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(54) Title: POLYPODAL SEROTONERGIC COMPOUNDS AND PRODRUGS OF SEROTONIN RECEPTOR AGONISTS AND ANTAGONISTS

(57) Abstract: Monopodal and polypodal serotonergic drugs, including prodrugs of serotonin receptor agonists and antagonists.

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POLYPODAL SEROTONERGIC COMPOUNDS AND PRODRUGS OF SEROTONIN RECEPTOR AGONISTS AND ANTAGONISTS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application No. 63/293,730, filed December 24, 2021, U.S. Provisional Application No. 63/299,817, filed January 14, 2022, and U.S. Provisional Application No. 63/338,994, filed May 6, 2022, with the entire contents of each being incorporated by reference herein for all purposes.

TECHNICAL FIELD

This disclosure relates to novel polypodal compounds and prodrugs of serotonergic compounds, including non-hallucinogenic variants comprising psilocin, as well as therapies for treating and preventing a variety of human conditions.

BACKGROUND

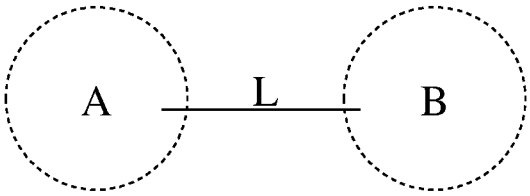
Many people worldwide are afflicted with psychological or mood disorders, such as depression, anxiety, compulsion, and post-traumatic stress disorders (PTSD). Altered synaptic connectivity has been observed in the brains of suffering from these types of diseases and disorders. Certain “psychedelic” drugs such as psilocybin and LSD have been found to alleviate symptoms of depression and PTSD in clinical trials. It is thought that this is due to the signaling of a 5-HT2A receptor, which sparks what’s called neuroplasticity. Neuroplasticity helps the brain form new neural connections, which is believed to generate quick and lasting positive mood effects. In studies, psilocybin-based psychotherapy has been demonstrated to almost immediately reduce depressive symptoms in patients after a single high dose.

However, psychedelic-based drug therapies have several limitations that have inhibited their widespread adoption. Most notably, tryptamine drugs like psilocybin and LSD are hallucinogenic and must be administered in a clinical setting in the presence of a medical professional. Secondarily, well-known 5-HT2A receptor agonists like psilocin (the active compound of the prodrug psilocybin) are known to be cardiotoxic due to their strong agonistic effects at the 5-HT2B receptor.

To date, very little (if any) work has been done in developing tryptamine-like analogs or tryptamine mimetics that are non-hallucinogenic and non-cardiotoxic. Accordingly, there remains a need to develop novel active compounds exhibiting these properties to provide patients with therapeutic options that can be administered daily/weekly in the privacy of their own home without the oversight of medical professionals.

SUMMARY

Disclosed herein are compounds of Formula I:



Formula I

wherein

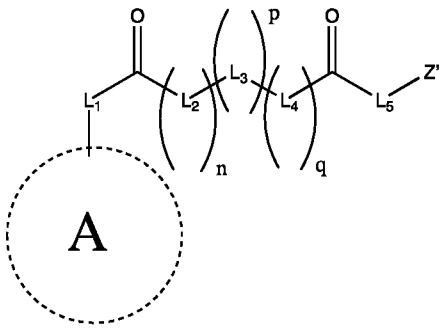
Group A is a residue of a first active compound comprising a serotonergic drug;

Group B is a residue of a second active compound; and

L is a covalent linkage between Group A and Group B,

and salts, solvates, hydrates, and prodrugs thereof.

Disclosed herein are compounds of Formula V:



Formula V

wherein:

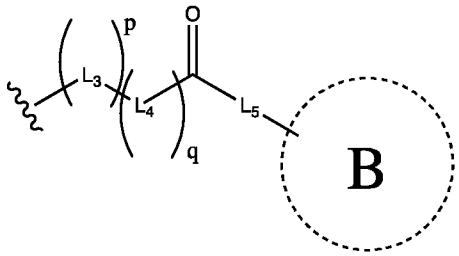
Group A is a residue of an active compound comprising a serotonergic drug;

L_1 and L_5 are independently selected from a covalent bond, O, NR_{10}, and S;

L_2 and L_4 for each occurrence are independently selected from O, $C(R_{10})_2$, NR_{10}, and S;

L_3 for each occurrence are independently selected from O, NR_{10}, S, $C(R_{10})_2$, $C(R_{10})=C(R_{10})$, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R_{10} for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, NO_2, -$N(R_9)_2$, -SR_9, halo, hydroxyl, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, $OP(O)(OR_9)_2$, -OSO_2R_8, and a structure of Formula IVB:



Formula IVB;

Group B is a residue of a second active compound;

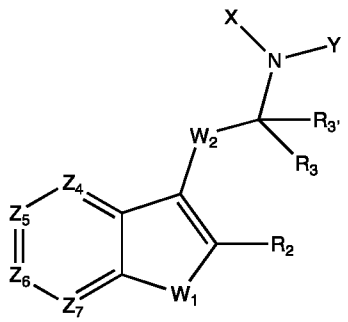
R_8 is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

R_9 is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

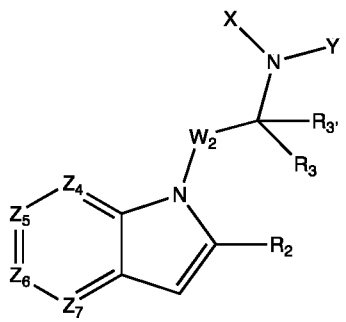
n, p, and q for each occurrence are integers independently selected from 0 to 10; and

Z' is selected from hydrogen, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, or, when L_5 is O, then Z' can also be selected from X^+, wherein X^+ is a pharmaceutically acceptable cation.

In some embodiments, Group A and/or Group B are independently selected from residues of compounds of Formulae II and III:



Formula II



Formula III

wherein

X and Y are each independently selected from hydrogen, deuterium, optionally

substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl, or Y is taken together with X and the nitrogen atom therebetween to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

W_1 is selected from NR_1, O, S, S(O), SO_2, Se, Se(O), and SeO_2;

W_2 is selected from -CD_2-, -CHD-, –$(CD_2)_2$-, -CH_2-, and –$(CH_2)_2$-;

Z_4 is selected from N and CR_4;

Z_5 is selected from N and CR_5;

Z_6 is selected from N and CR_6;

Z_7 is selected from N and CR_7;

R_1 is selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, -C(O)R_8, -C(O)OR_8, -P(O)$(OR_9)_2$, -C(O)N$(R_9)_2$, -SOR_8, and -SO_2R_8;

R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, -N$(R_9)_2$, -SR_9, halo, optionally substituted C_1-C_8 alkyl, -C_1-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl,

or Y is absent and R_3 is taken together with carbon to which it is attached and the nitrogen atom to which X is attached to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9,

or X is absent and R_2 is taken together with the carbon to which it is attached and the nitrogen atom to which Y is attached to form a 5- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

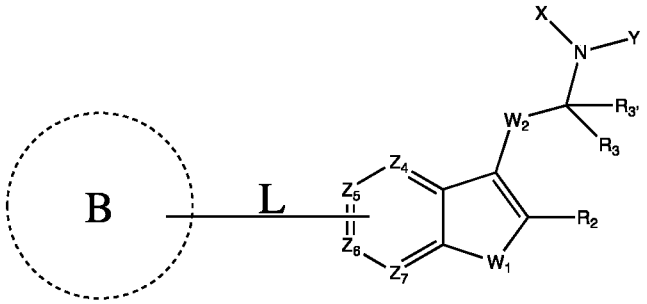
R_4 and R_5 are each independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, -N$(R_9)_2$, -SR_9, -C_1-C_8 alkoxy, -OC(O)R_8, -OC(O)OR_8, -OP(O)$(OR_9)_2$, and -OSO_2R_8;

each R_8 is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

each R_9 is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

and salts, solvates, hydrates, and prodrugs thereof.

In some embodiments, the compounds of Formula I are selected from compounds of Formula IA:



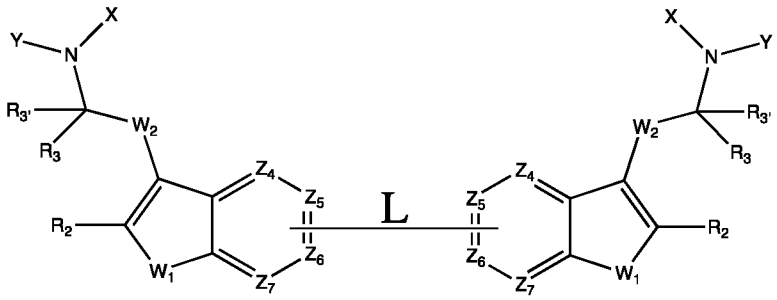
Formula IA

wherein Group B, linker L, X, Y, W_1, W_2, R_2, R_3, $R_{3'}$, Z_4, Z_5, Z_6, and Z_7 are as defined herein

and wherein L can replace a hydrogen in a R_4 group when Z_4 is CR_4, a hydrogen in a R_5 group when Z_5 is CR_5, a hydrogen in a R_6 group when Z_6 is CR_6, or a hydrogen in a R_7 group when Z_7 is CR_7,

and wherein L can replace X or a hydrogen atom in a R_2 group.

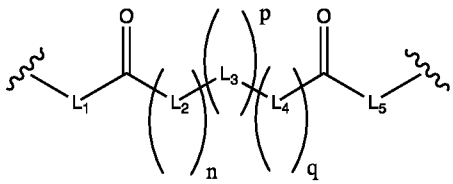
In some embodiments, the compounds of Formula I are selected from compounds of Formula IB:



Formula IB

wherein linker L, X, Y, W_1, W_2, R_2, R_3, $R_{3'}$, Z_4, Z_5, Z_6, and Z_7 are as defined herein.

In some embodiments, the linker "L" in Formula I is selected from Formula IV:



Formula IV

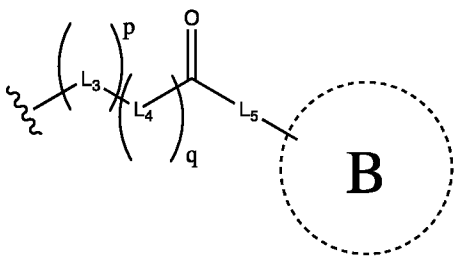
wherein

L_1 and L_5 for each occurrence are independently selected from a covalent bond, O, NR_{10}, and S;

L_2 and L_4 for each occurrence are independently selected from O, $C(R_{10})_2$, NR_{10}, and S;

L_3 for each occurrence are independently selected from O, NR_{10}, S, $C(R_{10})_2$, $C(R_{10})=C(R_{10})$, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R_{10} for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, NO_2, $-N(R_9)_2$, $-SR_9$, halo, hydroxyl, $-C_1$-C_8 alkoxy, $-OC(O)R_8$, $-OC(O)OR_8$, $-OP(O)(OR_9)_2$, $-OSO_2R_8$, and a structure of Formula IVA:



Formula IVA

and

n, p, and q for each occurrence are integers independently selected from 0 to 10.

The disclosure also related to compositions comprising, consisting of, or consisting essentially of a compound of Formula I and/or Formula V and an excipient. The disclosure further relates to pharmaceutical compositions comprising a therapeutically effective amount of a compound of Formula I and/or Formula V, wherein the excipient is a pharmaceutically acceptable carrier. Unless stated differently, a reference to Formula I shall generally include embodiments relevant to all subformulae (e.g., Formula IA, Formula IB, Formula IC, Formula ID, Formula IDd, Formula IDe, Formula IE, Formula IEa, Formula IF, Formula IG).

The disclosure also relates to compositions comprising, consisting of, or consisting essentially of a compound of Formula I and/or Formula V and an excipient. The disclosure further relates to pharmaceutical compositions comprising a therapeutically effective amount of

a compound of Formula I and/or Formula V, wherein the excipient is a pharmaceutically acceptable carrier.

The present disclosure further relates to a method of preventing or treating a psychological disorder comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound of Formula I and/or Formula V or a pharmaceutical composition containing the same.

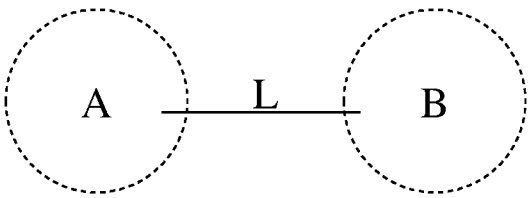
Embodiments of the disclosure also relate to a composition comprising, consisting of, or consisting essentially of a first compound selected from compounds of Formula I and/or Formula V; and a second active compound. In certain embodiments, the second active compound comprises a serotonergic compound.

Also described herein are methods of preventing or treating inflammation and/or pain comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula I and/or Formula V, or a composition (*e.g.*, a pharmaceutically-acceptable composition) containing said compound of Formula I and/or Formula V.

DETAILED DESCRIPTION

COMPOUNDS

Disclosed herein are compounds of Formula I:



Formula I

wherein

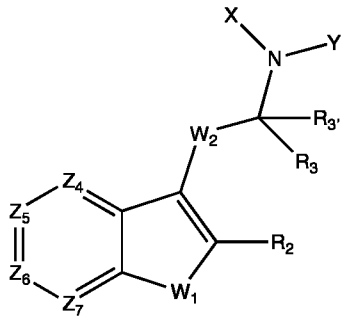
Group A is a residue of a first active compound comprising a serotonergic drug;

Group B is a residue of a second active compound; and

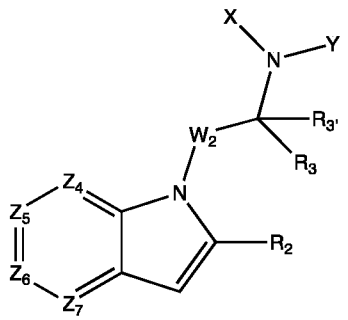
L is a covalent linkage between Group A and Group B,

and salts, solvates, hydrates, and prodrugs thereof.

In some embodiments, Group A and/or Group B are independently selected from residues of compounds of Formulae II and III:



Formula II



Formula III

wherein

X and Y are each independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl, or Y is taken together with X and the nitrogen atom therebetween to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

W_1 is selected from NR_1, O, S, S(O), SO_2, Se, Se(O), and SeO_2;

W_2 is selected from -CD_2-, -CHD-, –$(CD_2)_2$-, -CH_2-, and –$(CH_2)_2$-;

Z_4 is selected from N and CR_4;

Z_5 is selected from N and CR_5;

Z_6 is selected from N and CR_6;

Z_7 is selected from N and CR_7;

R_1 is selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, -C(O)R_8, -C(O)OR_8, -P(O)$(OR_9)_2$, -C(O)N$(R_9)_2$, -SOR_8, and -SO_2R_8;

R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, -N$(R_9)_2$, -SR_9, halo, optionally substituted C_1-C_8 alkyl, -C_1-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl,

or Y is absent and R_3 is taken together with carbon to which it is attached and the nitrogen atom to which X is attached to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9,

or X is absent and R_2 is taken together with carbon to which it is attached and the nitrogen atom to which Y is attached to form a 5- to 7-membered heterocyclic ring optionally

including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

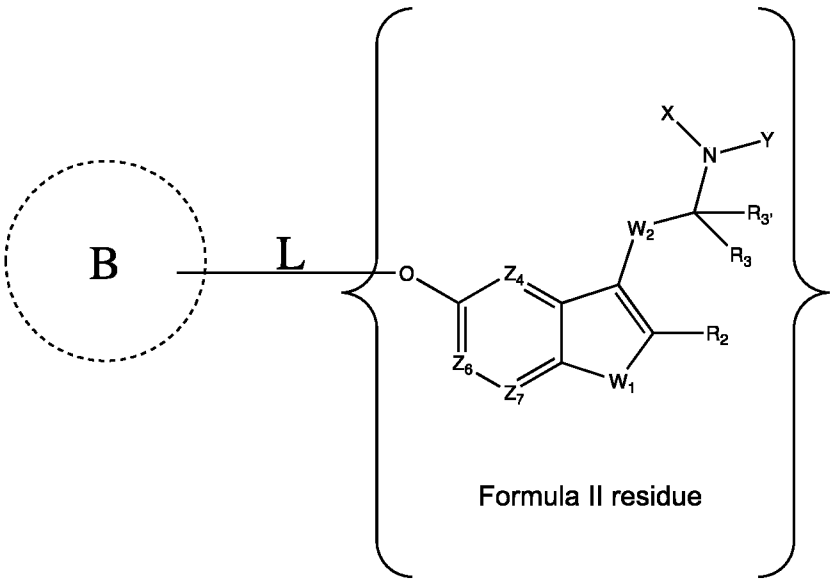
R_4 and R_5 are each independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, -$N(R_9)_2$, -SR_9, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8;

each R_8 is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

each R_9 is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

and salts, solvates, hydrates, and prodrugs thereof.

As used herein, a “residue” of an active compound, such as compounds of Formulae II and III, refers to the remaining portion of the compound after accounting for the attachment of covalent linker “L” to said compound. For example, when Group A is a residue of a compound of Formula II where Z_5 is CR_5, R_5 is -OH, and linker “L” is attached to the compound of Formula II by replacing the hydrogen on the -OH group of R_5, and then the “residue” of Formula II would be as follows:



Formula II residue

As used herein, the term “alkyl” refers to straight, branched or cyclic saturated hydrocarbon group. When the alkyl group is a cyclic alkyl group, it can be called a “cycloalkyl.” As used herein, alkyl has 1 to 20 carbon atoms, 1 to 10 carbon atoms, 1 to 8 carbon atoms, 1 to 6 carbon atoms or 1 to 3 carbon atoms. Examples of alkyl groups include methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl pentyl, isopentyl, hexyl, heptyl, octyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, and cyclodecyl. When an alkyl group having a specific number of carbons is named by chemical

name or identified by molecular formula, all positional isomers having that number of carbons may be encompassed; thus, for example, "butyl" includes n-butyl, isobutyl, sec-butyl, and tert-butyl; and "propyl" includes n-propyl and isopropyl. In some embodiments, a deuterium atom maybe be a replacement for a hydrogen atom. When the alkyl groups described herein are said to be "substituted," they may be substituted with any substituent or substituents as those found in the exemplary compounds and embodiments disclosed herein, as well as deuterium, aryl, heteroaryl, hydroxy, alkoxy, alkyl sulfonamido, aryl sulfonamido, and halo.

As used herein, the term "alkenyl" refers to an alkyl group that contains one or more carbon-carbon double bonds. An "alkynyl" group is an alkyl group that contains one or more carbon-carbon triple bonds. Examples of unsaturated alkyl groups include, but are not limited to, vinyl, allyl, $CH{=}CH(CH_3)$, $-CH{=}C(CH_3)_2$, $-C(CH_3){=}CH_2$, $-C(CH_3){=}CH(CH_3)$, $-C(CH_2CH_3){=}CH_2$, $-C{\equiv}CH$, $-C{\equiv}C(CH_3)$, $-C{\equiv}C(CH_2CH_3)$, $-CH_2C{\equiv}CH$, $CH_2C{\equiv}C(CH_3)$ and $CH_2C{\equiv}C(CH_2CH_3)$, among others. When the alkenyl and alkynyl groups described herein are said to be "substituted," they may be substituted with any substituent or substituents as those found in the exemplary compounds and embodiments disclosed herein, as well as deuterium, aryl, heteroaryl, hydroxy, alkoxy, alkyl sulfonamido, aryl sulfonamido, and halo.

As used herein, the term "cycloalkenyl" refers to a cyclic alkyl group that is partially saturated.

As used herein, the term "alkoxy" refers to -O-(alkyl), wherein alkyl is as defined above.

As used herein, the term "aryl" refers to an aromatic carbocyclic group of from 6 to 14 carbon atoms having a single ring (e.g., phenyl) or multiple condensed rings (e.g., naphthyl or anthryl). In some embodiments, aryl groups contain 6-14 carbons and in others from 6 to 12 or even 6 to 10 carbon atoms in the ring portions of the groups. Particular aryls include phenyl, biphenyl, naphthyl and the like. The phrase "aryl groups" also includes groups containing fused rings, such as fused aromatic-aliphatic ring systems (e.g., indanyl, tetrahydronaphthyl, and the like). When the aryl groups described herein are said to be "substituted," they may be substituted with any substituent or substituents as those found in the exemplary compounds and embodiments disclosed herein, as well as deuterium, aryl, alkyl, heteroaryl, hydroxyl, and halo.

As used herein, the term "heteroaryl" refers to an aromatic ring system having one to four heteroatoms as ring atoms in a heteroaromatic ring system, wherein the remainder of the atoms are carbon atoms. In some embodiments, heteroaryl groups contain 3 to 6 ring atoms, and in others from 6 to 9 or even 6 to 10 atoms in the ring portions of the groups. Suitable heteroatoms include oxygen, sulfur and nitrogen. In certain embodiments, the heteroaryl ring system is monocyclic or bicyclic.

As used herein, the term “heterocyclic ring” or “heterocyclyl” or “heterocycloalkyl” refers to a non-aromatic cycloalkyl in which one to four of the ring carbon atoms are independently replaced with a heteroatom selected from O, S and N. In some embodiments, heterocyclyl groups include 3 to 10 ring members, whereas other such groups have 3 to 5, 3 to 6, or 3 to 8 ring members. Heterocyclyls can also be bonded to other groups at any ring atom (i.e., at any carbon atom or heteroatom of the heterocyclic ring). A heterocycloalkyl group can be substituted or unsubstituted. Heterocyclyl groups encompass saturated and partially saturated ring systems. Further, the term heterocyclyl is intended to encompass any non-aromatic ring containing at least one heteroatom, which ring may be fused to an aryl or heteroaryl ring, regardless of the attachment to the remainder of the molecule. The phrase also includes bridged polycyclic ring systems containing a heteroatom. When the heterocyclyl groups described herein are said to be “substituted,” they may be substituted with any substituent or substituents as those found in the exemplary compounds and embodiments disclosed herein, as well as deuterium, aryl, alkyl, heteroaryl, hydroxyl, and halo.

As used herein, the term “heteromoieties” refers to any groups containing a heteroatom, for example, amino, O, Se, Se(O), SeO_2, S, S(O), and SO_2.

As used herein, the term “halo” or “halogen” refers to a fluorine, chlorine, bromine or iodine atom.

As used herein, the term “hydroxyl” refers to -OH group.

As used herein, the term “alkyl sulfonamido” refers to a moiety containing $-S(=O)_2-NR_2$, wherein each R group is chosen from an alkyl and H.

As used herein, the term “aryl sulfonamido” refers to a moiety containing $-S(=O)_2-NR_2$, wherein each R group is chosen from an aryl and H.

In some embodiments, the compound of Formulae I, II, III and V contains one or more stereocenters. In some circumstances, the compounds of Formulae I, II, III and V comprise a racemic mixture. In some embodiments, the compounds of Formulae I, II, III and V comprise the (S) enantiomer. In some embodiments, the compounds of Formulae I, II, III and V comprise the (R) enantiomer. In some embodiments, the (S) and (R) designations refer to the absolute stereochemistry of a compound having more than one stereocenter. In such cases, the conformation of one of those stereocenters may be referred to in terms of its relative (D) or (L) configuration.

In some embodiments, X and Y are independently selected from hydrogen, deuterium, and optionally substituted C_1-C_8 alkyl, wherein the alkyl group comprises a cycloalkyl moiety

(*e.g.*, cyclopropyl, cyclobutyl, etc.).

In some embodiments, R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, $-N(R_9)_2$, $-SR_9$, halo, optionally substituted C_1-C_8 alkyl, $-C_1$-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl, or Y is absent and R_3 taken together with carbon to which it is attached and the nitrogen atom to which X is attached form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9. In some embodiments, R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, halo, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl.

In some embodiments, R_4 and R_5 are each independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, $-N(R_9)_2$, $-SR_9$, $-C_1$-C_8 alkoxy, $-OC(O)R_8$, $-OC(O)OR_8$, $-OP(O)(OR_9)_2$, and $-OSO_2R_8$. In some embodiments, R_4 and R_5 are each independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, $-C_1$-C_8 alkoxy, $-OC(O)R_8$, $-OC(O)OR_8$, $-OP(O)(OR_9)_2$, and $-OSO_2R_8$.

In certain embodiments, at least one of R_4 and R_5 is selected from C_1-C_5 alkoxy group, or in some embodiments a C_2-C_4 alkoxy group, wherein it may be a straight chain or branched C_1-C_5 alkoxy group or C_2-C_4 alkoxy group, for example a straight chain, and may be methoxy or ethoxy. In some embodiments, R_5 is C_1-C_5 alkoxy. In some embodiments, R_4 is selected from hydrogen and fluorine, and R_5 is C_1-C_5 alkoxy. In some embodiments, at least one of R_4 and R_5 is selected from C_1-C_5 alkyl or C_1-C_4 alkyl, for example a straight chain C_1-C_4 alkyl. In some embodiments, R_5 is selected from methyl, ethyl, n-propyl or n-butyl, and for example methyl or ethyl. In some embodiments, at least one of R_4 and R_5 is halo. In some embodiments, R_4 is fluoro. In some embodiments, R_4 is fluoro and R_5 is selected from hydrogen and C_1-C_5 alkoxy. In some embodiments, at least one of R_4 or R_5 is $-OC(O)R_8$. In some embodiments, R_4 is selected from $-OC(O)R_8$ and R_5 is hydrogen or fluoro.

In some embodiments, R_8 is selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl. In some embodiments, R_9 is selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl. In some embodiments, R_8 is selected from methyl, ethyl, propyl, and isopropyl. In some embodiments, R_9 is selected from methyl, ethyl, propyl, and isopropyl.

Exemplary halo atoms for compounds of Formulae II and III include chloro, bromo, fluoro, and iodo. In certain embodiments, the compounds of Formula I and/or Formula V comprise at least one fluoro.

In some embodiments, W_1 is selected from NR_1, O, S, S(O), SO_2, Se, Se(O), and SeO_2 . In some embodiments, W_1 is NR_1. In some embodiments, W_1 is O. In some embodiments, W_1 is S. In some embodiments, W_1 is Se. In some embodiments, Z_6 is selected from N and CR_6; and Z_7 is selected from N and CR_7. In some embodiments, Z_6 is N. In some embodiments, Z_7 is N.

In some embodiments, R_1 is selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, $-C(O)R_8$, $-C(O)OR_8$, $-P(O)(OR_9)_2$, $-C(O)N(R_9)_2$, $-SOR_8$, and $-SO_2R_8$. In some embodiments, R_1 is hydrogen. In some embodiments, R_1 is optionally substituted C_1-C_8 alkyl. In some embodiments, R_1 is optionally substituted C_2-C_4 alkyl. In some embodiments, R_1 is methyl. In some embodiments, R_1 is ethyl. In some embodiments, R_1 is isopropyl.

In some embodiments, W_2 is selected from $-CD_2-$, -CDH-, $-(CD_2)_2-$, $-CH_2-$, and $-(CH_2)_2-$. In some embodiments, W_2 is selected from $-CH_2-$. In some embodiments, W_2 is selected from $-(CH_2)_2-$. In some embodiments, W_2 is selected from $-CD_2-$. In some embodiments, W_2 is selected from $-(CD_2)_2-$. In some embodiments, W_2 is -CDH-. In some embodiments, when W_2 is -CDH-, W_2 represents a stereocenter in the (R) or (S) conformation.

In certain embodiments, the alkyl groups of Formulae II and III are selected from C_1-C_8 alkyl, C_2-C_8 alkyl, C_3-C_8 alkyl, and C_4-C_8 alkyl, or methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl pentyl, isopentyl, hexyl, heptyl, octyl, etc. In certain embodiments, the alkenyl groups of Formulae II and III are selected from C_2-C_8 alkenyl, C_3-C_8 alkenyl, and C_4-C_8 alkenyl, or ethenyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl, etc.

In certain embodiments, the alkyl and alkenyl groups of Formulae II and III may be unsubstituted or substituted with one or more groups selected from aryl, heteroaryl, hydroxy, alkoxy, alkyl sulfonamido, aryl sulfonamido, and halo.

In certain embodiments, the cycloalkenyl and heterocyclyl groups of Formulae II and III may be unsubstituted or substituted with one or more groups selected from deuterium, alkyl, alkenyl, aryl, heteroaryl, hydroxy, alkoxy, alkyl sulfonamido, aryl sulfonamido, and halo.

In certain embodiments, the aryl and heteroaryl groups of Formulae II and III are unsubstituted or substituted with one or more groups selected from aryl, alkyl, heteroaryl, hydroxyl, and halo. In certain embodiments, the alkoxy groups of Formulae II and III may be unsubstituted or substituted with one or more groups selected from aryl, alkyl, heteroaryl, hydroxyl, and halo.

In some embodiments, X and/or Y may be a straight chain C_1-C_4 alkyl, or a C_2-C_4

alkenyl. In some embodiments, X and Y are each methyl, X and Y are each ethyl, or X is methyl and Y is ethyl. In certain embodiments, X and/or Y are an C_1-C_8 alkyl or C_2-C_8 alkenyl optionally substituted with at least one halo group, such as fluorine. In certain embodiments, at least one of X or Y comprises a group selected from $-CF_3$, $-CHF_2$, $-CH_2F$, $-CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$. In certain embodiments, at least one of X or Y comprises a group selected from $-CD_3$, $-CH_2CD_3$, $-CD_2CH_3$, and $-CD_2CD_3$.

In some embodiments, X is unsubstituted C_1-C_8 alkyl. In some embodiments, X is methyl. In some embodiments, X is ethyl. In some embodiments, X is n-propyl. In some embodiments, X is isopropyl. In some embodiments, X is cyclopropyl. In some embodiments, Y is hydrogen. In some embodiments, Y is unsubstituted C_1-C_8 alkyl. In some embodiments, Y is methyl. In some embodiments, Y is ethyl. In some embodiments, Y is n-propyl. In some embodiments, Y is isopropyl. In some embodiments, Y is cyclopropyl.

In some embodiments, R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, halo, or C_1-C_4 alkyl, for example a straight chain C_1-C_4 alkyl. In some embodiments, R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, halo, methyl, ethyl, n-propyl, isopropyl, n-butyl and isobutyl. In other embodiments, R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, methyl, and ethyl.

In some embodiments, R_2 is hydrogen. In some embodiments, R_3 and $R_{3'}$ are each independently selected from hydrogen, methyl, and ethyl. In some embodiments, R_3 is hydrogen. In some embodiments, R_3 is methyl and $R_{3'}$ is hydrogen. In some embodiments, R_3 and $R_{3'}$ are both hydrogen. In some embodiments, R_3 and $R_{3'}$ are both deuterium. In some embodiments, R_3 is hydrogen and $R_{3'}$ is deuterium. In some embodiments, when R_3 and $R_{3'}$ are not the same, it represents a stereocenter wherein the compound of Formulae II or III comprises a racemic mixture. In some embodiments, when R_3 and $R_{3'}$ are not the same, it represents a stereocenter wherein the compound of Formulae II or III comprises the (S) enantiomer. In some embodiments, when R_3 is not hydrogen, it represents a stereocenter wherein the compound of Formulae II or III comprises the (R) enantiomer. In some embodiments, a racemic mixture can be resolved to provide a pure enantiomer or a mixture enhanced with either the (R) or (S) enantiomer.

In some embodiments, R_6 and R_7 are each independently selected hydrogen, halo, methyl, ethyl, n-propyl, isopropyl, n-butyl and isobutyl. In some embodiments, R_6 is selected from hydrogen and halo. In some embodiments, R_6 is selected from hydrogen and fluorine. In some embodiments, R_6 is fluorine. In some embodiments, R_6 is selected from alkoxy and halo. In some embodiments, R_6 is selected from methoxy, chloro and fluoro. In some embodiments,

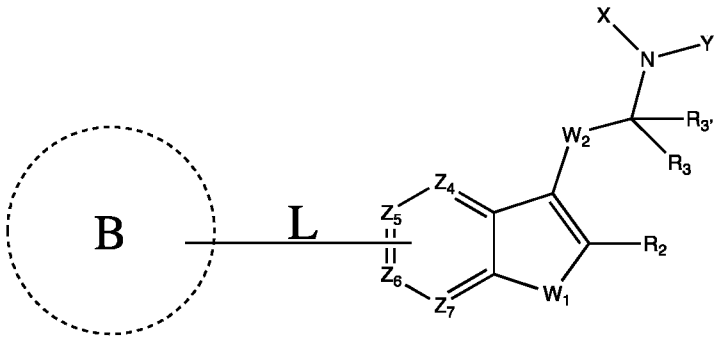
R_6 is fluorine. In some embodiments, R_6 is methoxy. In some embodiments, R_7 is selected from hydrogen and optionally substituted C_1-C_4 alkyl. In some embodiments, R_7 is selected from hydrogen, methyl and ethyl. In some embodiments, R_7 is optionally substituted C_1-C_4 alkyl. In some embodiments, when R_6 is fluoro, then R_7 is selected from hydrogen and optionally substituted C_1-C_4 alkyl.

In some embodiments, R_4 is hydrogen and R_5 is selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8. In some embodiments, R_5 is selected from C_1-C_8 alkyl, hydroxyl, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8. In some embodiments, R_5 is selected from C_2-C_8 alkyl, hydroxyl, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8. In some embodiments, R_5 is hydroxy. In some embodiments, R_5 is -$OC(O)R_8$. In some embodiments, R_8 is C_1-C_4 alkyl. In some embodiments, R_8 is methyl.

In some embodiments, R_5 is hydrogen and R_4 is selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8. In some embodiments, R_4 is selected from C_1-C_8 alkyl, hydroxyl, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8. In some embodiments, R_5 is selected from C_1-C_8 alkyl, -C_2-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8. In some embodiments, R_5 is -$OC(O)R_8$. In some embodiments, R_8 is C_1-C_4 alkyl. In some embodiments, R_8 is methyl.

In certain embodiments, one or more hydrogen atoms on a compound of Formulae II or III may be replaced with one or more deuterium atoms. For example, in certain embodiments, R_6 may comprise a deuterium atom as a replacement for a hydrogen, or when R_7 is a -CH_3, each hydrogen atom may be replaced to form a -CD_3. Similarly, another non-limiting example includes when X and/or Y is a -CH_3, each hydrogen atom may be replaced to form a -CD_3.

In some embodiments, the compounds of Formula I are selected from compounds of Formula IA:



Formula IA

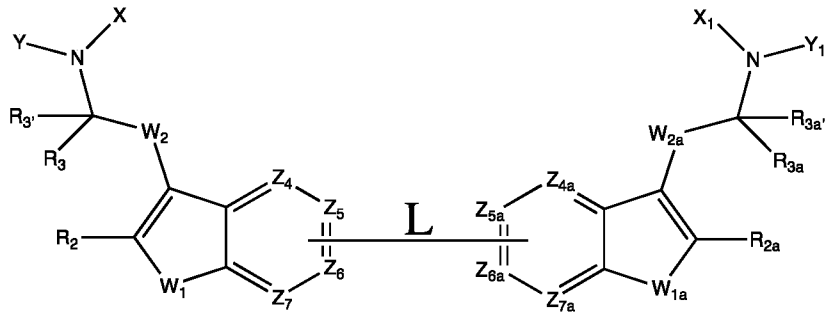
wherein Group B, linker L, X, Y, W_1, W_2, R_2, R_3, $R_{3'}$, Z_4, Z_5, Z_6, and Z_7 are as defined herein

and wherein L can replace a hydrogen in a R_4 group when Z_4 is CR_4, a hydrogen in a R_5 group when Z_5 is CR_5, a hydrogen in a R_6 group when Z_6 is CR_6, or a hydrogen in a R_7 group when Z_7 is CR_7,

and wherein L can replace X or a hydrogen atom in a R_2 group.

For the avoidance of doubt, linker L is not attached to Z_4, Z_5, Z_6, or Z_7 when they are N.

In some embodiments, the compounds of Formula I are selected from compounds of Formula IB:



Formula IB

wherein Lis a covalent linker;

X, X_1, Y and Y_1 for each occurrence are independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl, or Y or Y_1 is taken together with X or X_1, respectively, and the nitrogen atom therebetween to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

W_1 and W_{1a} are independently selected from NR_1, O, S, S(O), SO_2, Se, Se(O), and SeO_2;

W_2 and W_{2a} are independently selected from -CD_2-, -CHD-, –$(CD_2)_2$-, -CH_2-, and –$(CH_2)_2$-;

Z_4 and Z_{4a} are independently selected from N and CR_4;

Z_5 and Z_{5a} are independently selected from N and CR_5;

Z_6 and Z_{6a} are independently selected from N and CR_6;

Z_7 and Z_{7a} are independently selected from N and CR_7;

R_1 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, -$C(O)R_8$, -$C(O)OR_8$, -$OP(O)(OR_9)_2$, -$C(O)N(R_9)_2$, -SOR_8, and -SO_2R_8;

R_2, R_3, R_6, R_7, R_{2a}, R_{3a}, $R_{3'}$ and $R_{3a'}$ for each occurrence are independently selected from hydrogen, deuterium, -$N(R_9)_2$, -SR_9, halo, optionally substituted C_1-C_8 alkyl, -C_1-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl,

or Y or Y_1 is absent and R_3 or R_{3a} is taken together with carbon to which it is attached and the nitrogen atom to which X or X_1, respectively, is attached to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9,

or X or X_1 is absent and R_2 or R_{2a}, respectively, is taken together with carbon to which it is attached and the nitrogen atom to which Y or Y_1 is attached to form a 5- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

R_4 and R_5 for each occurrence are independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, -$N(R_9)_2$, -SR_9, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8;

R_8 for each occurrence is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

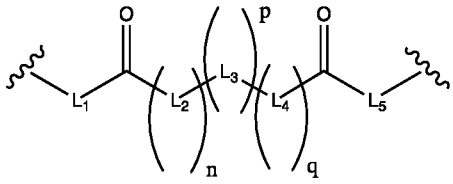
R_9 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

and wherein L can replace a hydrogen in a R_4 group when Z_4 and/or Z_{4a} is CR_4, a hydrogen in a R_5 group when Z_5 and/or Z_{5a} is CR_5, a hydrogen in a R_6 group when Z_6 and/or Z_{6a} is CR_6, or a hydrogen in a R_7 group when Z_7 and/or Z_{7a} is CR_7,

and wherein L can replace X or a hydrogen atom in a R_2 group.

For the avoidance of doubt, linker L is not attached to Z_4, Z_{4a}, Z_5, Z_{5a}, Z_6, Z_{6a}, Z_{7a}, or Z_7 when they are N.

In some embodiments, the linker "L" is selected from Formula IV:



Formula IV

wherein L_1, L_2, L_3, L_4, L_5, n, p, and q are as defined herein.

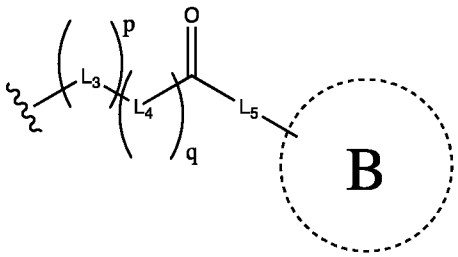
In some embodiments, L_1 and L_5 for each occurrence are independently selected from a covalent bond, O, NR_{10}, and S. In some embodiments, L_1 and L_5 are the same. In some embodiments, L_1 and L_5 are different. In some embodiments, L_1 and L_5 are both O. In some embodiments, L_1 and L_5 both represent covalent bonds.

In some embodiments, L_2 and L_4 for each occurrence are independently selected from a O, $C(R_{10})_2$, NR_{10}, and S. In some embodiments, L_2 and L_4 are the same. In some embodiments, L_2 and L_4 are different. In some embodiments, L_2 and L_4 are O. In some embodiments, L_2 and L_4 are independently selected from O and $C(R_{10})_2$ for each occurrence. In some embodiments, at least one of L_2 or L_4 is $C(R_{10})_2$.

In some embodiments, L_3 for each occurrence are independently selected from O, NR_{10}, S, $C(R_{10})_2$, $C(R_{10})=C(R_{10})$, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl. In some embodiments, L_3 for each occurrence is selected from S and $C(R_{10})_2$. In some embodiments, L_3 for each occurrence is S. In some embodiments, L_3 for each occurrence is selected from $C(R_{10})_2$.

In some embodiments, R_{10} for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, NO_2, $-N(R_9)_2$, $-SR_9$, halo, hydroxyl, $-C_1$-C_8 alkoxy, $-OC(O)R_8$, $-OC(O)OR_8$, $-OP(O)(OR_9)_2$, and $-OSO_2R_8$, wherein R_8 and R_9 are as defined herein. In some embodiments, R_{10} is hydrogen for each occurrence. In some embodiments, R_{10} is independently selected from hydrogen and methyl for each occurrence.

In other embodiments, R_{10} may be independently selected from any of the variables listed in the preceding paragraph and a structure of Formula IVA:



Formula IVA

wherein L_3, L_4, L_5, p, q, and Group B are as defined herein.

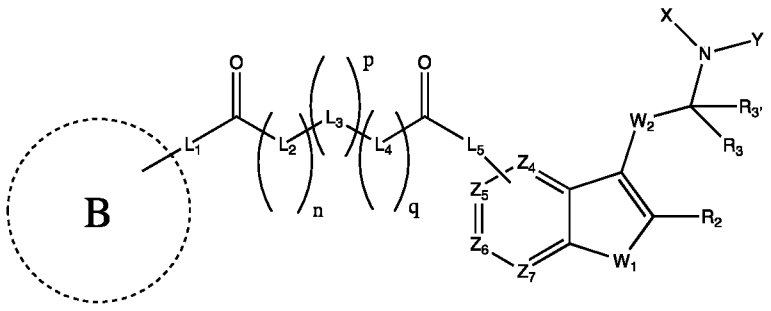
In some embodiments, when one R_{10} comprises a structure of Formula IVA, the compound of Formula I may be referred to as a "tripodal" derivative (*see, e.g.*, Compound [IIq] below). In some embodiments, when two of R_{10} comprises a structure of Formula IVA, the compound may be referred to as a "tetrapodal" derivative (*see, e.g.*, Compound [IIr] below).

In some embodiments, n is selected from 0 to 10, such as 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10. In some embodiments, n is 0. In some embodiments, n is 1. In some embodiments, n is 3.

In some embodiments, p is selected from 0 to 10, such as 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10. In some embodiments, p is 0. In some embodiments, p is 2.

In some embodiments, q is selected from 0 to 10, such as 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10. In some embodiments, q is 0. In some embodiments, q is 3. In some embodiments, q is 1.

In some embodiments, the compounds described herein are selected from Formula IC:



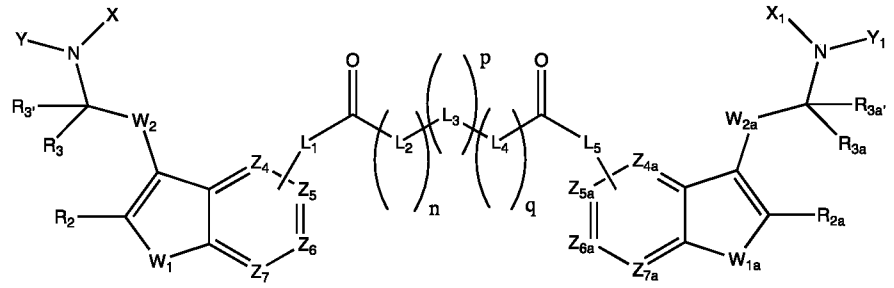
Formula IC

wherein Group B, X, Y, W_1, W_2, R_2, R_3, $R_{3'}$, Z_4, Z_5, Z_6, Z_7, L_1, L_2, L_3, L_4, L_5, n, p, q are as defined herein, and

wherein L_5 can replace a hydrogen in a R_4 group when Z_4 is CR_4, a hydrogen in a R_5 group when Z_5 is CR_5, a hydrogen in a R_6 group when Z_6 is CR_6, or a hydrogen in a R_7 group when Z_7 is CR_7,

and wherein L can replace X or a hydrogen atom in a R_2 group.

