distinguishing feature between depression and major depressive disorder.

Accordingly, the opposed patent fails to treat a new disease as second medical use requires (described in Section 5.1.), because 5-MeO-DMT for use in the treatment of depression is disclosed in the prior art.

5.3. Failed second medical use claims with known drug / know disease / new patient group

In order to comply with second medical use with known drug / known disease, the opposed patent tries to identify new groups (or subgroups) of patients, such as patients suffer from moderate, severe, and treatment-resistant major depressive disorder.

As described in Section 5.2., for second medical use with known drug / know disease, the new patient group should be distinguished from the former by its physiological or pathological status.

However, none of the alleged subgroups by the opposed patent fulfill those requirements. Instead, either the definition of subgroups is arbitrary, e.g. "a patient who is diagnosed with major depressive disorder by a licensed professional in accordance with accepted medical practice", or no therapeutic / pharmacological effects have been observed to the alleged subgroups, e.g. no comparison with patient who are not treatment-resistant.

This is unacceptable.

5.4. EPC proceedings

Not only with the shortcomings described above, but the opposed patent also has been objected during examination proceedings by the Examiner with Communication dated 16.12.2022 for the reasons: lack of clarity (Section 5 Article 84 EPC, Page 6), lack of technical effect thus leading to lack of inventive step (Section 8, Article 56 EPC, Page 7 to 12).
It is stated in the communication (Page 12):

> *"The Applicant is invited to file new claims which take account of the above comments […]*
>
> *Failure to overcome the objections above will lead to the appointment of oral proceedings as a next step". (*emphasis added*)*

Despite such statement and without any claim amendment to overcome the objections or any further correspondence to rebut the objections, the opposed patent got **mysteriously granted**, despite the responsible work done by the Examiner who painstakingly provided the rational opinions dated 16.12.2022 together with the 5 observations provided by the conscientious third parties.

For the sake of social stability and societal impact, more cautions should be taken into the

opposed patent, as it relates to the use of 5-MeO-DMT, a well-known strong psychedelic drug. Many European countries list 5-MeO-DMT as a controlled substance.

For example, in Sweden 5-MeO-DMT is listed as "health hazard" under the act Lagen om förbud mot vissa hälsofarliga varor (translated Act on the Prohibition of Certain Goods Dangerous to Health) in October 2004, making it illegal to sell or possess. In Germany 5-MeO-DMT is a controlled substance; It is illegal to manufacture, possess, import, export, buy, sell, procure or dispense it without a license. In Denmark, 5-MeO-DMT is legally restricted to "medical or scientific purposes".

Last but not the least, special attention should also be taken due to its side effects as described in the patent as well as its dangerous drug-drug interactions when co-administrated with other drugs, which is also known to a person skilled in the art.

Consequently, such inconsiderate decision of the EPO to grant this controlled substance for its falsely alleged second medical use would lead to the potential addition and drug abuse, which deteriorates EPO's credibility as well threatens EPO's responsibilities to citizens and society.

This is unacceptable.

5.5. Already for these reasons the patent needs to be revoked and **we herewith request to receive a full refund of the opposition fee.**

6. Prior art evidence relevant for the Opposition

The following documents and disclosures are referred to in the opposition:

Ref.	Document/Disclosure	Publication date	Document cited during examination
E1	Davis et al., Journal of Psychopharmacology, 32 (7). "The epidemiology of 5-Methoxy-N,N-Dimethyltryptamine (5-MeODMT) use: Benefits, consequences, patterns of use, subjective effects, and reasons for consumption"	30 April 2018	D4; D4a (in TIPA-2)
E2	Christopher Greer Ewing,	15 April 2017	

	"The practical tripper: Ground to Source- experiencing the Divine within"		
E3	American Psychiatric Association website page "What Is Depression?"	17 January 2019	
E4	Jaffe et al., BMC Psychiatry, 19(1). "The humanistic and economic burden of treatment-resistant depression in Europe: a cross-sectional study"	7 August 2019	
E5	Malhi et al., British Journal of Psychiatry, 214(1). "Treatment-resistant depression: problematic illness or a problem in our approach?"	January 2019	
E6	Barsuglia et al., Frontiers in Psychology, 9. "Intensity of Mystical Experiences Occasioned by 5-MeO-DMT and Comparison With a Prior Psilocybin Study"	6 December 2018	D2 (in TIPA-2)
E7	Quitty et al., International Journal of Methods in Psychiatric Research, 22(3). "The structure of the Montgomery-Åsberg depression rating scale over the course of treatment for depression."	19 August 2013	

Documents E1-E7 were published before the priority date of the opposed patent and are thus relevant state of the art under Art. 54(2) EPC.

