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Canadian Intellectual Property Office

CA 3125636 A1 2020/07/30

(21) 3 125 636

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

(86) Date de dépôt PCT/PCT Filing Date: 2020/01/24
(87) Date publication PCT/PCT Publication Date: 2020/07/30
(85) Entrée phase nationale/National Entry: 2021/07/02
(86) N° demande PCT/PCT Application No.: US 2020/015083
(87) N° publication PCT/PCT Publication No.: 2020/154683
(30) Priorité/Priority: 2019/01/25 (US62/796,941)

(51) Cl.Int./Int.Cl. *C07D 401/02* (2006.01), *C07D 401/10* (2006.01), *C07D 403/10* (2006.01)

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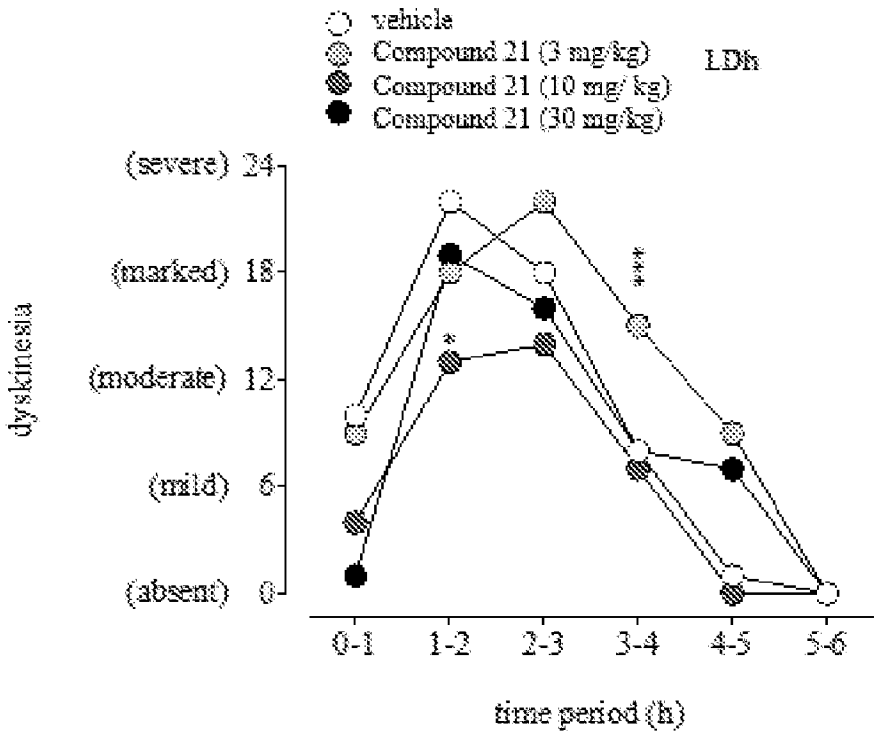
(54) Titre : METHODES DE TRAITEMENT D'UNE MALADIE A L'AIDE D'INHIBITEURS DE MAGL
(54) Title: METHODS OF TREATING DISEASE WITH MAGL INHIBITORS

FIG. 1C



(57) Abrégé/Abstract:
Provided herein are methods for the treatment of disease with monoacylglycerol lipase (MAGL) inhibitors.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 July 2020 (30.07.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/154683 A1

(51) International Patent Classification:
C07D 401/02 (2006.01) *C07D 403/10* (2006.01)
C07D 401/10 (2006.01)

(21) International Application Number:
PCT/US2020/015083

(22) International Filing Date:
24 January 2020 (24.01.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/796,941 25 January 2019 (25.01.2019) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

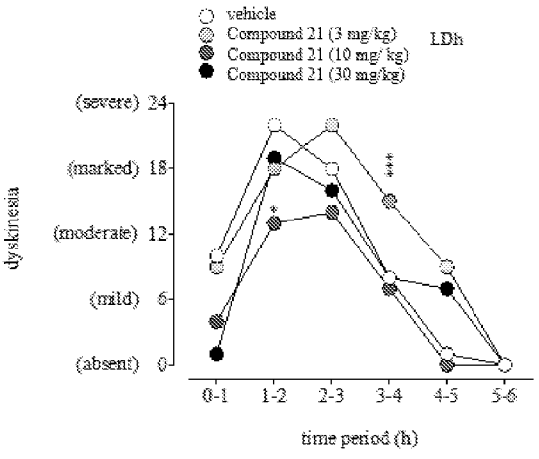
Published:
— *with international search report (Art. 21(3))*

WO 2020/154683 A1

(54) Title: METHODS OF TREATING DISEASE WITH MAGL INHIBITORS

(57) Abstract: Provided herein are methods for the treatment of disease with monoacylglycerol lipase (MAGL) inhibitors.

FIG. 1C



METHODS OF TREATING DISEASE WITH MAGL INHIBITORS

CROSS-REFERENCE

[0001] This application claims benefit of U.S. Provisional Application No. 62/796,941, filed on January 25, 2019, which is herein incorporated by reference in its entirety.

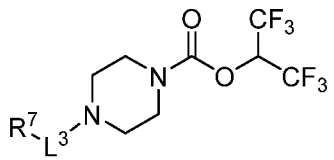
BACKGROUND

[0002] Monoacylglycerol lipase (MAGL) is an enzyme responsible for hydrolyzing endocannabinoids such as 2-AG (2-arachidonoylglycerol), an arachidonate based lipid, in the nervous system.

BRIEF SUMMARY OF THE INVENTION

[0003] This disclosure provides, for example, methods for treating dyskinesia with compounds and pharmaceutical compositions which are modulators of MAGL. The disclosure also provides for the use of disclosed compounds as medicaments and/or in the manufacture of medicaments for the inhibition of MAGL in warm-blooded animals such as humans.

[0004] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (I'):



Formula (I');

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is optionally substituted with one or two substituents independently selected from C_{1-}

$_{6}$haloalkyl, -C(O)OR^{9}, and -NR^{9}SO$_2$R^{8}; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

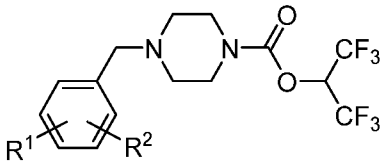
the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^{8} is independently selected from C_{1-6}alkyl; and

each R^{9} is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[0005] In some embodiments is method for treating dyskinesia with a compound of Formula (I'), wherein the compound of Formula (I') is a compound of Formula (III):



Formula (III);

wherein:

R^{1} is halogen, -OR^{3}, -SF$_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or -C(O)OR^{9};

R^{2} is -NR^{5}R^{6};

R^{3} is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^{5} and R^{6}, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one or two substituents independently selected from C_{1-6}haloalkyl, -C(O)OR^{9}, and -NR^{9}SO$_2$R^{8}; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^{8} is independently selected from C_{1-6}alkyl; and

each R^{9} is independently selected from H and C_{1-6}alkyl;

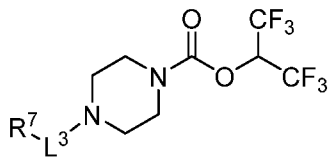
or a pharmaceutically acceptable salt or solvate thereof.

[0006] In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^{5} and R^{6}, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle, wherein the 4-6

membered saturated monocyclic heterocycle is substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; and

the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine and piperidine. In some embodiments is method for treating dyskinesia with a compound of Formula (I'), wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle. In some embodiments is method for treating dyskinesia with a compound of Formula (I'), wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 7-8 membered bridged heterocyclic ring. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^1 is halogen, -SF_5, or optionally substituted C_{1-6}alkyl optionally substituted by halogen. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^1 is halogen. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^1 is C_{1-6}alkyl optionally substituted by halogen. In some embodiments is method for treating dyskinesia with a compound of Formula (I') or (III), wherein R^1 is -CF_3.

[0007] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (I):



Formula (I);

wherein:

L^3 is a bond, $-CH_2-$, $-S(O)_2-$, or $-C(O)-$;

R^7 is phenyl; wherein R^7 is optionally substituted by one, two, or three moieties independently selected from R^h;

R^a and R^b are independently selected, for each occurrence, from the group consisting of hydrogen and C_{1-3}alkyl; wherein C_{1-3}alkyl is optionally substituted by one or more substituents selected from halogen, cyano, oxo, hydroxyl, heterocycle, and phenyl;

or R^a and R^b, when they occur together with the nitrogen to which they are attached, form a 4-6 membered saturated heterocyclic ring, which may have an additional heteroatom selected from O, S, and N, or a spirocyclic ring selected from 8-oxa-2-azaspiro[4.5]decane and 2,8-diazaspiro[4.5]decane, wherein the 4-6 membered saturated heterocyclic ring or the spirocyclic ring are optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, $-S(O)_w-C_{1-6}$alkyl (where w is 0, 1 or 2), hydroxyl, $-C(O)-C_{1-6}$alkyl, $-NH_2$, and $-NH-C(O)-C_{1-6}$alkyl;

R^c is selected from the group consisting of halogen, hydroxyl, C_{1-6}alkyl (optionally substituted by one, two, or three halogens), and C_{1-6}alkoxy (optionally substituted by one, two, or three halogens); and

R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from R^c), hydroxyl, cyano, C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), R^aR^bN-, $R^a-C(O)NR^a-$, $R^aR^bN-SO_2-$, $R^aR^bN-C(O)-$, $R^a-S(O)_w-$ (wherein w is 0, 1 or 2), $R^a-SO_2-NR^b-$, and heteroaryl (optionally substituted by one, two or three moieties each independently selected from R^c);

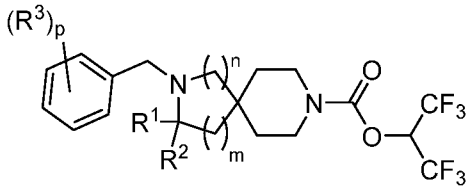
or a pharmaceutically acceptable salt or solvate thereof.

[0008] In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein L^3 is a $-CH_2-$. In some embodiments is method for treating

dyskinesia with a compound of Formula (I), wherein L^3 is a -CH_2-; and R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from halogen, methyl, ethyl, propyl, t-butyl, and CF_3), C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), R^aR^bN-, R^aR^bN-C(O)-, and heteroaryl (optionally substituted by one, two or three moieties each independently selected from C_{1-6}alkyl or halogen). In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein L^3 is a -CH_2-; and R^h is selected from the group consisting of: halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), and R^aR^bN-. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein R^7 is substituted by two moieties independently selected from R^h. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein L^3 is a -CH_2-; and R^7 is substituted by R^aR^bN- and a moiety selected from the group consisting of: halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens), and C_{1-6}alkoxy (optionally substituted by one, two or three halogens). In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein R^a and R^b, together with the nitrogen to which they are attached, form a 4-6 membered saturated heterocyclic ring, which may have an additional heteroatom selected from O, S, and N, and the 4-6 membered saturated heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein the 4-6 membered saturated heterocyclic ring is selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine, and the 4-6 membered saturated heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein the 4-6 membered saturated heterocyclic ring is pyrrolidine. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein the 4-6 membered saturated heterocyclic ring is morpholine. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein the 4-6 membered saturated heterocyclic ring is piperidine. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein L^3 is a -CH_2-;

and R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from halogen, methyl, ethyl, propyl, t-butyl, and CF_3), C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), and heteroaryl (optionally substituted by one, two or three moieties each independently selected from C_{1-6}alkyl or halogen). In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein R^7 is substituted by two moieties independently selected from R^h. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein L^3 is a $-CH_2-$; and R^h is selected from the group consisting of: halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), and R^aR^bN-. In some embodiments is method for treating dyskinesia with a compound of Formula (I), wherein R^7 is substituted by two moieties independently selected from R^h.

[0009] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (II):



Formula (II);

wherein:

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, heterocycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), heteroaryl, $-SF_5$, $-NR^5R^6$, $-OR^7$, $-CO_2R^8$, $-C(O)R^8$, and $-C(O)NR^8R^9$, wherein heterocycloalkyl and -C_{1-6}alkyl(heterocycloalkyl) are optionally substituted with one or two R^4; or two adjacent R^3 form a heterocycloalkyl ring optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, halogen, oxo, -CN, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$;

each R^5 and R^6 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -C_{1-6}alkyl-C(O)(heterocycloalkyl), heterocycloalkyl, aryl, and heteroaryl; or R^5 and R^6,

together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -C_{1-6}alkyl-C(O)(heterocycloalkyl), heterocycloalkyl, aryl, and heteroaryl, wherein heterocycloalkyl, aryl, and heteroaryl are optionally substituted with one or two groups selected from oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and $C(O)NH_2$;

each R^8 and R^9 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, aryl, and heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one or two groups selected from C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and $C(O)NH_2$;

each R^{10} is independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-6}haloalkyl, halogen, oxo, -CN, -CO_2R^8, -$C(O)R^8$, -$C(O)NR^8R^9$, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$;

p is 0, 1, 2, 3, 4, or 5;

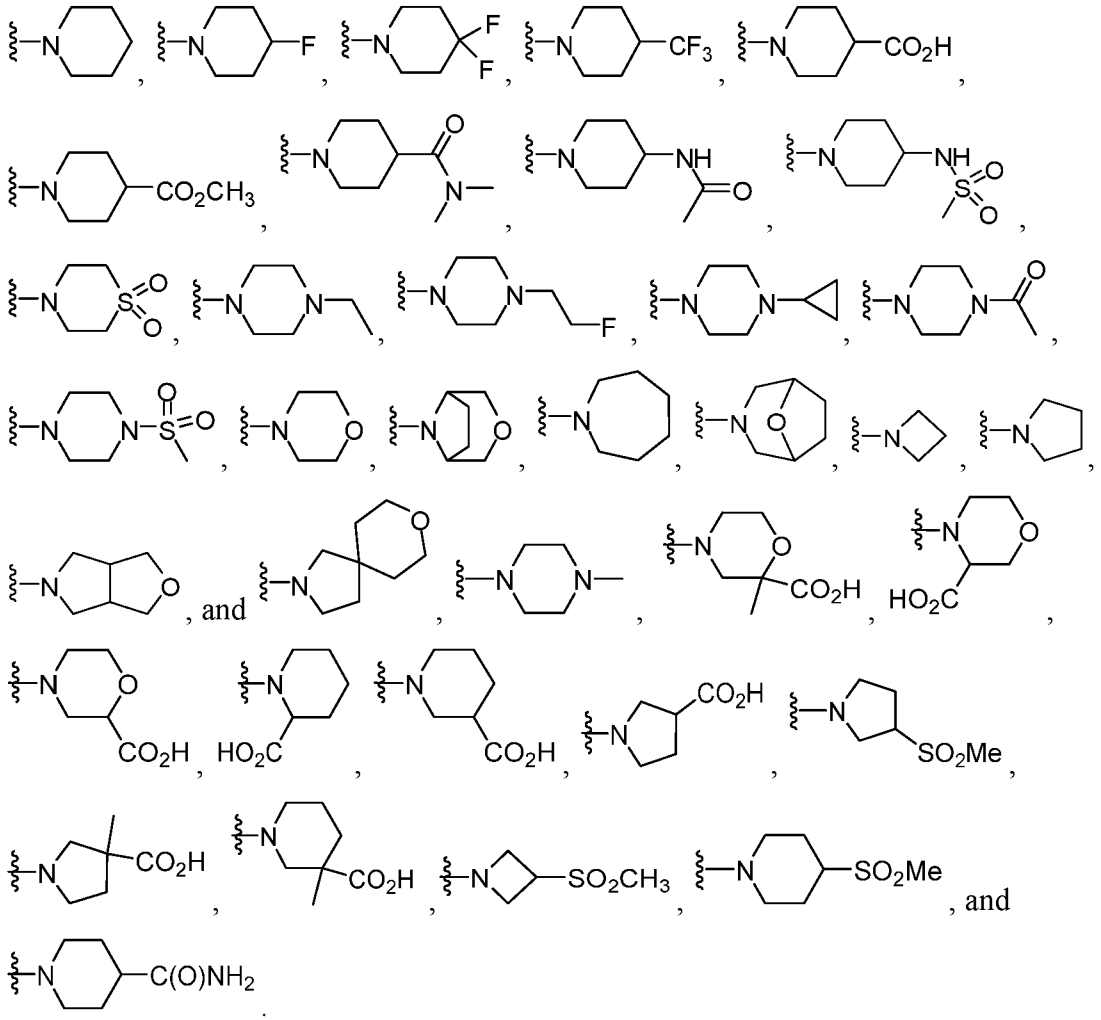
n is 0 or 1; and

m is 1 or 2; provided that when n is 0, then m is 2; and when n is 1, then m is 1;

or a pharmaceutically acceptable salt or solvate thereof.

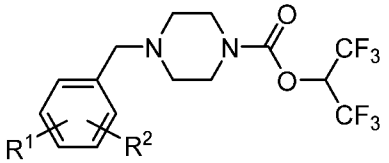
[0010] In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkynyl, halogen, -CN, C_{1-6}haloalkyl, heterocycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), heteroaryl, -SF_5, -NR^5R^6, -OR^7, -CO_2R^8, and -$C(O)NR^8R^9$. In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein R^1 and R^2 are both H. In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein each R^3 is independently selected from halogen, C_{1-6}haloalkyl, -NR^5R^6, and -OR^7. In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one or two R^{10} independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-6}haloalkyl, halogen, -CO_2R^8, -$C(O)R^8$, -$C(O)NR^8R^9$, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$. In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl and -CO_2H. In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted heterocycloalkyl ring. In some embodiments is method for treating dyskinesia with a

compound of Formula (II), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10} selected from:



[0011] In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein p is 1 or 2. In some embodiments is method for treating dyskinesia with a compound of Formula (II), wherein n is 0 and m is 2.

[0012] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (III):



Formula (III);

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

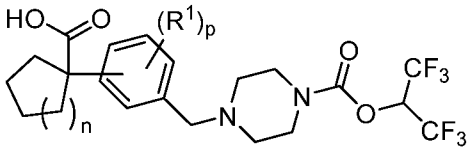
each R^9 is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[0013] In some embodiments is method for treating dyskinesia with a compound of Formula (III), wherein R^1 is halogen, $-SF_5$, or optionally substituted C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is $-CF_3$. In some embodiments is method for treating dyskinesia with a compound of Formula (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S. In some embodiments is method for treating dyskinesia with a compound of Formula (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments is method for treating dyskinesia with a compound of Formula (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected

from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine and piperidine. In some embodiments is method for treating dyskinesia with a compound of Formula (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (III), wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstitued 7-8 membered bridged heterocyclic ring.

[0014] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (IV):



Formula (IV);

wherein:

each R^1 is independently halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, -CN, or -SF_5;

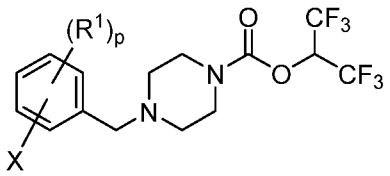
n is 1 or 2; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

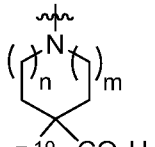
[0015] In some embodiments is method for treating dyskinesia with a compound of Formula (IV), wherein n is 1.

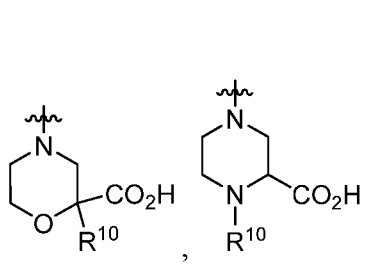
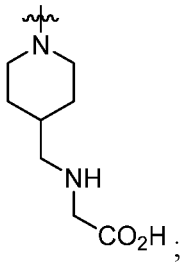
[0016] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (V):



Formula (V);

wherein:

X is -N(R^2)(R^3), -C_{1-6}alkyl-N(R^4)(R^5), -C(O)N(R^4)(R^5),  ,

 , , or  ;

each R^1 is independently halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, -CN, or -SF_5;

R^2 and R^3, together with the nitrogen to which they are attached, form

(i) a C_2-C_8heterocycloalkyl; or

(ii) a C_2-C_8heteroaryl;

wherein the C_2-C_8heterocycloalkyl or the C_2-C_8heteroaryl is substituted with one R^6 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^4 and R^5, together with the nitrogen to which they are attached, form

(i) a C_2-C_8heterocycloalkyl; or

(ii) a C_2-C_8heteroaryl;

wherein the C_2-C_8heterocycloalkyl or the C_2-C_8heteroaryl is substituted with one R^7 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^6 is -C_{1-6}alkyl-CO_2H or -N(R^8)-C_{1-6}alkyl-CO_2H;

R^7 is -CO_2H, -C_{1-6}alkyl-CO_2H, or -N(R^9)-C_{1-6}alkyl-CO_2H;

R^8 is H or C_{1-6}alkyl;

R^9 is H or C_{1-6}alkyl;

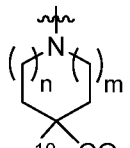
R^{10} is C_{1-6}alkyl;

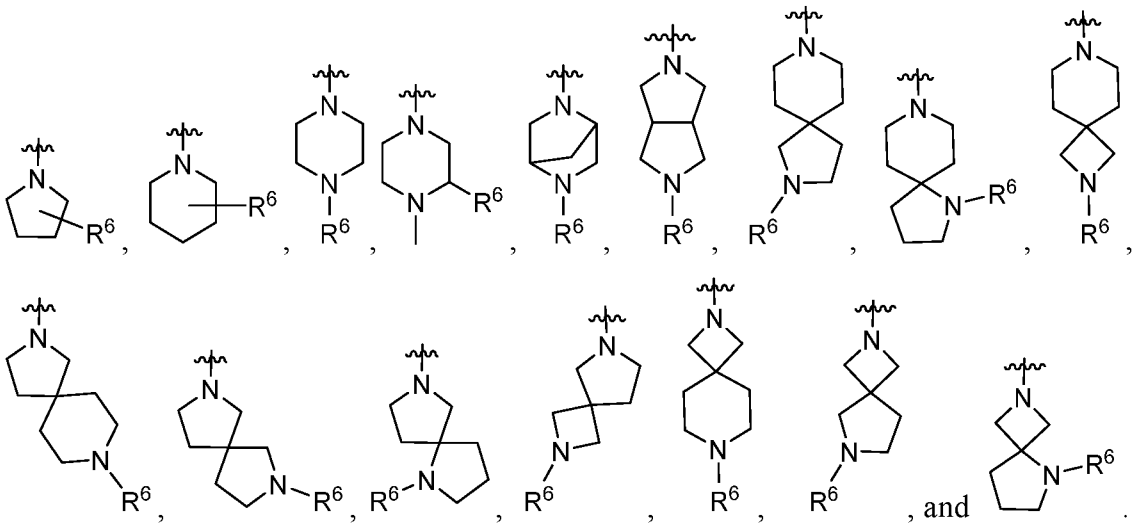
m is 0, 1, or 2;

n is 0 or 1; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

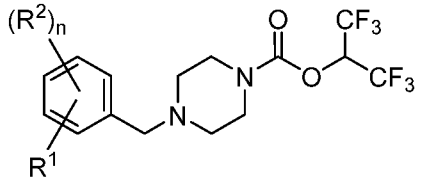
[0017] In some embodiments is method for treating dyskinesia with a compound of Formula (V), wherein X is  . In some embodiments is method for treating dyskinesia with a compound of Formula (V), wherein m is 1 and n is 1. In some embodiments is method for treating dyskinesia with a compound of Formula (V), wherein X is $-N(R^2)(R^3)$. In some embodiments is method for treating dyskinesia with a compound of Formula (V), wherein R^2 and R^3, together with the nitrogen to which they are attached, form a C_2-C_8heterocycloalkyl substituted with one R^6. In some embodiments is method for treating dyskinesia with a compound of Formula (V), wherein R^2 and R^3, together with the nitrogen to which they are attached, form a C_2-C_8heterocycloalkyl selected from:



[0018] In some embodiments is method for treating dyskinesia with a compound of Formula (V), wherein R^6 is $-C_{1-6}$alkyl-CO_2H.

[0019] In some embodiments is method for treating dyskinesia with a compound of Formula (IV) or (V), wherein each R^1 is independently halogen. In some embodiments is method for treating dyskinesia with a compound of Formula (IV) or (V), wherein each R^1 is independently C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (IV) or (V), wherein each R^1 is independently C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (IV) or (V), wherein p is 1.

[0020] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (VI):



Formula (VI);

wherein:

R^1 is $-N(R^3)(R^5)$ or $-NH(R^4)$;

each R^2 is independently selected from halogen, C_{1-6}alkyl, -CN, C_{1-6}haloalkyl, and $-OR^6$;

R^3 is $-CH_2CO_2H$, $-CH_2CH_2CO_2H$, or $-CH(CH_3)CO_2H$;

R^4 is $-(CH_2)_m-CO_2H$;

R^5 is H or C_{1-3}alkyl;

each R^6 is independently selected from H, C_{1-6}alkyl, and C_{1-6}haloalkyl;

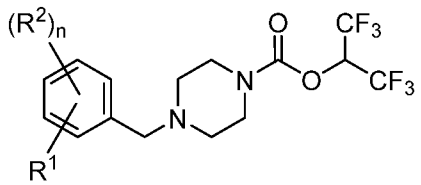
n is 0, 1, 2, 3, or 4; and

m is 3;

or a pharmaceutically acceptable salt or solvate thereof.

[0021] In some embodiments is method for treating dyskinesia with a compound of Formula (VI), wherein R^1 is $-N(R^3)(R^5)$. In some embodiments is method for treating dyskinesia with a compound of Formula (VI), wherein R^5 is H. In some embodiments is method for treating dyskinesia with a compound of Formula (VI), wherein R^1 is $-NH(R^4)$. In some embodiments is method for treating dyskinesia with a compound of Formula (VI), wherein each R^2 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (VI), wherein n is 1.

[0022] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (VII):



Formula (VII);

wherein:

R^1 is $-R^{14}$, $-OR^3$, $-SR^4$, $-S(O)_2R^4$, or $-C\equiv C-(CR^6R^7)-R^8$;

each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-OR^{17}$, and $-C(O)NR^{18}R^{19}$;

R^3 is $-(CR^6R^7)_m-R^8$, $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$, or $-(CR^6R^7)_t-C_{3-6}$cycloalkyl$-R^8$;

R^4 is $-(CR^6R^7)_m-R^{8'}$, $-(CR^6R^7)_v-C(O)OH$, or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

Y is -O- or $-N(R^{22})-$;

each R^6 and R^7 is each independently selected from H, F, and C_{1-6}alkyl; or R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring;

R^8 is $-C(O)OR^9$, $-C(O)R^{10}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

$R^{8'}$ is $-C(O)OR^{9'}$, $-C(O)R^{10'}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

R^9 is H or C_{1-6}alkyl;

$R^{9'}$ is C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl or $-NHSO_2R^{21}$;

$R^{10'}$ is C_{2-6}alkyl or $-NHSO_2R^{21}$;

R^{11} is C_{1-6}alkyl or C_{1-6}alkoxy;

R^{12} and R^{13} is each independently H or C_{1-6}alkyl;

R^{14} is $-(CR^{15}R^{16})_m-R^8$ or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

each R^{15} and R^{16} is each independently selected from H, F, and C_{1-6}alkyl;

each R^{17} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-6}cycloalkyl;

each R^{18} and R^{19} is each independently selected from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, aryl, and heteroaryl; or R^{18} and R^{19}, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{20};

each R^{20} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

R^{21} is C_{1-6}alkyl or C_{3-6}cycloalkyl;

R^{22} is H, C_{1-6}alkyl, or $-SO_2R^{23}$;

R^{23} is C_{1-6}alkyl;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3, or 4;

p is 2, 3, or 4;

q is 1, 2, or 3;

t is 0, 1, or 2; and

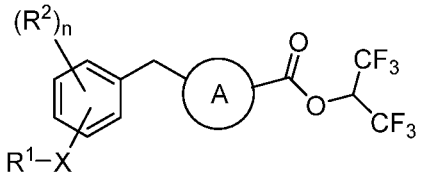
v is 3 or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[0023] In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein R^1 is $-OR^3$. In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein R^3 is $-(CR^6R^7)_m-R^8$. In some embodiments is method for treating dyskinesia with a compound of Formula (VII),

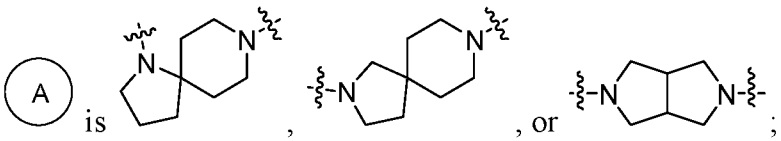
wherein m is 1, 2, or 3. In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein each R^6 and R^7 is each independently selected from H and C_{1-6}alkyl, or R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring. In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein R^8 is -C(O)OR^9. In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein R^9 is H. In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein each R^2 is independently selected from C_{1-6}alkyl, halogen, and C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein n is 2. In some embodiments is method for treating dyskinesia with a compound of Formula (VII), wherein n is 1.

[0024] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (VIII):



Formula (VIII);

wherein:

A is  ;

X is -O-, -S-, -SO_2-, -N(R^3)-, or -CH_2-;

Y is -O- or -N(R^7)-;

R^1 is -(CR^4R^5)$_m$-R^6, -(CR^4R^5)$_p$-Y-(CR^4R^5)$_q$-R^6, or -(CR^4R^5)$_t$-C_{3-6}cycloalkyl-R^6;

each R^2 is independently selected from halogen, -CN, C_{1-6}alkyl, C_{1-6}haloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -OR^{17}, and -C(O)N$R^{18}R^{19}$;

R^3 is H or C_{1-6}alkyl;

each R^4 and R^5 is each independently selected from H, F, and C_{1-6}alkyl; or R^4 and R^5, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring;

R^6 is -CO_2R^9, -C(O)R^{10}, or -C(O)O-($CR^{12}R^{13}$)-OC(O)R^{11};

R^7 is H, C_{1-6}alkyl, or -SO_2R^8;

R^8 is C_{1-6}alkyl;

R^9 is H or C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl or -$NHSO_2R^{21}$;

R^{11} is C_{1-6}alkyl or C_{1-6}alkoxy;

R^{12} and R^{13} is each independently H or C_{1-6}alkyl;

each R^{17} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, aminoalkyl, cycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -C_{1-6}alkyl-C(O)(heterocycloalkyl), optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

each R^{18} and R^{19} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, cycloalkyl, aryl, and heteroaryl; or R^{18} and R^{19}, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{20};

each R^{20} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

R^{21} is C_{1-6}alkyl;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3, or 4;

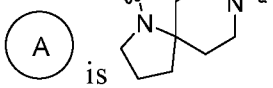
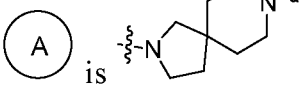
p is 2, 3, or 4;

q is 1, 2, or 3; and

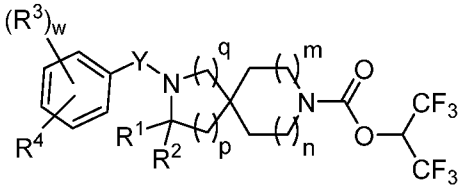
t is 0, 1, or 2;

or a pharmaceutically acceptable salt or solvate thereof.

