IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	MANFREDI, Paolo	Confirmation No.:
Serial No.:	17/435,571	Group No.:
Filing or 371(c) Date:	March 6, 2020	Examiner:

Entitled: COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON PSYCHEDELIC/PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS

THIRD-PARTY PRE-ISSUANCE SUBMISSION

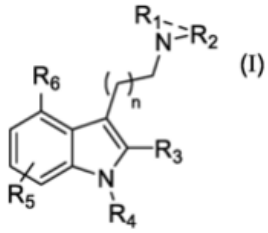
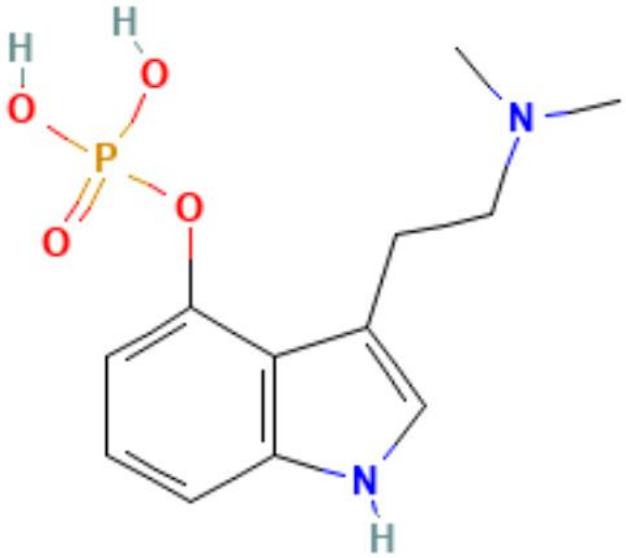
Examiner:

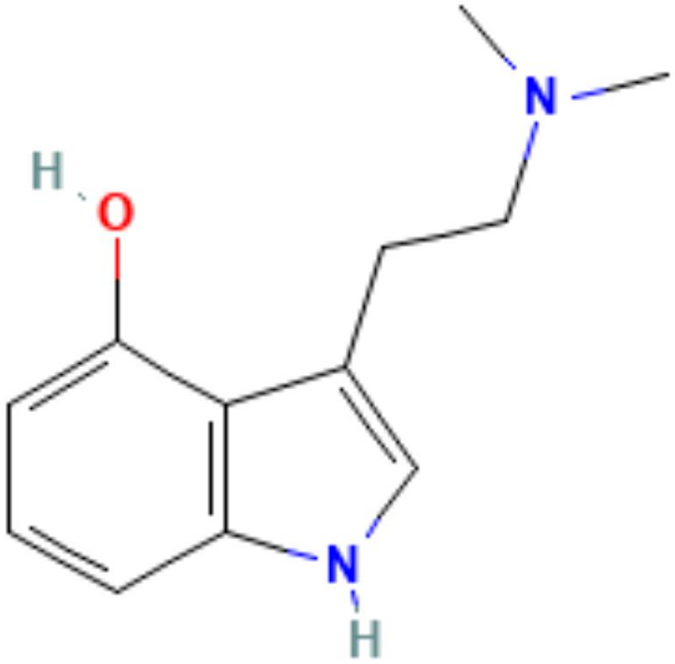
The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application:

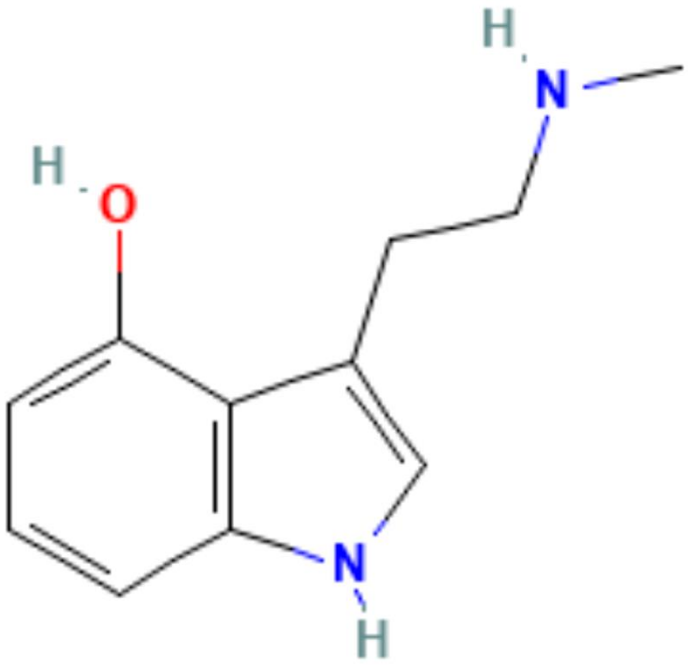
1. PUBCHEM (2005) “Psilocybine” https://pubchem.ncbi.nlm.nih.gov/compound/10624
2. PUBCHEM (2005) “Psilocin” https://pubchem.ncbi.nlm.nih.gov/compound/Psilocin
3. PUBCHEM (2007) “Norpsilocin” https://pubchem.ncbi.nlm.nih.gov/compound/14107683
4. PUBCHEM (2005) “Baeocystin” https://pubchem.ncbi.nlm.nih.gov/compound/Baeocystin
5. PUBCHEM (2005) “Norbaeocystin” https://pubchem.ncbi.nlm.nih.gov/compound/Norbaeocystin
6. PUBCHEM (2005) “N,N-Dimethyltryptamine” https://pubchem.ncbi.nlm.nih.gov/compound/N_N-Dimethyltryptamine
7. PUBCHEM (2005) “Lysergide” https://pubchem.ncbi.nlm.nih.gov/compound/Lysergide
8. PUBCHEM (2005) “Ibogaine” https://pubchem.ncbi.nlm.nih.gov/compound/Ibogaine
9. JOHNSTAD (2018) “Powerful substances in tiny amounts: An interview study of psychedelic microdosing” Nordic Studies on Alcohol and Drugs. 35(1):39-51.
10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012
11. MADSEN (2019) “Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels” Neuropsychopharmacology. 44(7):1336.

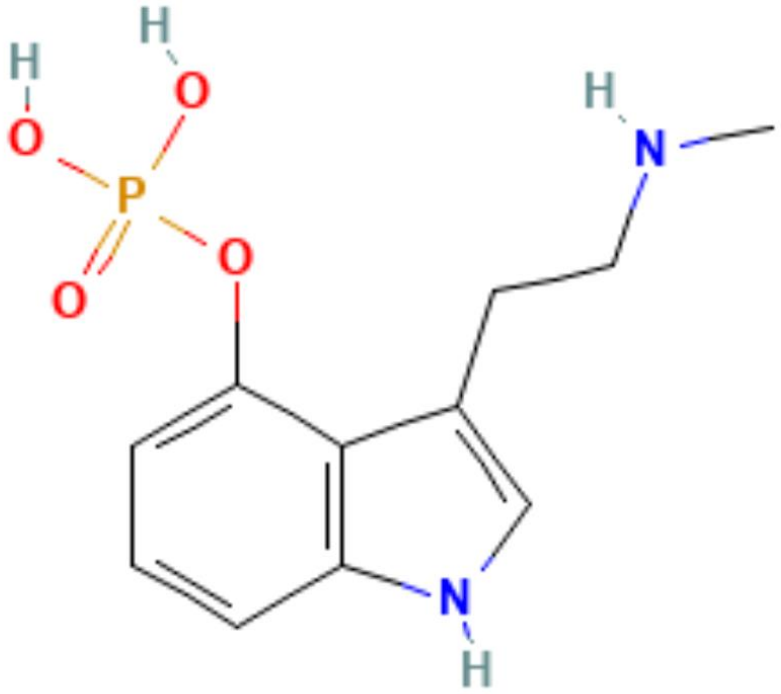
12. GREGORIO (2018) “d-Lysergic acid diethylamide, psilocybin, and other classic hallucinogens: Mechanism of action and potential therapeutic applications in mood disorders” Progress in Brain Research. 242:69-96.
13. FARBER (1998) “Serotonergic Agents That Activate 5HT2A Receptors Prevent NMDA Antagonist Neurotoxicity” Neuropsychopharmacology. 18:57-62.
14. U.S. Pat. App. Pub. No. US/2018/0021326 “Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin” (Published 25 January 2018)
15. Int’l Pat. App. Pub. No. WO/2020/097320 “REHABILITATION OF SUBJECTS WITH PHARMACOLOGICALLY INDUCED NEUROPLASTICITY” (Published 14 May 2020)
16. Int’l Pat. App. Pub. No. WO/2018/195455 “ASSESSING AND TREATING PSYCHEDELIC-RESPONSIVE SUBJECTS” (Published 20 April 2018)
17. U.S. Pat. App. Pub. No. US/2020/0330405 “COMPOSITIONS AND METHODS FOR TREATING OCULAR PATHOLOGIES” (Published 22 October 2020)
18. U.S. Pat. App. Pub. No. US/2012/0108510 “Methods of improving behavioral therapies” (Published May 3, 2012)
19. Int’l Pat. App. Pub. No. WO/2020/157569 “METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS” (Published 29 January 2020)
20. Int’l Pat. App. Pub. No. WO/2019/109124 “COMPOSITIONS AND METHODS FOR MODULATING LIVER ENDOTHELIAL CELL FENESTRATIONS” (Published 13 June 2019)
21. POLITO (2019) “A systematic study of microdosing psychedelics” PLOS One. 14(2):1-26.
22. Int’l Pat. App. Pub. No. WO/2018/148605 “COMPOSITIONS AND METHODS COMPRISING A PSILOCYBIN DERIVATIVE” (Published 16 August 2018)
23. Int’l Pat. App. Pub. No. WO/2006/079999 “INDUCTION OF A NOVEL STATE OF MIND WITH A 5-HT2A AGONIST AND A NMDA ANTAGONIST” (Published 3 August 2006)
24. AUFFRET (2018) “The Many Faces of Apomorphine: Lessons from the Past and Challenges for the Future” Drugs in R&D. 18:91-107.
25. PUBCHEM (2005) “2,5-Dimethoxy-N,N-dimethyl-4-iodoamphetamine" https://pubchem.ncbi.nlm.nih.gov/compound/2_5-Dimethoxy-N_N-dimethyl-4-iodoamphetamine
26. OLGUN (2007) “Deuteronation and Aging” Annals of the New York Academy of Sciences. 1100(1):400-403.

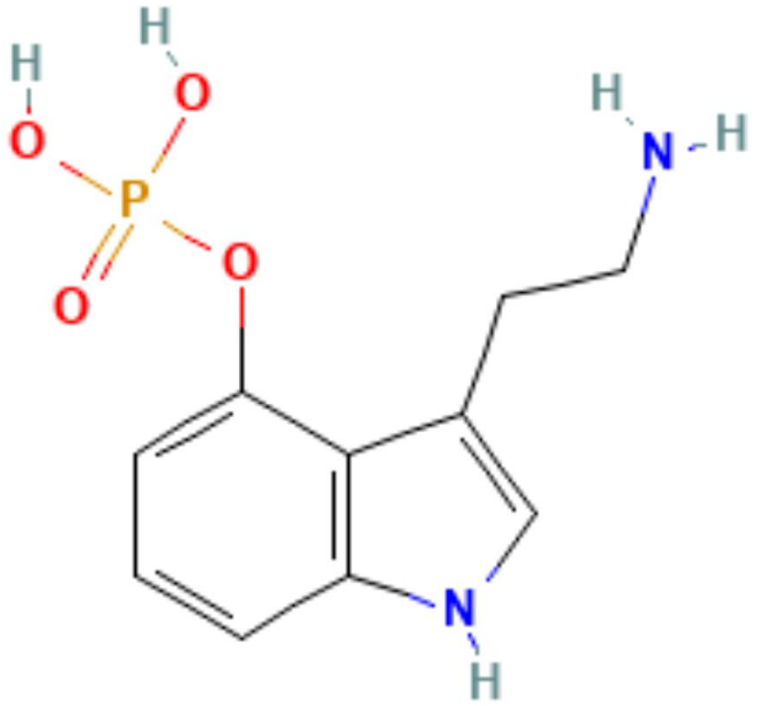
Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

U.S.S.N. 17/435,571 Pending Claims	References
1. A compound comprising a structural analogue to psilocin, norpsilocin, psilocybin, baeocystin, norbaeocystin or N,N-dimethyltryptamine, according to formula I:  (I) wherein R 1 and R 2 are, independently, hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl (independently or ring close with the nitrogen), C 3-C 8 cycloalkenyl (independently or ring close with the nitrogen), aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl,	1. PUBCHEM (2005) "Psilocybine" https://pubchem.ncbi.nlm.nih.gov/compound/10624 From Chemical Structure Description Section:  *Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 1 of said application:* *"A compound comprising a structural analogue to psilocin, norpsilocin,* ***psilocybin****, baeocystin, norbaeocystin or N,N-dimethyltryptamine, according to formula I wherein:* • *R1 and R2 are...C1-C8 alkyl* • *R3 is hydrogen* • *R4 is hydrogen* • *R5 represents...hydrogen.* • *R6 is... —OP(O)(OH) 2"*

thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; R 3 is hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 3 is selected from the group consisting of halogen, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryloxy, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, and nitrate; R 4 is hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, any of which are optionally substituted at one or	2. PUBCHEM (2005) “Psilocin” https://pubchem.ncbi.nlm.nih.gov/compound/Psilocin From Chemical Structure Description Section:  *Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 1 of said application:* *“A compound comprising a structural analogue to **psilocin**, norpsilocin, psilocybin, baeocystin, norbaeocystin or N,N-dimethyltryptamine, according to formula I wherein:* • *R1 and R2 are...C1-C8 alkyl* • *R3 is hydrogen* • *R4 is hydrogen* • *R5 represents...hydrogen* • *R6 is...hydroxy”* 3. PUBCHEM (2007) “Norpsilocin” https://pubchem.ncbi.nlm.nih.gov/compound/14107683 From Chemical Structure Description Section:

more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 4 is selected from the group consisting of alkyl ester, formyl, hydroxy, arylamido, alkylamido, alkylcarbamoyl, arylcarbamoyl, amino, alkylsulfonyl, and alkylamino; R 5 represents 1-3 substituents selected from the group consisting of hydrogen, deuterium, halogen, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate;	 *Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 1 of said application:* *"A compound comprising a structural analogue to psilocin,* ***norpsilocin****, psilocybin, baeocystin, norbaeocystin or N,N-dimethyltryptamine, according to formula I wherein:* • *R1 and R2 are independently hydrogen...C1-C8 alkyl.* • *R3 is hydrogen* • *R4 is hydrogen* • *R5 represents...hydrogen* • *R6 is...hydroxy"* 4. PUBCHEM (2005) "Baeocystin" https://pubchem.ncbi.nlm.nih.gov/compound/Baeocystin From Chemical Structure Description Section:

R 6 is hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl any of which are optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 6 is selected from the group consisting of halogen, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryloxy, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, nitrate, —OP(O)(OH) 2, —OC(O)R 7, —OSO 2OH, —OC(O)NHR 7, —OC(O)NR 7R 8 and —SONH; and n is 1 to 5.	 *Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 1 of said application:* *"A compound comprising a structural analogue to psilocin, norpsilocin, psilocybin, **baeocystin**, norbaeocystin or N,N-dimethyltryptamine, according to formula I wherein:* • *R1 and R2 are independently hydrogen...C1-C8 alkyl.* • *R3 is hydrogen* • *R4 is hydrogen* • *R5 represents...hydrogen* • *R6 is... —OP(O)(OH) 2"* 5. PUBCHEM (2005) "Norbaeocystin" https://pubchem.ncbi.nlm.nih.gov/compound/Norbaeocystin From Chemical Structure Description Section:



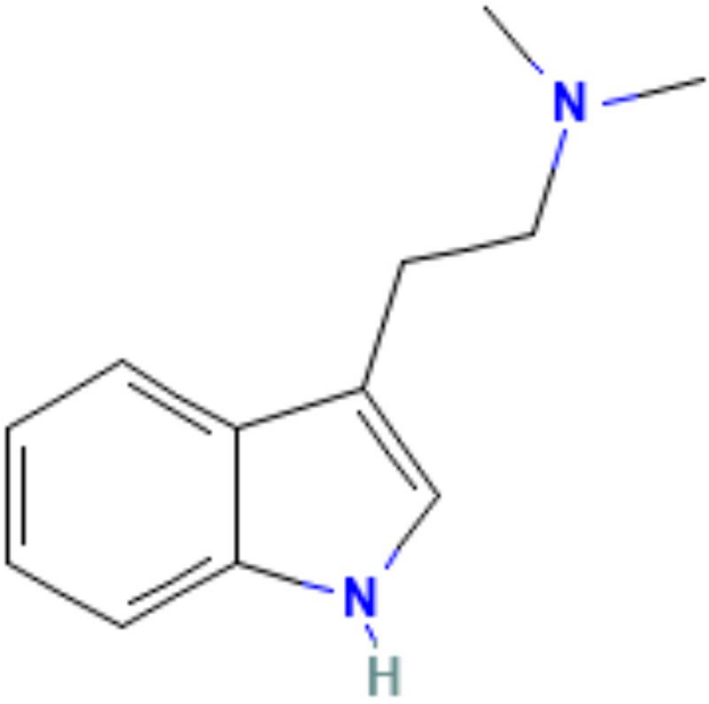
Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 1 of said application:

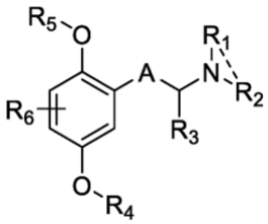
"A compound comprising a structural analogue to psilocin, norpsilocin, psilocybin, baeocystin, ***norbaeocystin*** *or N,N-dimethyltryptamine, according to formula I wherein:*

- *R1 and R2 are independently hydrogen*
- *R3 is hydrogen*
- *R4 is hydrogen*
- *R5 represents...hydrogen*
- *R6 is... —OP(O)(OH) 2"*

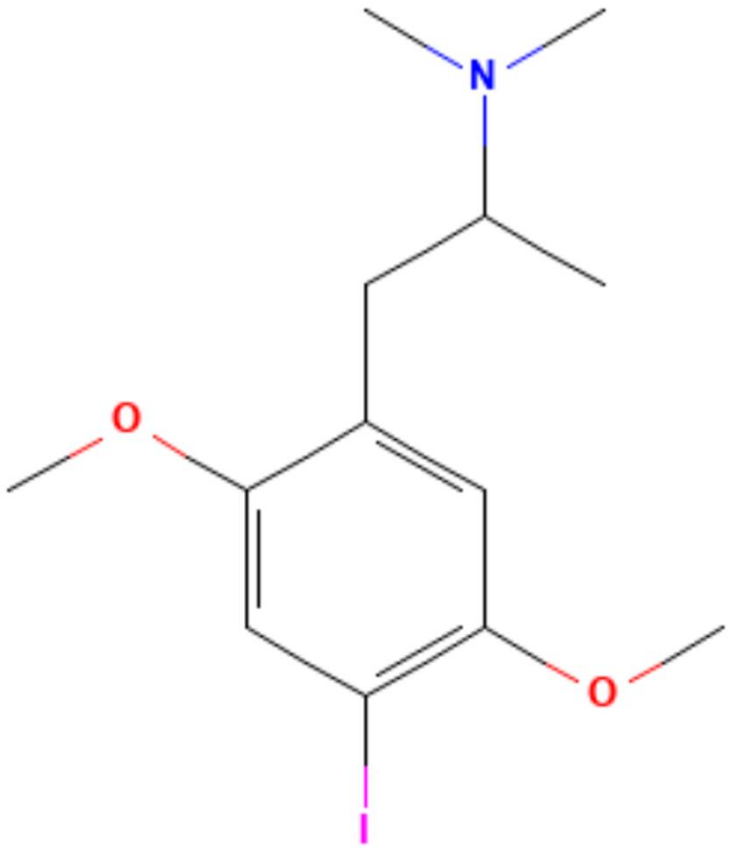
6. PUBCHEM (2005) "N,N-Dimethyltryptamine"
https://pubchem.ncbi.nlm.nih.gov/compound/N_N-Dimethyltryptamine

From Chemical Structure Description Section:

	 *Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 1 of said application:* *"A compound comprising a structural analogue to psilocin, norpsilocin, psilocybin, baeocystin, norbaeocystin or **N,N-dimethyltryptamine**, according to formula I wherein:* • *R1 and R2 are independently hydrogen* • *R3 is hydrogen* • *R4 is hydrogen* • *R5 represents...hydrogen* • *R6 is...hydrogen"*
2. A compound comprising a structural analogue to 2,5-Dimethoxy-4-iodoamphetamine, according to formula II:	25. PUBCHEM (2005) "2,5-Dimethoxy-N,N-dimethyl-4-iodoamphetamine" https://pubchem.ncbi.nlm.nih.gov/compound/2_5-Dimethoxy-N_N-dimethyl-4-iodoamphetamine From Chemical Structure Description Section:



wherein
A is C 1-C 6 alkylene, C 2-C 6 alkenylene, or C 2-C 6 alkynylene;
R 1 and R 2 are, independently, hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl (independently or ring close with the nitrogen), C 3-C 8 cycloalkenyl (independently or ring close with the nitrogen), aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate;
R 3 is hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by



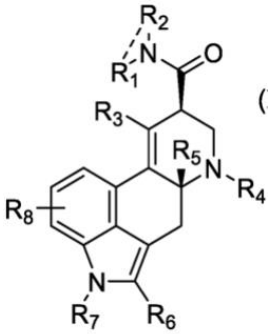
Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 2 of said application:

"A compound comprising a structural analogue to ***2,5-Dimethoxy-4-iodoamphetamine****, according to formula II wherein:*

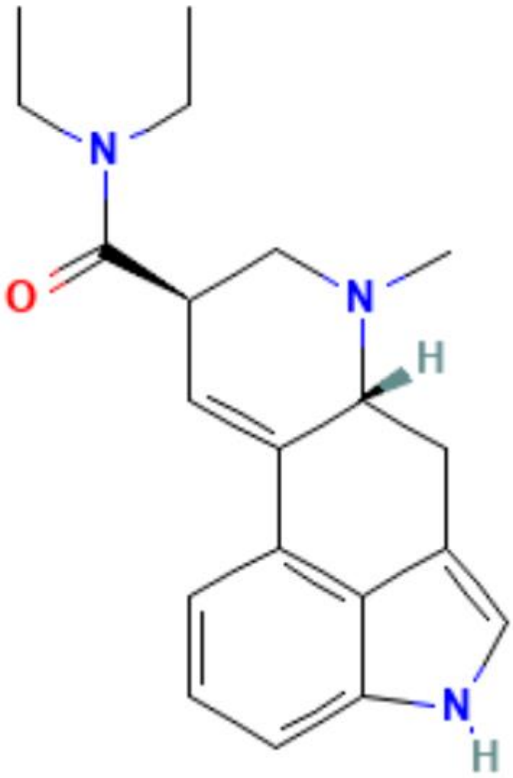
- *A is C1-C6 alkylene...*
- *R1 and R2 are, independently... C1 – C8 alkyl...*
- *R3 is C1 – C8 alkyl...*
- *R4 and R5 are independently C1 – C8 alkyl...halogen...*
- *R6 represents a C1 – C8 alkyl..."*

deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 3 is selected from the group consisting of halogen, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryloxy, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, and nitrate; R 4 and R 5 are, independently, hydrogen, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 4	

and R 5 are, independently, selected from the group consisting of alkyl ester, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, and nitrate; and R 6 represents 1-3 substituents selected from the group consisting of hydrogen, deuterium, halogen, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate.	
3. A compound comprising a structural analogue to Lysergic acid diethylamide, according to formula III:	7. PUBCHEM (2005) “Lysergide” https://pubchem.ncbi.nlm.nih.gov/compound/Lysergide From Chemical Structure Description Section:



wherein
R 1 and R 2 are, independently, hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl (independently or ring close with the nitrogen), C 3-C 8 cycloalkenyl (independently or ring close with the nitrogen), aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate;
R 3 is hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by



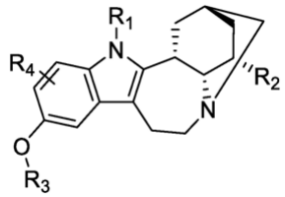
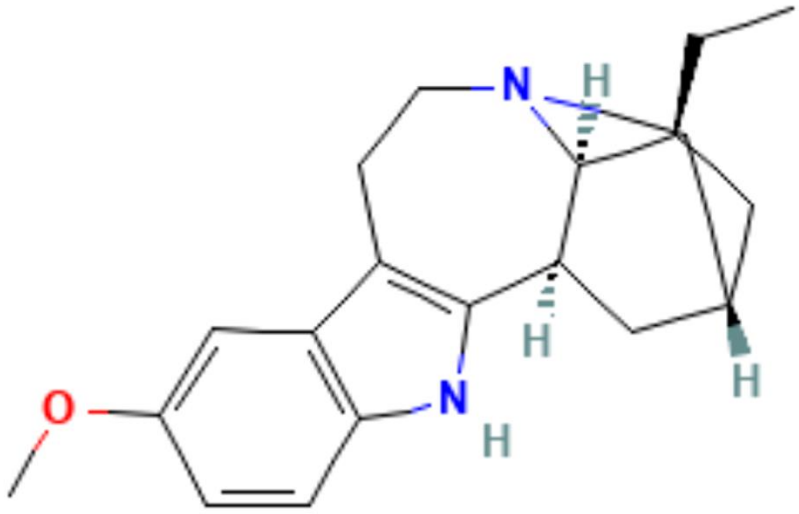
Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 3 of said application:

"A compound comprising a structural analogue to Lysergic acid diethylamide, according to formula III wherein:

- *R1 and R2 are independently... C1-C8 alkyl...*
- *R3 is hydrogen...*
- *R4 and R7 are independently hydrogen... C1-C8 alkyl...*
- *R5 and R6 are independently hydrogen...*
- *R8 represents hydrogen..."*

deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 3 is selected from the group consisting of halogen, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryloxy, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, and nitrate; R 4 and R 7 are, independently, hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl,	

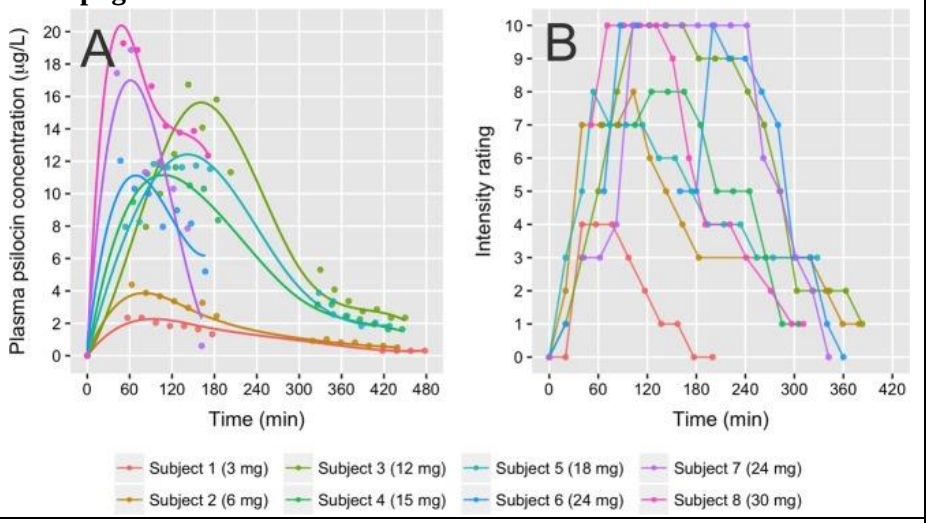
arylcarbamoyl, nitro, cyano, or nitrate; R 5 and R 6 are, independently, hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 5 and R 6 are, independently, selected from the group consisting of halogen, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryloxy, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, and nitrate; and R 8 represents 1-3 substituents selected from the group consisting of hydrogen, deuterium, halogen, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8	

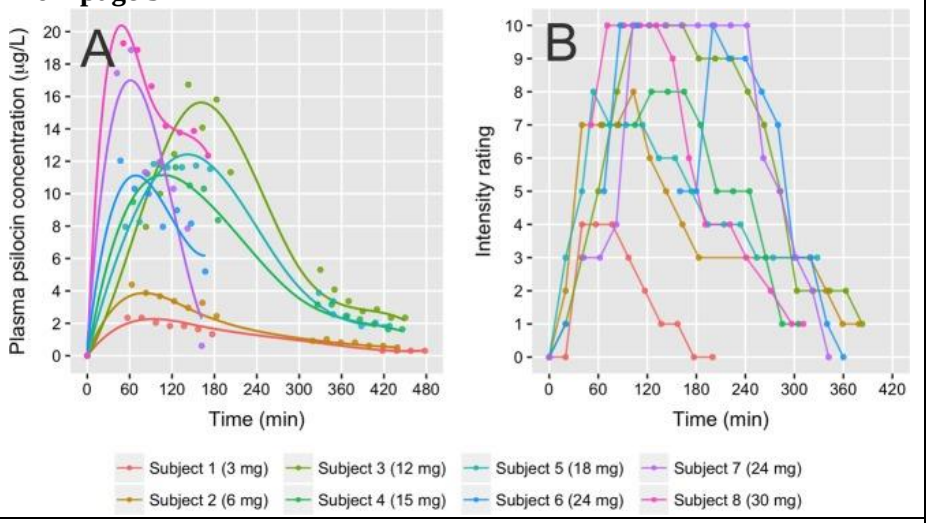
cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate.	
4. A compound comprising a structural analogue to ibogaine, according to formula IV:  wherein R 1 is deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido,	8. PUBCHEM (2005) "Ibogaine" https://pubchem.ncbi.nlm.nih.gov/compound/Ibogaine From Chemical Structure Description Section:  *Relevance of above figure to the application of interest, U.S. Application Number 17/435,571, as quoted from claim 4 of said application:* *"A compound comprising a structural analogue to* ***ibogaine****, according to formula IV wherein:*

thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; R 2 is hydrogen, deuterium, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 2 is selected from the group consisting of halogen, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryloxy, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, and nitrate; R 3 is hydrogen, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or	• *R1 is....deuterium...* • *R2 is...C1-C8 alkyl...* • *R3 is C1-C8 alkyl...* • *R4 represents...hydrogen...”* 26. OLGUN (2007) “Deuteronation and Aging” Annals of the New York Academy of Sciences. 1100(1):400-403. From page 400 “The **natural abundance of deuterium is 1 per ~6600 hydrogen atoms.**”