7. Novelty (Art. 54 and 100(a) EPC)

Notwithstanding the objections raised above and particularly not understanding the reason and results of the "allowed" claim language in this case, we herewith base our novelty attack **firstly** on a claim 1 as we would expect one after a proper EP examination namely without the untechnical features and thus similar to "5-MeO-DMT or a pharmaceutically acceptable salt thereof for use in treating 'a subgroup of patients with "major depressive disorder" (see 6.1.).

7.1. Lack of novelty in view of E1

E1 discloses in accordance with all the features of claim 1:

-> 5-MeO-DMT or a pharmaceutically acceptable salt thereof (Page 2-3, Measures, lines 1-3: "various types of 5-MeO-DMT (i.e. chemical/synthetic, toad venom, plant exact, yopo, and others)"; and Table 3, Type of 5-MeO-DMT ever used)

-> for use (Page 3, Measures, left column, lines 9-10: "the most common routes of administration (e.g., smoking/vaporizing, insufflation and injecting)"; and Table 3, typical route of administration)

-> in treating major depressive disorder (Page 6, right column, Line 6: "61% of respondents who had been diagnosed with depression". Page 6, right column, Lines 14-18: "Following 5-MeO-DMT use, the majority reports improvements in symptoms, including improvements in depression, post-traumatic stress disorder, anxiety, substance use problems and obsessive compulsive disorder"; Table 6).

E1 treats patients who are diagnosed with depression (in general). The patient group in E1 overlaps the patient subgroups in the opposed patent.

Thus, the subject-matter of the attacked claim 1 is not novel in the sense of Art. 54(1)(2) EPC, more details as described in section 4.2. above.

Additionally, the dependent claims do not contain any additional technical features which render the present subject-matter novel since their features are either known from the prior art.

Consequently, all the claims of the opposed patent are not allowable for lack of novelty.

7.2. Lack of novelty in view of E2

E2 discloses 5-MeO-DMT or a pharmaceutically acceptable salt thereof for use (Page 10, Lines 8 "after injecting myself with 5-MeO-DMT") in treating major depressive disorder (Page 3, Line 5: "have struggled for many years with suicidal ideation and severe depression"; Page 4, lines 18-19: "now several years after having tried something that the medical establishment that pushed dangerous drugs on me", referring to repetitive and unsuccessful treatments, which can obviously be understood not other than the patient has a treatment-resistant form of major depressive disorder).

The anti-depressant effects by using 5-MeO-DMT are shown in E2: "After one dose, the effects of which lasted for all of 20 minutes, I was more profoundly healed than through years of "treatment"…" (Page 10, Lines 9-13); "the beneficial effects continue to increase, affecting all

areas of my life and allowing me to be of better service to others and to my community" (Page 10, Lines 16-17).

The patient in E2 falls in all the patient subgroups in the opposed patent: suicidal ideation (paragraphs [0006] and [0138]), moderate or severe major depressive disorder (claims 3-4) and treatment resistant (claim 5 and Example 2).

So, even if E2, is less scientific; it includes and discloses the full teaching of the presently attacked claims, thus novelty must not be acknowledged.

All the features of the opposed claims have been disclosed in E2, rendering them to lack novelty based on Art. 54 EPC.

8. Inventive step (Art. 56 and 100(a) EPC)

8.1. Lack of inventive step over E1 with E2

Just in case the Division does acknowledge novelty due to any of the non-technical features, we herewith offer for the determination of inventive step, choosing E1 as the closest prior art.

E1 teaches the treatment of major depressive disorder with 5-MeO-DMT.

Regardless the insufficient disclosure of essential technical features or technical teaching, the dependent claims contain additional features: moderate or severe major depressive disorder and treatment-resistant form of major depressive disorder.

The technical effect of those additional features tries to elucidate the subgroup of patients to whom 5-MeO-DMT is used for the treatment.

If at all, it is this alleged subgroup of patients who might be considered a distinguishing feature between the closest state of the art and the opposed patent.

The objective technical problem can be defined as to extend a known treatment to a further specific subgroups of mental disorders amenable for treatment with the known psychoactive therapy (as similarly mentioned in the opposed patent, [0031] and [0034]).

E2 which refers also to the treatment by using 5-MeO-DMT in a patient who "have struggled for many years with suicidal ideation and severe depression" and "now several years after having

tried something that the medical establishment that pushed dangerous drugs on me" is clearly identifiable as relevant for the skilled practitioner. So, he not only could but would have identified the teaching of E2 as relevant, particularly where it is described to successfully treat one patient who has struggled for many years with suicidal ideation and severe depression and resistant to medical establishment, falling in all the patient subgroups of the opposed patent.

Knowing from E1 the general applicability of using 5-Me-DMT to treat major depressive disorder in general, the skilled practitioner would - knowing E2 - also consider the treatment of a so called "treatment-resistant form of major depressive disorder" as well as "severe depression" not only possible but obvious, particularly as E2 speaks about a successful treatment of that patient thus obviously was treatment-resistant and severe depression.