In some embodiments, the compounds described herein are selected from Formula ID:



Formula ID

wherein X, Y, W_1, W_{1a}, W_2, W_{2a}, R_2, R_{2a}, R_3, R_{3a}, $R_{3'}$, $R_{3a'}$, Z_4, Z_{4a}, Z_5, Z_{5a}, Z_6, Z_{6a}, Z_7, Z_{7a}, L_1, L_2, L_3, L_4, L_5, n, p, and q are as defined herein,

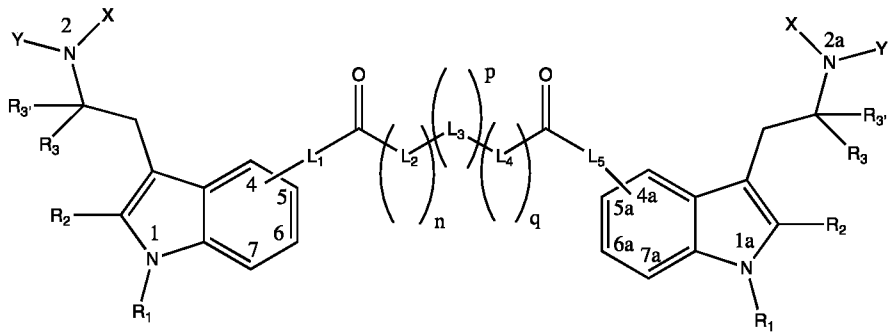
and wherein L_1 can replace a hydrogen in a R_4 group when Z_4 is CR_4, a hydrogen in a R_5 group when Z_5 is CR_5, a hydrogen in a R_6 group when Z_6 is CR_6, or a hydrogen in a R_7 group when Z_7 is CR_7,

and wherein L_1 can replace X or a hydrogen atom in a R_2 group,

and wherein L_5 can replace a hydrogen in a can replace a hydrogen in a R_4 group when Z_{4a} is CR_4, a hydrogen in a R_5 group when Z_{5a} is CR_5, a hydrogen in a R_6 group when Z_{6a} is CR_6, a hydrogen in a R_7 group when Z_{7a} is CR_7,

and wherein L_5 can replace X or a hydrogen atom in a R_2 group.

In some embodiments, the compounds described herein are selected from Formula IE:



Formula IE

wherein X, Y, R_1, R_2, R_3, $R_{3'}$, L_1, L_2, L_3, L_4, L_5, n, p, and q are as defined herein

and wherein L_1 is connected to the 4, 5, 6, or 7 carbon when L_1 replaces the hydrogen on that carbon

or L_1 is connected to the 1 or 2 nitrogen when R_1 or X is absent, respectively,

and wherein L_5 is connected to the 4a, 5a, 6a, or 7a carbon when L_5 replaces the hydrogen on that carbon

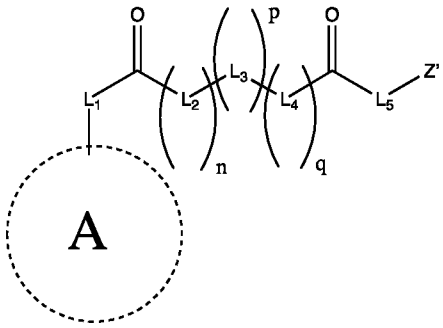
or L_5 is connected to the 1a or 2a nitrogen when R_1 or X is absent.

In some embodiments for compounds of Formula IE, the linker on one end is connected to the first indole skeleton by a covalent bond between L_1 and the 4, 5, 6, or 7 carbon of the indole skeleton. In some embodiments, L_1 is a covalent bond and the carbonyl of the linker is connected to the 4, 5, 6, or 7 carbon of the indole skeleton. Alternatively, in some embodiments, L_1 is a covalent bond and the carbonyl of the linker is connected to the 1 or 2 nitrogen, wherein R_1 or X is absent.

In some embodiments, the opposing end of the linker is connected to Group B by a covalent bond between L_5 and the 4a, 5a, 6a, or 7a carbon of the indole skeleton. In some embodiments, the opposing end of the linker is connected to Group B by a covalent bond between the C(=O) of the linker and the 4a, 5a, 6a, or 7a carbon of the indole skeleton. Alternatively, in some embodiments when L_5 is a covalent bond, the other end of the linker is connected to the indole by a covalent bond between the C(=O) of the linker and the 1a or 2a nitrogen, wherein R_1 or X is absent.

In certain embodiments, one or more hydrogen atoms on compounds of Formulae I, II, III, and/or V may be replaced with one or more deuterium atoms. For example, in certain embodiments, R_7 may comprise a deuterium atom as a replacement for a hydrogen, or when R_7 is a $-CH_3$, each hydrogen atom may be replaced to form a $-CD_3$. Similarly, another non-limiting example includes when X and/or Y is a $-CH_3$, each hydrogen atom may be replaced to form a $-CD_3$.

In some embodiments are described compounds of Formula V:



Formula V

wherein Group A, L_1, L_2, L_3, L_4, L_5, n, p, q, and Z' are as defined herein.

In some embodiments, Z' is selected from hydrogen, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and, when L_5 is O, then Z' can also be selected from X^+, wherein X^+ is a pharmaceutically acceptable cation. Exemplary X+ cations include, but are not limited to, NH_4+, K+, Na+, Ca+, etc. In some embodiments, Group A is a residue of a cannabinoid, such as Delta-8-THC, Delta-9-THC, THCA, THCV, THCVA, CBC, CBCA, CBCV, CBCVA, CBD, CBDA, CBDV, CBDVA, CBG, CBGA, CBGV, or CBGVA. In certain embodiments when A is a cannabinoid, L_1 is an oxygen derived from the phenolic oxygen of the cannabinoid. In some embodiments, L_5 is oxygen. In some embodiments, the sum of n, p, and q is greater than 2. In some embodiments, the sum of n, p, and q is an integer selected from 3 to about 16, such as 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 14, or 16. In some embodiments, L_2 and L_4 are both -CH_2- and L_3 is selected from -CH=CH- and -CH_2-.

In certain embodiments, it has been surprisingly discovered that compounds of Formula V wherein the sum of n, p, and q is greater than 2 can "self-cleave" rapidly *in vivo* to provide the active compound (*e.g.*, Delta-9-THC from prodrug Compound Vd described below). Without being bound to any particular theory, it is believed compounds in which the sum of n, p, and q is less than 3 do not effect such rapid self-cleavage *in vivo*, because doing so requires the intramolecular formation of a constrained ring of 5 atoms or less, which is suboptimal to a more flexible ring of 6 or greater that is formed with the sum of n, p, and q is 3 or greater.

In certain embodiments, Group A in the compounds of Formula I and/or V is a residue of a 5-HT1A agonist selected from buspirone (8-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]-8 -azaspiro[4.5]decane-7,9-dione) or its enolate (enol alcohol) equivalent, 5-OH-buspirone, 6-OH-buspirone, tandospirone ((1R,2R,6S,7S)-4-{4-[4-(pyrimidin -2-yl)piperazin-1-yl]butyl}-4-azatricyclo[5.2.1.02,6]decane-3,5-dione), gepirone (4,4-dimethyl-1-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]piperid- ine-2,6-dione), alnespirone ((+)-4-dihydro-2H-chromen-3-yl]-propylamino]butyl]-8-azaspiro[4.5]decane-- 7,9-dione), binospirone (8-[2-(2,3-dihydro-1,4-benzodioxin-2-ylmethylamino)ethyl]-8-azaspiro[4.5]- decane-7,9-dione), ipsapirone (9,9-dioxo-

8-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]-9.lamda.6-thia-8-a- zabicyclo[4.3.0]nona-1,3,5-trien-7-one), perospirone (3aR, 7aS) -2-{4-[4-(1,2-benzisothiazol-3-yl)piperazin-1-yl]butyl} hexahydro-1H-isoindole-1,3(2H)-dione, befiradol (F-13,640) (3-chloro-4-fluorophenyl-[4-fluoro-4-([(5-methylpyridin-2 -yl)methylamino]methyl)piperidin-1-yl]methanone, repinotan ((R)-(-)-2-[4-[(chroman-2 -ylmethyl)-amino]-butyl]-1,1-dioxo-benzo[d] isothiazolone), piclozotan (3-chloro-4-[4-[4-(2-pyridinyl)-1,2,3,6-tetrahydropyridin-1-yl]butyl]-1,4- -benzoxazepin-5(4H)-one), osemozotan (5-(3-[((2S)-1,4-benzodioxan-2-ylmethyl)amino]propoxy)-1,3-benzodioxole), flesinoxan (4-fluoro-N-[2-[4-[(3S)-3-(hydroxymethyl)-2,3-dihydro-1,4 -benzodioxin-8-yl]piperazin-1-yl]ethyl]benzamide), flibanserin (1-(2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,3-dihydro-2H-- benzimidazol-2-one), 8-OH-DPAT (7-(Dipropylamino)-5,6,7,8-tetrahydronaphthalen-1-ol), and sarizotan (EMD-128,130) (1-[(2R)-3,4-dihydro-2H-chromen-2-yl]-N-([5-(4 -fluorophenyl)pyridin-3-yl]methyl)methanamine), or a prodrug, salt, or derivative thereof. In certain embodiments, Group B in the compounds of Formula I is a residue of a 5-HT1A agonist selected from the 5-HT1A agonists above.

In certain embodiments, Group A in the compounds of Formula I and/or V is a residue of a serotonin 5-HT2B receptor antagonist selected from agomelatine, amisulpride, ariprazole, carprazine, clozapine, cyproheptadine, mCCP, sarpogrelate, lisuride, tegasurod, metadoxine, and promethazine. In certain embodiments, Group B in the compounds of Formula I is a residue of a serotonin 5-HT2B receptor antagonist selected from the 5-HT2B receptor antagonists above.

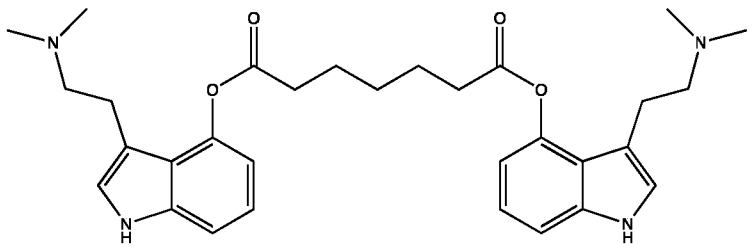
In certain embodiments, Group A in the compounds of Formula I and/or V is a residue of a 5-HT2C receptor agonist selected from lorcaserin, vabicaserin, aripiprazole, YM-348, PRX-00933, and meta-chlorophenylpiperazine. In certain embodiments, Group B in the compounds of Formula I is a residue of a 5-HT2C receptor agonist selected from the 5-HT2C receptor agonists above.

In certain embodiments, Group A in the compounds of Formula I and/or V is a residue of a serotonergic drug selected from any serotonergic drug listed herein. In certain embodiments, Group B in the compounds of Formula I is a residue of a serotonergic drug selected from any serotonergic drug listed herein. In certain embodiments, Group A in the compounds of Formula I and/or V is a residue of an antidepressant drug selected from any antidepressant drug listed herein. In certain embodiments, Group B in the compounds of Formula I is a residue of an antidepressant drug selected from any antidepressant drug listed herein.

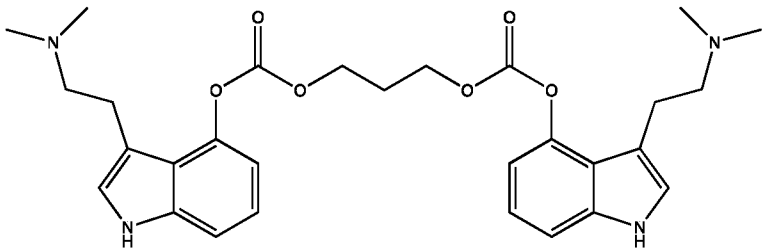
In certain embodiments, Group B in the compounds of Formula I and/or V is a residue of an adrenergic drug selected from any adrenergic drug listed herein. In certain embodiments, Group B in the compounds of Formula I and/or V is a residue of a dopaminergic drug selected

from any dopaminergic drug listed herein. In certain embodiments, Group B in the compounds of Formula I and/or V is a residue of an anxiolytic drug selected from any anxiolytic drug listed herein.

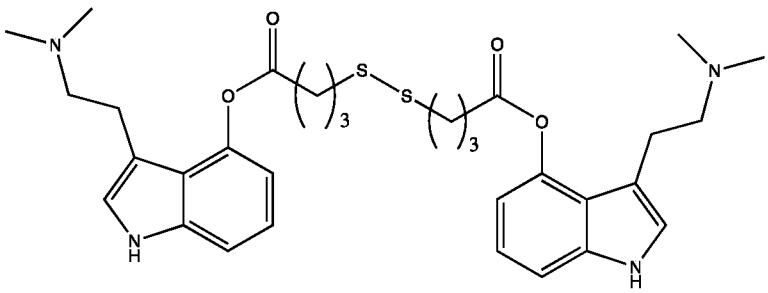
Exemplary compounds of Formula I include, but are not limited to, Dipsilocin™ variants set forth below:



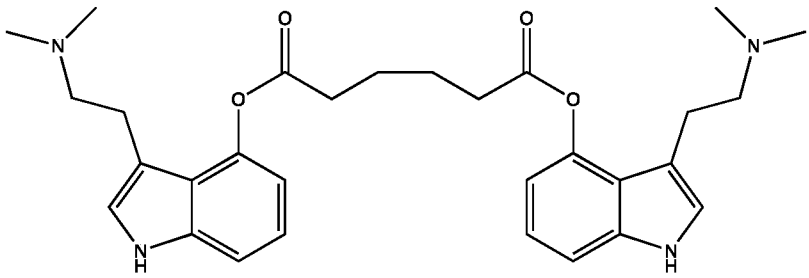
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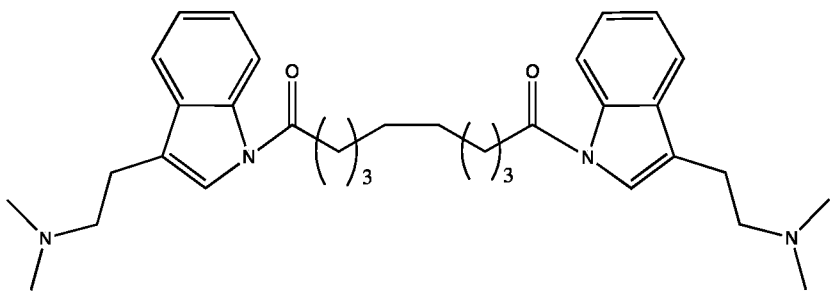
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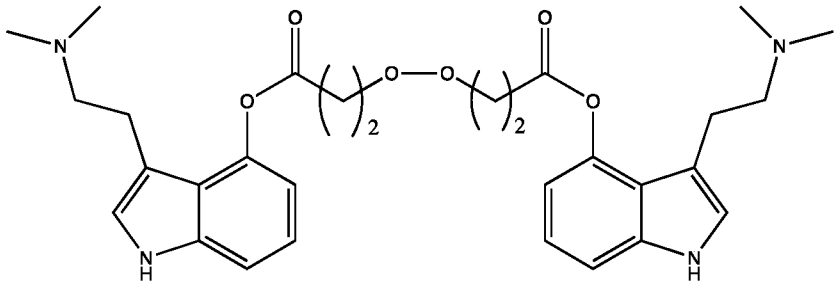
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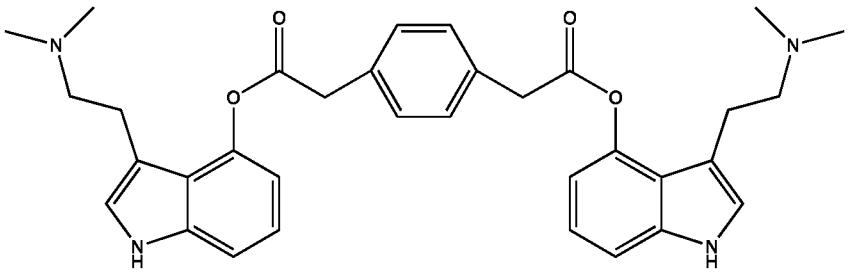
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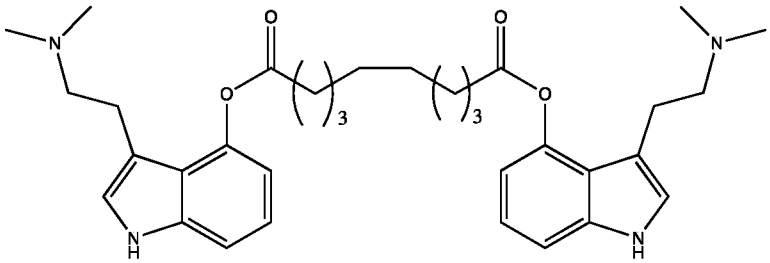
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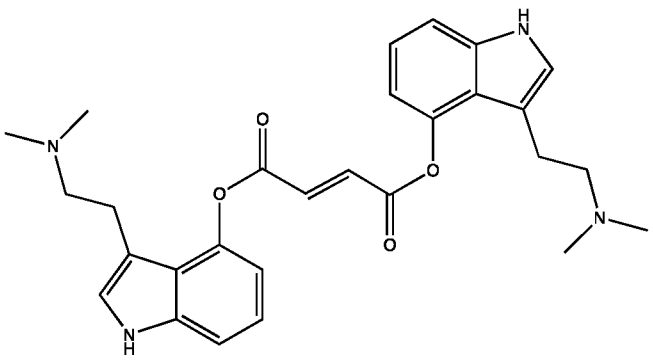
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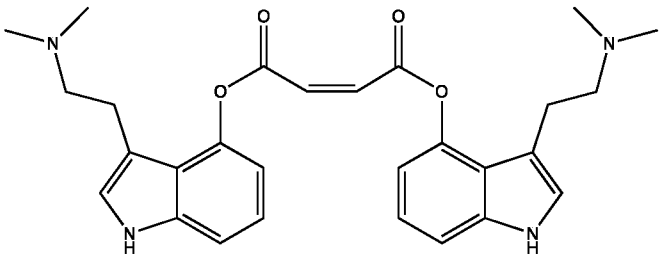
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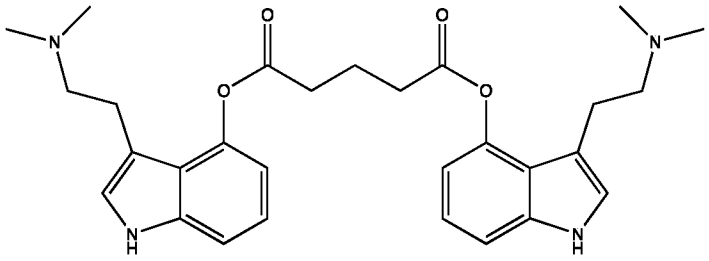
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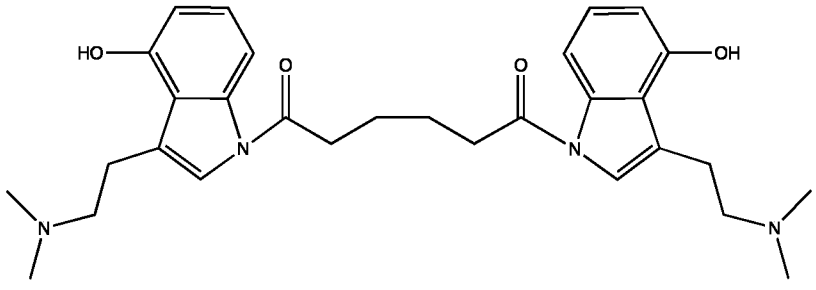
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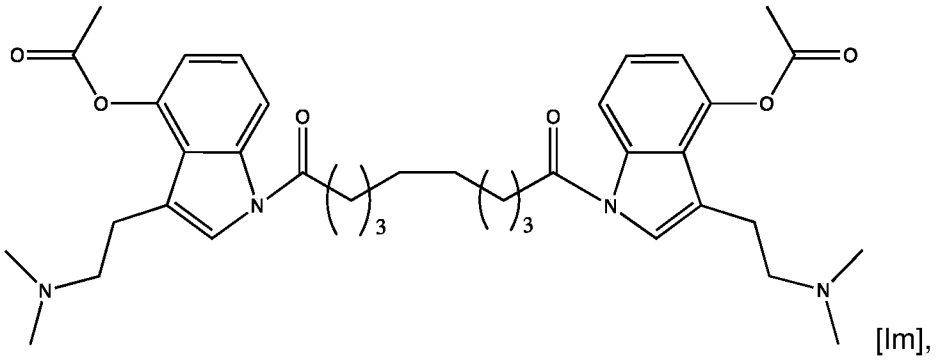
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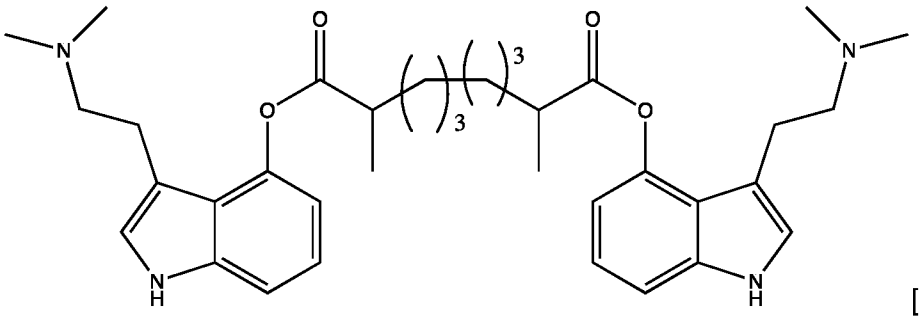
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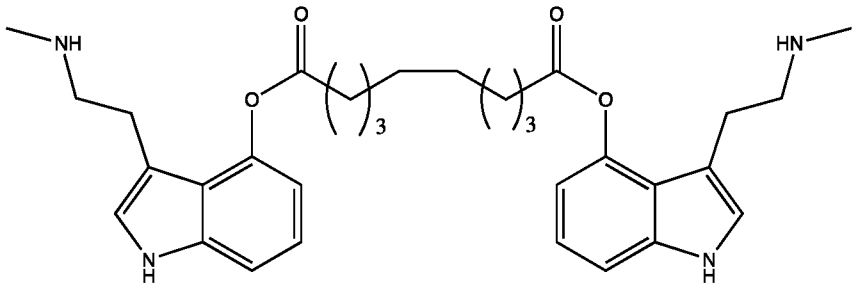
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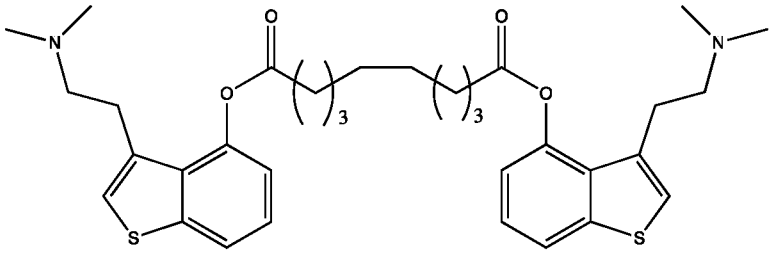
[In],

and salts, solvates, hydrates, and prodrugs of any of compounds [Ia] through [In].

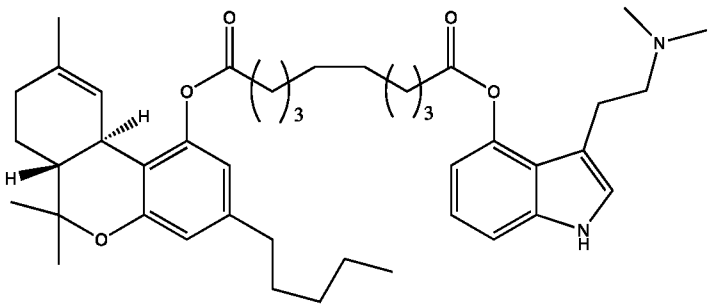
Other exemplary compounds of Formula I include:



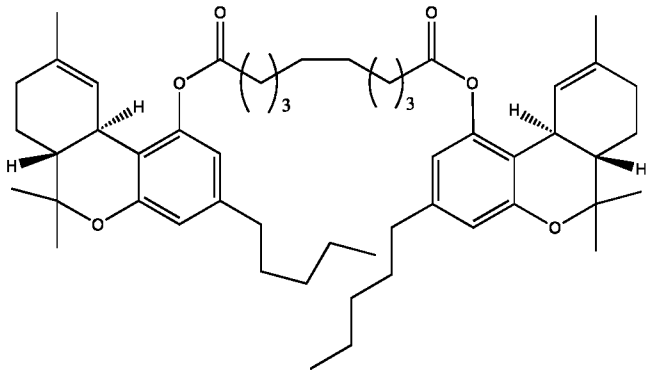
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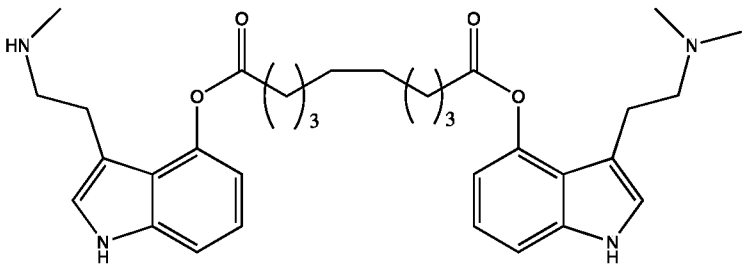
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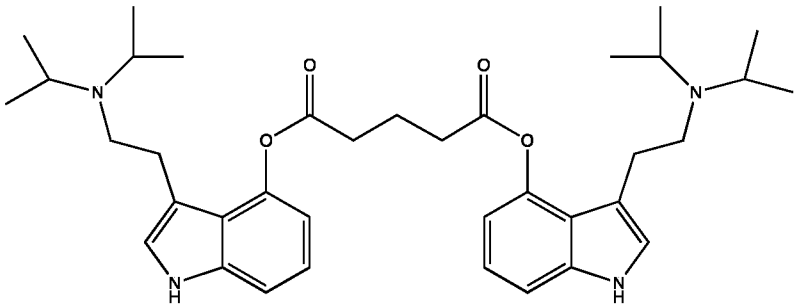
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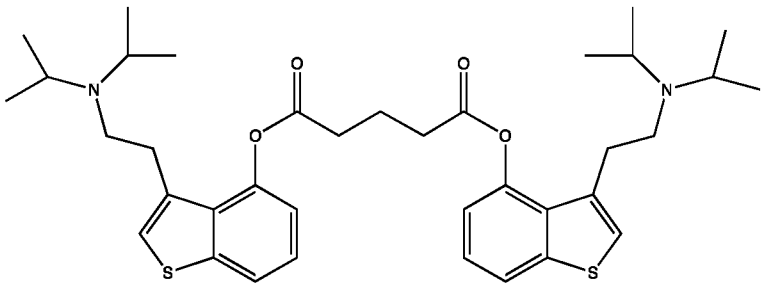
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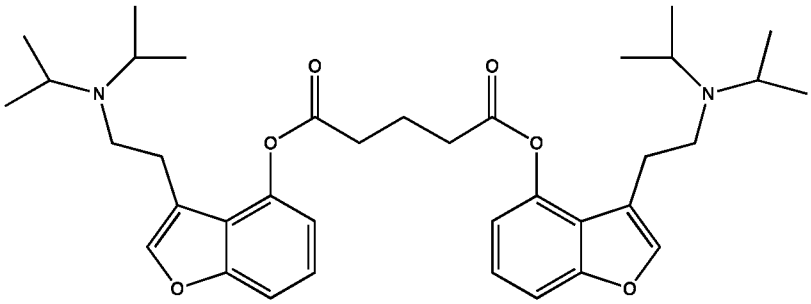
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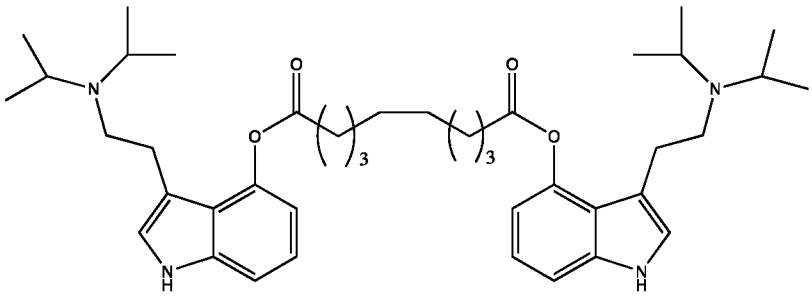
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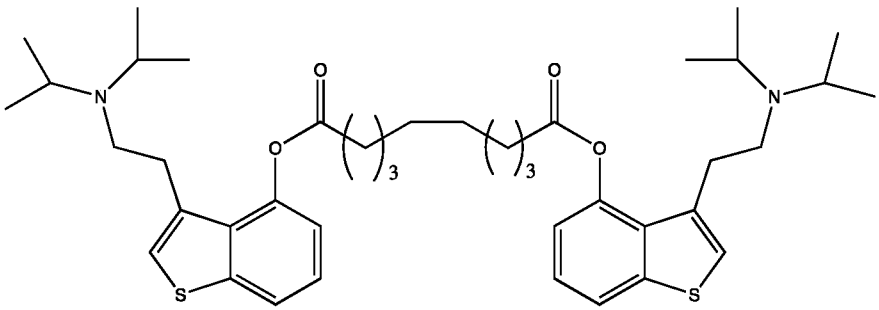
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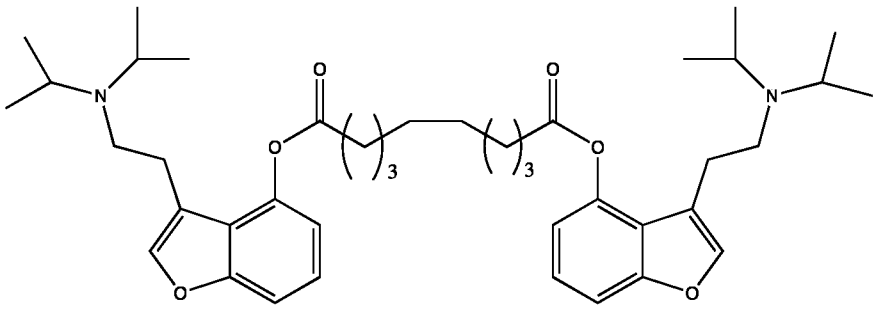
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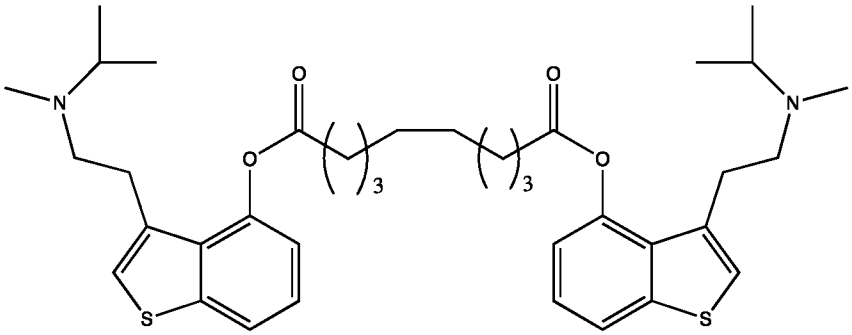
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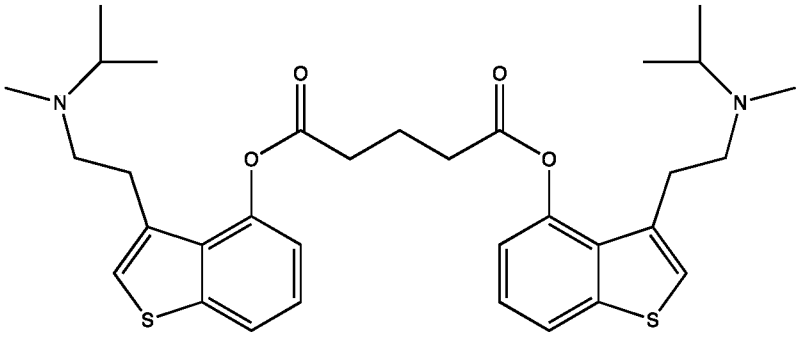
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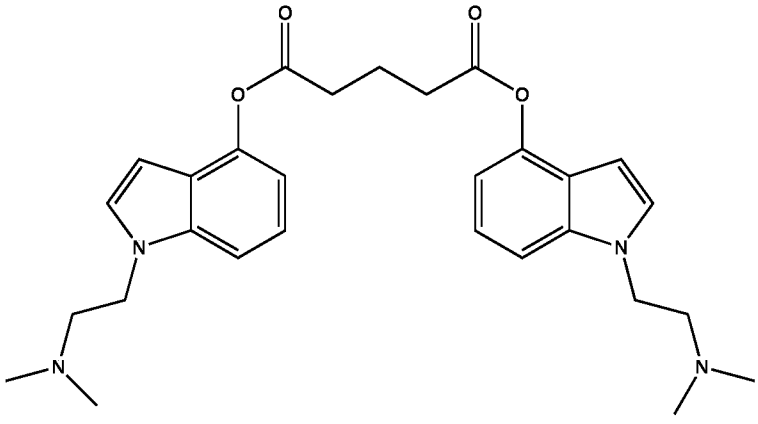
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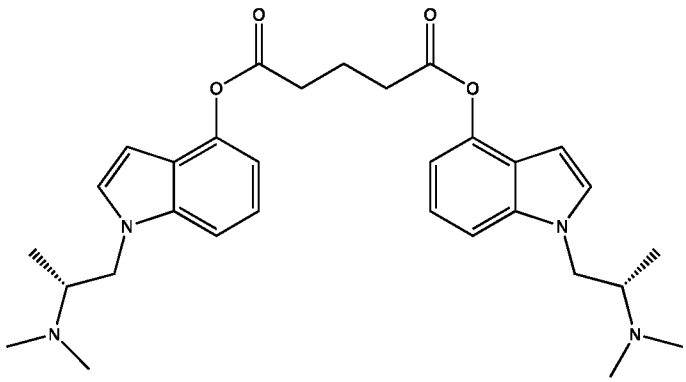
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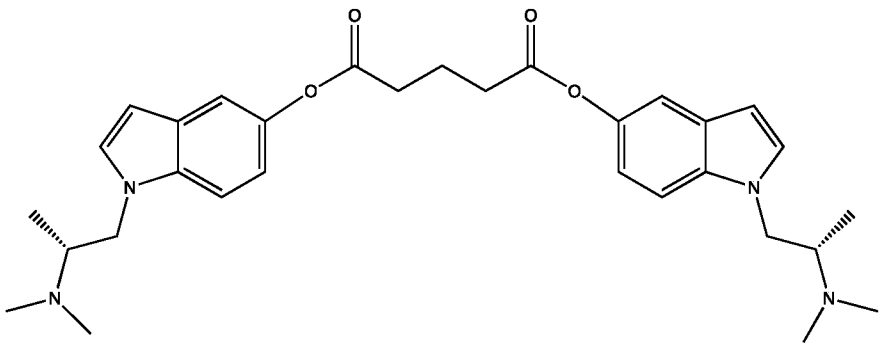
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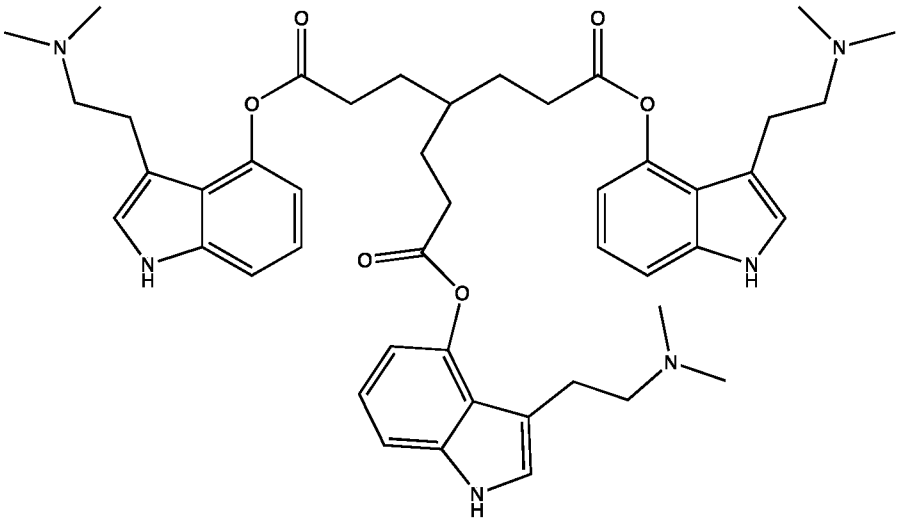
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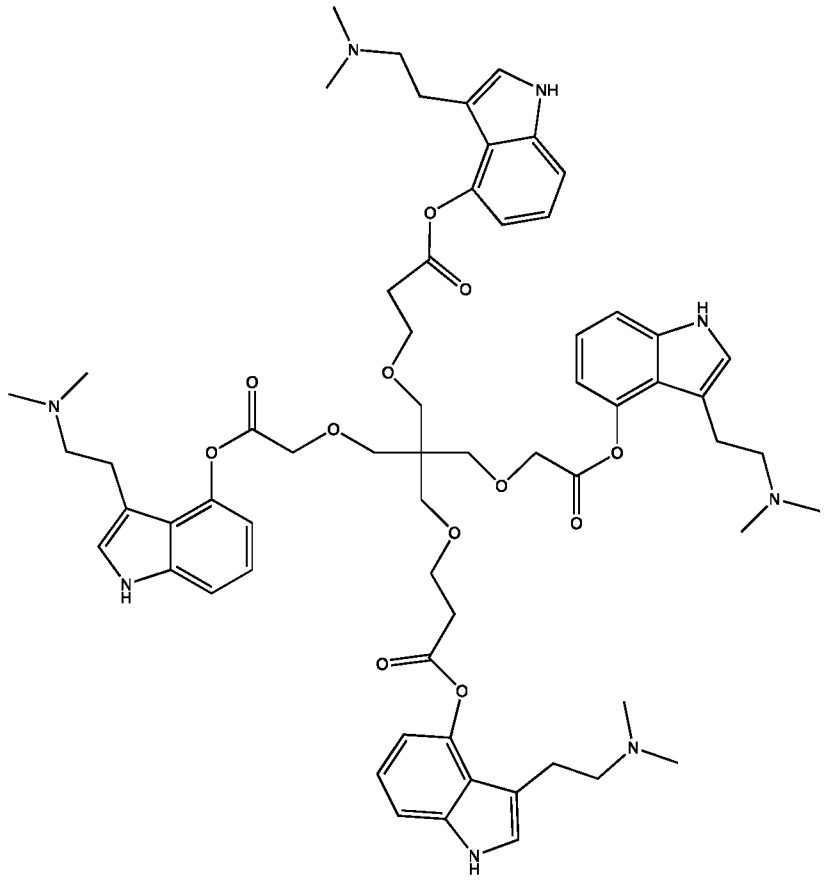
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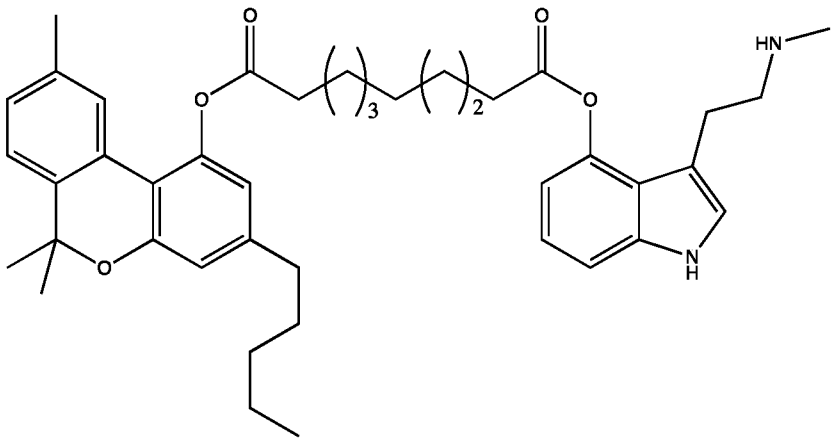
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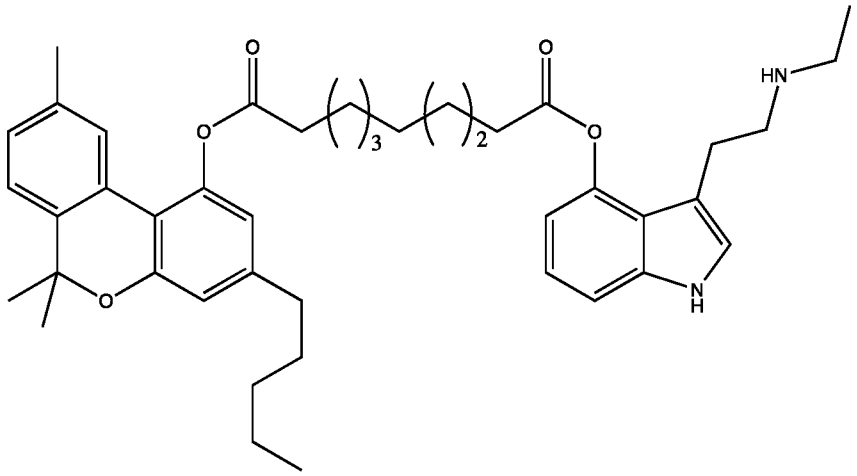
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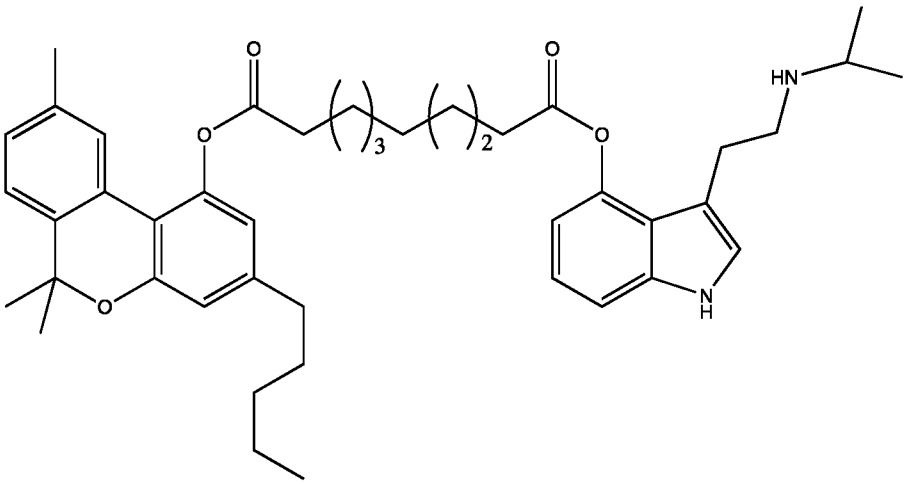
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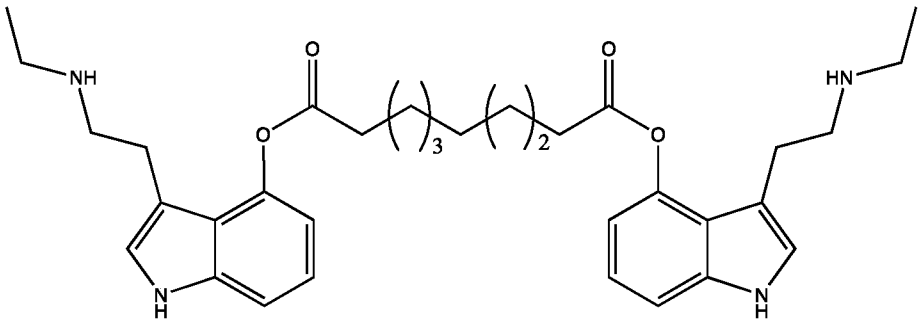
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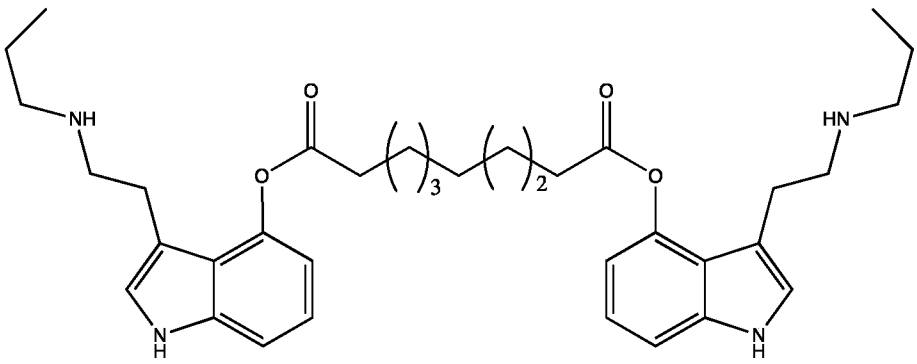
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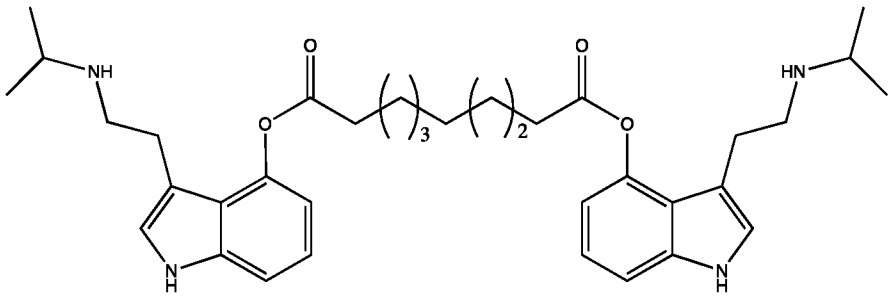
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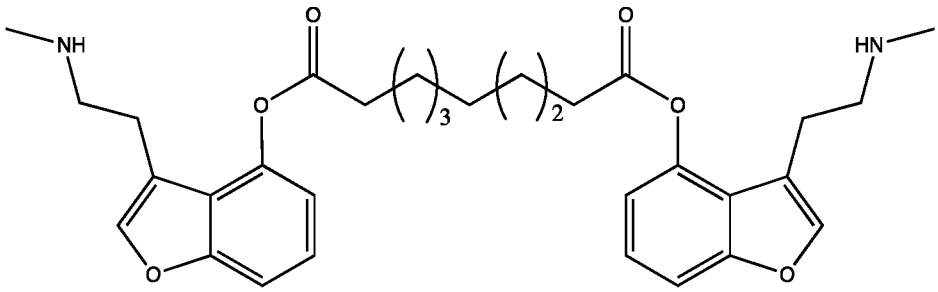
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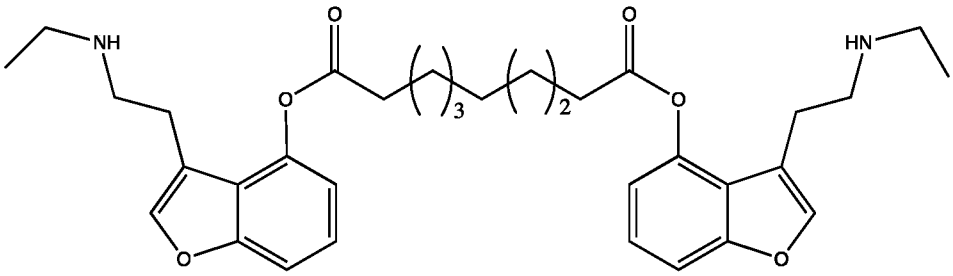
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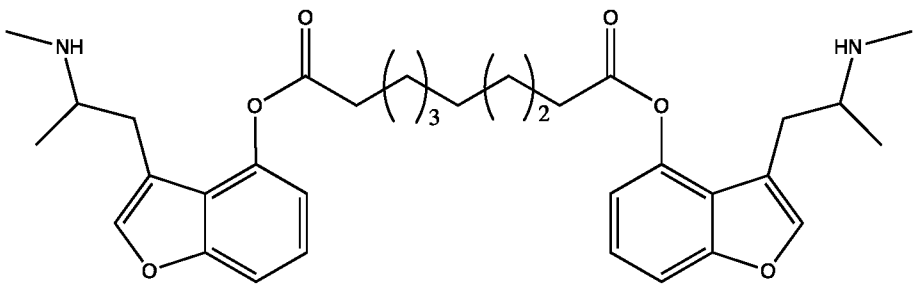
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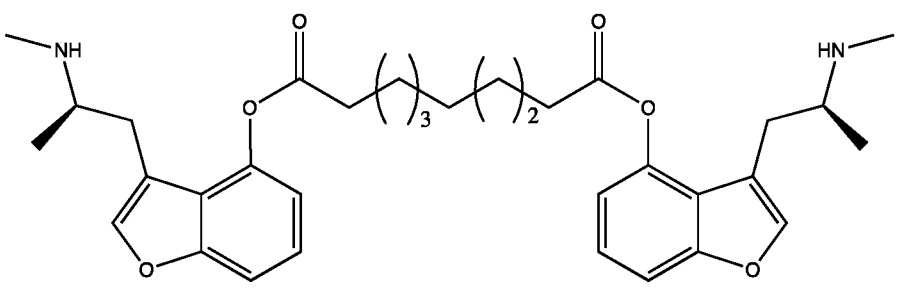
[IIz]

and salts, solvates, hydrates, and prodrugs of any of compounds [IIa] through [IIz].