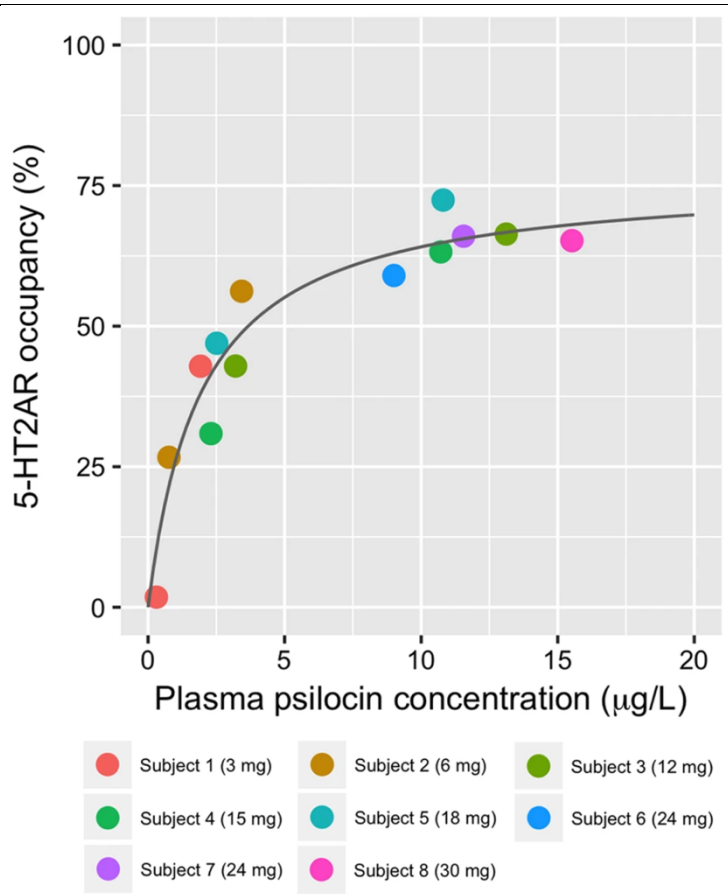
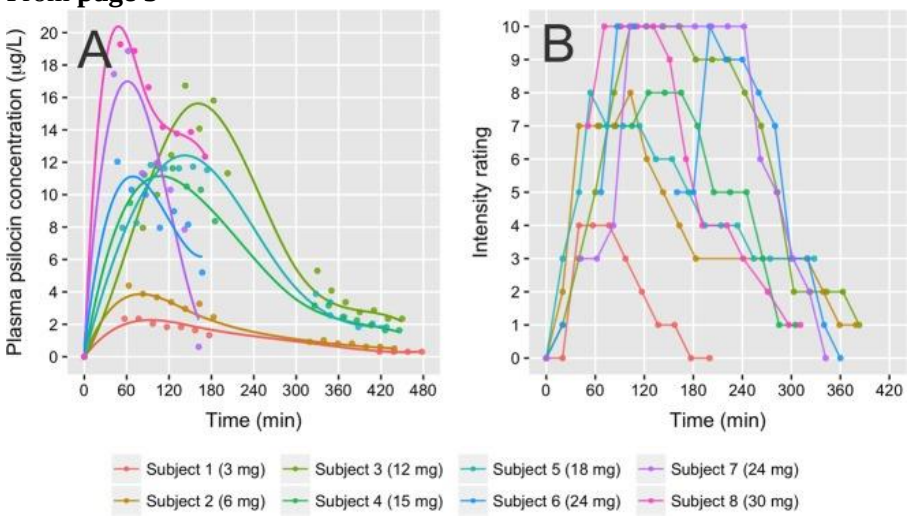
more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate; or R 3 is selected from the group consisting of alkyl ester, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, and nitrate; and R 4 represents 1-3 substituents selected from the group consisting of hydrogen, deuterium, halogen, C 1-C 8 alkyl, C 2-C 8 alkenyl, C 2-C 8 alkynyl, C 3-C 8 cycloalkyl, C 3-C 8 cycloalkenyl, aryl or heterocyclyl, optionally substituted at one or more positions by deuterium, halogen, alkyl, alkyl ester, hydroxy, alkoxy, carboxy, formyl, aryl, aryloxy, heterocyclyl, amino, alkylamino, arylamido, alkylamido, thiol, thioalkyl, thioaryl, alkylsulfonyl, alkylcarbamoyl, arylcarbamoyl, nitro, cyano, or nitrate.	

5. A method for preventing or treating diseases and conditions or improving functions in patients or subjects, the method comprising: administration of a compound of any of claims 1- 4 at doses, dosages, posology, or formulations devoid of clinically meaningful psychedelic or psychotomimetic actions or effects, and having clinical effects comparable to those exerted by human plasma psilocin Cmax of 4 ng/ml or less, or human 5-HT2A CNS receptor occupancy of 50% or less, or PD effects comparable to those exerted by human plasma psilocin Tmax in excess of 60 minutes.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 21. POLITO (2019) "A systematic study of microdosing psychedelics" PLOS One. 14(2):1-26. From page 1 "The phenomenon of 'microdosing', that is, regular ingestion of very small quantities of psychedelic substances, has seen a rapid explosion of popularity in recent years. Individuals who microdose report minimal acute effects from these substances yet claim **a range of long-term general health and wellbeing benefits**." From **page 2** "So, for example, a microdose of lysergic acid diethylamide (LSD) might be 6–25 micrograms, or **a microdose of psilocybin might be .1 to .5 grams of dried mushrooms**." From **page 19** "Longer term, **we found evidence that microdosing led to improved mental health**, **altered attentional capacities (reduced mind wandering and increased absorption),** and increased neuroticism."

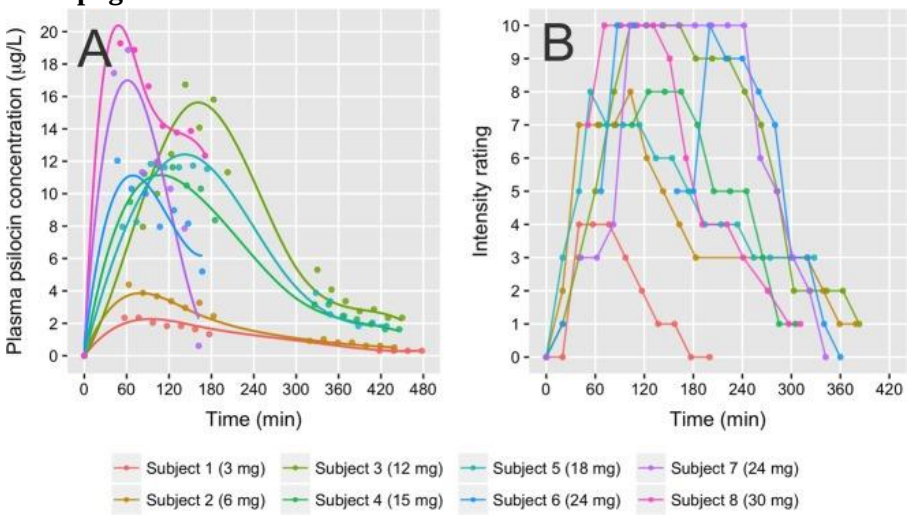
	11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 
6. The method of claim 5, wherein said clinical effects are comparable to those exerted by human plasma psilocin Cmax of 2 ng/ml or less or 5-HT2A human CNS receptor occupancy of 40% or less.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 21. POLITO (2019) "A systematic study of microdosing psychedelics" PLOS One. 14(2):1-26. From **page 1** "The phenomenon of 'microdosing', that is, regular ingestion of very small quantities of psychedelic substances, has seen a rapid explosion of popularity in recent years. Individuals who microdose report minimal acute effects from these substances yet claim **a range of long-term general health and wellbeing benefits**."

	From **page 2** "So, for example, a microdose of lysergic acid diethylamide (LSD) might be 6–25 micrograms, or **a microdose of psilocybin might be .1 to .5 grams of dried mushrooms**." From **page 19** "Longer term, **we found evidence that microdosing led to improved mental health**, **altered attentional capacities (reduced mind wandering and increased absorption),** and increased neuroticism." 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 
7. The method of claim 5, wherein said clinical effects are comparable to those exerted by human plasma psilocin Cmax of 1 ng/ml or less or 5-HT2A human CNS receptor occupancy of 30% or less.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use.

	Reported effects included improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 21. POLITO (2019) "A systematic study of microdosing psychedelics" PLOS One. 14(2):1-26. From **page 1** "The phenomenon of 'microdosing', that is, regular ingestion of very small quantities of psychedelic substances, has seen a rapid explosion of popularity in recent years. Individuals who microdose report minimal acute effects from these substances yet claim **a range of long-term general health and wellbeing benefits**." From **page 2** "So, for example, a microdose of lysergic acid diethylamide (LSD) might be 6–25 micrograms, or **a microdose of psilocybin might be .1 to .5 grams of dried mushrooms**." From **page 19** "Longer term, **we found evidence that microdosing led to improved mental health**, **altered attentional capacities (reduced mind wandering and increased absorption),** and increased neuroticism." 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 4**

	
8. The method of claim 5, wherein said PD effects are comparable to those exerted by human plasma psilocin Tmax in excess of 120 minutes.	11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 

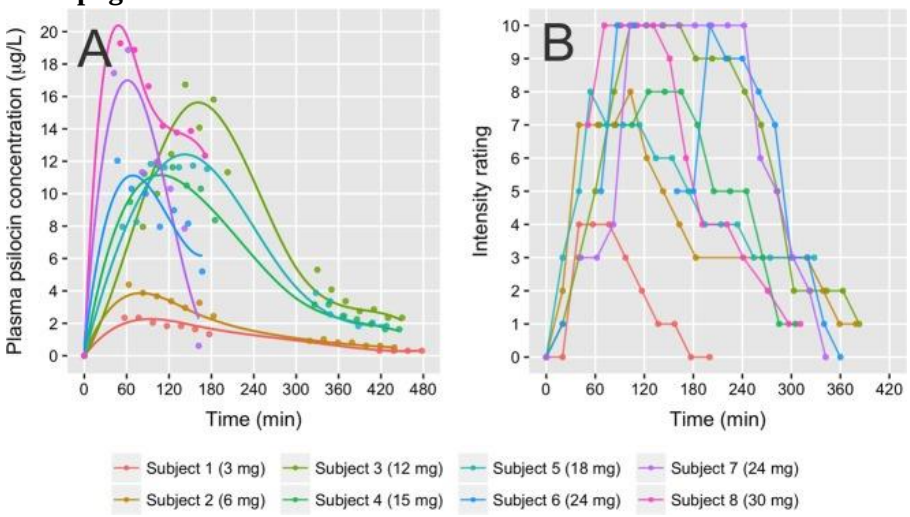
	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 1** "A method of managing a neurological condition or other symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof; and b) a pharmaceutically acceptable excipient" From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **claim 30** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component.**" From **paragraph [201]** "The controlled release dosage forms of certain embodiments attempt to deliver therapeutically effective amounts of active drug as a once-daily dose so that the ratio Cmax/Cmin in the plasma at steady state is less than the therapeutic index, and to **maintain drug levels at constant effective levels to provide a therapeutic benefit over a period of time (e.g. 24-hour period).**"

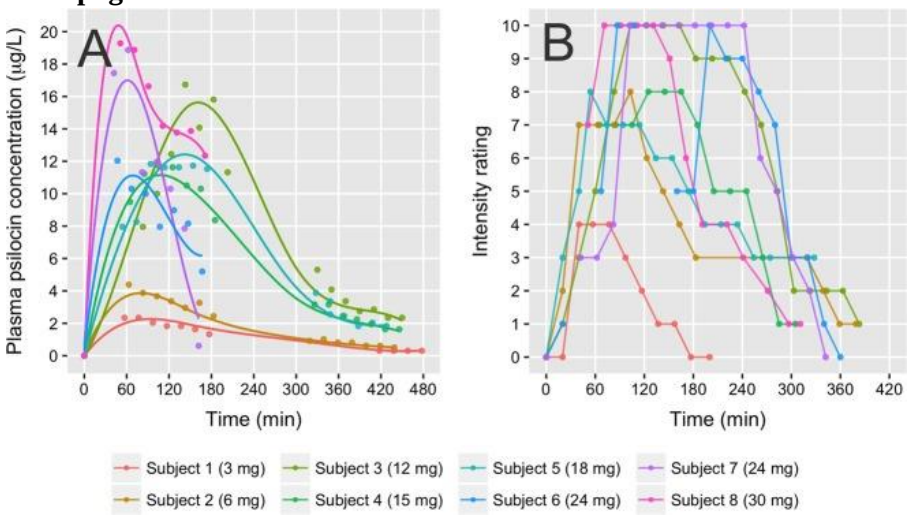
9. The method of claim 5, wherein said PD effects are comparable to those exerted by human plasma psilocin Tmax in excess of 180 minutes.	11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3**  19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 1** "A method of managing a neurological condition or other symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof; and b) a pharmaceutically acceptable excipient" From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**."

	From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **claim 30** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component.**" From **paragraph [201]** "The controlled release dosage forms of certain embodiments attempt to deliver therapeutically effective amounts of active drug as a once-daily dose so that the ratio Cmax/Cmin in the plasma at steady state is less than the therapeutic index, and to **maintain drug levels at constant effective levels to provide a therapeutic benefit over a period of time (e.g. 24-hour period).**"
10. The method of claim 5, wherein the administering of the compound occurs under conditions that may modulate NMDARs and their subunits in addition to modulate 5-HT2A receptors.	12. GREGORIO (2018) "d-Lysergic acid diethylamide, psilocybin, and other classic hallucinogens: Mechanism of action and potential therapeutic applications in mood disorders" Progress in Brain Research. 69-96:242. From **page 69** "**LSD**, belonging to the category of "classic halluginogens," **interacts with** the 5-HT system through 5HT1A, and 5HT2A receptors, with the DA system through D2 receptors, and indirectly also the glutamatergic neurotransmission thought the recruitment of **N-methyl- D-aspartate (NMDA) receptors**."
11. The method of claim 5, wherein the administering of the compound may provide excitotoxicity protection.	13. FARBER (1998) "Serotonergic Agents That Activate 5HT2A Receptors Prevent NMDA Antagonist Neurotoxicity" Neuropsychopharmacology. 18:57-62. From **page 57** "Among the **5HT2A agonists examined and found to be neuroprotective are LSD** and related hallucinogens" From **page 60** "Blockade of these **NMDA receptors inactivates the inhibitory mechanism thereby disinhibiting the excitatory pathways, and unleashing excitotoxic activity that serves as the proximal cause of neuronal injury**. Given evidence for serotonergic innervation of GABAergic interneurons via 5HT2A receptors (Mengod et al. 1990; Sheldon and Aghajanian 1990; Cornea-Hebert et al. 1996; Mathews et al. 1996; Shen and Andrade 1996), we postulate that a 5HT2A receptor is located on one or more of the GABAergic neurons in the NRH neurotoxicity circuit, and that **activation of this receptor by the 5HT2A agonist restores inhibition to the network and prevents neuronal injury**."