[0025] In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein R^1 is -$(CR^4R^5)_m$-R^6. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein each R^4 and R^5 is each independently selected from H and C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein each R^4 and R^5 is H. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein R^6 is -CO_2R^9. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein R^9 is H. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein R^6 is -$C(O)R^{10}$. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein R^{10} is -$NHSO_2R^{21}$. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein X is -O-. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein X is -$N(R^3)$-. In some embodiments is method for treating dyskinesia with a compound of

Formula (VIII), wherein  is . In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein  is . In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein each R^2 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (VIII), wherein n is 1.

[0026] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (IX):



Formula (IX);

wherein:

Y is $-CH_2-$ or $-C(O)-$;

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-SF_5$, and $-OR^7$;

R^4 is selected from $-C\equiv C-C_{1-6}$alkyl-CO_2H and $-C_{3-8}$cycloalkyl-CO_2H;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, and $-C_{1-6}$alkyl-C_{3-8}cycloalkyl;

w is 0, 1, 2, 3, or 4;

n is 0 or 1;

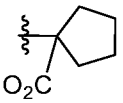
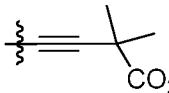
m is 0 or 1;

p is 0, 1, or 2; and

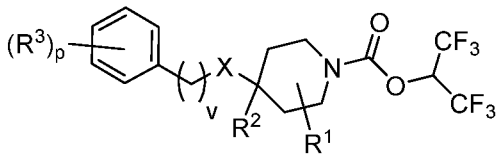
q is 0, 1, or 2; provided that when q is 0, then p is 2;

or a pharmaceutically acceptable salt or solvate thereof.

[0027] In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein R^4 is $-C_{3-8}$cycloalkyl-CO_2H. In some embodiments is method for

treating dyskinesia with a compound of Formula (IX), wherein R^4 is  . In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein R^4 is -C≡C-C_{1-6}alkyl-CO_2H. In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein R^4 is  . In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein Y is -CH_2-. In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein R^1 and R^2 are both H. In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein each R^3 is independently selected from halogen and C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein w is 1. In some embodiments is method for treating dyskinesia with a compound of Formula (IX), wherein m is 1, n is 1, q is 0, and p is 2.

[0028] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (X):



Formula (X);

wherein:

X is -O- or -N(R^{11})-;

R^1 is H or C_{1-6}alkyl;

R^2 is C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, -C≡C-C_{1-6}alkyl-CO_2H, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), C_{1-9}heteroaryl, -SF_5, -NR^5R^6, -OR^7, -CO_2R^8, and -$C(O)NR^8R^9$, wherein C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{1-9}heteroaryl are optionally substituted with one or two R^4; or two adjacent R^3 form a C_{2-9}heterocycloalkyl ring, wherein the C_{2-9}heterocycloalkyl ring is optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-6}haloalkyl, halogen, oxo, -CN, -CO_2R^8, -$C(O)R^8$, -$C(O)NR^8R^9$, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$;

each R^5 and R^6 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-C(O)(C_{2-9}heterocycloalkyl), C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl; or R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-C(O)(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-CO_2H, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl, wherein C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl are optionally substituted with one or two groups selected from oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and CO_2NH_2;

each R^8 and R^9 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one or two groups selected from C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and CO_2NH_2;

each R^{10} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, oxo, -CN, -CO_2R^8, -C(O)R^8, -C(O)NR^8R^9, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$;

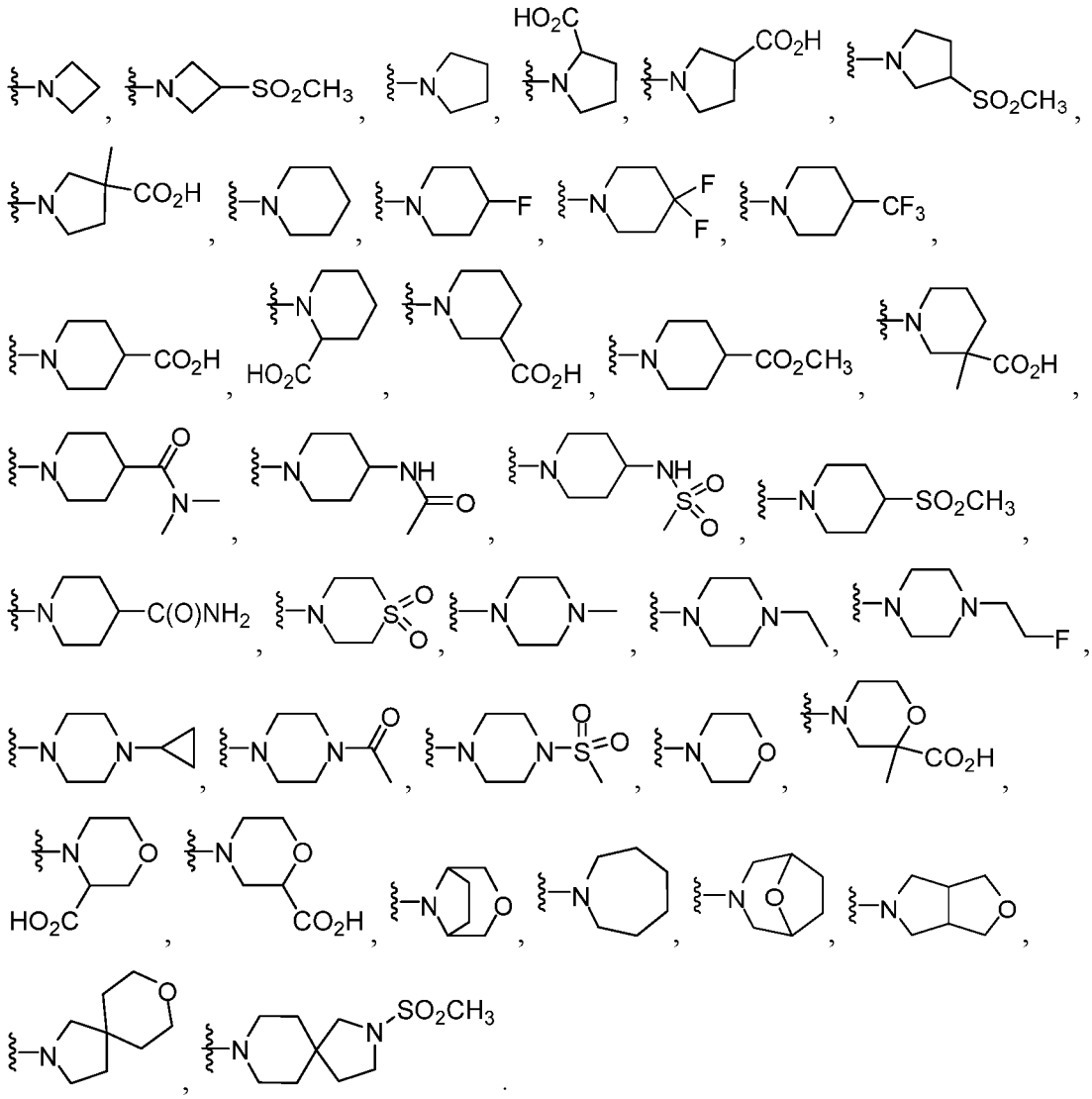
R^{11} is H, C_{1-6}alkyl, -C(O)-C_{1-6}alkyl, or -CH_2CO_2H;

p is 0, 1, 2, 3, 4, or 5; and

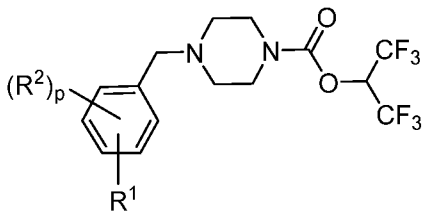
v is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

[0029] In some embodiments is method for treating dyskinesia with a compound of Formula (X), wherein each R^3 is independently selected from halogen, C_{1-6}haloalkyl, -NR^5R^6, and -OR^7. In some embodiments is method for treating dyskinesia with a compound of Formula (X), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10}. In some embodiments is method for treating dyskinesia with a compound of Formula (X), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl and -CO_2H. In some embodiments is method for treating dyskinesia with a compound of Formula (X), wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted C_{2-9}heterocycloalkyl ring. In some embodiments is method for treating dyskinesia with a compound of Formula (X), wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring selected from:

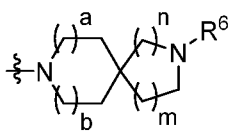
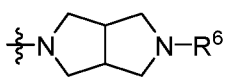


[0030] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (XI):



Formula (XI);

wherein:

R^1 is selected from  and  ;

each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, $-SF_5$, $-OR^3$, and $-C(O)NR^4R^5$;

each R^3 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, and -C_{1-6}alkyl-C_{3-8}cycloalkyl;

each R^4 and R^5 is independently selected from H, C_{1-6}alkyl, and C_{3-8}cycloalkyl;

R^6 is selected from C_{1-6}alkyl, -C(O)-C_{1-6}alkyl, and -$S(O)_2$-C_{1-6}alkyl;

a is 0 or 1;

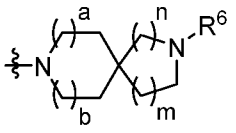
b is 0 or 1;

m is 0, 1, or 2;

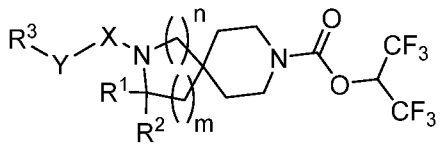
n is 0, 1, or 2; provided that when n is 0, then m is 2; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[0031] In some embodiments is method for treating dyskinesia with a compound of Formula (XI), wherein R^1 is  . In some embodiments is method for treating dyskinesia with a compound of Formula (XI), wherein R^6 is -C(O)-C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XI), wherein R^6 is -$S(O)_2$-C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XI), wherein each R^3 is independently selected from halogen and C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XI), wherein p is 1.

[0032] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (XII):



Formula (XII);

wherein:

X is -CH_2- or -C(O)-;

Y is a bond, C_{1-6}alkyl, C_{1-6}haloalkyl, or C_{3-8}cycloalkyl;

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

R^3 is a 5- to 6-membered heteroaryl ring or a 9- to 10-membered bicyclic heteroaryl ring; wherein the 5- to 6-membered heteroaryl ring and the 9- to 10-membered bicyclic heteroaryl ring are optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl-(C_{2-9}heterocycloalkyl), phenyl, -CH_2-phenyl, C_{1-9}heteroaryl, -OR^7, -CO_2R^6, -$CH_2CO_2R^6$, and -$CH_2C(O)N(H)SO_2R^8$; wherein C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), phenyl, and C_{1-9}heteroaryl are optionally substituted with one or two R^5; or two adjacent R^4 form a 6-membered cycloalkyl or 6-membered heterocycloalkyl ring, wherein the cycloalkyl and heterocycloalkyl ring are optionally substituted with one or two R^5;

each R^5 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}heteroalkyl, C_{1-6}alkoxy, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, -CO_2R^6, -$CH_2CO_2R^6$, and -C_{1-6}alkyl(C_{2-9}heterocycloalkyl) optionally substituted with C_{1-6}alkyl;

each R^6 is independently selected from H and C_{1-6}alkyl;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;

each R^8 is independently selected from C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;

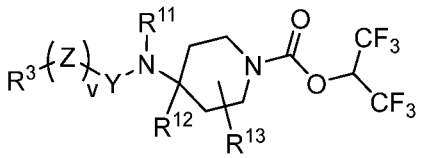
n is 0 or 1; and

m is 1 or 2; provided that when n is 0, then m is 2; and when n is 1, then m is 1;

or a pharmaceutically acceptable salt or solvate thereof.

[0033] In some embodiments is method for treating dyskinesia with a compound of Formula (XII), wherein Y is a bond. In some embodiments is method for treating dyskinesia with a compound of Formula (XII), wherein R^1 and R^2 are both H. In some embodiments is method for treating dyskinesia with a compound of Formula (XII), wherein X is -CH_2-. In some embodiments is method for treating dyskinesia with a compound of Formula (XII), wherein X is -C(O)-. In some embodiments is method for treating dyskinesia with a compound of Formula (XII), wherein n is 0 and m is 2.

[0034] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (XIII):



Formula (XIII);

wherein:

Y is -CH_2- or -C(O)-;

Z is C_{3-6}cycloalkyl;

R^3 is a 5- to 6-membered heteroaryl ring or a 9- to 10-membered bicyclic heteroaryl ring; wherein the 5- to 6-membered heteroaryl ring and the 9- to 10-membered bicyclic heteroaryl ring are optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl-(C_{2-9}heterocycloalkyl), phenyl, -CH_2-phenyl, C_{1-9}heteroaryl, -OR^7, -CO_2R^6, and -$CH_2CO_2R^6$; wherein C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), phenyl, and C_{1-9}heteroaryl are optionally substituted with one or two R^5; or two adjacent R^4 form a 6-membered cycloalkyl or 6-membered heterocycloalkyl ring, wherein the cycloalkyl and heterocycloalkyl ring are optionally substituted with one or two R^5;

each R^5 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}heteroalkyl, C_{1-6}alkoxy, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, -CO_2R^6, -$CH_2CO_2R^6$, and -C_{1-6}alkyl(C_{2-9}heterocycloalkyl) optionally substituted with C_{1-6}alkyl;

each R^6 is independently selected from H and C_{1-6}alkyl;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;

R^{11} is H, C_{1-6}alkyl, or -C_{1-6}alkyl-O-C_{1-6}alkyl;

R^{12} is C_{1-6}alkyl;

R^{13} is H or C_{1-6}alkyl; and

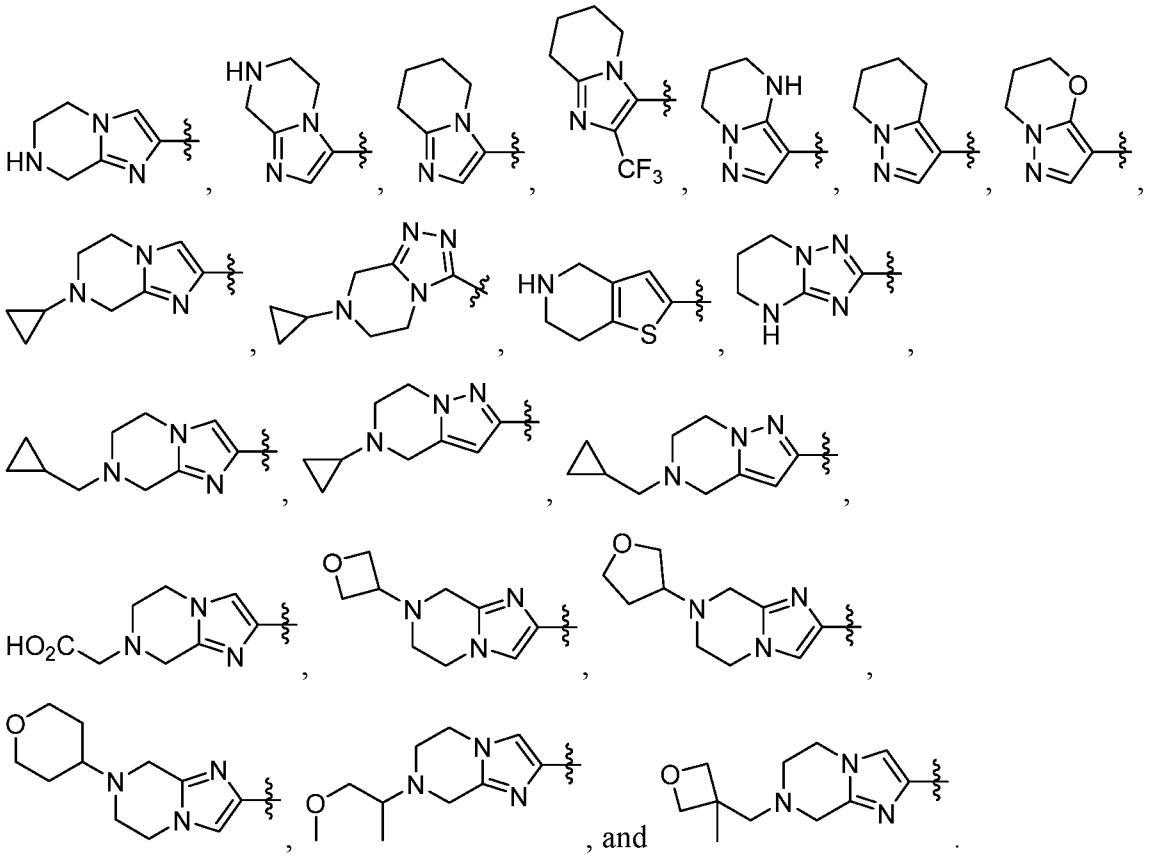
v is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

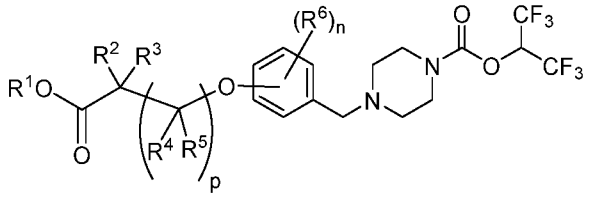
[0035] In some embodiments is method for treating dyskinesia with a compound of Formula (XIII), wherein R^{13} is H. In some embodiments is method for treating dyskinesia with a compound of Formula (XIII), wherein v is 0. In some embodiments is method for treating dyskinesia with a compound of Formula (XIII), wherein R^1 is Y is -C(O)-.

[0036] In some embodiments is method for treating dyskinesia with a compound of Formula (XII) or (XIII), wherein R^3 is a 5-membered heteroaryl ring substituted with one, two, or three R^4. In some embodiments is method for treating dyskinesia with a compound of Formula (XII) or (XIII), wherein R^3 is a 5-membered heteroaryl ring substituted with two or three R^4, wherein two adjacent R^4 form a 6-membered heterocycloalkyl ring optionally substituted with one or two R^5. In some embodiments is method for treating dyskinesia with a compound of Formula (XII) or (XIII), wherein R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form an unsubstituted 6-membered heterocycloalkyl ring. In some

embodiments is method for treating dyskinesia with a compound of Formula (XII) or (XIII), wherein R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5. In some embodiments is method for treating dyskinesia with a compound of Formula (XII) or (XIII), wherein R^5 is selected from C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, and -CH_2CO_2H. In some embodiments is method for treating dyskinesia with a compound of Formula (XII) or (XIII), wherein:



[0037] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (XIV):



Formula (XIV);

wherein:

R^1 is H or C_{1-6}alkyl;

R^2 is C_{1-6}alkyl;

R^3 is H or C_{1-6}alkyl;

R^4 and R^5 are independently selected from H and C_{1-6}alkyl;

each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, -OR^7, -$C(O)NR^8R^9$, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{2-9}heteroaryl, wherein C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{2-9}heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-6}cycloalkyl;

each R^8 and R^9 is each independently selected from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, aryl, and heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^{10} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

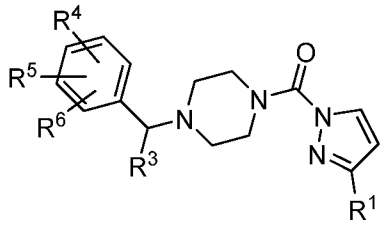
n is 0, 1, 2, 3, or 4; and

p is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

[0038] In some embodiments is method for treating dyskinesia with a compound of Formula (XIV), wherein p is 0. In some embodiments is method for treating dyskinesia with a compound of Formula (XIV), wherein p is 1. In some embodiments is method for treating dyskinesia with a compound of Formula (XIV), wherein R^4 and R^5 are H In some embodiments is method for treating dyskinesia with a compound of Formula (XIV), wherein R^3 is C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XIV), wherein each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, -OR^7, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl, wherein C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl are optionally substituted with one or two groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments is method for treating dyskinesia with a compound of Formula (XIV), wherein each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, and C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XIV), wherein n is 1 or 2.

[0039] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (XV):



Formula (XV);

wherein:

R^1 is $-N(R^2)C(O)R^{15}$ or $-N(H)SO_2R^{15}$;

R^2 is H or C_{1-6}alkyl;

R^3 is H or optionally substituted phenyl;

R^4 is H, halogen, $-OR^7$, C_{1-6}alkyl, C_{1-6}haloalkyl, optionally substituted heterocycloalkyl, optionally substituted C_{1-6}alkyl-heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, $-CO_2H$, or $-C(O)NR^8R^9$;

R^5 is H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or phenyl; or

R^4 and R^5 are combined to form a heterocycloalkyl ring;

R^6 is H, halogen or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, optionally substituted phenyl, optionally substituted C_{1-6}alkyl-phenyl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, or $-C_{1-6}$alkyl$C(O)NR^{10}R^{11}$;

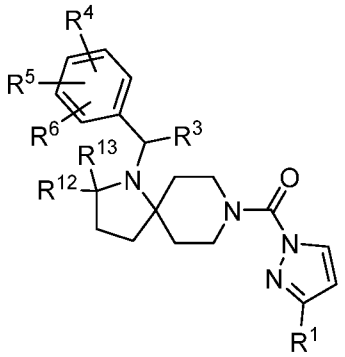
R^8 and R^9 are each independently H, or C_{1-6}alkyl; or R^8 and R^9 together with the nitrogen to which they are attached are combined to form an optionally substituted heterocycloalkyl ring;

R^{10} and R^{11} are each independently H, or C_{1-6}alkyl; or R^{10} and R^{11} together with the nitrogen to which they are attached are combined to form a heterocycloalkyl ring; and

R^{15} is optionally substituted C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[0040] In some embodiments is a method for treating dyskinesia in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (XVI):



Formula (XVI);

wherein:

R^1 is $-N(R^2)C(O)R^{15}$ or $-N(H)SO_2R^{15}$;

R^2 is H or C_{1-6}alkyl;

R^3 is H or optionally substituted phenyl;

R^4 is H, halogen, $-OR^7$, C_{1-6}alkyl, C_{1-6}haloalkyl, optionally substituted heterocycloalkyl, optionally substituted C_{1-6}alkyl-heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, $-CO_2H$, or $-C(O)NR^8R^9$;

R^5 is H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or phenyl; or

R^4 and R^5 are combined to form a heterocycloalkyl ring;

R^6 is H, halogen or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, optionally substituted phenyl, optionally substituted C_{1-6}alkyl-phenyl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, or $-C_{1-6}$alkyl$C(O)NR^{10}R^{11}$;

R^8 and R^9 are each independently H, or C_{1-6}alkyl; or R^8 and R^9 together with the nitrogen to which they are attached are combined to form an optionally substituted heterocycloalkyl ring;

R^{10} and R^{11} are each independently H, or C_{1-6}alkyl; or R^{10} and R^{11} together with the nitrogen to which they are attached are combined to form a heterocycloalkyl ring;

R^{12} is H or C_{1-6}alkyl;

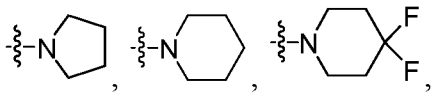
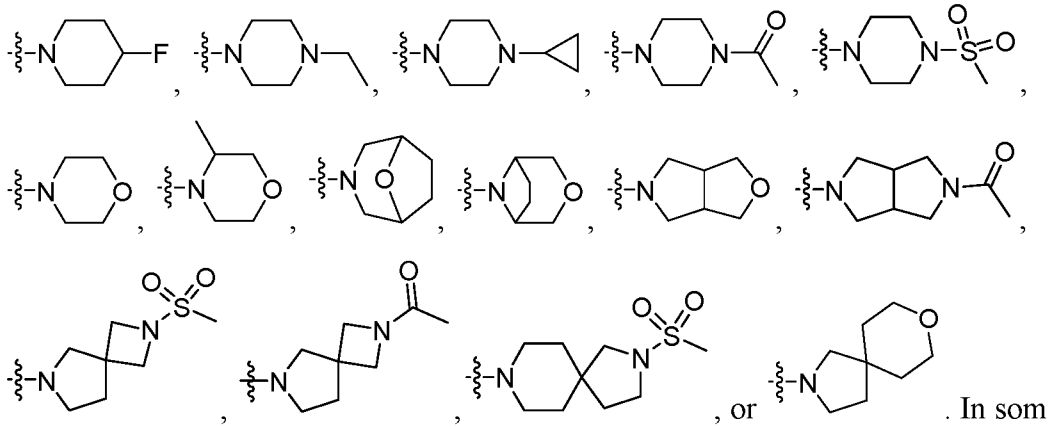
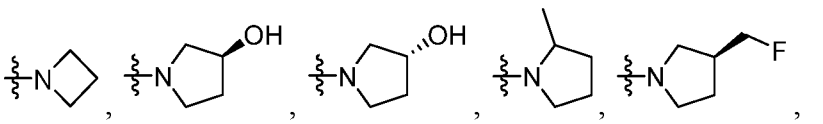
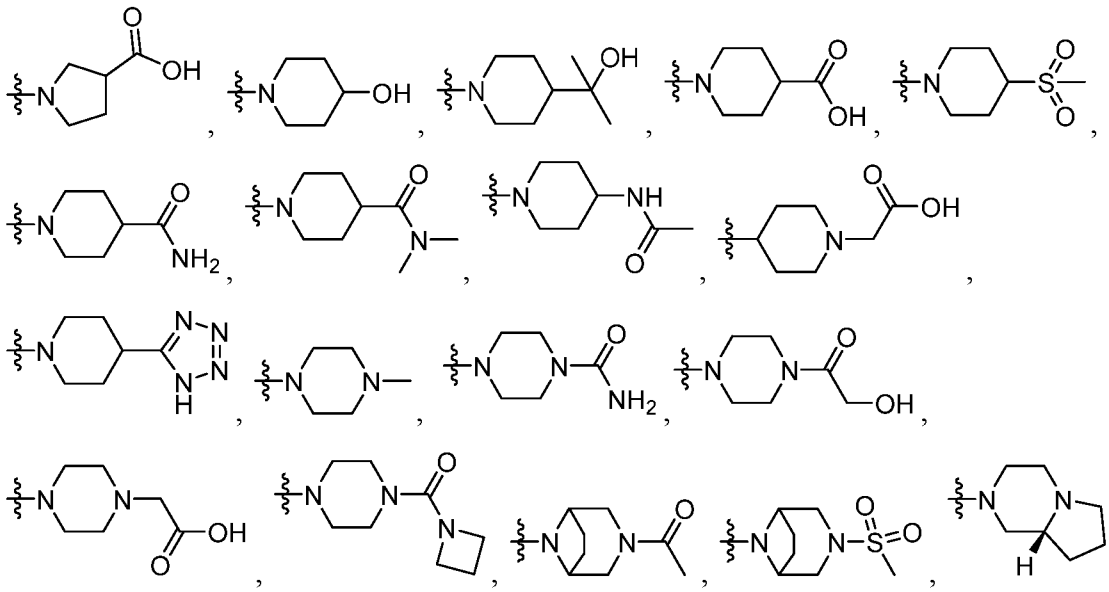
R^{13} is H or C_{1-6}alkyl; and

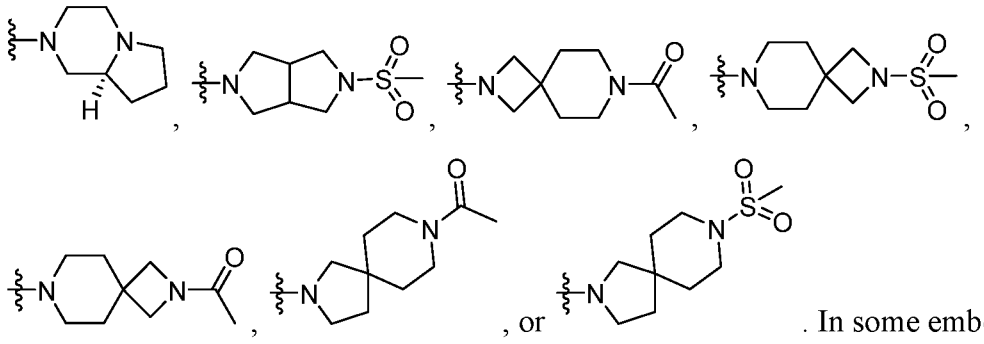
R^{15} is optionally substituted C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[0041] In some embodiments is method for treating dyskinesia with a compound of Formula (XVI), wherein R^{12} and R^{13} are H.

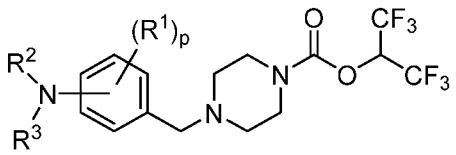
[0042] In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^4 is optionally substituted heterocycloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or

(XVI), wherein R^4 is heterocycloalkyl optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-6}alkyl, -C_{1-6}alkyl-OH, C_{1-6}fluoroalkyl, C_{3-6}cycloalkyl, heteroaryl, -CO_2H, -C_{1-6}alkyl-CO_2H, -$C(O)C_{1-6}$alkyl, -$C(O)C_{1-6}$alkyl-OH, -$N(H)C(O)C_{1-6}$alkyl, -$C(O)NH_2$, -$C(O)N(H)(C_{1-6}$alkyl), -$C(O)N(C_{1-6}$alkyl$)_2$, -$C(O)C_{2-7}$heterocycloalkyl, and -$S(O)_2C_{1-6}$alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^4 is optionally substituted heterocycloalkyl and the heterocycloalkyl is a 4-6 membered monocyclic heterocycloalkyl, a 8-9 membered bicyclic heterocycloalkyl, a 7-8 membered bridged heterocycloalkyl, a 5,5 fused heterocycloalkyl, or an 8-11 membered spirocyclic heterocycloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^4 is  ,  , or . In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^4 is  , 



. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^4 is halogen. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^4 is C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^5 is halogen. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^5 is C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^5 is C_{1-6}alkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^6 is H. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^3 is H. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^1 is $-N(R^2)C(O)R^{15}$. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^1 is $-N(H)SO_2R^{15}$. In some embodiments is method for treating dyskinesia with a compound of Formula (XV) or (XVI), wherein R^{15} is unsubstituted C_{1-6}alkyl.