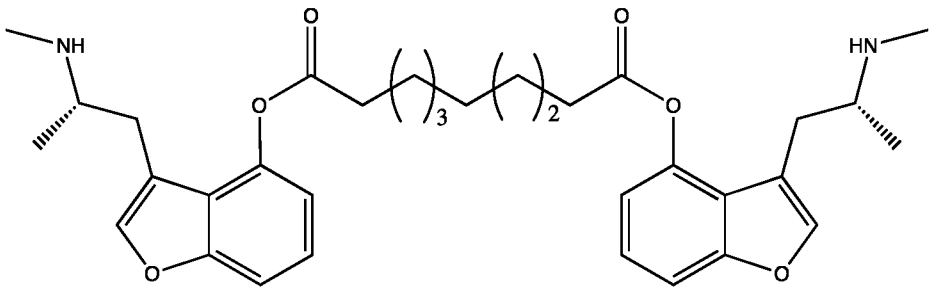
Other exemplary compounds of Formula I include:



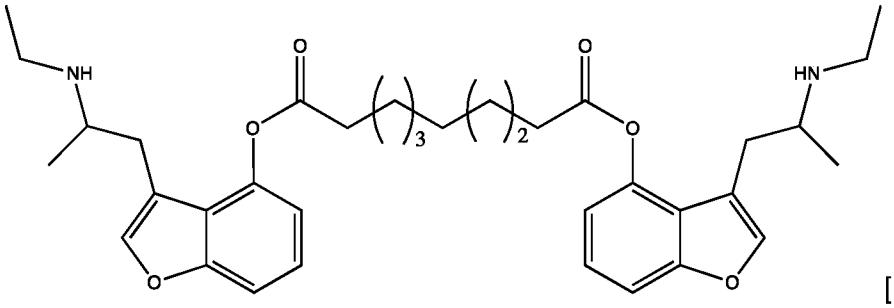
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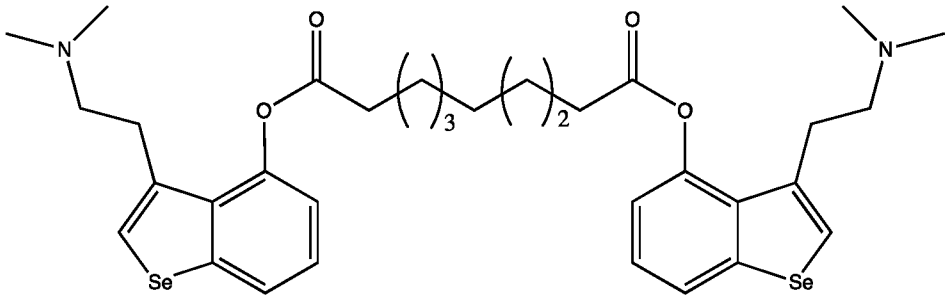
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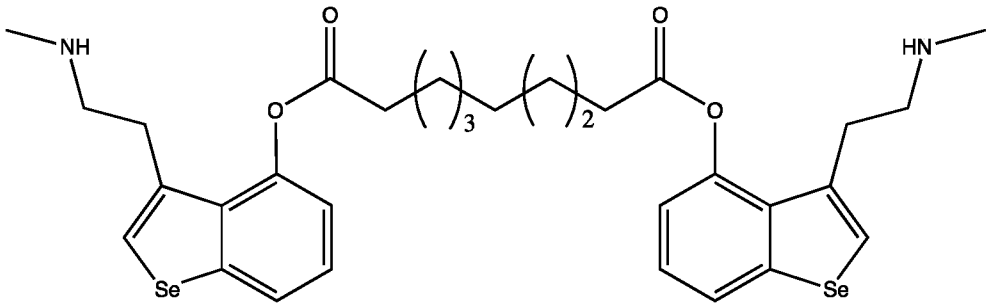
[IIIc],



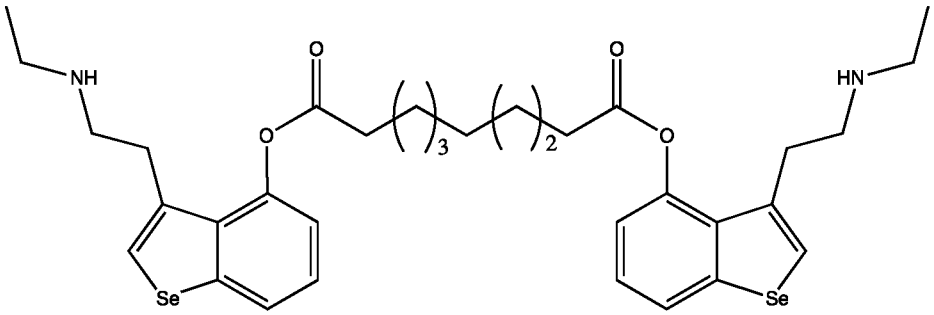
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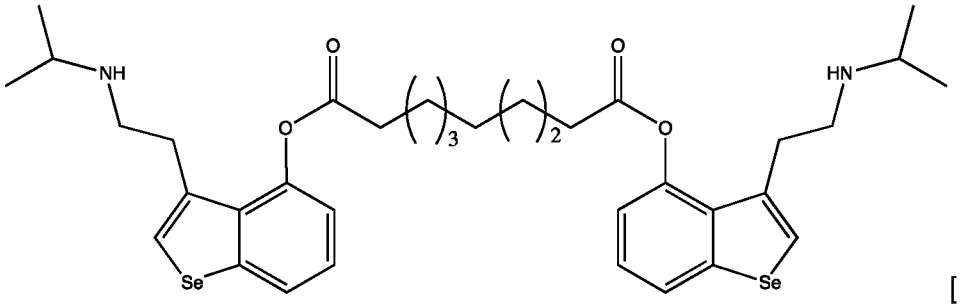
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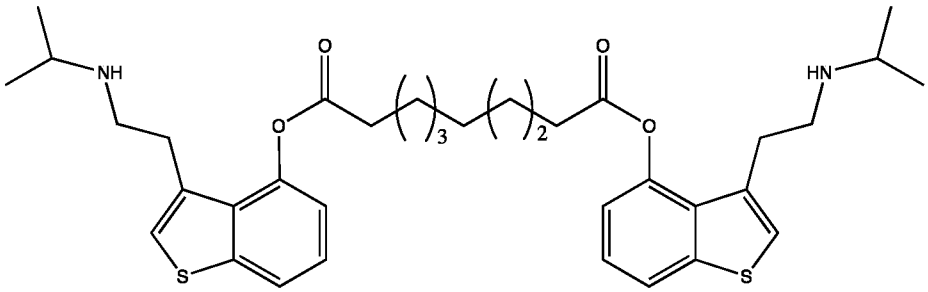
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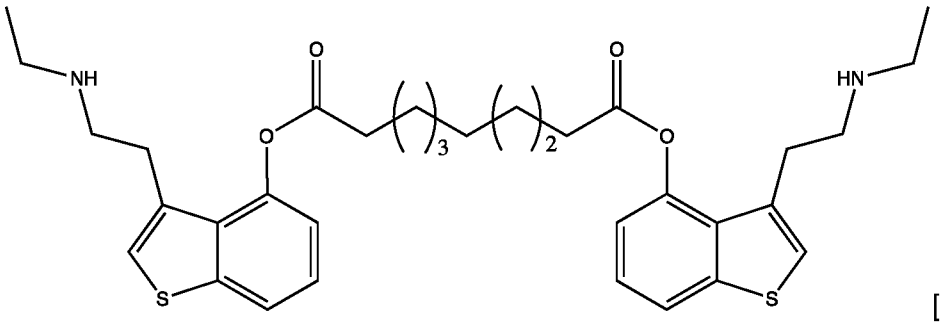
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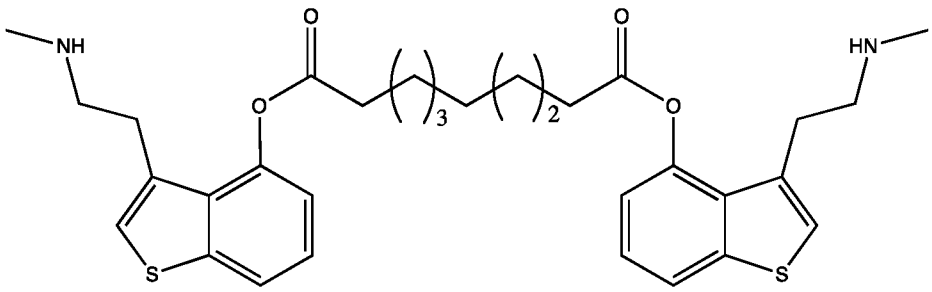
[IIIh],



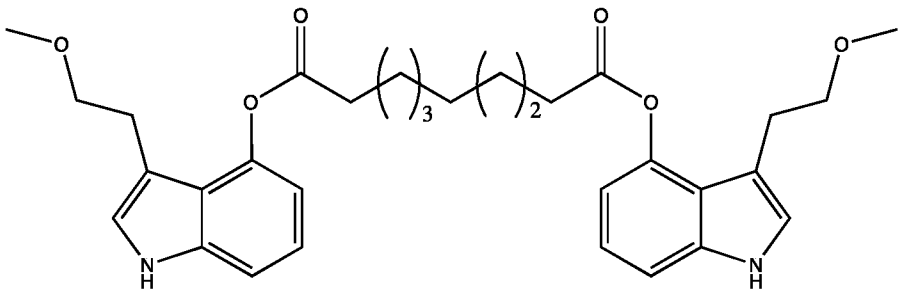
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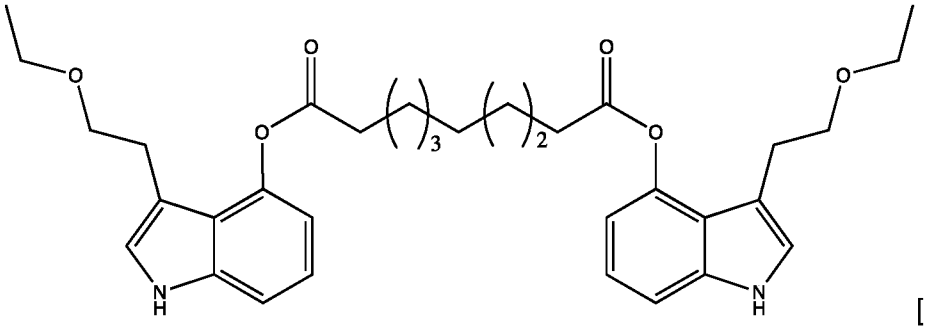
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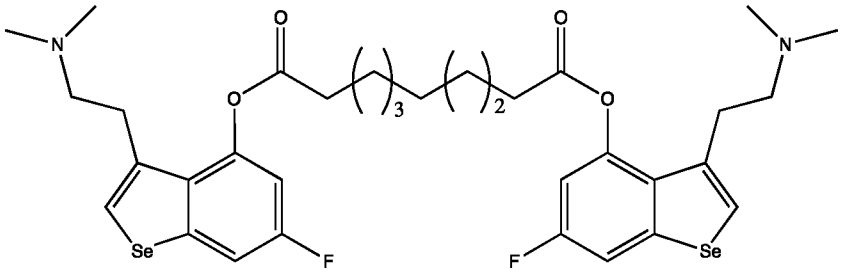
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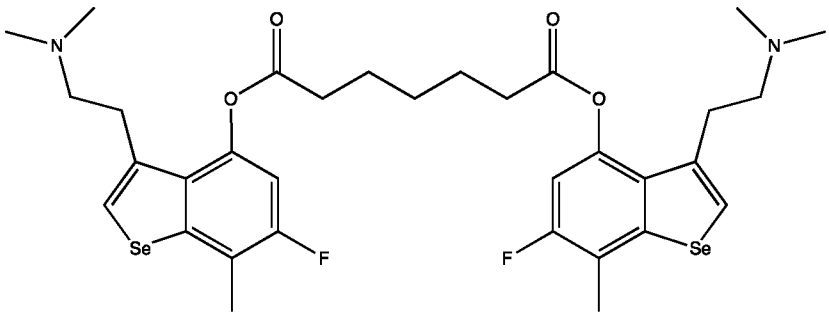
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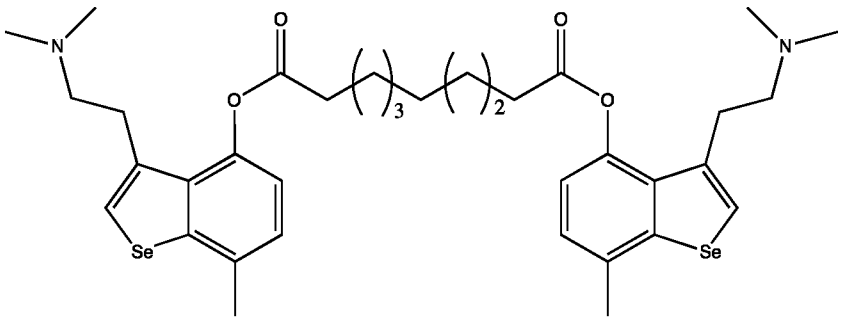
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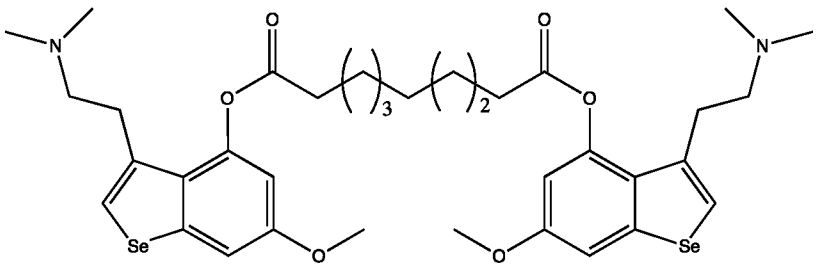
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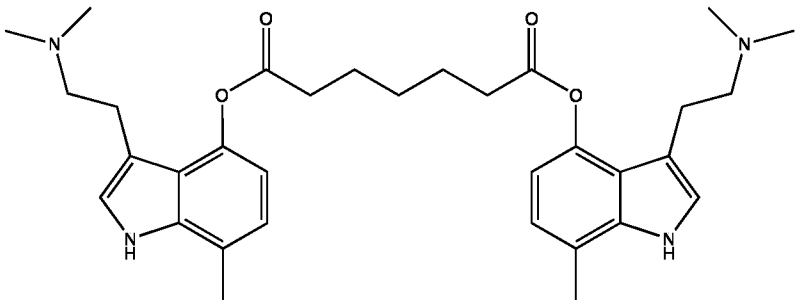
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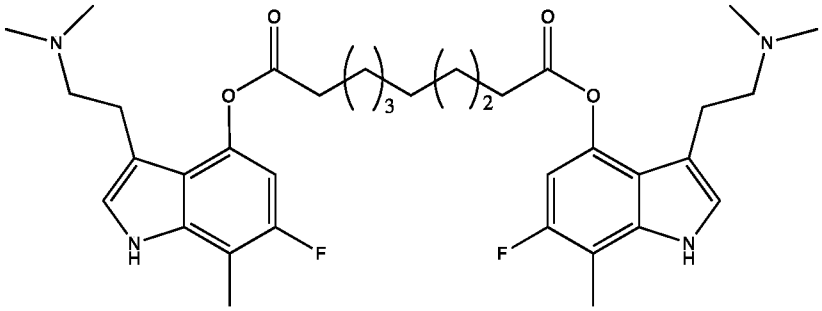
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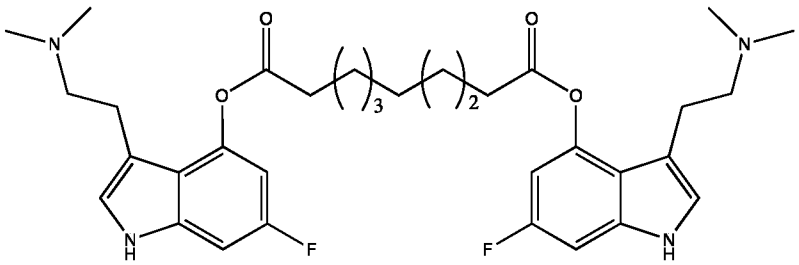
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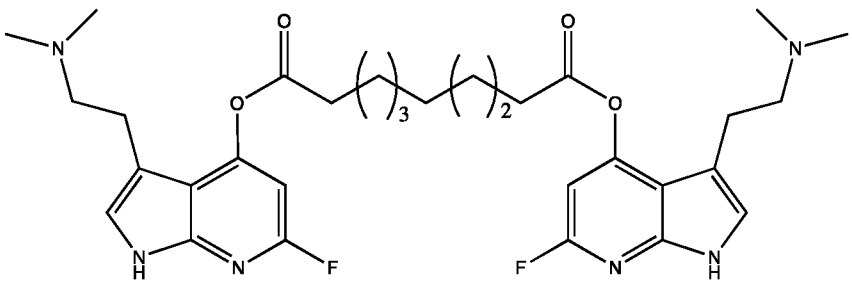
[IIIr],



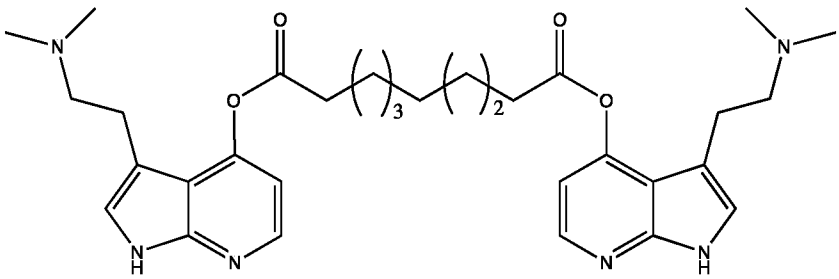
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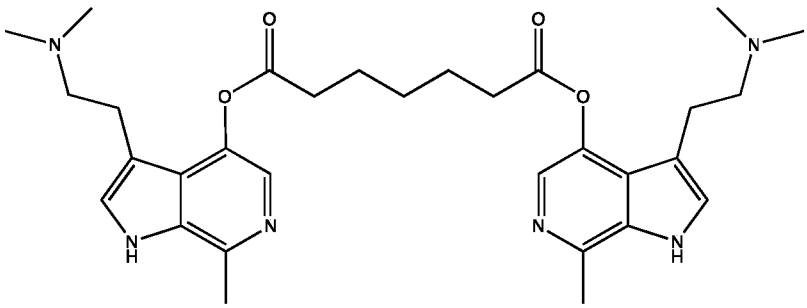
[IIIt],



[IIIu],



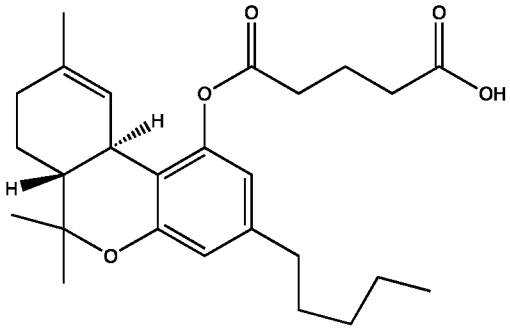
[IIIv],



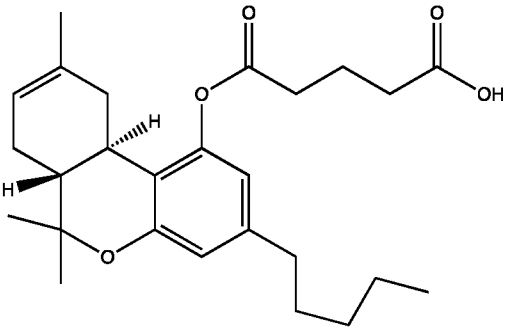
[IIIw],

and salts, solvates, hydrates, and prodrugs of any of compounds [IIIa] through [IIIw].

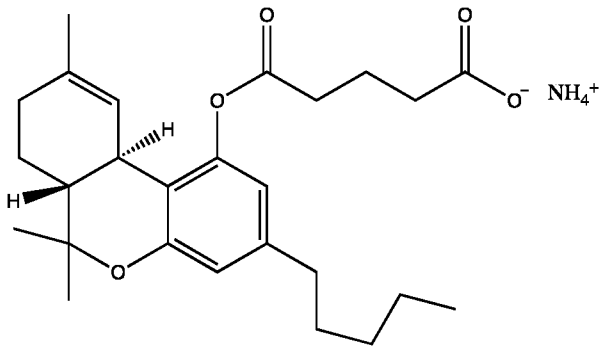
In some embodiments are described compounds of Formula V, including but not limited to:



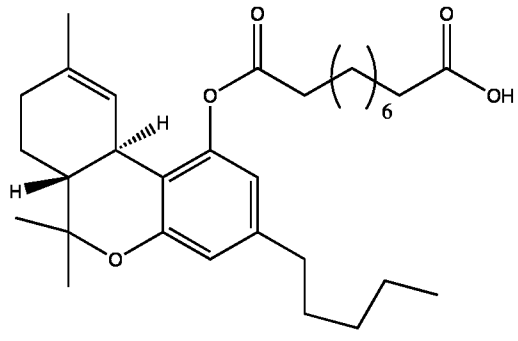
[Va],



[Vb],



[Vc],

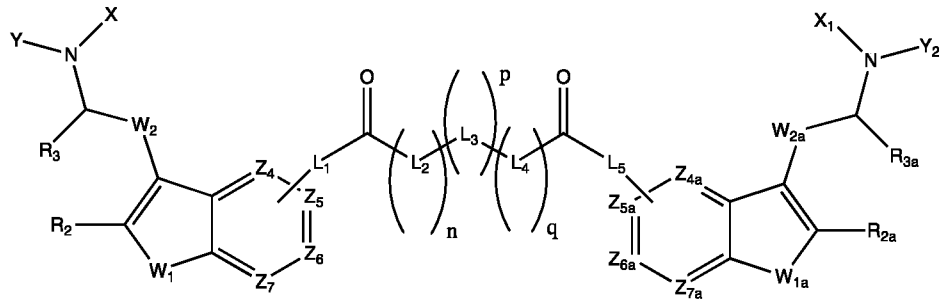


[Vd], and

and salts, solvates, hydrates, and prodrugs of any of compounds [Va] through [Vd].

In some embodiments, the compounds of Formula I and/or Formula V comprise salts. In some embodiments, the compounds of Formula I and/or Formula V comprise pharmaceutically-acceptable salts. Exemplary salts include, but are not limited to, HCl, HI, HBr, HF, ascorbate, hydrofumarate, fumarate, oxalate, maleate, and the like. In certain embodiments, the compound of Formula I and/or Formula V is in its free-base form. In some embodiments, the compound of Formula I and/or Formula V comprises a salt, such as a [1:1] salt (e.g., HCl, hydrofumarate) or a [2:1] salt (e.g., oxalate, fumarate). In some embodiments, for the [1:1] salts, one ammonium cation of one compound of Formulae II or III is balanced by a single anion (Cl-, I-, etc.). For the [2:1] salts, two ammonium cations of two molecules of Formulae II or III are balanced by a dianionic species, such as a dianion derived from di-acids such as oxalic acid and fumaric acid. Other exemplary salts include zwitterionic forms of compounds of Formulae II or III, such as when R_1 is $-P(O)(OH)_2$, wherein deprotonation of an -OH on R_1 may result in intramolecular coordination of the resulting $-O^-$ with the quaternary ethylammonium (e.g., $-(CH_2)_2N^+H(CH_3)_2$).

Other exemplary compounds of Formula ID include those of subgenus Formula IDd, as described below and in Table 1,



Formula IDd

wherein:

W_2 and W_{2a} are $-CH_2-$;

Z_4 and Z_{4a} are each CR_4 wherein L_1 and L_5 have replaced the R_4 groups;

Z_5 and Z_{5a} are CR_5;

Z_6 and Z_{6a} are CR_6;

Z_7 and Z_{7a} are CR_7;

L_1 and L_5 are O;

L_2 and L_4 for each occurrence are independently selected from O, CH_2, NH, and S;

L_3 for each occurrence is independently selected from S and CH_2;

p is an integer selected from 0, 1, 2, 3; and

n and q are each integers independently selected from 0, 1, 2, 3, 4, 5, and 6.

Table 1

Ref	X and X_1	Y and Y_1	R_2, R_{2a}	R_3, R_{3a}	R_5 (each occur.)	R_6 (each occur.)	R_7 (each occur.)	W_1, W_{1a}
1	$-CH_3$	$-CH_3$	H	H	H	H	H	NH
2	$-CH_3$	$-CH_2CH_3$	H	H	H	H	H	NH
3	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	NH
4	$-CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	NH
5	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NH
6	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NH
7	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	H	H	NH
8	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	NH
9	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	NH
10	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NH
11	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NH
12	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	NH
13	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	NH
14	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NH
15	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NH
16	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	H	H	NH
17	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	H	H	NH
18	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	NH
19	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NH
20	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NH
21	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	NH
21a	$-CH_3$	$-CH_3$	H	H	H	H	H	O

22	$-CH_3$	$-CH_2CH_3$	H	H	H	H	H	O
23	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	O
24	$-CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	O
25	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	O
26	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	O
27	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	H	H	O
28	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	O
29	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	O
30	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	O
31	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	O
32	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	O
33	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	O
34	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	O
35	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	O
36	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	H	H	O
37	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	H	H	O
38	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	O
39	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	O
40	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	O
41	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	O
42	$-CH_3$	$-CH_3$	H	H	H	H	H	S
43	$-CH_3$	$-CH_2CH_3$	H	H	H	H	H	S
44	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	S
45	$-CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	S
46	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	S
47	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	S
48	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	H	H	S
49	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	S
50	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	S
51	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	S
52	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	S
53	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	S
54	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	S
55	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	S
56	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	S
57	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	H	H	S
58	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	H	H	S
59	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	S
60	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	S
61	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	S
62	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	S
63	$-CH_3$	$-CH_3$	H	H	H	Br	H	NH
64	$-CH_3$	$-CH_2CH_3$	H	H	H	Br	H	NH

65	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	Br	H	NH
66	$-CH_3$	$-CH(CH_3)_2$	H	H	H	Br	H	NH
67	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	Br	H	NH
68	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	Br	H	NH
69	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	Br	H	NH
70	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	Br	H	NH
71	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	Br	H	NH
72	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	Br	H	NH
73	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	Br	H	NH
74	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	Br	H	NH
75	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	Br	H	NH
76	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	Br	H	NH
77	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	Br	H	NH
78	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	Br	H	NH
79	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	Br	H	NH
80	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	Br	H	NH
81	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	Br	H	NH
82	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	Br	H	NH
83	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	Br	H	NH
84	$-CH_3$	$-CH_2CH_3$	H	H	H	Cl	H	NH
85	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	Cl	H	NH
86	$-CH_3$	$-CH(CH_3)_2$	H	H	H	Cl	H	NH
87	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	Cl	H	NH
88	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	Cl	H	NH
89	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	Cl	H	NH
90	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	Cl	H	NH
91	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	Cl	H	NH
92	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	Cl	H	NH
93	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	Cl	H	NH
94	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	Cl	H	NH
95	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	Cl	H	NH
96	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	Cl	H	NH
97	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	Cl	H	NH
98	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	Cl	H	NH
99	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	Cl	H	NH
100	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	Cl	H	NH
101	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	Cl	H	NH
102	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	Cl	H	NH
103	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	Cl	H	NH
104	$-CH_3$	$-CH_3$	H	H	H	F	H	NH
105	$-CH_3$	$-CH_2CH_3$	H	H	H	F	H	NH
106	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	F	H	NH
107	$-CH_3$	$-CH(CH_3)_2$	H	H	H	F	H	NH

108	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NH
109	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NH
110	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	F	H	NH
111	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	F	H	NH
112	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	F	H	NH
113	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NH
114	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NH
115	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	F	H	NH
116	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	F	H	NH
117	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NH
118	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NH
119	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	F	H	NH
120	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	F	H	NH
121	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	F	H	NH
122	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NH
123	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NH
124	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	F	H	NH
125	$-CH_3$	$-CH_3$	H	H	H	H	H	Se
126	$-CH_3$	$-CH_2CH_3$	H	H	H	H	H	Se
127	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	Se
128	$-CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	Se
129	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	Se
130	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	Se
131	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	H	H	Se
132	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	Se
133	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	Se
134	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	Se
135	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	Se
135	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	Se
137	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	Se
138	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	Se
139	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	Se
140	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	H	H	Se
141	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	H	H	Se
142	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	Se
143	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	Se
144	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	Se
145	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	Se
145a	H	$-CH_3$	H	H	H	H	H	Se
146	H	$-CH_2CH_3$	H	H	H	H	H	Se
147	H	$-(CH_2)_2CH_3$	H	H	H	H	H	Se
148	H	$-CH(CH_3)_2$	H	H	H	H	H	Se

149	H	-$(CH_2)_3CH_3$	H	H	H	H	H	Se
150	H	-CH_2-$HC=CH_2$	H	H	H	H	H	Se
150a	H	-CH_3	H	H	H	H	H	NH
151	H	-CH_2CH_3	H	H	H	H	H	NH
152	H	-$(CH_2)_2CH_3$	H	H	H	H	H	NH
153	H	-$CH(CH_3)_2$	H	H	H	H	H	NH
154	H	-$(CH_2)_3CH_3$	H	H	H	H	H	NH
155	H	-CH_2-$HC=CH_2$	H	H	H	H	H	NH
156	H	-$(CH_2)_2CH_3$	H	H	H	H	H	NH
157	H	-$CH(CH_3)_2$	H	H	H	H	H	NH
158	H	-$(CH_2)_3CH_3$	H	H	H	H	H	NH
159	H	-CH_2-$HC=CH_2$	H	H	H	H	H	NH
159a	H	-CH_3	H	H	H	H	H	O
160	H	-CH_2CH_3	H	H	H	H	H	O
161	H	-$CH(CH_3)_2$	H	H	H	H	H	O
162	H	-$(CH_2)_3CH_3$	H	H	H	H	H	O
163	H	-CH_2-$HC=CH_2$	H	H	H	H	H	O
164	H	-$(CH_2)_3CH_3$	H	H	H	H	H	O
165	H	-CH_2-$HC=CH_2$	H	H	H	H	H	O
166	H	-CH_3	H	H	H	H	H	S
167	H	-CH_2CH_3	H	H	H	H	H	S
168	H	-$(CH_2)_2CH_3$	H	H	H	H	H	S
169	H	-$CH(CH_3)_2$	H	H	H	H	H	S
170	H	-$(CH_2)_3CH_3$	H	H	H	H	H	S
171	H	-CH_2-$HC=CH_2$	H	H	H	F	H	S
171a	H	-CH_3	H	H	H	F	H	NH
172	H	-CH_2CH_3	H	H	H	F	H	NH
173	H	-$(CH_2)_2CH_3$	H	H	H	F	H	NH
174	H	-$CH(CH_3)_2$	H	H	H	F	H	NH
175	H	-$(CH_2)_3CH_3$	H	H	H	F	H	NH
176	H	-CH_2-$HC=CH_2$	H	H	H	F	H	NH
176a	H	-CH_3	H	H	H	F	H	O
176b	H	-CH_2CH_3	H	H	H	F	H	O
177	H	-$(CH_2)_2CH_3$	H	H	H	F	H	O
178	H	-$CH(CH_3)_2$	H	H	H	F	H	O
179	H	-$(CH_2)_3CH_3$	H	H	H	F	H	O
180	H	-CH_2-$HC=CH_2$	H	H	H	F	H	O
180a	H	-CH_3	H	H	H	F	H	S
180b	H	-CH_2CH_3	H	H	H	F	H	S
180	H	-$(CH_2)_2CH_3$	H	H	H	F	H	S

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181	H	-$CH(CH_3)_2$	H	H	H	F	H	S
182	H	-$(CH_2)_3CH_3$	H	H	H	F	H	S
183	H	-CH_2- $HC=CH_2$	H	H	H	F	H	S
183a	H	-CH_3	H	H	H	H	F	Se
183b	H	-CH_2CH_3	H	H	H	F	H	Se
183c	H	-$(CH_2)_2CH_3$	H	H	H	F	H	Se
184	H	-$(CH_2)_3CH_3$	H	H	H	F	H	Se
185	H	-CH_2- $HC=CH_2$	H	H	H	F	H	Se
186	H	-CH_2- $HC=CH_2$	H	H	H	F	H	Se
187	-CH_3	-CH_3	H	H	Br	H	H	NH
188	-CH_3	-CH_2CH_3	H	H	Br	H	H	NH
189	-CH_3	-$(CH_2)_2CH_3$	H	H	Br	H	H	NH
190	-CH_3	-$CH(CH_3)_2$	H	H	Br	H	H	NH
191	-CH_3	-$(CH_2)_3CH_3$	H	H	Br	H	H	NH
192	-CH_3	-CH_2- $HC=CH_2$	H	H	Br	H	H	NH
193	-CH_2CH_3	-CH_2CH_3	H	H	Br	H	H	NH
194	-CH_2CH_3	-$(CH_2)_2CH_3$	H	H	Br	H	H	NH
195	-CH_2CH_3	-$CH(CH_3)_2$	H	H	Br	H	H	NH
196	-CH_2CH_3	-$(CH_2)_3CH_3$	H	H	Br	H	H	NH
197	-CH_2CH_3	-CH_2- $HC=CH_2$	H	H	Br	H	H	NH
198	-$(CH_2)_2CH_3$	-$(CH_2)_2CH_3$	H	H	Br	H	H	NH
199	-$(CH_2)_2CH_3$	-$CH(CH_3)_2$	H	H	Br	H	H	NH
200	-$(CH_2)_2CH_3$	-$(CH_2)_3CH_3$	H	H	Br	H	H	NH
201	-$(CH_2)_2CH_3$	-CH_2- $HC=CH_2$	H	H	Br	H	H	NH
202	-$CH(CH_3)_2$	-$CH(CH_3)_2$	H	H	Br	H	H	NH
203	-$CH(CH_3)_2$	-$(CH_2)_3CH_3$	H	H	Br	H	H	NH
204	-$CH(CH_3)_2$	-CH_2- $HC=CH_2$	H	H	Br	H	H	NH
205	-$(CH_2)_3CH_3$	-$(CH_2)_3CH_3$	H	H	Br	H	H	NH
206	-$(CH_2)_3CH_3$	-CH_2- $HC=CH_2$	H	H	Br	H	H	NH
207	-CH_2- $HC=CH_2$	-CH_2- $HC=CH_2$	H	H	Br	H	H	NH
208	-CH_3	-CH_2CH_3	H	H	Cl	H	H	NH
209	-CH_3	-$(CH_2)_2CH_3$	H	H	Cl	H	H	NH
210	-CH_3	-$CH(CH_3)_2$	H	H	Cl	H	H	NH
211	-CH_3	-$(CH_2)_3CH_3$	H	H	Cl	H	H	NH
212	-CH_3	-CH_2- $HC=CH_2$	H	H	Cl	H	H	NH
213	-CH_2CH_3	-CH_2CH_3	H	H	Cl	H	H	NH
214	-CH_2CH_3	-$(CH_2)_2CH_3$	H	H	Cl	H	H	NH
215	-CH_2CH_3	-$CH(CH_3)_2$	H	H	Cl	H	H	NH
216	-CH_2CH_3	-$(CH_2)_3CH_3$	H	H	Cl	H	H	NH
217	-CH_2CH_3	-CH_2- $HC=CH_2$	H	H	Cl	H	H	NH

218	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	Cl	H	H	NH
219	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	Cl	H	H	NH
220	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	Cl	H	H	NH
221	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	Cl	H	H	NH
222	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	Cl	H	H	NH
223	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	Cl	H	H	NH
224	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	Cl	H	H	NH
225	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	Cl	H	H	NH
226	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	Cl	H	H	NH
227	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	Cl	H	H	NH
228	$-CH_3$	$-CH_3$	H	H	F	H	H	NH
229	$-CH_3$	$-CH_2CH_3$	H	H	F	H	H	NH
230	$-CH_3$	$-(CH_2)_2CH_3$	H	H	F	H	H	NH
231	$-CH_3$	$-CH(CH_3)_2$	H	H	F	H	H	NH
232	$-CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NH
233	$-CH_3$	$-CH_2-HC=CH_2$	H	H	F	H	H	NH
234	$-CH_2CH_3$	$-CH_2CH_3$	H	H	F	H	H	NH
235	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	F	H	H	NH
236	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	F	H	H	NH
237	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NH
238	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	F	H	H	NH
239	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	F	H	H	NH
240	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	F	H	H	NH
241	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NH
242	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	F	H	H	NH
243	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	F	H	H	NH
244	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	F	H	H	NH
245	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	F	H	H	NH
246	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NH
247	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	F	H	H	NH
248	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	F	H	H	NH
249	$-CH_3$	$-CH_3$	$-CH_3$	H	H	H	H	NH
250	$-CH_3$	$-CH_2CH_3$	$-CH_3$	H	H	H	H	NH
251	$-CH_3$	$-(CH_2)_2CH_3$	$-CH_3$	H	H	H	H	NH
252	$-CH_3$	$-CH(CH_3)_2$	$-CH_3$	H	H	H	H	NH
253	$-CH_3$	$-(CH_2)_3CH_3$	$-CH_3$	H	H	H	H	NH
254	$-CH_3$	$-CH_2-HC=CH_2$	$-CH_3$	H	H	H	H	NH
255	$-CH(CH_3)_2$	$-CH(CH_3)_2$	$-CH_3$	H	H	H	H	NH
256	$-CH_3$	$-CH_3$	$-CH_3$	$-CH_3$	H	H	H	NH
257	$-CH_3$	$-CH_2CH_3$	$-CH_3$	$-CH_3$	H	H	H	NH
258	$-CH_3$	$-(CH_2)_2CH_3$	$-CH_3$	$-CH_3$	H	H	H	NH
259	$-CH_3$	$-CH(CH_3)_2$	$-CH_3$	$-CH_3$	H	H	H	NH
260	$-CH_3$	$-(CH_2)_3CH_3$	$-CH_3$	$-CH_3$	H	H	H	NH
261	$-CH_3$	$-CH_2-$	$-CH_3$	$-CH_3$	H	H	H	NH

