

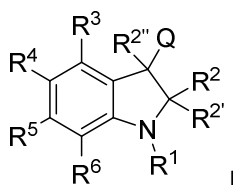
[0007] Some potential non-hallucinogenic psychedelic analogs have been reported (Cunningham M.J. et al., ACS Chem. Neurosci. 2023, 14, 1, 119-135, Hofman, A. LSD, My Problem Child: Reflections on Sacred Drugs, Mysticism, and Science; MAPS, Multidisciplinary Association for Psychedelic Studies: Santa Cruz, CA, 2009, Weingartner, H. et al., J. Clin. Pharmacol. New Drugs 1971, 11, 103-111, Shulgin, A.T. 2-Amino-1-(2,5-dimethoxyphenyl) butanes US Patent No. 4105695A, Shulgin, A.T. Soc. Pharmacol. 1987, 1, 279-290, Cameron, et al. Nature 2021, 589(7842) 474-479, Lu J. et al., Molecular Psychiatry, 2021, 26, 6237-6252, Cao et al., Science 2022, 375, 403-411, Vargas et al., Science, 2023, 379, 700-706). While results with these non-hallucinogenic 5-HT_{2A} agonists have been encouraging, non-hallucinogenic 5-HT_{2A} agonist therapeutic development remains in its infancy.

[0008] There remains a need to provide new psychedelic and non-hallucinogenic 5-HT_{2A} agonist molecules for the treatment, for example, of mental diseases.

SUMMARY OF THE APPLICATION

[0009] Compounds of the present application modulate the activity of serotonin receptor subtypes, in particular 5-HT_{2A}, by direct binding to these receptors.

[0009a] In one aspect, the present disclosure provides a compound of Formula I:

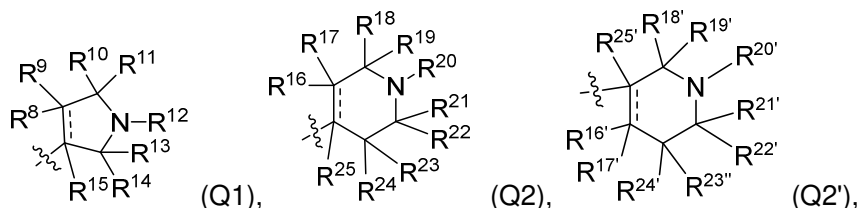


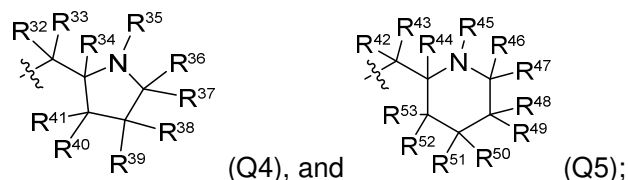
or a pharmaceutically acceptable salt, solvate, and/or prodrug thereof,

wherein:

R¹ is selected from C(O)R⁷, CO₂R⁷, C(O)N(R⁷)(R⁷), S(O)R⁷, SO₂R⁷, C₁₋₆alkyleneR⁷, and R⁷;

Q is selected from Q1, Q2, Q2', Q4, and Q5:





--- is a single bond or a double bond provided that when --- in Q1 is a double bond then R⁹ and R¹⁵ are not present, and when --- in Q2 is a double bond then R¹⁷ and R²⁵ are not present and when --- in Q2' is a double bond then R^{16'} and R^{25'} are not present;

$\sim$ over a bond means that the bond is attached to a remaining portion of the compound;

R², R^{2'}, and R^{2''} are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R^{2a})(R^{2b}), and SC₁₋₆alkyl;

R^{2a} and R^{2b} are independently selected from H and C₁₋₆alkyl;

R³, R⁴, R⁵, and R⁶ are independently selected from H, halo, N(R^{5'})(R^{6'}), C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R^{5'})(R^{6'}), and SC₁₋₆alkyl, the latter four groups being optionally substituted with one or two substituents independently selected from OH and C₁₋₆alkoxy, or

two adjacent R³, R⁴, R⁵, and R⁶ are linked together to form O-(CH₂)₁₋₂O and the remaining of R³, R⁴, R⁵, and R⁶ are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, N(R^{5'})(R^{6'}), C₁₋₆alkyleneN(R^{5'})(R^{6'}), and SC₁₋₆alkyl, or

one of R³, R⁴, R⁵, and R⁶ is selected from A, O-A, and C₁₋₄alkylene-A and the remaining of R³, R⁴, R⁵, and R⁶ are independently H or halo ;

R^{5'} and R^{6'} are independently selected from H and C₁₋₆alkyl;

A is selected from phenyl, C₃₋₆cycloalkyl, 3- to 6-membered heterocycloalkyl comprising 1 to 4 heteromoieties independently selected from O, S, S(O), SO₂, N, and NR⁵⁴, and 5- to 6-membered heteroaryl comprising 1 to 4 heteromoieties independently selected from O, S, S(O), SO₂, N, and NR⁵⁴, wherein the phenyl, C₃₋₁₀cycloalkyl, 3- to 6-membered heterocycloalkyl, and 5- to 6-membered heteroaryl are optionally substituted with one or more substituents independently selected from halo, C₁₋₄alkyl, OC₁₋₄alkyl, N(R^{54a})(R^{54b}), C₁₋₄alkyleneN(R^{54a})(R^{54b}), and SC₁₋₄alkyl;

R⁷ is selected from H, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, phenyl, C₃₋₆cycloalkyl, 3- to 6-membered heterocycloalkyl comprising 1 to 4 heteromoieties independently selected from O, S, N, and NR^{7''}, and 5- to 6-membered heteroaryl comprising 1 to 4 heteromoieties independently selected from O, S, N, and NR^{7''}, wherein the latter 7 groups are optionally substituted with one or more substituents independently selected from halo, OR⁵⁵,

$N(R^{55})(R^{56})$, and SR^{55} and/or the C_{1-6} alkyl is optionally interrupted by one to three heteromoieties independently selected from O, C(O), CO_2 , and NR^{57} ;