[0043] In some embodiments is a compound of Formula (XVII):



Formula (XVII);

wherein:

each R^1 is independently halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, or -CN;

R^2 and R^3, together with the carbon to which they are attached, form

(i) a C_2-C_7heterocycloalkyl; or

(ii) a C_2-C_9heteroaryl;

wherein the C_2-C_7heterocycloalkyl or the C_2-C_9heteroaryl is substituted with one R^4 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^4 is $-CO_2H$ or $-C_{1-6}$alkyl-CO_2H; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[0044] In some embodiments is method for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_7heterocycloalkyl substituted with one R^4 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments is method for treating dyskinesia with a compound of Formula (XVII), R^4 is $-CO_2H$. In some embodiments is method for treating dyskinesia with a compound of Formula (XVII), R^4 is $-C_{1-6}$alkyl-CO_2H. In some embodiments is method for treating dyskinesia with a compound of Formula (XVII), each R^1 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl. In some embodiments is method for treating dyskinesia with a compound of Formula (XVII), p is 1 or 2. In some embodiments is method for treating dyskinesia with a compound of Formula (XVII), p is 2. In some embodiments is method for treating dyskinesia with a compound of Formula (XVII), p is 1.

[0045] In some embodiments of the methods described herein for treating dyskinesia with a compound of Formula (I)-(XVII), the dyskinesia is levodopa-induced dyskinesia.

BRIEF DESCRIPTION OF THE FIGURES

[0046] Fig. 1A depicts dyskinesia in MPTP-lesioned cynomolgus macaques dosed with amantadine (AMT) (10 mg/kg, p.o.) or vehicle following L-DOPA administration.

[0047] Fig. 1B depicts dyskinesia in MPTP-lesioned cynomolgus macaques dosed with amantadine (AMT) (10 mg/kg, p.o.) or vehicle following L-DOPA administration.

[0048] Fig. 1C depicts dyskinesia in MPTP-lesioned cynomolgus macaques dosed with Compound 21 (3, 10, and 30 mg/kg, p.o.) or vehicle following L-DOPA administration.

[0049] Fig. 1D depicts dyskinesia in MPTP-lesioned cynomolgus macaques dosed with Compound 21 (3, 10, and 30 mg/kg, p.o.) or vehicle following L-DOPA administration.

[0050] Fig. 1E depicts Parkinson disability in MPTP-lesioned cynomolgus macaques dosed with amantadine (AMT) (10 mg/kg, p.o.) or vehicle following L-DOPA administration.

[0051] Fig. 1F depicts Parkinson disability in MPTP-lesioned cynomolgus macaques dosed with Compound 21 (3, 10, and 30 mg/kg, p.o.) or vehicle following L-DOPA administration.

DETAILED DESCRIPTION OF THE INVENTION

[0052] Dyskinesia is a type of hyperkinetic movement disorder. In Parkinson's disease, dyskinesia develops in response to long-term levodopa use and affects 90% of patients within approximately 10 years of treatment. Dyskinesia is characterized by involuntary, abnormal, purposeless movements and can be quite debilitating and disruptive to the patient. Dyskinesia can be broken down into subsets of hyperkinetic movements including chorea characterized by frequent, brief, unpredictable, purposeless movements flowing from body part to body part and dystonia which consists of intermittent muscle contractions causing abnormal, repetitive movements and postures. The clinical manifestation of dyskinesia can be categorized by the temporal occurrence after administration as peak-dose dyskinesias, biphasic dyskinesia and OFF dyskinesias.

[0053] Dyskinesia and hyperkinetic movements are also associated with other neurological disorders including tardive dyskinesia, Huntington's diseases, restless legs syndrome, tremor, traumatic brain injury and stroke.

[0054] This disclosure is directed, at least in part, to a method for treating dyskinesia with a MAGL inhibitor. In some embodiments described is a method for treating dyskinesia with a compound of Formula (I)-(XVII) described herein.

[0055] As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an agent" includes a plurality of such agents, and reference to "the cell" includes reference to one or more cells (or to a plurality of cells) and equivalents thereof. When ranges are used herein for physical properties, such as molecular weight, or chemical properties, such as chemical formulae, all combinations and subcombinations of ranges and specific embodiments therein are intended to be included. The term "about" when referring to a number or a numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and thus the number or numerical range varies between 1% and 15% of the stated number or numerical range. The term "comprising" (and related terms such as "comprise" or "comprises" or "having" or "including") is not intended to exclude that which in other certain embodiments, for example, an embodiment of any composition of matter, composition, method, or process,

or the like, described herein, may "consist of" or "consist essentially of" the described features.

Definitions

[0056] As used in the specification and appended claims, unless specified to the contrary, the following terms have the meaning indicated below.

[0057] "Amino" refers to the $-NH_2$ radical.

[0058] "Cyano" refers to the -CN radical.

[0059] "Nitro" refers to the $-NO_2$ radical.

[0060] "Oxa" refers to the -O- radical.

[0061] "Oxo" refers to the =O radical.

[0062] "Thioxo" refers to the =S radical.

[0063] "Imino" refers to the =N-H radical.

[0064] "Oximo" refers to the =N-OH radical.

[0065] "Alkyl" refers to a straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, containing no unsaturation, having from one to fifteen carbon atoms (*e.g.*, C_1-C_{15} alkyl). In certain embodiments, an alkyl comprises one to thirteen carbon atoms (*e.g.*, C_1-C_{13} alkyl). In certain embodiments, an alkyl comprises one to eight carbon atoms (*e.g.*, C_1-C_8 alkyl). In certain embodiments, an alkyl comprises one to eight carbon atoms (*e.g.*, C_1-C_6 alkyl). In other embodiments, an alkyl comprises one to five carbon atoms (*e.g.*, C_1-C_5 alkyl). In other embodiments, an alkyl comprises one to four carbon atoms (*e.g.*, C_1-C_4 alkyl). In other embodiments, an alkyl comprises one to three carbon atoms (*e.g.*, C_1-C_3 alkyl). In other embodiments, an alkyl comprises one to two carbon atoms (*e.g.*, C_1-C_2 alkyl). In other embodiments, an alkyl comprises one carbon atom (*e.g.*, C_1 alkyl). In other embodiments, an alkyl comprises five to fifteen carbon atoms (*e.g.*, C_5-C_{15} alkyl). In other embodiments, an alkyl comprises five to eight carbon atoms (*e.g.*, C_5-C_8 alkyl). In other embodiments, an alkyl comprises two to five carbon atoms (*e.g.*, C_2-C_5 alkyl). In other embodiments, an alkyl comprises three to five carbon atoms (*e.g.*, C_3-C_5 alkyl). In other embodiments, the alkyl group is selected from methyl, ethyl, 1-propyl (*n*-propyl), 1-methylethyl (*iso*-propyl), 1-butyl (*n*-butyl), 1-methylpropyl (*sec*-butyl), 2-methylpropyl (*iso*-butyl), 1,1-dimethylethyl (*tert*-butyl), 1-pentyl (*n*-pentyl). The alkyl is attached to the rest of the molecule by a single bond. Unless stated otherwise specifically in the specification, an alkyl group is optionally substituted by one or more of the following substituents: halo, cyano, nitro, oxo, thioxo, imino, oximo, trimethylsilanyl, $-OR^a$, $-SR^a$, $-OC(O)R^a$, $-N(R^a)_2$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)N(R^a)_2$, $-N(R^a)C(O)OR^f$, $-OC(O)-NR^aR^f$, $-N(R^a)C(O)R^f$, $-N(R^a)S(O)_tR^f$ (where t is 1

or 2), $-S(O)_tOR^a$ (where t is 1 or 2), $-S(O)_tR^f$ (where t is 1 or 2) and $-S(O)_tN(R^a)_2$ (where t is 1 or 2) where each R^a is hydrogen, alkyl, fluoroalkyl, cycloalkyl, aryl, aralkyl, heterocycloalkyl, heteroaryl or heteroarylalkyl, and each R^f is independently alkyl, fluoroalkyl, cycloalkyl, aryl, aralkyl, heterocycloalkyl, heteroaryl or heteroarylalkyl.

[0066] "Alkoxy" refers to a radical bonded through an oxygen atom of the formula –O-alkyl, where alkyl is an alkyl chain as defined above.

[0067] "Alkenyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one carbon-carbon double bond, and having from two to twelve carbon atoms. In certain embodiments, an alkenyl comprises two to eight carbon atoms. In certain embodiments, an alkenyl comprises two to six carbon atoms. In other embodiments, an alkenyl comprises two to four carbon atoms. The alkenyl is attached to the rest of the molecule by a single bond, for example, ethenyl (*i.e.*, vinyl), prop-1-enyl (*i.e.*, allyl), but-1-enyl, pent-1-enyl, penta-1,4-dienyl, and the like. Unless stated otherwise specifically in the specification, an alkenyl group is optionally substituted by one or more of the following substituents: halo, cyano, nitro, oxo, thioxo, imino, oximo, trimethylsilanyl, $-OR^a$, $-SR^a$, $-OC(O)R^a$, $-N(R^a)_2$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)N(R^a)_2$, $-N(R^a)C(O)OR^f$, $-OC(O)-NR^aR^f$, $-N(R^a)C(O)R^f$, $-N(R^a)S(O)_tR^f$ (where t is 1 or 2), $-S(O)_tOR^a$ (where t is 1 or 2), $-S(O)_tR^f$ (where t is 1 or 2) and $-S(O)_tN(R^a)_2$ (where t is 1 or 2) where each R^a is hydrogen, alkyl, fluoroalkyl, cycloalkyl, aryl, aralkyl, heterocycloalkyl, heteroaryl or heteroarylalkyl, and each R^f is independently alkyl, fluoroalkyl, cycloalkyl, aryl, aralkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl.

[0068] "Alkynyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one carbon-carbon triple bond, and having from two to twelve carbon atoms. In certain embodiments, an alkenyl comprises two to eight carbon atoms. In certain embodiments, an alkynyl comprises two to six carbon atoms. In other embodiments, an alkynyl comprises two to four carbon atoms. The alkynyl is attached to the rest of the molecule by a single bond, for example, ethynyl, propynyl, butynyl, pentynyl, hexynyl, and the like. Unless stated otherwise specifically in the specification, an alkynyl group is optionally substituted by one or more of the following substituents: halo, cyano, nitro, oxo, thioxo, imino, oximo, trimethylsilanyl, $-OR^a$, $-SR^a$, $-OC(O)R^a$, $-N(R^a)_2$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)N(R^a)_2$, $-N(R^a)C(O)OR^f$, $-OC(O)-NR^aR^f$, $-N(R^a)C(O)R^f$, $-N(R^a)S(O)_tR^f$ (where t is 1 or 2), $-S(O)_tOR^a$ (where t is 1 or 2), $-S(O)_tR^f$ (where t is 1 or 2) and $-S(O)_tN(R^a)_2$ (where t is 1 or 2) where each R^a is hydrogen, alkyl, fluoroalkyl, cycloalkyl, aryl, aralkyl,

heterocycloalkyl, heteroaryl or heteroarylalkyl, and each R^f is independently alkyl, fluoroalkyl, cycloalkyl, aryl, aralkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl.

[0069] "Alkylene" or "alkylene chain" refers to a straight or branched divalent hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing no unsaturation and having from one to twelve carbon atoms, for example, methylene, ethylene, propylene, *n*-butylene, and the like. The alkylene chain is attached to the rest of the molecule through a single bond and to the radical group through a single bond. The points of attachment of the alkylene chain to the rest of the molecule and to the radical group are through one carbon in the alkylene chain or through any two carbons within the chain. In certain embodiments, an alkylene comprises one to eight carbon atoms (*e.g.*, C_1-C_8 alkylene). In other embodiments, an alkylene comprises one to five carbon atoms (*e.g.*, C_1-C_5 alkylene). In other embodiments, an alkylene comprises one to four carbon atoms (*e.g.*, C_1-C_4 alkylene). In other embodiments, an alkylene comprises one to three carbon atoms (*e.g.*, C_1-C_3 alkylene). In other embodiments, an alkylene comprises one to two carbon atoms (*e.g.*, C_1-C_2 alkylene). In other embodiments, an alkylene comprises one carbon atom (*e.g.*, C_1 alkylene). In other embodiments, an alkylene comprises five to eight carbon atoms (*e.g.*, C_5-C_8 alkylene). In other embodiments, an alkylene comprises two to five carbon atoms (*e.g.*, C_2-C_5 alkylene). In other embodiments, an alkylene comprises three to five carbon atoms (*e.g.*, C_3-C_5 alkylene). Unless stated otherwise specifically in the specification, an alkylene chain is optionally substituted by one or more of the following substituents: halo, cyano, nitro, oxo, thioxo, imino, oximo, trimethylsilanyl, $-OR^a$, $-SR^a$, $-OC(O)-R^a$, $-N(R^a)_2$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)N(R^a)_2$, $-N(R^a)C(O)OR^f$, $-OC(O)-NR^aR^f$, $-N(R^a)C(O)R^f$, $-N(R^a)S(O)_tR^f$ (where t is 1 or 2), $-S(O)_tOR^a$ (where t is 1 or 2), $-S(O)_tR^f$ (where t is 1 or 2) and $-S(O)_tN(R^a)_2$ (where t is 1 or 2) where each R^a is independently hydrogen, alkyl, fluoroalkyl, carbocyclyl, carbocyclylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl, and each R^f is independently alkyl, fluoroalkyl, carbocyclyl, carbocyclylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.

[0070] "Aryl" refers to a radical derived from an aromatic monocyclic or multicyclic hydrocarbon ring system by removing a hydrogen atom from a ring carbon atom. The aromatic monocyclic or multicyclic hydrocarbon ring system contains only hydrogen and carbon from five to eighteen carbon atoms, where at least one of the rings in the ring system is fully unsaturated, *i.e.*, it contains a cyclic, delocalized (4n+2) π–electron system in accordance with the Hückel theory. The ring system from which aryl groups

are derived include, but are not limited to, groups such as benzene, fluorene, indane, indene, tetralin and naphthalene. Unless stated otherwise specifically in the specification, the term "aryl" or the prefix "ar-" (such as in "aralkyl") is meant to include aryl radicals optionally substituted by one or more substituents independently selected from alkyl, alkenyl, alkynyl, halo, fluoroalkyl, cyano, nitro, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted carbocyclyl, optionally substituted carbocyclylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl,

heteroarylalkyl, $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 1 or 2) and $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2), where each R^a is independently hydrogen, alkyl, fluoroalkyl, cycloalkyl, cycloalkylalkyl, aryl (optionally substituted with one or more halo groups), aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl, each R^b is independently a direct bond or a straight or branched alkylene or alkenylene chain, and R^c is a straight or branched alkylene or alkenylene chain, and where each of the above substituents is unsubstituted unless otherwise indicated.

[0071] "Aryloxy" refers to a radical bonded through an oxygen atom of the formula –O-aryl, where aryl is as defined above.

[0072] "Aralkyl" refers to a radical of the formula $-R^c$-aryl where R^c is an alkylene chain as defined above, for example, methylene, ethylene, and the like. The alkylene chain part of the aralkyl radical is optionally substituted as described above for an alkylene chain. The aryl part of the aralkyl radical is optionally substituted as described above for an aryl group.

[0073] "Aralkenyl" refers to a radical of the formula $–R^d$-aryl where R^d is an alkenylene chain as defined above. The aryl part of the aralkenyl radical is optionally substituted as described above for an aryl group. The alkenylene chain part of the aralkenyl radical is optionally substituted as defined above for an alkenylene group.

[0074] "Aralkynyl" refers to a radical of the formula $-R^e$-aryl, where R^e is an alkynylene chain as defined above. The aryl part of the aralkynyl radical is optionally substituted as described above for an aryl group. The alkynylene chain part of the aralkynyl radical is optionally substituted as defined above for an alkynylene chain.

[0075] "Carbocyclyl" refers to a stable non-aromatic monocyclic or polycyclic hydrocarbon radical consisting solely of carbon and hydrogen atoms, which includes fused or bridged ring systems, having from three to fifteen carbon atoms. In certain embodiments, a carbocyclyl comprises three to ten carbon atoms. In other embodiments, a carbocyclyl comprises five to seven carbon atoms. The carbocyclyl is attached to the rest of the molecule by a single bond. Carbocyclyl is saturated, (*i.e.*, containing single C-C bonds only) or unsaturated (*i.e.*, containing one or more double bonds or triple bonds). A fully saturated carbocyclyl radical is also referred to as "cycloalkyl." Examples of monocyclic cycloalkyls include, *e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. In certain embodiments, a cycloalkyl comprises three to eight carbon atoms (*e.g.*, C_3-C_8 cycloalkyl). In other embodiments, a cycloalkyl comprises three to seven carbon atoms (*e.g.*, C_3-C_7 cycloalkyl). In other embodiments, a cycloalkyl comprises three to six carbon atoms (*e.g.*, C_3-C_6 cycloalkyl). In other embodiments, a cycloalkyl comprises three to five carbon atoms (*e.g.*, C_3-C_5 cycloalkyl). In other embodiments, a cycloalkyl comprises three to four carbon atoms (*e.g.*, C_3-C_4 cycloalkyl). An unsaturated carbocyclyl is also referred to as "cycloalkenyl." Examples of monocyclic cycloalkenyls include, *e.g.*, cyclopentenyl, cyclohexenyl, cycloheptenyl, and cyclooctenyl. Polycyclic carbocyclyl radicals include, for example, adamantyl, norbornyl (*i.e.*, bicyclo[2.2.1]heptanyl), norbornenyl, decalinyl, 7,7-dimethyl-bicyclo[2.2.1]heptanyl, and the like. Unless otherwise stated specifically in the specification, the term "carbocyclyl" is meant to include carbocyclyl radicals that are optionally substituted by one or more substituents independently selected from alkyl, alkenyl, alkynyl, halo, fluoroalkyl, oxo, thioxo, cyano, nitro, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted carbocyclyl, optionally substituted carbocyclylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl, heteroarylalkyl, $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 1 or 2) and $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2), where each R^a is independently hydrogen, alkyl, fluoroalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl, each R^b is independently a direct bond or a straight or branched alkylene or alkenylene chain, and R^c is a straight or

branched alkylene or alkenylene chain, and where each of the above substituents is unsubstituted unless otherwise indicated.

[0076] "Carbocyclylalkyl" refers to a radical of the formula $–R^c$-carbocyclyl where R^c is an alkylene chain as defined above. The alkylene chain and the carbocyclyl radical is optionally substituted as defined above.

[0077] "Halo" or "halogen" refers to bromo, chloro, fluoro or iodo substituents.

[0078] "Fluoroalkyl" refers to an alkyl radical, as defined above, that is substituted by one or more fluoro radicals, as defined above, for example, trifluoromethyl, difluoromethyl, fluoromethyl, 2,2,2-trifluoroethyl, 1-fluoromethyl-2-fluoroethyl, and the like. In some embodiments, the alkyl part of the fluoroalkyl radical is optionally substituted as defined above for an alkyl group.

[0079] "Heterocyclyl" refers to a stable 3- to 18-membered non-aromatic ring radical that comprises two to twelve carbon atoms and from one to six heteroatoms selected from nitrogen, oxygen and sulfur. Unless stated otherwise specifically in the specification, the heterocyclyl radical is a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which includes fused or bridged ring systems. The heteroatoms in the heterocyclyl radical are optionally oxidized. One or more nitrogen atoms, if present, are optionally quaternized. The heterocyclyl radical is partially or fully saturated. In some embodiments, the heterocyclyl is attached to the rest of the molecule through any atom of the ring(s). Examples of such heterocyclyl radicals include, but are not limited to, dioxolanyl, thienyl[1,3]dithianyl, decahydroisoquinolyl, imidazolinyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, octahydroindolyl, octahydroisoindolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, oxazolidinyl, piperidinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, pyrazolidinyl, quinuclidinyl, thiazolidinyl, tetrahydrofuryl, trithianyl, tetrahydropyranyl, thiomorpholinyl, thiamorpholinyl, 1-oxo-thiomorpholinyl, and 1,1-dioxo-thiomorpholinyl. Unless stated otherwise specifically in the specification, the term "heterocyclyl" is meant to include heterocyclyl radicals as defined above that are optionally substituted by one or more substituents selected from alkyl, alkenyl, alkynyl, halo, fluoroalkyl, oxo, thioxo, cyano, nitro, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted carbocyclyl, optionally substituted carbocyclylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR$

^{a}, -R^{b}-N(R^{a})C(O)R^{a}, -R^{b}-N(R^{a})S(O)$_{t}R^{a}$ (where t is 1 or 2), -R^{b}-S(O)$_{t}OR^{a}$ (where t is 1 or 2), -R^{b}-S(O)$_{t}R^{a}$ (where t is 1 or 2) and -R^{b}-S(O)$_{t}$N(R^{a})$_{2}$ (where t is 1 or 2), where each R^{a} is independently hydrogen, alkyl, fluoroalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl, each R^{b} is independently a direct bond or a straight or branched alkylene or alkenylene chain, and R^{c} is a straight or branched alkylene or alkenylene chain, and where each of the above substituents is unsubstituted unless otherwise indicated. The terms "heterocyclyl", “heterocycle”, and “heterocycloalkyl” are used interchangeably.

[0080] "Heterocyclylalkyl" refers to a radical of the formula –R^{c}-heterocyclyl where R^{c} is an alkylene chain as defined above. If the heterocyclyl is a nitrogen-containing heterocyclyl, the heterocyclyl is optionally attached to the alkyl radical at the nitrogen atom. The alkylene chain of the heterocyclylalkyl radical is optionally substituted as defined above for an alkylene chain. The heterocyclyl part of the heterocyclylalkyl radical is optionally substituted as defined above for a heterocyclyl group.

[0081] "Heterocyclylalkoxy" refers to a radical bonded through an oxygen atom of the formula –O-R^{c}-heterocyclyl where R^{c} is an alkylene chain as defined above. If the heterocyclyl is a nitrogen-containing heterocyclyl, the heterocyclyl is optionally attached to the alkyl radical at the nitrogen atom. The alkylene chain of the heterocyclylalkoxy radical is optionally substituted as defined above for an alkylene chain. The heterocyclyl part of the heterocyclylalkoxy radical is optionally substituted as defined above for a heterocyclyl group.

[0082] "Heteroaryl" refers to a radical derived from a 3- to 18-membered aromatic ring radical that comprises two to seventeen carbon atoms and from one to six heteroatoms selected from nitrogen, oxygen and sulfur. As used herein, the heteroaryl radical is a monocyclic, bicyclic, tricyclic or tetracyclic ring system, wherein at least one of the rings in the ring system is fully unsaturated, *i.e.*, it contains a cyclic, delocalized (4n+2) π–electron system in accordance with the Hückel theory. Heteroaryl includes fused or bridged ring systems. The heteroatom(s) in the heteroaryl radical is optionally oxidized. One or more nitrogen atoms, if present, are optionally quaternized. The heteroaryl is attached to the rest of the molecule through any atom of the ring(s). Examples of heteroaryls include, but are not limited to, azepinyl, acridinyl, benzimidazolyl, benzindolyl, 1,3-benzodioxolyl, benzofuranyl, benzooxazolyl, benzo[d]thiazolyl, benzothiadiazolyl, benzo[*b*][1,4]dioxepinyl, benzo[b][1,4]oxazinyl, 1,4-benzodioxanyl, benzonaphthofuranyl, benzoxazolyl, benzodioxolyl, benzodioxinyl, benzopyranyl, benzopyranonyl, benzofuranyl, benzofuranonyl, benzothienyl (benzothiophenyl),

benzothieno[3,2-d]pyrimidinyl, benzotriazolyl, benzo[4,6]imidazo[1,2-a]pyridinyl, carbazolyl, cinnolinyl, cyclopenta[d]pyrimidinyl, 6,7-dihydro-5H-cyclopenta[4,5]thieno[2,3-d]pyrimidinyl, 5,6-dihydrobenzo[h]quinazolinyl, 5,6-dihydrobenzo[h]cinnolinyl, 6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazinyl, dibenzofuranyl, dibenzothiophenyl, furanyl, furanonyl, furo[3,2-c]pyridinyl, 5,6,7,8,9,10-hexahydrocycloocta[d]pyrimidinyl, 5,6,7,8,9,10-hexahydrocycloocta[d]pyridazinyl, 5,6,7,8,9,10-hexahydrocycloocta[d]pyridinyl, isothiazolyl, imidazolyl, indazolyl, indolyl, indazolyl, isoindolyl, indolinyl, isoindolinyl, isoquinolyl, indolizinyl, isoxazolyl, 5,8-methano-5,6,7,8-tetrahydroquinazolinyl, naphthyridinyl, 1,6-naphthyridinonyl, oxadiazolyl, 2-oxoazepinyl, oxazolyl, oxiranyl, 5,6,6a,7,8,9,10,10a-octahydrobenzo[h]quinazolinyl, 1-phenyl-1*H*-pyrrolyl, phenazinyl, phenothiazinyl, phenoxazinyl, phthalazinyl, pteridinyl, purinyl, pyrrolyl, pyrazolyl, pyrazolo[3,4-d]pyrimidinyl, pyridinyl, pyrido[3,2-d]pyrimidinyl, pyrido[3,4-d]pyrimidinyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrrolyl, quinazolinyl, quinoxalinyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, 5,6,7,8-tetrahydroquinazolinyl, 5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidinyl, 6,7,8,9-tetrahydro-5H-cyclohepta[4,5]thieno[2,3-d]pyrimidinyl, 5,6,7,8-tetrahydropyrido[4,5-c]pyridazinyl, thiazolyl, thiadiazolyl, triazolyl, tetrazolyl, triazinyl, thieno[2,3-d]pyrimidinyl, thieno[3,2-d]pyrimidinyl, thieno[2,3-c]pyridinyl, and thiophenyl (*i.e.* thienyl). Unless stated otherwise specifically in the specification, the term "heteroaryl" is meant to include heteroaryl radicals as defined above which are optionally substituted by one or more substituents selected from alkyl, alkenyl, alkynyl, halo, fluoroalkyl, haloalkenyl, haloalkynyl, oxo, thioxo, cyano, nitro, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted carbocyclyl, optionally substituted carbocyclylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 1 or 2) and $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2), where each R^a is independently hydrogen, alkyl, fluoroalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl, each R^b is independently a direct bond or a straight or branched alkylene or alkenylene chain, and R^c is a straight or

branched alkylene or alkenylene chain, and where each of the above substituents is unsubstituted unless otherwise indicated.

[0083] "*N*-heteroaryl" refers to a heteroaryl radical as defined above containing at least one nitrogen and where the point of attachment of the heteroaryl radical to the rest of the molecule is through a nitrogen atom in the heteroaryl radical. An *N*-heteroaryl radical is optionally substituted as described above for heteroaryl radicals.

[0084] "*C*-heteroaryl" refers to a heteroaryl radical as defined above and where the point of attachment of the heteroaryl radical to the rest of the molecule is through a carbon atom in the heteroaryl radical. A *C*-heteroaryl radical is optionally substituted as described above for heteroaryl radicals.

[0085] "Heteroaryloxy" refers to radical bonded through an oxygen atom of the formula –O-heteroaryl, where heteroaryl is as defined above.

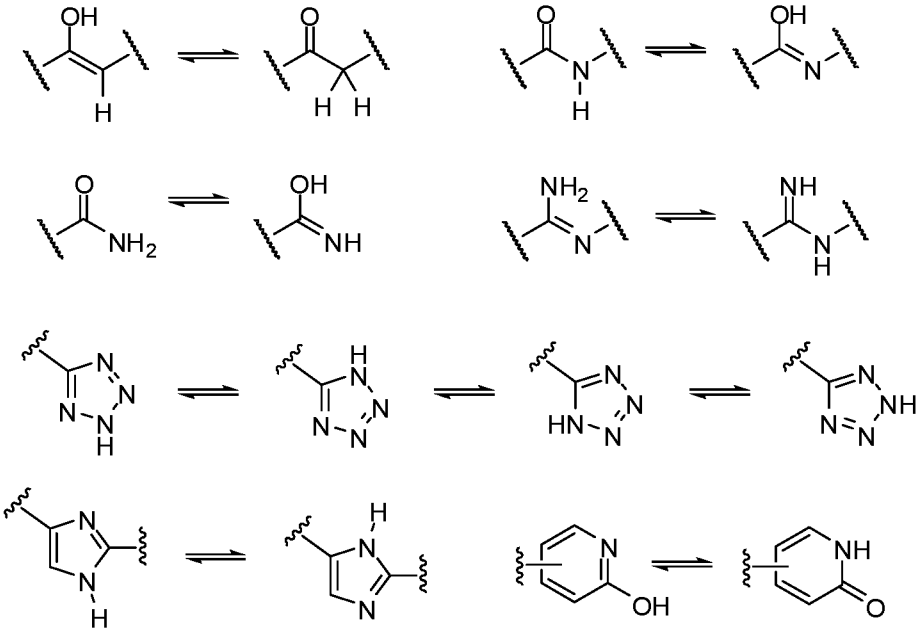
[0086] "Heteroarylalkyl" refers to a radical of the formula –R^c-heteroaryl, where R^c is an alkylene chain as defined above. If the heteroaryl is a nitrogen-containing heteroaryl, the heteroaryl is optionally attached to the alkyl radical at the nitrogen atom. The alkylene chain of the heteroarylalkyl radical is optionally substituted as defined above for an alkylene chain. The heteroaryl part of the heteroarylalkyl radical is optionally substituted as defined above for a heteroaryl group.

[0087] "Heteroarylalkoxy" refers to a radical bonded through an oxygen atom of the formula –O-R^c-heteroaryl, where R^c is an alkylene chain as defined above. If the heteroaryl is a nitrogen-containing heteroaryl, the heteroaryl is optionally attached to the alkyl radical at the nitrogen atom. The alkylene chain of the heteroarylalkoxy radical is optionally substituted as defined above for an alkylene chain. The heteroaryl part of the heteroarylalkoxy radical is optionally substituted as defined above for a heteroaryl group.