		$HC=CH_2$						
262	$-CH(CH_3)_2$	$-CH(CH_3)_2$	$-CH_3$	$-CH_3$	H	H	H	NH
263	$-CH_3$	$-CH_3$	H	H	H	$-CH_3$	H	NH
264	$-CH_3$	$-CH_2CH_3$	H	H	H	$-CH_3$	H	NH
265	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	$-CH_3$	H	NH
266	$-CH_3$	$-CH(CH_3)_2$	H	H	H	$-CH_3$	H	NH
267	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	$-CH_3$	H	NH
268	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	$-CH_3$	H	NH
269	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	$-CH_3$	H	NH
270	$-CH_3$	$-CH_3$	H	H	H	H	$-CH_3$	NH
271	$-CH_3$	$-CH_2CH_3$	H	H	H	H	$-CH_3$	NH
272	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	$-CH_3$	NH
273	$-CH_3$	$-CH(CH_3)_2$	H	H	H	H	$-CH_3$	NH
274	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	$-CH_3$	NH
275	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	$-CH_3$	NH
276	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	H	$-CH_3$	NH
277	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	NCH_2CH_3
278	$-CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	NCH_2CH_3
279	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NCH_2CH_3
280	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NCH_2CH_3
281	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	H	H	NCH_2CH_3
282	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	NCH_2CH_3
283	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	NCH_2CH_3
284	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NCH_2CH_3
285	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NCH_2CH_3
286	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	H	NCH_2CH_3
287	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	H	NCH_2CH_3
288	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NCH_2CH_3
289	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NCH_2CH_3
290	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	H	H	NCH_2CH_3
291	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	H	H	NCH_2CH_3
292	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	NCH_2CH_3
293	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	H	NCH_2CH_3
294	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	H	NCH_2CH_3
295	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	H	H	NCH_2CH_3
296	$-CH_3$	$-CH_2CH_3$	H	H	H	H	H	NCH_2CH_3
297	$-CH_3$	$-CH_3$	H	H	H	H	H	NCH_2CH_3
298	$-CH_3$	$-(CH_2)_2CH_3$	H	H	F	H	H	NCH_2CH_3
299	$-CH_3$	$-CH(CH_3)_2$	H	H	F	H	H	NCH_2CH_3
300	$-CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NCH_2CH_3
301	$-CH_3$	$-CH_2-HC=CH_2$	H	H	F	H	H	NCH_2CH_3
302	$-CH_2CH_3$	$-CH_2CH_3$	H	H	F	H	H	NCH_2CH_3
303	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	F	H	H	NCH_2CH_3
304	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	F	H	H	NCH_2CH_3
305	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NCH_2CH_3
306	$-CH_2CH_3$	$-CH_2-$	H	H	F	H	H	NCH_2CH_3

		$HC=CH_2$						
307	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	F	H	H	NCH_2CH_3
308	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	F	H	H	NCH_2CH_3
309	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NCH_2CH_3
310	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	F	H	H	NCH_2CH_3
311	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	F	H	H	NCH_2CH_3
312	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	F	H	H	NCH_2CH_3
313	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	F	H	H	NCH_2CH_3
314	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	F	H	H	NCH_2CH_3
315	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	F	H	H	NCH_2CH_3
316	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	F	H	H	NCH_2CH_3
317	$-CH_3$	$-CH_2CH_3$	H	H	F	H	H	NCH_2CH_3
318	$-CH_3$	$-CH_3$	H	H	F	H	H	NCH_2CH_3
319	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	F	H	NCH_2CH_3
320	$-CH_3$	$-CH(CH_3)_2$	H	H	H	F	H	NCH_2CH_3
321	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NCH_2CH_3
322	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
323	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	F	H	NCH_2CH_3
324	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	F	H	NCH_2CH_3
325	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	F	H	NCH_2CH_3
326	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NCH_2CH_3
327	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
328	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	F	H	NCH_2CH_3
329	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	F	H	NCH_2CH_3
330	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NCH_2CH_3
331	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
332	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	F	H	NCH_2CH_3
333	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	F	H	NCH_2CH_3
334	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
335	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	F	H	NCH_2CH_3
336	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
337	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
338	$-CH_3$	$-CH_2CH_3$	H	H	H	F	H	NCH_2CH_3
339	$-CH_3$	$-CH_3$	H	H	H	F	H	NCH_2CH_3
340	$-CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	F	NCH_2CH_3
341	$-CH_3$	$-CH(CH_3)_2$	H	H	H	H	F	NCH_2CH_3
342	$-CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	F	NCH_2CH_3
343	$-CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
344	$-CH_2CH_3$	$-CH_2CH_3$	H	H	H	H	F	NCH_2CH_3
345	$-CH_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	F	NCH_2CH_3
346	$-CH_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	F	NCH_2CH_3
347	$-CH_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	F	NCH_2CH_3
348	$-CH_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3

349	$-(CH_2)_2CH_3$	$-(CH_2)_2CH_3$	H	H	H	H	F	NCH_2CH_3
350	$-(CH_2)_2CH_3$	$-CH(CH_3)_2$	H	H	H	H	F	NCH_2CH_3
351	$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	F	NCH_2CH_3
352	$-(CH_2)_2CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
353	$-CH(CH_3)_2$	$-CH(CH_3)_2$	H	H	H	H	F	NCH_2CH_3
354	$-CH(CH_3)_2$	$-(CH_2)_3CH_3$	H	H	H	H	F	NCH_2CH_3
355	$-CH(CH_3)_2$	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
356	$-(CH_2)_3CH_3$	$-(CH_2)_3CH_3$	H	H	H	H	F	NCH_2CH_3
357	$-(CH_2)_3CH_3$	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
358	$-CH_2-HC=CH_2$	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
359	$-CH_3$	$-CH_2CH_3$	H	H	H	H	F	NCH_2CH_3
360	$-CH_3$	$-CH_3$	H	H	H	H	F	NCH_2CH_3
361	H	$-(CH_2)_2CH_3$	H	H	H	H	H	NCH_2CH_3
362	H	$-CH(CH_3)_2$	H	H	H	H	H	NCH_2CH_3
363	H	$-(CH_2)_3CH_3$	H	H	H	H	H	NCH_2CH_3
364	H	$-CH_2-HC=CH_2$	H	H	H	H	H	NCH_2CH_3
365	H	$-CH_2CH_3$	H	H	H	H	H	NCH_2CH_3
366	H	$-CH_3$	H	H	H	H	H	NCH_2CH_3
367	H	$-(CH_2)_2CH_3$	H	H	F	H	H	NCH_2CH_3
368	H	$-CH(CH_3)_2$	H	H	F	H	H	NCH_2CH_3
369	H	$-(CH_2)_3CH_3$	H	H	F	H	H	NCH_2CH_3
370	H	$-CH_2-HC=CH_2$	H	H	F	H	H	NCH_2CH_3
371	H	$-CH_2CH_3$	H	H	F	H	H	NCH_2CH_3
372	H	$-CH_3$	H	H	F	H	H	NCH_2CH_3
373	H	$-(CH_2)_2CH_3$	H	H	H	H	H	NCH_2CH_3
374	H	$-CH(CH_3)_2$	H	H	H	F	H	NCH_2CH_3
375	H	$-(CH_2)_3CH_3$	H	H	H	F	H	NCH_2CH_3
376	H	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
377	H	$-(CH_2)_2CH_3$	H	H	H	F	H	NCH_2CH_3
378	H	$-CH(CH_3)_2$	H	H	H	F	H	NCH_2CH_3
379	H	$-(CH_2)_3CH_3$	H	H	H	F	H	NCH_2CH_3
380	H	$-CH_2-HC=CH_2$	H	H	H	F	H	NCH_2CH_3
381	H	$-CH(CH_3)_2$	H	H	H	F	H	NCH_2CH_3
382	H	$-CH_3$	H	H	H	F	H	NCH_2CH_3
383	H	$-(CH_2)_3CH_3$	H	H	H	H	F	NCH_2CH_3
384	H	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
385	H	$-(CH_2)_3CH_3$	H	H	H	H	F	NCH_2CH_3
386	H	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
387	H	$-CH_2-HC=CH_2$	H	H	H	H	F	NCH_2CH_3
388	H	$-CH_2CH_3$	H	H	H	H	F	NCH_2CH_3
389	H	$-CH_3$	H	H	H	H	F	NCH_2CH_3
390	H	$-(CH_2)_2CH_3$	H	$-CH_3$	H	H	H	NH
391	H	$-CH(CH_3)_2$	H	$-CH_3$	H	H	H	NH
392	H	$-(CH_2)_3CH_3$	H	$-CH_3$	H	H	H	NH

393	H	-CH_2-$HC=CH_2$	H	-CH_3	H	H	H	NH
394	H	-CH_2CH_3	H	-CH_3	H	H	H	NH
395	H	-$(CH_2)_2CH_3$	H	-CH_3	H	H	H	NH
396	H	-CH_3	H	-CH_3	H	H	H	NH
397	H	-$(CH_2)_2CH_3$	H	-CH_3	H	H	H	NH
398	H	-$CH(CH_3)_2$	H	-CH_3	H	H	H	NCH_2CH_3
399	H	-$(CH_2)_3CH_3$	H	-CH_3	H	H	H	NCH_2CH_3
400	H	-CH_2-$HC=CH_2$	H	-CH_3	H	H	H	NCH_2CH_3
401	H	-CH_2CH_3	H	-CH_3	H	H	H	NCH_2CH_3
402	H	-$(CH_2)_2CH_3$	H	-CH_3	H	H	H	NCH_2CH_3
403	H	-CH_3	H	-CH_3	H	H	H	NCH_2CH_3
404	H	-$(CH_2)_2CH_3$	H	-CH_3	F	H	H	NH
405	H	-$CH(CH_3)_2$	H	-CH_3	F	H	H	NH
406	H	-$(CH_2)_3CH_3$	H	-CH_3	F	H	H	NH
407	H	-CH_2-$HC=CH_2$	H	-CH_3	F	H	H	NH
408	H	-CH_2CH_3	H	-CH_3	F	H	H	NH
409	H	-$(CH_2)_2CH_3$	H	-CH_3	F	H	H	NH
410	H	-CH_3	H	-CH_3	F	H	H	NH
411	H	-$(CH_2)_2CH_3$	H	-CH_3	H	F	H	NH
412	H	-$CH(CH_3)_2$	H	-CH_3	H	F	H	NH
413	H	-$(CH_2)_3CH_3$	H	-CH_3	H	F	H	NH
414	H	-CH_2-$HC=CH_2$	H	-CH_3	H	F	H	NH
415	H	-CH_2CH_3	H	-CH_3	H	F	H	NH
416	H	-$(CH_2)_2CH_3$	H	-CH_3	H	F	H	NH
417	H	-CH_3	H	-CH_3	H	F	F	NH
418	H	-$(CH_2)_2CH_3$	H	-CH_3	H	H	F	NH
419	H	-$CH(CH_3)_2$	H	-CH_3	H	H	F	NH
420	H	-$(CH_2)_3CH_3$	H	-CH_3	H	H	F	NH
421	H	-CH_2-$HC=CH_2$	H	-CH_3	H	H	F	NH
422	H	-CH_2CH_3	H	-CH_3	H	H	F	NH
423	H	-$(CH_2)_2CH_3$	H	-CH_3	H	H	F	NH
424	H	-CH_3	H	-CH_3	H	H	F	NH
425	H	-$(CH_2)_2CH_3$	H	-CH_3	H	F	H	NCH_2CH_3
426	H	-$CH(CH_3)_2$	H	-CH_3	H	F	H	NCH_2CH_3
427	H	-$(CH_2)_3CH_3$	H	-CH_3	H	F	H	NCH_2CH_3
428	H	-CH_2-$HC=CH_2$	H	-CH_3	H	F	H	NCH_2CH_3
429	H	-CH_2CH_3	H	-CH_3	H	F	H	NCH_2CH_3
430	H	-$(CH_2)_2CH_3$	H	-CH_3	H	F	H	NCH_2CH_3
431	H	-CH_3	H	-CH_3	H	F	H	NCH_2CH_3

COMPOSITIONS AND METHODS

As used herein, the term “5-HT1A” refers to a 5-HT1A receptor. As used herein, the term “5-HT2A” refers to a 5-HT2A receptor.

As used herein, the term “effective amount” in connection with a compound disclosed

herein means an amount capable of treating or preventing a disorder, disease or condition, or symptoms thereof, disclosed herein.

As used herein, the term "hallucination" (and related terms such as “hallucinogenic” and “hallucinogen”) refers to a perception in the absence of external stimulus that has qualities of real perception. In some embodiments, hallucinations may be vivid, substantial, and are perceived to be located in external objective space. As used herein, hallucinations may occur in any sensory modality including, but not limited to visual, auditory, olfactory, gustatory, tactile, proprioceptive, equilibrioceptive, nociceptive, thermoceptive and chronoceptive. In some embodiments, the hallucinations are selected from visual hallucinations, auditory hallucinations, olfactory hallucinations, gustatory hallucinations, tactile hallucinations, proprioceptive hallucinations, equilibrioceptive hallucinations, nociceptive hallucinations, thermoceptive hallucinations, chronoceptive hallucinations and any combination thereof. In some embodiments, hallucinations are visual hallucinations.

As used herein, the terms “prevent” or “preventing” refers to means a method of delaying and/or precluding the onset, recurrence or spread, in whole or in part, of a disorder, disease or condition; barring a subject from acquiring a disorder, disease, or condition; or reducing a subject’s risk of acquiring a disorder, disease, or condition.

As used herein, the term “treat” or “treating” refers to an alleviation, in whole or in part, of a disorder, disease or condition, or one or more of the symptoms associated with a disorder, disease, or condition, or slowing or halting of further progression or worsening of those symptoms, or alleviating or eradicating the cause(s) of the disorder, disease, or condition itself.

In further embodiments of the present disclosure, described are novel compounds and compositions, as well as methods of administering the same. In some embodiments, a compound provided herein is for use in the methods provided herein. In some embodiments, the disclosure provides the use of a compound provided herein in the preparation of a medicament for treating one or more of the diseases or disorders provided herein.

In certain embodiments, the method comprises administering a serotonin 5-HT1A agonist and a serotonin 5-HT2A agonist. Without being bound to any particular theory, in certain embodiments it has been surprisingly discovered that administering a serotonin 5-HT1A agonist and a serotonin 5-HT2A agonist can be effective in preventing or treating one or more of the conditions described herein. In certain embodiments, it has also been surprisingly discovered that administering a serotonin 5-HT1A agonist and a hallucinogenic 5-HT2A agonist can effectively treat patients without the patients experiencing the hallucinogenic effects of the 5-HT2A agonist. Without intending to be bound by any particular theory, it is believed that the patient can experience a therapeutic effect without experiencing a hallucinogenic manifestation

that typically results from the administration of a 5-HT2A agonist because the 5-HT1A agonist can "turn off" the hallucinogenic effects of the of the 5-HT2A agonist without otherwise significantly altering its agonism at a 5-HT2A receptor. In some embodiments, the 5-HT1A agonist is a partial agonist. In some embodiments, the 5-HT1A agonist is a full agonist. In some embodiments, the 5-HT2A agonist is a partial agonist. In some embodiments, the 5-HT2A agonist is a full agonist. In some embodiments, the 5-HT1A and/or 5-HT2A agonists may be selected from compounds of Formula I and Formula V herein. In some embodiments, the 5-HT1A and the 5-HT2A agonists are the same compound (*e.g.*, a compound of Formulae II or III).

In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered at the same time. In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered at different times. In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered at the same time in the same composition. In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered together as part of a compound of Formula I, wherein Group A is a 5-HT1A agonist residue (*e.g.*, 8-OH-DPAT or 6-OH-buspirone attached to the linker "L" via the free hydroxyl group) and Group B is a 5-HT2A agonist residue (*e.g.*, psilocin or attached to the linker "L" via the free hydroxyl group).

In some embodiments, it has been surprisingly discovered that polypodal (*e.g.*, dimeric) compounds of Formula I can be implemented to effectively deliver two or more active compounds efficiently past the blood-brain barrier (BBB). For example, in some embodiments it has been surprisingly discovered that linking a first compound (*e.g.*, serotonergic drug A) with a second compound (*e.g.*, active compound B) can enhance the BBB penetration, half-life, and/or overall efficacy of the target actives when administered to a patient in need thereof, as the co-administration of certain compounds (*e.g.*, serotonergic drugs) with other drugs (*e.g.*, cannabinoids) can have a synergistic effect on the resulting therapeutic properties of said compounds.

As defined herein, a "full agonist" shall mean an agonist having an Emax% of at least 90% for the relevant serotonin receptor agonist assay (*e.g.*, BRET2, calcium mobilization, beta-arrestin) when compared to an industry-accepted control compound for that particular receptor assay (*e.g.*, serotonin (5-OH-tryptamine)). In some embodiments, a "full agonist" will exhibit an Emax% of at least 90, at least 91, at least 92, at least 93, at least 94, at least 95, at least 96, at least 97, at least 98, or at least 99%. Also defined herein, a "partial agonist" shall mean an agonist having an Emax% of less than 90% for the relevant serotonin receptor when compared to an industry-accepted control compound for that particular receptor (*e.g.*, serotonin (5-OH-tryptamine)). In some embodiments, a "partial agonist" will exhibit an Emax% of less than 85,

80, 75, 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or even less than 5%. In some embodiments, a partial agonist will exhibit an Emax% of about 0.1 to about 89.9%, such as about 1 to about 89, about 5 to about 85, about 50 to about 88, about 40 to about 85, about 35 to about 75, about 25 to about 65, or about 20 to about 55%.

In some embodiment, the 5-HT1A agonist as used herein is selected from buspirone (8-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]-8 -azaspiro[4.5]decane-7,9-dione) or its enolate (enol alcohol) equivalent, 5-OH-buspirone, 6-OH-buspirone, tandospirone ((1R,2R,6S,7S)-4-{4-[4-(pyrimidin -2-yl)piperazin-1-yl]butyl}-4-azatricyclo[5.2.1.02,6]decane-3,5-dione), gepirone (4,4-dimethyl-1-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]piperid- ine-2,6-dione), alnespirone ((+)-4-dihydro-2H-chromen-3-yl]-propylamino]butyl]-8-azaspiro[4.5]decane-- 7,9-dione), binospirone (8-[2-(2,3-dihydro-1,4-benzodioxin-2-ylmethylamino)ethyl]-8-azaspiro[4.5]- decane-7,9-dione), ipsapirone (9,9-dioxo-8-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]-9.lamda.6-thia-8-a-zabicyclo[4.3.0]nona-1,3,5-trien-7-one), perospirone (3aR, 7aS) -2-{4-[4-(1,2-benzisothiazol-3-yl)piperazin-1-yl]butyl} hexahydro-1H-isoindole-1,3(2H)-dione, befiradol (F-13,640) (3-chloro-4-fluorophenyl-[4-fluoro-4-([(5-methylpyridin-2 -yl)methylamino]methyl)piperidin-1-yl]methanone, repinotan ((R)-(-)-2-[4-[(chroman-2 -ylmethyl)-amino]-butyl]-1,1-dioxo-benzo[d] isothiazolone), piclozotan (3-chloro-4-[4-[4-(2-pyridinyl)-1,2,3,6-tetrahydropyridin-1-yl]butyl]-1,4- -benzoxazepin-5(4H)-one), osemozotan (5-(3-[((2S)-1,4-benzodioxan-2-ylmethyl)amino]propoxy)-1,3-benzodioxole), flesinoxan (4-fluoro-N-[2-[4-[(3S)-3-(hydroxymethyl)-2,3-dihydro-1,4 -benzodioxin-8-yl]piperazin-1-yl]ethyl]benzamide), flibanserin (1-(2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,3-dihydro-2H-- benzimidazol-2-one), 8-OH-DPAT (7-(Dipropylamino)-5,6,7,8-tetrahydronaphthalen-1-ol), and sarizotan (EMD-128,130) (1-[(2R)-3,4-dihydro-2H-chromen-2-yl]-N-([5-(4 -fluorophenyl)pyridin-3-yl]methyl)methanamine), a compound of Formula II or III, or a prodrug, salt, or derivative thereof.

In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered at the same time. In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered at different times. In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered sequentially. In some embodiments, the serotonin 5-HT1A agonist is administered first, and 5-HT2A agonist is administered second. In some embodiments, the serotonin 5-HT2A agonist is administered about 30 minutes to about 12hrs after administration of 5-HT1A agonist, such as about 1hr to about 6hrs afterwards. In some embodiments, the serotonin 5-HT1A agonist and 5-HT2A agonist are administered at the same time in the same composition. In some embodiments, 5-HT1A agonist is selected from buspirone, 5-OH-buspirone, 6-OH-buspirone, and 8-OH-DPAT. In some embodiments, the 5-HT1A agonist is buspirone. In some embodiments, the 5-HT1A agonist is selected from compounds of Formula I, such as for example compounds of Formula IE, and compounds of Formula V. In some embodiments, the 5-HT2A agonist is hallucinogenic. In some

embodiments, the 5-HT2A agonist is non-hallucinogenic. In some embodiments, the 5-HT2A agonist is selected from compounds of Formula I, such as for example compounds of Formula IE, and compounds of Formula V.

In some embodiments, the 5-HT2A agonist and the 5-HT1A agonist may comprise the same compound. In some embodiments, the compounds of Formulae II and III described herein can act as both 5-HT1A and 5-HT2A receptor agonists. In some embodiments, the compounds described herein are full agonists for both 5-HT1A and 5-HT2A.

In some embodiments, the 5-HT1A agonist and 5-HT2A agonist are full agonists for a 5-HT1A receptor and a 5-HT2A receptor, respectively. In some embodiments, the 5-HT1A agonist exhibits a higher level of molar potency (*i.e.*, lower EC_{50}) for activating a 5-HT1A receptor than the 5-HT2A agonist exhibits for activating the 5-HT2A receptor. Without being bound to any particular scientific theory, in certain embodiments it has been surprisingly discovered that compounds that are agonists for 5-HT1A and 5-HT2A – but which exhibit a higher molar potency for 5-HT1A – may be useful to patients needing/desiring non-hallucinogenic 5-HT2A modulation. In other embodiments, the 5-HT1A agonist is a partial agonist (*e.g.*, buspirone) and 5-HT2A agonist is a full agonist for a 5-HT1A receptor and a 5-HT2A receptors, respectively. In other embodiments, the 5-HT1A agonist is a partial agonist (*e.g.*, buspirone) and 5-HT2A agonist is a partial agonist for a 5-HT1A receptor and a 5-HT2A receptors, respectively.

In certain embodiments are described methods for treating, preventing, ameliorating, or curing a disease or disorder via a non-hallucinogenic therapeutic treatment regimen that includes modulation of a 5-HT1A receptor. In certain embodiments, the method comprises identifying a subject in need of treatment for a disease or condition associated with modulation of a 5-HT1A receptor; selecting a compound of Formula I (*e.g.*, Formula IE) and/or Formula V; and administering the compound to the subject in need of treatment, wherein the compound modulates activity at both a 5-HT1A and 5-HT2A receptor. In certain embodiments, the compound of Formula I and/or Formula V is a full agonist of a 5-HT1A receptor. In certain embodiments, the compound of Formula I and/or Formula V is a full agonist for both 5-HT1A and 5-HT2A receptors. In certain embodiments, the compound of Formula I and/or Formula V is a partial agonist for a 5-HT1A receptor and a full agonist for a 5-HT2A receptor. In certain embodiments, the compound of Formula I and/or Formula V is a partial agonist for a 5-HT1A receptor and a partial agonist for a 5-HT2A receptor. In certain embodiments, the compound of Formula I and/or Formula V exhibits a higher molar potency (lower EC_{50}) for a 5-HT1A receptor when compared to a 5-HT2A receptor.

In certain embodiments, the 5-HT1A agonist has an EC_{50} for activating a 5-HT1A

receptor of less than about 100nM, such as less than about 75nm, less than about 50nm, less than about 25nm, less than about 15nm, less than about 10nm, or less than about 5nm. In certain embodiments, the 5-HT2A agonist has an EC_{50} for activating a 5-HT2A receptor of less than about 100nM, such as less than about 75nm, less than about 50nm, less than about 25nm, less than about 15nm, less than about 10nm, or less than about 5nm. In certain embodiments, the 5-HT1A agonist exhibits an EC_{50} for activating a 5-HT1A receptor of about 0.01nM to about 100nM, such as about 0.05 to about 50nm, about 0.1 to about 25nM, or about 0.5 to about 10nM. In certain embodiments, the 5-HT2A agonist has an EC_{50} for activating a 5-HT2A receptor of about 0.01nM to about 100nM, such as about 0.05 to about 50nm, about 0.1 to about 25nM, or about 0.5 to about 10nM. In certain embodiments, the 5-HT2A agonist has an EC_{50} for activating a 5-HT2A receptor of about 5 to about 75nM, such as about 10 to about 60nm, about 15 to about 50nM, or about 20 to about 40nM. In some embodiments, the 5-HT1A agonist/5-HT2A agonist exhibits a 5-HT1A receptor: 5-HT2A receptor EC_{50} ratio range of about 1:2 to about 1:100, such as about 1:5 to about 1:50 or about 1:10 to about 1:40. In some embodiments, the active drugs of compounds of Formula I (*e.g.*, first active compound of Group A and second active compound of Group B, respectively) independently exhibit a 5-HT1A receptor: 5-HT2A receptor EC_{50} ratio range of about 1:2 to about 1:100, such as about 1:5 to about 1:50 or about 1:10 to about 1:40 when said compounds are liberated (for example, *in vivo*). Relevant testing parameters to determine full vs. partial agonism (Emax%) and molar potency (EC_{50}) include those known to persons of skill in the art, such as the 5-HT Functional Assays described further in the Biological Examples below.

In some embodiments, also described are novel compounds and compositions, as well as methods of administering the same. In certain embodiments, the method comprises administering a serotonin 5-HT2A agonist and a serotonin 5-HT2B antagonist. Without being bound to any particular theory, in certain embodiments it has been surprisingly discovered that administering a serotonin 5-HT2A agonist and a serotonin 5-HT2B antagonist can be effective in preventing or treating one or more of the conditions described herein. In some embodiments, it has been surprisingly discovered that administering a serotonin 5-HT2A agonist and a serotonin 5-HT2B antagonist can effectively treat patients while also reducing serotonin 5-HT2B-induced cardiotoxicity (*e.g.*, heart valve fibrosis and hypertrophy). In certain embodiments, it has also been surprisingly discovered that administering a serotonin 5-HT2B antagonist and a 5-HT2A agonist can be safely and effectively used treat patients as described herein without the patients experiencing the hallucinogenic effects that can be associated with hallucinogenic 5-HT2A agonists. In some embodiments, the 5-HT2A agonist is a full agonist. In some embodiments, the 5-HT2A agonist is a partial agonist. In some embodiments, the 5-HT2B antagonist is a full antagonist. In some embodiments, the 5-HT2B antagonist is a partial antagonist.

Exemplary serotonin 5-HT2B receptor antagonists include, but are not limited to, agomelatine, amisulpride, ariprazole, carprazine, clozapine, cyproheptadine, mCCP, sarpogrelate, lisuride, tegasurod, metadoxine, and promethazine. In certain embodiments, the 5-HT2B antagonist is not an antagonist at any of the other serotonin 5-HT type receptor subtypes, such as 5-HT1A and 5-HT2A. In certain embodiments, the 5-HT2B receptor antagonist will also be a full or partial agonist at a 5-HT1A and/or 5-HT2A receptor.

In some embodiments, the serotonin 5-HT2A agonist and 5-HT2B antagonist are administered at the same time. In some embodiments, the serotonin 5-HT2A agonist and 5-HT2B antagonist are administered at different times. In some embodiments, the serotonin 5-HT2A agonist and 5-HT2B antagonist are administered at the same time in the same composition. In some embodiments, the serotonin 5-HT2A agonist and 5-HT2B antagonist are administered together as part of a compound of Formula I, wherein Group A is a 5-HT2B antagonist residue and Group B is a 5-HT2A agonist residue (*e.g.*, psilocin attached to the linker "L" via the free hydroxyl group). In some embodiments, the serotonin 5-HT1A agonist and 5-HT2B antagonist are administered sequentially. In some embodiments, the serotonin 5-HT2B antagonist is administered first, and 5-HT2A agonist is administered second. In some embodiments, the serotonin 5-HT2A agonist is administered about 30 minutes to about 12 hrs after administration of 5-HT2B antagonist, such as about 1 hr to about 6 hrs afterwards. In some embodiments, the 5-HT2A agonist is hallucinogenic. In some embodiments, the 5-HT2A agonist is non-hallucinogenic. In some embodiments, the 5-HT2A agonist is selected from compounds of Formula I, such as for example compounds of Formula IE, and Formula V.

In some embodiments, also described are novel compounds and compositions, as well as methods of administering the same. In certain embodiments, the method comprises administering a serotonin 5-HT2A agonist and a serotonin 5-HT2C agonist. Without being bound to any particular theory, in certain embodiments it has been surprisingly discovered that administering a serotonin 5-HT2A agonist and a serotonin 5-HT2C agonist can be effective in preventing or treating one or more of the conditions described herein. In some embodiments, it has been surprisingly discovered that administering a serotonin 5-HT2A agonist and a serotonin 5-HT2C agonist can effectively treat patients while also reducing or eliminating the hallucinogenic "trip" typically associated with 5-HT2A agonists. In some embodiments, the 5-HT2A agonist is a full agonist. In some embodiments, the 5-HT2A agonist is a partial agonist. In some embodiments, the 5-HT2C agonist is a full agonist. In some embodiments, the 5-HT2C agonist is a partial agonist.

Exemplary serotonin 5-HT2C receptor agonists include, but are not limited to, lorcaserin, vabicaserin, aripiprazole, YM-348, PRX-00933, and meta-chlorophenylpiperazine. In certain embodiments, the 5-HT2C agonist is not an agonist at any of the other serotonin 5-

HT type receptor subtypes, such as 5-HT1A and 5-HT2B. In certain embodiments, the 5-HT2C receptor agonist will be inactive or only a partial agonist at a 5-HT1A and/or 5-HT2B receptor.

In some embodiments, the serotonin 5-HT2A agonist and 5-HT2C agonist are administered at the same time. In some embodiments, the serotonin 5-HT2A agonist and 5-HT2C agonist are administered at different times. In some embodiments, the serotonin 5-HT2A agonist and 5-HT2C agonist are administered at the same time in the same composition. In some embodiments, the serotonin 5-HT2A agonist and 5-HT2C agonist are administered together as part of a compound of Formula I, wherein Group A is a 5-HT2C agonist residue and Group B is a 5-HT2A agonist residue (*e.g.*, psilocin attached to the linker "L" via the free hydroxyl group). In some embodiments, the serotonin 5-HT2A agonist and 5-HT2C agonist are administered sequentially. In some embodiments, the serotonin 5-HT2C agonist is administered first, and 5-HT2A agonist is administered second. In some embodiments, the serotonin 5-HT2A agonist is administered about 30 minutes to about 12 hrs after administration of 5-HT2C agonist, such as about 1 hr to about 6 hrs afterwards. In some embodiments, the 5-HT2A agonist is hallucinogenic. In some embodiments, the 5-HT2A agonist is non-hallucinogenic. In some embodiments, the 5-HT2A agonist is selected from compounds of Formula I, such as for example compounds of Formula IE, and Formula V.

In some embodiments, the 5-HT2A agonist and the 5-HT2C agonist may comprise the same compound. In some embodiments, the compounds of Formula I (*e.g.*, compounds of Formula IE) and Formula V can act as both 5-HT2C and 5-HT2A receptor agonists. In some embodiments, the compounds described herein are full agonists for both 5-HT2A and 5-HT2C. In some embodiments, the compounds described herein act as partial agonists at 5-HT2A and full agonists at 5-HT2C. In some embodiments, the compounds described herein are partial agonists for both 5-HT2A and 5-HT2C. In some embodiments, the compounds described herein act as agonists at 5-HT2A and 5-HT2C, but are only partial agonists (or inactive) at a 5-HT2B receptor.

In certain embodiments for compounds described herein, Applicant has discovered that the size and nature of alkyl groups for X and/or Y can dramatically affect the metabolism of such compounds. For example, it has been theorized that compounds such as 5-MeO-Dimethyltryptamine (5-MeO-DMT) and Dimethyltryptamine (DMT) are inactive upon oral administration due to rapid metabolism of the methylamino groups by monoamine oxidase (MAO) enzymes. It has also been theorized that the oral stability of psilocin (4-OH-dimethyltryptamine), on the other hand, is due largely to intramolecular coordination (hydrogen bonding) between the 4-OH group and the dimethylamino group, which effectively shields/inhibits rapid MAO degradation.

Without being bound to any particular scientific theory, Applicant has surprisingly found that substituting the alkyl groups X and/or Y with substituents such as deuterium and fluorine can help inhibit MAO degradation of those groups, despite the absence of a hydrogen bond donor (e.g., -OH) at the 4-position. In addition, or in the alternative, Applicant has discovered that using non-methyl alkyl groups such as ethyl or n-propyl for X and/or Y can also slow or inhibit rapid MAO metabolism upon oral administration. This, in turn, permits the preparation of orally available compounds of Formula I and/or Formula V that are highly active serotonergic drugs that do not require special formulating procedures (*e.g.*, dosages containing MAO inhibitors), or the presence of hydrogen bond-forming donors at the 4-position that – in some cases – can negatively impact the properties of the underlying compound (*e.g.*, reduction of 5-HT1A and/or 5-HT2A agonism).

In some embodiments, Applicant has also surprisingly discovered that alpha-deuteration of the compounds described herein (wherein R_3 and/or $R_{3'}$ are deuterium) can dramatically improve the pharmacokinetics of those compounds. Without being bound to any particular scientific theory, it is believed that the heavier deuterium isotope disrupts the enzymatic metabolism of those compounds. However, in some embodiments it may not be desirable to "over deuterate" the compound, such as further including deuterated species for groups for X and Y or deuteration at the beta position (*i.e.*, W_2), which can further alter the compounds' pharmacokinetic profiles (*e.g.*, greatly extended half lives) in an undesirable manner. Accordingly, in some embodiments, Applicant has discovered that minimal deuteration may be used to achieve the desired pharmacokinetic outcome. For example, in some embodiments adding a single deuterium atom at the alpha position (*i.e.*, R_3 or $R_{3'}$) can greatly enhance the desired pharmacokinetic profile. It is theorized that this may be due, in part, to the creation of a stereocenter at the alpha position upon deuteration that impacts the enzymes' ability to metabolize the compound (*e.g.*, hindrance of MAO degradation and/or the ability of enzymes to oxidize the alpha position during metabolic processes).

In one embodiment, the compounds, the methods, and the pharmaceutical compositions described herein are used to modulate the activity of a neurotransmitter receptor by administering a therapeutically effective amount of a compound of Formula I and/or Formula V. Methods include the administration of a therapeutically effective amount of a compound of Formula I and/or Formula V to prevent or treat a psychological disorder such as those discussed herein. Compounds described herein may be administered neat or as a pharmaceutical composition comprising a compound of Formula I and/or Formula V as discussed herein.

In some embodiments, the compounds described herein may be used to prevent and/or treat a psychological disorder. The disclosure provides a method for preventing and/or treating

a psychological disorder by administering to a subject in need thereof a therapeutically effective amount of a compound of Formula I and/or Formula V, including the exemplary embodiments discussed herein. The psychological disorder may be chosen from depression; psychotic disorder; schizophrenia; schizophreniform disorder (acute schizophrenic episode); schizoaffective disorder; bipolar I disorder (mania, manic disorder, manic-depressive psychosis); bipolar II disorder; major depressive disorder; major depressive disorder with psychotic feature (psychotic depression); delusional disorders (paranoia); Shared Psychotic Disorder (Shared paranoia disorder); Brief Psychotic disorder (Other and Unspecified Reactive Psychosis); Psychotic disorder not otherwise specified (Unspecified Psychosis); paranoid personality disorder; schizoid personality disorder; schizotypal personality disorder; anxiety disorder; social anxiety disorder; substance-induced anxiety disorder; selective mutism; panic disorder; panic attacks; agoraphobia; attention deficit syndrome; posttraumatic stress disorder (PTSD); premenstrual dysphoric disorder (PMDD); and premenstrual syndrome (PMS).

In some embodiments, the compounds described herein may be used to prevent and/or treat a brain disorder. The disclosure provides a method for preventing and/or treating a brain disorder by administering to a subject in need thereof a therapeutically effective amount of a compound of Formula I and/or Formula V, including the exemplary embodiments discussed above. The brain disorder may be chosen from Huntington's disease, Alzheimer's disease, dementia, and Parkinson's disease.

In some embodiments, the compounds described herein may be used to prevent and/or treat developmental disorders, delirium, dementia, amnestic disorders and other cognitive disorders, psychiatric disorders due to a somatic condition, drug-related disorders, schizophrenia and other psychotic disorders, mood disorders, anxiety disorders, somatoform disorders, factitious disorders, dissociative disorders, eating disorders, sleep disorders, impulse control disorders, adjustment disorders, or personality disorders. The disclosure provides a method for preventing and/or treating these disorders by administering to a subject in need thereof a therapeutically effective amount of a compound of Formula I and/or Formula V, including the exemplary embodiments discussed above.

In some embodiments, the compounds described herein may be used to prevent and/or treat inflammation and/or pain, such as, for example, inflammation and/or pain associated with inflammatory skeletal or muscular diseases or conditions. Accordingly, the disclosure relates to a method for preventing and/or treating inflammation and/or pain by administering to a subject in need thereof a therapeutically effective amount of a compound of Formula I and/or Formula V, including the exemplary embodiments discussed herein. Generally speaking, treatable "pain" includes nociceptive, neuropathic, and mix-type. A method of the disclosure may reduce or alleviate the symptoms associated with inflammation, including, but not limited to, treating

localized manifestation of inflammation characterized by acute or chronic swelling, pain, redness, increased temperature, or loss of function in some cases. A method of the disclosure may reduce or alleviate the symptoms of pain regardless of the cause of the pain, including, but not limited to, reducing pain of varying severity, *i.e.* mild, moderate and severe pain, acute pain and chronic pain. A method of the disclosure is effective in treating joint pain, muscle pain, tendon pain, burn pain, and pain caused by inflammation such as rheumatoid arthritis. Skeletal or muscular diseases or conditions which may be treated include, but are not limited to, musculoskeletal sprains, musculoskeletal strains, tendinopathy, peripheral radiculopathy, osteoarthritis, joint degenerative disease, polymyalgia rheumatica, juvenile arthritis, gout, ankylosing spondylitis, psoriatic arthritis, systemic lupus erythematosus, costochondritis, tendonitis, bursitis, such as the common lateral epicondylitis (tennis elbow), medial epicondylitis (pitchers elbow) and trochanteric bursitis, temporomandibular joint syndrome, and fibromyalgia.

In other embodiments, the methods and compositions disclosed herein comprise regulating the activity of a neurotransmitter receptor with a formulation comprising a compound described herein, including compounds of Formula I and/or Formula V. In one embodiment, the methods and compositions disclosed herein comprise administering a first dosage formulation comprising at least one compound of Formula I and/or Formula V, which may comprise a serotonergic drug (Group A) and a second active compound (Group B). In one embodiment, the second active compound comprises neurotransmitter activity modulator (*e.g.*, a second serotonergic drug). In one embodiment, the second active compound comprises at least one cannabinoid, at least one terpene, or a second serotonergic drug.

The present disclosure relates to compositions comprising, consisting essentially of, or consisting of an effective amount of a compound of Formula I and/or Formula V and an excipient. The terms “composition” and “formulation” are used interchangeably herein. Other embodiments relate to pharmaceutical compositions comprising, consisting essentially of, or consisting of a therapeutically effective amount of a compound of Formula I and/or Formula V, including those discussed above, and a pharmaceutically acceptable excipient (also known as a pharmaceutically acceptable carrier). As discussed above, a compound of Formula I and/or Formula V may be therapeutically useful to prevent and/or treat, for example, psychological disorders, brain disorders, pain and inflammation as well as other disorders such as those discussed above.

In some embodiments, the compositions described herein may comprise at least one compound of Formula I, which itself comprises a residue of a first active compound comprising a serotonergic drug and a residue of a second active compound selected from at least one of a second serotonergic drug, a cannabinoid, a terpene, or an MAO inhibitor. In certain embodiments, the second compound may be derived from natural sources, such as fungi (*e.g.*, Psilocybe mushrooms; Lion’s Mane mushrooms (containing terpenes such as erinacines and

hericenones)) and plants (*e.g.*, Cannabis). Accordingly, in certain embodiments the second compound may derived or "extracted" from fungus or plant material, meaning said second compound may or may not be "purified" depending on the manner in which it was sourced and extracted.

Within the context of this disclosure, the term "purified" means separated from other compounds or materials, such as plant or fungal material, *e.g.*, protein, chitin, cellulose, or water. In one embodiment, the term "purified" refers to a compound substantially free of other materials. In one embodiment, the term "purified" refers to a compound that is substantially free from a second compound (*e.g.* an enantiomeric compound of Formula I and/or Formula V exhibiting 99% enantiomeric excess after resolution). In one embodiment, the term "purified" refers to a compound substantially free from a biological material, such as mold, fungus, plant mater, or bacteria.

In one embodiment, the term "purified" refers to a compound or composition that has been crystallized. In one embodiment, the term "purified" refers to a compound or composition that has been chromatographed, for example by gas chromatography, liquid chromatography (e.g., LC, HPLC, etc.), etc. In one embodiment, the term "purified" refers to a compound or composition that has been distilled. In one embodiment, the term "purified" refers to a compound or composition that has been sublimed. In one embodiment, the term "purified" refers to a compound or composition that has been subject to two or more steps chosen from crystallization, chromatography, distillation, and sublimation.

In one embodiment, the term "purified" refers to a compound that has a purity ranging from about 80% to about 100%, meaning that the compound makes up about 80% to about 100%of the total mass of the composition. In one embodiment, the term "purified" refers to a compound that is has a purity ranging from about 90% to about 100%, meaning that the compound makes up about 90% to about 100% of the total mass of the composition. In one embodiment, the term "purified" refers to a compound that has a purity ranging from about 95% to about 100%, meaning that the compound makes up about 95% to about 100% of the total mass of the composition. In one embodiment, the term "purified" refers to a compound that has a purity ranging from about 99% to about 100% pure, meaning that the compound makes up about 99% to about 100% of the total mass of the composition. In one embodiment, the term "purified" refers to a compound that has a purity ranging from about 99.9% to about 100%, meaning that the compound makes up about 99.9% to about 100% of the total mass of the composition.