$R^{7'}$ is selected from H and C_{1-6} alkyl;

$R^{7''}$ is selected from H and C_{1-6} alkyl;

$R^8, R^9, R^{10}, R^{11}, R^{13}, R^{14}, R^{15}, R^{16}, R^{16'}, R^{17}, R^{17'}, R^{18}, R^{19}, R^{19'}, R^{21}, R^{22}, R^{22'}, R^{23}, R^{23'}, R^{24}, R^{24'}, R^{25}, R^{25'}, R^{32}, R^{33}, R^{34}, R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52}$, and R^{53} are independently selected from H, halo, and C_{1-6} alkyl;

$R^{12}, R^{20}, R^{20'}, R^{35}$, and R^{45} are independently selected from H, C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl;

R^{54}, R^{55}, R^{56} , and R^{57} are independently selected from H and C_{1-6} alkyl;

R^{54a} and R^{54b} are independently selected from H and C_{1-6} alkyl; and

available hydrogen atoms are optionally and independently substituted with a fluorine atom or a chlorine atom and available atoms are optionally substituted with alternate isotope thereof.

[0009b] In another aspect, the present disclosure provides a pharmaceutical composition comprising one or more compounds of the disclosure and pharmaceutically acceptable carrier.

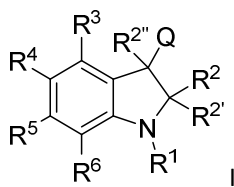
[0009c] In another aspect, the present disclosure provides a use of a therapeutically effective amount of one or more compounds of the disclosure in the manufacture of a medicament for treating a central nervous system (CNS) disease, disorder, or condition.

[0009d] In another aspect, the present disclosure provides a use of a therapeutically effective amount of any one or more compounds of the disclosure in the manufacture of a medicament for treating a mental illness.

[0009e] In another aspect, the present disclosure provides a use of a therapeutically effective amount of one or more compounds of the disclosure in the manufacture of a medicament for treating a neurological disease.

[0009f] In another aspect, the present disclosure provides a use of a therapeutically effective amount of one or more compounds of the disclosure in the manufacture of a medicament for treating a central nervous system (CNS) disease, disorder, or condition and/or a neurological disease, disorder, or condition.

[0010] Accordingly, the present application includes compounds of Formula I:

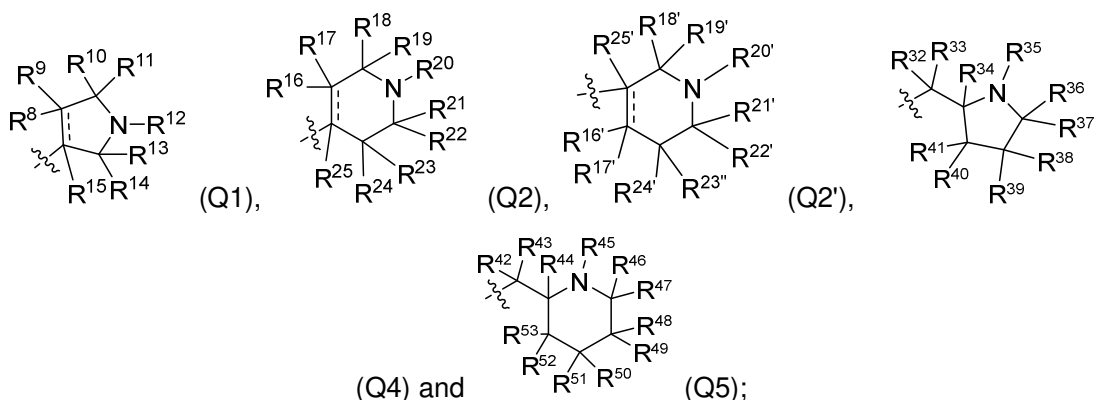


or a pharmaceutically acceptable salt, solvate and/or prodrug thereof,

wherein:

R¹ is selected from C(O)R⁷, CO₂R⁷, C(O)N(R⁷)(R⁷), S(O)R⁷, SO₂R⁷, C₁₋₆alkyleneR⁷ and R⁷;

Q is selected from Q1, Q2, Q2', Q4 and Q5:



--- is a single bond or a double bond provided that when --- in Q1 is a double bond then R⁹ and R¹⁵ are not present, and when --- in Q2 is a double bond then R¹⁷ and R²⁵ are not present;

R², R^{2'} and R^{2''} are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R^{2a})(R^{2b}) and SC₁₋₆alkyl;

R^{2a} and R^{2b} are independently selected from H and C₁₋₆alkyl;

R³, R⁴, R⁵ and R⁶ are independently selected from H, halo, N(R⁵)(R⁶), C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R⁵)(R⁶) and SC₁₋₆alkyl, the latter four groups being optionally substituted with one or two substituents selected from OH and C₁₋₆alkoxy; or

two adjacent of R³, R⁴, R⁵ and R⁶ are linked together to form O-(CH₂)₁₋₂O and the remaining of R³, R⁴, R⁵ and R⁶ are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, N(R⁵)(R⁶), C₁₋₆alkyleneN(R⁵)(R⁶) and SC₁₋₆alkyl, or

one of R³, R⁴, R⁵ and R⁶ is selected from A, O-A and C₁₋₄alkylene A and the remaining of R³, R⁴, R⁵ and R⁶ are independently H or halo;

R⁵ and R⁶ are independently selected from H and C₁₋₆alkyl;

A is selected from phenyl, C₃₋₆cycloalkyl, 3- to 6-membered heterocycloalkyl comprising 1 to 4 heteromoeities independently selected from O, S, S(O), SO₂, N and NR⁵⁴ and 5- to 6-membered heteroaryl comprising 1 to 4 heteromoeities independently selected from O, S, S(O), SO₂, N and NR⁵⁴, wherein the phenyl, C₃₋₁₀cycloalkyl, 3- to 6-membered heterocycloalkyl and 5- to 6-membered heteroaryl are optionally substituted with one or more substituents independently selected from halo, C₁₋₄alkyl, OC₁₋₄alkyl, N(R^{54a})(R^{54b}), C₁₋₄alkyleneN(R^{54a})(R^{54b}) and SC₁₋₄alkyl;