[0088] In some embodiments, he compounds disclosed herein contain one or more asymmetric centers and thus give rise to enantiomers, diastereomers, and other stereoisomeric forms that are defined, in terms of absolute stereochemistry, as (*R*)- or (*S*)-. Unless stated otherwise, it is intended that all stereoisomeric forms of the compounds disclosed herein are contemplated by this disclosure. When the compounds described herein contain alkene double bonds, and unless specified otherwise, it is intended that this disclosure includes both *E* and Z geometric isomers (*e.g., cis* or *trans*.) Likewise, all possible isomers, as well as their racemic and optically pure forms, and all tautomeric forms are also intended to be included. The term "geometric isomer" refers to *E* or Z geometric isomers (*e.g., cis* or *trans*) of an alkene double bond. The term

"positional isomer" refers to structural isomers around a central ring, such as *ortho*-, *meta*-, and *para*- isomers around a benzene ring.

[0089] A "tautomer" refers to a molecule wherein a proton shift from one atom of a molecule to another atom of the same molecule is possible. In certain embodiments, the compounds presented herein exist as tautomers. In circumstances where tautomerization is possible, a chemical equilibrium of the tautomers will exist. The exact ratio of the tautomers depends on several factors, including physical state, temperature, solvent, and pH. Some examples of tautomeric equilibrium include:



[0090] "Optional" or "optionally" means that a subsequently described event or circumstance may or may not occur and that the description includes instances when the event or circumstance occurs and instances in which it does not. For example, "optionally substituted aryl" means that the aryl radical may or may not be substituted and that the description includes both substituted aryl radicals and aryl radicals having no substitution.

[0091] "Pharmaceutically acceptable salt" includes both acid and base addition salts. A pharmaceutically acceptable salt of any one of the compounds described herein is intended to encompass any and all pharmaceutically suitable salt forms. Preferred pharmaceutically acceptable salts of the compounds described herein are pharmaceutically acceptable acid addition salts and pharmaceutically acceptable base addition salts.

[0092] "Pharmaceutically acceptable acid addition salt" refers to those salts which retain the biological effectiveness and properties of the free bases, which are not biologically or otherwise undesirable, and which are formed with inorganic acids such as hydrochloric

acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, hydroiodic acid, hydrofluoric acid, phosphorous acid, and the like. Also included are salts that are formed with organic acids such as aliphatic mono- and dicarboxylic acids, phenyl-substituted alkanoic acids, hydroxy alkanoic acids, alkanedioic acids, aromatic acids, aliphatic and. aromatic sulfonic acids, etc. and include, for example, acetic acid, trifluoroacetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. Exemplary salts thus include sulfates, pyrosulfates, bisulfates, sulfites, bisulfites, nitrates, phosphates, monohydrogenphosphates, dihydrogenphosphates, metaphosphates, pyrophosphates, chlorides, bromides, iodides, acetates, trifluoroacetates, propionates, caprylates, isobutyrates, oxalates, malonates, succinate suberates, sebacates, fumarates, maleates, mandelates, benzoates, chlorobenzoates, methylbenzoates, dinitrobenzoates, phthalates, benzenesulfonates, toluenesulfonates, phenylacetates, citrates, lactates, malates, tartrates, methanesulfonates, and the like. Also contemplated are salts of amino acids, such as arginates, gluconates, and galacturonates (see, for example, Berge S.M. et al., "Pharmaceutical Salts," *Journal of Pharmaceutical Science,* 66:1-19 (1997)). Acid addition salts of basic compounds are prepared by contacting the free base forms with a sufficient amount of the desired acid to produce the salt.

[0093] "Pharmaceutically acceptable base addition salt" refers to those salts that retain the biological effectiveness and properties of the free acids, which are not biologically or otherwise undesirable. These salts are prepared from addition of an inorganic base or an organic base to the free acid. In some embodiments, pharmaceutically acceptable base addition salts are formed with metals or amines, such as alkali and alkaline earth metals or organic amines. Salts derived from inorganic bases include, but are not limited to, sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Salts derived from organic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, for example, isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, diethanolamine, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, *N,N*-dibenzylethylenediamine, chloroprocaine, hydrabamine, choline, betaine, ethylenediamine, ethylenedianiline, *N*-methylglucamine, glucosamine, methylglucamine,

theobromine, purines, piperazine, piperidine, *N*-ethylpiperidine, polyamine resins and the like. See Berge et al., *supra*.

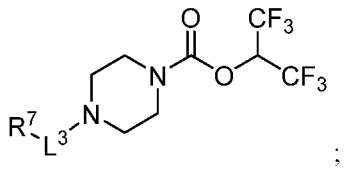
[0094] As used herein, "treatment" or "treating " or "palliating" or "ameliorating" are used interchangeably herein. These terms refers to an approach for obtaining beneficial or desired results including but not limited to therapeutic benefit and/or a prophylactic benefit. By "therapeutic benefit" is meant eradication or amelioration of the underlying disorder being treated. Also, a therapeutic benefit is achieved with the eradication or amelioration of one or more of the physiological symptoms associated with the underlying disorder such that an improvement is observed in the patient, notwithstanding that the patient is still afflicted with the underlying disorder. For prophylactic benefit, the compositions are administered to a patient at risk of developing a particular disease, or to a patient reporting one or more of the physiological symptoms of a disease, even though a diagnosis of this disease has not been made.

Embodiments of the Invention

[0095] In the following, embodiments of the invention are disclosed. The first embodiment is denoted E1, the second embodiment E2 and so forth.

[0096] In a first embodiment E1 the present invention relates to a method of treating a disease with a compound of Formula (I).

[0097] E1: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (I):



;

Formula (I);

wherein:

L^3 is a bond, -CH_2-, -$S(O)_2$-, or -C(O)-;

R^7 is phenyl; wherein R^7 is optionally substituted by one, two, or three moieties independently selected from R^h;

R^a and R^b are independently selected, for each occurrence, from the group consisting of hydrogen and C_{1-3}alkyl; wherein C_{1-3}alkyl is optionally substituted by one or more substituents selected from halogen, cyano, oxo, hydroxyl, heterocycle, and phenyl;

or R^a and R^b, when they occur together with the nitrogen to which they are attached, form a 4-6 membered saturated heterocyclic ring, which may have an additional

heteroatom selected from O, S, and N, or a spirocyclic ring selected from 8-oxa-2-azaspiro[4.5]decane and 2,8-diazaspiro[4.5]decane, wherein the 4-6 membered saturated heterocyclic ring or the spirocyclic ring are optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl;

R^c is selected from the group consisting of halogen, hydroxyl, C_{1-6}alkyl (optionally substituted by one, two, or three halogens), and C_{1-6}alkoxy (optionally substituted by one, two, or three halogens); and

R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from R^c), hydroxyl, cyano, C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), R^aR^bN-, R^a-C(O)NR^a-, R^aR^bN-SO_2-, R^aR^bN-C(O)-, R^a-$S(O)_w$- (wherein w is 0, 1 or 2), R^a-SO_2-NR^b-, and heteroaryl (optionally substituted by one, two or three moieties each independently selected from R^c);

or a pharmaceutically acceptable salt or solvate thereof.

[0098] E2: The method of embodiment 1, wherein L^3 is a -CH_2-.

[0099] E3: The method of embodiment 1, wherein L^3 is a -CH_2-; and R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from halogen, methyl, ethyl, propyl, t-butyl, and CF_3), C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), R^aR^bN-, R^aR^bN-C(O)-, and heteroaryl (optionally substituted by one, two or three moieties each independently selected from C_{1-6}alkyl or halogen).

[00100] E4: The method of embodiment 1, wherein L^3 is a -CH_2-; and R^h is selected from the group consisting of: halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), and R^aR^bN-.

[00101] E5: The method of embodiment 1, wherein R^7 is substituted by two moieties independently selected from R^h.

[00102] E6: The method of embodiment 1, wherein L^3 is a -CH_2-; and R^7 is substituted by R^aR^bN- and a moiety selected from the group consisting of: halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens), and C_{1-6}alkoxy (optionally substituted by one, two or three halogens).

[00103] E7: The method of embodiment 6, wherein R^a and R^b, together with the nitrogen to which they are attached, form a 4-6 membered saturated heterocyclic ring, which may have an additional heteroatom selected from O, S, and N, and the 4-6 membered saturated heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl.

[00104] E8: The method of embodiment 7, wherein the 4-6 membered saturated heterocyclic ring is selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine, and the 4-6 membered saturated heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl.

[00105] E9: The method of embodiment 7, wherein the 4-6 membered saturated heterocyclic ring is pyrrolidine.

[00106] E10: The method of embodiment 7, wherein the 4-6 membered saturated heterocyclic ring is morpholine.

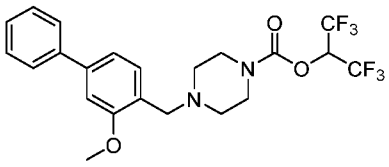
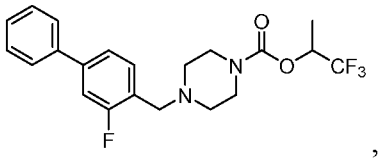
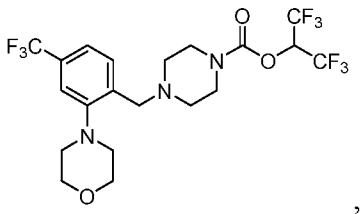
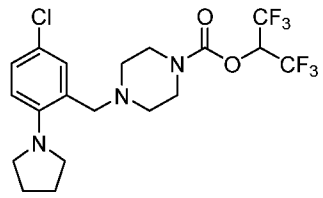
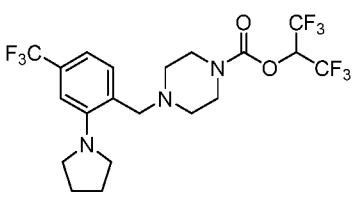
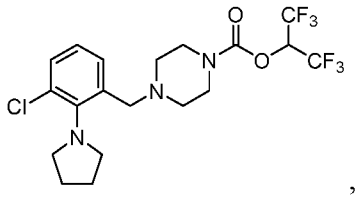
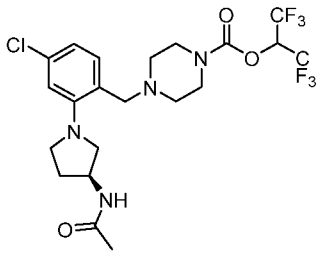
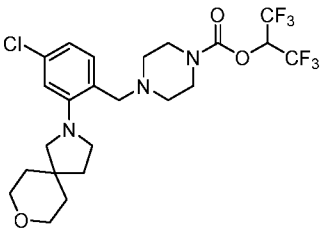
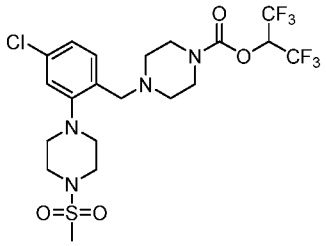
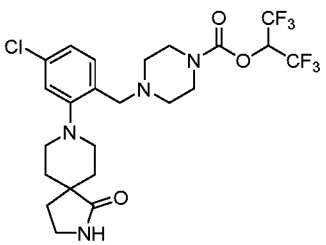
[00107] E11: The method of embodiment 7, wherein the 4-6 membered saturated heterocyclic ring is piperidine.

[00108] E12: The method of embodiment 1, wherein L^3 is a -CH_2-; and R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from halogen, methyl, ethyl, propyl, t-butyl, and CF_3), C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), and heteroaryl (optionally substituted by one, two or three moieties each independently selected from C_{1-6}alkyl or halogen).

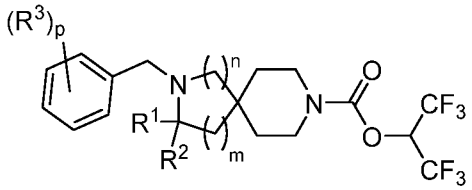
[00109] E13: The method of embodiment 12, wherein R^7 is substituted by two moieties independently selected from R^h.

[00110] E14: The method of embodiment 1, wherein L^3 is a -CH_2-; and R^h is selected from the group consisting of: halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), and R^aR^bN-.

[00111] E15: The method of embodiment 14, wherein R^7 is substituted by two moieties independently selected from R^h.

[00112] E16: The method of embodiment 1, wherein the compound of Formula (I) is selected from:  ,  ,  ,  ,  ,  ,  ,  ,  , and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00113] E17: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (II):



Formula (II);

wherein:

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, heterocycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), heteroaryl, -SF_5, -NR^5R^6, -OR^7, -CO_2R^8, -$C(O)R^8$, and -$C(O)NR^8R^9$, wherein heterocycloalkyl and -C_{1-6}alkyl(heterocycloalkyl) are optionally substituted with

one or two R^4; or two adjacent R^3 form a heterocycloalkyl ring optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, halogen, oxo, -CN, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$;

each R^5 and R^6 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-C_{1-6}$alkyl-C(O)(heterocycloalkyl), heterocycloalkyl, aryl, and heteroaryl; or R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-C_{1-6}$alkyl-C(O)(heterocycloalkyl), heterocycloalkyl, aryl, and heteroaryl, wherein heterocycloalkyl, aryl, and heteroaryl are optionally substituted with one or two groups selected from oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and $C(O)NH_2$;

each R^8 and R^9 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, aryl, and heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one or two groups selected from C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and $C(O)NH_2$;

each R^{10} is independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-6}haloalkyl, halogen, oxo, -CN, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$;

p is 0, 1, 2, 3, 4, or 5;

n is 0 or 1; and

m is 1 or 2; provided that when n is 0, then m is 2; and when n is 1, then m is 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00114] E18: The method of embodiment 17, wherein each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkynyl, halogen, -CN, C_{1-6}haloalkyl, heterocycloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), heteroaryl, $-SF_5$, $-NR^5R^6$, $-OR^7$, $-CO_2R^8$, and $-C(O)NR^8R^9$.

[00115] E19: The method of embodiment 17 or embodiment 18, wherein R^1 and R^2 are both H.

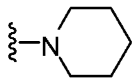
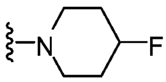
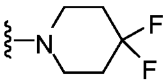
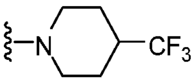
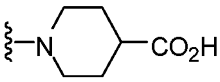
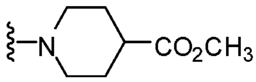
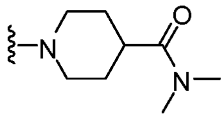
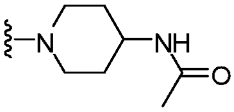
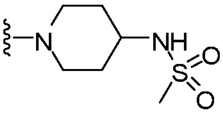
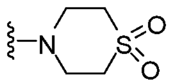
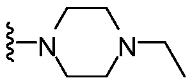
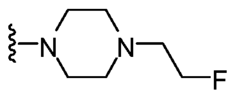
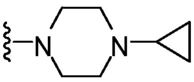
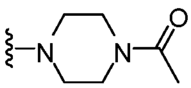
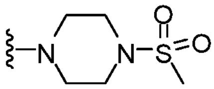
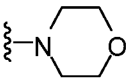
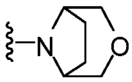
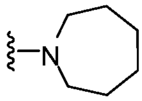
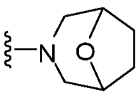
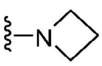
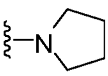
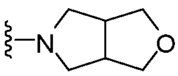
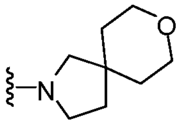
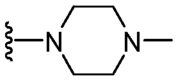
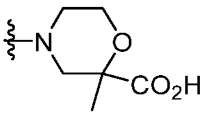
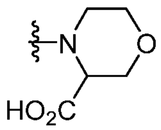
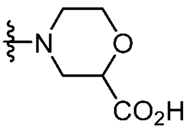
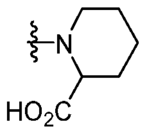
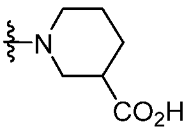
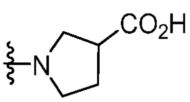
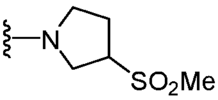
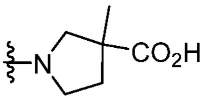
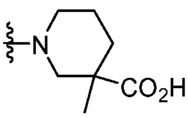
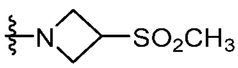
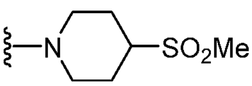
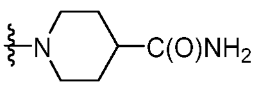
[00116] E20: The method of any one of embodiments 17-19, wherein each R^3 is independently selected from halogen, C_{1-6}haloalkyl, $-NR^5R^6$, and $-OR^7$.

[00117] E21: The method of any one of embodiments 17-20, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one or two R^{10} independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-}

${}_6$haloalkyl, halogen, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$.

[00118] E22: The method of embodiment 21, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring substituted with one or two R^{10} independently selected from $C_{1\text{-}6}$alkyl and $-CO_2H$.

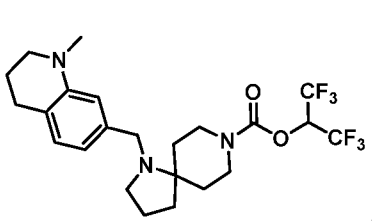
[00119] E23: The method of embodiment 21, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted heterocycloalkyl ring.

[00120] E24: The method of any one of embodiments 17-20, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10} selected from:  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  .

[00121] E25: The method of any one of embodiments 17-24, wherein p is 1 or 2.

[00122] E26: The method of any one of embodiments 17-25, wherein n is 0 and m is 2.

[00123] E27: The method of embodiment 17, wherein the compound of Formula (II) is selected from: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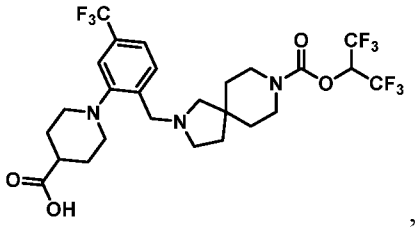
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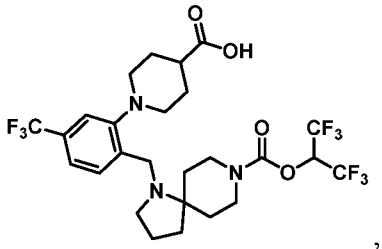
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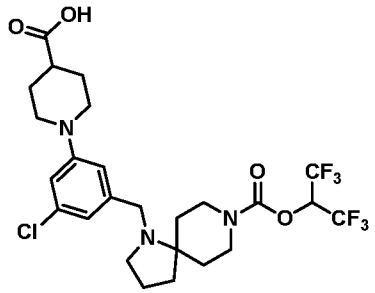
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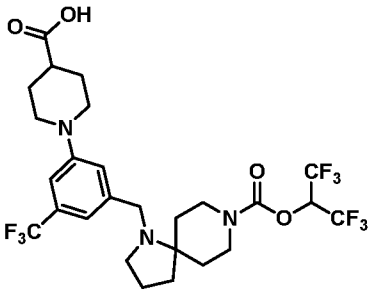
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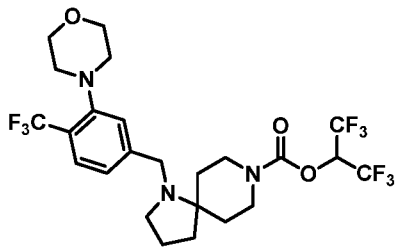
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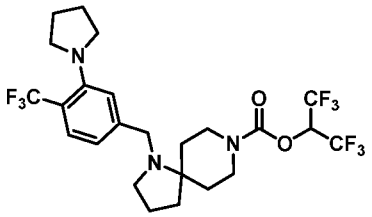
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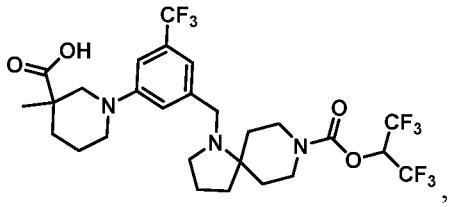
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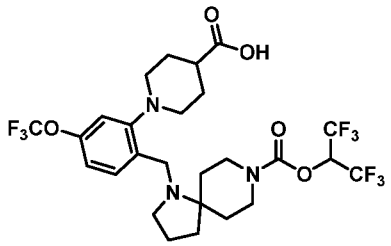
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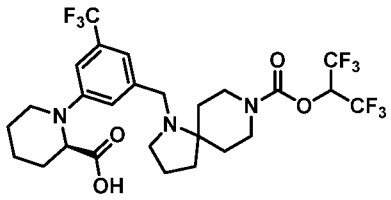
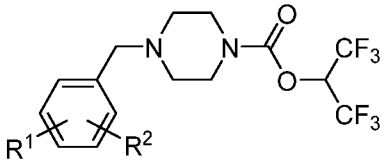

; or a pharmaceutically acceptable salt or solvate thereof.

[00124] E28: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (III):



Formula (III);

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

each R^9 is independently selected from H and C_{1-6}alkyl;

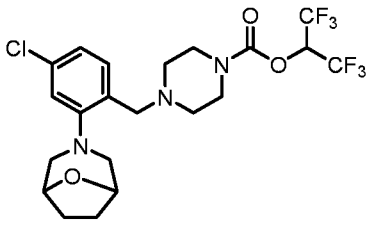
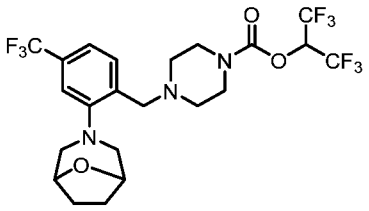
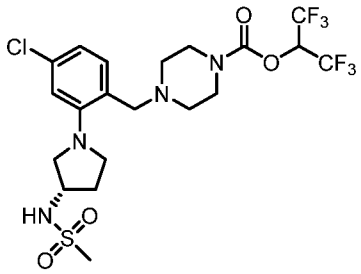
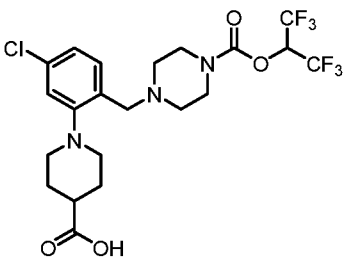
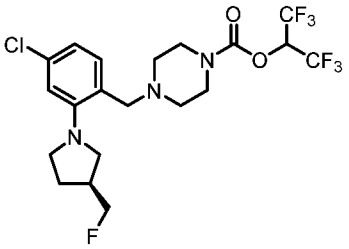
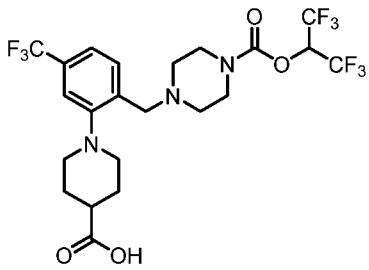
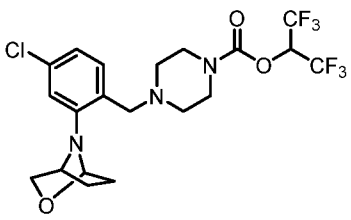
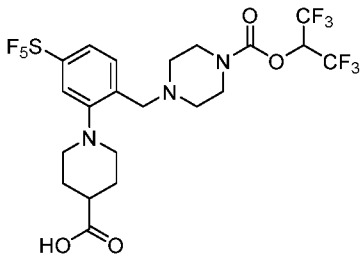
or a pharmaceutically acceptable salt or solvate thereof.

[00125] E29: The method of embodiment 28, wherein R^1 is halogen, $-SF_5$, or optionally substituted C_{1-6}alkyl optionally substituted by halogen.

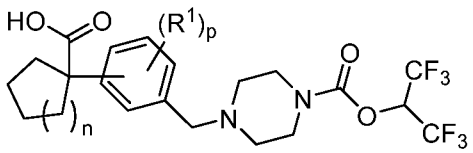
[00126] E30: The method of embodiment 28 or embodiment 29, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S.

[00127] E31: The method of embodiment 30, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine.

[00128] E32: The method of embodiment 28 or embodiment 29, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl.

[00129] E33: The method of embodiment 28, wherein the compound of Formula (III) is selected from:  ,  ,  ,  ,  ,  ,  , and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00130] E34: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (IV):



Formula (IV);

wherein:

each R^1 is independently halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, -CN, or $-SF_5$;

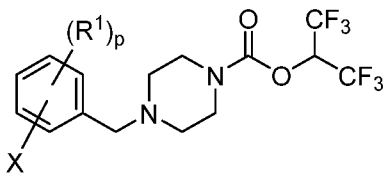
n is 1 or 2; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

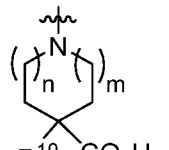
[00131] E35: The method of embodiment 34, wherein n is 1.

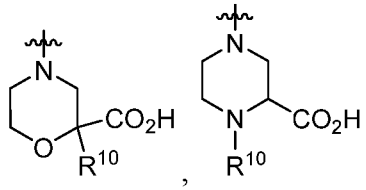
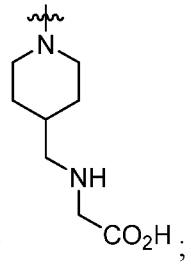
[00132] E36: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (V):



Formula (V);

wherein:

X is $-N(R^2)(R^3)$, $-C_{1-6}$alkyl$-N(R^4)(R^5)$, $-C(O)N(R^4)(R^5)$,  ,

 , , or  ;

each R^1 is independently halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, -CN, or $-SF_5$;

R^2 and R^3, together with the nitrogen to which they are attached, form

(i) a C_2-C_8heterocycloalkyl; or

(ii) a C_2-C_8heteroaryl;

wherein the C_2-C_8heterocycloalkyl or the C_2-C_8heteroaryl is substituted with one R^6 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^4 and R^5, together with the nitrogen to which they are attached, form

(i) a C_2-C_8heterocycloalkyl; or

(ii) a C_2-C_8heteroaryl;

wherein the C_2-C_8heterocycloalkyl or the C_2-C_8heteroaryl is substituted with one R^7 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^6 is $-C_{1-6}$alkyl$-CO_2H$ or $-N(R^8)-C_{1-6}$alkyl$-CO_2H$;

R^7 is $-CO_2H$, $-C_{1-6}$alkyl$-CO_2H$, or $-N(R^9)-C_{1-6}$alkyl$-CO_2H$;

R^8 is H or C_{1-6}alkyl;

R^9 is H or C_{1-6}alkyl;

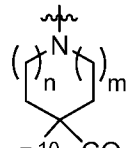
R^{10} is C_{1-6}alkyl;

m is 0, 1, or 2;

n is 0 or 1; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.



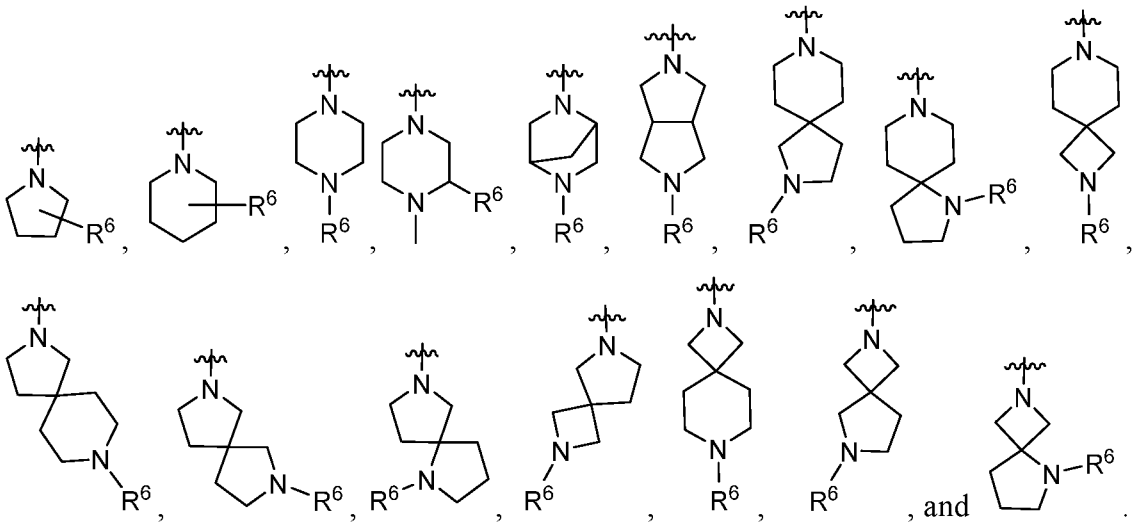
[00133] E37: The method of embodiment 36, wherein X is .

[00134] E38: The method of embodiment 37, wherein m is 1 and n is 1.

[00135] E39: The method of embodiment 36, wherein X is $-N(R^2)(R^3)$.

[00136] E40: The method of embodiment 39, wherein R^2 and R^3, together with the nitrogen to which they are attached, form a C_2-C_8heterocycloalkyl substituted with one R^6.

[00137] E41: The method of embodiment 40, wherein R^2 and R^3, together with the nitrogen to which they are attached, form a C_2-C_8heterocycloalkyl selected from:



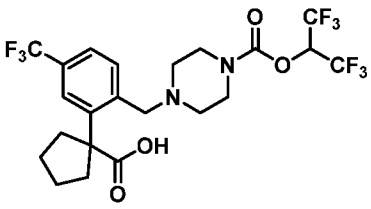
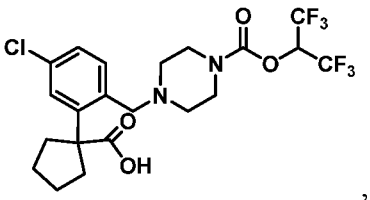
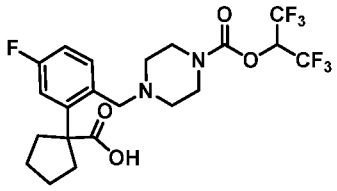
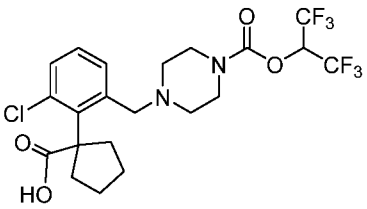
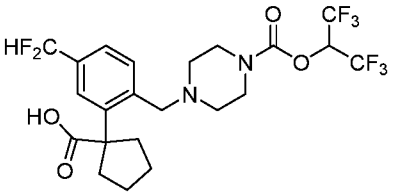
[00138] E42: The method of embodiment 40 or embodiment 41, wherein R^6 is $-C_{1-6}$alkyl-CO_2H.