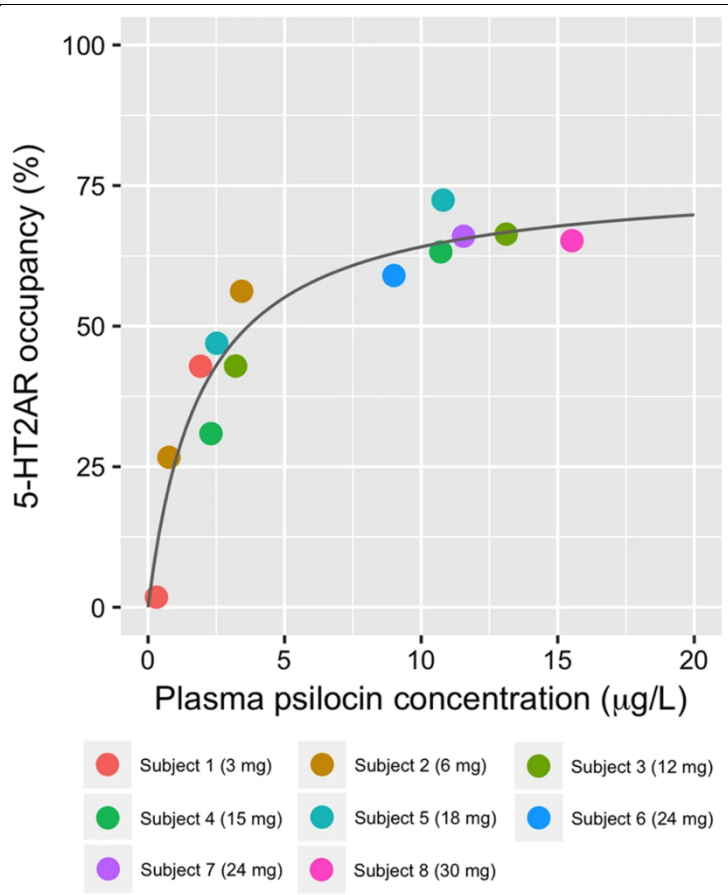
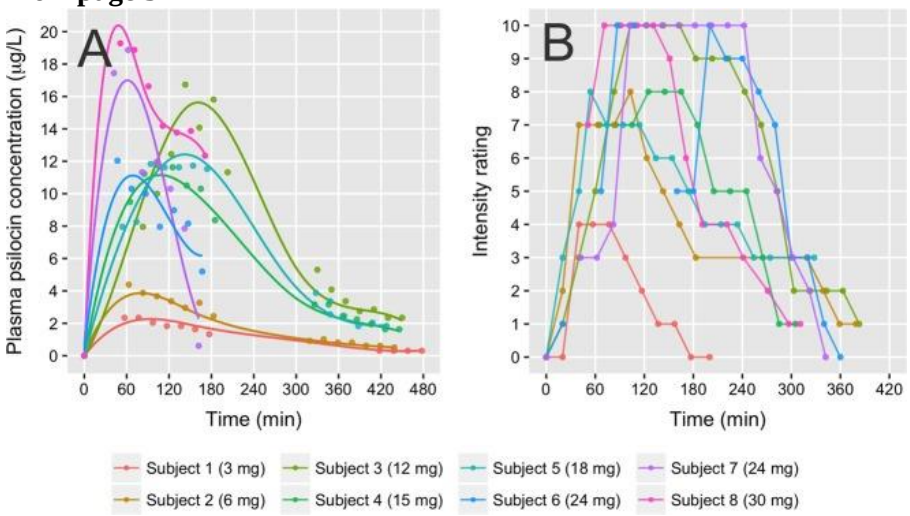
12. The method of claim 5, wherein the administering of the compound may modulate neurogenesis.	14. U.S. App. Pub. No. US/2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published 25 January 2018) From claim 1 "A method for **improving neurological health** of an animal **comprising: administering** a therapeutically effective amount of a composition to an animal, wherein the composition comprises one or more of **psilocybin**, **psilocin, baeocystin, norbaeocystin,** salts thereof, or combinations thereof, one or more of erinacines, hericenones or combinations thereof, and niacin." From claim 10 "The method of claim 1, wherein the composition additionally **promotes neurogenesis**." From claim 14 "A method for improving neurological health comprising: administering a daily dose of a composition for at least one month to a patient, wherein the composition comprises: one or more of about **0.1 to 10 mg of psilocybin**, **psilocin, baeocystin, norbaeocystin,** or salts thereof, one or more of about 0.1 to 1 gram of psilocybin mushrooms, or combinations thereof; about 0.1 to 200 mg of one or more of erinacines, hericenones, or combinations thereof; and about 1 to 200 mg of niacin." From Brief Summary of Invention section "As niacin activates nerve endings, the inventor suggests that the addition of niacin contributes an added benefit by **enhancing the neurogenic effects of psilocybin**, psilocin, erinacines and hericenones by helping these nootropics cross the blood brain barrier, and migrate throughout the nervous systems, and to its end points."
13. The method of claim 5, wherein the administering of the compound occurs under conditions effective for the substance to exert neuroplastogen effects, including modulation of neural plasticity.	15. Int'l Pat. App. Pub. No. WO/2020/097320 "REHABILITATION OF SUBJECTS WITH PHARMACOLOGICALLY INDUCED NEUROPLASTICITY" (Published 14 May 2020) From claim 2 "The Neurological Rehabilitation method according to claim 1 wherein **the neuroplasticity medicament is comprising** at least one of an selective serotonin reuptake inhibitor, a Brain Derived Neuro trophic factor enhancer, a steroid, **a psychedelic**, valproic acid, NDRI's, lithium carbonate, Metformin, N-Acety ley stine, and Human Growth Hormone." From **paragraph [0094]** "Another manifestation of the method will be the use of OVVR in combination with **neuroplasticity medicaments in the form of pharmacological psychedelics**, which have been shown to promote neuroplasticity both structurally and functionally, **including** but not limited to: **tryptamines** (N,N-dimethyltryptamine [DMT] and **psilocin**) amphetamines (2,5-dimethoxy-4-iodoamphetamine [DOI] and MDMA) **ergolines** (**lysergic acid diethylamide [LSD]**)."

14. The method of claim 5, wherein the administration of the compound is repeated over days or months or is chronic.	14. U.S. App. Pub. No. US/2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published 25 January 2018) From claim 14 "A method for improving neurological health comprising: administering **a daily dose of a composition for at least one month** to a patient, wherein the composition comprises: one or more of about **0.1 to 10 mg of psilocybin**, psilocin, baeocystin, norbaeocystin, or salts thereof, one or more of about 0.1 to 1 gram of psilocybin mushrooms, or combinations thereof; about 0.1 to 200 mg of one or more of erinacines, hericenones, or combinations thereof; and about 1 to 200 mg of niacin."
15. The method of claim 5, wherein the administration of the compound is intermittent and occurs every second day, every third day or every other week or every 2 weeks or every other month.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof; and b) a pharmaceutically acceptable excipient." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist is psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **claim 44** "The method of any one of the preceding claims, wherein the pharmaceutical composition is administered to a subject in need thereof once a day, **every alternate day, three times a week, twice a week, once a week, every other week, two weeks per month, three weeks per month, once a month, twice a month** or three times per month."

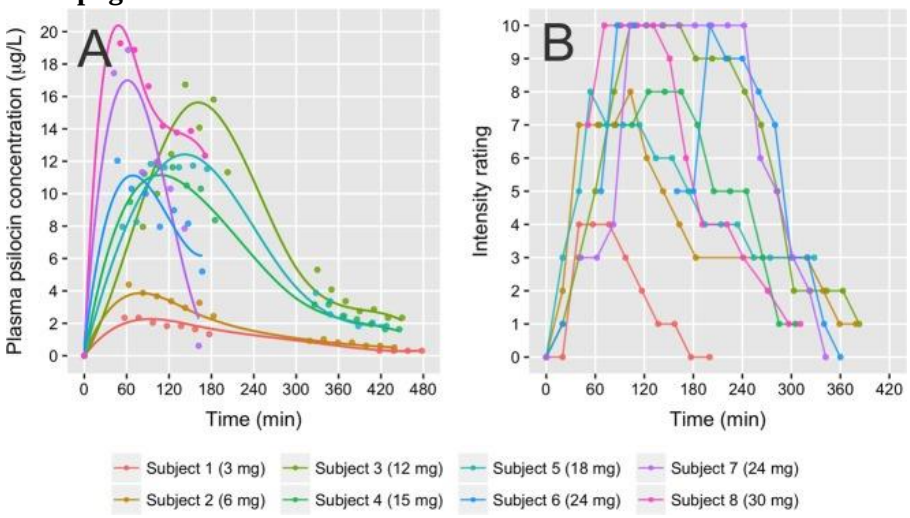
16. A method for preventing or treating diseases and conditions or improving functions in patients or subjects, the method comprising: administration of a 5-HT2A agonist substance at doses, dosages, posology, or formulations devoid of clinically meaningful psychedelic or psychotomimetic actions or effects, and having clinical effects comparable to those exerted by human plasma psilocin Cmax of 4 ng/ml or less, or human 5-HT2A CNS receptor occupancy of 50% or less, or PD effects comparable to those exerted by human plasma psilocin Tmax in excess of 60 minutes.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 

17. The method of claim 16, wherein said clinical effects are comparable to those exerted by human plasma psilocin Cmax of 2 ng/ml or less or 5-HT2A human CNS receptor occupancy of 40% or less.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 

18. The method of claim 16, wherein said clinical effects are comparable to those exerted by human plasma psilocin Cmax of 1 ng/ml or less or 5-HT2A human CNS receptor occupancy of 30% or less.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 4**

	
19. The method of claim 16, wherein said PD effects are comparable to those exerted by human plasma psilocin Tmax in excess of 120 minutes.	11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 

	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 1** "A method of managing a neurological condition or other symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof; and b) a pharmaceutically acceptable excipient" From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **claim 30** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component.**" From **paragraph [201]** "The controlled release dosage forms of certain embodiments attempt to deliver therapeutically effective amounts of active drug as a once-daily dose so that the ratio Cmax/Cmin in the plasma at steady state is less than the therapeutic index, and to **maintain drug levels at constant effective levels to provide a therapeutic benefit over a period of time (e.g. 24-hour period).**"

20. The method of claim 16, wherein said PD effects are comparable to those exerted by human plasma psilocin Tmax in excess of 180 minutes.	11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3**  19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 1** "A method of managing a neurological condition or other symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof; and b) a pharmaceutically acceptable excipient" From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**."

	From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **claim 30** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component.**" From **paragraph [201]** "The controlled release dosage forms of certain embodiments attempt to deliver therapeutically effective amounts of active drug as a once-daily dose so that the ratio Cmax/Cmin in the plasma at steady state is less than the therapeutic index, and to **maintain drug levels at constant effective levels to provide a therapeutic benefit over a period of time (e.g. 24-hour period).**"
21. The method of claim 16, wherein the administering of the 5-HT2A agonist substance occurs under conditions that may modulate NMDARs and their subunits in addition to modulate 5-HT2A receptors.	12. GREGORIO (2018) "d-Lysergic acid diethylamide, psilocybin, and other classic hallucinogens: Mechanism of action and potential therapeutic applications in mood disorders" Progress in Brain Research. 69-96:242. From **page 69** "**LSD**, belonging to the category of "classic halluginogens," **interacts with** the 5-HT system through 5HT1A, and 5HT2A receptors, with the DA system through D2 receptors, and indirectly also the glutamatergic neurotransmission thought the recruitment of **N-methyl- D-aspartate (NMDA) receptors**."
22. The method of claim 16, wherein the administering of the 5-HT2A agonist substance may provide excitotoxicity protection.	13. FARBER (1998) "Serotonergic Agents That Activate 5HT2A Receptors Prevent NMDA Antagonist Neurotoxicity" Neuropsychopharmacology. 18:57-62. From **page 57** "Among the **5HT2A agonists examined and found to be neuroprotective are LSD** and related hallucinogens" From **page 60** "Blockade of these **NMDA receptors inactivates the inhibitory mechanism thereby disinhibiting the excitatory pathways, and unleashing excitotoxic activity that serves as the proximal cause of neuronal injury**. Given evidence for serotonergic innervation of GABAergic interneurons via 5HT2A receptors (Mengod et al. 1990; Sheldon and Aghajanian 1990; Cornea-Hebert et al. 1996; Mathews et al. 1996; Shen and Andrade 1996), we postulate that a 5HT2A receptor is located on one or more of the GABAergic neurons in the NRH neurotoxicity

	circuit, and that **activation of this receptor by the 5HT2A agonist restores inhibition to the network and prevents neuronal injury**."
23. The method of claim 16, wherein the administering of the 5-HT2A agonist substance may modulate neurogenesis.	14. U.S. App. Pub. No. US/2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published 25 January 2018) From claim 1 "A method for **improving neurological health** of an animal **comprising: administering** a therapeutically effective amount of a composition to an animal, wherein the composition comprises one or more of **psilocybin**, **psilocin, baeocystin, norbaeocystin,** salts thereof, or combinations thereof, one or more of erinacines, hericenones or combinations thereof, and niacin." From claim 10 "The method of claim 1, wherein the composition additionally **promotes neurogenesis**." From claim 14 "A method for improving neurological health comprising: administering a daily dose of a composition for at least one month to a patient, wherein the composition comprises: one or more of about **0.1 to 10 mg of psilocybin**, psilocin, baeocystin, norbaeocystin, or salts thereof, one or more of about 0.1 to 1 gram of psilocybin mushrooms, or combinations thereof; about 0.1 to 200 mg of one or more of erinacines, hericenones, or combinations thereof; and about 1 to 200 mg of niacin." From Brief Summary of Invention section "As niacin activates nerve endings, the inventor suggests that the addition of niacin contributes an added benefit by **enhancing the neurogenic effects of psilocybin**, psilocin, erinacines and hericenones by helping these nootropics cross the blood brain barrier, and migrate throughout the nervous systems, and to its end points."
24. The method of claim 16, wherein the administering of the 5-HT2A agonist substance occurs under conditions effective for the substance to exert neuroplastogen effects, including modulation of neural plasticity.	15. Int'l Pat. App. Pub. No. WO/2020/097320 "REHABILITATION OF SUBJECTS WITH PHARMACOLOGICALLY INDUCED NEUROPLASTICITY" (Published 14 May 2020) From claim 2 "The Neurological Rehabilitation method according to claim 1 wherein **the neuroplasticity medicament is comprising** at least one of an selective serotonin reuptake inhibitor, a Brain Derived Neuro trophic factor enhancer, a steroid, **a psychedelic**, valproic acid, NDRI's, lithium carbonate, Metformin, N-Acety ley stine, and Human Growth Hormone."
25. The method of claim 16, wherein the administration of the 5-HT2A agonist substance is repeated	14. U.S. App. Pub. No. US/2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published 25 January 2018)

over days or months or is chronic.	From claim 14 "A method for improving neurological health comprising: administering **a daily dose of a composition for at least one month** to a patient, wherein the composition comprises: one or more of about **0.1 to 10 mg of psilocybin**, psilocin, baeocystin, norbaeocystin, or salts thereof, one or more of about 0.1 to 1 gram of psilocybin mushrooms, or combinations thereof; about 0.1 to 200 mg of one or more of erinacines, hericenones, or combinations thereof; and about 1 to 200 mg of niacin."
26. The method of claim 16, wherein the administration of the 5-HT2A agonist substance is intermittent and occurs every second day, every third day or every other week or every 2 weeks or every other month.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof; and b) a pharmaceutically acceptable excipient." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist is psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **claim 44** "The method of any one of the preceding claims, wherein the pharmaceutical composition is administered to a subject in need thereof once a day, **every alternate day, three times a week, twice a week, once a week, every other week, two weeks per month, three weeks per month, once a month, twice a month** or three times per month."
27. The method of claim 16, wherein the method includes the treatment of the metabolic syndrome and its complications.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020)

	From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, **metabolic diseases such as obesity and diabetes**, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
28. The method of claim 16, wherein the method includes the treatment of impaired glucose tolerance, diabetes and their complication.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist is psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof."