R⁷ is selected from H, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, phenyl, C₃₋₆cycloalkyl, 3- to 6-membered heterocycloalkyl comprising 1 to 4 heteromoeities independently selected from O, S, N and NR^{7m} and 5- to 6-membered heteroaryl comprising 1 to 4 heteromoeities

independently selected from O, S, N and $\text{NR}^{7''}$, wherein the latter 7 groups are optionally substituted with one or more substituents independently selected from halo, OR^{55} , $\text{N}(\text{R}^{55})(\text{R}^{56})$ and SR^{55} and/or the $\text{C}_{1-6}\text{alkyl}$ is optionally interrupted by one to three heteromoieties independently selected from O, $\text{C}(\text{O})$, CO_2 and NR^{57} ;

$\text{R}^{7'}$ is selected from H and $\text{C}_{1-6}\text{alkyl}$;

$\text{R}^{7''}$ is selected from H and $\text{C}_{1-6}\text{alkyl}$;

$\text{R}^8, \text{R}^9, \text{R}^{10}, \text{R}^{11}, \text{R}^{13}, \text{R}^{14}, \text{R}^{15}, \text{R}^{16}, \text{R}^{16'}, \text{R}^{17}, \text{R}^{17'}, \text{R}^{18}, \text{R}^{19}, \text{R}^{19'}, \text{R}^{21}, \text{R}^{22}, \text{R}^{22'}, \text{R}^{23}, \text{R}^{23'}, \text{R}^{24}, \text{R}^{24'}, \text{R}^{25}, \text{R}^{25'}, \text{R}^{32}, \text{R}^{33}, \text{R}^{34}, \text{R}^{36}, \text{R}^{37}, \text{R}^{38}, \text{R}^{39}, \text{R}^{40}, \text{R}^{41}, \text{R}^{42}, \text{R}^{43}, \text{R}^{44}, \text{R}^{46}, \text{R}^{47}, \text{R}^{48}, \text{R}^{49}, \text{R}^{50}, \text{R}^{51}, \text{R}^{52}$ and R^{53} are independently selected from H, halo and $\text{C}_{1-6}\text{alkyl}$;

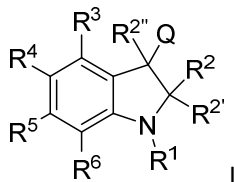
$\text{R}^{12}, \text{R}^{20}, \text{R}^{20'}, \text{R}^{35}$ and R^{45} are independently selected from H, $\text{C}_{1-6}\text{alkyl}$ and $\text{C}(\text{O})\text{C}_{1-6}\text{alkyl}$;

$\text{R}^{54}, \text{R}^{55}, \text{R}^{56}$ and R^{57} are independently selected from H and $\text{C}_{1-6}\text{alkyl}$;

R^{54a} and R^{54b} are independently selected from H and $\text{C}_{1-6}\text{alkyl}$; and

all available hydrogen atoms are optionally and independently substituted with a fluorine atom or chlorine atom and all available atoms are optionally substituted with alternate isotope thereof.

[0011] In some examples, the compound of Formula I is defined as follows:

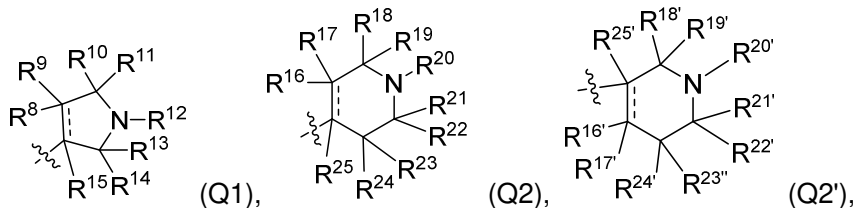


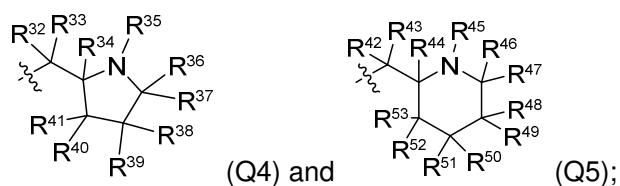
or a pharmaceutically acceptable salt, solvate and/or prodrug thereof,

wherein:

R^1 is H;

Q is selected from Q1, Q2, Q2', Q4 and Q5:





--- is a single bond or a double bond provided that when --- in Q1 is a double bond then R⁹ and R¹⁵ are not present, and when --- in Q2 is a double bond then R¹⁷ and R²⁵ are not present and when --- in Q2' is a double bond then R^{16'} and R^{25'} are not present;

~ over a bond means that the bond is attached to a remaining portion of the compound;

R², R^{2'} and R^{2''} are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R^{2a})(R^{2b}) and SC₁₋₆alkyl;

R^{2a} and R^{2b} are independently selected from H and C₁₋₆alkyl;

R³, R⁴, R⁵ and R⁶ are independently selected from H, halo, N(R^{5'})(R^{6'}), C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R^{5'})(R^{6'}) and SC₁₋₆alkyl, the latter four substituents selected from OH and C₁₋₆alkoxy, or

two adjacent of R³, R⁴, R⁵ and R⁶ are linked together to form O-(CH₂)₁₋₂O and the remaining of R³, R⁴, R⁵ and R⁶ are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, N(R^{5'})(R^{6'}), C₁₋₆alkyleneN(R^{5'})(R^{6'}) and SC₁₋₆alkyl;

R^{5'} and R^{6'} are independently selected from H and C₁₋₆alkyl;

R⁸, R⁹, R¹⁰, R¹¹, R¹³, R¹⁴, R¹⁵, R¹⁶, R^{16'}, R¹⁷, R^{17'}, R¹⁸, R¹⁹, R^{19'}, R²¹, R²², R^{22'}, R²³, R^{23'}, R²⁴, R^{24'}, R²⁵, R^{25'}, R³², R³³, R³⁴, R³⁶, R³⁷, R³⁸, R³⁹, R⁴⁰, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹, R⁵² and R⁵³ are independently selected from H, halo and C₁₋₆alkyl;

R¹², R²⁰, R^{20'}, R³⁵ and R⁴⁵ are independently selected from H, C₁₋₆alkyl and C(O)C₁₋₆alkyl;

all available hydrogen atoms are optionally and independently substituted with a fluorine atom or chlorine atom and all available atoms are optionally substituted with alternate isotope thereof.