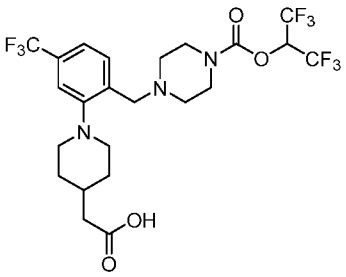
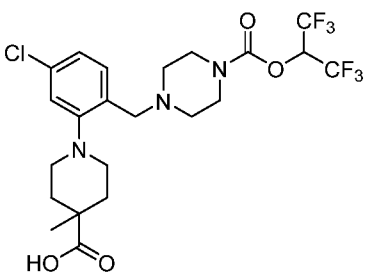
[00139] E43: The method of any one of embodiments 34-42, wherein each R^1 is independently halogen.

[00140] E44: The method of any one of embodiments 34-42, wherein each R^1 is independently C_{1-6}haloalkyl.

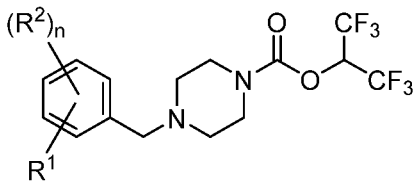
[00141] E45: The method of any one of embodiments 34-42, wherein each R^1 is independently C_{1-6}alkyl.

[00142] E46: The method of any one of embodiments 34-45, wherein p is 1.

[00143] E47: The method of embodiment 34, wherein the compound of Formula (IV) is selected from:  ,  ,  ,  , and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00144] E48: The method of embodiment 36, wherein the compound of Formula (V) is selected from:  and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00145] E49: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VI):



Formula (VI);

wherein:

R^1 is $-N(R^3)(R^5)$ or $-NH(R^4)$;

each R^2 is independently selected from halogen, C_{1-6}alkyl, -CN, C_{1-6}haloalkyl, and $-OR^6$;

R^3 is $-CH_2CO_2H$, $-CH_2CH_2CO_2H$, or $-CH(CH_3)CO_2H$;

R^4 is $-(CH_2)_m-CO_2H$;

R^5 is H or C_{1-3}alkyl;

each R^6 is independently selected from H, C_{1-6}alkyl, and C_{1-6}haloalkyl;

n is 0, 1, 2, 3, or 4; and

m is 3;

or a pharmaceutically acceptable salt or solvate thereof.

[00146] E50: The method of embodiment 49, wherein R^1 is -N(R^3)(R^5).

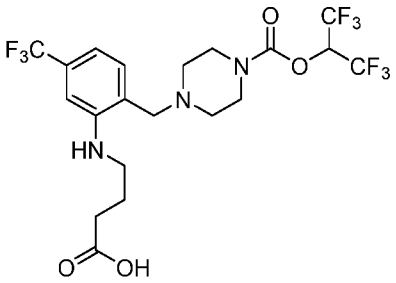
[00147] E51: The method of embodiment 50, wherein R^5 is H.

[00148] E52: The method of embodiment 49, wherein R^1 is -NH(R^4).

[00149] E53: The method of any one of embodiments 49-52, wherein each R^2 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl.

[00150] E54: The method of any one of embodiments 49-53, wherein n is 1.

[00151] E55: The method of embodiment 49, wherein the compound of Formula (VI) is selected from: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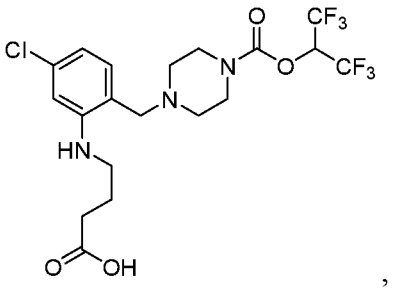
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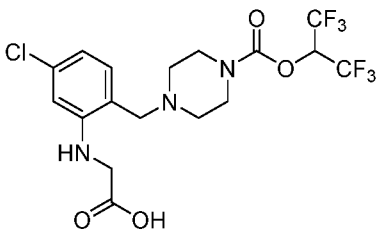
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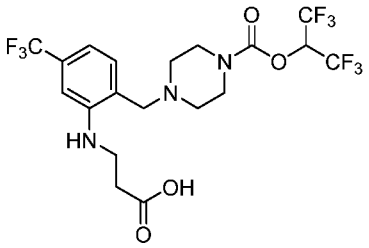
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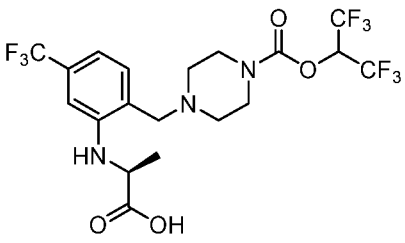
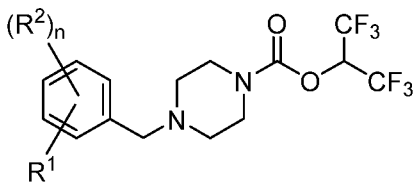

; or a pharmaceutically acceptable salt or solvate thereof.

[00152] E56: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VII):



Formula (VII);

wherein:

R^1 is $-R^{14}$, $-OR^3$, $-SR^4$, $-S(O)_2R^4$, or $-C\equiv C-(CR^6R^7)-R^8$;

each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-OR^{17}$, and $-C(O)NR^{18}R^{19}$;

R^3 is $-(CR^6R^7)_m-R^8$, $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$, or $-(CR^6R^7)_t-C_{3-6}$cycloalkyl-R^8;

R^4 is $-(CR^6R^7)_m-R^{8'}$, $-(CR^6R^7)_v-C(O)OH$, or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

Y is -O- or $-N(R^{22})-$;

each R^6 and R^7 is each independently selected from H, F, and C_{1-6}alkyl; or R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring;

R^8 is $-C(O)OR^9$, $-C(O)R^{10}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

$R^{8'}$ is $-C(O)OR^{9'}$, $-C(O)R^{10'}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

R^9 is H or C_{1-6}alkyl;

$R^{9'}$ is C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl or $-NHSO_2R^{21}$;

$R^{10'}$ is C_{2-6}alkyl or $-NHSO_2R^{21}$;

R^{11} is C_{1-6}alkyl or C_{1-6}alkoxy;

R^{12} and R^{13} is each independently H or C_{1-6}alkyl;

R^{14} is $-(CR^{15}R^{16})_m-R^8$ or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

each R^{15} and R^{16} is each independently selected from H, F, and C_{1-6}alkyl;

each R^{17} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-6}cycloalkyl;

each R^{18} and R^{19} is each independently selected from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, aryl, and heteroaryl; or R^{18} and R^{19}, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{20};

each R^{20} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

R^{21} is C_{1-6}alkyl or C_{3-6}cycloalkyl;

R^{22} is H, C_{1-6}alkyl, or $-SO_2R^{23}$;

R^{23} is C_{1-6}alkyl;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3, or 4;

p is 2, 3, or 4;

q is 1, 2, or 3;

t is 0, 1, or 2; and

v is 3 or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[00153] E57: The method of embodiment 56, wherein R^1 is $-OR^3$.

[00154] E58: The method of embodiment 57, wherein R^3 is $-(CR^6R^7)_m-R^8$.

[00155] E59: The method of embodiment 58, wherein m is 1, 2, or 3.

[00156] E60: The method of embodiment 59, wherein each R^6 and R^7 is each independently selected from H and C_{1-6}alkyl, or R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring.

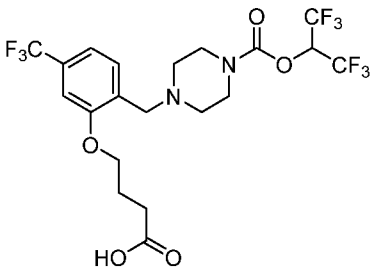
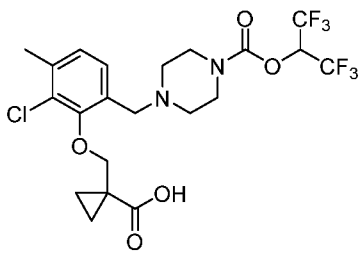
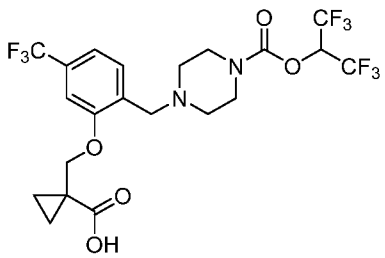
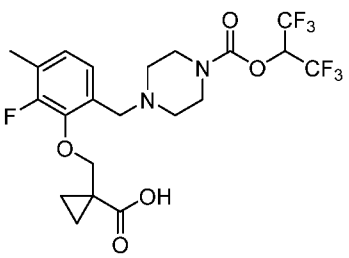
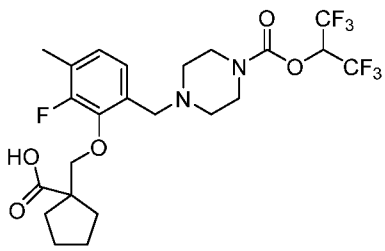
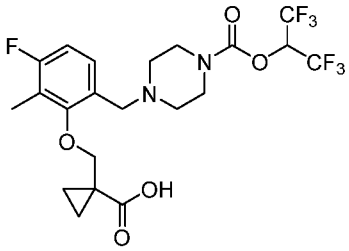
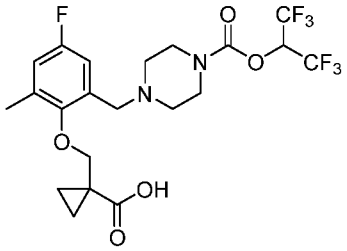
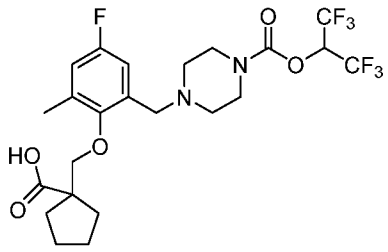
[00157] E61: The method of embodiment 60, wherein R^8 is $-C(O)OR^9$.

[00158] E62: The method of embodiment 61, wherein R^9 is H.

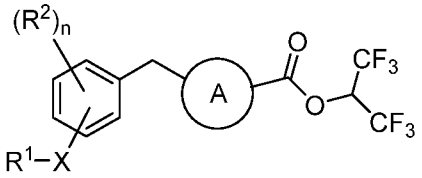
[00159] E63: The method of any one of embodiments 56-62, wherein each R^2 is independently selected from C_{1-6}alkyl, halogen, and C_{1-6}haloalkyl.

[00160] E64: The method of embodiment 63, wherein n is 2.

[00161] E65: The method of embodiment 63, wherein n is 1.

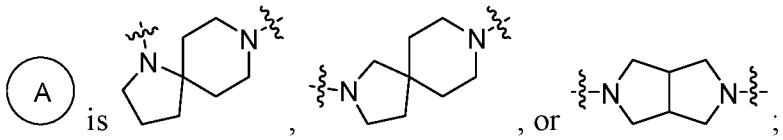
[00162] E66: The method of embodiment 56, wherein the compound of Formula (VII) is selected from:  ,  ,  ,  ,  ,  ,  , and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00163] E67: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VIII):



Formula (VIII);

wherein:

A is  ;

X is -O-, -S-, -SO_2-, -N(R^3)-, or -CH_2-;

Y is -O- or -N(R^7)-;

R^1 is -(CR^4R^5)$_m$-R^6, -(CR^4R^5)$_p$-Y-(CR^4R^5)$_q$-R^6, or -(CR^4R^5)$_t$-C_{3-6}cycloalkyl-R^6;

each R^2 is independently selected from halogen, -CN, C_{1-6}alkyl, C_{1-6}haloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -OR^{17}, and -C(O)$NR^{18}R^{19}$;

R^3 is H or C_{1-6}alkyl;

each R^4 and R^5 is each independently selected from H, F, and C_{1-6}alkyl; or R^4 and R^5, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring;

R^6 is -CO_2R^9, -C(O)R^{10}, or -C(O)O-($CR^{12}R^{13}$)-OC(O)R^{11};

R^7 is H, C_{1-6}alkyl, or -SO_2R^8;

R^8 is C_{1-6}alkyl;

R^9 is H or C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl or -$NHSO_2R^{21}$;

R^{11} is C_{1-6}alkyl or C_{1-6}alkoxy;

R^{12} and R^{13} is each independently H or C_{1-6}alkyl;

each R^{17} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, aminoalkyl, cycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -C_{1-6}alkyl-C(O)(heterocycloalkyl), optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

each R^{18} and R^{19} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, cycloalkyl, aryl, and heteroaryl; or R^{18} and R^{19}, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{20};

each R^{20} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

R^{21} is C_{1-6}alkyl;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3, or 4;

p is 2, 3, or 4;

q is 1, 2, or 3; and

t is 0, 1, or 2;

or a pharmaceutically acceptable salt or solvate thereof.

[00164] E68: The method of embodiment 67, wherein R^1 is $-(CR^4R^5)_m-R^6$.

[00165] E69: The method of embodiment 67 or embodiment 68, wherein each R^4 and R^5 is each independently selected from H and C_{1-6}alkyl.

[00166] E70: The method of any one of embodiments 67-69, wherein each R^4 and R^5 is H.

[00167] E71: The method of any one of embodiments 67-70, wherein R^6 is $-CO_2R^9$.

[00168] E72: The method of any one of embodiments 67-71, wherein R^9 is H.

[00169] E73: The method of any one of embodiments 67-70, wherein R^6 is $-C(O)R^{10}$.

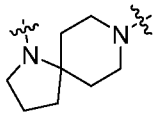
[00170] E74: The method of embodiment 73, wherein R^{10} is $-NHSO_2R^{21}$.

[00171] E75: The method of any one of embodiments 67-74, wherein X is -O-.

[00172] E76: The method of any one of embodiments 67-74, wherein X is $-N(R^3)-$.

[00173] E77: The method of any one of embodiments 67-76, wherein 

is



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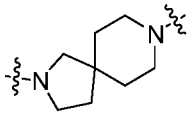
[00174] E78: The method of any one of embodiments 67-76, wherein 

is



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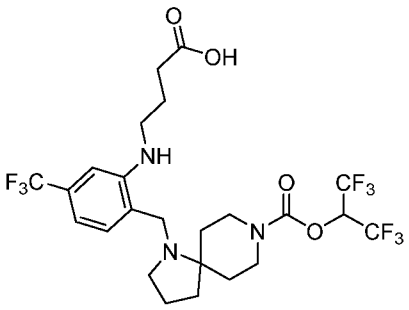
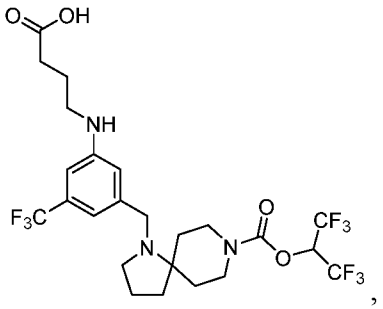
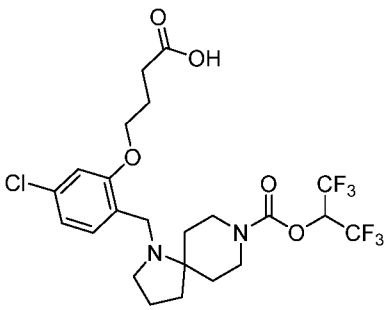
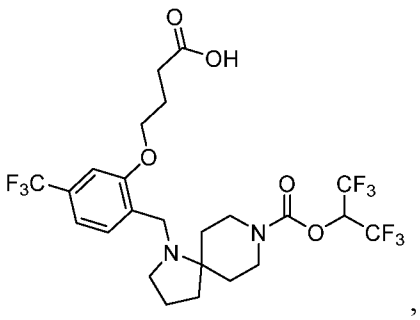
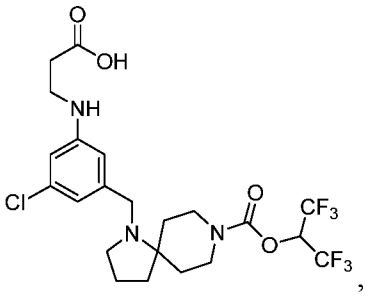
[00175] E79: The method of any one of embodiments 67-78, wherein each R^2 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl.

[00176] E80: The method of any one of embodiments 67-79, wherein n is 1.

[00177] E81: The method of embodiment 67, wherein the compound of Formula (VIII) is selected from:


,

,

,

,

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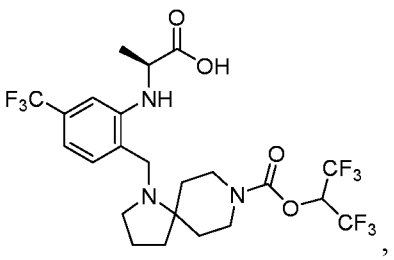
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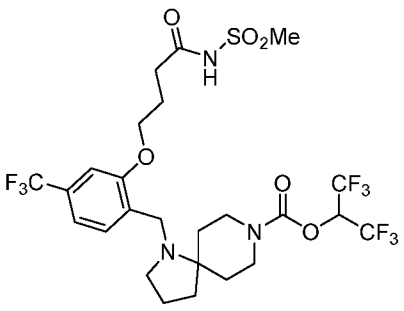
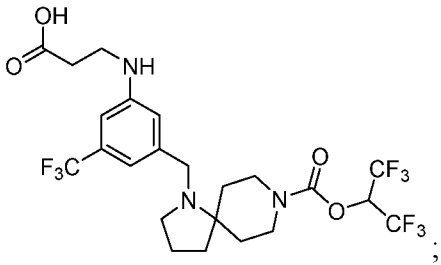
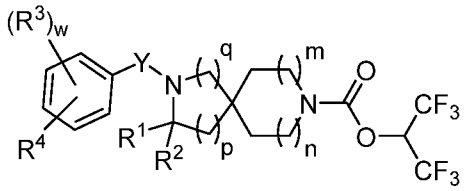

, and

; or a pharmaceutically acceptable salt or solvate thereof.

[00178] E82: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (IX):



Formula (IX);

wherein:

Y is $-CH_2-$ or -C(O)-;

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-SF_5$, and $-OR^7$;

R^4 is selected from $-C\equiv C-C_{1-6}$alkyl-CO_2H and $-C_{3-8}$cycloalkyl-CO_2H;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, and $-C_{1-6}$alkyl-C_{3-8}cycloalkyl;

w is 0, 1, 2, 3, or 4;

n is 0 or 1;

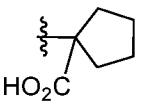
m is 0 or 1;

p is 0, 1, or 2; and

q is 0, 1, or 2; provided that when q is 0, then p is 2;

or a pharmaceutically acceptable salt or solvate thereof.

[00179] E83: The method of embodiment 82, wherein R^4 is $-C_{3-8}$cycloalkyl-CO_2H.

[00180] E84: The method of embodiment 83, wherein R^4 is 

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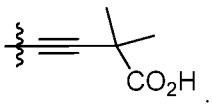
[00181] E85: The method of embodiment 82, wherein R^4 is $-C\equiv C-C_{1-6}$alkyl-CO_2H.

[00182] E86: The method of embodiment 85, wherein R^4 is 

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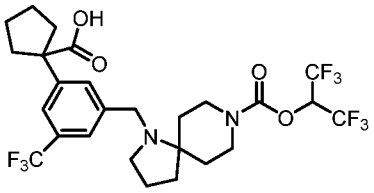
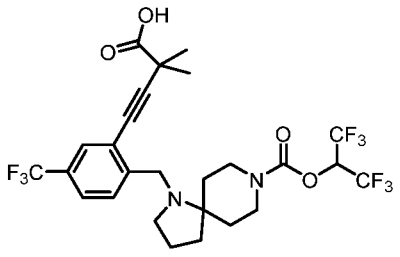
[00183] E87: The method of any one of embodiments 82-86, wherein Y is $-CH_2-$.

[00184] E88: The method of any one of embodiments 82-87, wherein R^1 and R^2 are both H.

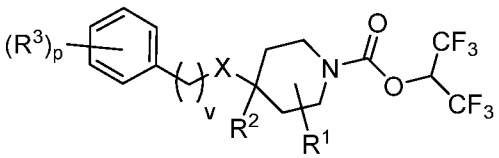
[00185] E89: The method of any one of embodiments 82-88, wherein each R^3 is independently selected from halogen and C_{1-6}haloalkyl.

[00186] E90: The method of any one of embodiments 82-89, wherein w is 1.

[00187] E91: The method of any one of embodiments 82-90, wherein m is 1, n is 1, q is 0, and p is 2.

[00188] E92: The method of embodiment 82, wherein the compound of Formula (IX) is selected from:  and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00189] E93: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (X):



Formula (X);

wherein:

X is -O- or -N(R^{11})-;

R^1 is H or C_{1-6}alkyl;

R^2 is C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, -C≡C-C_{1-6}alkyl-CO_2H, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), C_{1-9}heteroaryl, -SF_5, -NR^5R^6, -OR^7, -CO_2R^8, and -$C(O)NR^8R^9$, wherein C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{1-9}heteroaryl are optionally substituted with one or two R^4; or two adjacent R^3 form a C_{2-9}heterocycloalkyl ring, wherein the C_{2-9}heterocycloalkyl ring is optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-6}haloalkyl, halogen, oxo, -CN, -CO_2R^8, -$C(O)R^8$, -$C(O)NR^8R^9$, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$;

each R^5 and R^6 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-C(O)(C_{2-9}heterocycloalkyl), C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl; or R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-C(O)(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-CO_2H, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-}

$_{9}$heteroaryl, wherein C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl are optionally substituted with one or two groups selected from oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and CO_2NH_2;

each R^8 and R^9 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one or two groups selected from C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and CO_2NH_2;

each R^{10} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, oxo, -CN, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$;

R^{11} is H, C_{1-6}alkyl, $-C(O)-C_{1-6}$alkyl, or $-CH_2CO_2H$;

p is 0, 1, 2, 3, 4, or 5; and

v is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

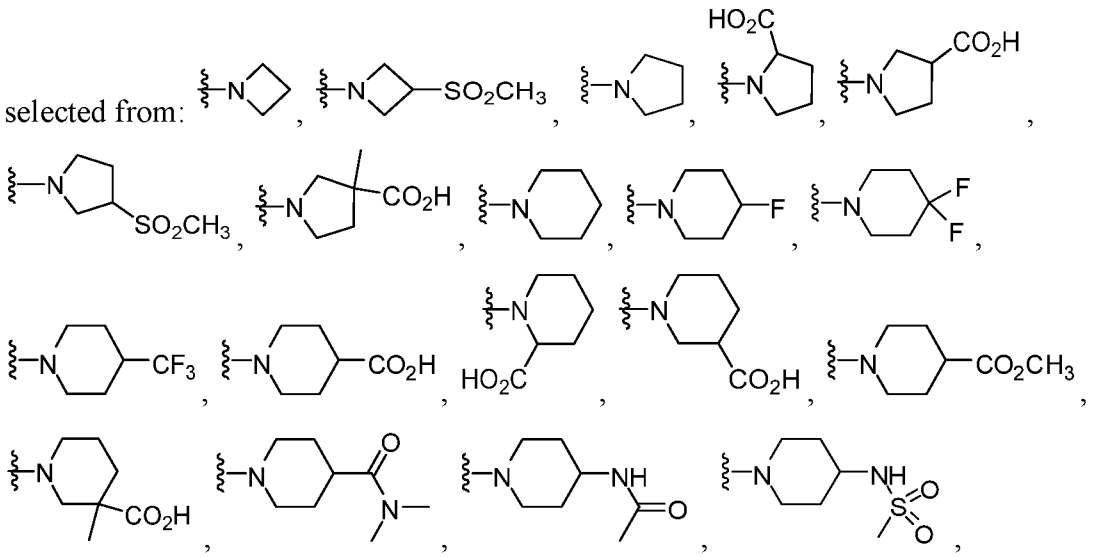
[00190] E94: The method of embodiment 93, wherein each R^3 is independently selected from halogen, C_{1-6}haloalkyl, $-NR^5R^6$, and $-OR^7$.

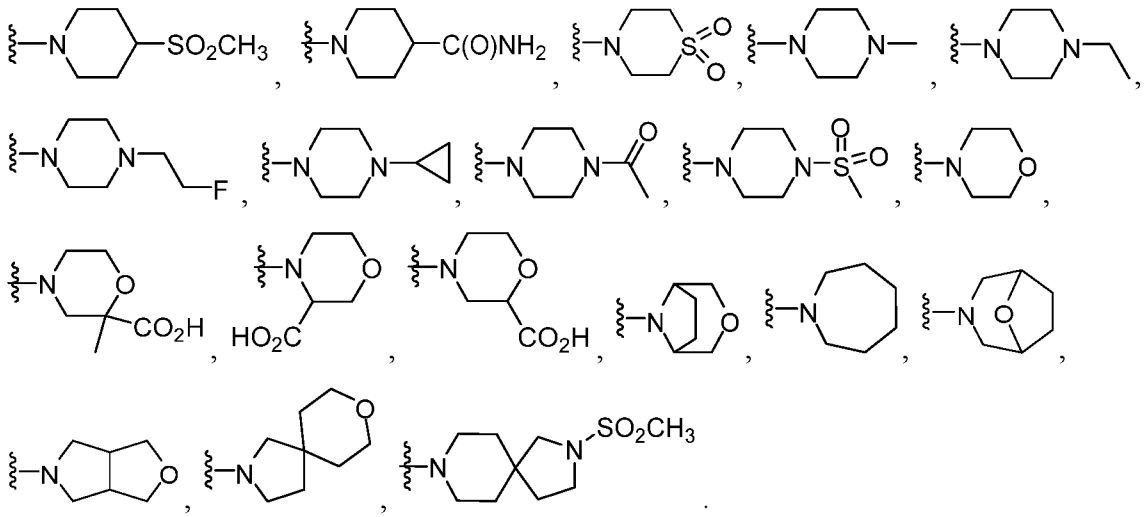
[00191] E95: The method of embodiment 93 or embodiment 94, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10}.

[00192] E96: The method of embodiment 95, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl and $-CO_2H$.

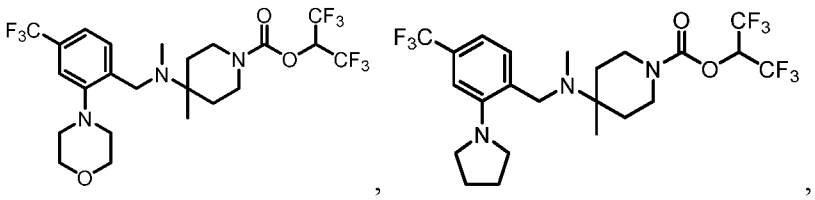
[00193] E97: The method of embodiment 95, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted C_{2-9}heterocycloalkyl ring.

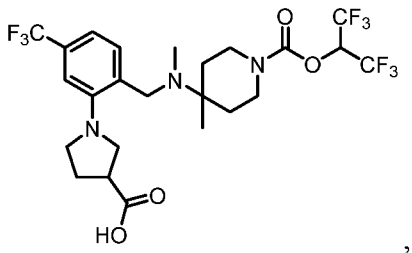
[00194] E98: The method of embodiment 93 or embodiment 94, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring selected from:



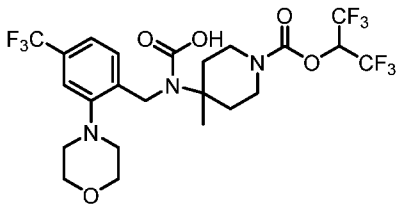


[00195] E99: The method of embodiment 93, wherein the compound of Formula (X) is selected from:



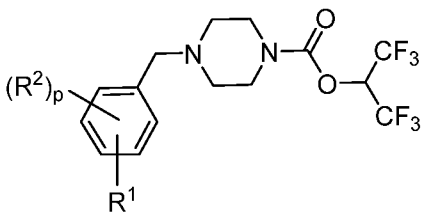


, and



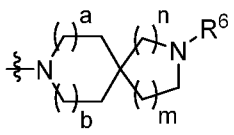
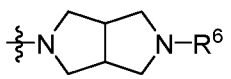
; or a pharmaceutically acceptable salt or solvate thereof.

[00196] E100: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XI)



Formula (XI);

wherein:

R^1 is selected from  and  ;

each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, $-SF_5$, $-OR^3$, and $-C(O)NR^4R^5$;

each R^3 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, and -C_{1-6}alkyl-C_{3-8}cycloalkyl;

each R^4 and R^5 is independently selected from H, C_{1-6}alkyl, and C_{3-8}cycloalkyl;

R^6 is selected from C_{1-6}alkyl, -C(O)-C_{1-6}alkyl, and -$S(O)_2$-C_{1-6}alkyl;

a is 0 or 1;

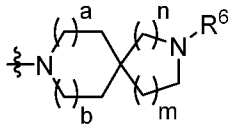
b is 0 or 1;

m is 0, 1, or 2;

n is 0, 1, or 2; provided that when n is 0, then m is 2; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

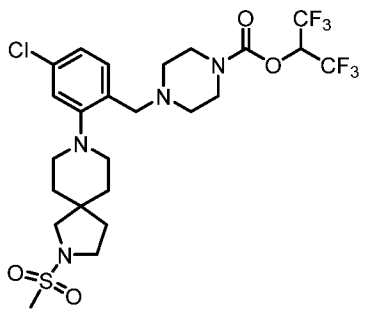
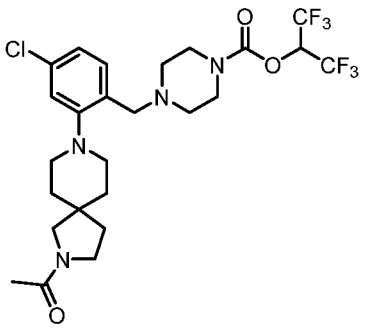
[00197] E101: The method of embodiment 100, wherein R^1 is  .

[00198] E102: The method of embodiment 100 or embodiment 101, wherein R^6 is -C(O)-C_{1-6}alkyl.