	From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, metabolic diseases such as obesity and **diabetes**, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
29. The method of claim 16, wherein the method includes the treatment of NAFL, NAFLD, NASH and their complications.	20. Int'l Pat. App. Pub. No. WO/2019/109124 "COMPOSITIONS AND METHODS FOR MODULATING LIVER ENDOTHELIAL CELL FENESTRATIONS" (Published 13 June 2019) From **claim 11** "The composition of any one of claims 1 to 5 wherein the 5-HT receptor agonist is selected from 2,5-Dimethoxy-4-iodoamphetamine (DOI), haloperidol, aripiprazole, asenapine, buspirone, vortioxetine, ziprasidone, methylphenidate, dihydroergotamine, ergotamine, methysergide, almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan, yohimbine, lasmiditan, naratriptan, bufotenin,

	egonovine, lisuride, **LSD,** mescaline, myristicin, **psilocin, psilocybin,** fenfluramine, MDMA, norfenfluramine, methylphenidate, ergonovine, lorcaserin, tazodone, methyl-5-HT, qipazine, ,cinitapride, cisapride, dazopride, metoclopramide, mosapride, prucalopride, renzapride, tegaserod, za copride, ergotamine, and valerenic acid." From **claim 12** "A method of modulating one or more of endothelial cell fenestration, porosity, diameter and frequency in a subject, the method comprising administering to the subject an effective amount of a composition of any one of claims 1 to 11." From **claim 13** "The method of claim 12 wherein the subject is a subject with an **age related disease or condition**." From **claim 14** "The method of claim 12 or 13 wherein the **age related disease or condition** is selected from atherosclerosis, cardiovascular disease, arthritis, cataracts, **age-related** macular degeneration, hearing loss, osteoporosis, osteoarthritis, type 2 diabetes, hypertension, Parkinson's disease, dementia, Alzheimer's disease, age-related changes in the liver microcirculation, age-related dyslipidaemia, insulin resistance, **fatty liver,** liver fibrosis and liver cirrhosis." From **paragraph [0143]** "**A composition may contain the therapeutic** or conjugate **in the range of about 0.1 mg to 2000 mg**, typically in the range of about 0.5 mg to 500 mg and more typically between about 1 mg and 200 mg. A daily dose of about 0.01 mg/kg to 100 mg/kg body weight, typically between about 0.1 mg/kg and about 50 mg/kg body weight, may be appropriate, depending on the route and frequency of administration. The daily dose will typically be administered in one or multiple, e.g., two, three or four, doses per day.
30. The method of claim 16, wherein the method includes the treatment of obesity and its complications.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate,

	metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, **metabolic diseases such as obesity and diabetes**, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
31. The method of claim 16, wherein the method includes the treatment of vision impairment and visual loss including macular degeneration and retinopathies.	17. U.S. Pat. App. Pub. No. US/2020/0330405 "COMPOSITIONS AND METHODS FOR TREATING OCULAR PATHOLOGIES" (Published 22 October 2020) From **claim 1** "A method of treating a condition associated with pathological ocular neovascularization, the method comprising administering to a subject in need thereof a therapeutically effective amount of a serotonin receptor agonist in a pharmaceutically acceptable carrier or salt thereof." From **claim 2** "The method of claim 1, wherein the pathological ocular neovascularization is: a corneal neovascularization or a choroidal neovascularization; and/or associated with **macular degeneration**, keratoconjunctivitis, conjunctivitis, diabetic retinitis, **retinopathy** of prematurity, polypoidal choroidal vasculopathy, ischemic proliferative retinopathy, retinitis pigmentosa, cone dystrophy, proliferative vitreoretinopathy, retinal artery occlusion, retinal vein occlusion, Leber's disease, retinal detachment, retinal pigment epithelial detachment, rubeosis iridis, corneal neovascularization, retinal neovascularization, choroidal neovascularization, retinochoroidal neovascularization, or a combination

	thereof." From **claim 11** "The method of claim 1, wherein the serotonin receptor agonist is a 5-HT 2A receptor agonist." From Detailed Description of the Invention section, paragraph 51 "The term "5-HT 2A agonists" can refer to any compound or ligand that increases the activity of a 5-hydroxytryptamine 2A receptor." From Detailed Description of the Invention section, paragraph 53 "In embodiments, the serotonin receptor agonist can be a Phenethylamine, a **Tryptamine**, an Ergoline, or a combination thereof." From Detailed Description of the Invention section, paragraph 54 "Non-limiting examples of a Tryptamine comprises DMT, [3-(2-Dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate (**Psilocybin**), 3-[2-(Dimethylamino)ethyl]-1H-indol-4-ol (Psilocin), and 5MEO-DMT." From Agonists section, paragraph 28 "In some embodiments, the **therapeutically effective amount of a compound of the invention (e.g., the serotonin receptor agonist and/or additional therapeutic agent) administered to a subject is at least about 0.0001 mg/kg body weight, 0.0005 mg/kg body weight, 0.001 mg/kg body weight, 0.005 mg/kg body weight, 0.01 mg/kg body weight, 0.05 mg/kg body weight, 0.1 mg/kg body weight**, at least about 0.25 mg/kg body weight, at least about 0.5 mg/kg body weight, at least about 0.75 mg/kg body weight, at least about 1 mg/kg body weight, at least about 2 mg/kg body weight, at least about 3 mg/kg body weight, at least about 4 mg/kg body weight, at least about 5 mg/kg body weight, at least about 6 mg/kg body weight, at least about 7 mg/kg body weight, at least about 8 mg/kg body weight, at least about 9 mg/kg body weight, at least about 10 mg/kg body weight, at least about 15 mg/kg body weight, at least about 20 mg/kg body weight, at least about 25 mg/kg body weight, at least about 30 mg/kg body weight, at least about 40 mg/kg body weight, at least about 50 mg/kg body weight, at least about 75 mg/kg body weight, at least about 100 mg/kg body weight, at least about 200 mg/kg body weight, at least about 250 mg/kg body weight, at least about 300 mg/kg body weight, at least about 350 mg/kg body weight, at least about 400 mg/kg body weight, at least about 450 mg/kg body weight, at least about 500 mg/kg body weight, at least about 550 mg/kg body weight, at least about 600 mg/kg body weight, at least about 650 mg/kg body weight, at least about 700 mg/kg body weight, at least about 750 mg/kg body weight, at least about 800 mg/kg body weight, at least about 900 mg/kg body weight, or at least about 1000 mg/kg body weight."
32. The method of claim 16, wherein the method includes the	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE,

treatment of neurological diseases, including neurodevelopmental diseases and neurodegenerative diseases that may benefit from modulation of neural plasticity, including: Neurological diseases and their symptoms and signs that may respond to neuroplastogen drugs and SMSNs include: Alzheimer's disease; presenile dementia; senile dementia; vascular dementia; Lewy body dementia; cognitive impairment, including mild cognitive impairment associated with aging and with chronic disease and its treatment, including chemotherapy, immunotherapy and radiotherapy, Parkinson's disease and Parkinsonian related disorders including but not limited to Parkinson dementia; disorders associated with accumulation of beta amyloid protein (including but not limited to cerebrovascular amyloid angiopathy, posterior cortical atrophy); disorders associated with accumulation or disruption of tau protein	BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, **autism and autism spectrum disorders**, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, **neurodegenerative diseases**, inflammatory diseases, autoimmune diseases, metabolic diseases such as obesity and diabetes, central nervous system disorders, peripheral nervous system disorders, **Alzheimer's disease**, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."

and its metabolites including but not limited to frontotemporal dementia and its variants, frontal variant, primary progressive aphasias (semantic dementia and progressive non fluent aphasia), corticobasal degeneration, supranuclear palsy; epilepsy; NS trauma; NS infections; NS inflammation, including inflammation from autoimmune disorders, including NMDAR encephalitis, and cytopathology from toxins, (including microbial toxins, heavy metals, and pesticides etc.); stroke; multiple sclerosis; Huntington's disease; mitochondrial disorders; Fragile X syndrome; Angelman syndrome; hereditary ataxias; neuro-otological and eye movement disorders; neurodegenerative diseases of the retina like glaucoma, diabetic retinopathy and age-related macular degeneration; amyotrophic lateral sclerosis; tardive dyskinesias; hyperkinetic disorders; attention deficit hyperactivity disorder and attention deficit disorders; restless leg	

syndrome; Tourette's syndrome; schizophrenia; autism spectrum disorders; tuberous sclerosis; Rett syndrome; cerebral palsy; disorders of the reward system including eating disorders [including anorexia nervosa (“AN”) and bulimia nervosa (“BN”); and binge eating disorder (“BED”), trichotillomania, dermotillomania, nail biting; migraine; fibromyalgia; and peripheral neuropathy of any etiology. Symptoms or manifestations of nervous system disorders that may be treated or prevented by neuroplastogen substances and drugs include: a decline, impairment, or abnormality in cognitive abilities including executive function, attention, cognitive speed, memory, language functions (speech, comprehension, reading and writing), orientation in space and time, praxis, ability to perform actions, ability to recognize faces or objects, concentration, and alertness; abnormal movements including akathisia, bradykinesia,	

tics, myoclonus, dyskinesias, including dyskinesias relate to Huntington's disease, levodopa induced dyskinesias and neuroleptic induced dyskinesias, dystonias, tremors, including essential tremor, and restless leg syndrome; parasomnias, insomnia, disturbed sleep pattern; psychosis; delirium; agitation; headache; motor weakness, spasticity, impaired physical endurance; sensory impairment, including impairment of vision and visual field defects, smell, taste, hearing and balance, and dysesthesias; dysautonomia; and ataxia, impairment of balance or coordination, tinnitus, neuro-otological and eye movement impairments, neurological symptoms of alcohol withdrawal, including delirium, headache, tremors, hallucinations, hypertension.	
33. The method of claim 16, wherein the method includes the treatment of psychiatric diseases as defined by DMS5 and ICD11 that may benefit from modulation of neural plasticity, including Schizophrenia spectrum	18. U.S. Pat. App. Pub. No. US/2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012) From **claim 1** "A method of improving the efficacy of psychotherapeutic treatment comprising administering a pharmaceutical composition comprising an oxytocin releasing agent to a subject diagnosed with a psychiatric or behavioral disorder." From **claim 3** "The method of claim 1, wherein the **psychiatric disorder is selected from the group consisting of depression, bi-polar disorders**,

and other psychotic disorders, Bipolar and related disorders, Depressive disorders, Anxiety disorders, Obsessive-compulsive and related disorders, Trauma- and stressor-related disorders, Dissociative disorders, Somatic symptom and related disorders, Feeding and eating disorders, Elimination disorders, Sleep-wake disorders, Sexual dysfunctions, Gender dysphoria, Disruptive, impulse-control, and conduct disorders, Substance-related and addictive disorders, Neurocognitive disorders, Personality disorders, Paraphilic disorders.	**anxiety disorders,** panic attacks, agoraphobia, attention deficit syndrome, mid-cycle dysphoria, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS), **addiction, obsessive-compulsive disorder,** Tourette's Syndrome, post-traumatic stress disorder (PTSD), and schizophrenia." From **claim 13** "The method of claim 1, wherein **the oxytocin releasing agent is** buspirone, gepirone, tandospirone serotonin, ergine, ergotamine, lysergic acid, **lysergic acid diethylamide**, **psilocybin**, 4-hydroxy-dimethyltryptamine, N,N-dimethyltryptamine, 5-methoxy-dimethyltryptamine, mescaline, 4-bromo-2,5-dimethoxyphenethylamine, 3,4-methylenedioxymethamphetamine, methylenedioxyethylamphetamine, tenamfetamine, lorcaserin or salts thereof." From paragraph [0077] "The **oxytocin-releasing agent is administered in a therapeutically effective amount**, which is that amount that provides improved therapeutic benefit relative to that achieved by psychotherapy alone. Dosage levels **from about 0.001 mg/kg to about 140 mg/kg of body weight** per day are useful for the purpose of the present disclosure or about 0.05 mg to about 7 g per patient per day."

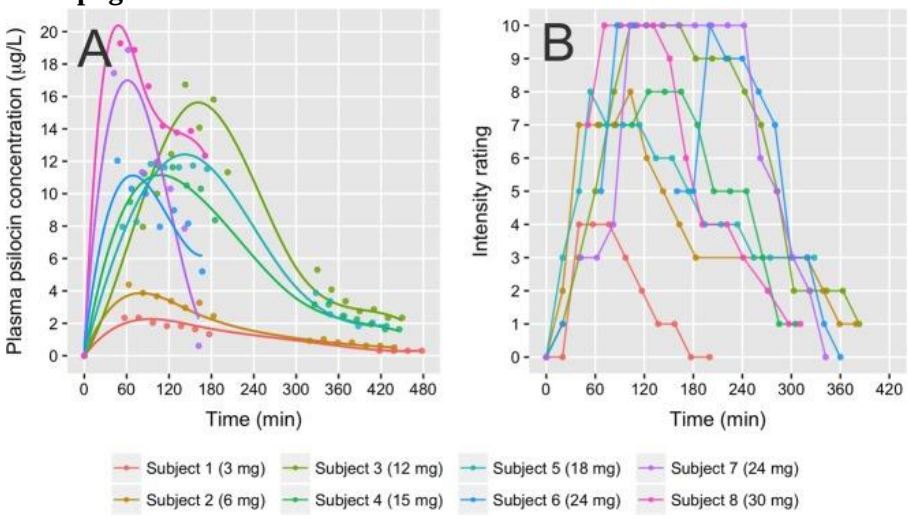
34. The method of claim 16, wherein the method includes the treatment of systemic inflammatory states and autoimmune disorders.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist is psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, **inflammatory diseases, autoimmune diseases**, metabolic diseases such as obesity and diabetes, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."