[0012] In a further example, the compounds of the application are used as medicaments. Accordingly, the application also includes a compound of the application for use as a medicament.

[0013] The present application also includes a method of treating psychosis or psychotic symptoms comprising administering a therapeutically effective amount of one or more compounds of the application to a subject in need thereof.

[0014] The present application also includes a method of treating a mental illness comprising administering a therapeutically effective amount of one or more compounds of the application to a subject in need thereof.

[0015] The present application also includes a method of treating a central nervous system (CNS) disease, disorder or condition and/or a neurological disease, disorder or condition.

[0016] The present application also includes a method of treating an endophenotype and/or symptom cluster associated with a disease, disorder or condition that is treated by activation of a serotonin receptor.

[0017] The application additionally provides a process for the preparation of compounds of the application. General and specific processes are discussed in more detail below and set forth in the examples below.

[0018] Other features and advantages of the present application will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating examples of the application, are given by way of illustration only and the scope of the claims should not be limited by these examples but should be given the broadest interpretation consistent with the description as a whole.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The present application will be described in greater detail with reference to the attached drawings in which:

[0020] Figure 1 shows the scores for exemplary compound I-I-54 in the mouse head twitch assays at doses of up to 60 mg/kg.

DETAILED DESCRIPTION

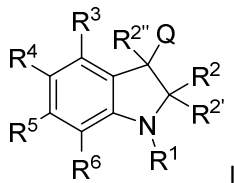
II. Definitions

[0021] Unless otherwise indicated, the definitions and embodiments described in this and other sections are intended to be applicable to all embodiments and aspects of the present application herein described for which they are suitable as would be understood by a person skilled in the art.

[0022] The term “compound(s) of the application” or “compound(s) of the present application” and the like as used herein refers to a compound of Formula I and includes pharmaceutically acceptable salts, solvates and/or prodrugs thereof as well as all stereoisomers and regioisomers.

Claims:

1. A compound of Formula I:

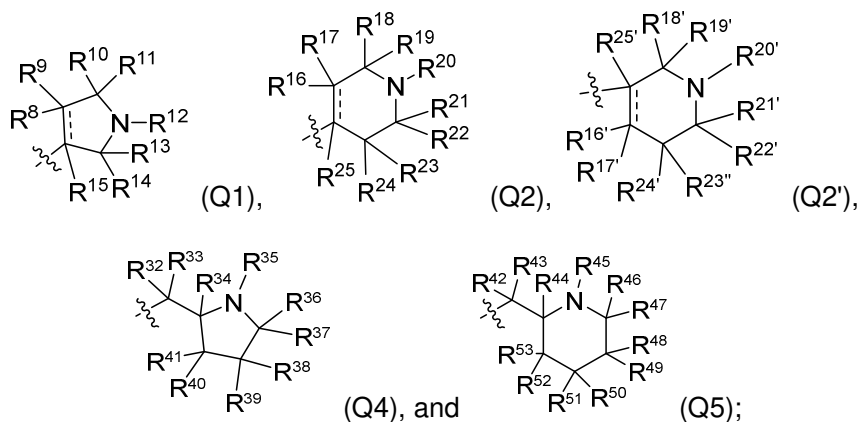


or a pharmaceutically acceptable salt, solvate, and/or prodrug thereof,

wherein:

R¹ is selected from C(O)R⁷, CO₂R⁷, C(O)N(R⁷)(R⁷), S(O)R⁷, SO₂R⁷, C₁₋₆alkyleneR⁷, and R⁷;

Q is selected from Q1, Q2, Q2', Q4, and Q5:



$\equiv$ is a single bond or a double bond provided that when $\equiv$ in Q1 is a double bond then R⁹ and R¹⁵ are not present, and when $\equiv$ in Q2 is a double bond then R¹⁷ and R²⁵ are not present and when $\equiv$ in Q2' is a double bond then R^{16'} and R^{25'} are not present;

~ over a bond means that the bond is attached to a remaining portion of the compound;

R², R^{2'}, and R^{2''} are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R^{2a})(R^{2b}), and SC₁₋₆alkyl;

R^{2a} and R^{2b} are independently selected from H and C₁₋₆alkyl;

R³, R⁴, R⁵, and R⁶ are independently selected from H, halo, N(R⁵)(R⁶), C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkyleneN(R⁵)(R⁶), and SC₁₋₆alkyl, the latter four groups being optionally substituted with one or two substituents independently selected from OH and C₁₋₆alkoxy, or

two adjacent R³, R⁴, R⁵, and R⁶ are linked together to form O-(CH₂)₁₋₂O and the remaining of R³, R⁴, R⁵, and R⁶ are independently selected from H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, N(R^{5'})(R^{6'}), C₁₋₆alkyleneN(R^{5'})(R^{6'}), and SC₁₋₆alkyl, or

one of R³, R⁴, R⁵, and R⁶ is selected from A, O-A, and C₁₋₄alkylene-A and the remaining of R³, R⁴, R⁵, and R⁶ are independently H or halo ;

R^{5'} and R^{6'} are independently selected from H and C₁₋₆alkyl;

A is selected from phenyl, C₃₋₆cycloalkyl, 3- to 6-membered heterocycloalkyl comprising 1 to 4 heteromoieties independently selected from O, S, S(O), SO₂, N, and NR⁵⁴, and 5- to 6-membered heteroaryl comprising 1 to 4 heteromoieties independently selected from O, S, S(O), SO₂, N, and NR⁵⁴, wherein the phenyl, C₃₋₁₀cycloalkyl, 3- to 6-membered heterocycloalkyl, and 5- to 6-membered heteroaryl are optionally substituted with one or more substituents independently selected from halo, C₁₋₄alkyl, OC₁₋₄alkyl, N(R^{54a})(R^{54b}), C₁₋₄alkyleneN(R^{54a})(R^{54b}), and SC₁₋₄alkyl;