As used herein, the term "particular ratio" refers to the amount of a compound in relation to the amount of another compound or compounds. In one embodiment, there is about 1:1 ratio of a 4-acetoxy-3-[2-(dimethylamino)ethyl]-benzo[*b*]thiophene) to 4-hydroxy-N,N-dimethyltryptamine. In one embodiment, a particular ratio of compounds is measured by the

same unit, *e.g.*, grams, kilograms, pounds, ounces, etc. In one embodiment, a particular ratio of compounds is measured in moles, i.e., molar proportions or molar ratios.

As used herein, the term "particular amount" refers to the quantity of a compound or compounds. In one embodiment, a particular amount is the combined quantity of two compounds within a sample. In one embodiment, a particular amount is measured by dry weight. In one embodiment, the particular amount has 1, 2, 3, or 4 significant figures.

Disclosed herein are also compositions comprising a compound of Formula I and/or Formula V and an additional compound. In one embodiment, the compositions disclosed herein comprise a molar ratio ranging from about 10:1 to about 1:10 of the compound of Formula I and/or Formula V (*e.g.*, a 5-HT2A receptor agonist) to the additional compound (*e.g.*, a 5-HT1A receptor agonist). In one embodiment, the compositions disclosed herein comprise a molar ratio ranging from about 100:1 to about 1:100 of the compound of Formula I and/or Formula V to the additional compound. In one embodiment, the compositions disclosed herein comprise a molar ratio ranging from about 1,000:1 to about 1:1,000 of the compound of Formula I and/or Formula V to the additional compound. In one embodiment, the compositions disclosed herein comprise a molar ratio ranging from about 10,000:1 to about 1:10,000 of the compound of Formula I and/or Formula V to the additional compound.

Within the context of this disclosure, unless otherwise specified, the serotonergic compounds (*e.g.*, tryptamine compounds) described herein may be present in their protonated or deprotonated (salt or freebase) forms or mixtures thereof depending on the context, for example, the pH of the solution or composition. However, in certain embodiments, the serotonergic compounds described herein are lipophilic, meaning they will tend to combine with lipids and fats and can readily pass though biological membranes in the body of an animal or human (*e.g.*, blood brain barrier). In certain embodiments, the serotonergic compound in free base form are lipophilic.

As used herein, the term "salt" refers to a neutralized ionic compound. In one embodiment, a salt is formed from the neutralization of acids and bases. In one embodiment, a salt is electrically neutral.

In one embodiment, the compositions and methods disclosed herein comprise administering a first cannabinoid. In one embodiment, a first cannabinoid is a first purified cannabinoid.

As used herein, the term "cannabinoid" refers to a compound from a class of molecules commonly found in plants of the genus cannabis and their derivatives. In one embodiment, the cannabinoid is endogenous to an animal, *i.e.*, an endocannabinoid. In one embodiment, the cannabinoid is derived from a plant, *e.g.*, a plant of genus cannabis, *e.g.*, a phytocannabinoid. In one embodiment, the cannabinoid is artificially made in a lab, i.e., a synthetic cannabinoid.

Many cannabinoids can be identified by the "cannabi" text in their chemical name. There are at least 113 different cannabinoids isolated from cannabis, exhibiting varied (similar and different) effects.

Examples of cannabinoids within the context of this disclosure include the following molecules: Cannabichromene (CBC), Cannabichromenic acid (CBCA), Cannabichromevarin (CBCV), Cannabichromevarinic acid (CBCVA), Cannabicyclol (CBL), Cannabicyclolic acid (CBLA), Cannabicyclovarin (CBLV), Cannabidiol (CBD), Cannabidiol monomethylether (CBDM), Cannabidiolic acid (CBDA), Cannabidiorcol (CBD-C1), Cannabidivarin (CBDV), Cannabidivarinic acid (CBDVA), Cannabielsoic acid B (CBEA-B), Cannabielsoin (CBE), Cannabielsoin acid A (CBEA-A), Cannabigerol (CBG), Cannabigerol monomethylether (CBGM), Cannabigerolic acid (CBGA), Cannabigerolic acid monomethylether (CBGAM), Cannabigerovarin (CBGV), Cannabigerovarinic acid (CBGVA), Cannabinodiol (CBND), Cannabinodivarin (CBDV), Cannabinol (CBN), Cannabinol methylether (CBNM), Cannabinol-C2 (CBN-C2), Cannabinol-C4 (CBN-C4), Cannabinolic acid (CBNA), Cannabiorcool (CBN-C1), Cannabivarin (CBV), Cannabitriol (CBT), Cannabitriolvarin (CBTV), 10-Ethoxy-9-hydroxy-delta-6a-tetrahydrocannabinol, Cannbicitran (CBT), Cannabiripsol (CBR), 8,9-Dihydroxy-delta-6a-tetrahydrocannabinol, Delta-8-tetrahydrocannabinol (.DELTA.8-THC), Delta-8-tetrahydrocannabinolic acid (.DELTA.8-THCA), Delta-9-tetrahydrocannabinol (THC), Delta-9-tetrahydrocannabinol-C4 (THC-C4), Delta-9-tetrahydrocannabinolic acid A (THCA-A), Delta-9-tetrahydrocannabinolic acid B (THCA-B), Delta-9-tetrahydrocannabinolic acid-C4 (THCA-C4), Delta-9-tetrahydrocannabiorcol (THC-C1), Delta-9-tetrahydrocannabiorcolic acid (THCA-C1), Delta-9-tetrahydrocannabivarin (THCV), Delta-9-tetrahydrocannabivarinic acid (THCVA), 10-Oxo-delta-6a-tetrahydrocannabinol (OTHC), Cannabichromanon (CBCF), Cannabifuran (CBF), Cannabiglendol, Delta-9-cis-tetrahydrocannabinol (cis-THC), Tryhydroxy-delta-9-tetrahydrocannabinol (triOH-THC), Dehydrocannabifuran (DCBF), and 3,4,5,6-Tetrahydro-7-hydroxy-alpha-alpha-2-trimethyl-9-n-propyl-2,6-metha- no-2H-1-benzoxocin-5-methanol.

In one embodiment, the term "cannabinoid" refers to a compound chosen from THC, THCA, THCV, THCVA, CBC, CBCA, CBCV, CBCVA, CBD, CBDA, CBDV, CBDVA, CBG, CBGA, CBGV, and CBGVA.

Within the context of this disclosure, the term "THC" comprises any derivative of Delta-9-tetrahydrocannabinol and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a THC residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "THCA" comprises any derivative of tetrahydrocannabinolic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a THCA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "THCV" comprises any derivative of Delta-9-tetrahydrocannabivarin and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a THCV residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "THCVA" comprises any derivative of Delta-9-tetrahydrocannabivarinic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a THCVA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBC" comprises any derivative of Cannabichromene and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBC residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBCA" comprises any derivative of Cannabichromenic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBCA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBCV" comprises any derivative of Cannabichromevarin and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBCV residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBCVA" comprises any derivative of Cannabichromevarinic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBCVA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBD" comprises any derivative of Cannabidiol and/or salt thereof. In one embodiment, the compounds of Formula I may comprise a CBD residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBDA" comprises any derivative of Cannabidiolic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBDA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBDV" comprises any derivative of Cannabidivarin and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBDV residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBDVA" comprises any derivative of

Cannabidivarinic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBDVA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBG" comprises any derivative of Cannabigerol and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBG residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBGA" comprises any derivative of Cannabigerolic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBGA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBGV" comprises any derivative of Cannabigerovarin and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBGV residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

Within the context of this disclosure, the term "CBGVA" comprises any derivative of Cannabigerovarinic acid and/or salts thereof. In one embodiment, the compounds of Formula I may comprise a CBGVA residue (*i.e.* Group B) and a serotonergic drug such as psilocin (*i.e.*, Group A).

In one embodiment, the compositions and methods disclosed herein comprise a compound of Formula I, wherein the compound comprises a first cannabinoid compound (Group A) and a second cannabinoid compound (Group B). In one embodiment, the cannabinoids are selected from THC, THCA, THCV, THCVA, CBC, CBCA, CBCV, CBCVA, CBD, CBDA, CBDV, CBDVA, CBG, CBGA, CBGV, and CBGVA.

In one embodiment, the compositions and methods disclosed herein comprise administering a compound of Formula I, the compound comprising a terpenoid residue (Group B) and a first serotonergic drug such as psilocin (Group A).

As used herein, the term "terpene" refers to a compound belonging to a large class of compounds often biosynthesized from 5-carbon isoprene units. In one embodiment, a terpene is isolated from a plant, *e.g.*, conifers, cannabis, basil, etc. In one embodiment, a terpene is produced by an insect, *e.g.*, termites or swallowtail butterflies. In one embodiment, a terpene is a volatile compound. In one embodiment, a terpene produces an odor. In one embodiment, a terpene is a major component of a natural resin, *e.g.*, turpentine produced from resin. In one embodiment, a terpene is derived biosynthetically from units of isoprene, which has the molecular formula C_5H_8. In one embodiment, the molecular formula of terpenes are multiples of $(C_5H_8)_n$, where n is the number of linked isoprene units, such as 1 to 5.

Within the context of this disclosure when a terpene is modified chemically, such as by oxidation or rearrangement of the carbon skeleton, the resulting compound is referred to as a "terpenoid." In the relevant arts, terpenoids are sometimes referred to as isoprenoids.

In one embodiment, a terpene is the primary constituent or constituents of an essential oil from a plant and/or flower. Essential oils are used widely as fragrances in perfumery, medicine, and alternative medicines, e.g., aromatherapy.

In one embodiment, a terpene is categorized according to the number of isoprene (C_5H_8) units in the compound, for example, a monoterpene ($C_{10}H_{16}$), a sesquiterpene ($C_{15}H_{24}$), a diterpene ($C_{20}H_{32}$), a triterpene ($C_{30}H_{48}$), or a tetraterpene ($C_{40}H_{64}$).

Examples of terpenes within the context of this disclosure include acetanisole, acetyl cedrene, anethole, anisole, benzaldehyde, bornyl acetate, borneol, cadinene, cafestol, caffeic acid, camphene, camphor, capsaicin, carene, carotene, carvacrol, carvone, alpha-caryophyllene, beta-caryophyllene, caryophyllene oxide, cedrene, cedrene epoxide, cecanal, cedrol, cembrene, cinnamaldehyde, cinnamic acid, citronellal, citronellol, cymene, eicosane, elemene, estragole, ethyl acetate, ethyl cinnamate, ethyl maltol, eucalyptol/1,8-cineole, eudesmol, eugenol, euphol, farnesene, farnesol, fenchone, geraniol, geranyl acetate, guaia-1(10),11-diene, guaiacol, guaiol, guaiene, gurjunene, herniarin, hexanaldehyde, hexanoic acid, humulene, ionone, ipsdienol, isoamyl acetate, isoamyl alcohol, isoamyl formate, isoborneol, isomyrcenol, isoprene, isopulegol, isovaleric acid, lavandulol, limonene, gamma-linolenic acid, linalool, longifolene, lycopene, menthol, methyl butyrate, 3-mercapto-2-methylpentanal, beta-mercaptoethanol, mercaptoacetic acid, methyl salicylate, methylbutenol, methyl-2-methylvalerate, methyl thiobutyrate, beta-myrcene, gamma-muurolene, nepetalactone, nerol, nerolidol, neryl acetate, nonanaldehyde, nonanoic acid, ocimene, octanal, octanoic acid, pentyl butyrate, phellandrene, phenylacetaldehyde, phenylacetic acid, phenylethanethiol, phytol, pinene, propanethiol, pristimerin, pulegone, retinol, rutin, sabinene, squalene, taxadiene, terpineol, terpine-4-ol, terpinolene, thujone, thymol, umbelliferone, undecanal, verdoxan, and vanillin.

In one embodiment, a purified terpene is chosen from bornyl acetate, alpha-bisabolol, borneol, camphene, camphor, carene, beta-caryophyllene, cedrene, cymene, elemene, eucalyptol, eudesmol, farnesene, fenchol, geraniol, guaiacol, humulene, isoborneol, limonene, linalool, menthol, beta-myrcene, nerolidol, ocimene, phellandrene, phytol, pinene, pulegone, sabinene, terpineol, terpinolene, and valencene.

Within the context of this disclosure, the term "bornyl acetate" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a bornyl acetate residue.

Within the context of this disclosure, the term "alpha-bisabolol" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise an alpha-bisabolol residue.

Within the context of this disclosure, the term "borneol" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a borneol residue.

Within the context of this disclosure, the term "camphene" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a camphene residue.

Within the context of this disclosure, the term "camphor" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a camphor residue.

Within the context of this disclosure, the term "carene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a carene residue.

Within the context of this disclosure, the term "beta-caryophyllene" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a beta-caryophyllene residue.

Within the context of this disclosure, the term "cedrene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a cedrene residue.

Within the context of this disclosure, the term "cymene" comprises any derivative and/or salt to thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a cymene residue.

Within the context of this disclosure, the term "elemene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise an elemene residue.

Within the context of this disclosure, the term "eucalyptol" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a eucalyptol residue.

Within the context of this disclosure, the term "eudesmol" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In

one embodiment, the compounds of Formula I and/or Formula V comprise a eudesmol residue.

Within the context of this disclosure, the term "farnesene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a farnesene residue.

Within the context of this disclosure, the term "fenchol" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a fenchol residue.

Within the context of this disclosure, the term "geraniol" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a geraniol residue.

Within the context of this disclosure, the term "guaiacol" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a guaiacol residue.

Within the context of this disclosure, the term "humulene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a humulene residue.

Within the context of this disclosure, the term "isoborneol" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise an isoborneol residue.

Within the context of this disclosure, the term "limonene" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a limonene residue.

Within the context of this disclosure, the term "linalool" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a linalool residue.

Within the context of this disclosure, the term "menthol" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a residue.

Within the context of this disclosure, the term "beta-myrcene" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a beta-myrcene residue.

Within the context of this disclosure, the term "nerolidol" comprises any derivative and/or

salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a nerolidol residue.

Within the context of this disclosure, the term "ocimene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise an ocimene residue.

Within the context of this disclosure, the term "phellandrene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a phellandrene residue.

Within the context of this disclosure, the term "phytol" comprises any derivative and/or salt thereof, including any isomeric, structural and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a phytol residue.

Within the context of this disclosure, the term "pinene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a pinene residue.

Within the context of this disclosure, the term "pulegone" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a pulegone residue.

Within the context of this disclosure, the term "sabinene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a sabinene residue.

Within the context of this disclosure, the term "terpineol" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a terpineol residue.

Within the context of this disclosure, the term "terpinolene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a terpinolene residue.

Within the context of this disclosure, the term "valencene" comprises any derivative and/or salt thereof, including any isomeric, structural, and/or enantiomeric, variations thereof. In one embodiment, the compounds of Formula I and/or Formula V comprise a valencene residue.

In one embodiment, the compositions and methods disclosed herein include one or more erinacine molecules. In one embodiment, the compositions and methods disclosed herein comprise erinacine A. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine B residue. In one embodiment, the compounds of

Formula I and/or Formula V disclosed herein comprise an erinacine C residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine D residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine E residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine F residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine G residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine H residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine I residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine J residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine K residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine L residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine M residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine N residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine O residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine Q residue. In one embodiment, the compounds of Formula I and/or Formula V disclosed herein comprise an erinacine R residue.

The erinacine chemical structures are taken from Li I-C, Lee L-Y, Tzeng T W, et al. Neurohealth properties of Hericium erinaceus mycelia enriched with erinacines. In: *Behavioural Neurology*. 2018. doi:10.1155/2018/5802634

In one embodiment, the compounds of Formula I and/or Formula V may comprise a hericenone residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone A residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone B residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone C residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone D residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone E residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone F residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone G residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone H residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone I residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone J residue. In one embodiment, the compounds of Formula I and/or Formula V comprise a hericenone K residue.

In one embodiment, the compounds of Formula I and/or Formula V may comprise active compound residues that are derived from extracting and subsequently purifying one or more compounds from an organism chosen from Bacopa monnieri (for example, the purified molecule bacoside A3), Centella asiatica (for example, the purified molecule asiaticoside), Gingko biloba (for example, the purified molecule myricetin), Zingiber officinale (for example, the purified molecule zingerone), Ocimum sanctum (for example, the purified molecule linalool), Polygonum cuspidatum (for example, the purified molecule resveratrol), Origanum vulgare (for example, the purified molecule carvacrol), Origanum onites (for example, the purified molecule thymol), Rosmarinus officinalis (for example, the purified molecule rosmarinic acid), Rosmarinus eriocalyx (for example, the purified molecule camphor), Curcuma longa (for example, the purified molecule curcumin), Camellia sinensis (for example, the purified molecule theobromine), Lavandula spica (for example, the purified molecule caryophyllene), Scutellaria lateriflora (for example, the purified molecule baicalin), Avena sativa (for example, the purified molecule avenalin), Avena byzantina (for example, the purified molecule beta-glucan), Salvia divinorum (for example, the purified molecule salvinorin A), Banisteriopsis caapi (for example, the purified molecule harmine), Psychotria species (for example, the purified molecule dimethyltryptamine), Tabernanthe iboga (for example, the purified molecule ibogaine), Voacanga africana (for example, the purified molecule voacangine), Tabernaemontana undulata (for example, the purified molecule ibogamine), Lophophora williamsii (for example, the purified molecule mescaline), Ipomoea tricolor (for example, the purified molecule ergonovine), and Argyreia nervosa (for example, the purified molecule ergine).

As used herein, the term "serotonergic drug" refers to a compound that binds to, blocks, or otherwise influences (*e.g.*, via an allosteric reaction) activity at a serotonin receptor. In one embodiment, a serotonergic drug binds to a serotonin receptor. In one embodiment, a serotonergic drug indirectly affects a serotonin receptor, e.g., via interactions affecting the reactivity of other molecules at the serotonin receptor. In one embodiment, a serotonergic drug is an agonist, e.g., a compound activating a serotonin receptor. In one embodiment, a serotonergic drug is an antagonist, e.g., a compound binding but not activating a serotonin receptor, e.g., blocking a receptor. In one embodiment, a serotonergic drug is an effector molecule, e.g., a compound binding to an enzyme for allosteric regulation. In one embodiment, a serotonergic drug acts (either directly or indirectly) at more than one type of receptor (e.g., SHT, dopamine, adrenergic, acetylcholine, etc.).

In one embodiment, a serotonergic drug is an antidepressant.

In one embodiment, a serotonergic drug is an anxiolytic.

In one embodiment, a serotonergic drug is a selective serotonin reuptake inhibitor.

In one embodiment, a serotonergic drug is a selective serotonin norepinephrine

reuptake inhibitor.

In some embodiments, the compounds of Formula I comprise a first serotonergic drug residue (Group A, which may selected from compounds of Formulae II and III) and a second serotonergic drug residue (Group B, which may be selected from compounds below and compounds of Formulae II and III).

Some exemplary serotonergic drugs include the following molecules: 4-hydroxy-N-methyltryptamine (aka 3[2-(methylamino)ethyl]-1H-indol-4-ol), aeruginascin (aka [3-[2-(trimethylazaniumyl)ethyl]-1H-indol-4-yl] hydrogen phosphate), baeocystin (aka [3-[2-(methylamino)ethyl]-1H-indol-4-yl] dihydrogen phosphate), bufotenidine (aka 3-[2-(trimethylazaniumypethyl]-1H-indol-5-olate), bufotenin (aka 3-[2-(dimethylamino)ethyl]-1H-indol-5-ol), ethocybin (aka [3-[2-(diethylamino)ethyl]-1H-indol-4-yl] dihydrogen phosphate), norbaeocystin (aka [3-(2-aminoethyl)-1H-indol-4-yl] dihydrogen phosphate), norpsilocin, psilocin (aka 3-[2-(dimethylamino)ethyl]-1H-indol-4-ol), psilocybin (aka [3-[2-(dimethylamino)ethyl]-1H-indol-4-yl] dihydrogen phosphate), serotonin (aka 3-(2-aminoethyl)-1H-indol-5-ol), 1P-LSD (aka (6aR,9R)-N,N-diethyl-7-methyl-4-propanoyl-6,6a,8,9-tetrahydroindolo [4,3-fg] quinoline-9-carboxamide), ALD-52 (aka (6aR,9R)-4-acetyl-N,N-diethyl-7-methyl-6,6a,8,9-tetrahydroindolo[4,3-fg]q- uinoline-9-carboxamide), AL-LAD (aka (6aR,9R)-N,N-diethyl-7-prop-2-enyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]q- uinoline-9-carboxamide), BU-LAD (aka (6aR,9R)-7-butyl-N,N-diethyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoli- ne-9-carboxamide), DAL (aka (6aR,9R)-7-methyl-N,N-bis(prop-2-enyl)-6,6a,8,9-tetrahydro-4H-indolo[4,3-- fg]quinoline-9-carboxamide), DAM-57 (aka (6aR,9R)-N,N,7-trimethyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-9- -carboxamide), EIPLA (aka (6aR,9R)-N-ethyl-7-methyl-N-propan-2-yl-6,6a,8,9-tetrahydro-4H-indolo[4,3- -fg]quinoline-9-carboxamide), ETH-LAD (aka (6aR,9R)-N,N,7-triethyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-9-- carboxamide), LAE-32 (aka (6aR,9R)-N-ethyl-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-- 9-carboxamide), LPD-824 (aka [(6aR,9R)-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-9-yl]-p- yrrolidin-1-ylmethanone), LSB (aka (6aR,9R)-N-butan-2-yl-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quino- line-9-carboxamide), LSA (aka (6aR,9R)-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-9-carbox- amide), LSD-25 (aka (6aR,9R)-N,N-diethyl-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinol- ine-9-carboxamide), LSD-PiP (aka (7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-9-yl)-piperidin-- 1-ylmethanone), LSM-775 (aka [(6aR,9R)-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-9-yl]-m- orpholin-4-ylmethanone), LSP (aka (6aR,9R)-7-methyl-N-pentan-3-yl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quin- oline-9-carboxamide), LSZ (aka [(6aR,9R)-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinoline-9-yl]-[- (2S,4S)-2,4-dimethylazetidin-1-yl]methanone), methergine (aka (6aR,9R)-N-(1-hydroxybutan-2-yl)-7-methyl-6,6a,8,9-tetrahydro-4H-indolo[4- ,3-fg]quinoline-9-carboxamide), MiPLA (aka (6aR,9R)-N,7-dimethyl-N-propan-2-yl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]-

quinoline-9-carboxamide), NDTDI, PARGY-LAD, PRO-LAD (aka (6aR,9R)-N,N-diethyl-7-propyl-6,6a,8,9-tetrahydro-4H-indolo[4,3-fg]quinol- ine-9-carboxamide), 2-Me-DET (aka N,N-diethyl-2-(2-methyl-1H-indol-3-yl)ethanamine), 2-Me-DMT (aka N,N-dimethyl-2-(2-methyl-1H-indol-3-yl)ethanamine), 2,alpha-DMT (aka 1-(2-methyl-1H-indol-3-yl)propan-2-amine), 4-AcO-DALT (aka [3-[2-[bis(prop-2-enyl)amino]ethyl]-1H-indol-4-yl] acetate), 4-AcO-DET (aka [3-[2-(diethylamino)ethyl]-1H-indol-4-yl] acetate), 4-AcO-DIPT (aka 3-[2-(Diisopropylamino)ethyl]-1H-indol-4-yl acetate), 4-AcO-DMT (aka [3-[2-(dimethylamino)ethyl]-1H-indol-4-yl] acetate), 4-AcO-DPT (aka [3-[2-(dipropylamino)ethyl]-1H-indol-4-yl] acetate), 4-AcO-EPT (aka 3-{2-[Ethyl(propyl)amino]ethyl}-1H-indol-4-yl acetate), 4-AcO-MET (aka [3-[2-[ethyl(methyl)amino]ethyl]-1H-indol-4-yl] acetate), 4-AcO-MIPT (aka [3-[2-[methyl(propan-2-yl)amino]ethyl]-1H-indol-4-yl] acetate), 4-AcO-MPT, 4-HO-DBT (aka 3-[2-(dibutylamino)ethyl]-1H-indol-4-ol), 4-HO-DET (aka 3-[2-(diethylamino)ethyl]-1H-indol-4-ol), 4-HO-DIPT (aka 3-[2-[di(propan-2-yl)amino]ethyl]-1H-indol-4-ol), 4-HO-DPT (aka 3-[2-(dipropylamino)ethyl]-1H-indol-4-ol), 4-HO-EPT, 4-HO-MCPT, 4-HO-MET (aka 3-[2-[ethyl(methyl)amino]ethyl]-1H-indol-4-ol), 4-HO-MIPT (aka 3-[2-[methyl(propan-2-yl)amino]ethyl]-1H-indol-4-ol), 4-HO-MPMI (aka 3-[(1-methylpyrrolidin-2-yl)methyl]-1H-indol-4-ol), 4-HO-MPT (aka 3-[2-[methyl(propyl)amino]ethyl]-1H-indol-4-ol), 4-HO-pyr-T (aka 3-(2-pyrrolidin-1-ylethyl)-1H-indol-4-ol), 4-MeO-MIPT (aka N-[2-(4-methoxy-1H-indol-3-yl)ethyl]-N-methylpropan-2-amine), 4,5-MDO-DIPT (aka N-[2-(6H-[1,3]dioxolo[4,5-e]indol-8-yl)ethyl]-N-propan-2-ylpropan-2-amine-), 4,5-MDO-DMT (aka 2-(6H-[1,3]dioxolo[4,5-e]indol-8-yl)-N,N-dimethylethanamine), 5-BROMO-DMT (aka 2-(5-bromo-1H-indol-3-yl)-N,N-dimethylethanamine), 5-chloro-alpha-MT (aka 1-(5-chloro-1H-indol-3-yl)propan-2-amine), 5-fluoro-AMT (aka 1-(5-fluoro-1H-indol-3-yl)propan-2-amine), 5-MeO-AET (aka 1-(5-methoxy-1H-indol-3-yl)butan-2-amine), 5-MeO-AMT (aka 1-(5-methoxy-1H-indol-3-yl)propan-2-amine), 5-MeO-DALT (aka N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-N-prop-2-enylprop-2-en-1-amine), 5-MeO-DET (aka N,N-diethyl-2-(5-methoxy-1H-indol -3- yl)ethanamine), 5-MeO-DiPT (aka N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-N-propan-2-ylpropan-2-amine), 5-MeO-DMT (aka 2-(5-methoxy-1H-indol-3-yl)-N,N-dimethylethanamine), 5-MeO -DPT (aka N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-N-propylpropan-1-amine), 5-MeO-EiPT (aka N-ethyl-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]propan-2-amine), 5-MeO-MALT (aka N-[2-(5-Methoxy-1H-indol-3-yl)ethyl]-N-methylprop-2-en-1-amine), 5-MeO-MiPT (aka N-[2-(5-methoxy-1H-indol -3-yl)ethyl]-N-methylpropan-2-amine), 5-MeO-NMT (aka 2-(5-methoxy-1H-indol-3-yl)-N-methylethanamine;hydrochloride), 5-MeO-pyr-T (aka 4-fluoro-5-methoxy-3-(2-pyrrolidin-1-ylethyl)-1H-indole), 5-MeO-TMT (aka 2-(5-methoxy-2-methyl-1H-indol-3-yl)-N,N-dimethylethanamine), 5-MeS-DMT (aka N,N-dimethyl-2-(5-methylsulfanyl-1H-indol-3-yl)ethanamine), 5,6-MDO-DIPT (aka N-[2-(5H-[1,3]dioxolo[4,5-f]indol-7-yl)ethyl]-N-propan-2-ylpropan-2-amine-), 5,6-MDO-DMT (aka 2-(5H-[1,3]dioxolo[4,5-f]indol-7-yl)-N,N-dimethylethanamine), 5,6-MDO-MIPT (aka N-[2-(5H-[1,3]dioxolo[4,5-f]indol-7-yl)ethyl]-N-ethylpropan-2-amine), 5,6-MeO-MIPT (aka N-[2-(5,6-dimethoxy-1H-indol-3-yl)ethyl]-N-

methylpropan-2-amine), 5,N,N-TMT (aka N,N-dimethyl-2-(5-methyl-1H-indol-3-ethanamine), 6-MeO-THH (aka 6-methoxy-1-methyl-2,3,4,9-tetrahydro-1H-pyrido [3,4-b]indole), alpha-ET (aka 1-(1H-indol-3-yl)butan-2-amine), alpha-MT (aka 1-(1H-indol-3-yl)propan-2-amine), alpha-TMT (aka 1-(1H-indol-3-yl)-N,N-dimethylpropan-2-amine), alpha,N-DMT (aka 2-(1H-indol-3-yl)-N,N-dimethylethanamine), alpha,N,O-TMS (aka 1-(5-methoxy-1H-indol-3-yl)-N-methylpropan-2-amine), alpha,O-DMS (aka 1-(5-methoxy-1H-indol-3-yl)propan-2-amine), DALT (aka N-[2-(1H-indol-3-ypethyl]-N-prop-2-enylprop-2-en-1-amine), DBT (aka N-butyl-N-[2-(1H-indol-3-yl)ethyl]butan-1-amine), DET (aka N,N-diethyl-2-(1H-indol-3-yl)ethanamine), DiPT (aka N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-N-propan-2-ylpropan-2-amine), DMT (aka 2-(1H-indol-3-yl)-N,N-dimethylethanamine), DPT (aka N-[2-(1H-indol-3-yl)ethyl]-N-propylpropan-1-amine), EiPT (aka N-ethyl-N-[2-(1H-indol-3-yl)ethyl]propan-2-amine), Harmaline (aka 7-methoxy-1-methyl-3,4-dihydro-2H-pyrido [3,4-b]indole), Harmine (aka 7-methoxy-1-methyl-9H-pyrido[3,4-b]indole), MALT, MBT (aka 3H-1,3-benzothiazole-2-thione), Melatonin (aka N-[2-(5-methoxy-1H-indol-3-yl)ethyl]acetamide), MET (aka N-ethyl-2-(1H-indol-3-yl)-N-methylethanamine), MiPT (aka N-[2-(1H-indol-3-yl)ethyl]-N-methylpropan-2-amine), MPT (aka 3-[2-[methyl(propyl)amino]ethyl]-1H-indol-4-ol), NET (aka N-ethyl-2-(1H-indol-3-yl)ethanamine), NMT (aka 2-(1H-indol-3-yl)-N-methylethanamine), PiPT (aka N-[2-(1H-indol-3-yl)ethyl]-N-propan-2-ylpropan-1-amine), pyr-T (aka 3-(2-pyrrolidin-1-ylethyl)-1H-indole), T (aka 2-(1H-indol-3-yl)ethanamine), Tetrahydroharmine (aka 7-methoxy-1-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole), 2-Br-4,5-MDA (aka 1-(6-bromo-1,3-benzodioxol-5-yl)propan-2-amine), 2-TIM (aka 2-(3,4-dimethoxy-2-methylsulfanylphenyl)ethanamine), 2-TOET (aka 1-(4-ethyl-5-methoxy-2-methylsulfanylphenyl)propan-2-amine), 2-TOM (aka 1-(5-methoxy-4-methyl-2-methylsulfanylphenyl)propan-2-amine), 2,4-DMA (aka 1-(2,4-dimethoxyphenyl)propan-2-amine), 2,5-DMA (aka 1-(2,5-dimethoxyphenyl)propan-2-amine), 2C-B (aka 2-(4-bromo-2,5-dimethoxyphenyl)ethanamine), 2C-C (aka 2-(4-chloro-2,5-dimethoxyphenyl)ethanamine), 2C-D (aka 2-(2,5-dimethoxy-4-methylphenyl)ethanamine), 2C-E (aka 2-(4-ethyl-2,5-dimethoxyphenyl)ethanamine), 2C-F (aka 2-(4-fluoro-2,5-dimethoxyphenyl)ethanamine), 2C-G (aka 2-(2,5-dimethoxy-3,4-dimethylpheny)ethanamine), 2C-G-3 (aka 2-(4,7-dimethoxy-2,3-dihydro-1H-inden-5-yl)ethanamine), 2C-G-4 (aka 2-(1,4-dimethoxy-5,6,7,8-tetrahydronaphthalen-2-yl)ethanamine), 2C-G-5 (aka CAS 207740-20-3), 2C-G-N (aka 2-(1,4-dimethoxynaphthalen-2-yl)ethanamine), 2C-H (aka 2-(2,5-dimethoxyphenyl)ethanamine), 2C-I (aka 2-(4-iodo-2,5-dimethoxyphenyl)ethanamine), 2C-N (aka 2-(2,5-dimethoxy-4-nitrophenyl)ethanamine), 2C-O-4 (aka 2-(2,5-dimethoxy-4-propan-2-yloxyphenyl)ethanamine), 2C-P (aka 2-(2,5-dimethoxy-4-propylphenyl)ethanamine), 2C-SE (aka 2-(2,5-dimethoxy-4-methylselanylphenyl)ethanamine), 2C-T (aka 2-(2,5-dimethoxy-4-methylsulfanylphenyl)ethanamine), 2C-T-13 (aka 2-[2,5-dimethoxy-4-(2-methoxyethylsulfanyl)phenyl]ethanamine), 2C-T-15 (aka 2-(4-cyclopropylsulfanyl-2,5-dimethoxyphenyl)ethanamine), 2C-T-17 (aka 2-(4-butan-2-ylsulfanyl-2,5-

dimethoxyphenyl)ethanamine), 2C-T-2 (aka 2-(4-ethylsulfanyl-2,5-dimethoxypheny)ethanamine), 2C-T-2 (aka 2-[4-(2-fluoroethylsulfanyl)-2,5-dimethoxyphenyl]ethanamine), 2C-T-4 (aka 2-(2,5-dimethoxy-4-propan-2-ylsulfanylpheny)ethanamine), 2C-T-7 (aka 2-(2,5-dimethoxy-4-propylsulfanylphenyl)ethanamine), 2C-T-8 (aka 2-[4-(cyclopropylmethylsulfanyl)-2,5-dimethoxyphenyl]ethanamine), 2C-T-9 (aka 2-(4-butylsulfanyl-2,5-dimethoxypheny)ethanamine), 2C-TFM (aka 2-[2,5-dimethoxy-4-(trifluoromethyl)phenyl]ethanamine), 2T-MMDA-3a (aka 1-(4-methylsulfanyl-1,3-benzodioxol-5-yl)propan-2-amine), 3-T-TRIS (aka 2-(3,4-diethoxy-5-ethylsulfanylphenyl)ethanamine), 3-TASB (aka 2-(3-ethoxy-4-ethylsulfanyl-5-methoxyphenyl)ethanamine), 3-TE (aka 2-(4-ethoxy-3-methoxy-5-methylsulfanylphenyl)ethanamine), 3-TFM (aka 2-(2,4-dimethoxy-3-methylsulfanylphenyl)ethanamine), 3-TM (aka 2-(3,4-dimethoxy-5-methylsulfanylpheny)ethanamine), 3-TME (aka 2-(3-ethylsulfanyl-4,5-dimethoxyphenyl)ethanamine), 3-TSB (aka 2-(3-ethoxy-5-ethylsulfanyl-4-methoxyphenyl)ethanamine), 3,4-DMA (aka 1-(3,4-dimethoxyphenyl)propan-2-amine), 3C-BZ (aka 1-(3,5-dimethoxy-4-phenylmethoxyphenyl)propan-2-amine), 3C-E (aka 1-(4-ethoxy-3,5-dimethoxyphenyl)propan-2-amine), 4-Br-3,5-DMA (aka 1-(4-bromo-3,5-dimethoxyphenyl)propan-2-amine), 4-D (aka CAS 1020518-87-9), 4-MA (aka 1-(4-methoxyphenyl)propan-2-amine), 4-T-TRIS (aka 2-(3,5-diethoxy-4-ethylsulfanylphenyl)ethanamine), 4-TASB (aka 2-(3-ethoxy-4-ethylsulfanyl-5-methoxypheny)ethanamine), 4-TE (aka 2-(4-ethylsulfanyl-3,5-dimethoxyphenyl)ethanamine), 4-TIM (aka 2-(2,3-dimethoxy-4-methylsulfanylphenyl)ethanamine), 4-TM (aka 2-(3,5-dimethoxy-4-methylsulfanylphenyl)ethanamine), 4-TME (aka 2-(3-ethoxy-5-methoxy-4-methylsulfanylpheny)ethanamine), 4-TSB (aka 2-(3,5-diethoxy-4-methylsulfanylphenyl)ethanamine), 4T-MMDA-2 (aka 1-(5-methoxy-1,3-benzoxathiol-6-yl)propan-2-amine), 5-TASB (aka 2-(3,4-diethoxy-5-methylsulfanylphenyl)ethanamine), 5-TME (aka 2-(3-ethoxy-4-methoxy-5-methylsulfanylphenyl)ethanamine), 5-TOET (aka 1-(4-ethyl-2-methoxy-5-methylsulfanylphenyl)propan-2-amine), 5-TOM (aka 1-(2-methoxy-4-methyl-5-methylsulfanylphenyl)propan-2-amine), 25B-NBF (aka 2-(4-bromo-2,5-dimethoxyphenyl)-N-[(2-fluorophenyl)methyl]ethanamine-), 25B-NBOH (aka 2-[[2-(4-bromo-2,5-dimethoxypheny)ethylaminolmethyl]phenol), 25B-NBOMe (aka 2-(4-bromo-2,5-dimethoxyphenyl)-N[(2-methoxyphenyl)methyl]ethanamine-), 25C-NB3OMe (aka 2-(4-chloro-2,5-dimethoxyphenyl)-N-[((3-methoxypheny)methyl]ethanamine), 25C-NB4OMe (aka 2-(4-chloro-2,5-dimethoxyphenyl)-N-[(4-methoxyphenyl)methyl]ethanamine), 25C-NBF (aka 2-(4-chloro-2,5-dimethoxyphenyl)-N-[(2-fluorophenyl)methyl]ethanamine), 25C-NBOH (aka 2-(4-chloro-2,5-dimethoxyphenyl)ethylaminolmethyl]phenol), 25C-NBOMe (aka 2-(4-chloro-2,5-dimethoxyphenyl)-N[(2-methoxyphenyl)methyl]ethanamine), 25CN-NBOH (aka 4-[2-[(2-hydroxyphenyl)methylaminolethyl]-2,5-dimethoxybenzonitrile), 25CN-NBOMe (aka CAS