35. The method of claim 16, wherein the method includes the treatment of aging, senescence and associated deficits, including osteoporosis.	20. Int'l Pat. App. Pub. No. WO/2019/109124 "COMPOSITIONS AND METHODS FOR MODULATING LIVER ENDOTHELIAL CELL FENESTRATIONS" (Published 13 June 2019) From **claim 11** "The composition of any one of claims 1 to 5 wherein the 5-HT receptor agonist is selected from 2,5-Dimethoxy-4-iodoamphetamine (DOI), haloperidol, aripiprazole, asenapine, buspirone, vortioxetine, ziprasidone, methylphenidate, dihydroergotamine, ergotamine, methysergide, almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan, yohimbine, lasmiditan, naratriptan, bufotenin, egonovine, lisuride, **LSD,** mescaline, myristicin, **psilocin, psilocybin,** fenfluramine, MDMA, norfenfluramine, methylphenidate, ergonovine, lorcaserin, tazodone, methyl-5-HT, qipazine, ,cinitapride, cisapride, dazopride, metoclopramide, mosapride, prucalopride, renzapride, tegaserod, za copride, ergotamine, and valerenic acid." From **claim 12** "A method of modulating one or more of endothelial cell fenestration, porosity, diameter and frequency in a subject, the method comprising administering to the subject an effective amount of a composition of any one of claims 1 to 11." From **claim 13** "The method of claim 12 wherein the subject is a subject with an **age related disease or condition**." From **claim 14** "The method of claim 12 or 13 wherein the **age related disease or condition** is selected from atherosclerosis, cardiovascular disease, arthritis, cataracts, **age-related** macular degeneration, hearing loss, **osteoporosis**, osteoarthritis, type 2 diabetes, hypertension, Parkinson's disease, dementia, Alzheimer's disease, age-related changes in the liver microcirculation, age-related dyslipidaemia, insulin resistance, fatty liver, liver fibrosis and liver cirrhosis." From **paragraph [0143]** "**A composition may contain the therapeutic or conjugate in the range of about 0.1 mg to 2000 mg**, typically in the range of about 0.5 mg to 500 mg and more typically between about 1 mg and 200 mg. A daily dose of about 0.01 mg/kg to 100 mg/kg body weight, typically between about 0.1 mg/kg and about 50 mg/kg body weight, may be appropriate, depending on the route and frequency of administration. The daily dose will typically be administered in one or multiple, e.g., two, three or four, doses per day."
36. The method of claim 16, wherein the method includes the treatment of dry eye syndrome.	17. U.S. App. Pub. No. US/2020/0330405 "COMPOSITIONS AND METHODS FOR TREATING OCULAR PATHOLOGIES" (Published 22 October 2020) From **claim 5** "A method of **treating dry eye**, the method comprising administering to a subject in need thereof a therapeutically effective amount

	of a serotonin receptor agonist in a pharmaceutically acceptable carrier or salt thereof." From **Detailed Description of the Invention section, paragraph 51** "The term "5-HT 2A agonists" can refer to any compound or ligand that increases the activity of a 5-hydroxytryptamine 2A receptor." From **Detailed Description of the Invention section, paragraph 53** "In embodiments, the serotonin receptor agonist can be a Phenethylamine, a **Tryptamine**, an Ergoline, or a combination thereof." From **Detailed Description of the Invention section, paragraph 54** "Non-limiting examples of a Tryptamine comprises DMT, [3-(2-Dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate (**Psilocybin**), 3-[2-(Dimethylamino)ethyl]-1H-indol-4-ol (Psilocin), and 5MEO-DMT." From **Detailed Description of the Invention section, paragraph 76** "In some embodiments, the therapeutically effective amount of a compound of the invention (e.g., the serotonin receptor agonist and/or additional therapeutic agent) administered to a subject is at least about **0.0001 mg/kg body weight, 0.0005 mg/kg body weight, 0.001 mg/kg body weight, 0.005 mg/kg body weight, 0.01 mg/kg body weight, 0.05 mg/kg body weight, 0.1 mg/kg body weight, at least about 0.25 mg/kg body weight**..."
37. The method of claim 16, wherein the method includes the treatment of restless leg syndrome.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug

	thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, metabolic diseases such as obesity and diabetes, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, **restless legs syndrome**, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
38. The method of claim 16, wherein the function is chosen from visual, auditory, sense of balance, olfactory, gustatory.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis* mushrooms to 0.1–0.3 g."** 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*, which contains 10–12 mg of psilocybin per gram of dried mushrooms**"

	17. U.S. App. Pub. No. US/2020/0330405 "COMPOSITIONS AND METHODS FOR TREATING OCULAR PATHOLOGIES" (Published 22 October 2020) From **claim 1** "A method of treating a condition associated with pathological ocular neovascularization, the method comprising administering to a subject in need thereof a therapeutically effective amount of a serotonin receptor agonist in a pharmaceutically acceptable carrier or salt thereof." From **claim 2** "The method of claim 1, wherein the pathological ocular neovascularization is: a corneal neovascularization or a choroidal neovascularization; and/or associated with **macular degeneration**, keratoconjunctivitis, conjunctivitis, diabetic retinitis, **retinopathy** of prematurity, polypoidal choroidal vasculopathy, ischemic proliferative retinopathy, retinitis pigmentosa, cone dystrophy, proliferative vitreoretinopathy, retinal artery occlusion, retinal vein occlusion, Leber's disease, retinal detachment, retinal pigment epithelial detachment, rubeosis iridis, corneal neovascularization, retinal neovascularization, choroidal neovascularization, retinochoroidal neovascularization, or a combination thereof." From **claim 11** "The method of claim 1, wherein the serotonin receptor agonist is a 5-HT 2A receptor agonist." From **Detailed Description of the Invention section, paragraph 51** "The term "5-HT 2A agonists" can refer to any compound or ligand that increases the activity of a 5-hydroxytryptamine 2A receptor." From **Detailed Description of the Invention section, paragraph 53** "In embodiments, the serotonin receptor agonist can be a Phenethylamine, a **Tryptamine**, an Ergoline, or a combination thereof." From **Detailed Description of the Invention section, paragraph 54** "Non-limiting examples of a Tryptamine comprises DMT, [3-(2-Dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate (**Psilocybin**), 3-[2-(Dimethylamino)ethyl]-1H-indol-4-ol (Psilocin), and 5MEO-DMT." From **Detailed Description of the Invention section, paragraph 76** "In some embodiments, the therapeutically effective amount of a compound of the invention (e.g., the serotonin receptor agonist and/or additional therapeutic agent) administered to a subject is at least about **0.0001 mg/kg body weight, 0.0005 mg/kg body weight, 0.001 mg/kg body weight, 0.005 mg/kg body weight, 0.01 mg/kg body weight, 0.05 mg/kg body weight, 0.1 mg/kg body weight, at least about 0.25 mg/kg body weight**..."

39. The method of claim 16, where the substance is psilocybin, psilocin, norpsilocin, baeocystin, nor-baeocystin or a mixture thereof.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 

40. The method of claim 16, where the substance is a modified release formulation of psilocybin, psilocin, norpsilocin, baeocystin, nor-baeocystin or a mixture thereof.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 1** "A method of managing a neurological condition or other symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof; and b) a pharmaceutically acceptable excipient" From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **claim 30** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component.**"
41. The method of claim 16, where the drug is a combination of at least two drugs, the first drug chosen among 5-HT2A agonists, including psilocybin or psilocin or norpsilocin or baeocystin or	23. Int'l Pat. App. Pub. No. WO/2006/079999 "INDUCTION OF A NOVEL STATE OF MIND WITH A 5-HT2A AGONIST AND A NMDA ANTAGONIST" (Published 3 August 2006) From **claim 1** "The method of inducing a novel and particular state or mode of the human mind by concurrently antagonizing **NMDA receptors** and activating or stimulating **5-HT2A receptors** in the human brain."

norbaeocystin at doses of 0.01-24 mg and the second drug chosen among an open-channel low-affinity uncompetitive NMDAR antagonist, including dextromethorphan, dextromethadone, ketamine and its isomers, memantine, amantadine, noribogaine at doses of 0.01-50 mg; wherein the administering of the combination substance provides synergistic effects and or improved safety over the administration of either substance alone.	From **claim 2** "The method of inducing a novel and particular state or mode of the human mind by the **concurrent administration of a NMDA antagonist and a 5-HT2A agonist** to a human being." From **paragraph 14** "Due to the psychosis-inducing effects of either **NMDA antagonists or 5-HT2Aagonists in human beings, a combination of drugs of these two classes can** only be expected to also have, and likely **have even stronger**, psychosis-inducing **effects**..." From **paragraph 37** "Since it has now been found that the **psychosis inducing effects of NMDA antagonists can be prevented by concurrent administration of a 5-HT2A agonist**..." From **paragraph 49** "Using the well known **5-HT2A agonist (±)-DOI and the well known NMDA antagonist (+)-MK-801**, also known as dizocilpine, the above described mental state has been induced in an adult human being of about 85 kg body weight with a dose of **0.5 mg (+)-MK-801 and 1.8 mg (±)-DOI.**"
42. The method of claim 16, further comprising administration of the compound of claims 1-4 or the 5-HT2A agonist substance in combination with magnesium and or zinc and or lithium and salts thereof; wherein the administering of the combination substance provides synergistic effects and or improved safety over the administration of either substance alone.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist is psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof" From **claim 32** "The method of any one of the preceding claims, further comprising administering an effective amount of a second agent" From **claim 36** "The method of claim 32, wherein the second agent is a stimulant, an antihistamine, an antiemetic, an antidepressant, an anti-inflammatory, a growth factor, **a lithium compound**, resveratrol, phosphatidylcholine, curcumin, **magnesium**, melatonin, pregnenolone, ginseng, lysergic acid diethylamide, or combination thereof"
43. The method of claim 16, the method comprising daily oral administration psilocybin and or psilocin and or	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51.

baeocystin containing fungi and or extracts thereof.	From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**." From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** From page 47 "The microdosing practices reported in this study generally conformed in regimen and dose to the recommendations published by Fadiman (2011), although **some users experimented with daily microdoses. LSD and psilocybin-containing mushrooms were most commonly used** but some respondents also microdosed a wide range of lesser-known psychedelics and other psychoactive drugs." 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**"
44. A method for preventing and treating diseases and conditions in a subject, the method comprising administering a 5-HT2A agonist derivative, including carbamate derivatives, fluoro-derivatives and including nitro-derivatives and their deuterated versions including deuterated carbamate derivatives, deuterated fluoro-derivatives and including nitro-	16. Int'l Pat. App. Pub. No. WO/2018/195455 "ASSESSING AND TREATING PSYCHEDELIC-RESPONSIVE SUBJECTS" (Published 20 April 2018) From **claim 1** "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**." From **claim 53** "The method of any one of claims 1 -52, wherein the psychedelic agent is selected from **lysergic acid diethylamide, psilocybin,** and pharmaceutically acceptable salts thereof." From **Summary of the Invention section, paragraph 84** "As used herein, the term "treating" refers to administering a pharmaceutical composition for therapeutic purposes. To "treat a disorder" or use for "therapeutic treatment"

derivatives and deuterated fluoro-nitroderivatives, including compounds of any of claims 1- 4.	refers to **administering treatment to a patient already suffering from a disease to ameliorate the disease or** one or more symptoms thereof to improve the patient's condition. The methods of the invention can also be used **as a primary prevention measure**, i.e., to prevent a condition or to reduce the risk of developing a condition. Prevention refers to prophylactic treatment of a patient who may not have fully developed a condition or disorder, but who is susceptible to, or otherwise at risk of, the condition. Thus, in the claims and embodiments, the methods of the invention can be used either for therapeutic or prophylactic purposes.
45. The method of claim 5, wherein the substance is coated with an emetic drug to lower the abuse potential of the substance.	22. Int'l Pat. App. Pub. No. WO/2018/148605 "COMPOSITIONS AND METHODS COMPRISING A PSILOCYBIN DERIVATIVE" (Published 16 August 2018) From **claim 82** "A method of modulating activity at a neurotransmitter receptor comprising **administering a neurotransmitter activity modulator, and administering a** first dosage formulation comprising a first purified **psilocybin derivative** to the person in need of treatment, wherein the first dosage formulation modulates activity at a neurotransmitter receptor." From **claim 86** "The method of claim 82, wherein the neurotransmitter receptor is chosen from a serotonin receptor, a cannabinoid receptor, an adrenergic receptor, a dopamine receptor, a GABAergic receptor, a glutaminergic receptor, a histaminergic receptor, a cholinergic receptor, an opioid receptor, or a glycinergic receptor." From **claim 93** "The method of claim 86, wherein the neurotransmitter receptor is a dopaminergic receptor." From **claim 94** "The method of claim 93, wherein the neurotransmitter activity modulator is a dopaminergic drug." From **claim 95** "The method of claim 94, wherein the dopaminergic drug is chosen from amineptine, **apomorphine**, benzylpiperazine, bromocriptine, cabergoline, chlorpromazine, clozapine, dihydrexidine, domperidone, dopamine, fluphenazine, haloperidol, ketamine, loxapine, methamphetamine, olanzapine, pemoline, perphenazine, pergolide, phencyclidine, phenethylamine, phenmetrazine, pimozide, piribedil, a psychostimulant, reserpine, risperidone, ropinirole, tetrabenazine, or thioridazine." 24. AUFFRET (2018) "The Many Faces of Apomorphine: Lessons from the Past and Challenges for the Future" Drugs in R&D. 18:91-107.

	From **page 91** "Throughout history, **three main clinical indications stood out: emetic** (gastric emptying, respiratory disorders, aversive conditioning), sedative (mental disorders, clinical anesthesia, alcoholism), and antiparkinsonian (fluctuations)."
46. The method of claim 5, wherein the administering of substance is performed orally, buccally, sublingually, rectally, vaginally, nasally, via aerosol, trans-dermally, trans-mucosal, parenterally (e.g., intravenous, intradermal, subcutaneous, and intramuscular injection), epidurally, intrathecally, intra-auricularly, intraocularly, including implanted depot formulations, or topically, including creams, lotions, gels and ointments for the skin or for the eyes and eye drops.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph [25]** "Further provided herein are methods wherein the pharmaceutical composition in an **oral formulation, a buccal formulation, a nasal formulation, or an inhalation formulation**." From **paragraph [26]** "Further provided herein are methods wherein the pharmaceutical composition in a form selected from a spray, **aerosol**, mist, nebulae, **ointment, cream, gel**, paste, salve, solution, suspension, tincture, patch, and atomized vapor."
47. The method of claim 5, wherein the method includes the treatment of the metabolic syndrome and its complications.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020)

	From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, **metabolic diseases such as obesity and diabetes**, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
48. The method of claim 5, wherein the method includes the treatment of impaired glucose tolerance, diabetes and their complication.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof."

	From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, metabolic diseases such as obesity and **diabetes**, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
49. The method of claim 5, wherein the method includes the treatment of NAFL, NAFLD, NASH and their complications.	20. Int'l Pat. App. Pub. No. WO/2019/109124 "COMPOSITIONS AND METHODS FOR MODULATING LIVER ENDOTHELIAL CELL FENESTRATIONS" (Published 13 June 2019) From **claim 11** "The composition of any one of claims 1 to 5 wherein the 5-HT receptor agonist is selected from 2,5-Dimethoxy-4-iodoamphetamine (DOI), haloperidol, aripiprazole, asenapine, buspirone, vortioxetine, ziprasidone, methylphenidate, dihydroergotamine, ergotamine, methysergide, almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan, yohimbine, lasmiditan, naratriptan, bufotenin, egonovine, lisuride, **LSD,** mescaline, myristicin, **psilocin, psilocybin,** fenfluramine, MDMA, norfenfluramine, methylphenidate, ergonovine, lorcaserin, tazodone, methyl-5-HT, qipazine, ,cinitapride, cisapride,

	dazopride, metoclopramide, mosapride, prucalopride, renzapride, tegaserod, za copride, ergotamine, and valerenic acid." From **claim 12** "A method of modulating one or more of endothelial cell fenestration, porosity, diameter and frequency in a subject, the method comprising administering to the subject an effective amount of a composition of any one of claims 1 to 11." From **claim 13** "The method of claim 12 wherein the subject is a subject with an **age related disease or condition**." From **claim 14** "The method of claim 12 or 13 wherein the **age related disease or condition** is selected from atherosclerosis, cardiovascular disease, arthritis, cataracts, **age-related** macular degeneration, hearing loss, osteoporosis, osteoarthritis, type 2 diabetes, hypertension, Parkinson's disease, dementia, Alzheimer's disease, age-related changes in the liver microcirculation, age-related dyslipidaemia, insulin resistance, **fatty liver,** liver fibrosis and liver cirrhosis." From **paragraph [0143]** "**A composition may contain the therapeutic** or conjugate **in the range of about 0.1 mg to 2000 mg**, typically in the range of about 0.5 mg to 500 mg and more typically between about 1 mg and 200 mg. A daily dose of about 0.01 mg/kg to 100 mg/kg body weight, typically between about 0.1 mg/kg and about 50 mg/kg body weight, may be appropriate, depending on the route and frequency of administration. The daily dose will typically be administered in one or multiple, e.g., two, three or four, doses per day.
50. The method of claim 5, wherein the method includes the treatment of obesity and its complications.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**."