Therefore, all the claims do not involve an inventive step in view of the combination of E1 and E2.

8.2. Lack of inventive step over E1 with E6

For the sake of discussion, a similar line of argumentation can be established starting from E1 as the closest prior art and the technical effect of additional features as well as the objective technical problem namely to extend the treatment of depression to a new suitable subgroup of patients for the treatment with 5-MeO-DMT as described above.

E6 demonstrates administration of vaporized 5-MeO-DMT reliably occasions complete mystical experiences in 75% of individuals and is similar in intensity to high dose psilocybin administrated in a laboratory setting. It further suggests already in the abstract that the short duration of action may be advantageous for clinical interventions (Abstract, Lines 17-19). This may make 5-MeO-DMT easier to use than psilocybin.

E6 discloses more details by using MEQ30 scores, shown in Table 1 and Figure 1. After applying 5-MeO-DMT, MEQ30 subscale mystical, positive mode, transcendence of time and space, and ineffability is 79.27, 88.67, 85.67 and 88.67, respectively.

In comparison, the maximum possible MEQ 30 score on each of the four subscales in the opposed patent is 75, 30, 30 and 15, which is clearly less than those in E6.

Based on the MEQ30 scores in E6, it is evident that inhaled 5-MeO-DMT renders potent anti-depressant effect and is speculative or incentive for a skilled person to at least try to use 5-MeO-

DMT for treatment of patients who have not only the general depression but those who have treatment-resistant or severe depression, with a reasonable expectation of success.

With the knowledge of E1 and E6, it is obvious and is possible to extrapolate for a person skilled in the art to use 5-MeO-DMT to all forms of depressions and particularly also subgroups of patients suffering from a moderate / severe or treatment-resistant major depressive disorder.

Therefore, also in the light of a combination of E1 and E6 the claims are not inventive.

9. Insufficient disclosure (Art. 83 and 100(b) EPC)

The patent does not disclose the invention in claims 1 to 5 in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, contrary to Article 100(b) EPC.

9.1 Level of disclosure required for medical use - plausibility

Principles established by the case law

According to the established case law of the boards of appeal, attaining the claimed therapeutic effect is regarded as a functional technical feature of claims relating to a further medical use. In order to meet the requirement of sufficiency of disclosure of Art. 83 EPC, the therapeutic efficacy of the composition and dosage regime for the claimed therapeutic indication must therefore be credible (principle reiterated in e.g. T 421/14 (dosage regime involving twice-daily treatment – multiple sclerosis), where the claims related to a further medical use).

The decision in T 1959/15, in which granted claim 1 was a second medical use claim in the format of a purpose-restricted product claim pursuant to Art. 54(5) EPC, also helpfully summarizes the applicable notions and reasoning (point 4.2 of the Reasons): According to Art. 54(5) EPC, patentability is not excluded for substances or compositions comprised in the state of the art for a specific use in a method referred to in Art. 53(c) EPC, provided that such use is not comprised in the state of the art. When a technical effect (which, in the case of a second medical use claim, is the therapeutic effect) is a feature of a claim, whether this effect is achieved by substantially all embodiments covered by the claim is a question of sufficiency of disclosure. Hence, because the subject-matter of second medical use claims is commonly limited to a known therapeutic agent for use in a new therapeutic application, it is usually only necessary that the patent renders it plausible that the known therapeutic agent (i.e. the product) is suitable for the claimed therapeutic application (i.e. the purpose: the technical effect).

Evidence of the therapeutic effect

The question is whether or not the skilled person, knowing the disclosure of the patent and the common general knowledge at the relevant date of the application, would have considered that the compounds referred to in the claim are suitable to achieve the therapeutical effect (see T 609/02, point 9 of the Reasons). Or, in other words, whether it was plausible (or, in yet other words, whether it was credible) that the therapeutic effect could be achieved by the claimed composition (as recapitulated in T 966/18).

Either the application must provide suitable evidence for the claimed therapeutic effect or it must be derivable from the prior art or common general knowledge. The disclosure of experimental results in the application is not always required to establish sufficiency, in particular if the application discloses a plausible technical concept and there are no substantiated doubts that the claimed concept can be put into practice (T 950/13 citing T 578/06).

A claimed therapeutic application may be proven by any kind of evidence as long as it reflects the therapeutic effect on which the therapeutic application relies (T 814/12, referring to T 609/02 in particular).

For the acceptance of sufficient disclosure of a therapeutic application, it is not always necessary for results of clinical trials to be provided at the relevant date, but the patent/patent application **must** provide some information showing that **the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease**.