R⁷ is selected from H, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, phenyl, C₃₋₆cycloalkyl, 3- to 6-membered heterocycloalkyl comprising 1 to 4 heteromoieties independently selected from O, S, N, and NR^{7"}, and 5- to 6-membered heteroaryl comprising 1 to 4 heteromoieties independently selected from O, S, N, and NR^{7"}, wherein the latter 7 groups are optionally substituted with one or more substituents independently selected from halo, OR⁵⁵, N(R⁵⁵)(R⁵⁶), and SR⁵⁵ and/or the C₁₋₆alkyl is optionally interrupted by one to three heteromoieties independently selected from O, C(O), CO₂, and NR⁵⁷;

R^{7'} is selected from H and C₁₋₆alkyl;

R^{7"} is selected from H and C₁₋₆alkyl;

R⁸, R⁹, R¹⁰, R¹¹, R¹³, R¹⁴, R¹⁵, R¹⁶, R^{16'}, R¹⁷, R^{17'}, R¹⁸, R^{19'}, R¹⁹, R^{19'}, R²¹, R^{22'}, R²², R^{22'}, R²³, R^{23'}, R²⁴, R^{24'}, R²⁵, R^{25'}, R³², R³³, R³⁴, R³⁶, R³⁷, R³⁸, R³⁹, R⁴⁰, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹, R⁵², and R⁵³ are independently selected from H, halo, and C₁₋₆alkyl;

R¹², R²⁰, R^{20'}, R³⁵, and R⁴⁵ are independently selected from H, C₁₋₆alkyl, and C(O)C₁₋₆alkyl;

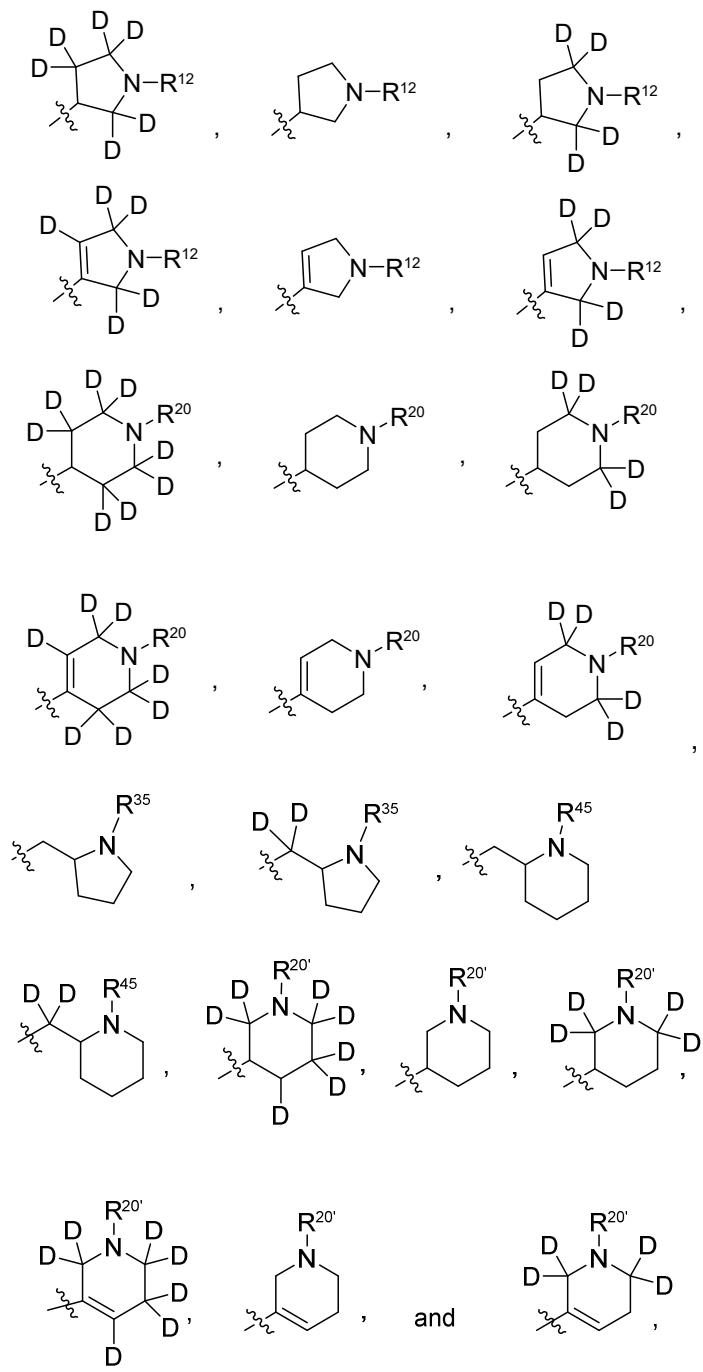
R⁵⁴, R⁵⁵, R⁵⁶, and R⁵⁷ are independently selected from H and C₁₋₆alkyl;

R^{54a} and R^{54b} are independently selected from H and C₁₋₆alkyl; and

available hydrogen atoms are optionally and independently substituted with a fluorine atom or a chlorine atom and available atoms are optionally substituted with alternate isotope thereof.

2. The compound of claim 1, wherein $R^8, R^9, R^{10}, R^{11}, R^{13}, R^{14}, R^{15}, R^{16}, R^{16'}, R^{17}, R^{17'}, R^{18}, R^{19}, R^{19'}, R^{21}, R^{22}, R^{22'}, R^{23}, R^{23'}, R^{24}, R^{24'}, R^{25}, R^{25'}, R^{32}, R^{33}, R^{34}, R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52},$ and R^{53} are independently selected from H and D.