	From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, **metabolic diseases such as obesity and diabetes**, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
51. The method of claim 5, wherein the method includes the treatment of vision impairment and visual loss including macular degeneration and retinopathies.	17. U.S. App. Pub. No. US/2020/0330405 "COMPOSITIONS AND METHODS FOR TREATING OCULAR PATHOLOGIES" (Published 22 October 2020) From **claim 1** "A method of treating a condition associated with pathological ocular neovascularization, the method comprising administering to a subject in need thereof a therapeutically effective amount of a serotonin receptor agonist in a pharmaceutically acceptable carrier or salt thereof." From **claim 2** "The method of claim 1, wherein the pathological ocular neovascularization is: a corneal neovascularization or a choroidal neovascularization; and/or associated with **macular degeneration**, keratoconjunctivitis, conjunctivitis, diabetic retinitis, **retinopathy** of prematurity, polypoidal choroidal vasculopathy, ischemic proliferative retinopathy, retinitis pigmentosa, cone dystrophy, proliferative vitreoretinopathy, retinal artery occlusion, retinal vein occlusion, Leber's disease, retinal detachment, retinal pigment epithelial detachment, rubeosis iridis, corneal neovascularization, retinal neovascularization, choroidal neovascularization, retinochoroidal neovascularization, or a combination thereof." From **claim 11** "The method of claim 1, wherein the serotonin receptor

	agonist is a 5-HT 2A receptor agonist." From **Detailed Description of the Invention section, paragraph 51** "The term "5-HT 2A agonists" can refer to any compound or ligand that increases the activity of a 5-hydroxytryptamine 2A receptor." From **Detailed Description of the Invention section, paragraph 53** "In embodiments, the serotonin receptor agonist can be a Phenethylamine, a **Tryptamine**, an Ergoline, or a combination thereof." From **Detailed Description of the Invention section, paragraph 54** "Non-limiting examples of a Tryptamine comprises DMT, [3-(2-Dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate (**Psilocybin**), 3-[2-(Dimethylamino)ethyl]-1H-indol-4-ol (Psilocin), and 5MEO-DMT." From **Detailed Description of the Invention section, paragraph 76** "In some embodiments, the therapeutically effective amount of a compound of the invention (e.g., the serotonin receptor agonist and/or additional therapeutic agent) administered to a subject is at least about 0.0001 mg/kg body weight, 0.0005 mg/kg body weight, 0.001 mg/kg body weight, 0.005 mg/kg body weight, 0.01 mg/kg body weight, 0.05 mg/kg body weight, 0.1 mg/kg body weight, at least about 0.25 mg/kg body weight..."
52. The method of claim 5, wherein the method includes the treatment of neurological diseases, including neurodevelopmental diseases and neurodegenerative diseases that may benefit from modulation of neural plasticity, including: Neurological diseases and their symptoms and signs that may respond to neuroplastogen drugs and SMSNs include: Alzheimer's disease; presenile dementia; senile dementia; vascular dementia; Lewy body dementia; cognitive impairment, including mild cognitive impairment	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**."

associated with aging and with chronic disease and its treatment, including chemotherapy, immunotherapy and radiotherapy, Parkinson's disease and Parkinsonian related disorders including but not limited to Parkinson dementia; disorders associated with accumulation of beta amyloid protein (including but not limited to cerebrovascular amyloid angiopathy, posterior cortical atrophy); disorders associated with accumulation or disruption of tau protein and its metabolites including but not limited to frontotemporal dementia and its variants, frontal variant, primary progressive aphasias (semantic dementia and progressive non fluent aphasia), corticobasal degeneration, supranuclear palsy; epilepsy; NS trauma; NS infections; NS inflammation, including inflammation from autoimmune disorders, including NMDAR encephalitis, and cytopathology from toxins, (including microbial toxins, heavy metals, and pesticides etc.); stroke; multiple sclerosis; Huntington's disease; mitochondrial	From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, **autism and autism spectrum disorders**, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, **neurodegenerative diseases**, inflammatory diseases, autoimmune diseases, metabolic diseases such as obesity and diabetes, central nervous system disorders, peripheral nervous system disorders, **Alzheimer's disease**, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."

disorders; Fragile X syndrome; Angelman syndrome; hereditary ataxias; neuro-otological and eye movement disorders; neurodegenerative diseases of the retina like glaucoma, diabetic retinopathy and age-related macular degeneration; amyotrophic lateral sclerosis; tardive dyskinesias; hyperkinetic disorders; attention deficit hyperactivity disorder and attention deficit disorders; restless leg syndrome; Tourette's syndrome; schizophrenia; autism spectrum disorders; tuberous sclerosis; Rett syndrome; cerebral palsy; disorders of the reward system including eating disorders [including anorexia nervosa ("AN") and bulimia nervosa ("BN"); and binge eating disorder ("BED"), trichotillomania, dermotillomania, nail biting; migraine; fibromyalgia; and peripheral neuropathy of any etiology. Symptoms or manifestations of nervous system disorders that may be treated or prevented by neuroplastogen substances and drugs include: a decline, impairment, or abnormality in	

cognitive abilities including executive function, attention, cognitive speed, memory, language functions (speech, comprehension, reading and writing), orientation in space and time, praxis, ability to perform actions, ability to recognize faces or objects, concentration, and alertness; abnormal movements including akathisia, bradykinesia, tics, myoclonus, dyskinesias, including dyskinesias relate to Huntington's disease, levodopa induced dyskinesias and neuroleptic induced dyskinesias, dystonias, tremors, including essential tremor, and restless leg syndrome; parasomnias, insomnia, disturbed sleep pattern; psychosis; delirium; agitation; headache; motor weakness, spasticity, impaired physical endurance; sensory impairment, including impairment of vision and visual field defects, smell, taste, hearing and balance, and dysesthesias; dysautonomia; and ataxia, impairment of balance or coordination, tinnitus, neuro-otological and eye movement impairments, neurological symptoms of alcohol withdrawal, including delirium, headache, tremors,	

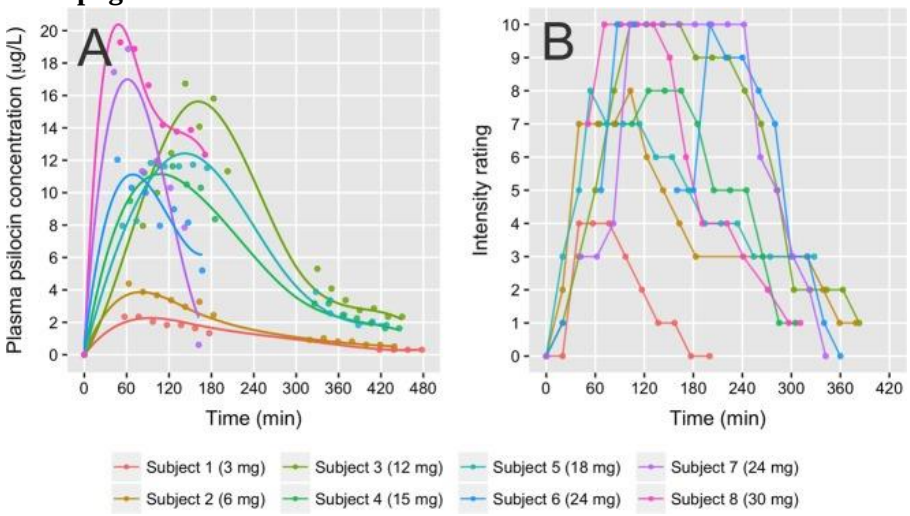
hallucinations, hypertension.	
53. The method of claim 5, wherein the method includes the treatment of psychiatric diseases as defined by DMS5 and ICD11 that may benefit from modulation of neural plasticity, including Schizophrenia spectrum and other psychotic disorders, Bipolar and related disorders, Depressive disorders, Anxiety disorders, Obsessive-compulsive and related disorders, Trauma- and stressor-related disorders, Dissociative disorders, Somatic symptom and related disorders, Feeding and eating disorders, Elimination disorders, Sleep-wake disorders, Sexual dysfunctions, Gender dysphoria, Disruptive, impulse-control, and conduct disorders, Substance-related and addictive disorders, Neurocognitive disorders, Personality disorders, Paraphilic disorders.	18. U.S. Pat. App. Pub. No. US/2012/0108510 "Methods of improving behavioral therapies" (Published May 3, 2012) From **claim 1** "A method of improving the efficacy of psychotherapeutic treatment comprising administering a pharmaceutical composition comprising an oxytocin releasing agent to a subject diagnosed with a psychiatric or behavioral disorder." From **claim 3** "The method of claim 1, wherein the psychiatric disorder is selected from the group consisting of **depression**, **bi-polar disorders**, **anxiety disorders**, panic attacks, agoraphobia, attention deficit syndrome, mid-cycle dysphoria, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS), **addiction**, obsessive-compulsive disorder, Tourette's Syndrome, **post-traumatic stress disorder (PTSD)**, and **schizophrenia**." From **claim 13** "The method of claim 1, wherein the oxytocin releasing agent is buspirone, gepirone, tandospirone serotonin, ergine, ergotamine, lysergic acid, **lysergic acid diethylamide**, **psilocybin**, 4-hydroxy-dimethyltryptamine, N,N-dimethyltryptamine, 5-methoxy-dimethyltryptamine, mescaline, 4-bromo-2,5-dimethoxyphenethylamine, 3,4-methylenedioxymethamphetamine, methylenedioxyethylamphetamine, tenamfetamine, lorcaserin or salts thereof." From paragraph [0077] "The **oxytocin-releasing agent is administered in a therapeutically effective amount**, which is that amount that provides improved therapeutic benefit relative to that achieved by psychotherapy alone. Dosage levels **from about 0.001 mg/kg to about 140 mg/kg of body weight** per day are useful for the purpose of the present disclosure or about 0.05 mg to about 7 g per patient per day."
54. The method of claim 5, wherein the method includes the treatment of systemic inflammatory states and autoimmune disorders.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020)

	From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of **5HT2A agonism facilitates treatment or management of disorders involving** cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD), eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, **inflammatory diseases, autoimmune diseases**, metabolic diseases such as obesity and diabetes, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, restless legs syndrome, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
55. The method of claim 5, wherein the method includes the treatment of aging, senescence and associated deficits, including osteoporosis.	20. Int'l Pat. App. Pub. No. WO/2019/109124 "COMPOSITIONS AND METHODS FOR MODULATING LIVER ENDOTHELIAL CELL FENESTRATIONS" (Published 13 June 2019) From **claim 11** "The composition of any one of claims 1 to 5 wherein the 5-HT receptor agonist is selected from 2,5-Dimethoxy-4-iodoamphetamine (DOI), haloperidol, aripiprazole, asenapine, buspirone, vortioxetine, ziprasidone, methylphenidate, dihydroergotamine, ergotamine, methysergide, almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan, yohimbine, lasmiditan, naratriptan, bufotenin,

	egonovine, lisuride, **LSD,** mescaline, myristicin, **psilocin, psilocybin,** fenfluramine, MDMA, norfenfluramine, methylphenidate, ergonovine, lorcaserin, tazodone, methyl-5-HT, qipazine, ,cinitapride, cisapride, dazopride, metoclopramide, mosapride, prucalopride, renzapride, tegaserod, za copride, ergotamine, and valerenic acid." From claim 12 "A method of modulating one or more of endothelial cell fenestration, porosity, diameter and frequency in a subject, the method comprising administering to the subject an effective amount of a composition of any one of claims 1 to 11." From claim 13 "The method of claim 12 wherein the subject is a subject with an **age related disease or condition**." From claim 14 "The method of claim 12 or 13 wherein the **age related disease or condition** is selected from atherosclerosis, cardiovascular disease, arthritis, cataracts, **age-related** macular degeneration, hearing loss, **osteoporosis**, osteoarthritis, type 2 diabetes, hypertension, Parkinson's disease, dementia, Alzheimer's disease, age-related changes in the liver microcirculation, age-related dyslipidaemia, insulin resistance, fatty liver, liver fibrosis and liver cirrhosis." From **paragraph [0143]** "**A composition may contain the therapeutic** or conjugate **in the range of about 0.1 mg to 2000 mg**, typically in the range of about 0.5 mg to 500 mg and more typically between about 1 mg and 200 mg. A daily dose of about 0.01 mg/kg to 100 mg/kg body weight, typically between about 0.1 mg/kg and about 50 mg/kg body weight, may be appropriate, depending on the route and frequency of administration. The daily dose will typically be administered in one or multiple, e.g., two, three or four, doses per day.
56. The method of claim 5, wherein the method includes the treatment of dry eye syndrome.	17. U.S. App. Pub. No. US/2020/0330405 "COMPOSITIONS AND METHODS FOR TREATING OCULAR PATHOLOGIES" (Published 22 October 2020) From claim 5 "A method of treating **dry eye**, the method comprising administering to a subject in need thereof a therapeutically effective amount of a serotonin receptor agonist in a pharmaceutically acceptable carrier or salt thereof." From Detailed Description of the Invention section, paragraph 51 "The term "5-HT 2A agonists" can refer to any compound or ligand that increases the activity of a 5-hydroxytryptamine 2A receptor." From Detailed Description of the Invention section, paragraph 53 "In embodiments, the serotonin receptor agonist can be a Phenethylamine, a **Tryptamine**, an Ergoline, or a combination thereof."