9.2 Lack of plausible therapeutic effect

No plausible therapeutic effect associated with the alleged patient subgroups

The opposed patent aims to use 5-MeO-DMT to treat major depressive disorder (or depression), and further attempts to use 5-MeO-DMT to treat patients with moderate or severe major depressive disorder and treatment-resistant major depressive disorder.

Neither with the physiological or pathological status of the patient subgroups as described above, nor providing plausible therapeutic data for the selected patient subgroups.

Firstly, the opposed patent fails in providing any therapeutic data to the alleged patient subgroup who suffer from moderate or severe major depressive disorder. Claims 3 and 4 are

targeted to the patients who suffer from moderate or severe major depressive disorder. However, the targeted patient subgroup with moderate or severe major depressive disorder is totally absent in the whole patent.

Additionally, two patients with major depressive disorder are applied in the opposed patent, and they are considered as treatment-resistant based on their inadequate improvement to at least two adequate courses of pharmacological therapy in the episode of depression.

To investigate the anti-depressive effect of 5-MeO-DMT to those two patients, measures of the intensity of psychedelic effects, measures of depressive severity and additional psychological measures were recorded at different time points (paragraph [0184]).

However, all those measurements cannot clearly and unambiguously reflect the claimed therapeutic effect. Incredibly, there is no comparison in this study between patients and blanks who are not treatment-resistant (Example 2). There are no tests on physiological or pathological status of the patients or pharmacological analysis of 5-MeO-DMT.

No effect of 5-MeO-DMT on a metabolic mechanism specially involved in the disease / patient subgroups

The opposed patent applies measures of the intensity of psychedelic effects, measures of depressive severity and additional psychological measures to demonstrate the anti-depressive effect (paragraph [0184]).

However, the entire patent specification is void of any data that demonstrate 5-MeO-DMT has a direct effect on a metabolic mechanism specifically involved in major depressive disorder or the selected patient subgroups, which is required for the acceptance of sufficient disclosure of a therapeutic application regarding the opposed patent.

9.3. Lack of technical features

In claim 1, the expression “by a licensed professional in accordance with accepted medical practice” does not have limiting character since it is non-technical and, in accordance with established EPO practice, should be ignored as a feature of the claim.

In claim 2, the expression “the disorder is diagnosed in accordance with the Diagnostic and Statistical Manual of Mental Disorder – Fifth Edition (DSM-5) published by the American Psychiatric Association” does not contain any technical nature.

E3 shows the definition of depression (major depressive disorder) published by the American Psychiatric Association.

As it is non-technical in nature, the term in claim 2 fails to delimit major depressive disorder compared to depression disclosed in the prior art.

In claims 3 and 4, MADRS scores are tried to indicate severity of major depressive disorder (see [0198]).

E7 demonstrated temporal and gender invariance for the MADRS (Page 183, left column, last paragraph). It has been noted by previous investigators that different populations might exhibit different factor structures of the MADRS. It further described that the comparison of MADRS scores within and between patients requires the demonstration of consistent properties (Abstract, lines 4-5).

Thus, severity of major depressive disorder as indicated by MADRS scores in claims 3 and 4 cannot and does not result in the selection of a specific subgroup of patients.

In claim 5, “treatment-resistant form of major depressive disorder” is described, and the definition of “treatment-resistant” for major depressive disorder is shown in [0069]. According to the opposed patent, “adequateness is assessed and documented by a physician or a psychologist using a defined set of criteria and …”

Firstly, this definition of the opposed patent is empirical, and does not contain technical features.

Moreover, there is no currently agreed definition of what “treatment-resistant” means.

E4, for example, states (Abstract, first line of ‘Background’) that a “patient is considered to suffer from treatment resistant depression when consecutive treatment with two products of different pharmacological classes, used for a sufficient length of time at an adequate dose, fail to induce a clinically meaningful effect (inadequate response)”.

E5 states that treatment-resistant depression “is widely defined as non-response to two ‘adequate’ courses of treatment”, but the definitions of treatment and depression are inconsistent reflecting gaps in our understanding (page 1, Summary, lines 1-3). It further urges that the definition of treatment-resistant disorder needs to be revised with an emphasis on diagnosis rather than treatment (Page 3, Conclusions, lines 1-2).

10. Summary

For each and any of the reasons given above, it is submitted that the Patent should be revoked in its entirety on the grounds of Article 100(a) EPC, that the subject matter of the European Patent is not patentable according to Articles 54 and 56 EPC; on the grounds of Article 100(b) EPC, that the European Patent does not disclose the invention of claim in a manner sufficiently clear and complete for to be carried out by a person skilled in the art; and on the grounds of Article 100(c) EPC, that the subject matter of the European Patent extends beyond the content of the application as filed.

Oral proceedings are hereby requested in the event that the Opposition Division does not revoke the Patent in its entirety.

Dr. Andrea Fleuchaus
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Encl.:
– Documents E1 to E7