1354632-16-8), 25D-NBOMe (aka 2-(2,5-dimethoxy-4-methylphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine), 25E-NBOMe (aka 2-(4-ethyl-2,5-dimethoxyphenyl)-N4(2-methoxyphenyl)methyl]ethanamine), 25G-NBOMe (aka 2-(2,5-dimethoxy-3,4-dimethylphenyl)-N-[(2-methoxyphenyl)methyl]ethanamin- e), 25H-NBOMe (aka 2-(2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine), 25H-NB34MD (aka N-(1,3-benzodioxol-5-ylmethyl)-2-(4-iodo-2,5-dimethoxyphenyl)ethanamine), 25I-NB3OMe (aka 2-(4-iodo-2,5-dimethoxyphenyl)-N-[(3-methoxyphenyl)methyl]ethanamine), 25I-NB4OMe (aka 2-(4-iodo-2,5-dimethoxyphenyl)-N-[(4-methoxyphenyl)methyl]ethanamine), 25I-NBF (aka N-[(2-fluorophenyl)methyl]-2-(4-iodo-2,5-dimethoxyphenyl)ethanamine), 25I-NBMD (aka N-(1,3-benzodioxol-4-ylmethyl)-2-(4-iodo-2,5-dimethoxyphenyl)ethanamine), 25I-NBOH (aka 2-[[2-(4-iodo-2,5-dimethoxypheny)ethylamino]methyl]phenol), 25I-NBOMe (aka 2-(4-iodo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine), 25iP-NBOMe (aka 2-(2,5-dimethoxy-4-propan-2-ylphenyl)-N-[(2-methoxypheny)methyl]ethanamin- e), 25N-NBOMe (aka 2-(2,5-dimethoxy-4-nitrophenyl)-N-[(2-methoxypheny)methyl]ethanamine), 25P-NBOMe (aka 2-(2,5-dimethoxy-4-propylphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine), 25TFM-NBOMe (aka 2-[2,5-dimethoxy-4-(trifluoromethyl)phenyl]-N-[(2-methoxyphenyl)methyl]et- hanamine), 2CBCB-NBOMe (aka 1-[(7R)-3-bromo-2,5-dimethoxy-7-bicyclo[4.2.0]octa-1(6),2,4-trienyl]-N-[(- 2-methoxypheny)methyl]methanamine), 2CBFly-NBOMe (aka 2-(4-bromo-2,3,6,7-tetrahydrofuro[2,3-f][1]benzofuran-8-yl)-N-[(2-methoxy- phenyl)methyl]thanamine), AEM (aka 1-(3,4,5-trimethoxyphenyl)butan-2-amine), AL (aka 2-(3,5-dimethoxy-4-prop-2-enoxyphenyl)ethanamine), ALEPH (aka 1-(2,5-dimethoxy-4-methylsulfanylphenyl)propan-2-amine; hydrochloride), ALEPH-2 (aka 1-(4-ethylsulfanyl-2,5-dimethoxyphenyl)propan-2-amine), ALEPH-4 (aka 1-(2,5-dimethoxy-4-propan-2-ylsulfanylphenyl)propan-2-amine), ALEPH-6 (aka 1-(2,5-dimethoxy-4-phenylsulfanylphenyl)propan-2-amine), ALEPH-7 (aka 1-(2,5-dimethoxy-4-propylsulfanylphenyl)propan-2-amine), ARIADNE (aka (2R)-1-(2,5-dimethoxy-4-methylphenyl)butan-2-amine), ASB (aka 2-(3,4-diethoxy-5-methoxyphenyl)ethanamine), B (aka 2-(4-butoxy-3,5-dimethoxyphenyl)ethanamine), BEATRICE (aka 1-(2,5-dimethoxy-4-methylphenyl)-N-methylpropan-2-amine), beta-D (aka 2,2-dideuterio-2-(3,4,5-trimethoxyphenyl)ethanamine), BIS-TOM (aka 1-[4-methyl-2,5-bis(methylsulfanyl)phenyl]propan-2-amine), bk-2C-B (aka 2-amino-1-(4-bromo-2,5-dimethoxyphenyl)ethanone), BOB (aka 2-(4-bromo-2,5-dimethoxyphenyl)-2-methoxyethanamine), BOD (aka 2-(2,5-dimethoxy-4-methylphenyl)-2-methoxyethanamine), BOH (aka 2-(1,3-benzodioxol-5-yl)-2-methoxyethanamine), BOHD (aka 2-amino-1-(2,5-dimethoxy-4-methylpheny)ethanol), BOM (aka 2-methoxy-2-(3,4,5-trimethoxyphenyl)ethanamine), bromo-dragonFLY (aka 1-(4-bromofuro[2,3-f][1]benzofuran-8-yl)propan-2-amine), butylone (aka 1-(1,3-benzodioxl-5-yl)-2-(methylamino)butan-1-one), CPM (aka 2-[4-(cyclopropylmethoxy)-3,5-dimethoxyphenyl]ethanamine), DESOXY (aka 2-(3,5-dimethoxy-4-methylpheny)ethanamine), DMCPA (aka 2-(2,5-dimethoxy-4-

methylphenyl)cyclopropan-1-amine), DME (aka 2-amino-1-(3,4-dimethoxyphenyl)ethanol), DMMDA (aka 1-(4,7-dimethoxy-1,3-benzodioxol-5-yl)propan-2-amine), DMMDA-2 (aka 1-(6,7-dimethoxy-1,3-benzodioxol-5-yl)propan-2-amine), DMPEA (aka 2-(3,4-dimethoxyphenyl)ethanamine), DOAM (aka 1-(2,5-dimethoxy-4-pentylphenyl)propan-2-amine), DOB (aka 1-(4-bromo-2,5-dimethoxyphenyl)propan-2-amine), DOBU (aka 1-(4-butyl-2,5-dimethoxyphenyl)propan-2-amine), DOC (aka 1-(4-chloro-2,5-dimethoxyphenyl)propan-2-amine), DOEF (aka 1-[4-(2-fluoroethyl)-2,5-dimethoxyphenyl]propan-2-amine), DOET (aka 1-(4-ethyl-2,5-dimethoxyphenyl)propan-2-amine), DOF (aka 1-(4-fluoro-2,5-dimethoxyphenyl)propan-2-amine), DOI (aka 1-(4-iodo-2,5-dimethoxyphenyl)propan-2-amine), DOM (aka 1-(2,5-dimethoxy-4-methylphenyl)propan-2-amine), DON (aka 1-(2,5-dimethoxy-4-nitrophenyl)propan-2-amine), DOPR (aka 1-(2,5-dimethoxy-4-propylphenyl)propan-2-amine), DOTFM (aka 1-[2,5-dimethoxy-4-(trifluoromethyl)phenyl]propan-2-amine), E (aka 2-(4-ethoxy-3,5-dimethoxyphenyl)ethanamine), EBDP (aka 1-(1,3-benzodioxol-5-yl)-N-ethylpentan-2-amine), EEE (aka 1-(2,4,5-triethoxyphenyl)propan-2-amine), EEM (aka 1-(2,4-diethoxy-5-methoxyphenyl)propan-2-amine), EME (aka 1-(2,5-diethoxy-4-methoxyphenyl)propan-2-amine), EMM (aka 1-(2-ethoxy-4,5-dimethoxyphenyl)propan-2-amine), ETHYL-J (aka 1-(1,3-benzodioxol-5-yl)-N-ethylbutan-2-amine), ETHYL-K (aka 1-(1,3-benzodioxol-5-yl)-N-ethylpentan-2-amine), F-2 (aka 1-(5-methoxy-2-methyl-2,3-dihydro-1-benzofuran-6-yl)propan-2-amine), F-22 (aka 1-(5-methoxy-2,2-dimethyl-3H-1-benzofuran-6-yl)propan-2-amine), FLEA (aka N-[1-(1,3-benzodioxol-5-yl)propan-2-yl]-N-methylhydroxylamine), G-3 (aka 1-(4,7-dimethoxy-2,3-dihydro-1H-inden-5-yl)propan-2-amine), G-4 (aka 1-(1,4-dimethoxy-5,6,7,8-tetrahydronaphthalen-2-yl)propan-2-amine), G-5 (aka 3,6-dimethoxy-4-(2-aminopropyl)benzonorbornane), G-N (aka 1-(1,4-dimethoxynaphthalen-2-yl)propan-2-amine), GANESHA (aka 1-(2,5-dimethoxy-3,4-dimethylphenyl)propan-2-amine), HOT-17 (aka N-[2-(4-butan-2-ylsulfanyl-2,5-dimethoxypheny)ethyl]hydroxylamine), HOT-2 (aka N-[2-(4-ethylsulfanyl-2,5-dimethoxypheny)ethyl]hydroxylamine), HOT-7 (aka N-[2-(2,5-dimethoxy-4-propylsulfanylpheny)ethyl]hydroxylamine), IDNNA (aka 1-(4-iodo-2,5-dimethoxyphenyl)-N,N-dimethylpropan-2-amine), IM (aka 2-(2,3,4-trimethoxyphenyl)e thanamine), IP (aka 2-(3,5-dimethoxy-4-propan-2-yloxyphenyl)ethanamine), IRIS (aka 1-(5-ethoxy-2-methoxy-4-methylphenyl)propan-2-amine), J (aka 1-(1,3-benzodioxol-5-yl)butan-2-amine), jimscaline (aka [(1R)-4,5,6-trimethoxy-2,3-dihydro-1H-inden-1-yl]methanamine), LOPHOPHINE (aka 2-(7-methoxy-1,3-benzodioxol-5-yl)ethanamine), M (aka 2-(3,4,5-trimethoxypheny)ethanamine), MADAM-6 (aka N-methyl-1-(6-methyl-1,3-benzodioxol-5-yl)propan-2-amine), MAL (aka 2-[3,5-dimethoxy-4-(2-methylprop-2-enoxy)phenyl]ethanamine), MDA (aka 1-(1,3-benzodioxol-5-yl)propan-2-amine), MDAL (aka 1-(1,3-benzodioxol-5-yl)-N-prop-2-enylpropan-2-amine), MDBU (aka N-[1-(1,3-benzodioxol-5-yl)propan-2-yl]butan-1-amine), MDBZ (aka 1-(1,3-benzodioxol-5-yl)-N-benzylpropan-2-amine), MDCPM (aka 1-(3a,7a-dihydro-1,3-benzodioxol-5-yl)-N-(cyclopropylmethyl)propan-2-amin- e), MDDM (aka 1-(1,3-benzodioxol-5-yl)-N,N-

dimethylpropan-2-amine), MDE (aka 1-(1,3-benzodioxol-5-yl)-N-ethylpropan-2-amine), MDHOET (aka 2-[1-(1,3-benzodioxol-5-yl)propan-2-ylamino]ethanol), MDIP (aka 1-(1,3-benzodioxol-5-yl)-N-propan-2-ylpropan-2-amine), MDMA (aka 1-(1,3-benzodioxol-5-yl)-N-methylpropan-2-amine), MDMC (aka 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-N-methylpropan-2-amine), MDMEO (aka 1-(1,3-benzodioxol-5-yl)-N-methoxypropan-2-amine), MDMEOET (aka 1-(1,3-benzodioxol-5-yl)-N-(2-methoxyethyl)propan-2-amine), MDMP (aka 1-(1,3-benzodioxol-5-yl)-N,2-dimethylpropan-2-amine), MDOH (aka N-[1-(1,3-benzodioxol-5-yl)propan-2-yl]hydroxylamine), MDPEA (aka 2-(1,3-benzodioxol-5-yl)ethanamine), MDPH (aka 1-(1,3-benzodioxol-5-yl)-2-methylpropan-2-amine), MDPL (aka 1-(1,3-benzodioxol-5-yl)-N-prop-2-ynylpropan-2-amine), MDPR (aka 1-(1,3-benzodioxol-5-yl)-N-propylpropan-2-amine), ME (aka 2-(3-ethoxy-4,5-dimethoxyphenyl)ethanamine), MEDA (aka 1-(5-methoxy-2,3-dihydro-1,4-benzodioxin-7-yl)propan-2-amine), MEE (aka 1-(4,5-diethoxy-2-methoxyphenyl)propan-2-amine), MEM (aka 1-(4-ethoxy-2,5-dimethoxyphenyl)propan-2-amine), MEPEA (aka 2-(4-ethoxy-3-methoxyphenyl)ethanamine), META-DOB (aka 1-(5-bromo-2,4-dimethoxyphenyl)propan-2-amine), META-DOT (aka 1-(2,4-dimethoxy-5-methylsulfanylphenyl)propan-2-amine), METHYL-DMA (aka 1-(2,5-dimethoxyphenyl)-N-methylpropan-2-amine), METHYL-DOB (aka 1-(4-bromo-2,5-dimethoxyphenyl)-N-methylpropan-2-amine), METHYL-J (aka 1-(1,3-benzodioxol-5-yl)-N-methylbutan-2-amine), METHYL-K (aka 1-(1,3-benzodioxol-5-yl)-N-methylpentan-2-amine), METHYL-MA (aka 1-(4-methoxyphenyl)-N-methylpropan-2-amine), METHYL-MMDA-2 (aka 1-(6-methoxy-1,3-benzodioxol-5-yl)-N-methylpropan-2-amine), MMDA (aka 1-(7-methoxy-1,3-benzodioxol-5-yl)propan-2-amine), MMDA-2 (aka 1-(6-methoxy-1,3-benzodioxol-5-yl)propan-2-amine), MMDA-3a (aka 1-(4-methoxy-1,3-benzodioxol-5-yl)propan-2-amine), MMDA-3b (aka 1-(7-methoxy-1,3-benzodioxol-4-yl)propan-2-amine), MME (aka 1-(5-ethoxy-2,4-dimethoxyphenyl)propan-2-amine), MP (aka 2-(3,4-dimethoxy-5-propoxyphenyl)ethanamine), MPM (aka 1-(2,4-dimethoxy-5-propoxyphenyl)propan-2-amine), NBOMe-mescaline (aka N-[(2-methoxyphenyl)methyl]-2-(3,4,5-trimethoxypheny)ethanamine), ORTHO-DOT (aka 1-(4,5-dimethoxy-2-methylsulfanylphenyl)propan-2-amine), P (aka 2-(3,5-dimethoxy-4-propoxyphenyl)ethanamine), PE (aka 2-[3,5-dimethoxy-4-(2-phenylethoxy)phenyl]ethanamine), PEA (aka 2-phenylethanamine), PROPYNYL (aka 2-(3,5-dimethoxy-4-prop-2-ynoxyphenyl)ethanamine), psi-2C-T-4, psi-DOM (aka 1-(2,6-dimethoxy-4-methylphenyl)propan-2-amine), SB (aka 2-(3,5-diethoxy-4-methoxyphenyl)ethanamine), TA (aka 1-(2,3,4,5-tetramethoxyphenyl)propan-2-amine), TB (aka 2-(4-butylsulfanyl-3,5-dimethoxypheny)ethanamine), TCB-2 (aka (3-bromo-2,5-dimethoxy-7-bicyclo[4.2.0]octa-1(6),2,4-trienyl)methanamine;hydrobromide), TMA (aka 1-(3,4,5-trimethoxyphenyl)propan-2-amine), TMA-2 (aka 1-(2,4,5-trimethoxyphenyl)propan-2-amine), TMA-3 (aka 1-(2,3,4-trimethoxyphenyl)propan-2-amine), TMA-4 (aka 1-(2,3,5-trimethoxyphenyl)propan-2-amine), TMA-5 (aka 1-(2,3,6-trimethoxyphenyl)propan-2-amine), TMA-6 (aka 1-(2,4,6-

trimethoxyphenyl)propan-2-amine), TMPEA (aka 2-(2,4,5-trimethoxyphenyl)ethanamine), TOMSO (aka 1-(2-methoxy-4-methyl-5-methylsulfinylphenyl)propan-2-amine), TP (aka 2-(3,5-dimethoxy-4-propylsulfanylphenyl)ethanamine), and TRIS (aka 2-(3,4,5-triethoxyphenyl)ethanamine).

In one embodiment, a serotonergic drug is chosen from alprazolam, amphetamine, aripiprazole, azapirone, a barbiturate, bromazepam, bupropion, buspirone, a cannabinoid, chlordiazepoxide, citalopram, clonazepam, clorazepate, dextromethorphan, diazepam, duloxetine, escitalopram, fluoxetine, flurazepam, fluvoxamine, lorazepam, lysergic acid diethylamide, lysergamide, 3,4-methylenedioxymethamphetamine, milnacipran, mirtazapine, naratriptan, paroxetine, pethidine, phenethylamine, psicaine, oxazepam, reboxetine, serenic, serotonin, sertraline, temazepam, tramadol, triazolam, a tryptamine, venlafaxine, vortioxetine, and derivatives thereof.

In one embodiment, serotonin acts at a serotonin receptor, *e.g.*, by acting as a ligand at a 5-HT receptor. In one embodiment, serotonin is produced by an organism for use as a neurotransmitter within that organism. In one embodiment, the compositions and methods disclosed herein increase the activity at a serotonin receptor. In one embodiment, the compositions and methods disclosed herein decrease the activity at a serotonin receptor.

As used herein, the term "serotonin receptor" refers to a collection of proteins outside a cell capable of receiving signals and activating internal signal transduction pathways causing a cellular response. In one embodiment, a serotonin receptor is found on a cell within the central nervous system of an organism. In one embodiment, a serotonin receptor is found on a cell within the peripheral nervous system of an organism. In one embodiment, serotonin is the natural ligand for a serotonin receptor. In one embodiment, a serotonin receptor modulates the release of a neurotransmitter, e.g., glutamate, gamma-Aminobutyric acid, dopamine, epinephrine (a.k.a. norepinephrine), acetylcholine, etc. In one embodiment, a serotonin receptor modulates the release of a hormone, e.g., oxytocin, prolactin, vasopressin, cortisol, corticotropin, substance P, etc.

Examples of serotonin receptors include, but are not limited to, 5-HT_{1A}, 5-HT_{1B}, 5-HT_{1D}, 5-HT_{1E}, 5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_{3}, 5-HT_{4}, 5-HT_{5A}, 5-HT_{5B}, 5-HT_{6}, and 5-HT_{7}.

As used herein, the term "adrenergic drug" refers to a compound that binds, blocks, or otherwise influences (e.g., via an allosteric reaction) activity at an adrenergic receptor. In one embodiment, an adrenergic drug binds to an adrenergic receptor. In one embodiment, an adrenergic drug indirectly affects an adrenergic receptor, e.g., via interactions affecting the reactivity of other molecules at the adrenergic receptor. In one embodiment, an adrenergic drug is an agonist, e.g., a compound activating an adrenergic receptor. In one embodiment, an adrenergic drug is an antagonist, e.g., a compound binding but not activating an adrenergic

receptor, e.g., blocking a receptor. In one embodiment, an adrenergic drug is an effector molecule, e.g., a compound binding to an enzyme for allosteric regulation. In one embodiment, an adrenergic drug acts (either directly or indirectly) at more than one type of receptor (e.g., 5HT, dopamine, adrenergic, acetylcholine, etc.).

In one embodiment, an adrenergic drug is an antidepressant.

In one embodiment, an adrenergic drug is a norepinephrine transporter inhibitor.

In one embodiment, an adrenergic drug is a vesicular monoamine transporter inhibitor.

In one embodiment, an adrenergic drug is chosen from adrenaline, agmatine, amoxapine, aptazapine, atomoxetine, bupropion, clonidine, doxepin, duloxetine, esmirtazpine, mianserin, mirabegron, mirtazapine, norepinephrine, phentolamine, phenylephrine, piperoxan, reserpine, ritodrine, setiptiline, tesofensine, timolol, trazodone, trimipramine, and xylazine.

In one embodiment, an adrenergic drug acts at an adrenergic receptor, e.g., by acting as a ligand at an adrenergic receptor. In one embodiment, adrenaline is produced by an organism for use as a neurotransmitter within that organism. In one embodiment, norepinephrine is produced by an organism for use as a neurotransmitter within that organism. In one embodiment, the compositions and methods disclosed herein increase the activity at an adrenergic receptor. In one embodiment, the compositions and methods disclosed herein decrease the activity at an adrenergic receptor.

As used herein, the term "adrenergic receptor" refers to a collection of proteins outside a cell capable of receiving signals and activating internal signal transduction pathways causing a cellular response. In one embodiment, an adrenergic receptor is found on a cell within the central nervous system of an organism. In one embodiment, an adrenergic receptor is found on a cell within the sympathetic nervous system of an organism.

As used herein, the term "dopaminergic drug" refers to a compound that binds, blocks, or otherwise influences (e.g., via an allosteric reaction) activity at a dopamine receptor. In one embodiment, a dopaminergic drug binds to a dopamine receptor. In one embodiment, a dopaminergic drug indirectly affects a dopamine receptor, e.g., via interactions affecting the reactivity of other molecules at the dopamine receptor. In one embodiment, a dopaminergic drug is an agonist, e.g., a compound activating a dopamine receptor. In one embodiment, a dopaminergic drug is an antagonist, e.g., a compound binding but not activating a dopamine receptor, e.g., blocking a receptor. In one embodiment, a dopaminergic drug is an effector molecule, e.g., a compound binding to an enzyme for allosteric regulation. In one embodiment, a dopaminergic drug acts (either directly or indirectly) at more than one type of receptor (e.g., 5HT, dopamine, adrenergic, acetylcholine, etc.).

In one embodiment, a dopaminergic drug is a dopamine transporter inhibitor.

In one embodiment, a dopaminergic drug is a vesicular monoamine transporter inhibitor.

In one embodiment, a 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, and thioridazine.

In one embodiment, a dopaminergic drug acts at a dopamine receptor, e.g., by acting as a ligand at a dopamine receptor. In one embodiment, dopamine is produced by an organism for use as a neurotransmitter within that organism. In one embodiment, the compositions and methods disclosed herein increase the activity at a dopamine receptor. In one embodiment, the compositions and methods disclosed herein decrease the activity at a dopamine receptor.

As used herein, the term "dopamine receptor" refers to a collection of proteins outside a cell capable of receiving signals and activating internal signal transduction pathways causing a cellular response. In one embodiment, a dopamine receptor is found on a cell within the central nervous system of an organism.

In one embodiment, the compound of Formula I and/or Formula V may yield active compounds that modulate the activity of a neurotransmitter at its native receptor, e.g., serotonin at a serotonin receptor, dopamine at a dopaminergic drug, norephedrine at an adrenergic receptor, etc.

In one embodiment, the compound of Formula I and/or Formula V may yield compounds that are active at one or more receptors, e.g., a serotonin 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.

In one embodiment, the compositions disclosed herein comprise a monoamine oxidase inhibitor.

As used herein, the term "monoamine oxidase inhibitor" refers to a molecule binding to a monoamine oxidase enzyme thereby reducing the activity of the monoamine oxidase enzyme. Within the context of this disclosure, examples of monoamine oxidase inhibitors include aurorix, deprenyl, eldepryl, emsam, humoryl, hydracarbazine, isocarboxazid, linezolid, manerix, nydrazid, phenelzine, pirazidol, procarbazine, rasagiline, and tranylcypromine. In one embodiment, monoamine oxidase catalyzes the oxidation of a monoamine, e.g., serotonin, dopamine, norepinephrine, amphetamine, adrenaline, etc.

In one embodiment, the compositions disclosed herein comprise a stabilizer. As used herein, the term "stabilizer" refers to a compound useful for preventing the degradation of an

active ingredient, e.g., a compound of Formula I and/or Formula V, a psilocybin derivative, a cannabinoid, a terpene, etc. In one embodiment, a stabilizer prevents an active ingredient from degrading. In one embodiment, a stabilizer prevents a serotonergic drug from reacting with other compounds in the composition, e.g., a cannabinoid, a terpene, a base, an acid, etc. In one embodiment, a stabilizer prevents a serotonergic drug from reacting with the ambient atmosphere, e.g., heat, light, water, and/or oxygen. In one embodiment, a stabilizer comprises an antioxidant. In one embodiment, a stabilizer comprises a pH buffer.

In one embodiment, the methods and compositions disclosed herein comprise an antioxidant. As used herein, the term "antioxidant" refers to a compound and/or a composition useful for preventing oxidation. In one embodiment, an antioxidant protects an active ingredient from "free radicals". Within the context of this disclosure, a "free radical" is an atom, molecule, or an ion with an unpaired valence electron. In one embodiment, an antioxidant is an electron donor.

In one embodiment, an antioxidant is chosen from ascorbic acid, lycopene, tocopherol, melatonin, retinol, astaxanthin, lutein, apigenin, carnosine, selenium, zinc, cucurmin, and a salt or derivative thereof.

In one embodiment, an antioxidant is ascorbic acid and/or its salts or derivatives. Within the context of this disclosure, the term "ascorbic acid" comprises Vitamin C and/or a salt or derivative thereof.

In one embodiment, an antioxidant prevents the oxidation of a composition comprising one or more compounds disclosed herein, e.g., compounds of Formula I and/or Formula V, psilocybin derivatives, cannabinoids, terpenes, and/or mixtures thereof. For example, preventing the oxidation of a phenolic group attached to a psilocybin derivative.

As used herein, the term "oxidation" refers to the formal loss of electrons and/or the increase of the formal oxidation state and/or the addition of an oxygen atom or atoms. As used herein, "reduction" refers to the formal gain of electrons and/or the decrease of the formal oxidation state. Zumdahl, Steven S., et al. Chemistry, 7th. Cengage Learning, 2018.

In one embodiment, the methods and compositions disclosed herein comprise a pH buffer.

As used herein, the term "pH buffer" refers to a compound or a composition useful for maintaining the pH of a composition. In one embodiment, a pH buffer comprises a weak acid and a corresponding conjugate base. In one embodiment, a pH buffer comprises a weak base and a corresponding conjugate acid. In one embodiment, a pH buffer does not change the pH of a composition with the addition of a strong acid and/or base.

In one embodiment, a pH buffer maintains the pH of a composition around 7. In one

embodiment, a pH buffer maintains the pH of a composition below about 7. In one embodiment, a pH buffer maintains the pH of a composition above about 7. In one embodiment, a pH buffer maintains the pH of a composition ranging from about 2 to about 6. In one embodiment, a pH buffer maintains the pH of a composition ranging from about 5 to about 7. In one embodiment, a pH buffer maintains the pH of a composition ranging from about 6 to about 8. In one embodiment, a pH buffer maintains the pH of a composition ranging from about 7 to about 10.

In one embodiment, a pH buffer comprises citric acid, acetic acid, monosodium phosphate, N-Cyclohexyl-2-aminoethanesulfonic acid, borate, hydrochloric acid, and/or sodium hydroxide.

In one embodiment, the methods disclosed herein comprise administering a composition comprising an acid.

As used herein, the term "acid" refers to a molecule or ion capable of donating a proton, i.e., H^+ and/or accepting electrons. In one embodiment, an "acid" refers to a Lewis acid. In one embodiment, an "acid" refers to a Bronsted acid. In one embodiment, an acid is determined by a composition's pH. In one embodiment, a pH below 7 indicates the presence of an acid.

In one embodiment, the compositions and methods disclosed herein comprise administering a formulation comprising a base.

As used herein, the term "base" refers to a molecule or ion capable of accepting a proton, i.e., an H^+. In one embodiment, a "base" refers to a molecule capable of donating an electron pair, i.e., a Lewis base. In one embodiment, the presence of a base is determined by a compound's pH. In one embodiment, a pH above 7 indicates the presence of a base.

In one embodiment, the compositions and methods disclosed herein comprise administering a non water-soluble composition.

In some embodiments, the compositions described herein are non-aqueous.

As used herein, the term "water soluble" refers to a compound or composition capable of dissolving in water at standard temperature and pressure. In one example, 1 g of a compound dissolves in 1 L of water. In one example, 2 g of a compound dissolves in 1 L of water. In one example, 5 g of a compound dissolves in 1 L of water. In one example, 10 g of a compound dissolves in 1 L of water. In one embodiment, a compound's solubility in water is an inherent property of a compound. In one embodiment, a compound's solubility in water is facilitated by another compound, e.g., an excipient.

In one embodiment, the compositions and methods disclosed herein comprise administering a compound of Formula I and/or Formula V present as and/or within a homogenous mixture within a dosage formulation.

In one embodiment, the compositions and methods disclosed herein comprise

administering a compound of Formula I and/or Formula V and at least one additional compound (*e.g.*, serotonergic drug, cannabinoid, terpene, excipient, stabilizer, antioxidant, etc.) present as and/or within a homogenous mixture within a dosage formulation.

As used herein, the term "homogeneous mixture" refers to a solid, liquid, or gaseous composition that has two or more compounds present within one state or thing, e.g., a clear, colorless solution. In one embodiment, the homogeneous mixtures disclosed herein have the same proportion, concentration, and/or ratio of its components across different samples. In one embodiment, the components in the homogeneous mixture are in the same state of matter. In one embodiment, a homogeneous mixture comprises one or more compounds within a solution, e.g., a compound of Formula I and/or Formula V and a cannabinoid within a clear solution. In one embodiment, the compositions disclosed herein are present as a homogenous mixture, e.g., a solution with no particulates, a solution with equal concentrations across samples, a powder of similar particle size, etc.

Disclosed herein is a method of modulating activity at a neurotransmitter receptor, comprising:

administering a dosage formulation comprising a compound of Formula I and/or Formula V to the person in need of treatment, wherein the dosage formulation modulates activity at a neurotransmitter receptor.

As used herein, the term "modulating activity of the neurotransmitter activity modulator" refers to changing, manipulating, and/or adjusting the ability of a compound or composition to affect a neurotransmitter receptor. In one embodiment, modulating the activity of a neurotransmitter activity modulator comprises administering an agonist at a neurotransmitter receptor. In one embodiment, modulating the activity of a neurotransmitter activity modulator comprises administering an antagonist at a neurotransmitter receptor.

As used herein, the term "administering" (e.g., administering a drug) refers to dosing, treating, giving, and/or providing. In one embodiment, administering a neurotransmitter activity modulator comprises providing a neurotransmitter activity modulator to an organism (e.g., a human being) with a neurotransmitter receptor. In one embodiment, administering a neurotransmitter activity modulator comprises providing a neurotransmitter activity modulator along with a compound of Formula I and/or Formula V, e.g., a formulation having each of a neurotransmitter activity modulator and a compound of Formula I and/or Formula V in a single dosage. In one embodiment, administering a neurotransmitter activity modulator comprises applying a transdermal composition, e.g., applying a topical composition to the skin having each of a neurotransmitter activity modulator and a compound of Formula I and/or Formula V. In one embodiment, administering a neurotransmitter activity modulator comprises giving a transmucosal preparation, e.g., providing rapidly dissolving a tablet with an absorption

enhancer having each of a neurotransmitter activity modulator and a compound of Formula I and/or Formula V.

In one embodiment, the methods disclosed herein comprise administering a composition by inhalation for crossing a blood-brain barrier.

As used herein, the term "neurotransmitter activity modulator" refers to a compound or composition that reacts or influences activity at a neurotransmitter receptor, e.g., a compound of Formula I and/or Formula V, a serotonergic drug, 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, etc. In one embodiment, a neurotransmitter activity modulator binds on a neurotransmitter receptor. In one embodiment, a neurotransmitter activity modulator indirectly affects a neurotransmitter receptor, e.g., via interactions affecting the reactivity of other molecules at a neurotransmitter receptor. In one embodiment, a neurotransmitter activity modulator is an agonist. In one embodiment, a neurotransmitter activity modulator is an antagonist. In one embodiment, a neurotransmitter activity modulator acts (either directly or indirectly) at more than one type of neurotransmitter receptor.

In one embodiment, a neurotransmitter activity modulator is chosen from aripiprazole, bupropion, citalopram, clomipramine, dextroamphetamine, duloxetine, escitalopram, fluoxetine, fluvoxamine, milnacipran, mirtazapine, paroxetine, quetiapine, reboxetine, risperidone, sertraline, and venlafaxine.

As used herein, the term "first dosage formulation" refers to a compound or compounds selected for the purposes of causing a reaction, effect, and/or result, e.g., causing activity at a neurotransmitter receptor, reacting with other compounds, enhancing the effects of other active ingredients, inhibiting the biosynthesis of a compound, etc., within an organism. In one embodiment, a first dosage formulation comprises a compound of Formula I and/or Formula V.

In one embodiment, a second dosage formulation comprises a compound of Formula I and/or Formula V. In one embodiment, a second dosage formulation comprises a second compound of Formula I and/or Formula V. In one embodiment, a second dosage formulation comprises an additional serotonergic drug.

In one embodiment, the methods disclosed herein comprise administering a second dosage formulation. In one embodiment, the methods disclosed herein comprise administering a third dosage formulation. In one embodiment, the methods disclosed herein comprise administering a fourth dosage formulation. In one embodiment, the methods disclosed herein comprise administering more than four dosage formulations.

In certain embodiments, the dosage formulation contains a desired amount of at least one compound of Formula I and/or Formula V. In certain embodiments, the dosage formulation

contains about 0.01 to about 1,000 mg of the compound, such as about 0.1 to about 500 mg, about 0.5 to about 100 mg, or about 1 to about 50 mg. In certain embodiments, the dosage formulation is calculated to contain an amount of a compound of Formula I and/or Formula V based on mg of compound per kg of the subject (mg/kg). In certain embodiments, the mg/kg range can be about 0.001 to about 10mg/kg, such as about 0.01 to about 5, about 0.05 to about 4, about 0.05 to about 3, about 0.05 to about 3, about 0.05 to about 2, or about 0.05 to about 1 mg/kg. In some embodiments, the compound is dosed in an amount that is less than about 1 mg/kg, such as about 0.001 to about 0.99, about 0.01 to about 0.85, about 0.05 to about 0.75, about 0.01 to about 0.50, about 0.01 to about 0.25 or about 0.01 to about 0.10 mg/kg.

In one embodiment, the methods disclosed herein comprise administering one or more active ingredients, *e.g.*, a compounds of Formula I and/or Formula V that yields active ingredients upon metabolism *in vivo*, such as cannabinoids, terpenes, serotonergic drugs, neurotransmitter activity modulators, etc.

Disclosed herein is a method of treating a psychological problem, comprising:

administering a compound of Formula I and/or Formula V to the person in need of treatment. In one embodiment, the method further comprises a step of identifying a person in need of treatment prior to administering the compound of Formula I and/or Formula V. In one embodiment, the compound of Formula I and/or Formula V yields one or more active compounds *in vivo* that modulate activity at a neurotransmitter receptor.

As used herein, the term "identifying a person in need of treatment" refers to analyzing, diagnosing, and/or determining whether a person requires treatment for a disease or condition. In one embodiment, identifying a person in need of treatment comprises diagnosing a person with a medical condition, e.g., a neurological disorder, a chemical imbalance, a hereditary condition, etc. In one embodiment, identifying a person in need of treatment comprises performing a psychiatric evaluation. In one embodiment, identifying a person in need of treatment comprises performing a blood test. In one embodiment, identifying a person in need of treatment comprises determining whether a person has a compulsive disorder. In one embodiment, identifying a person in need of treatment comprises self-identifying as having a compulsive disorder.

As used herein, the term "psychological disorder" refers to a condition wherein a person exhibits a pattern of behavioral and/or psychological symptoms that impact multiple life areas and create distress for the person experiencing these symptoms. In one embodiment, a psychological disorder is caused by a genetic disorder. In one embodiment, a psychological disorder is caused by a biological condition, e.g., excess hormone production, a lack of activity at a neurotransmitter receptor, a lack of producing neurotransmitters, etc. In one embodiment, the neurotransmitter receptor is a serotonin receptor.

In one embodiment, the psychological problem is an anxiety disorder. In one embodiment, the psychological problem is a depressive disorder. In one embodiment, the psychological problem is a compulsive disorder. In one embodiment, the psychological problem is characterized by neurodegeneration.

As used herein, the term "anxiety disorder" refers to a state of apprehension, uncertainty, and/or fear resulting from the anticipation of an event and/or situation. An anxiety disorder can disrupt the physical and psychological functions of a person. These disruptions can cause a small hindrance to a debilitating handicap for a person's everyday life. An anxiety disorder can cause a physiological symptom, e.g., muscle tension, heart palpitations, sweating, dizziness, shortness of breath, etc. An anxiety disorder can also cause a psychological symptom, e.g., fear of dying, fear of embarrassment or humiliation, fear of an event occurring, etc.

In one embodiment, an anxiety disorder comprises acute stress disorder, anxiety due to a medical condition, generalized anxiety disorder, panic disorder, panic attack, a phobia, post-traumatic stress disorder, separation anxiety disorder, social anxiety disorder, substance-induced anxiety disorder, or selective mutism.

As used herein, the term "acute stress disorder" refers to a condition developed after exposure to one or more traumatic events. Examples of traumatic events include, but are not limited to, exposure to war, rape or sexual violence, a physical attack, a mugging, childhood physical or sexual violence, kidnapping or being taken hostage, terrorist attacks, torture, natural disasters, and/or severe accidents. In one embodiment, acute stress disorder occurs within a day of experiencing a traumatic event. In one embodiment, acute stress disorder occurs within three days of experiencing a traumatic event. In some instances, acute stress disorder occurs within a week of experiencing a traumatic event. In some instances, acute stress disorder occurs within a month of experiencing a traumatic event.

As used herein, the term "anxiety due to another medical condition" refers to a condition wherein anxiety symptoms are developed because of a physiological and psychological consequence of a non-related disease, injury, and/or illness, e.g., an endocrine disease, a cardiovascular disorder, respiratory illness, a metabolic disturbance, a neurological illness, etc.

As used herein, the term "generalized anxiety disorder" refers to a condition of persistent and excessive anxiety and worry about various domains, e.g., work, school, social settings, etc., that an individual finds difficult to control. In addition, the individual experiences physical symptoms including restlessness, alertness, and/or nervousness; being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and sleep disturbance.

As used herein, the term "panic disorder" refers to a condition wherein an individual

experiences recurrent and unexpected panic attacks. The individual is persistently concerned about having more panic attacks and changes his or her behavior in maladaptive ways because of these panic attacks, e.g. avoidance of exercise, unfamiliar locations, new people, etc.

As used herein, the term "panic attack" refers to an abrupt surge of intense fear or intense discomfort that reaches a peak within a short period of time, e.g., seconds, minutes, hours, etc. In some instances, a panic attack comprises a physical and/or cognitive symptom. Panic attacks may be predictable, such as in response to a typically feared object or situation. In some instances, a panic attack occurs for no apparent reason.

As used herein, the term "phobia" refers to a condition of being fearful, anxious about, or avoidant of a circumscribed object and/or situation. In some instances, a phobia comprises a fear, anxiety, or avoidance that is induced by a situation to a degree that is persistent and out of proportion to the actual risk posed. Examples of phobias include, but are not limited to, a fear or anxiety of an animal, a natural environment, an injection-injury, etc.

As used herein, the term "post-traumatic stress disorder" refers to a condition developed after experiencing and/or witnessing a traumatic event or learning that a traumatic event has happened to a loved one. In some instances, a person shows symptoms of post-traumatic stress disorder within a week of experiencing the traumatic event. In some instances, a person shows symptoms of post-traumatic stress disorder within a month of experiencing the traumatic event. In some instances, a person shows symptoms of post-traumatic stress disorder within a year of experiencing the traumatic event. In some instances, a person shows symptoms of post-traumatic stress disorder after a year or more of experiencing the traumatic event. In some instances, post-traumatic stress disorder comprises a person re-experiencing the trauma event through intrusive distressing recollections of the event, flashbacks, and/or nightmares. In some instances, a symptom of post-traumatic stress disorder comprises emotional numbness and avoidance of places, people, and activities that are reminders of the trauma. In some instances, a symptom of post-traumatic stress disorder comprises increased arousal such as difficulty sleeping and concentrating, feeling anxious, and being easily irritated and angered.

As used herein the term "neurodegeneration" refers to the progressive loss of structure or function of neurons, including but not limited to the death of neurons. Many neurodegenerative diseases--including amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, and Huntington's disease--occur as a result of neurodegenerative processes. Such diseases are incurable, resulting in progressive degeneration and/or death of neuron cells. Some attempts have been made to treat such diseases and conditions using fungal and plant extracts. But those methods all suffer from a common flaw in that the fungal and/or plants extracts fail to provide consistent or reliable amounts of the therapeutic compounds on account of relying on the highly variable chemical compositions of particular naturally occurring organisms.

As used herein, the term "separation anxiety disorder" refers to a condition wherein an individual is fearful and/or anxious about separation from an attachment figure to a degree that is developmentally inappropriate. In some instances, a separation anxiety disorder comprises a fear or anxiety about harm coming to an attachment figure. In some instances, a separation anxiety disorder comprises a fear of an event leading to the loss of or separation from an attachment figure and reluctance to go away from attachment figures. In some instances, a separation anxiety disorder comprises a nightmare and/or psychical symptom of distress.

As used herein, the term "social anxiety disorder" refers to a condition wherein an individual is fearful, anxious about, or avoidant of social interactions and situations that involve the possibility of being scrutinized. These social interactions and situations include meeting unfamiliar people, situations in which the individual may be observed eating or drinking, situations in which the individual performs in front of others, etc. In some instances, a social anxiety disorder is caused by the fear of being negatively evaluated by others, by being embarrassed, humiliated, rejected, and/or offending others.

As used herein, the term "substance-induced anxiety disorder" refers to a condition wherein anxiety caused by a substance intoxication and/or a withdrawal or to a medical treatment. In some instances, a withdrawal from a substance increases anxiety.

As used herein, the term "selective mutism" refers to a condition characterized by an individual's consistent failure to speak in social situations in which there is an expectation to speak, e.g., school, a lecture, a meeting, etc., even though the individual speaks in other situations. Failure to speak has significant consequences on achievement in academics, occupational settings, and/or otherwise interferes with normal social communication.

In some instances, an anxiety disorder comprises a medical diagnosis based on the criteria and classification from the Diagnostic and Statistical Manual of Medical Disorders, 5th Ed. In some instances, an anxiety disorder comprises a medical diagnosis based on an independent medical evaluation. In some instances, an anxiety disorder comprises a medical diagnosis based on a self-evaluation.

In one embodiment, the methods and compositions disclosed herein comprise administering an anxiolytic drug.

As used herein, the term "anxiolytic drug" refers to a compound or composition that reacts or influences activity at a neurotransmitter receptor, *e.g.*, a compound of Formula I and/or Formula V, a serotonergic drug, 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, etc. In one embodiment, an anxiolytic drug binds on a neurotransmitter receptor. In one embodiment, an anxiolytic drug indirectly affects a neurotransmitter receptor, e.g., via interactions affecting the reactivity of other molecules at a

neurotransmitter receptor. In one embodiment, an anxiolytic drug is an agonist. In one embodiment, an anxiolytic drug is an antagonist. In one embodiment, an anxiolytic drug acts (either directly or indirectly) at more than one type of neurotransmitter receptor.

In one embodiment, an anxiolytic drug is chosen from alprazolam, an alpha blocker, an antihistamine, a barbiturate, a beta blocker, bromazepam, a carbamate, chlordiazepoxide, clonazepam, clorazepate, diazepam, flurazepam, lorazepam, an opioid, oxazepam, temazepam, and triazolam.

As used herein, the term "depressive disorder" refers to a condition of low mood and aversion to activity that can affect a person's thoughts, behavior, feelings, and sense of well-being lasting for a time period. In one embodiment, a depressive disorder disrupts the physical and psychological functions of a person. In one embodiment, a depressive disorder causes a physiological symptom, e.g., weight loss, aches or pains, headaches, cramps, digestive problems, etc. In one embodiment, a depressive disorder causes a psychological symptom, e.g., persistent sadness; anxiety; feelings of hopelessness and irritability; feelings of guilt, worthlessness, or helplessness; loss of interest or pleasure in hobbies and activities; difficulty concentrating, remembering, or making decisions, etc.

In one embodiment, a depressive disorder is chosen from atypical depression, bipolar disorder, catatonic depression, depressive disorder due to a medical condition, major depressive disorder, postpartum depression, premenstrual dysphoric disorder, and seasonal affective disorder.

As used herein, the term "atypical depression" refers to a condition wherein an individual shows signs of mood reactivity (i.e., mood brightens in response to actual or potential positive events), significant weight gain, increase in appetite, hypersomnia, heavy, leaden feelings in arms or legs, and/or long-standing pattern of interpersonal rejection sensitivity that results in significant social or occupational impairment. Exemplary symptoms of atypical depression include, but are not limited to, daily sadness or depressed mood; loss of enjoyment in things that were once pleasurable; major changes in weight (gain or loss) or appetite; insomnia or excessive sleep almost every day; a state of physical restlessness or being rundown that is noticeable by others; daily fatigue or loss of energy; feelings of hopelessness, worthlessness, or excessive guilt almost every day; problems with concentration or making decisions almost every day; recurring thoughts of death or suicide, suicide plan, or suicide attempt.

As used herein, the term "bipolar disorder" refers to a condition that causes an individual to experience unusual shifts in mood, energy, activity levels, and the ability to carry out day-to-day tasks. Individuals with bipolar disorder experience periods of unusually intense emotion, changes in sleep patterns and activity levels, and unusual behaviors. These distinct

periods are called "mood episodes." Mood episodes are drastically different from the moods and behaviors that are typical for the person. Exemplary symptoms of mania, excessive behavior, include, but are not limited to, abnormally upbeat, jumpy, or wired behavior; increased activity, energy, or agitation; exaggerated sense of well-being and self-confidence; decreased need for sleep; unusual talkativeness; racing thoughts; distractibility; and poor decision-making--for example, going on buying sprees, taking sexual risks, or making foolish investments. Exemplary symptoms of depressive episodes, low mood, include, but are not limited by, depressed mood, such as feelings of sadness, emptiness, hopelessness, or tearfulness; marked loss of interest or feeling no pleasure in all--or almost all--activities; significant weight loss, weight gain, or decrease or increase in appetite; insomnia or sleeping too much; restlessness or slowed behavior; fatigue or loss of energy; feelings of worthlessness or excessive or inappropriate guilt; decreased ability to think or concentrate, or indecisiveness; and thinking about, planning or attempting suicide.

As used herein, the term "catatonic depression" refers to a condition causing an individual to remain speechless and motionless for an extended period. Exemplary symptoms of catatonic depression include, but are not limited to, feelings of sadness, which can occur daily, a loss of interest in most activities, sudden weight gain or loss, a change in appetite, trouble falling asleep, trouble getting out of bed, feelings of restlessness, irritability, feelings of worthlessness, feelings of guilt, fatigue, difficulty concentrating, difficulty thinking, difficulty making decisions, thoughts of suicide or death, and/or a suicide attempt.

As used herein, the term "depressive disorder due to a medical condition" refers to a condition wherein an individual experiences a depressive symptom(s) caused by another illness. Examples of medical conditions known to cause a depressive disorder include, but are not limited to, HIV/AIDS, diabetes, arthritis, strokes, brain disorders such as Parkinson's disease, Huntington's disease, multiple sclerosis, and Alzheimer's disease, metabolic conditions (e.g. vitamin B12 deficiency), autoimmune conditions (e.g., lupus and rheumatoid arthritis), viral or other infections (hepatitis, mononucleosis, herpes), back pain, and certain cancers (e.g., pancreatic).

As used herein, the term "major depressive disorder" refers to a condition characterized by a time period of low mood that is present across most situations. Major depressive disorder is often accompanied by low self-esteem, loss of interest in normally enjoyable activities, low energy, and pain without a clear cause. In some instances, major depressive order is characterized by two weeks. In some instances, an individual experiences periods of depression separated by years. In some instances, an individual experiences symptom of depression that are nearly always present. Major depressive disorder can negatively affect a person's personal, work, or school life, as well as sleeping, eating habits, and general health. 2-7% of adults with major depressive disorder commit suicide, and up to 60% of people who

commit suicide had a major depressive disorder or another related mood disorder. Dysthymia is a subtype of major depressive disorder consisting of the same cognitive and physical problems as a major depressive disorder with less severe but longer-lasting symptoms. Exemplary symptoms of a major depressive disorder include, but are not limited to, feelings of sadness, tearfulness, emptiness or hopelessness; angry outbursts, irritability or frustration, even over small matters; loss of interest or pleasure in most or all normal activities; sleep disturbances, including insomnia or sleeping too much; tiredness and lack of energy; reduced appetite, weight loss or gain; anxiety, agitation or restlessness; slowed thinking, speaking, or body movements; feelings of worthlessness or guilt, fixating on past failures or self-blame; trouble thinking, concentrating, making decisions, and remembering things; frequent thoughts of death, suicidal thoughts, suicide attempts, or suicide; and unexplained physical problems, such as back pain or headaches.