3. The compound of claim 1, wherein Q is selected from one of the following groups:

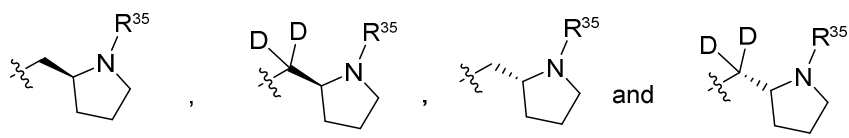


wherein $R^{12}, R^{20}, R^{20'}, R^{35},$ and R^{45} are as defined in claim 1.

4. The compound of claim 3, wherein R^{12} , R^{20} , $R^{20'}$, R^{35} , and R^{45} are independently selected from H, D, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{1-4} deuteroalkyl, $C(O)C_{1-4}$ alkyl, $C(O)C_{1-4}$ fluoroalkyl, and $C(O)C_{1-4}$ deuteroalkyl.

5. The compound of claim 4, wherein R^{12} , R^{20} , $R^{20'}$, R^{35} , and R^{45} are independently selected from H, CH_3 , and CD_3 .

6. The compound of claim 3, wherein Q is selected from



wherein R^{35} is selected from H, D, C_{1-6} alkyl, C_{1-6} fluoroalkyl, and C_{1-6} deuteroalkyl.

7. The compound of claim 6, wherein R^{35} is selected from H, CH_3 , CD_3 , CF_2H , and CF_3 .

8. The compound of any one of claims 1 to 5, wherein R^1 is selected from $C(O)R^7$, CO_2R^7 , $C(O)N(R^7)(R^7)$, $S(O)R^7$, SO_2R^7 , C_{1-4} alkylene R^7 , and R^7 , wherein available hydrogen atoms are optionally and independently substituted with a fluorine atom or a deuterium atom.

9. The compound of any one of claims 1 to 8, wherein R^7 is selected from H, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, C_{3-6} cycloalkyl, 3- to 6-membered heterocycloalkyl comprising 1 to 4 heteromoiety independently selected from O, S, N, and $NR^{7''}$, and 5- to 6-membered heteroaryl comprising 1 to 4 heteromoiety independently selected from O, S, N, and $NR^{7''}$, wherein the latter 7 groups are optionally substituted with one or more substituents independently selected from halo, OR^{55} , $N(R^{55})(R^{56})$, and SR^{55} and/or the C_{1-4} alkyl is optionally interrupted by one to three heteromoiety independently selected from O, $C(O)$, CO_2 , and NR^{57} , and wherein available hydrogen atoms are optionally and independently substituted with a fluorine atom or a deuterium atom.

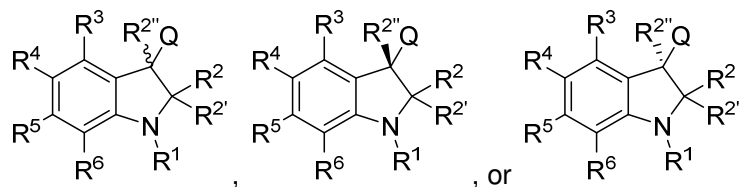
10. The compound of claim 9, wherein R^7 is selected from H and C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from F, Cl, OR^{55} , $N(R^{55})(R^{56})$, and SR^{55} and/or the C_{1-4} alkyl is optionally interrupted by one to three heteromoiety independently selected from O, $C(O)$, CO_2 , and NR^{57} , and wherein available hydrogen atoms are optionally and independently substituted with a fluorine atom or a deuterium atom.

11. The compound of claim 9, wherein R^7 is selected from H, D, C_{1-4} alkyl, C_{1-4} fluoroalkyl, and C_{1-4} deuteroalkyl.

12. The compound of claim 1, wherein R^3 , R^4 , R^5 , and R^6 are independently selected from H, D, F, Cl, Br, $N(R^5)(R^6)$, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{1-4} deuteroalkyl, C_{1-4} alkoxy, C_{1-4} alkoxy,

₄fluoroalkoxy, C₁₋₄deuteroalkoxy, C₁₋₄alkyleneN(R⁵)(R⁶), SC₁₋₄alkyl, SC₁₋₄fluoroalkyl, and SC₁₋₄deuteroalkyl, the latter ten groups being optionally substituted with one or two substituents selected from OH, C₁₋₄alkoxy, C₁₋₄fluoroalkoxy, and C₁₋₄deuteroalkoxy.

13. The compound of any one of claims 1 to 12, wherein the compound of Formula I has one of the following structures:



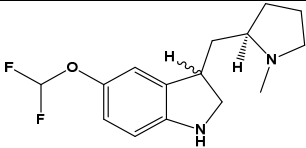
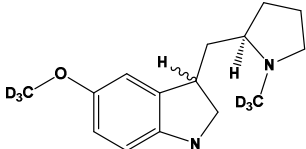
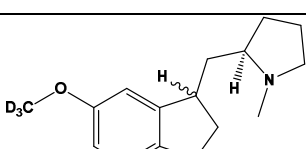
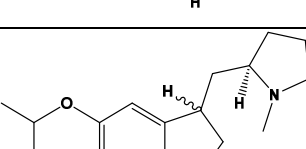
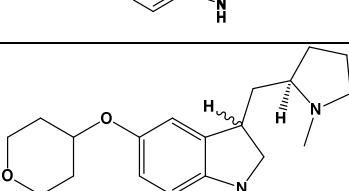
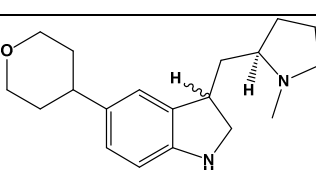
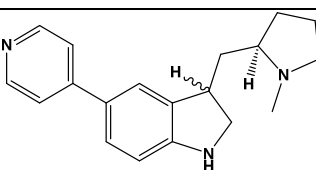
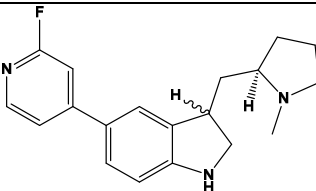
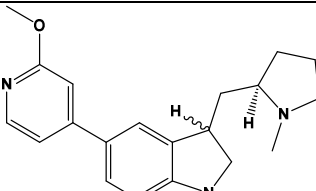
or a mixture thereof.