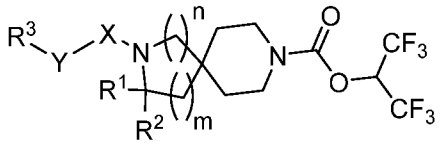
[00199] E103: The method of embodiment 100 or embodiment 101, wherein R^6 is -$S(O)_2$-C_{1-6}alkyl.

[00200] E104: The method of any one of embodiments 100-103, wherein each R^3 is independently selected from halogen and C_{1-6}haloalkyl.

[00201] E105: The method of any one of embodiments 100-104, wherein p is 1.

[00202] E106: The method of embodiment 100, wherein the compound of Formula (XI) is selected from:  and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00203] E107: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XII):



Formula (XII);

wherein:

X is $-CH_2-$ or -C(O)-;

Y is a bond, C_{1-6}alkyl, C_{1-6}haloalkyl, or C_{3-8}cycloalkyl;

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

R^3 is a 5- to 6-membered heteroaryl ring or a 9- to 10-membered bicyclic heteroaryl ring; wherein the 5- to 6-membered heteroaryl ring and the 9- to 10-membered bicyclic heteroaryl ring are optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl-(C_{2-9}heterocycloalkyl), phenyl, $-CH_2-$phenyl, C_{1-9}heteroaryl, $-OR^7$, $-CO_2R^6$, $-CH_2CO_2R^6$, and $-CH_2C(O)N(H)SO_2R^8$; wherein C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), phenyl, and C_{1-9}heteroaryl are optionally substituted with one or two R^5; or two adjacent R^4 form a 6-membered cycloalkyl or 6-membered heterocycloalkyl ring, wherein the cycloalkyl and heterocycloalkyl ring are optionally substituted with one or two R^5;

each R^5 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}heteroalkyl, C_{1-6}alkoxy, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, $-CO_2R^6$, $-CH_2CO_2R^6$, and -C_{1-6}alkyl(C_{2-9}heterocycloalkyl) optionally substituted with C_{1-6}alkyl;

each R^6 is independently selected from H and C_{1-6}alkyl;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;

each R^8 is independently selected from C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;

n is 0 or 1; and

m is 1 or 2; provided that when n is 0, then m is 2; and when n is 1, then m is 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00204] E108: The method of embodiment 107, wherein Y is a bond.

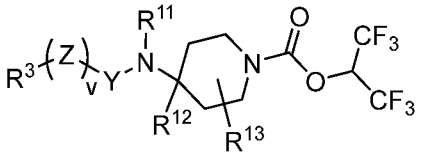
[00205] E109: The method of embodiment 107 or embodiment 108, wherein R^1 and R^2 are both H.

[00206] E110: The method of any one of embodiments 107-109, wherein X is $-CH_2-$.

[00207] E111: The method of any one of embodiments 107-109, wherein X is -C(O)-.

[00208] E112: The method of any one of embodiments 107-111, wherein n is 0 and m is 2.

[00209] E113: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XIII):



Formula (XIII);

wherein:

Y is $-CH_2-$ or $-C(O)-$;

Z is C_{3-6}cycloalkyl;

R^3 is a 5- to 6-membered heteroaryl ring or a 9- to 10-membered bicyclic heteroaryl ring; wherein the 5- to 6-membered heteroaryl ring and the 9- to 10-membered bicyclic heteroaryl ring are optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl-(C_{2-9}heterocycloalkyl), phenyl, $-CH_2-$phenyl, C_{1-9}heteroaryl, $-OR^7$, $-CO_2R^6$, and $-CH_2CO_2R^6$; wherein C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), phenyl, and C_{1-9}heteroaryl are optionally substituted with one or two R^5; or two adjacent R^4 form a 6-membered cycloalkyl or 6-membered heterocycloalkyl ring, wherein the cycloalkyl and heterocycloalkyl ring are optionally substituted with one or two R^5;

each R^5 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}heteroalkyl, C_{1-6}alkoxy, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, $-CO_2R^6$, $-CH_2CO_2R^6$, and -C_{1-6}alkyl(C_{2-9}heterocycloalkyl) optionally substituted with C_{1-6}alkyl;

each R^6 is independently selected from H and C_{1-6}alkyl;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;

R^{11} is H, C_{1-6}alkyl, or -C_{1-6}alkyl-O-C_{1-6}alkyl;

R^{12} is C_{1-6}alkyl;

R^{13} is H or C_{1-6}alkyl; and

v is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00210] E114: The method of embodiment 113, wherein R^{13} is H.

[00211] E115: The method of embodiment 113 or embodiment 114, wherein v is 0.

[00212] E116: The method of any one of embodiments 113-115, wherein Y is -C(O)-.

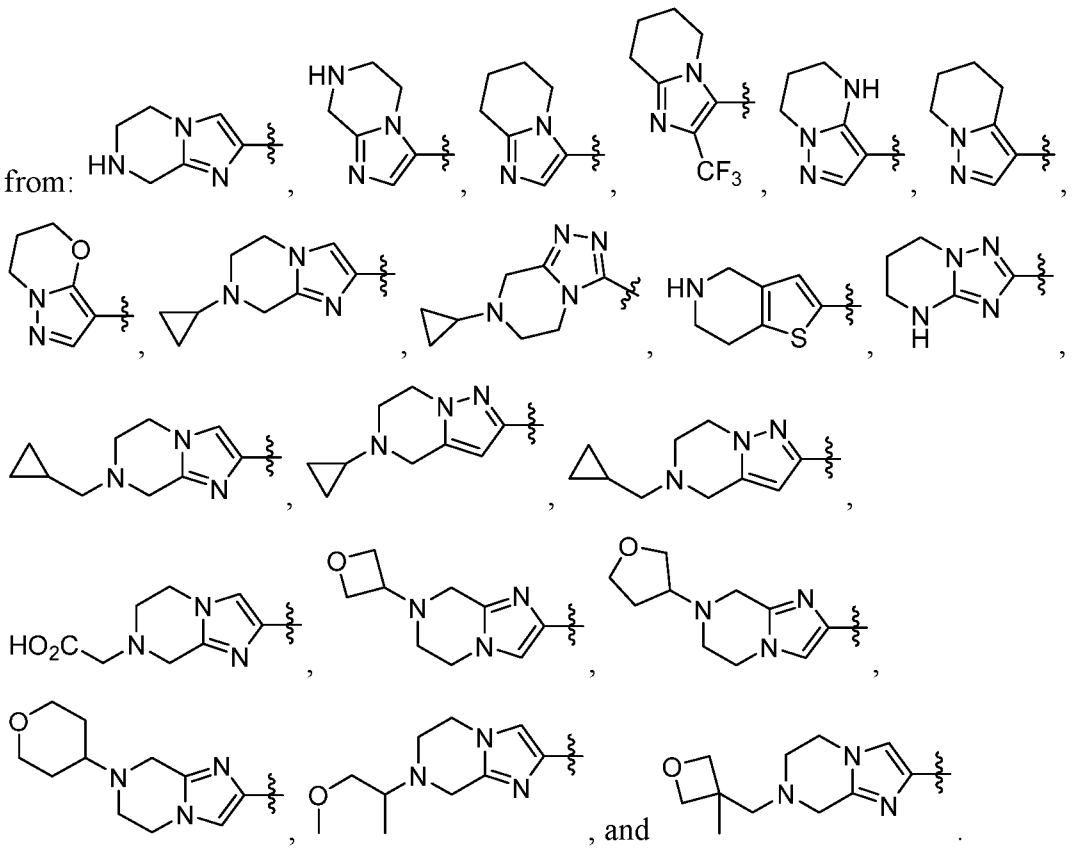
[00213] E117: The method of any one of embodiments 107-116, wherein R^3 is a 5-membered heteroaryl ring substituted with one, two, or three R^4.

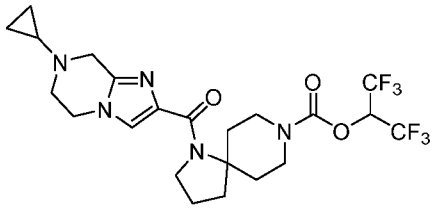
[00214] E118: The method of embodiment 117, wherein R^3 is a 5-membered heteroaryl ring substituted with two or three R^4, wherein two adjacent R^4 form a 6-membered heterocycloalkyl ring optionally substituted with one or two R^5.

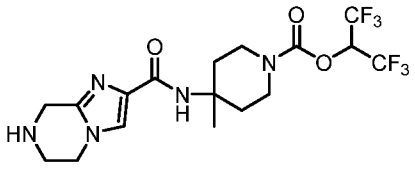
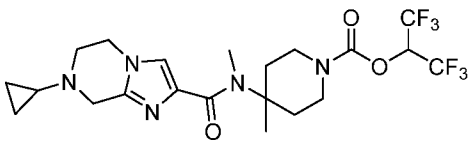
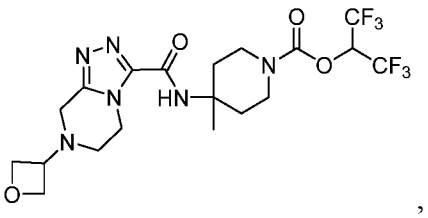
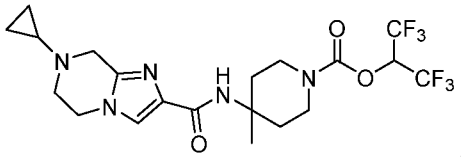
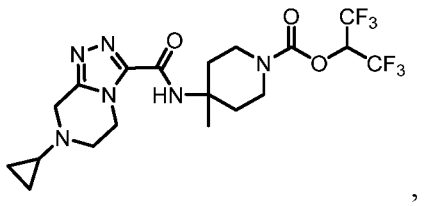
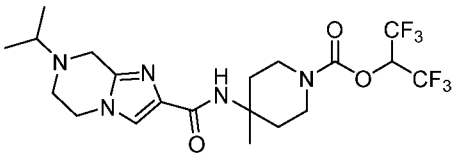
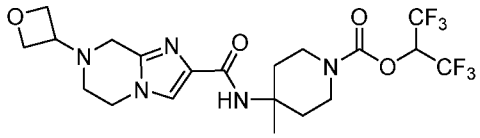
[00215] E119: The method of embodiment 118, wherein R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form an unsubstituted 6-membered heterocycloalkyl ring.

[00216] E120: The method of embodiment 118, wherein R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5.

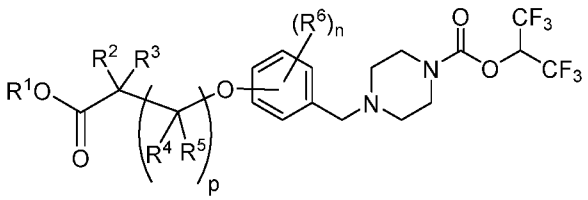
[00217] E121: The method of embodiment 120, wherein R^5 is selected from $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$heteroalkyl, $C_{3\text{-}8}$cycloalkyl, -$C_{1\text{-}6}$alkyl($C_{3\text{-}8}$cycloalkyl), $C_{2\text{-}9}$heterocycloalkyl, and -CH_2CO_2H.

[00218] E122: The method of any one of embodiments 107-116, wherein R^3 is selected from:  , and .

[00219] E123: The method of embodiment 107, wherein the compound of Formula (XII) is:  ; or a pharmaceutically acceptable salt or solvate thereof.

[00220] E124: The method of embodiment 113, wherein the compound of Formula (XIII) is selected from:  ,   ,  ,  ,  , and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00221] E125: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XIV):



Formula (XIV);

wherein:

R^1 is H or $C_{1\text{-}6}$alkyl;

R^2 is $C_{1\text{-}6}$alkyl;

R^3 is H or $C_{1\text{-}6}$alkyl;

R^4 and R^5 are independently selected from H and C_{1-6}alkyl;

each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, -OR^7, -$C(O)NR^8R^9$, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{2-9}heteroaryl, wherein C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{2-9}heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-6}cycloalkyl;

each R^8 and R^9 is each independently selected from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, aryl, and heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^{10} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

n is 0, 1, 2, 3, or 4; and

p is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00222] E126: The method of embodiment 125, wherein p is 0.

[00223] E127: The method of embodiment 125, wherein p is 1.

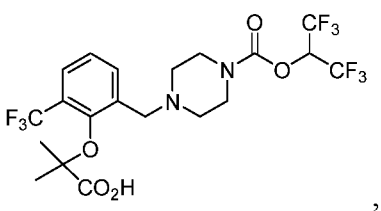
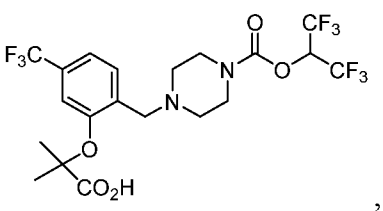
[00224] E128: The method of any one of embodiments 125-127, wherein R^4 and R^5 are H.

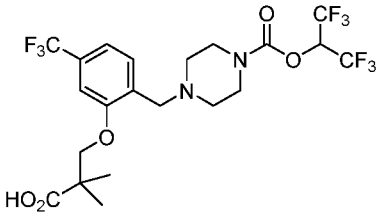
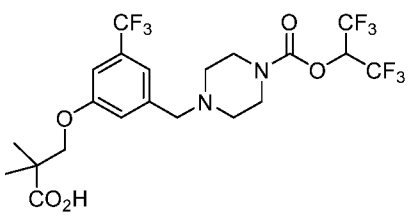
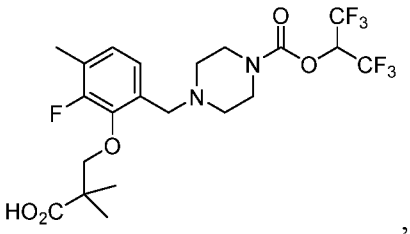
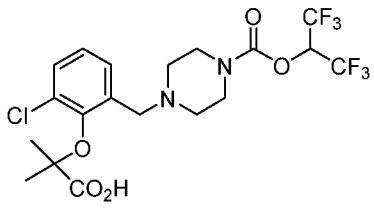
[00225] E129: The method of any one of embodiments 125-128, wherein R^3 is C_{1-6}alkyl.

[00226] E130: The method of any one of embodiments 125-129, wherein each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, -OR^7, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl, wherein C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl are optionally substituted with one or two groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy.

[00227] E131: The method of any one of embodiments 125-130, wherein each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, and C_{1-6}haloalkyl.

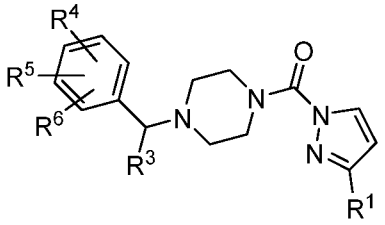
[00228] E132: The method of any one of embodiments 125-131, wherein n is 1 or 2.

[00229] E133: The method of embodiment 125, wherein the compound of Formula (XIV) is selected from:  ,  ,

; or a pharmaceutically acceptable salt or solvate thereof.

[00230] E134: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XV):



Formula (XV);

wherein:

R^1 is $-N(R^2)C(O)R^{15}$ or $-N(H)SO_2R^{15}$;

R^2 is H or C_{1-6}alkyl;

R^3 is H or optionally substituted phenyl;

R^4 is H, halogen, $-OR^7$, C_{1-6}alkyl, C_{1-6}haloalkyl, optionally substituted heterocycloalkyl, optionally substituted C_{1-6}alkyl-heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, $-CO_2H$, or $-C(O)NR^8R^9$;

R^5 is H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or phenyl; or

R^4 and R^5 are combined to form a heterocycloalkyl ring;

R^6 is H, halogen or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, optionally substituted phenyl, optionally substituted C_{1-6}alkyl-phenyl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, or $-C_{1-6}$alkyl$C(O)NR^{10}R^{11}$;

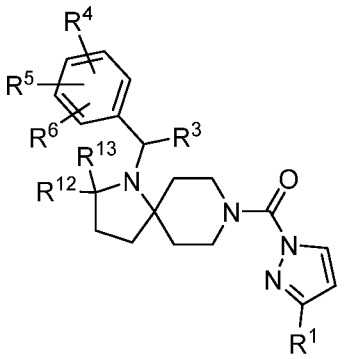
R^8 and R^9 are each independently H, or C_{1-6}alkyl; or R^8 and R^9 together with the nitrogen to which they are attached are combined to form an optionally substituted heterocycloalkyl ring;

R^{10} and R^{11} are each independently H, or C_{1-6}alkyl; or R^{10} and R^{11} together with the nitrogen to which they are attached are combined to form a heterocycloalkyl ring; and

R^{15} is optionally substituted C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[00231] E135: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XVI):



Formula (XVI);

wherein:

R^1 is $-N(R^2)C(O)R^{15}$ or $-N(H)SO_2R^{15}$;

R^2 is H or C_{1-6}alkyl;

R^3 is H or optionally substituted phenyl;

R^4 is H, halogen, $-OR^7$, C_{1-6}alkyl, C_{1-6}haloalkyl, optionally substituted heterocycloalkyl, optionally substituted C_{1-6}alkyl-heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, $-CO_2H$, or $-C(O)NR^8R^9$;

R^5 is H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or phenyl; or

R^4 and R^5 are combined to form a heterocycloalkyl ring;

R^6 is H, halogen or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, optionally substituted phenyl, optionally substituted C_{1-6}alkyl-phenyl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, or $-C_{1-6}$alkyl$C(O)NR^{10}R^{11}$;

R^8 and R^9 are each independently H, or C_{1-6}alkyl; or R^8 and R^9 together with the nitrogen to which they are attached are combined to form an optionally substituted heterocycloalkyl ring;

R^{10} and R^{11} are each independently H, or C_{1-6}alkyl; or R^{10} and R^{11} together with the nitrogen to which they are attached are combined to form a heterocycloalkyl ring;

R^{12} is H or C_{1-6}alkyl;

R^{13} is H or C_{1-6}alkyl; and

R^{15} is optionally substituted C_{1-6}alkyl;

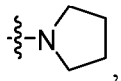
or a pharmaceutically acceptable salt or solvate thereof.

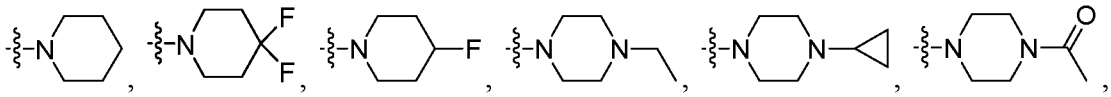
[00232] E136: The method of embodiment 135, wherein R^{12} and R^{13} are H.

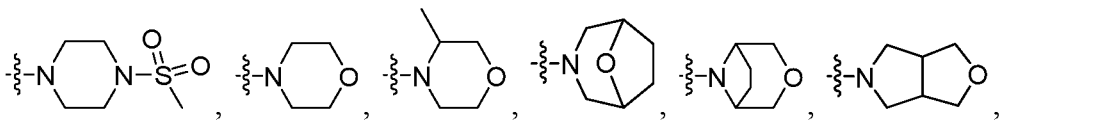
[00233] E137: The method of any one of embodiments 134-136, wherein R^4 is optionally substituted heterocycloalkyl.

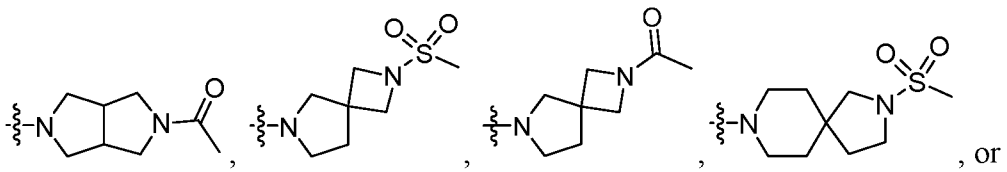
[00234] E138: The method of any one of embodiments 134-137, wherein R^4 is heterocycloalkyl optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-6}alkyl, -C_{1-6}alkyl-OH, C_{1-6}fluoroalkyl, C_{3-6}cycloalkyl, heteroaryl, -CO_2H, -C_{1-6}alkyl-CO_2H, -C(O)C_{1-6}alkyl, -C(O)C_{1-6}alkyl-OH, -N(H)C(O)C_{1-6}alkyl, -$C(O)NH_2$, -C(O)N(H)(C_{1-6}alkyl), -C(O)N(C_{1-6}alkyl)$_2$, -C(O)C_{2-7}heterocycloalkyl, and -$S(O)_2C_{1-6}$alkyl.

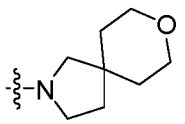
[00235] E139: The method of any one of embodiments 134-138, wherein R^4 is optionally substituted heterocycloalkyl and the heterocycloalkyl is a 4-6 membered monocyclic heterocycloalkyl, a 8-9 membered bicyclic heterocycloalkyl, a 7-8 membered bridged heterocycloalkyl, a 5,5 fused heterocycloalkyl, or an 8-11 membered spirocyclic heterocycloalkyl.

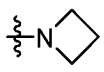
[00236] E140: The method of any one of embodiments 134-136, wherein R^4 is  ,

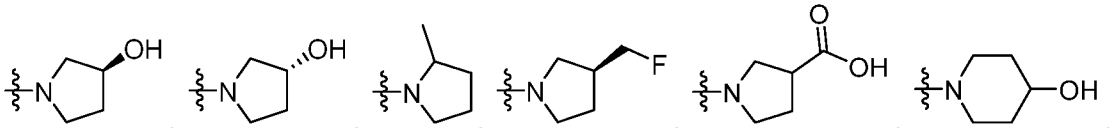


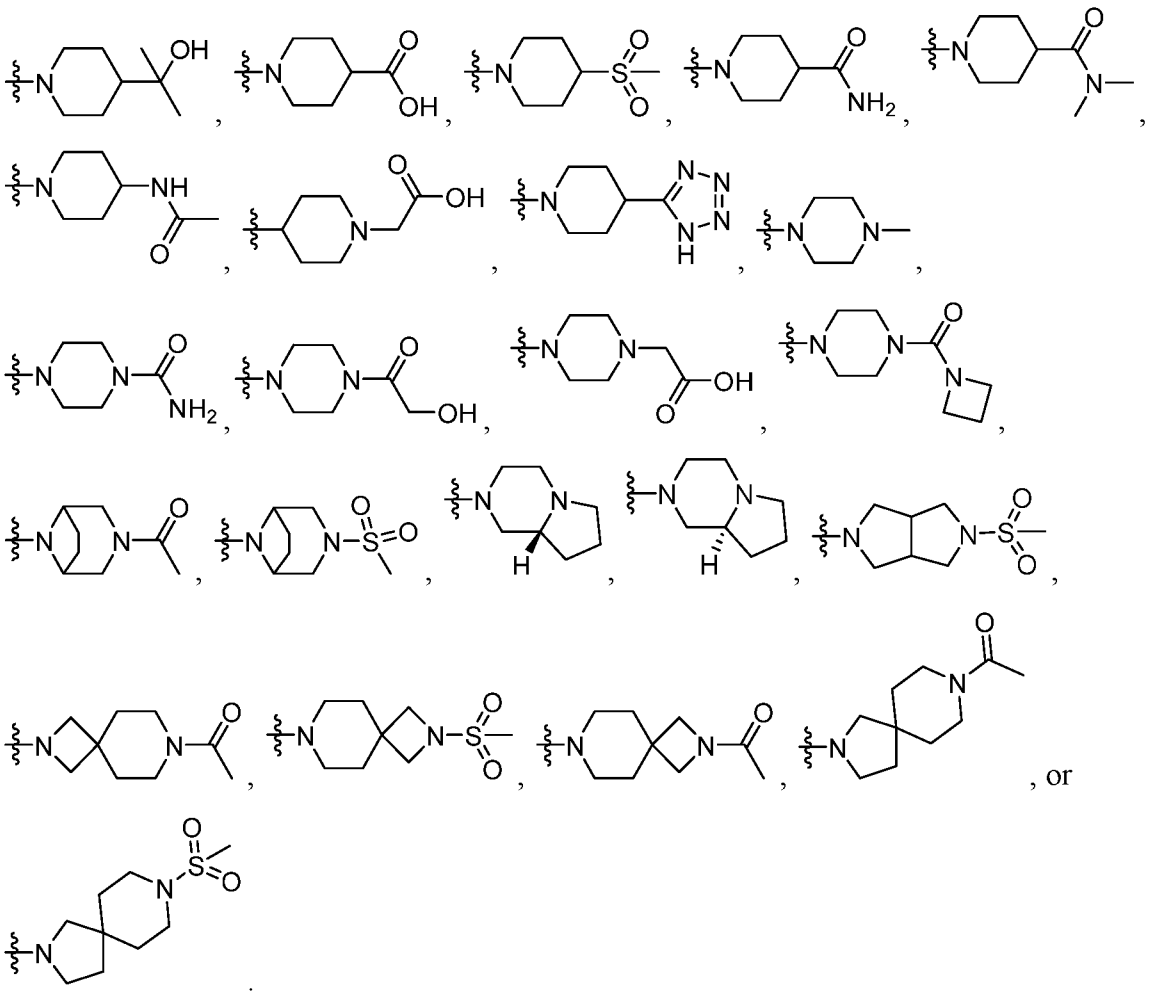


 , or

 .

[00237] E141: The method of any one of embodiments 134-136, wherein R^4 is  ,





[00238] E142: The method of any one of embodiments 134-136, wherein R^4 is halogen.

[00239] E143: The method of any one of embodiments 134-136, wherein R^4 is C_{1-6}haloalkyl.

[00240] E144: The method of any one of embodiments 134-143, wherein R^5 is halogen.

[00241] E145: The method of any one of embodiments 134-143, wherein R^5 is C_{1-6}haloalkyl.

[00242] E146: The method of any one of embodiments 134-143, wherein R^5 is C_{1-6}alkyl.

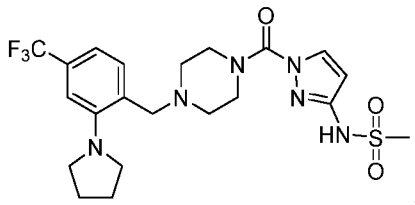
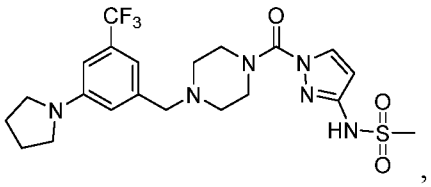
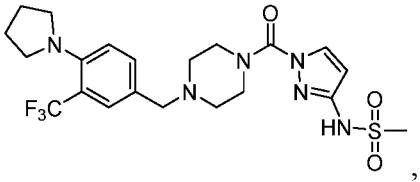
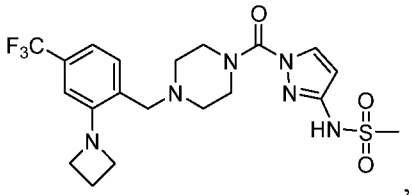
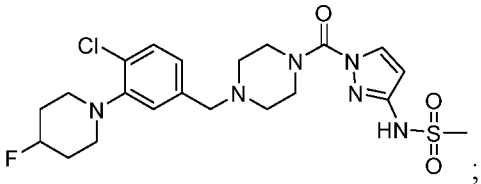
[00243] E147: The method of any one of embodiments 134-146, wherein R^6 is H.

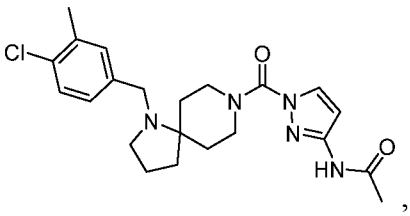
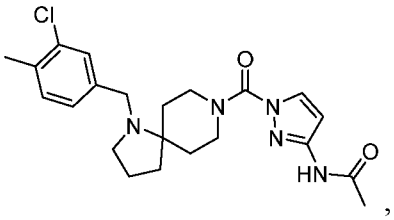
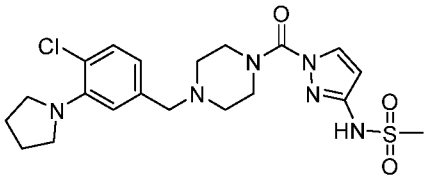
[00244] E148: The method of any one of embodiments 134-146, wherein R^3 is H.

[00245] E149: The method of any one of embodiments 134-148, wherein R^1 is -$N(R^2)C(O)R^{15}$.

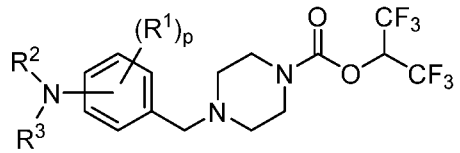
[00246] E150: The method of any one of embodiments 134-148, wherein R^1 is -$N(H)SO_2R^{15}$.

[00247] E151: The method of any one of embodiments 134-150, wherein R^{15} is unsubstituted C_{1-6}alkyl.

[00248] E152: The method of embodiment 134, wherein the compound of Formula (XV) is selected from:  ,  ,  ,  , and  ; or a pharmaceutically acceptable salt or solvate thereof.

[00249] E153: The method of embodiment 135, wherein the compound of Formula (XVI) is selected from:  ,  ,  , and ; or a pharmaceutically acceptable salt or solvate thereof.

[00250] E154: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XVII):



Formula (XVII);

wherein:

each R^1 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, and -CN;

R^2 and R^3, together with the carbon to which they are attached, form

(i) a C_2-C_7heterocycloalkyl; or

(ii) a C_2-C_9heteroaryl;

wherein the C_2-C_7heterocycloalkyl or the C_2-C_9heteroaryl is substituted with one R^4 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^4 is $-CO_2H$ or $-C_{1-6}$alkyl-CO_2H; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[00251] E155: The method of embodiment 154, wherein R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_7heterocycloalkyl substituted with one R^4 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy.

[00252] E156: The method of embodiment 154 or embodiment 155, wherein R^4 is $-CO_2H$.

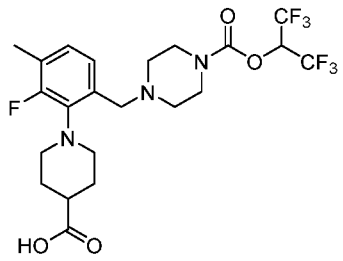
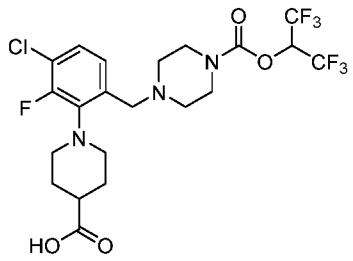
[00253] E157: The method of embodiment 154 or embodiment 155, wherein R^4 is $-C_{1-6}$alkyl-CO_2H.