As used herein, the term "postpartum depression" refers to a condition as the result of childbirth and hormonal changes, psychological adjustment to parenthood, and/or fatigue. Postpartum depression is often associated with women, but men can also suffer from postpartum depression as well. Exemplary symptoms of postpartum depression include, but are not limited to, feelings of sadness, hopeless, emptiness, or overwhelmed; crying more often than usual or for no apparent reason; worrying or feeling overly anxious; feeling moody, irritable, or restless; oversleeping, or being unable to sleep even when the baby is asleep; having trouble concentrating, remembering details, and making decisions; experiencing anger or rage; losing interest in activities that are usually enjoyable; suffering from physical aches and pains, including frequent headaches, stomach problems, and muscle pain; eating too little or too much; withdrawing from or avoiding friends and family; having trouble bonding or forming an emotional attachment with the baby; persistently doubting his or ability to care for the baby; and thinking about harming themselves or the baby.

As used herein, the term "premenstrual dysphoric disorder" refers to a condition wherein an individual expresses mood lability, irritability, dysphoria, and anxiety symptoms that occur repeatedly during the premenstrual phase of the cycle and remit around the onset of menses or shortly thereafter. Exemplary symptoms of premenstrual dysphoric disorder include, but are not limited to, lability (e.g., mood swings), irritability or anger, depressed mood, anxiety, and tension, decreased interest in usual activities, difficulty in concentration, lethargy and lack of energy, change in appetite (e.g., overeating or specific food cravings), hypersomnia or insomnia, feeling overwhelmed or out of control, physical symptoms (e.g., breast tenderness or swelling, joint or muscle pain, a sensation of `bloating` and weight gain), self-deprecating thoughts, feelings of being keyed up or on edge, decreased interest in usual activities (e.g., work, school, friends, hobbies), subjective difficulty in concentration, and easy fatigability.

As used herein, the term "seasonal affective disorder" refers to a condition wherein an

individual experiences mood changes based on the time of the year. In some instances, an individual experiences low mood, low energy, or other depressive symptoms during the fall and/or winter season. In some instances, an individual experiences low mood, low energy, or other depressive symptoms during the spring and/or summer season. Exemplary symptoms of seasonal affective disorder include, but are not limited to, feeling depressed most of the day or nearly every day; losing interest in activities once found enjoyable; having low energy; having problems with sleeping; experiencing changes in appetite or weight; feeling sluggish or agitated; having difficulty concentrating; feeling hopeless, worthless, or guilty; and having frequent thoughts of death or suicide.

In one embodiment, a depressive disorder comprises a medical diagnosis based on the criteria and classification from Diagnostic and Statistical Manual of Medical Disorders, 5th Ed. In one embodiment, a depressive disorder comprises a medical diagnosis based on an independent medical evaluation.

In one embodiment, the methods and compositions disclosed herein comprise administering an antidepressant.

As used herein, the term "antidepressant" refers to a compound that reacts or influences activity at a neurotransmitter receptor, e.g., a compound of Formula I and/or Formula V, a serotonergic drug, 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, etc. In one embodiment, an antidepressant binds on a neurotransmitter receptor. In one embodiment, an antidepressant indirectly affects a neurotransmitter receptor, e.g., via interactions affecting the reactivity of other molecules at a neurotransmitter receptor. In one embodiment, an antidepressant is an agonist. In one embodiment, an antidepressant is an antagonist. In one embodiment, an antidepressant acts (either directly or indirectly) at more than one type of neurotransmitter receptor.

In one embodiment, an antidepressant is chosen from bupropion, citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, milnacipran, mirtazapine, paroxetine, reboxetine, sertraline, and venlafaxine.

Disclosed herein is a method of treating headaches and/or migraines, comprising identifying a person in need of treatment and administering a composition disclosed herein to the person in need of treatment.

Disclosed herein is a method of treating nicotine addiction, comprising identifying a person in need of treatment and administering a composition disclosed herein to the person in need of treatment.

Disclosed herein is a method of treating drug addiction, comprising identifying a person in need of treatment and administering a composition disclosed herein to the person in need of

treatment.

Disclosed herein is a method of treating alcohol addiction, comprising identifying a person in need of treatment and administering a composition disclosed herein to the person in need of treatment.

The compositions disclosed herein are useful for the treatment of compulsive disorders in humans, a variety of intractable psychiatric disorders, chronic depression, post-traumatic stress disorder, and drug or alcohol dependency. The compositions disclosed herein are also useful within the context of meditative, spiritual, and religious practices within a variety of contexts.

As used herein, the term "compulsive disorder" refers to a condition wherein an individual has an obsession causing a feeling of anxiety, fear, apprehension, etc., and has a compulsion to perform tasks to relieve said feeling of anxiety. An obsession is a thought that recurs and persists despite the efforts of an individual to ignore or confront them. In some instances, an obsession is relatively vague involving a general sense of disarray or tension accompanied by a belief that life cannot proceed as normal while the imbalance remains. In other instances, an obsession is more intense and could be a preoccupation with the thought or image of someone close to them dying or intrusions related to relationship rightness. Other obsessions concern the possibility that someone or something other than oneself--such as God, the Devil, or disease--will harm either the person, the people or things that the person cares about. In some instances, individuals perform compulsive rituals because they inexplicably feel they have to. In some instances, individuals perform compulsive rituals to mitigate the anxiety that stems from a particular obsession. The person feels that these actions will somehow either prevent a dreaded event from occurring or will push the event from their thoughts.

In one embodiment, a compulsive disorder is chosen from addiction, body dysmorphic disorder, excoriation disorder, hoarding disorder, obsessive-compulsive disorder, and trichotillomania.

As used herein, the term "addiction" refers to a physical and/or psychological dependence on a substance, activity, and/or any other habit. In one embodiment, an addiction is caused by the altered brain chemistry of an individual in response to a stimulus, e.g., a substance releasing large amounts of serotonin, an activity releasing large amounts of adrenaline, etc. In one embodiment, an addiction is a dependence on a substance, e.g., a drug, an alcohol, nicotine, a food, etc. In one embodiment, an addiction is a dependence on an activity, e.g., gambling, eating, shopping, etc.

As used herein, the term "body dysmorphic disorder" refers to a condition characterized by the obsessive idea that some aspect of an individual's appearance is severely flawed and

warrants exceptional measures to hide or fix it. Exemplary symptoms of body dysmorphic disorder includes, but are not limited to, being extremely preoccupied with a perceived flaw in appearance that to others can't be seen or appears minor; a belief that a defect in appearance makes an individual ugly or deformed; a belief that others take special notice of an individual's appearance in a negative way or mock the individual; engaging in behaviors aimed at fixing or hiding the perceived flaw that are difficult to resist or control, such as frequently checking the mirror, grooming, or skin picking; attempting to hide perceived flaws with styling, makeup, or clothes; constantly comparing one's appearance with others; always seeking reassurance about one's appearance from others; having perfectionist tendencies; seeking frequent cosmetic procedures with little satisfaction; avoiding social situations; and being so preoccupied with one's appearance that it causes major distress or problems in a person's social life, work, school, or other areas of functioning.

As used herein, the term "excoriation disorder" refers to a condition of having a repeated urge to pick at one's own skin. In some instances, an excoriation disorder causes a person to often pick their skin to the extent that damage is caused.

As used herein, the term "hoarding disorder" refers to a condition of persistent difficulty in discarding or parting with possessions, regardless of their value. Exemplary symptoms of a hoarding disorder include, but are not limited to, inability to throw away possessions; severe anxiety when attempting to discard items; great difficulty categorizing or organizing possessions; indecision about what to keep or where to put things; distress, such as feeling overwhelmed or embarrassed by possessions; suspicion of other people touching items; obsessive thoughts and actions; fear of running out of an item or of needing it in the future; checking the trash for accidentally discarded objects; and functional impairments, e.g., loss of living space, social isolation, family or marital discord, financial difficulties, health hazards, etc.

As used herein, the term "obsessive-compulsive disorder" refers to a condition in which an individual has uncontrollable, reoccurring thoughts and behaviors that he or she feels the urge to repeat over and over. In some instances, an obsessive-compulsive disorder manifests itself as an individual needing to clean in order to reduce the fear that germs, dirt, or chemicals will contaminate the individual and the individual will spend many hours washing themselves or cleaning their surroundings. In some instances, an obsessive-compulsive disorder manifests itself as an individual needing to dispel anxiety. An individual may utter a name, phrase or repeat a behavior several times. The individual knows these repetitions will not actually prevent injury, but fear of harm will occur if the repetitions are not performed. In some instances, an obsessive-compulsive disorder manifests itself as an individual needing to reduce the fear of harming oneself or others by, e.g., forgetting to lock the door or turning off appliances, developing checking rituals, etc. In some instances, an obsessive-compulsive disorder manifests itself as an individual needing to order and arrange his or her surroundings to reduce

discomfort, e.g., putting objects in a certain order, arranging household items in a particular manner or in a symmetric fashion, etc. In some instances, an obsessive-compulsive disorder manifests itself as an individual needing to respond to intrusive obsessive thoughts, e.g., praying or saying phrases to reduce anxiety or prevent a dreaded future event. In some instances, obsessive-compulsive disorder is caused by another medical condition. In some instances, obsessive-compulsive disorder is caused by a substance.

As used herein, the term "trichotillomania" refers to a condition of self-induced and recurrent loss of hair, e.g., pulling one's own hair out. In some instances, trichotillomania comprises an individual pulling their hair out at one location. In some instances, trichotillomania comprises an individual pulling their hair out at multiple locations. Exemplary symptoms of trichotillomania include, but are not limited to, recurrent pulling out of one's hair resulting in noticeable hair loss; an increased sense of tension immediately before pulling out the hair or when resisting the behavior; pleasure, gratification, or relief when pulling out the hair; the disturbance is not accounted for by another mental disorder and is not due to a general medical condition (i.e., dermatological condition); repeated attempts have been made to decrease or stop hair pulling; disturbances caused significant distress or impairment in social, occupational, or other important areas of functioning; distress including feelings of loss of control, embarrassment, shame; and impairment due to avoidance of work, school, or other public situations.

In one embodiment, a compulsive disorder comprises a medical diagnosis based on the criteria and classification from Diagnostic and Statistical Manual of Medical Disorders, 5th Ed. In one embodiment, a compulsive disorder comprises a medical diagnosis based on an independent medical evaluation.

In some embodiments, the compositions described herein further comprise at least one compound not acting on a serotonin receptor.

In some embodiments, the compositions described herein comprise a compound of Formula I and/or Formula V. In some embodiments, the compound of Formula I and/or Formula V comprises a single active serotonergic drug.

Although the compounds disclosed herein have been described with reference to various exemplary embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present disclosure. Those having skill in the art would recognize that various modifications to the exemplary embodiments may be made, without departing from the scope of the disclosure.

Where reference is made to a particular compound, it should be understood that this disclosure also contemplates salts and derivatives of that compound as well as degradation products, such as oxidized versions of explicitly disclosed molecules.

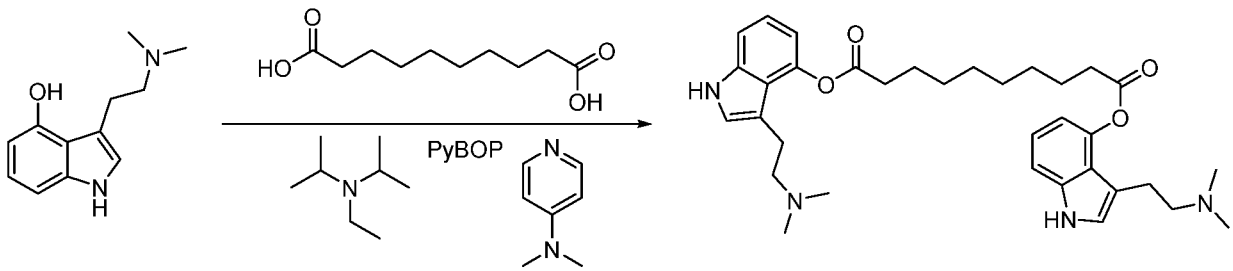
Moreover, it should be understood that various features and/or characteristics of differing embodiments herein may be combined with one another. It is, therefore, to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the scope of the disclosure.

Furthermore, other embodiments of the disclosure will be apparent to those skilled in the art from consideration of the specification and practice of the disclosure disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a scope and spirit being indicated by the claims.

In the present description, any concentration range, percentage range, ratio range, or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated. As used herein, the terms "about" and "approximately" mean ± 20%, ± 10%, ± 5%, or ± 1% of the indicated range, value, or structure, unless otherwise indicated.

Examples

Example 1. Dispsilocin™ L-10 Dimer



To a suspension of sebacic acid (0.5 mmol) and PyBOP (1.0 mmol) in DCM (0.15 M) was added Hunig's base (1.0 mmol) and the mixture was stirred at RT until the solution turned homogenous (about 30 min). To this solution was added psilocin (1.0 mmol) and DMAP (0.15 mmol) as a mixed solid in one portion. The resulting heterogeneous solution was allowed to stir at RT. After 16 hrs, the reaction mixture was diluted with an equal volume of hexanes. The supernatant was decanted, leaving behind a reddish oil. The red oil was washed with chloroform three times to afford a crude reddish-brown oil.

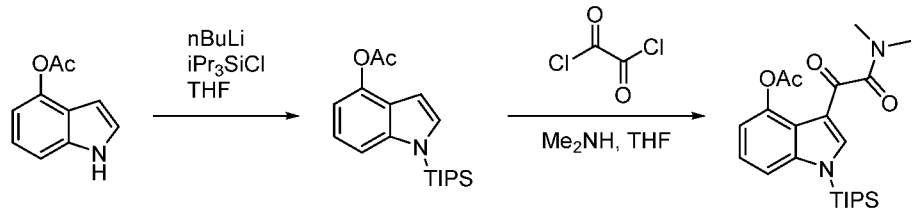
CPC Purification

The crude material was dissolved in $CHCl_3$ and then partitioned between ethyl acetate and hexanes in a Quattro CPC Lab Prep (250 mL) to afford a white crystalline solid, following concentration, in 68% yield.

CPC General Information

Centrifugal Partition Chromatography (CPC) is a sub-type of counter current chromatography, an application of liquid-liquid chromatography. CPC extrapolates small differences in partition coefficients through repetitive partitioning across multiple small chambers, called cells, which are linked in series. Components of the mixture are separated by partitioning between the two non-miscible liquid phases. During the operation, the liquid stationary phase is retained in the centrifugal rotor by centrifugal force and the mobile phase is then eluted through the stationary phase. The mobile phase is collected into fractions containing resolved analytes as detected most commonly by UV-Diode Array detection. Mobile phase containing the target component(s) is collected and concentrated to recover the target analyte(s). Nontarget analytes can be recovered from the mobile phase, with strongly retained non-target analytes being recovered from the stationary phase by purging the apparatus.

Example 2.



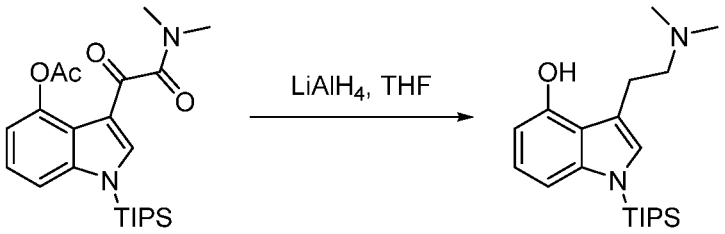
To a cooled solution of 4-acetoxyindole (6.8 mmol) in anhyd. THF (3 mL) at -78 °C was added a 1.6 M solution of nBuLi in hexane (7.0 mL, 11.0 mmol) dropwise, and the temperature was raised to -10 °C. After 15 min the reaction mixture was cooled to -50 °C, and TIPSCl (1.64 g, 11.0 mmol) was added. The solution was warmed to 0 °C, stirred for 3 h, and poured into water (10 mL). The mixture was extracted with DCM three times, and the combined organic extracts were dried, filtered, and concentrated *in vacuo*. The crude 1-(triisopropylsilyl)-1H-indol-4-yl acetate was used without further purification.

To 5 mL of anhyd. THF at 0 °C under an inert atmosphere was added oxalyl chloride (0.865 mL, 10.2 mmol). A solution of the crude 1-(triisopropylsilyl)-1H-indol-4-yl acetate (assumed as 6.8 mmol, 1 eq) in THF was added dropwise via an addition funnel and stirred at 0°C for 1 hour. The reaction mixture was diluted with anhyd. hexanes. The resulting solid was filtered and washed several times with (3/1) hexanes/diethylether mixture and used without further purification.

The filtered acid chloride (assumed as 6.8 mmol, 1 eq) was dissolved in THF (10 mL) under an inert atmosphere and 2.0 M dimethylamine in THF (11.5 mmol, 1.7 eq) followed by triethylamine (1.39 mL, 10.2 mmol, 1.5 eq) were added via syringe. The reaction mixture was stirred at rt for 3 h. Anhyd. hexanes (10 mL) was then added and allowed to stir at 40°C for 30 min. The resulting hydrochloride salt was filtered off and the ketoamide precipitated from the

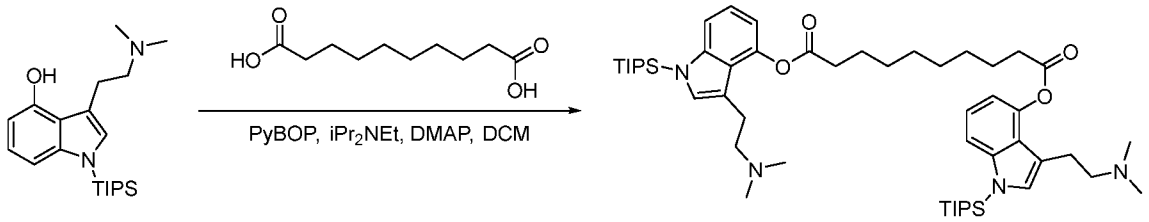
mother liquor and was collected to afford an off-white solid in 51% yield over 3 steps.

Example 3.



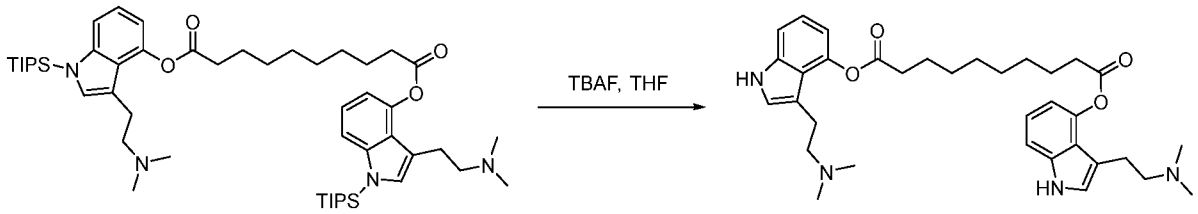
To a solution of ketoamide prepared according to the procedure of Example 2 (1.0 g, 2.32 mmol) in THF (50 mL) at 0°C under an inert atmosphere was added $LiAlH_4$ (12.7 mmol, 5.5 eq) as a 2.0 M solution in THF and the mixture was heated at reflux for 8 hrs. The reaction was quenched by addition of water (10 mL) and the aqueous layer was extracted thrice with diethyl ether. The combined organic layer was washed with brine, dried over anhyd. sodium sulfate and concentrated *in vacuo*. The crude solid was purified via SiO_2 column chromatography to yield the desired product in about 64% yield.

Example 4.



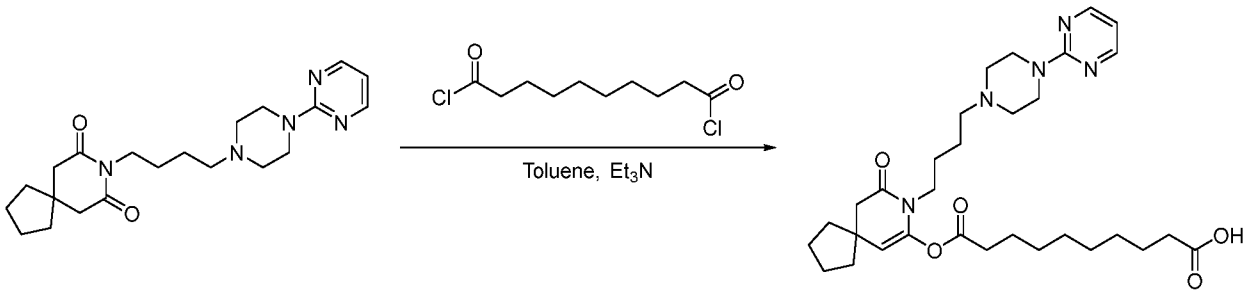
The procedure according to Example 1 was repeated with the TIPS-protected phenol prepared according to Example 3 to yield the desired TIPS-protected dimer.

Example 5.



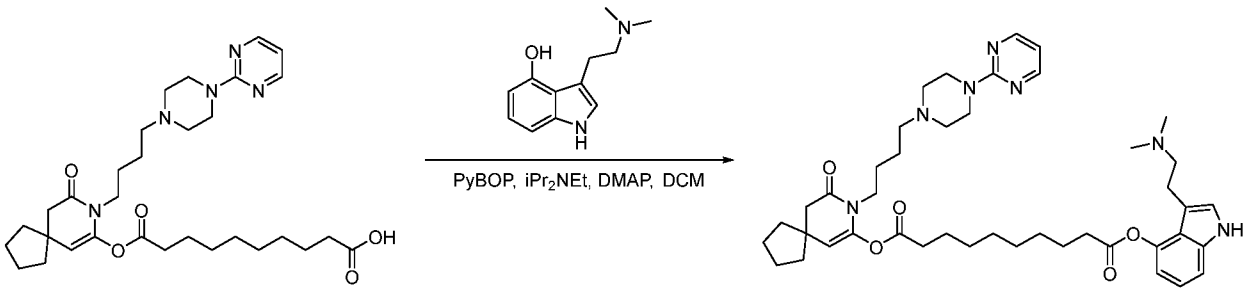
A 1.0 M solution of Bu_4NF(0.6 mmol) in THF was added to a 0.2 M solution of purified TIPS protected Dipsilocin$_{TM}$ dimer prepared according to the procedure of Example 4 (0.5 mmol) in anhyd THF, and the mixture was stirred at RT for 10 min. After quenching with saturated aqueous sodium carbonate, the mixture was extracted with DCM, and the combined organic layers were dried over anhyd. sodium sulfate and concentrated in vacuo. The residue was passed through a plug of silica to provide analytically pure bis(3-(2-(dimethylamino)ethyl)-1H-indol-4-yl) decanedioate as a crystalline white solid in 89% yield.

Example 6.



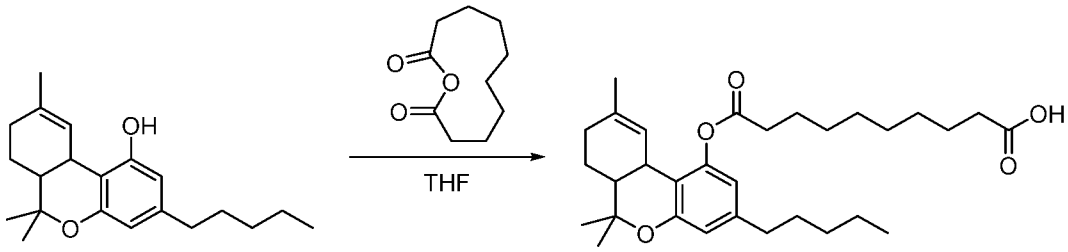
To a heated solution of buspirone (2.00 mmol, 1 equiv.) in toluene (5 mL) at 50°C is added triethylamine (0.52 mL, 4 mmol, 2 equiv.) followed by the slow addition of sebacoyl chloride (1.9 mmol, 0.95 equiv.) in toluene (5 mL) via an addition funnel. After 2 hrs the solution is quenched with water and diluted with ethyl acetate before washing with saturated sodium bicarbonate. The organic layer is then dried over anhyd. sodium sulfate, filtered and concentrated in vacuo. The crude residue is purified by column chromatography on silica gel (30% ethyl acetate in hexanes) to afford 10-oxo-10-((9-oxo-8-(4-(4-(pyrimidin-2-yl)piperazin-1-yl)butyl)-8-azaspiro[4.5]dec-6-en-7-yl)oxy)decanoic acid.

Example 7.



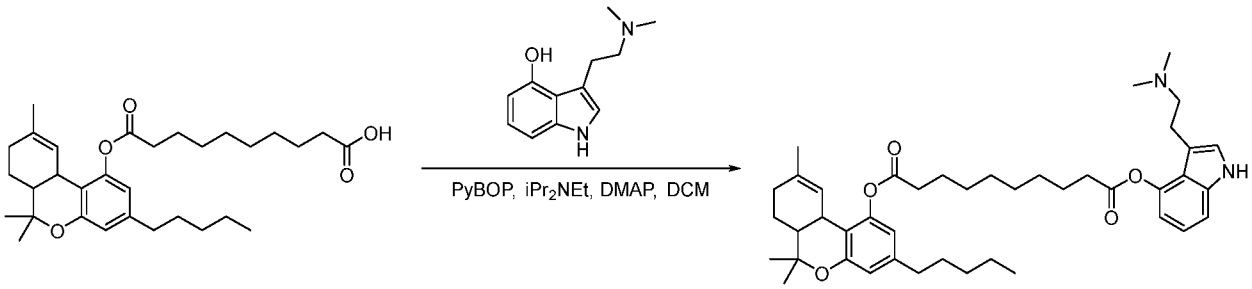
To a suspension of 10-oxo-10-((9-oxo-8-(4-(4-(pyrimidin-2-yl)piperazin-1-yl)butyl)-8-azaspiro[4.5]dec-6-en-7-yl)oxy)decanoic acid prepared according to the procedure of Example 6 (0.5 mmol) and PyBOP (0.6 mmol) in DCM (0.15 M) is added Hunig's base (0.6 mmol) and the mixture is permitted to stir at RT until it becomes homogenous (around 30 min). To this is added psilocin (0.5 mmol) and DMAP (0.15 mmol) as a mixed solid in one portion. The reaction mixture is stirred at RT for 16 hours then diluted with an equal volume of hexanes. The supernatant is then decanted, leaving behind the crude material which is washed with chloroform three times to afford a crude product which is purified via HPLC to afford 1-(3-(2-(dimethylamino)ethyl)-1H-indol-4-yl) 10-(9-oxo-8-(4-(4-(pyrimidin-2-yl)piperazin-1-yl)butyl)-8-azaspiro[4.5]dec-6-en-7-yl) decanedioate.

Example 8.



To a solution of delta-9-tetrahydrocannabinol (1.0 mmol) in anhydrous THF (5 mL) is added sebacic anhydride (1.0 mmol) in one portion before refluxing for 16 hours. The crude reaction mixture is then concentrated *in vacuo* to afford the target 10-oxo-10-((6,6,9-trimethyl-3-pentyl-6a,7,8,10a-tetrahydro-6H-benzo[c]chromen-1-yl)oxy)decanoic acid as a crude material.

Example 9.



The procedure of Example 7 is repeated with the starting material produced according to Example 8 to yield the desired THC-Psilocin L-10 dimer product in good yield, which is purified by silica gel chromatography and/or the HPLC or CPC methods described herein.

Biological Studies

Head-Twitch Response (HTR) Experiments.

Dose-response studies. Dose-response studies for compounds of Formula I and/or Formula V are performed in four consecutive steps:

(a). Formulation work. A suitable (non-toxic) vehicle is identified that can be used to dissolve the compound.

(b). Pilot dose-finding study. HTR-inducing drugs typically have biphasic bell-shaped (inverted U-shaped) dose-response functions, with ascending and descending phases. To quantify the potency of a drug in a HTR dose-response study, doses covering the entire extent of the ascending phase should be included, as well as at least one dose that falls on the descending phase. A pilot dose-finding study is performed to identify a set of doses that matches those requirements. For the pilot, male C57BL/6J mice are injected with a range of doses (typically 0.3–30 mg/kg) by the IP or SC route and then behaviors are recorded in a magnetometer chamber for up to 150 minutes.

(c). Dose-response study. Groups of male C57BL/6J mice with a magnet implant are injected with vehicle or 4-5 doses of the compound (n=5-7 mice/group) by the IP or SC route and then behaviors are recorded in a magnetometer chamber for at least 30 minutes.

(d). Repeated testing. Although potency can typically be quantified based on a single dose-response study, in some instances repeated testing may be necessary. For example, the doses selected for testing may not have been ideal to calculate the median effective dose (ED50 value). If necessary, a second or third dose-response study is performed.

Analysis: The following analyses are performed for dose-response studies:

HTR counts are analyzed using a 1-way ANOVA followed by a post-hoc test (Dunnett's test).

The median effective dose (ED_{50} value) for the compounds (in mg/kg or moles/kg) will calculated by nonlinear regression using a gaussian or sigmoidal model. The potencies of compounds and other reference compounds can also be compared statistically using an extra-sum-of-squares F-test.

HTR counts can be binned (e.g., blocks of 1, 2, 5, or 10 minutes) and analyzed using a 2-way ANOVA (drug x time) followed by a post-hoc test (Dunnett's test or Tukey's test).

5-HT_{2A} Antagonist blockade studies. Four groups of male C57BL/6J mice with a magnet implant are pretreated SC with the selective 5-HT_{2A} antagonist M100907 (vehicle, 0.001, 0.01, or 0.1 mg/kg). Twenty minutes later, all of the animals are injected IP or SC with one dose of the compound (n=5-7 mice/group) and then behaviors are recorded in a magnetometer chamber for 30 minutes.

5-HT_{1A} Antagonist blockade studies. Four groups of male C57BL/6J mice (n=5-7 mice/group) with a magnet implant are pretreated SC with the selective 5-HT_{1A} antagonist WAY-100635 (vehicle or 1 mg/kg). Twenty minutes later, the animals are injected IP or SC with vehicle or one dose of the compound and then behaviors are recorded in a magnetometer chamber for at least 30 minutes.

Extended time-course studies. Male C57BL/6J mice with a magnet implant are injected IP or SC with up to three different treatments (n=5-6 mice/group) and then behaviors are recorded in a magnetometer chamber for up to 5 hours (the exact assessment period used will depend on the duration-of-action of the Material being tested).

Brain penetration testing. These studies are used to test whether 5-HT2A ligands that do not induce the HTR are brain penetrant in mice. Male C57BL/6J mice with a magnet implant are pretreated IP or SC with vehicle or three doses of the 5-HT2A ligand (n=5-7 mice/group); 20 minutes later, all of the mice are injected IP with 1 mg/kg (±)-DOI HCl, and then behaviors are recorded in a magnetometer chamber for 20-30 minutes.

hERG inhibition studies.

All experiments are conducted manually using a HEKA EPC-10 amplifier at room temperature in the whole-cell mode of the patch-clamp technique. HEK293 cells stably expressing hKv11.1 (hERG) under G418 selection can be sourced from the University of Wisconsin, Madison. Cells are cultured in DMEM containing 10% fetal bovine serum, 2 mM glutamine, 1 mM sodium pyruvate, 100 U ml−1 streptomycin, and 500 mg ml−1 penicillin, 100 μ g ml−1 G418. The cell line is not authenticated or tested for mycoplasma contamination. Before experiments, cells are grown to 60–80% confluency, lifted using TrypLE, and plated onto poly-l-lysine-coated coverslips. Patch pipettes are pulled from soda lime glass (micro-haematocrit tubes) and should exhibit resistances of 2–4 MΩ. For the external solution, normal sodium Ringer is used (160 mM NaCl, 4.5 mM KCl, 2 mM $CaCl_2$, 1 mM $MgCl_2$, 10 mM HEPES, pH 7.4 and 290–310 mOsm). The internal solution used is potassium fluoride with ATP (160 mM KF, 2 mM MgCl2, 10 mM EGTA, 10 mM HEPES, 4 mM NaATP, pH = 7.2 and 300–320 mOsm). A two-step pulse (applied every 10 s) from −80 mV initially to 40 mV for 2 s and then to −60 mV for 4 s, is used to elicit hERG currents. The percentage reduction of tail current amplitude by the compounds of Formula I and/or Formula V that are tested is determined and data are shown as mean ± s.d. (n = 3–4 per data point). For all experiments, solutions of the drugs are prepared fresh from 10 mM stocks in DMSO. The final DMSO concentration never exceeds 1%.

Serotonin and opioid receptor functional assays.

Functional assay screens at 5-HT and opioid receptors are performed in parallel using the same compound dilutions and 384-well-format high-throughput assay platforms. Assays are used to assess activity at all human isoforms of the receptors, except where noted for the mouse 5-HT_{2A} receptor. Receptor constructs in pcDNA vectors are generated from the Presto-Tango GPCR library39 with minor modifications. All tested compounds of Formula I and/or Formula V are serially diluted in drug buffer (HBSS, 20 mM HEPES, pH 7.4 supplemented with 0.1% bovine serum albumin and 0.01% ascorbic acid) and dispensed into 384-well assay plates using a FLIPR Tetra automated dispenser head (Molecular Devices). Every plate includes a positive control such as 5-HT (for all 5-HT receptors), DADLE (DOR), salvinorin A (KOR), and DAMGO (MOR). For measurements of 5-HT_{2A} 5-HT_{2B}, and 5-HT_{2C} Gq-mediated calcium flux function, HEK Flp-In 293, T-Rex stable cell lines (Invitrogen) are loaded with Fluo-4 dye for one hour, stimulated with compounds and read for baseline (0–10 s) and peak fold-over-basal fluorescence (5 min) at 25 °C on the FLIPR Tetra system. For measurement of 5-HT_6 Gs and 5-HT_{7a} functional assays, -mediated cAMP accumulation is detected using the split-luciferase GloSensor assay in HEKT cells measuring luminescence on a Microbeta Trilux (Perkin Elmer) with a 15 min drug incubation at 25 °C. For 5-HT_{1A}, 5-HT_{1B}, 5-HT_{1F}, MOR, KOR and DOR functional assays, Gi/o, -mediated cAMP inhibition is measured using the split-

luciferase GloSensor assay in HEKT cells, conducted similarly to that above, but in combination with either 0.3 μM isoproterenol (5-HT_{1A}, 5-HT_{1B}, 5-HT_{1F}) or 1 μM forskolin (MOR, KOR and DOR) to stimulate endogenous cAMP accumulation. For measurement of 5-HT_{1D}, 5-HT_{1E}, 5-HT_4, and 5-HT_{5A} functional assays, β-arrestin2 recruitment is measured by the Tango assay using HTLA cells expressing tobacco etch virus (TEV) fused-β-arrestin2, as described previously with minor modifications. Cell lines are not authenticated, but they are purchased mycoplasma-free and tested for mycoplasma contamination. Data for all assays are plotted and nonlinear regression is performed using "log(agonist) vs. response" in GraphPad Prism to yield estimates of the efficacy (Emax and half-maximal effective concentration (EC_{50})).

Pharmacokinetic studies.

Male and female C57/BL6J mice (12 weeks old) are administered a compound of Formula I and/or Formula V via i.p. injection at doses of either 50 mg kg−1, 10 mg kg−1 or 1 mg kg−1. Mice are euthanized 15 min or 3 h after injection by cervical dislocation. Two males and two females are used per dose and time point. Brain and liver are collected, flash-frozen in liquid nitrogen, and stored at −80 °C until metabolomic processing. Whole brain and liver sections are lyophilized overnight to complete dryness, then homogenized with 3.2mm diameter stainless-steel beads using a GenoGrinder for 50 s at 1,500 rpm. Ground tissue is then extracted using 225 μl cold methanol, 190 μl water, 750 μl methyl tert-butyl ether (MTBE). Seven method blanks and seven quality-control samples (pooled human serum, BioIVT) are extracted at the same time as the samples. The nonpolar fraction of MTBE is dried under vacuum and reconstituted in 60 μl of 90:10 (v/v) methanol: toluene containing 1-cyclohexyldodecanoic acid urea as an internal standard. Samples are then vortexed, sonicated and centrifuged before analysis.

For analysis of the tested compound in liver and brain, samples are randomized before injection with method blanks and quality-control samples are analyzed between every ten study samples. A six-point calibration curve is analyzed after column equilibration using blank injections, and then after all study samples. Blanks are injected after the calibration curve to ensure no that none of the tested compound is retained on the column and carried over to samples. Reconstituted sample (5 μl) is injected onto a Waters Acquity UPLC CSH C18 column (100 mm × 2.1 mm, 1.7 μm particle size) with an Acquity UPLC CSH C18 VanGuard precolumn (Waters) using a Vanquish UHPLC coupled to a TSQ Altis triple quadrupole mass spectrometer (Thermo Fisher Scientific). Mobile phase A consists of 60:40 v/v acetonitrile/ water with 10 mM ammonium formate and 0.1% formic acid. Mobile phase B consists of 90:10 v/v isopropanol/acetonitrile with 10 mM ammonium formate and 0.1% formic acid. Gradients are run from 0–2 min at 15% B; 2–2.5 min 30% B; 2.5–4.5 min 48% B; 4.5–7.3 min 99% B; 7.3–10 min 15% B. The flow rate is 0.600 ml/min and the column is heated to 65 °C. Mass

spectrometer conditions are optimized for the target compound by direct infusion. Selected reaction monitoring is performed for the top five ions, with collision energy, source fragmentation, and radiofrequency optimized for the test compound. Data are processed with TraceFinder 4.1 (Thermo Fisher Scientific). Organ weights are recorded. The concentration in the brain is calculated using the experimentally determined number of moles of the target compound in the whole organ divided by the weight of the organ.

5-HT Receptor Functional Assays.

Various assays for measuring serotonin receptor activation are known to those of skill in the art, including those methods described in Olsen et al., *Nat. Chem. Biol.*, 2020 Aug.; 16(8):841-49, incorporated herein by reference in its entirety for all purposes. The assays described therein may be utilized to measure the functional activity of any of the serotonin receptor subtypes described herein, including 5-HT1A, 5-HT2A, 5-HT2B, and 5-HT2C. In certain embodiments, serotonin (5-hydroxytryptamine) is used as the reference compound.

Cell culture

HEK293T cells are maintained, passaged, and transfected in DMEM medium containing 10% FBS, 100 Units/mL penicillin, and 100 μg/mL streptomycin (Gibco-ThermoFisher, Waltham, MA) in a humidified atmosphere at 37°C and 5% CO2. After transfection, cells are plated in DMEM containing 1% dialyzed FBS, 100 Units/mL penicillin, and 100 μg/mL streptomycin for BRET2, calcium, and GloSensor assays.

BRET2 assays

Cells are plated either in six-well dishes at a density of 700,000–800,000 cells/well, or 10-cm dishes at 7–8 million cells/dish. Cells are transfected 2–4 hours later, using a 1:1:1:1 DNA ratio of receptor:Gα-RLuc8:Gβ:Gγ-GFP2 (100 ng/construct for six-well dishes, 750 ng/construct for 10-cm dishes), except for the Gγ-GFP2 screen, where an ethanol co-precipitated mixture of Gβ1–4- is used at twice its normal ratio (1:1:2:1). Transit 2020 (Mirus Biosciences, Madison, WI) is used to complex the DNA at a ratio of 3 μL Transit/μg DNA, in OptiMEM (Gibco-ThermoFisher, Waltham, MA) at a concentration of 10 ng DNA/μL OptiMEM. The next day, cells are harvested from the plate using Versene (0.1M PBS + 0.5 mM EDTA, pH 7.4), and plated in poly-D-lysine-coated white, clear bottom 96-well assay plates (Greiner Bio-One, Monroe, NC) at a density of 30,000–50,000 cells/well.

One day after plating in 96-well assay plates, white backings (Perkin Elmer, Waltham, MA) are applied to the plate bottoms, and growth medium is carefully aspirated and replaced immediately with 60 μL of assay buffer (1x HBSS + 20 mM HEPES, pH 7.4), followed by a 10 μL addition of freshly prepared 50 μM coelenterazine 400a (Nanolight Technologies, Pinetop, AZ). After a five-minute equilibration period, cells are treated with 30 μL of drug for an

additional 5 minutes. Plates are then read in an LB940 Mithras plate reader (Berthold Technologies, Oak Ridge, TN) with 395 nm (RLuc8-coelenterazine 400a) and 510 nm (GFP2) emission filters, at 1 second/well integration times. Plates are read serially six times, and measurements from the sixth read are used in all analyses. BRET2 ratios are computed as the ratio of the GFP2 emission to RLuc8 emission.

Calcium Mobilization Assays

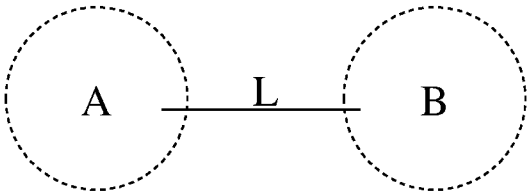
Cells are plated in 10-cm plates as described in the BRET2 protocol and co-transfected with receptor (1 μg) and Gα-subunit (1 μg) cDNA. The next day, cells are plated at 15,000 cells/well in poly-D-lysine coated black, clear bottom 384-well plates (Greiner Bio-One, Monroe, NC). The following day, growth medium are aspirated and replaced with 20 μL assay buffer containing 1x Fluo-4 Direct Calcium Dye (ThermoFisher Scientific, Waltham, MA) and incubated for 60 minutes at 37°C (no CO_2). Plates are brought to RT for 10 minutes in the dark before being loaded into a FLIPR Tetra® liquid-handling robot and plate reader (Molecular Devices, San Jose, CA). Baseline fluorescence measurements are taken for 10 seconds followed by robotic drug addition (10 μL) and a 60-second measurement (1 measurement/second). For antagonist assays, cells are first treated with antagonist and kept in the dark at room temperature for ten minutes before agonist addition by the FLIPR Tetra® robot. Maximal response during this time is used to calculate amplitude of the calcium transients. Measurements are analyzed as percentage of maximum signal amplitude for the construct.

Glosensor cAMP Assays

Cells are plated in 10-cm plates as previously described. Cells are transfected with plasmids encoding cDNA for the Glosensor reporter (Promega, Madison, WI), receptor, and Gα-subunit at a ratio of 2:1:1 (2 μg: 1 μg: 1 μg). The next day, cells are plated in black, clear-bottom, 384-well white plates. After aspiration of the medium on the day of the assay, cells are incubated for 60 minutes at 37°C with 20 μL of 5 mM luciferin substrate (GoldBio, St. Louis, MO) freshly prepared in assay buffer. For Gαs activity, 10 μL of drugs are added using the FLIPR Tetra® liquid-handling robot and read after 15 minutes in a Spectramax luminescence plate reader (Molecular Devices, San Jose, CA) with a 0.5 second signal integration time. For Gαi activity, 10 μL of drugs are added for a 15-minute incubation period. Subsequently, 10 μL of isoproterenol (final concentration of 200 nM) are added and incubated for an additional 15-minute period before reading.