14. The compound of claim 1 selected from:

(R)-I-46	
(S),(R)-I-46	
(R),(R)-I-46	
(R)-I-47	
(S),(R)-I-47	

(R),(R)-I-47	
(S)-I-48	
(R)-I-49	
(S)-I-49	
(R)-I-51	
(R)-I-52	
(R)-I-53	
(S)-I-54	

(R)-I-54	
(S),(R)-I-54	
(R),(R)-I-54	
(R)-I-55	
(R)-I-56	
(S)-I-56	
(R)-I-56	
(R)-I-58	

(R)-I-59	
(R)-I-60	
(R)-I-61	
(R)-I-62	
(R)-I-63	
(R)-I-64	
(R)-I-65	
(R)-I-66	
(R)-I-67	

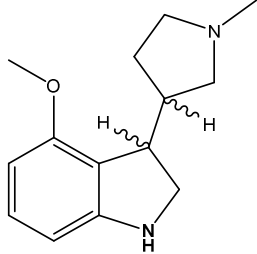
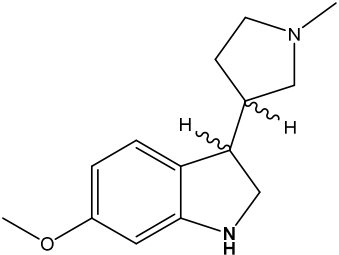
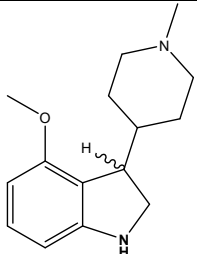
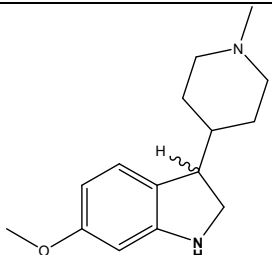
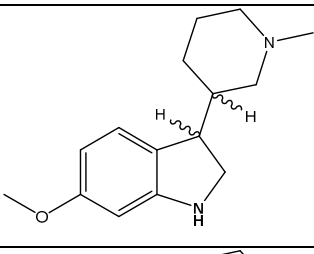
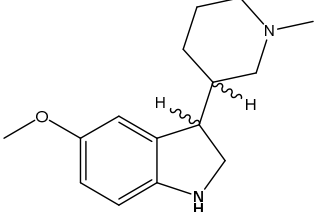
(R)-I-68	
(R)-I-69	
(R)-I-70	
(R)-I-71	
(R)-I-72	
(S),(R)-I-72	
(R),(R)-I-72	
(R)-I-73	
(R)-I-74	

(R)-I-75	
(R)-I-76	
(R)-I-77	
(R)-I-78	
(R)-I-79	
(R)-I-80	
(R)-I-81	
(R)-I-82	
(R)-I-83	

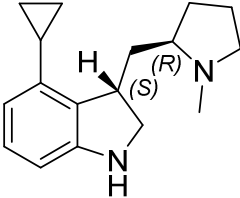
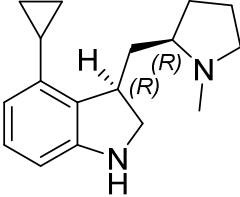
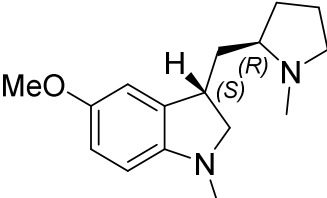
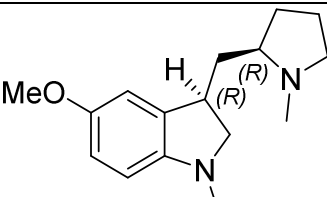
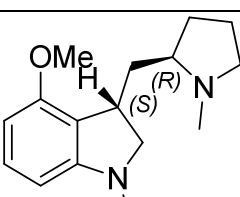
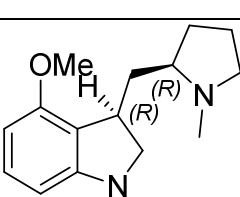
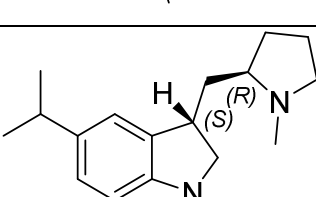
(R)-I-84	
(R)-I-85	
(R)-I-86	
(R)-I-87	
(R)-I-88	
(R)-I-89	
(R)-I-90	
(R)-I-91	
(R)-I-92	

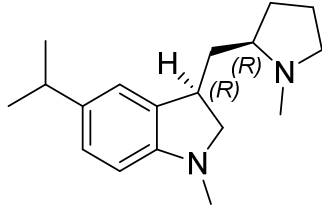
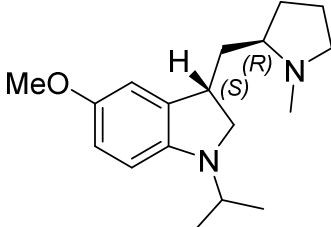
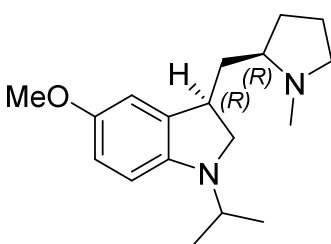
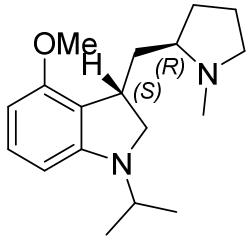
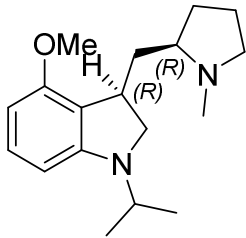
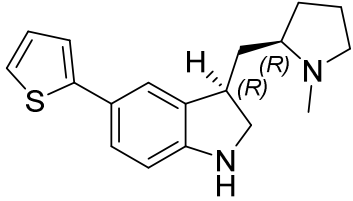
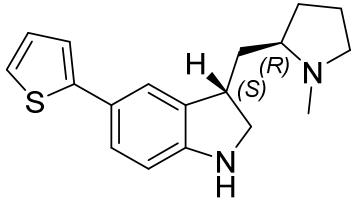
(R)-I-93	
(R)-I-94	
(S),(R)-I-94	
(R),(R)-I-94	
(R)-I-95	
(R)-I-96	
(R)-I-97	
(R)-I-98	