	From Detailed Description of the Invention section, paragraph 54 "Non-limiting examples of a Tryptamine comprises DMT, [3-(2-Dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate (**Psilocybin**), 3-[2-(Dimethylamino)ethyl]-1H-indol-4-ol (Psilocin), and 5MEO-DMT." From **Detailed Description of the Invention section, paragraph 76** "In some embodiments, the therapeutically effective amount of a compound of the invention (e.g., the serotonin receptor agonist and/or additional therapeutic agent) administered to a subject is at least about **0.0001 mg/kg body weight, 0.0005 mg/kg body weight, 0.001 mg/kg body weight, 0.005 mg/kg body weight, 0.01 mg/kg body weight, 0.05 mg/kg body weight, 0.1 mg/kg body weight, at least about 0.25 mg/kg body weight**..."
57. The method of claim 5, wherein the method includes the treatment of restless leg syndrome.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 18** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** is **psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 21** "The method of any one of the preceding claims, wherein the **5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is present in an amount of from about **0.1 mg to about 2 mg**." From **claim 23** "The method of any one of the preceding claims, wherein the therapeutically effective amount of the **5HT receptor agonist** or pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof is provided to the subject in need thereof **in an amount insufficient to provide a hallucinogenic experience**." From **paragraph 52** "In some instances, agonism of 5HT2A agonism facilitates treatment or management of disorders involving cognitive function and social interaction, or the symptoms thereof, as evidenced by the extensive localization of the 5-HT2A receptor in brain areas that mediate cognitive functions and social interaction. In some instances, disorders in which the 5HT2A receptor are involved include, but are not limited to schizophrenia, depression/suicide, anxiety, obsessive compulsive disorders (OCD), bipolar disorders, attention deficit hyperactivity disorder (ADHD),

	eating disorders such as anorexia nervosa, autism and autism spectrum disorders, Asperger's, neuropsychiatric diseases and disorders, sexual disorders such as erectile dysfunction, neurodegenerative diseases, inflammatory diseases, autoimmune diseases, metabolic diseases such as obesity and diabetes, central nervous system disorders, peripheral nervous system disorders, Alzheimer's disease, snoring, sleep apnea (obstructive sleep apnea, central sleep apnea), insomnia, sleep deprivation, **restless legs syndrome**, parasomnia, nightmares, night terrors, sleepwalking, hypersomnia (daytime sleepiness), narcolepsy and pain."
58. The method of claim 5, wherein the function is chosen from visual, auditory, sense of balance, olfactory, gustatory.	17. U.S. App. Pub. No. US/2020/0330405 "COMPOSITIONS AND METHODS FOR TREATING OCULAR PATHOLOGIES" (Published 22 October 2020) From **claim 5** "A method of treating **dry eye**, the method comprising administering to a subject in need thereof a therapeutically effective amount of a serotonin receptor agonist in a pharmaceutically acceptable carrier or salt thereof." From **Detailed Description of the Invention section, paragraph 51** "The term "5-HT 2A agonists" can refer to any compound or ligand that increases the activity of a 5-hydroxytryptamine 2A receptor." From **Detailed Description of the Invention section, paragraph 53** "In embodiments, the serotonin receptor agonist can be a Phenethylamine, a **Tryptamine**, an Ergoline, or a combination thereof." From **Detailed Description of the Invention section, paragraph 54** "Non-limiting examples of a Tryptamine comprises DMT, [3-(2-Dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate (**Psilocybin**), 3-[2-(Dimethylamino)ethyl]-1H-indol-4-ol (Psilocin), and 5MEO-DMT." From **Detailed Description of the Invention section, paragraph 76** "In some embodiments, the therapeutically effective amount of a compound of the invention (e.g., the serotonin receptor agonist and/or additional therapeutic agent) administered to a subject is at least about **0.0001 mg/kg body weight, 0.0005 mg/kg body weight, 0.001 mg/kg body weight, 0.005 mg/kg body weight, 0.01 mg/kg body weight, 0.05 mg/kg body weight, 0.1 mg/kg body weight, at least about 0.25 mg/kg body weight**..."
59. The method of claim 5, where the substance is psilocybin, psilocin, norpsilocin, baeocystin, nor-baeocystin or a mixture thereof.	9. JOHNSTAD (2018) "Powerful substances in tiny amounts: An interview study of psychedelic microdosing" Nordic Studies on Alcohol and Drugs. 35(1):39-51. From **page 39** "This article presents a qualitative interview study of people who **microdose with psychedelic drugs**, which means that the user takes about **one tenth of an ordinary recreational dose**."

	From **page 39** "Respondents tended to experiment with microdosing in phases, reporting mostly positive consequences from this form of drug use. **Reported effects included** improved mood, cognition, and creativity, which often served to **counteract symptoms especially from conditions of anxiety and depression**." From **page 44** "For LSD, this amounted to somewhere between 10 and 25 mcg, and for ***Psilocybe cubensis*** **mushrooms to 0.1–0.3 g."** 10. ARONSON (2014) Manson's Tropical Infectious Diseases (Twenty-Third Edition). ISBN: 9780702051012 From **page 1146** "Psilocybin content varies based on such factors as species and preparation. The most commonly used mushroom is ***Psilocybe cubensis*****, which contains 10–12 mg of psilocybin per gram of dried mushrooms**" 11. MADSEN (2019) "Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels" Neuropsychopharmacology. 44(7): 1336. From **page 3** 
60. The method of claim 5, where the drug is a combination of at least two drugs, the first drug chosen among 5-HT2A agonists, including psilocybin or psilocin or norpsilocin	23. Int'l Pat. App. Pub. No. WO/2006/079999 "INDUCTION OF A NOVEL STATE OF MIND WITH A 5-HT2A AGONIST AND A NMDA ANTAGONIST" (Published 3 August 2006) From **claim 1** "The method of inducing a novel and particular state or mode of the human mind by concurrently antagonizing **NMDA receptors** and activating or stimulating **5-HT2A receptors** in the human brain."

or baeocystin or norbaeocystin at doses of 0.01-24 mg and the second drug chosen among an open-channel low-affinity uncompetitive NMDAR antagonist, including dextromethorphan, dextromethadone, ketamine and its isomers, memantine, amantadine, noribogaine at doses of 0.01-50 mg; wherein the administering of the combination substance provides synergistic effects and or improved safety over the administration of either substance alone.	From **claim 2** "The method of inducing a novel and particular state or mode of the human mind by the **concurrent administration of a NMDA antagonist and a 5-HT2A agonist** to a human being." From paragraph 14 "Due to the psychosis-inducing effects of either **NMDA antagonists or 5-HT2Aagonists in human beings, a combination of drugs of these two classes can** only be expected to also have, and likely **have even stronger**, psychosis-inducing **effects**..." From paragraph 37 "Since it has now been found that the **psychosis inducing effects of NMDA antagonists can be prevented by concurrent administration of a 5-HT2A agonist**..." From **paragraph 49** "Using the well known **5-HT2A agonist** (±)-DOI and the well known **NMDA antagonist (**+)-MK-801, also known as dizocilpine, the above described mental state has been induced in an adult human being of about 85 kg body weight with a dose of **0.5 mg** (+)-MK-801 and **1.8 mg** (±)-DOI."
61. The method of claim 5, further comprising administration of the compound or the 5-HT2A agonist substance in combination with magnesium and or zinc and or lithium and salts thereof; wherein the administering of the combination substance provides synergistic effects and or improved safety over the administration of either substance alone.	19. Int'l Pat. App. Pub. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published 29 January 2020) From **claim 19** "The method of any one of the preceding claims, wherein the **5HT receptor agonist is psilocybin** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof" From **claim 32** "The method of any one of the preceding claims, further comprising administering an effective amount of a second agent" From **claim 36** "The method of claim 32, wherein the second agent is a stimulant, an antihistamine, an antiemetic, an antidepressant, an anti-inflammatory, a growth factor, **a lithium compound**, resveratrol, phosphatidylcholine, curcumin, magnesium, melatonin, pregnenolone, ginseng, lysergic acid diethylamide, or combination thereof"
62. The method of claim 5, the method comprising daily oral administration psilocybin and or psilocin and or	14. U.S. App. Pub. No. US/2018/0021326 "Compositions and methods for enhancing neuroregeneration and cognition by combining mushroom extracts containing active ingredients psilocin or psilocybin with erinacines or hericenones enhanced with niacin" (Published 25 January 2018)

baeocystin containing fungi and or extracts thereof.	From claim 14 “A method for improving neurological health comprising: administering a **daily dose** of a composition for at least one month to a patient, wherein the composition comprises: one or more of about 0.1 to 10 mg **of psilocybin, psilocin, baeocystin, norbaeocystin, or salts thereof, one or more of about 0.1 to 1 gram of psilocybin mushrooms,** or combinations thereof; about 0.1 to 200 mg of one or more of erinacines, hericenones, or combinations thereof; and about 1 to 200 mg of niacin.”

Electronic Acknowledgement Receipt

EFS ID:	47364134
Application Number:	17435571
International Application Number:	
Confirmation Number:	4510
Title of Invention:	COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON-PSYCHEDELIC/ PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS
First Named Inventor/Applicant Name:	Paolo L. Manfredi
Customer Number:	26875
Filer:	Shahin Shams
Filer Authorized By:	
Attorney Docket Number:	RELM-53US
Receipt Date:	12-JAN-2023
Filing Date:	01-SEP-2021
Time Stamp:	18:32:44
Application Type:	

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$72
RAM confirmation Number	E20231BI32404514
Deposit Account	
Authorized User	

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

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Concise Description of Relevance	Concise-description-generated.pdf	50961 9c563514f3feb5b2abd39f028ced7ee6ba8f6baa	no	11
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Information:					
2	Third-Party Submission Under 37 CFR 1.290	Third-party-preissuance-submission.pdf	75322 4554c1ffbc0e4127a40c2538300a4495554c8f30	no	5
Warnings:					
Information:					
3	Request for Notification of Non-compliant Third-Party Submission	Third-party-notification-request.pdf	23720 b4d6b05d01954233aa6114d63132908dfa80d74d	no	1
Warnings:					
Information:					
4	Concise Description of Relevance	US20220143051ClaimsChartComp.pdf	541585 69d2f177c610b4ae00046403ca2c0fe2dbe51d4e	no	73
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Information:					
5	Evidence of Publication	1-Psilocybine.pdf	223340 61689644d871ff272070a3e2c5aa32acac37941c	no	2
Warnings:					
Information:					
6	Evidence of Publication	2-Psilocin.pdf	204906 3874a00e829e015ae93bad5cffb01a83194cd152	no	2
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7	Evidence of Publication	3-Norpsilocin.pdf	129807 439543b4a8faf18b356f1bb8180fd8d787a45551	no	2
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Information:					
8	Evidence of Publication	4-Baeocystin.pdf	131366 910c64c69d924893a8018eb8d9de73236b628716	no	2
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Information:					
9	Evidence of Publication	5-Norbaeocystin.pdf	131508 190f621784c442d879224915b5e8e464ebe7a507	no	2
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10	Evidence of Publication	6-NNDimethyltryptamine.pdf	128216 c1e344e620d7e17dc81c363f0bb3d9539e0c609a	no	2
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Information:					
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13	Evidence of Publication	9-Johnstad.pdf	225979 e7edc345a13b7a276b7c54f250c0499e858c6987	no	13
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14	Evidence of Publication	10-ARONSON.pdf	13367882 252cf29c6013a6f448688c03eb0503555ebb9a5b	no	29
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Information:					
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New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

Electronic Acknowledgement Receipt

EFS ID:	47364236
Application Number:	17435571
International Application Number:	
Confirmation Number:	4510
Title of Invention:	COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON-PSYCHEDELIC/ PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS
First Named Inventor/Applicant Name:	Paolo L. Manfredi
Customer Number:	26875
Filer:	Shahin Shams
Filer Authorized By:	
Attorney Docket Number:	RELM-53US
Receipt Date:	12-JAN-2023
Filing Date:	01-SEP-2021
Time Stamp:	19:03:05
Application Type:	

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$72
RAM confirmation Number	E20231BJ02584846
Deposit Account	
Authorized User	

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

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Concise Description of Relevance	Concise-description-generated.pdf	44687 647f5cb2e0d9ca28f959e9d7d5016e5b3109b133	no	6
Warnings:					
Information:					
2	Third-Party Submission Under 37 CFR 1.290	Third-party-preissuance-submission.pdf	71719 0cbf5882c7153c594f9d49d044735a8bfbc14869	no	3
Warnings:					
Information:					
3	Request for Notification of Non-compliant Third-Party Submission	Third-party-notification-request.pdf	23720 c2bd000efe101221e7f1b8f10d58395703a656d6	no	1
Warnings:					
Information:					
4	Concise Description of Relevance	US20220143051ClaimsChartComp.pdf	541585 69d2f177c610b4ae00046403ca2c0fe2dbe51d4e	no	73
Warnings:					
Information:					
5	Evidence of Publication	11-Madsen.pdf	1199032 8c91dca48225d69fc3072862efd41250b8c548be	no	7
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6	Evidence of Publication	12-Gregorio.pdf	546186 c1fa9f6e976fc3948054f3455677128e31a4211b	no	28
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7	Evidence of Publication	13-Farber.pdf	117185 10e71ea78246c61268d3ab94b669391bcff7281c	no	6
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8	Evidence of Publication	14-US20180021326A1.pdf	1286444 7e248e6162e441351fa6b6fe4779429427729a3f	no	9
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9	Evidence of Publication	15-PriorityDocWO2020097320.pdf	2579032 8c4fa2baed4d7f9b387aceb2b7dd7bb86de1bcd1	no	42
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Warnings:					
Information:					
13	Evidence of Publication	19-PriorityDocWO2020157569.pdf	7185233 385c2c1d16fec2764b263a8d3bf50ce2435d1c03	no	131
Warnings:					
Information:					

14	Evidence of Publication	20-WO2019109124A1.pdf	12171261 5ac0a71a22e9585298cbdb1066ce42d3a509487f	no	84
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Information:					
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New Applications Under 35 U.S.C. 111

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

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

New International Application Filed with the USPTO as a Receiving Office

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

Electronic Acknowledgement Receipt

EFS ID:	47364402
Application Number:	17435571
International Application Number:	
Confirmation Number:	4510
Title of Invention:	COMPOSITIONS AND METHODS OF USE COMPRISING SUBSTANCES WITH NEURAL PLASTICITY ACTIONS ADMINISTERED AT NON-PSYCHEDELIC/ PSYCHOTOMIMETIC DOSAGES AND FORMULATIONS
First Named Inventor/Applicant Name:	Paolo L. Manfredi
Customer Number:	26875
Filer:	Shahin Shams
Filer Authorized By:	
Attorney Docket Number:	RELM-53US
Receipt Date:	12-JAN-2023
Filing Date:	01-SEP-2021
Time Stamp:	19:12:23
Application Type:	

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$72
RAM confirmation Number	E20231BJ12204948
Deposit Account	
Authorized User	

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

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Information:					
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Information:					
3	Request for Notification of Non-compliant Third-Party Submission	Third-party-notification-request.pdf	23720 fedca2c49d6fd7da7f13ae8334641ac30faf997c	no	1
Warnings:					
Information:					
4	Concise Description of Relevance	US20220143051ClaimsChartComp.pdf	541585 69d2f177c610b4ae00046403ca2c0fe2dbe51d4e	no	73
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5	Evidence of Publication	21-POLITO.pdf	1181902 dce9cdea3f5a2f7a05022a54ba87efdb2ce83bfe	no	26
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Information:					
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7	Evidence of Publication	23-WO2006079999A2.pdf	978398 58a437ccaf2ad25b755a404cf6b0fc62998e3068	no	17
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8	Evidence of Publication	24-Auffret.pdf	1065303 b5e06159ff91bd457273061c84189cef861502d8	no	17
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9	Evidence of Publication	25-DOI.pdf	121289 d862dda20350fd9980e8f9e34ef910c093a38417	no	1
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10	Evidence of Publication	26-OLGUN.pdf	54272 41a61edb39a3b1bd9bd61b8bdd7b78997e9fa80a	no	4
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11	Fee Worksheet (SB06)	fee-info.pdf	37468 da2fde6aaa9424aa00a96ee3243d90c5620ba871	no	2
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Information:					
			Total Files Size (in bytes):	8027463	

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New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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