[00254] E158: The method of any one of embodiments 154-157, wherein each R^1 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl.

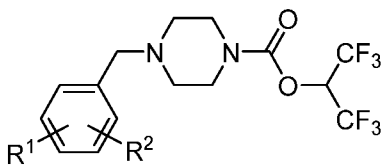
[00255] E159: The method of any one of embodiments 154-158, wherein p is 1 or 2.

[00256] E160: The method of any one of embodiments 154-159, wherein p is 2.

[00257] E161: The method of any one of embodiments 154-159, wherein p is 1.

[00258] E162: The method of embodiment 153, wherein the compound of Formula (XVII) is selected from:  and  .

[00259] E163: A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (I'):



Formula (I');

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is optionally substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

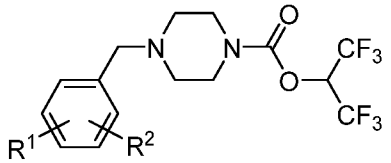
the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

each R^9 is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[00260] E164: The method of embodiment 163, wherein the compound of Formula (I') is a compound of Formula (III):



Formula (III);

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$,

and -$NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

each R^9 is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[00261] E165: The method of embodiment 163 or embodiment 164, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S.

[00262] E166: The method of embodiment 165, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine.

[00263] E167: The method of embodiment 166, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine and piperidine.

[00264] E168: The method of embodiment 163, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle.

[00265] E169: The method of embodiment 168, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine.

[00266] E170: The method of embodiment 163 or embodiment 164, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl.

[00267] E171: The method of embodiment 170, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 7-8 membered bridged heterocyclic ring.

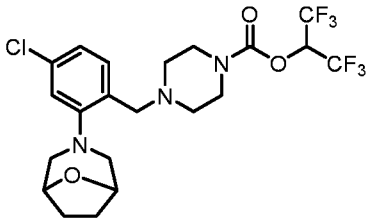
[00268] E172: The method of any one of embodiments 163-171, wherein R^1 is halogen, -SF_5, or optionally substituted C_{1-6}alkyl optionally substituted by halogen.

[00269] E173: The method of any one of embodiments 163-172, wherein R^1 is halogen.

[00270] E174: The method of any one of embodiments 163-172, wherein R^1 is C_{1-6}alkyl optionally substituted by halogen.

[00271] E175: The method of embodiment 174, wherein R^1 is -CF_3.

[00272] E176: The method of embodiment 163, wherein the compound is selected from: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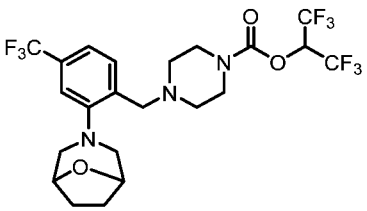
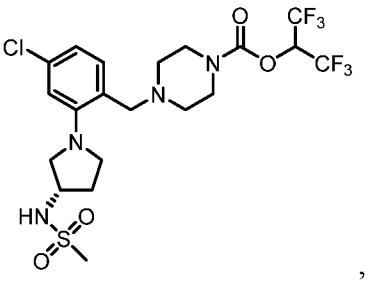
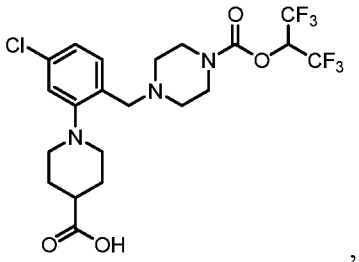

,

,

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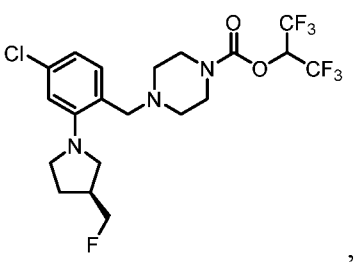
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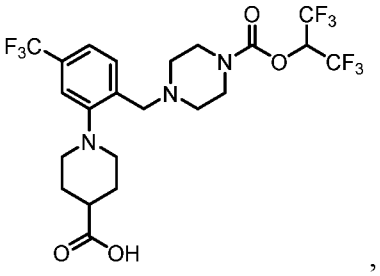
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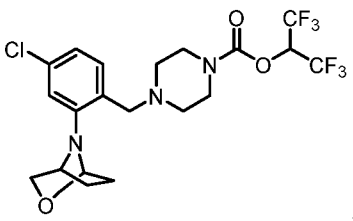
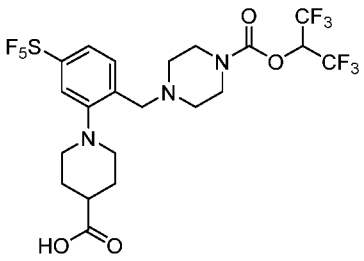
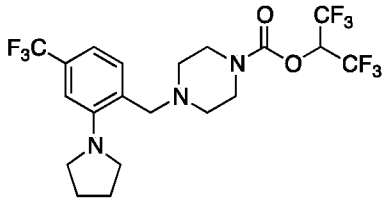

, and

; or a pharmaceutically acceptable salt or solvate thereof.

[00273] E177: The method of embodiment 163, wherein the compound is:


; or a pharmaceutically acceptable salt or solvate thereof.

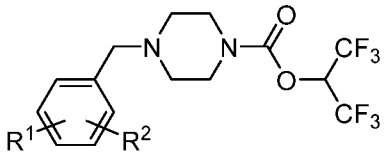
[00274] E178: The method of any one of embodiments 1-177, wherein the dyskinesia is levodopa-induced dyskinesia.

Methods

[00275] In some embodiments disclosed herein are methods of modulating the activity of MAGL. Contemplated methods, for example, comprise exposing said enzyme to a compound described herein. The ability of compounds described herein to modulate or inhibit MAGL is evaluated by procedures known in the art and/or described herein. Another aspect of this disclosure provides methods of treating a disease associated with expression or activity of MAGL in a patient.

[00276] Compounds described herein are modulators of MAGL. In some embodiments, these compounds and pharmaceutical compositions comprising these compounds, are useful for the treatment of dyskinesia. In some embodiments, these compounds and pharmaceutical compositions comprising these compounds, are useful for the treatment of levadopa-induced dyskinesia.

[00277] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (I'):



Formula (I');

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is optionally substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

each R^9 is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[00278] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (I'), wherein the dyskinesia is levodopa-induced dyskinesia.

[00279] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine and piperidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is pyrrolidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is piperidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered

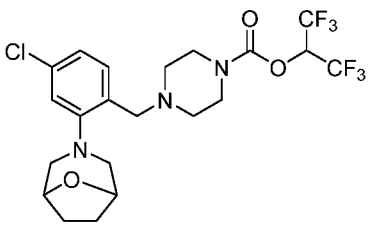
saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is morpholine.

[00280] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is pyrrolidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is piperidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is morpholine.

[00281] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 7-8 membered bridged heterocyclic ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring is substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring is substituted with one substituent selected from halogen, oxo, and C_{1-6}alkyl.

[00282] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is halogen, $-OR^3$, $-SF_5$, or C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is halogen, $-CH_3$, $-CF_3$, $-OCH_3$, or $-OCF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is halogen, $-SF_5$, or C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is $-SF_5$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is $-OCH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), R^1 is $-OCF_3$.

[00283] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), the compound is selected from: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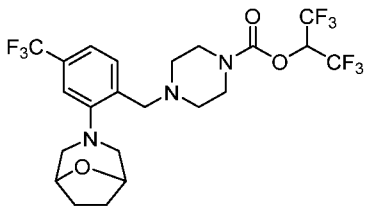
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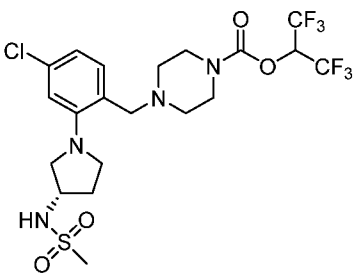
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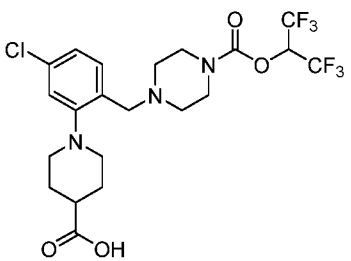
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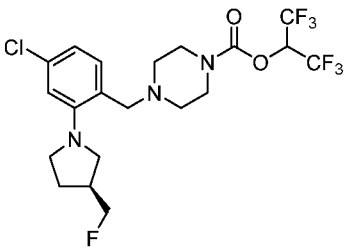
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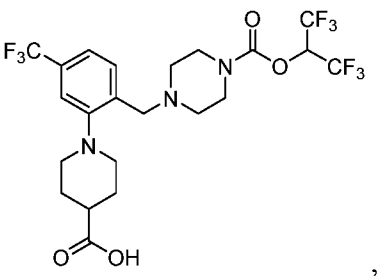
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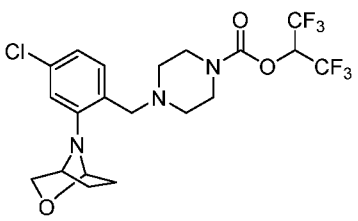
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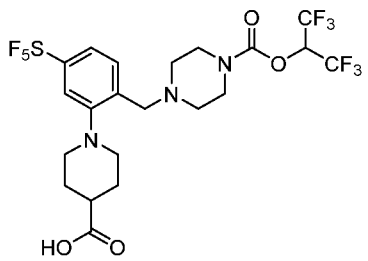
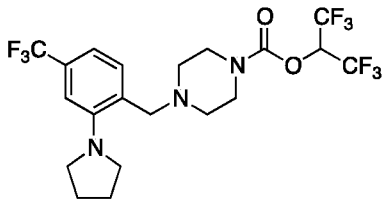
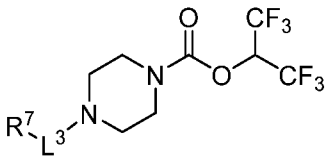

; or a pharmaceutically acceptable salt or solvate thereof.

[00284] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I'), the compound is:



; or a pharmaceutically acceptable salt or solvate thereof.

[00285] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (I):



Formula (I);

wherein:

L^3 is a bond, $-CH_2-$, $-S(O)_2-$, or $-C(O)-$;

R^7 is phenyl; wherein R^7 is optionally substituted by one, two, or three moieties independently selected from R^h;

R^a and R^b are independently selected, for each occurrence, from the group consisting of hydrogen and C_{1-3}alkyl; wherein C_{1-3}alkyl is optionally substituted by one or more substituents selected from halogen, cyano, oxo, hydroxyl, heterocycle, and phenyl;

or R^a and R^b, when they occur together with the nitrogen to which they are attached, form a 4-6 membered saturated heterocyclic ring, which may have an additional heteroatom selected from O, S, and N, or a spirocyclic ring selected from 8-oxa-2-azaspiro[4.5]decane and 2,8-diazaspiro[4.5]decane, wherein the 4-6 membered saturated heterocyclic ring or the spirocyclic ring are optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, $-S(O)_w-C_{1-6}$alkyl (where w is 0, 1 or 2), hydroxyl, $-C(O)-C_{1-6}$alkyl, $-NH_2$, and $-NH-C(O)-C_{1-6}$alkyl;

R^c is selected from the group consisting of halogen, hydroxyl, C_{1-6}alkyl (optionally substituted by one, two, or three halogens), and C_{1-6}alkoxy (optionally substituted by one, two, or three halogens); and

R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from R^c), hydroxyl, cyano, C_{1-6}alkyl (optionally substituted by one, two or three halogens), C_{1-6}alkoxy (optionally substituted by one, two or three halogens), R^aR^bN-, $R^a-C(O)NR^a-$, R^aR^bN-

SO_2-, R^aR^bN-C(O)-, R^a-$S(O)_w$- (wherein w is 0, 1 or 2), R^a-SO_2-NR^b-, and heteroaryl (optionally substituted by one, two or three moieties each independently selected from R^c);

or a pharmaceutically acceptable salt or solvate thereof.

[00286] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (I), wherein the dyskinesia is levodopa-induced dyskinesia.

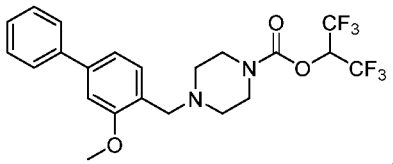
[00287] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), L^3 is -CH_2-. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), L^3 is a bond. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), L^3 is -$S(O)_2$-. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), L^3 is -C(O)-.

[00288] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), R^7 is phenyl optionally substituted by one or two moieties independently selected from R^h. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), R^7 is phenyl optionally substituted by one or two R^h moieties independently selected from the group consisting of halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from halogen, methyl, ethyl, propyl, t-butyl, and CF_3), $C_{1\text{-}6}$alkyl (optionally substituted by one, two or three halogens), $C_{1\text{-}6}$alkoxy (optionally substituted by one, two or three halogens), R^aR^bN-, R^aR^bN-C(O)-, and heteroaryl (optionally substituted by one, two or three moieties each independently selected from $C_{1\text{-}6}$alkyl or halogen). In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), R^7 is phenyl optionally substituted by one or two R^h moieties independently selected from the group consisting of halogen, $C_{1\text{-}6}$alkyl (optionally substituted by one, two or three halogens), $C_{1\text{-}6}$alkoxy (optionally substituted by one, two or three halogens), and R^aR^bN-.

[00289] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), L^3 is -CH_2- and R^7 is substituted by R^aR^bN- and a moiety selected from the group consisting of: halogen, $C_{1\text{-}6}$alkyl (optionally substituted by one, two or three halogens), and $C_{1\text{-}6}$alkoxy (optionally substituted by one, two or three halogens). In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), R^a and R^b, together with the nitrogen to which they are attached, form a 4-6 membered saturated heterocyclic ring, which may have an additional heteroatom selected from O, S, and N, and the 4-6 membered saturated heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, $C_{1\text{-}}$

$_{6}$alkyl, -S(O)$_w$-C$_{1-6}$alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C$_{1-6}$alkyl, -NH$_2$, and -NH-C(O)-C$_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), the 4-6 membered saturated heterocyclic ring is selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine, and the 4-6 membered saturated heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C$_{1-6}$alkyl, -S(O)$_w$-C$_{1-6}$alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C$_{1-6}$alkyl, -NH$_2$, and -NH-C(O)-C$_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), the 4-6 membered saturated heterocyclic ring is pyrrolidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), the 4-6 membered saturated heterocyclic ring is piperidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), the 4-6 membered saturated heterocyclic ring is morpholine.

[00290] In some embodiments of the methods for treating dyskinesia with a compound of Formula (I), the compound is selected from: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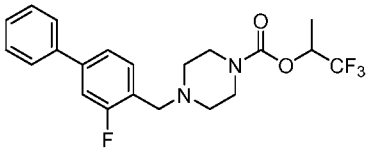
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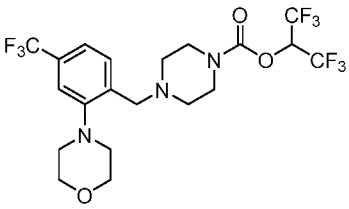
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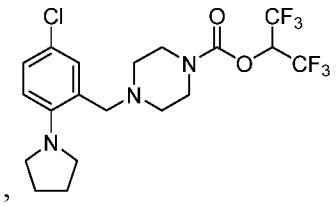
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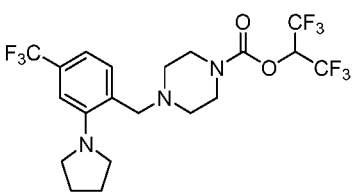
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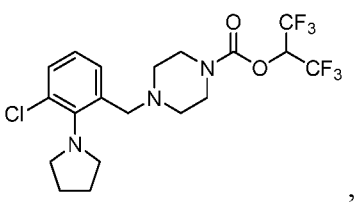
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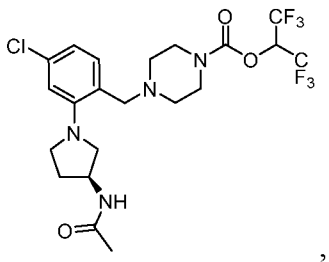
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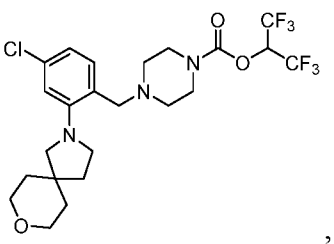
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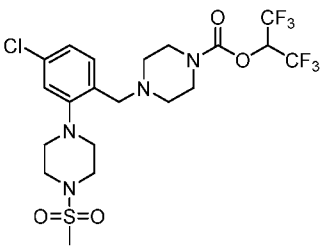
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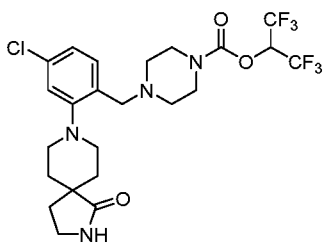
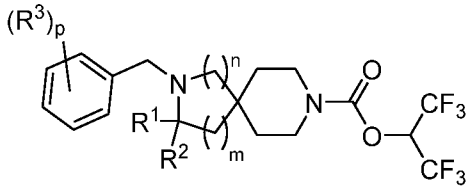

; or a pharmaceutically acceptable salt or solvate thereof.

[00291] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (II):



Formula (II);

wherein:

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, heterocycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), heteroaryl, -SF_5, -NR^5R^6, -OR^7, -CO_2R^8, -$C(O)R^8$, and -$C(O)NR^8R^9$, wherein heterocycloalkyl and -C_{1-6}alkyl(heterocycloalkyl) are optionally substituted with one or two R^4; or two adjacent R^3 form a heterocycloalkyl ring optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, halogen, oxo, -CN, -CO_2R^8, -$C(O)R^8$, -$C(O)NR^8R^9$, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$;

each R^5 and R^6 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -C_{1-6}alkyl-C(O)(heterocycloalkyl), heterocycloalkyl, aryl, and heteroaryl; or R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(heterocycloalkyl), -C_{1-6}alkyl-C(O)(heterocycloalkyl), heterocycloalkyl, aryl, and heteroaryl, wherein heterocycloalkyl, aryl, and heteroaryl are optionally substituted with one or two groups selected from oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and $C(O)NH_2$;

each R^8 and R^9 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, aryl, and heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one or two groups selected from C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and $C(O)NH_2$;

each R^{10} is independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-6}haloalkyl, halogen, oxo, -CN, -CO_2R^8, -$C(O)R^8$, -$C(O)NR^8R^9$, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$;

p is 0, 1, 2, 3, 4, or 5;

n is 0 or 1; and

m is 1 or 2; provided that when n is 0, then m is 2; and when n is 1, then m is 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00292] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (II), wherein the dyskinesia is levodopa-induced dyskinesia.

[00293] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), n is 0 and m is 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), n is 1 and m is 1.

[00294] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), R^1 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), R^2 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), wherein R^1 and R^2 are both H.

[00295] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 0, 1, 2, or 3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 1 or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2. some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 3.

[00296] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 1 and R^3 is selected from $C_{1\text{-}6}$alkyl, halogen, $C_{1\text{-}6}$haloalkyl, -$C_{1\text{-}6}$alkyl(heterocycloalkyl), -NR^5R^6, -OR^7, -CO_2R^8, and -$C(O)NR^8R^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 1 and R^3 is selected from halogen, $C_{1\text{-}6}$haloalkyl, -NR^5R^6, and -OR^7.

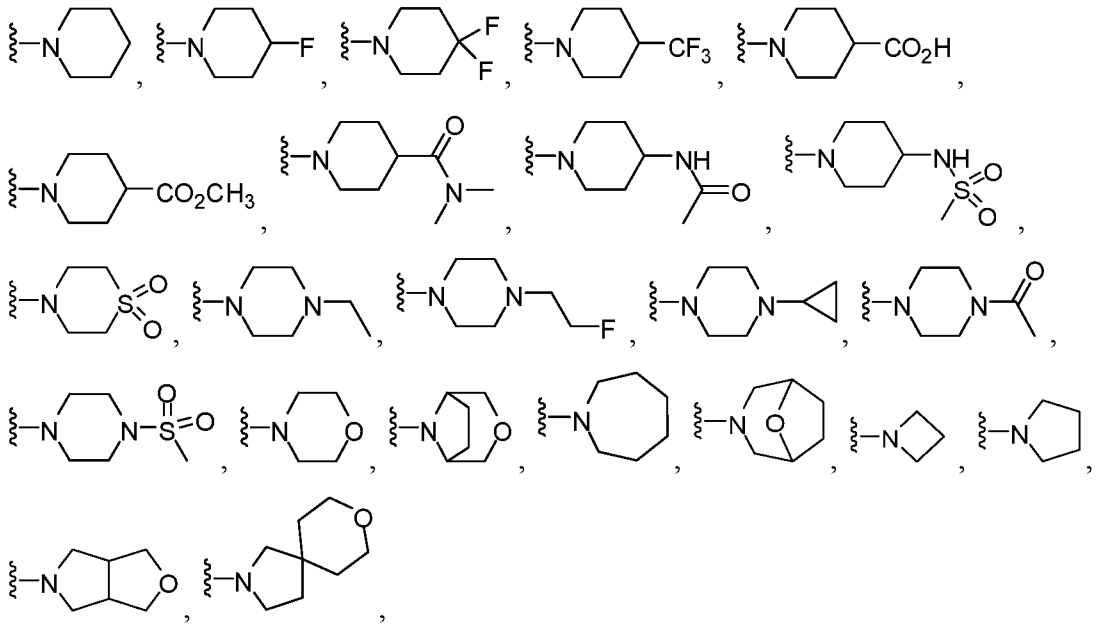
[00297] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 1 and R^3 is -NR^5R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), R^3 is -NR^5R^6, and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 1, R^3 is -NR^5R^6, and R^5 and R^6, together with the nitrogen to which they are attached, form an

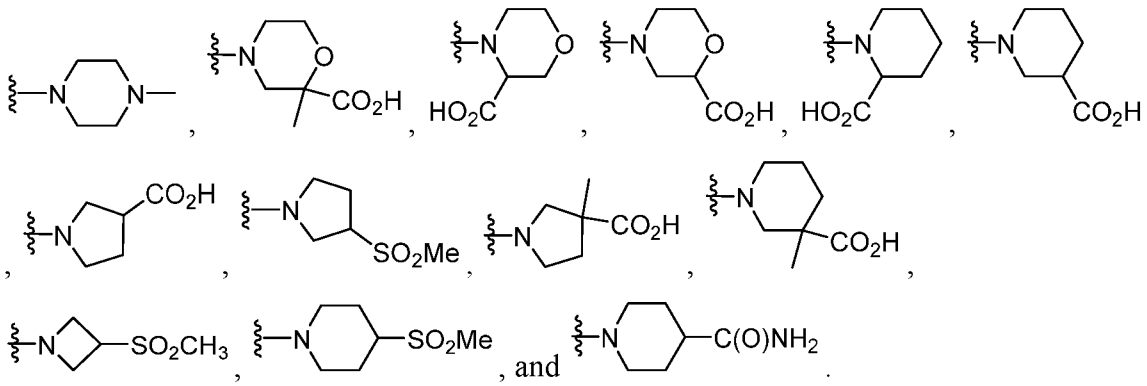
unsubstituted heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 1, R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl, cycloalkyl, C_{1-6}haloalkyl, halogen, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$.

[00298] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2 and each R^3 is independently selected from C_{1-6}alkyl, halogen, C_{1-6}haloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-NR^5R^6$, $-OR^7$, $-CO_2R^8$, and $-C(O)NR^8R^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is halogen, and one R^3 is $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is -Cl, one R^3 is $-OR^7$, and R^7 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is -Cl, one R^3 is $-OR^7$, and R^7 is $-C_{1-6}$alkyl(heterocycloalkyl). In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is halogen, and one R^3 is $-NR^5R^6$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is halogen, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is halogen, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl, cycloalkyl, C_{1-6}haloalkyl, halogen, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is -Cl, and one R^3 is $-NR^5R^6$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is -Cl, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is -Cl, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl, cycloalkyl, C_{1-6}haloalkyl, halogen, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is C_{1-}

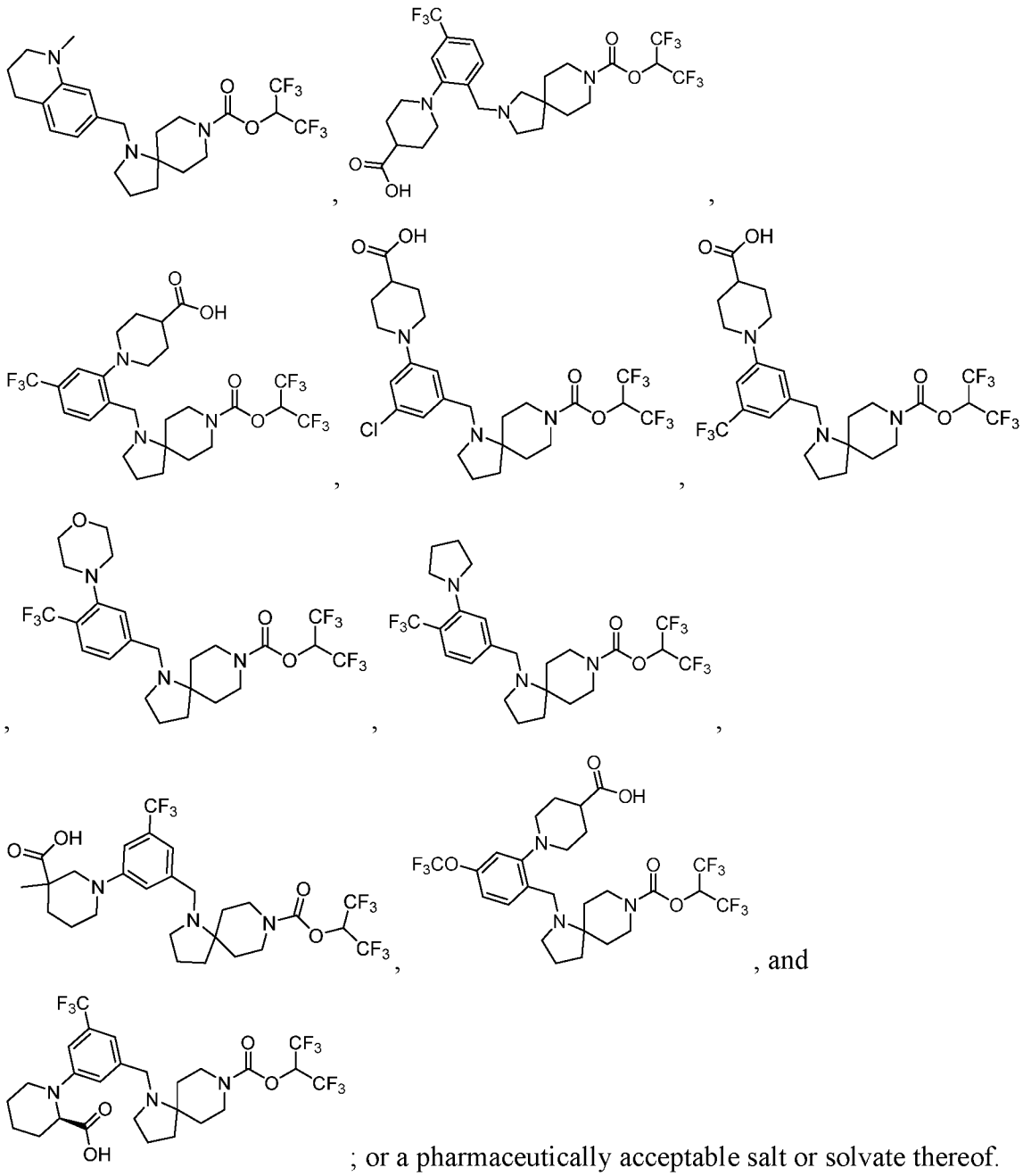
$_{6}$haloalkyl, and one R^3 is $-NR^5R^6$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is C_{1-6}haloalkyl, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is C_{1-6}haloalkyl, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl, cycloalkyl, C_{1-6}haloalkyl, halogen, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is $-CF_3$, and one R^3 is $-NR^5R^6$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is $-CF_3$, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is $-CF_3$, one R^3 is $-NR^5R^6$, and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring substituted with one or two R^{10} independently selected from C_{1-6}alkyl, cycloalkyl, C_{1-6}haloalkyl, halogen, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$.

[00299] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), p is 2, one R^3 is C_{1-6}alkyl, halogen, C_{1-6}haloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-OR^7$, $-CO_2R^8$, or $-C(O)NR^8R^9$, and one R^3 is $-NR^5R^6$, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a heterocycloalkyl ring selected from:



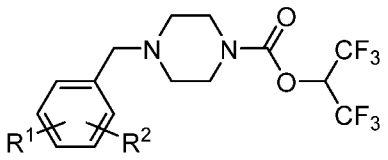


[00300] In some embodiments of the methods for treating dyskinesia with a compound of Formula (II), the compound is selected from:



; or a pharmaceutically acceptable salt or solvate thereof.

[00301] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (III):



Formula (III);

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(iii) a 4-6 membered saturated monocyclic heterocycle; or

(iv) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

each R^9 is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[00302] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (III), wherein the dyskinesia is levodopa-induced dyskinesia.

[00303] In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-

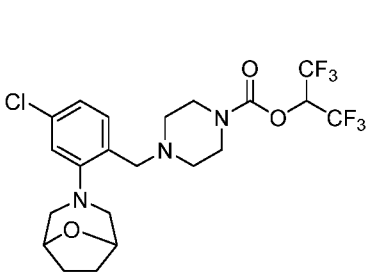
6 membered saturated monocyclic heterocycle substituted with one or two substituents independently selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine and piperidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is pyrrolidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is piperidine. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$; wherein the 4-6 membered saturated monocyclic heterocycle is morpholine.

[00304] In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 7-8 membered bridged heterocyclic ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the

nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring is substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring is substituted with one substituent selected from halogen, oxo, and C_{1-6}alkyl.

[00305] In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is halogen, $-OR^3$, $-SF_5$, or C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is halogen, $-CH_3$, $-CF_3$, $-OCH_3$, or $-OCF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is halogen, $-SF_5$, or C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is C_{1-6}alkyl optionally substituted by halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is $-SF_5$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is $-OCH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), R^1 is $-OCF_3$.