Exemplary Embodiments

Embodiment 1: A compound of Formula I:



Formula I

wherein

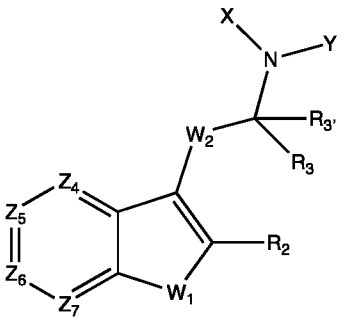
Group A is a residue of a first active compound comprising a serotonergic drug;

Group B is a residue of a second active compound; and

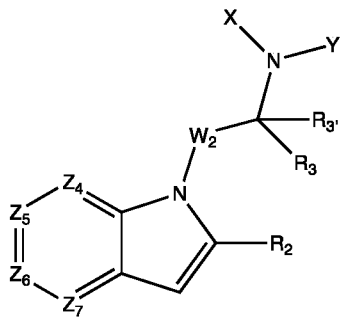
L is a covalent linkage between Group A and Group B,

and salts, solvates, hydrates, and prodrugs thereof.

Embodiment 2: The compound of Embodiment 1, wherein at least one of Group A or Group B is a residue of a serotonergic drug selected from Formulae II and III:



Formula II



Formula III

wherein

X and Y are each independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl, or Y is taken together with X and the nitrogen atom therebetween to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

W_1 is selected from NR_1, O, S, S(O), SO_2, Se, Se(O), and SeO_2;

W_2 is selected from -CD_2-, -CHD-, –$(CD_2)_2$-, -CH_2-, and –$(CH_2)_2$-;

Z_4 is selected from N and CR_4;

Z_5 is selected from N and CR_5;

Z_6 is selected from N and CR_6;

Z_7 is selected from N and CR_7;

R_1 is selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, $-C(O)R_8$, $-C(O)OR_8$, $-P(O)(OR_9)_2$, $-C(O)N(R_9)_2$, $-SOR_8$, and $-SO_2R_8$;

R_2, R_3, $R_{3'}$, R_6 and R_7 are each independently selected from hydrogen, deuterium, $-N(R_9)_2$, $-SR_9$, halo, optionally substituted C_1-C_8 alkyl, $-C_1$-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl, or Y is absent and R_3 is taken together with carbon to which it is attached and the nitrogen atom to which X is attached to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9, or X is absent and R_2 is taken together with carbon to which it is attached and the nitrogen atom to which Y is attached to form a 5- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

R_4 and R_5 are each independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, $-N(R_9)_2$, $-SR_9$, $-C_1$-C_8 alkoxy, $-OC(O)R_8$, $-OC(O)OR_8$, $-OP(O)(OR_9)_2$, and $-OSO_2R_8$;

each R_8 is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

each R_9 is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

and salts, solvates, hydrates, and prodrugs thereof.

Embodiment 3: The compound according to Embodiment 2, wherein R_3 and $R_{3'}$ are hydrogen for each occurrence.

Embodiment 4: The compound according to Embodiment 2 or 3, wherein X and Y for each occurrence are independently selected from C_1-C_8 alkyl.

Embodiment 5: The compound according to Embodiment 4, wherein X is methyl.

Embodiment 6: The compound according to Embodiment 4, wherein X is ethyl.

Embodiment 7: The compound according to Embodiment 4, wherein X is n-propyl.

Embodiment 8: The compound according to Embodiment 4, wherein X is isopropyl.

Embodiment 9: The compound according to any one of Embodiments 2-3, wherein X is hydrogen.

Embodiment 10: The compound according to any one of Embodiments 2-9, wherein Y is methyl.

Embodiment 11: The compound according to any one of Embodiments 2-9, wherein Y is ethyl.

Embodiment 12: The compound according to any one of Embodiments 2-9, wherein Y is n-propyl.

Embodiment 13: The compound according to any one of Embodiments 2-9, wherein Y is isopropyl.

Embodiment 14: The compound according to any one of Embodiments 2-13, wherein W_2 is independently selected from $-CD_2-$, -CHD-, and $-CH_2-$ for each occurrence.

Embodiment 15: The compound according to any one of Embodiments 2-14, wherein R_2 is hydrogen for each occurrence.

Embodiment 16: The compound according to any one of Embodiments 2 and 4-15, wherein R_3 and $R_{3'}$ for each occurrence are independently selected from hydrogen, deuterium, and C_1-C_4 alkyl.

Embodiment 17: The compound according to Embodiment 16, wherein R_3 and $R_{3'}$ are each independently selected from methyl and hydrogen.

Embodiment 18: The compound according to any one of Embodiments 2-17, wherein R_7 is selected from hydrogen and C_1-C_4 alkyl.

Embodiment 19: The compound according to Embodiment 18, wherein R_7 is methyl.

Embodiment 20: The compound according to Embodiment 18, wherein R_7 is hydrogen.

Embodiment 21: The compound according to any one of Embodiments 2-20, wherein R_6 is selected from hydrogen, -C_1-C_8 alkoxy, and halo.

Embodiment 22: The compound according to Embodiment 21, wherein R_6 is selected from halo and methoxy.

Embodiment 23: The compound according to Embodiment 21, wherein R_6 is fluoro.

Embodiment 24: The compound according to Embodiments 21, wherein R_6 is chloro.

Embodiment 25: The compound according to Embodiments 21, wherein R_6 is bromo.

Embodiment 26: The compound according to any one of Embodiments 2-25, wherein at least one of R_4 and R_5 is hydroxyl.

Embodiment 27: The compound according to Embodiment 26, wherein linker "L" is linked to a residue of a compound of Formula II via the hydroxyl group.

Embodiment 28: The compound according to any one of Embodiments 2-21 and 26-27, wherein Z_6 is N.

Embodiment 29: The compound according to any one of Embodiments 2-17 and 21-28, wherein Z_7 is N.

Embodiment 30: The compound according to any one of Embodiments 2-29, wherein W_1 is NR_1.

Embodiment 31: The compound according to any one of Embodiments 2-29, wherein W_1 is O.

Embodiment 32: The compound according to any one of Embodiments 2-29, wherein W_1 is S.

Embodiment 33: The compound according to any one of Embodiments 2-29, wherein W_1 is Se.

Embodiment 34: The compound according to any one of claims 2-33, wherein Group A is a residue of a compound of Formula II.

Embodiment 35: The compound according to any one of claims 2-33, wherein Group A is a residue of a compound of Formula III.

Embodiment 36: The compound according to any of the preceding Embodiments, wherein Group B is a residue of a cannabinoid.

Embodiment 37: The compound of Embodiment 36, wherein the cannabinoid is selected from Delta-8-THC, Delta-9-THC, THCA, THCV, THCVA, CBC, CBCA, CBCV, CBCVA, CBD, CBDA, CBDV, CBDVA, CBG, CBGA, CBGV, and CBGVA.

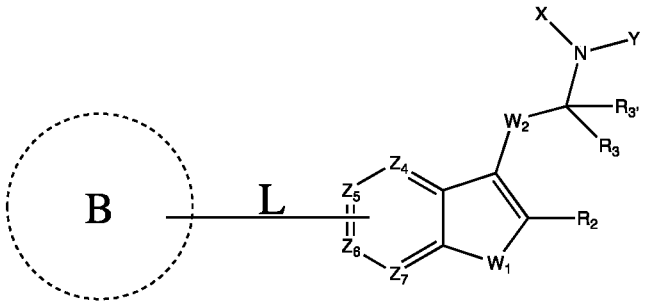
Embodiment 38: The compound according to any of the preceding Embodiments, wherein Group B is a residue of an active compound that is a serotonin receptor 5-HT2A agonist.

Embodiment 39: The compound according to Embodiment 38, wherein the serotonin receptor 5-HT1A agonist is a full agonist.

Embodiment 40: The compound according to any one of Embodiments 38-39, wherein the serotonin receptor 5-HT1A agonist is a compound of Formula II.

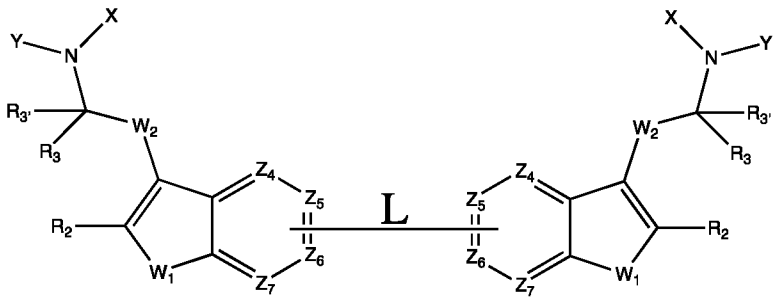
Embodiment 41: The compound according to Embodiment 38, wherein the serotonin receptor 5-HT2A agonist is selected from buspirone (8-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]-8-azaspiro[4.5]decane-7,9-dione), 5-OH-buspirone, 6-OH-buspirone, tandospirone ((1R,2R,6S,7S)-4-{4-[4-(pyrimidin -2-yl)piperazin-1-yl]butyl}-4-azatricyclo[5.2.1.02,6]decane-3,5-dione), gepirone (4,4-dimethyl-1-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]piperid- ine-2,6-dione), alnespirone ((+)-4-dihydro-2H-chromen-3-yl]-propylamino]butyl]-8-azaspiro[4.5]decane--7,9-dione), binospirone (8-[2-(2,3-dihydro-1,4-benzodioxin-2-ylmethylamino)ethyl]-8-azaspiro[4.5]- decane-7,9-dione), ipsapirone (9,9-dioxo-8-[4-(4-pyrimidin-2-ylpiperazin-1-yl)butyl]-9.lamda.6-thia-8-a- zabicyclo[4.3.0]nona-1,3,5-trien-7-one), perospirone (3aR, 7aS) -2-{4-[4-(1,2-benzisothiazol-3-yl)piperazin-1-yl]butyl} hexahydro-1H-isoindole-1,3(2H)-dione, befiradol (F-13,640) (3-chloro-4-fluorophenyl-[4-fluoro-4-([(5-methylpyridin-2 -yl)methylamino]methyl)piperidin-1-yl]methanone, repinotan ((R)-(-)-2-[4-[(chroman-2 -ylmethyl)-amino]-butyl]-1,1-dioxo-benzo[d] isothiazolone), piclozotan (3-chloro-4-[4-[4-(2-pyridinyl)-1,2,3,6-tetrahydropyridin-1-yl]butyl]-1,4- -benzoxazepin-5(4H)-one), osemozotan (5-(3-[((2S)-1,4-benzodioxan-2-ylmethyl)amino]propoxy)-1,3-benzodioxole), flesinoxan (4-fluoro-N-[2-[4-[(3S)-3-(hydroxymethyl)-2,3-dihydro-1,4 -benzodioxin-8-yl]piperazin-1-yl]ethyl]benzamide), flibanserin (1-(2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,3-dihydro-2H--benzimidazol-2-one), 8-OH-DPAT (7-(Dipropylamino)-5,6,7,8-tetrahydronaphthalen-1-ol), and sarizotan (EMD-128,130) (1-[(2R)-3,4-dihydro-2H-chromen-2-yl]-N-([5-(4 -fluorophenyl)pyridin-3-yl]methyl)methanamine).

Embodiment 42: The compound according to any one of Embodiments 1-35 and 38-40, wherein the compound of Formula I is a compound of Formula IA:



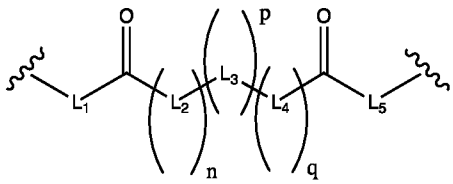
Formula IA.

Embodiment 43: The compound according to any one of Embodiments 1-35, 38-40 and 42, wherein the compound of Formula I is a compound of Formula IB:



Formula IB.

Embodiment 44: The compound according to any one of the preceding Embodiments, wherein the linker "L" is selected from Formula IV:



Formula IV

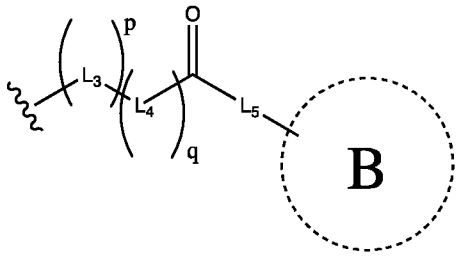
wherein

L_1 and L_5 for each occurrence are independently selected from a covalent bond, O, NR_{10}, and S;

L_2 and L_4 for each occurrence are independently selected from O, $C(R_{10})_2$, NR_{10}, and S;

L_3 for each occurrence are independently selected from O, NR_{10}, S, $C(R_{10})_2$, $C(R_{10})=C(R_{10})$, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R_{10} for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, NO_2, -$N(R_9)_2$, -SR_9, halo, hydroxyl, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, -OSO_2R_8, and a residue of Formula IVB:



Formula IVB;

R_8 is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

R_9 is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

and

n, p, and q for each occurrence are integers independently selected from 0 to 10.

Embodiment 45: The compound according to Embodiment 44, wherein L_1 and L_5 are O.

Embodiment 46: The compound according to any one of Embodiments 44-45, wherein L_2 and L_4 are, for each occurrence, independently selected from O and $C(R_{10})_2$.

Embodiment 47: The compound according to any one of Embodiments 44-46, wherein R_{10} is, for each occurrence, independently selected from hydrogen and C_1-C_4 alkyl.

Embodiment 48: The compound according to any one of Embodiments 44-47, wherein n and q are integers independently selected from 1, 2, 3, and 4.

Embodiment 49: The compound according to any one of Embodiments 44-48, wherein L_3 for each occurrence is independently selected from O, S, and $C(R_{10})_2$.

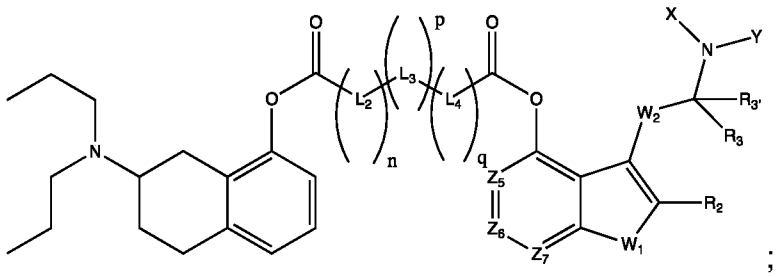
Embodiment 50: The compound according to any one of Embodiments 44-49, wherein R_{10} is hydrogen for each occurrence.

Embodiment 51: The compound according to any one of Embodiments 44-50, wherein p is an integer selected from 1, 2, 3 and 4.

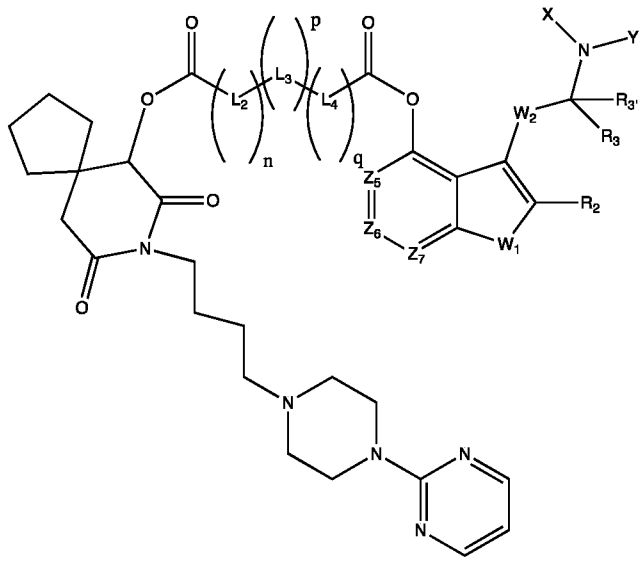
Embodiment 52: The compound according to any one of Embodiments 2-35, 42, and

44-51, wherein Group B is a residue of buspirone enolate, 6-OH-buspirone or 8-OH-DPAT.

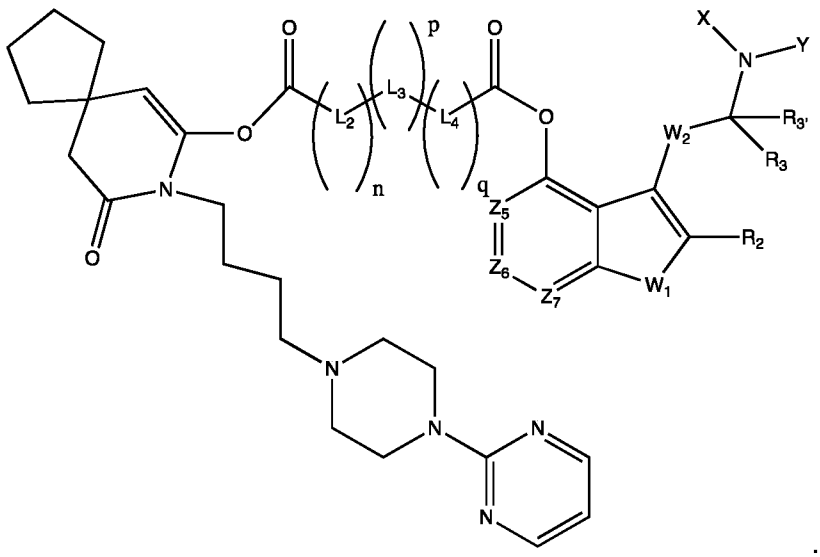
Embodiment 53: The compound according to Embodiment 52, wherein the compound is selected from:



;

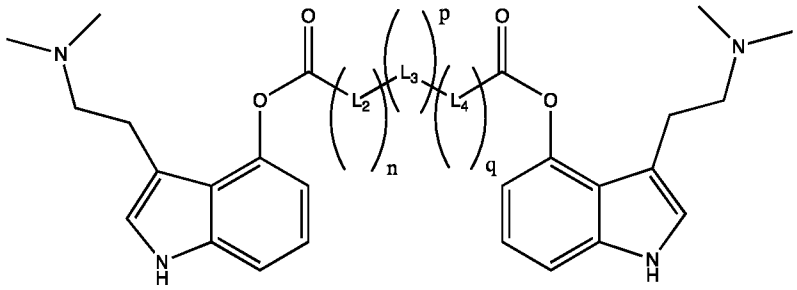


; and



.

Embodiment 54: The compound according to Embodiment 42-51, wherein the compound is a Dipsilocin™ analog selected from Formula IF:



Formula IF.

Embodiment 55: The compound according to any one of Embodiments 1-54, wherein the compound is a salt.

Embodiment 56: The compound according to any one of Embodiments 1-55, wherein the compound is crystalline.

Embodiment 57: A composition comprising, consisting essentially of, or consisting of a compound according to any one of Embodiments 1-56 and 62-117, and an excipient.

Embodiment 58: A composition according to Embodiment 57, wherein the composition is a pharmaceutical composition comprising, consisting essentially of, or consisting of a therapeutically effective amount of a compound according to any one of Embodiments 1-56 and 62-117, and a pharmaceutically acceptable excipient.

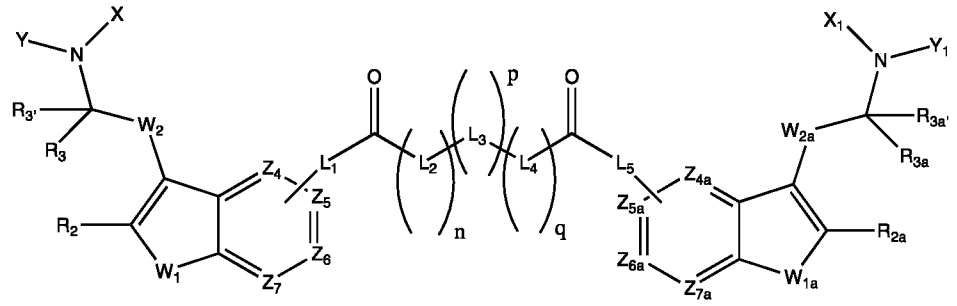
Embodiment 59: A method of preventing or treating a psychological disorder comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of Embodiments 1-56 and 62-117, or a composition according to any one of Embodiments 57-58.

Embodiment 60: A method of preventing or treating inflammation and/or pain comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of Embodiments 1-56 and 62-117, or a composition according to any one of Embodiments 57-58.

Embodiment 61: A method of modulating activity at a neurotransmitter receptor, comprising:

administering a compound according to any one of Embodiments 1-56 and 62-117, or a composition according to any one of Embodiments 57-58, to the subject in need of treatment.

Embodiment 62: A compound of Formula IDe:



Formula IDe

wherein

X, X_1, Y and Y_1 for each occurrence are independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl, or Y or Y_1 is taken together with X or X_1, respectively, and the nitrogen atom therebetween to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

W_1 and W_{1a} are independently selected from NR_1, O, S, S(O), SO_2, Se, Se(O), and SeO_2;

W_2 and W_{2a} are independently selected from -CD_2-, -CHD-, –$(CD_2)_2$-, -CH_2-, and –$(CH_2)_2$-;

Z_4 and Z_{4a} are independently selected from N and CR_4;

Z_5 and Z_{5a} are independently selected from N and CR_5;

Z_6 and Z_{6a} are independently selected from N and CR_6;

Z_7 and Z_{7a} are independently selected from N and CR_7;

R_1 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, -C(O)R_8, -C(O)OR_8, -OP(O)$(OR_9)_2$, -C(O)N$(R_9)_2$, -SOR_8, and -SO_2R_8;

R_2, R_3, R_6, R_7, R_{2a}, R_{3a}, $R_{3'}$ and $R_{3a'}$ for each occurrence are independently selected from hydrogen, deuterium, -N$(R_9)_2$, -SR_9, halo, optionally substituted C_1-C_8 alkyl, -C_1-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl,

or Y or Y_1 is absent and R_3 or R_{3a} is taken together with carbon to which it is attached and the nitrogen atom to which X or X_1, respectively, is attached to form a 3- to

7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9,

or X or X_1 is absent and R_2 or R_{2a}, respectively, is taken together with carbon to which it is attached and the nitrogen atom to which Y or Y_1 is attached to form a 5- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

R_4 and R_5 for each occurrence are independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, -$N(R_9)_2$, -SR_9, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8;

R_8 for each occurrence is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

R_9 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

L_1 and L_5 for each occurrence are independently selected from a covalent bond, O, NR_{10}, and S;

L_2 and L_4 for each occurrence are independently selected from O, $C(R_{10})_2$, NR_{10}, and S;

L_3 for each occurrence are independently selected from O, NR_{10}, S, $C(R_{10})_2$, $C(R_{10})=C(R_{10})$, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R_{10} for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl; and

n, p and q for each occurrence are integers independently selected from 0 to 10;

wherein L_1 can replace a hydrogen in a R_4 group when Z_4 is CR_4, a hydrogen in a R_5 group when Z_5 is CR_5, a hydrogen in a R_6 group when Z_6 is CR_6, or a hydrogen in a R_7 group when Z_7 is CR_7,

or L_1 can replace X or a hydrogen atom in a R_2 group,

and wherein L_5 can replace a hydrogen in a can replace a hydrogen in a R_4 group when Z_{4a} is CR_4, a hydrogen in a R_5 group when Z_{5a} is CR_5, a hydrogen in a R_6 group when Z_{6a} is

CR_6, a hydrogen in a R_7 group when Z_{7a} is CR_7,

or L_5 can replace X or a hydrogen atom in a R_2 group,

or salts, solvates, hydrates, and prodrugs thereof.

Embodiment 63: The compound according to Embodiment 62, wherein X is hydrogen.

Embodiment 64: The compound according to Embodiment 62, wherein X, X_1, Y and Y_1 are selected from optionally substituted C_1-C_8 alkyl and optionally substituted C_2-C_8 alkenyl.

Embodiment 65: The compound according to Embodiment 62 or 64, wherein X is methyl.

Embodiment 66: The compound according to any one of Embodiments 62-65, wherein X_1 is methyl.

Embodiment 67: The compound according to any one of Embodiment 62, 64 and 66, wherein X is ethyl.

Embodiment 68: The compound according to Embodiments 62-65 and 67, wherein X_1 is ethyl.

Embodiment 69: The compound according to any one of Embodiments 62-63 and 65-68, wherein Y is hydrogen.

Embodiment 70: The compound according to any one of Embodiments 62-63 and 65-69, wherein Y_1 is hydrogen.

Embodiment 71: The compound according to any one of Embodiments 62-68 and 70, wherein Y is methyl.

Embodiment 72: The compound according to any one of Embodiments 62-69 and 70, wherein Y_1 is methyl.

Embodiment 73: The compound according to any one of Embodiments 62-68 and 70, wherein Y is ethyl.

Embodiment 74: The compound according to any one of Embodiments 62-69, 71 and 73, wherein Y_1 is ethyl.

Embodiment 75: The compound according to any one of Embodiments 62-74, wherein W_2 and W_{2a} are each independently selected from $-CD_2-$, -CHD- and $-CH_2-$.

Embodiment 76: The compound according to any one of Embodiments 62-75, wherein R_3 and $R_{3'}$ are each independently selected from hydrogen, deuterium and C_1-C_4 alkyl.

Embodiment 77: The compound according to any one of Embodiments 62-76, wherein R_{3a} and $R_{3a'}$ are each independently selected from hydrogen, deuterium and C_1-C_4 alkyl.

Embodiment 78: The compound according to any one of Embodiments 62-77, wherein R_2 and R_{2a} are hydrogen.

Embodiment 79: The compound according to any one of Embodiments 62-78, wherein at least one of Z_6, Z_{6a}, Z_7 or Z_{7a} is N.

Embodiment 80: The compound according to any one of Embodiments 62-79, wherein at least one of Z_7 or Z_{7a} is N.

Embodiment 81: The compound according to any one of Embodiments 62-80, wherein Z_6 and Z_{6a} are both CR_6 respectively.

Embodiment 82: The compound according to Embodiment 81, wherein each R_6 is independently selected from C_1-C_8 alkoxy, hydrogen and halo.

Embodiment 83: The compound according to Embodiment 82, wherein each R_6 is independently selected from methoxy, fluoro, chloro and bromo.

Embodiment 84: The compound according to any one of Embodiments 62-80, wherein at least one of Z_6 or Z_{6a} is N.

Embodiment 85: The compound according to any one of Embodiments 62-79 and 81-84, wherein Z_7 and Z_{7a} are both CR_7 respectively.

Embodiment 86: The compound according to Embodiment 85, wherein each R_7 is independently selected from C_1-C_4 alkyl and hydrogen.

Embodiment 87: The compound according to Embodiment 86, wherein each R_7 is methyl.

Embodiment 88: The compound according to any one of Embodiments 62-87, wherein at least one of Z_4 or Z_5 is CR_4 and CR_5 respectively.

Embodiment 89: The compound according to any one of Embodiments 62-88, wherein at least one of Z_{4a} or Z_{5a} is CR_4 and CR_5 respectively.

Embodiment 90: The compound according to any one of Embodiments 62-89, wherein

Z_4 is CR_4 wherein R_4 is replaced by L_1.

Embodiment 91: The compound according to any one of Embodiments 62-89, wherein Z_5 is CR_5 wherein R_5 is replaced by L_1.

Embodiment 92: The compound according to any one of Embodiments 62-91, wherein Z_{4a} is CR_4 wherein R_{4a} is replaced by L_5.

Embodiment 93: The compound according to any one of Embodiments 62-91, wherein Z_{5a} is CR_5 wherein R_{5a} is replaced by L_5.

Embodiment 94: The compound according to any one of Embodiments 62-93, wherein L_1 is O.

Embodiment 95: The compound according to any one of Embodiments 62-94, wherein L_5 is O.

Embodiment 96: The compound according to any one of Embodiments 62-95, wherein W_1 is NR_1.

Embodiment 97: The compound according to any one of Embodiments 62-96, wherein R_1 is selected from hydrogen and C_1-C_4 alkyl.

Embodiment 98: The compound according to any one of Embodiments 62-95, wherein W_1 is O.

Embodiment 99: The compound according to any one of Embodiments 62-95, wherein W_1 is S.

Embodiment 100: The compound according to any one of Embodiments 62-95, wherein W_1 is Se.

Embodiment 101: The compound according to any one of Embodiments 62-100, wherein W_{1a} is NR_1.

Embodiment 102: The compound according to Embodiment 101, wherein R_1 is selected from hydrogen and C_1-C_4 alkyl.

Embodiment 103: The compound according to any one of Embodiments 62-100, wherein W_{1a} is O.

Embodiment 104: The compound according to any one of Embodiments 62-100, wherein W_{1a} is S.

Embodiment 105: The compound according to any one of Embodiments 62-100, wherein W_{1a} is Se.

Embodiment 106: The compound according to any one of Embodiments 62-105, wherein L_2 and L_4 for each occurrence are independently selected from O and $C(R_{10})_2$.

Embodiment 107: The compound according to Embodiment 106, wherein R_{10} for each occurrence is independently selected from hydrogen and C_1-C_4 alkyl.

Embodiment 108: The compound according to Embodiment 104, wherein R_{10} for each occurrence is independently selected from hydrogen and methyl.

Embodiment 109: The compound according to any one of Embodiments 62-108, wherein n and q are independently selected from 1, 2, 3 and 4.

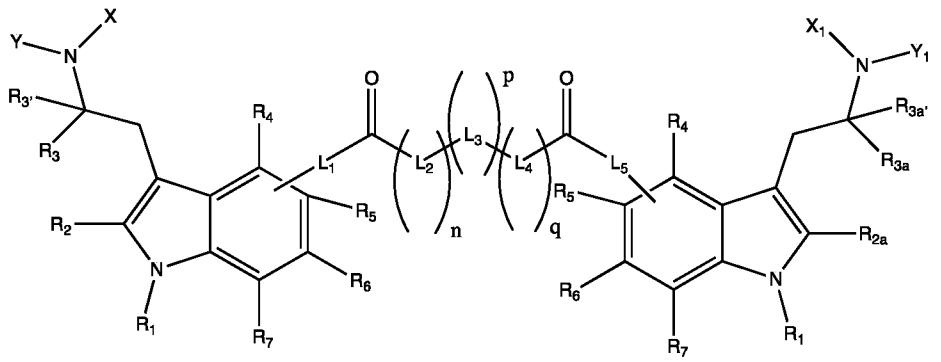
Embodiment 110: The compound according to any one of Embodiments 62-109, wherein L_3 for each occurrence is independently selected from O, S and $C(R_{10})_2$.

Embodiment 111: The compound according to Embodiment 110, wherein R_{10} for each occurrence with respect to L_3 is independently selected from hydrogen and C_1-C_4 alkyl.

Embodiment 112: The compound according to Embodiment 111, wherein R_{10} for each occurrence with respect to L_3 is hydrogen.

Embodiment 113: The compound according to any one of Embodiments 62-112, wherein p is selected from 1, 2, 3 and 4.

Embodiment 114: The compound according to any one of Embodiments 62-78, 81-83, 85-97, 101-102, and 106-113, wherein the compound of Formula IDe is selected from Formula IEa:



Formula IEa.

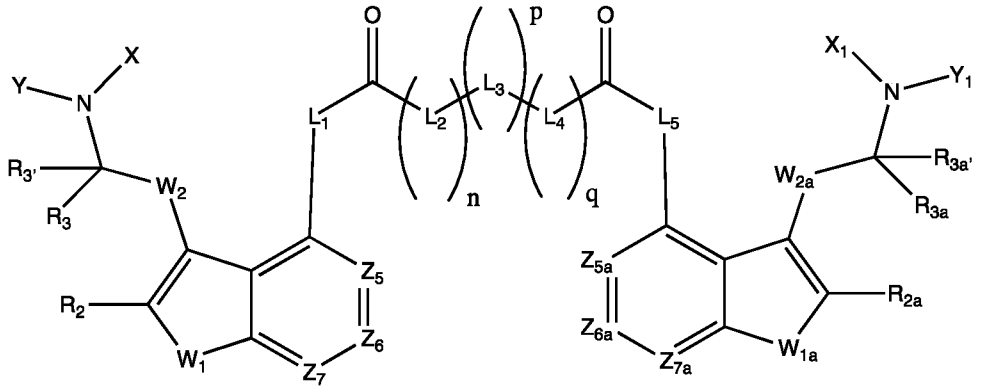
Embodiment 115: The compound according to Embodiment 114, wherein L_1 and L_5 are

O.

Embodiment 116: The compound according to Embodiment 114 or 115, wherein L_1 replaces R_4 on the first indole skeleton.

Embodiment 117: The compound according to any one of Embodiments 113-114, wherein L_5 replaces R_4 on the second indole skeleton.

1. Embodiment 118: A compound of Formula IG:



Formula IG

wherein

X, X_1, Y and Y_1 for each occurrence are independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl, or Y or Y_1 is taken together with X or X_1, respectively, and the nitrogen atom therebetween to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

W_1 and W_{1a} are independently selected from NR_1, O, S, S(O), Se, Se(O), and SeO_2;

W_2 and W_{2a} are independently selected from -CD_2-, -CHD-, –$(CD_2)_2$-, -CH_2-, and –$(CH_2)_2$-;

Z_5 and Z_{5a} are independently selected from N and CR_5;

Z_6 and Z_{6a} are independently selected from N and CR_6;

Z_7 and Z_{7a} are independently selected from N and CR_7;

R_1 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, -C(O)R_8, -

$C(O)OR_8$, $-P(O)(OR_9)_2$, $-C(O)N(R_9)_2$, $-SOR_8$, and $-SO_2R_8$;

R_2, R_3, $R_{6,}$ R_7, R_{2a}, R_{3a}, $R_{3'}$ and $R_{3a'}$ for each occurrence are independently selected from hydrogen, deuterium, $-N(R_9)_2$, $-SR_9$, halo, optionally substituted C_1-C_8 alkyl, $-C_1$-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl,

or Y or Y_1 is absent and R_3 or R_{3a} is taken together with carbon to which it is attached and the nitrogen atom to which X or X_1, respectively, is attached to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9,

or X or X_1 is absent and R_2 or $R_{2a,}$ respectively, is taken together with carbon to which it is attached and the nitrogen atom to which Y or Y_1 is attached to form a 5- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

R_5 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, $-N(R_9)_2$, $-SR_9$, $-C_1$-C_8 alkoxy, $-OC(O)R_8$, $-OC(O)OR_8$, $-OP(O)(OR_9)_2$, and $-OSO_2R_8$;

R_8 for each occurrence is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

R_9 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

L_1 and L_5 for each occurrence are independently selected from a covalent bond, O, NR_{10}, and S;

L_2 and L_4 for each occurrence are independently selected from O, $C(R_{10})_2$, NR_{10}, and S;

L_3 for each occurrence are independently selected from O, NR_{10}, S, $C(R_{10})_2$, $C(R_{10})=C(R_{10})$, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R_{10} for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl; and

n, p and q for each occurrence are integers independently selected from 0 to 10;

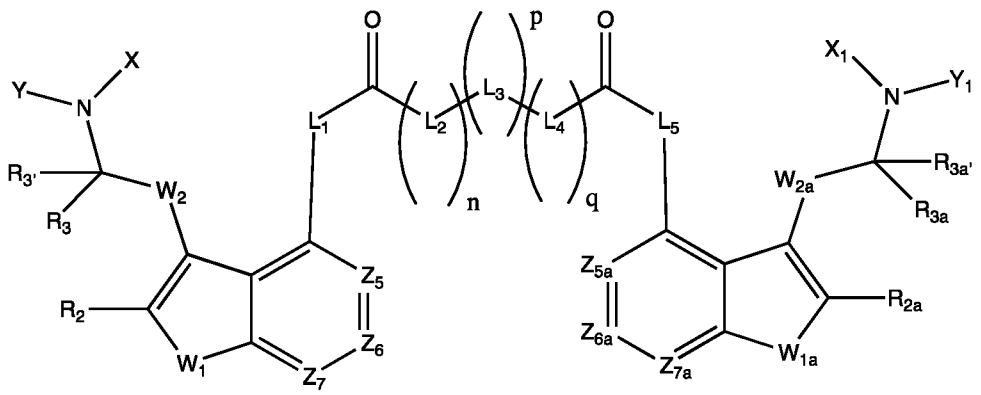
or

salts, solvates, hydrates, and prodrugs thereof.

Finally, it is noted that, as used in this specification and the appended claims, the singular forms "a," "an," and "the," include plural referents unless expressly and unequivocally limited to one referent and vice versa. As used herein, the term "include" or "comprising" and its grammatical variants are intended to be non-limiting, such that recitation of an item or items is not to the exclusion of other like items that can be substituted or added to the recited item(s).

WHAT IS CLAIMED IS:

1. A compound of Formula IG:



Formula IG

wherein

X, X_1, Y and Y_1 for each occurrence are independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl, or Y or Y_1 is taken together with X or X_1, respectively, and the nitrogen atom therebetween to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

W_1 and W_{1a} are independently selected from NR_1, O, S, S(O), Se, Se(O), and SeO_2;

W_2 and W_{2a} are independently selected from -CD_2-, -CHD-, –$(CD_2)_2$-, -CH_2-, and –$(CH_2)_2$-;

Z_5 and Z_{5a} are independently selected from N and CR_5;

Z_6 and Z_{6a} are independently selected from N and CR_6;

Z_7 and Z_{7a} are independently selected from N and CR_7;

R_1 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, -$C(O)R_8$, -$C(O)OR_8$, -$P(O)(OR_9)_2$, -$C(O)N(R_9)_2$, -SOR_8, and -SO_2R_8;

R_2, R_3, R_6, R_7, R_{2a}, R_{3a}, $R_{3'}$ and $R_{3a'}$ for each occurrence are independently selected from hydrogen, deuterium, -$N(R_9)_2$, -SR_9, halo, optionally substituted C_1-C_8 alkyl, -C_1-C_8 alkoxy, and optionally substituted C_2-C_8 alkenyl,

or Y or Y_1 is absent and R_3 or R_{3a} is taken together with carbon to which it is

attached and the nitrogen atom to which X or X_1, respectively, is attached to form a 3- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9,

or X or X_1 is absent and R_2 or R_{2a}, respectively, is taken together with carbon to which it is attached and the nitrogen atom to which Y or Y_1 is attached to form a 5- to 7-membered heterocyclic ring optionally including 1 to 2 additional ring heteromoieties selected from O, S, S(O), SO_2, and NR_9;

R_5 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, halo, hydroxyl, -$N(R_9)_2$, -SR_9, -C_1-C_8 alkoxy, -$OC(O)R_8$, -$OC(O)OR_8$, -$OP(O)(OR_9)_2$, and -OSO_2R_8;

R_8 for each occurrence is independently selected from optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

R_9 for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, optionally substituted C_2-C_8 alkenyl, and optionally substituted aryl;

L_1 and L_5 for each occurrence are independently selected from a covalent bond, O, NR_{10}, and S;

L_2 and L_4 for each occurrence are independently selected from O, $C(R_{10})_2$, NR_{10}, and S;

L_3 for each occurrence are independently selected from O, NR_{10}, S, $C(R_{10})_2$, $C(R_{10})=C(R_{10})$, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R_{10} for each occurrence is independently selected from hydrogen, deuterium, optionally substituted C_1-C_8 alkyl, and optionally substituted C_2-C_8 alkenyl; and

n, p and q for each occurrence are integers independently selected from 0 to 10; or

salts, solvates, hydrates, and prodrugs thereof.

2. The compound according to claim 1, wherein X and X_1 are independently selected from C_1-C_8 alkyl.

3. The compound according to any one of the preceding claims, wherein Y and Y_1 are

independently selected from C_1-C_8 alkyl.

4. The compound according to any one of the preceding claims, wherein W_2 and W_{2a} are independently selected from -CD_2-, -CHD-, and -CH_2-.

5. The compound according to any one of the preceding claims, wherein R_{2a} and R_2 are hydrogen.

6. The compound according to any one of the preceding claims, wherein R_3, $R_{3'}$, R_{3a} and $R_{3'}$ are each independently selected from hydrogen, deuterium, and methyl.

7. The compound according to any one of the preceding claims, wherein R_3, $R_{3'}$, R_{3a} and $R_{3'}$ are each independently selected from hydrogen and deuterium.

8. The compound according to any one of the preceding claims, wherein Z_5 and Z_{5a} for each occurrence are independently CR_5.

9. The compound according to claim 8, wherein R_5 for each occurrence is independently selected from hydrogen and halogen.

10. The compound according to any one of the preceding claims, wherein at least one of Z_6, Z_{6a}, Z_7 and Z_{7a} is N.

11. The compound according to any one of the preceding claims, wherein Z_6 and Z_{6a} are N.

12. The compound according to any one of the preceding claims, wherein Z_7 and Z_{7a} are N.

13. The compound according to any one of claims 1-10 and 12, wherein Z_6 and Z_{6a} are both CR_6.

14. The compound according to claim 13, wherein R_6 for each occurrence is independently selected from C_1-C_4 alkoxy, halo, and hydrogen.

15. The compound according to claim 14, wherein R_6 for each occurrence is independently selected from methoxy, fluoro, chloro and bromo.

16. The compound according to any one of claims 1-11 and 13-15, wherein Z_7 and Z_{7a} are both CR_7.

17. The compound according to claim 16, wherein each R_7 is independently selected from hydrogen and C_1-C_4 alkyl.

18. The compound of claim 17, wherein R_7 is methyl for each occurrence.

19. The compound according to any one of the preceding claims, wherein W_1 and W_{1a} are both NR_1.

20. The compound according to claim 19, wherein R_1 for each occurrence is independently selected from hydrogen and C_1-C_4 alkyl.

21. The compound according to any one of claims 1-18, wherein W_1 and W_{1a} are each independently selected from Se, S and O.

22. The compound according to claim 21, wherein W_1 and W_{1a} are both Se.

23. The compound according to any one of the preceding claims, wherein L_1 and L_5 are both O.

24. The compound according to any one of the preceding claims, wherein L_2 and L_4 for each occurrence are independently selected from O and $C(R_{10})_2$.

25. The compound according to any one of the preceding claims, wherein R_{10} for each occurrence, with respect to L_2 and L_4, is independently selected from hydrogen and C_1-C_4 alkyl.

26. The compound according to any one of the preceding claims, wherein R_{10} for each occurrence, with respect to L_2 and L_4, is independently selected from hydrogen and methyl.

27. The compound according to any one of the preceding claims, wherein n and q are independently selected from 1, 2, 3 and 4.

28. The compound according to any one of the preceding claims, wherein L_3 for each occurrence is independently selected from O, S and $C(R_{10})_2$.

29. The compound according to claim 28, wherein R_{10} for each occurrence, with respect to L_3, is independently selected from hydrogen and C_1-C_4 alkyl.

30. The compound according to claim 29, wherein R_{10} for each occurrence, with respect to L_3, is hydrogen.

31. The compound according to any one of the preceding claims, wherein p is selected from 1, 2, 3 and 4.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/53910

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. C07D 209/16, C07D 401/14, C07D 401/12 (2023.01)
ADD. C07D 413/12, C07D 403/06, A61K 31/4045, A61P 25/22 (2023.01)

CPC - INV. C07D 209/16, C07D 401/14, C07D 401/12
ADD. C07D 413/12, C07D 403/06, A61K 31/4045, A61P 25/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2016/0130279 A1 (NESTEC S.A.) 12 May 2016 (12.05.2016); para [0273]	1-3
A	Simonetti et al. "Synthesis of Novel Tryptamine Derivatives and Their Biological Activity as Antitumor Agents" Molecules. 28 January 2021 (28.01.2021) vol 26, pg. 1-13; pg. 4, Scheme 1	1-3
A	WO 2021/155467 A1 (MINDSET PHARMA INC.) 12 August 2021 (12.08.2021); para [00181]	1-3
A	US 2018/0221396 A1 (CaaMTech, LLC) 09 August 2018 (09.08.2018); entire document	1-3
P, X	WO 2022/038299 A1 (COMPASS PATHFINDER LIMITED) 24 February 2022 (24.02.2022); entire document	1-3

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
03 March 2023 (03.03.2023)	APR 05 2023
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Kari Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/53910

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 4-31
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.