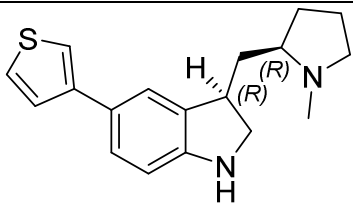
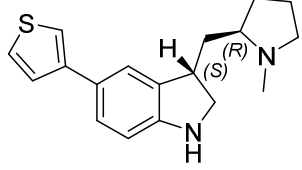
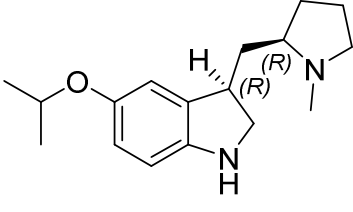
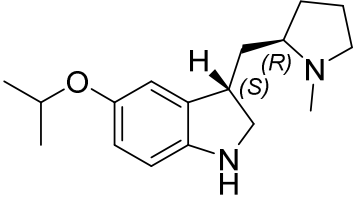
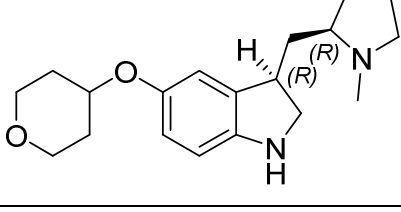
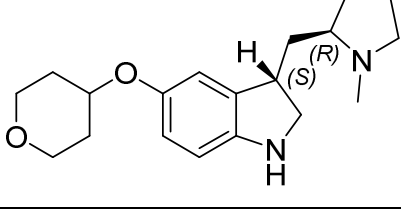
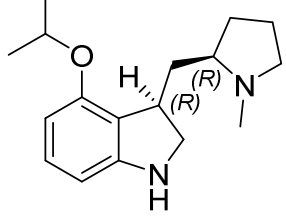
(S)-I-99	
(R),(S)-I-99	
(S),(S)-I-99	
I-102	
I-103	
I-104	
I-105	

I-139	
I-140	
I-141	
I-142	
I-143	
I-144	

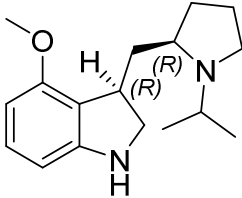
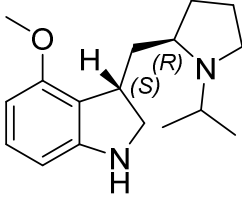
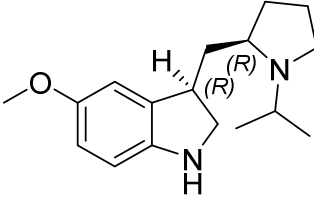
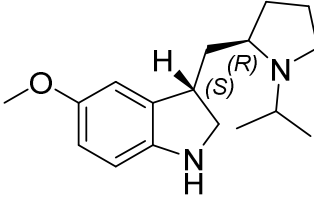
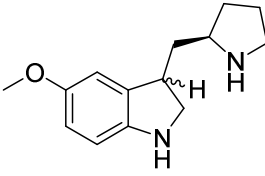
I-145	
(S),(R)-I-146	
(R),(R)-I-146	
(S),(R)-I-147	
(R),(R)-I-147	
(S),(R)-I-148	
(R),(R)-I-148	

(S),(R)-I-149	
(R),(R)-I-149	
(S),(R)-I-150	
(R),(R)-I-150	
(S),(R)-I-151	
(R),(R)-I-151	
(S),(R)-I-152	

(R),(R)-I-152	
(S),(R)-I-153	
(R),(R)-I-153	
(S),(R)-I-154	
(R),(R)-I-154	
(R),(R)-I-155	
(S),(R)-I-155	

(R),(R)-I-156	
(S),(R)-I-156	
(R),(R)-I-157	
(S),(R)-I-157	
(R),(R)-I-158	
(S),(R)-I-158	
(R),(R)-I-159	

(S),(R)-I-159	
(R),(R)-I-160	
(S),(R)-I-160	
(R),(R)-I-161	
(S),(R)-I-161	
(R),(R)-I-162	
(S),(R)-I-162	

(R),(R)-I-163	
(S),(R)-I-163	
(R),(R)-I-164	
(S),(R)-I-164	 and
(R)-I-165	

or a pharmaceutically acceptable salt, solvate, and/or prodrug thereof.

15. A pharmaceutical composition comprising one or more compounds of any one of claims 1 to 14 and pharmaceutically acceptable carrier.

16. Use of a therapeutically effective amount of one or more compounds of any one of claims 1 to 14 in the manufacture of a medicament for treating a central nervous system (CNS) disease, disorder, or condition.

17. The use of claim 16, wherein the disease, disorder, or condition is (are) selected from: Alzheimer's disease, Lewy body dementia, cognitive impairment, Parkinson's disease, depression, post-traumatic stress disorder (PTSD), attention deficit hyperactivity disorder, attention deficit disorder; schizophrenia; autism spectrum disorders; eating disorders, nail biting; migraine; fibromyalgia; peripheral neuropathy, and combinations thereof.

18. Use of a therapeutically effective amount of any one or more compounds of claims 1 to 14 in the manufacture of a medicament for treating a mental illness.
19. Use of a therapeutically effective amount of one or more compounds of any one of claims 1 to 14 in the manufacture of a medicament for treating a neurological disease.
20. Use of a therapeutically effective amount of one or more compounds of any one of claims 1 to 14 in the manufacture of a medicament for treating a central nervous system (CNS) disease, disorder, or condition and/or a neurological disease, disorder, or condition.