[00306] In some embodiments of the methods for treating dyskinesia with a compound of Formula (III), the compound is selected from: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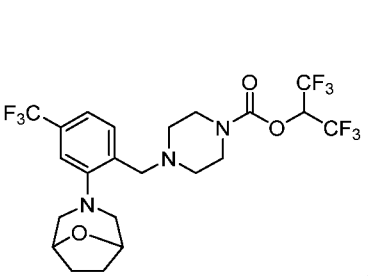
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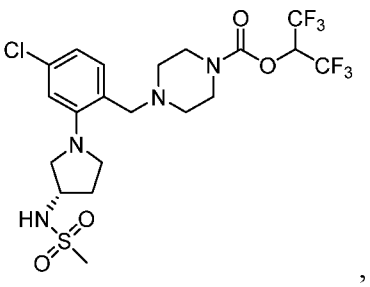
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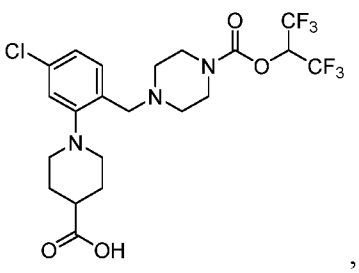
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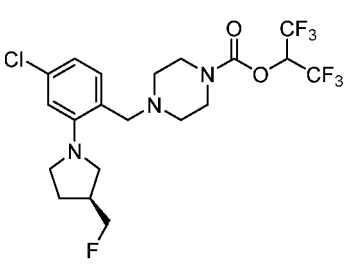
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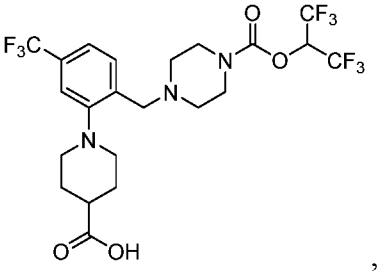
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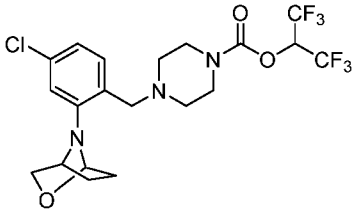
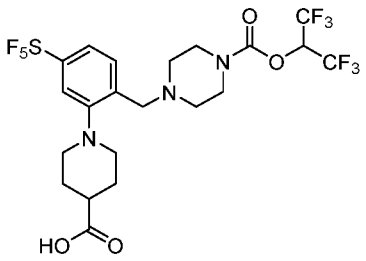
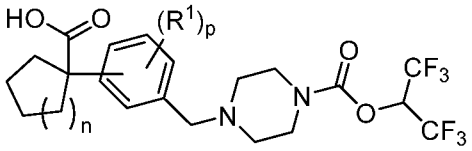



; or a pharmaceutically acceptable salt or solvate thereof.

[00307] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (IV):



Formula (IV);

wherein:

each R^1 is independently halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, -CN, or $-SF_5$;

n is 1 or 2; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[00308] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (IV), wherein the dyskinesia is levodopa-induced dyskinesia.

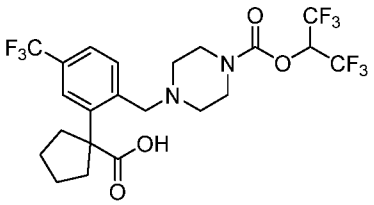
[00309] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), n is 2.

[00310] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 2.

[00311] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is halogen, C_{1-6}alkyl, or C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is

halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), p is 1 and R^1 is $-CF_3$.

[00312] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IV), the compound is selected from: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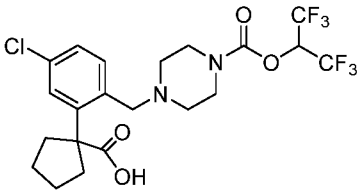
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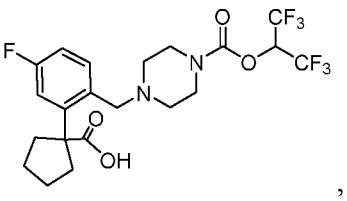
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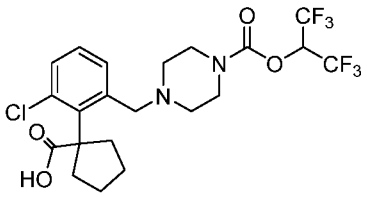
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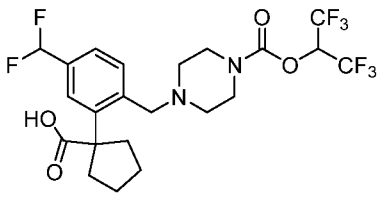
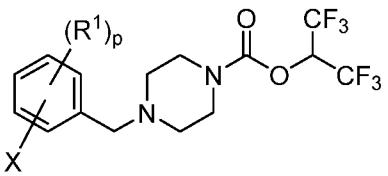
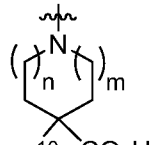

; or a pharmaceutically acceptable salt or solvate thereof.

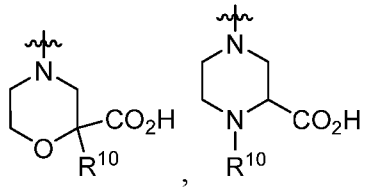
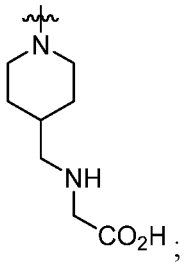
[00313] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (V):



Formula (V);

wherein:

X is -N(R^2)(R^3), -C_{1-6}alkyl-N(R^4)(R^5), -C(O)N(R^4)(R^5),  ,

 , , or  ;

each R^1 is independently halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, -CN, or -SF_5;

R^2 and R^3, together with the nitrogen to which they are attached, form

(iii) a C_2-C_8heterocycloalkyl; or

(iv) a C_2-C_8heteroaryl;

wherein the C_2-C_8heterocycloalkyl or the C_2-C_8heteroaryl is substituted with one R^6 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^4 and R^5, together with the nitrogen to which they are attached, form

(iii) a C_2-C_8heterocycloalkyl; or

(iv) a C_2-C_8heteroaryl;

wherein the C_2-C_8heterocycloalkyl or the C_2-C_8heteroaryl is substituted with one R^7 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^6 is -C_{1-6}alkyl-CO_2H or -N(R^8)-C_{1-6}alkyl-CO_2H;

R^7 is -CO_2H, -C_{1-6}alkyl-CO_2H, or -N(R^9)-C_{1-6}alkyl-CO_2H;

R^8 is H or C_{1-6}alkyl;

R^9 is H or C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl;

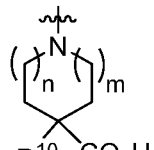
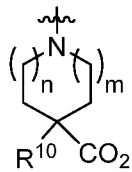
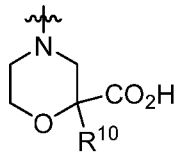
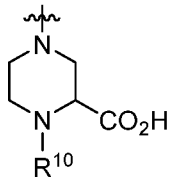
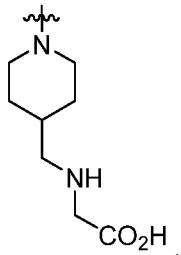
m is 0, 1, or 2;

n is 0 or 1; and

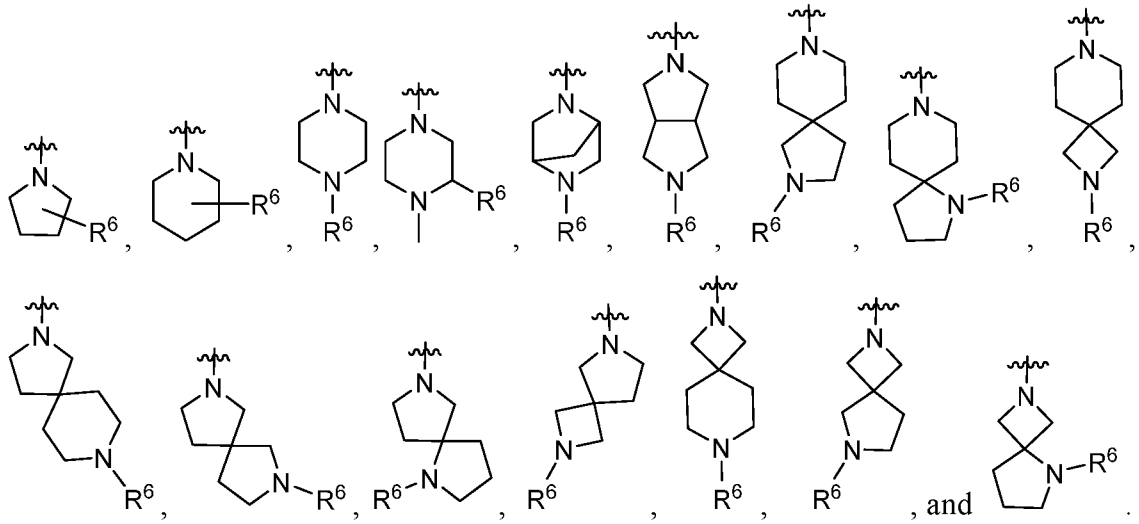
p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[00314] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (V), wherein the dyskinesia is levodopa-induced dyskinesia.

[00315] In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is  , m is 1, and n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), R^{10} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is  .

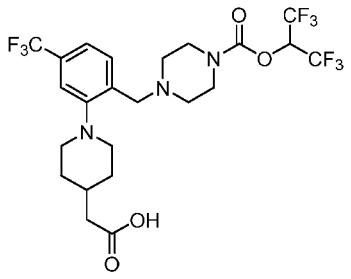
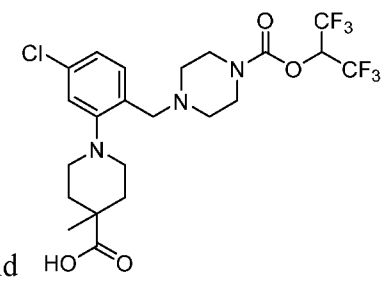
[00316] In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is $-N(R^2)(R^3)$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is $-N(R^2)(R^3)$ and R^2 and R^3, together with the nitrogen to which they are attached, form a C_2-C_8heterocycloalkyl substituted with one R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), X is $-N(R^2)(R^3)$ and R^2 and R^3, together with the nitrogen to which they are attached, form a C_2-C_8heterocycloalkyl selected from



[00317] In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 2.

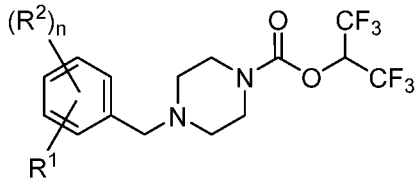
[00318] In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is halogen, C_{1-6}alkyl, or C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), p is 1 and R^1 is $-CF_3$.

[00319] In some embodiments of the methods for treating dyskinesia with a compound of Formula (V), the compound is selected from:

and ; or a pharmaceutically acceptable salt or solvate thereof.

[00320] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VI):



Formula (VI);

wherein:

R^1 is $-N(R^3)(R^5)$ or $-NH(R^4)$;

each R^2 is independently selected from halogen, C_{1-6}alkyl, -CN, C_{1-6}haloalkyl, and $-OR^6$;

R^3 is $-CH_2CO_2H$, $-CH_2CH_2CO_2H$, or $-CH(CH_3)CO_2H$;

R^4 is $-(CH_2)_m-CO_2H$;

R^5 is H or C_{1-3}alkyl;

each R^6 is independently selected from H, C_{1-6}alkyl, and C_{1-6}haloalkyl;

n is 0, 1, 2, 3, or 4; and

m is 3;

or a pharmaceutically acceptable salt or solvate thereof.

[00321] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VI), wherein the dyskinesia is levodopa-induced dyskinesia.

[00322] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is $-N(R^3)(R^5)$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is $-N(R^3)(R^5)$ and R^5 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is $-N(R^3)(R^5)$, R^5 is H, and R^3 is $-CH_2CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is $-N(R^3)(R^5)$, R^5 is H, and R^3 is $-CH_2CH_2CO_2H$. In some embodiments of

the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is -$N(R^3)(R^5)$, R^5 is H, and R^3 is -$CH(CH_3)CO_2H$.

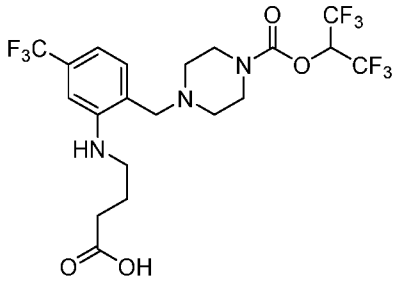
[00323] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is -$N(R^3)(R^5)$ and R^5 is C_{1-3}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is -$N(R^3)(R^5)$, R^5 is C_{1-3}alkyl, and R^3 is -CH_2CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is -$N(R^3)(R^5)$, R^5 is C_{1-3}alkyl, and R^3 is -$CH_2CH_2CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is -$N(R^3)(R^5)$, R^5 is C_{1-3}alkyl, and R^3 is -$CH(CH_3)CO_2H$.

[00324] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein R^1 is -$NH(CH_2)_3CO_2H$.

[00325] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein n is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein n is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein n is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), wherein n is 2.

[00326] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or -OR^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is halogen, C_{1-6}alkyl, or C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is -CH_3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), n is 1 and R^2 is -CF_3.

[00327] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VI), the compound is selected from: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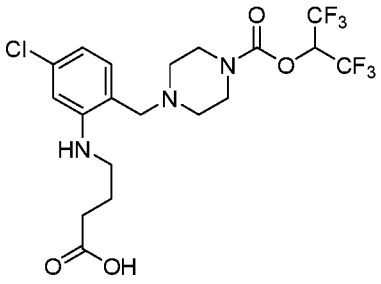
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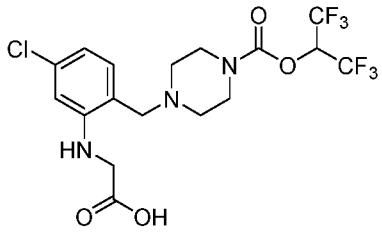
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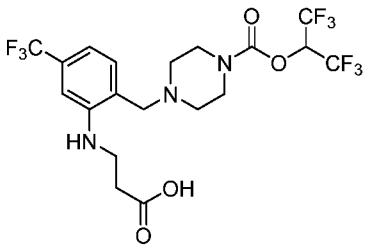
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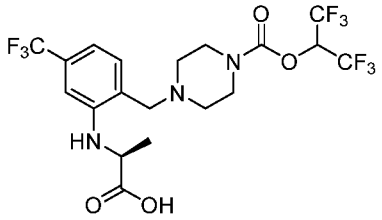
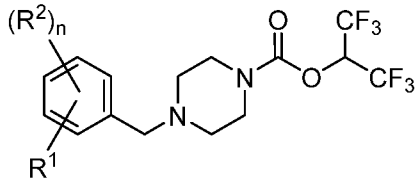

; or a pharmaceutically acceptable salt or solvate thereof.

[00328] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VII):



Formula (VII);

wherein:

R^1 is $-R^{14}$, $-OR^3$, $-SR^4$, $-S(O)_2R^4$, or $-C\equiv C-(CR^6R^7)-R^8$;

each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-OR^{17}$, and $-C(O)NR^{18}R^{19}$;

R^3 is $-(CR^6R^7)_m-R^8$, $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$, or $-(CR^6R^7)_t-C_{3-6}$cycloalkyl$-R^8$;

R^4 is $-(CR^6R^7)_m-R^{8'}$, $-(CR^6R^7)_v-C(O)OH$, or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

Y is -O- or $-N(R^{22})-$;

each R^6 and R^7 is each independently selected from H, F, and C_{1-6}alkyl; or R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring;

R^8 is $-C(O)OR^9$, $-C(O)R^{10}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

$R^{8'}$ is $-C(O)OR^{9'}$, $-C(O)R^{10'}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

R^9 is H or C_{1-6}alkyl;

$R^{9'}$ is C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl or $-NHSO_2R^{21}$;

$R^{10'}$ is C_{2-6}alkyl or $-NHSO_2R^{21}$;

R^{11} is C_{1-6}alkyl or C_{1-6}alkoxy;

R^{12} and R^{13} is each independently H or C_{1-6}alkyl;

R^{14} is $-(CR^{15}R^{16})_m-R^8$ or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

each R^{15} and R^{16} is each independently selected from H, F, and C_{1-6}alkyl;

each R^{17} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-6}cycloalkyl;

each R^{18} and R^{19} is each independently selected from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, aryl, and heteroaryl; or R^{18} and R^{19}, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{20};

each R^{20} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

R^{21} is C_{1-6}alkyl or C_{3-6}cycloalkyl;

R^{22} is H, C_{1-6}alkyl, or $-SO_2R^{23}$;

R^{23} is C_{1-6}alkyl;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3, or 4;

p is 2, 3, or 4;

q is 1, 2, or 3;

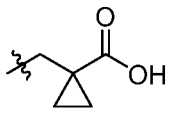
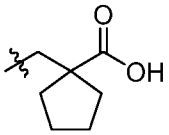
t is 0, 1, or 2; and

v is 3 or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[00329] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VII), wherein the dyskinesia is levodopa-induced dyskinesia.

[00330] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-(CR^6R^7)_m-R^8$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a

compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is $-CH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$ and R^{10} is $-NHSO_2R^{21}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$, R^{10} is $-NHSO_2R^{21}$, and R^{21} is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$, R^{10} is $-NHSO_2R^{21}$, and R^{21} is C_{3-6}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$ and R^{11} is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$ and R^{11} is C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH(CH_3)CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2C(O)OCH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2C(O)OCH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2C(O)OC(CH_3)_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2CH_2C(O)OCH_3$. In some embodiments of the methods for treating dyskinesia

with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2CH_2C(O)OCH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-CH_2CH_2CH_2C(O)OC(CH_3)_3$.

[00331] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is $-(CR^6R^7)_t-C_{3-6}$cycloalkyl-R^8. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$, R^3 is $-(CR^6R^7)_t-C_{3-6}$cycloalkyl-R^8, and t is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$, R^3 is $-(CR^6R^7)_t-C_{3-6}$cycloalkyl-R^8, and t is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$, R^3 is $-(CR^6R^7)_t-C_{3-6}$cycloalkyl-R^8, and t is 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is -cyclopropyl-C(O)OH. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is -cyclobutyl-C(O)OH. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-OR^3$ and R^3 is -cyclopentyl-C(O)OH.

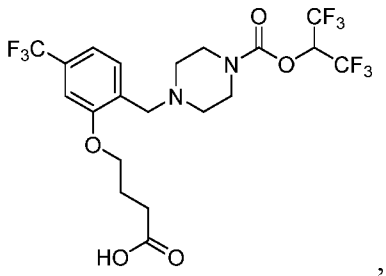
[00332] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-(CR^{15}R^{16})_m-R^8$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^{14} is $-(CR^{15}R^{16})_m-R^8$ and m is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^{14} is $-(CR^{15}R^{16})_m-R^8$ and m is 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^{14} is $-(CR^{15}R^{16})_m-R^8$ and m is 3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^{14} is $-(CR^{15}R^{16})_m-R^8$ and m is 4. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)OR^9$ and R^9 is $-CH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$

and R^{10} is $-NHSO_2R^{21}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$, R^{10} is $-NHSO_2R^{21}$, and R^{21} is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)R^{10}$, R^{10} is $-NHSO_2R^{21}$, and R^{21} is C_{3-6}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$ and R^{11} is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$ and R^{11} is C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH(CH_3)CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2C(O)OCH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2C(O)OCH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2C(O)OC(CH_3)_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2C(O)OCH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2C(O)OCH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2C(O)OC(CH_3)_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2CH_2C(O)OCH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2CH_2C(O)OCH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), R^1 is $-R^{14}$ and R^{14} is $-CH_2CH_2CH_2CH_2C(O)OC(CH_3)_3$.

[00333] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 2.

[00334] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or $-OR^{17}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, or C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is halogen, C_{1-6}alkyl, or C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), n is 1 and R^2 is $-CF_3$.

[00335] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VII), the compound is selected from: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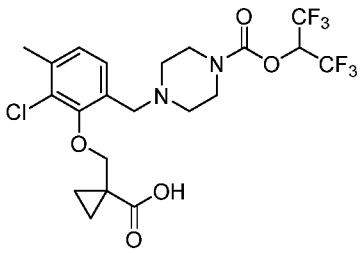
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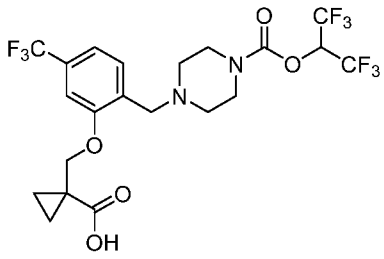
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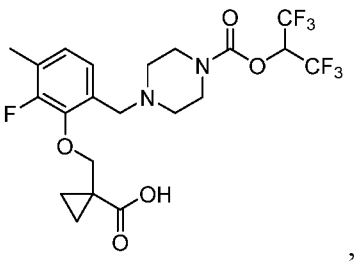
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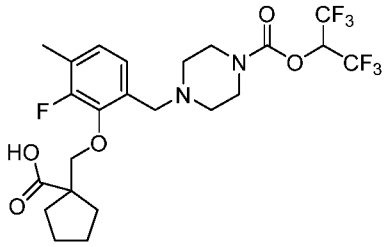
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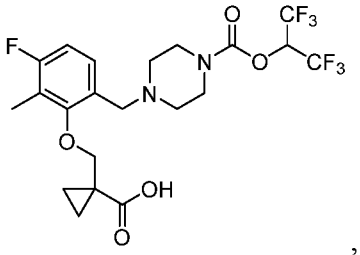
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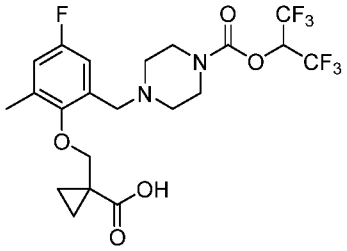
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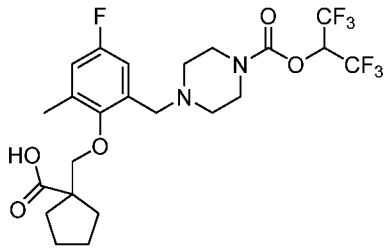
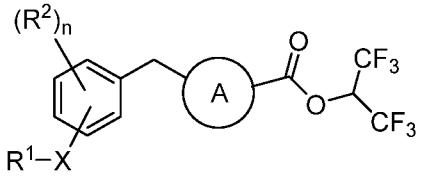
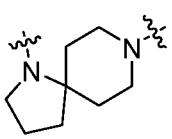
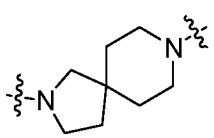
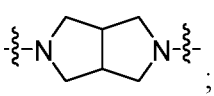

and ; or a pharmaceutically acceptable salt or solvate thereof.

[00336] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VIII):



Formula (VIII);

wherein:

A is 
, 
, or 
;

X is -O-, -S-, -SO_2-, -N(R^3)-, or -CH_2-;

Y is -O- or -N(R^7)-;

R^1 is $-(CR^4R^5)_m-R^6$, $-(CR^4R^5)_p-Y-(CR^4R^5)_q-R^6$, or $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6;

each R^2 is independently selected from halogen, -CN, C_{1-6}alkyl, C_{1-6}haloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-OR^{17}$, and $-C(O)NR^{18}R^{19}$;

R^3 is H or C_{1-6}alkyl;

each R^4 and R^5 is each independently selected from H, F, and C_{1-6}alkyl; or R^4 and R^5, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring;

R^6 is $-CO_2R^9$, $-C(O)R^{10}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

R^7 is H, C_{1-6}alkyl, or $-SO_2R^8$;

R^8 is C_{1-6}alkyl;

R^9 is H or C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl or $-NHSO_2R^{21}$;

R^{11} is C_{1-6}alkyl or C_{1-6}alkoxy;

R^{12} and R^{13} is each independently H or C_{1-6}alkyl;

each R^{17} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, aminoalkyl, cycloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-C_{1-6}$alkyl-C(O)(heterocycloalkyl), optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

each R^{18} and R^{19} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, cycloalkyl, aryl, and heteroaryl; or R^{18} and R^{19}, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{20};

each R^{20} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

R^{21} is C_{1-6}alkyl;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3, or 4;

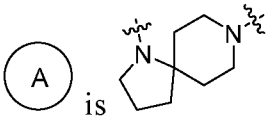
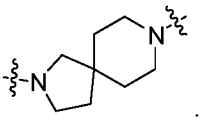
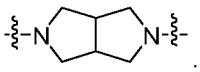
p is 2, 3, or 4;

q is 1, 2, or 3; and

t is 0, 1, or 2;

or a pharmaceutically acceptable salt or solvate thereof.

[00337] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (VIII), wherein the dyskinesia is levodopa-induced dyskinesia.

[00338] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII),  is . In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII),  is  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII),  is  .

[00339] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), X is -O-. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), X is $-N(R^3)-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), X is -N(H)-. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), X is $-N(CH_3)-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), X is $-N(CH_2CH_3)-$.

[00340] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and R^6 is $-CO_2R^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and R^6 is $-CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and R^6 is $-CO_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and R^6 is $-CO_2CH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and R^6 is $-C(O)R^{10}$.

[00341] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and R^6 is $-C(O)NHSO_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and m is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and m is 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and m is 3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and m is 4.

[00342] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and each R^4 and R^5 is each independently selected from H and C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$ and each R^4 and R^5 is H.

[00343] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$, R^6 is $-CO_2H$, m is 1, and R^4 and R^5 are H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$, R^6 is $-CO_2H$, m is 2, and each R^4 and R^5 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$, R^6 is $-CO_2H$, m is 3, and each R^4 and R^5 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_m-R^6$, R^6 is $-CO_2H$, m is 4, and each R^4 and R^5 is H.

[00344] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-$cyclopropyl-R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t$-cyclobutyl-R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-$cyclopentyl-R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t$-cyclohexyl-R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6 and R^6 is $-CO_2R^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6 and R^6 is $-CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6 and R^6 is $-CO_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6 and R^6 is $-CO_2CH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6 and t is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6 and t is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6 and t is 2.

[00345] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is $-(CR^4R^5)_t-C_{3-6}$cycloalkyl-R^6, R^6 is $-CO_2H$, t is 0, and R^4 and R^5 are H. In some embodiments of the methods for treating dyskinesia with a compound of

Formula (VIII), R^1 is -$(CR^4R^5)_t$-C_{3-6}cycloalkyl-R^6, R^6 is -CO_2H, t is 1, and each R^4 and R^5 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), R^1 is -$(CR^4R^5)_t$-C_{3-6}cycloalkyl-R^6, R^6 is -CO_2H, t is 2, and each R^4 and R^5 is H.

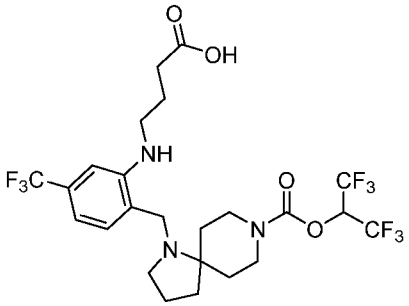
[00346] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$OCH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$N(H)CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$OCH(CH_3)C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$N(H)CH(CH_3)C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$OCH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$N(H)CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$OCH_2CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$N(H)CH_2CH_2CH_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$OCH_2CH_2C(CH_3)_2C(O)OH$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -$N(H)CH_2CH_2C(CH_3)_2C(O)OH$.

[00347] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -O-cyclopropyl-C(O)OH. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -N(H)-cyclopropyl-C(O)OH. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -O-cyclobutyl-C(O)OH. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), -X-R^1 is -N(H)-cyclobutyl-C(O)OH.

[00348] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 2.

[00349] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or -OR^{17}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is halogen, C_{1-6}alkyl, or C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is -CH_3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), n is 1 and R^2 is -CF_3.

[00350] In some embodiments of the methods for treating dyskinesia with a compound of Formula (VIII), the compound is selected from: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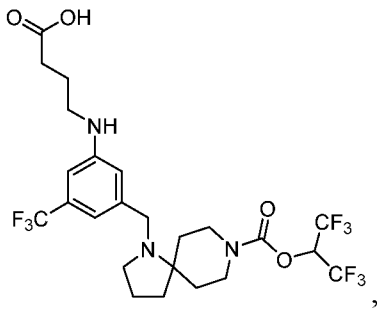
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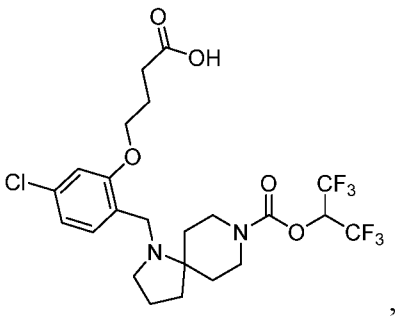
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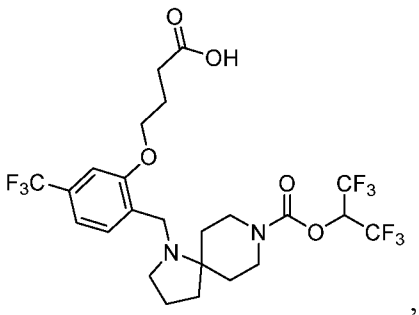
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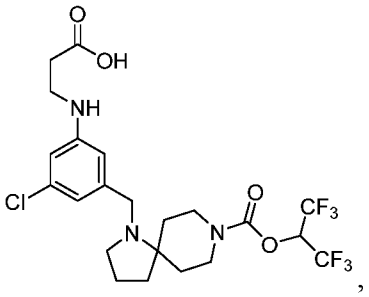
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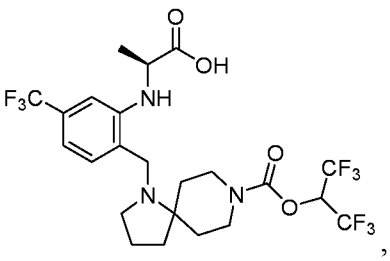
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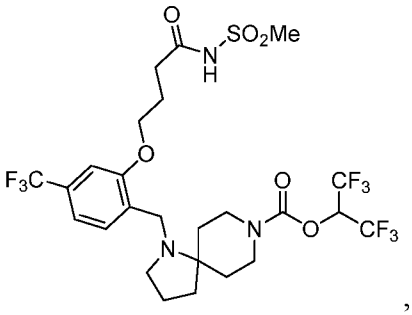

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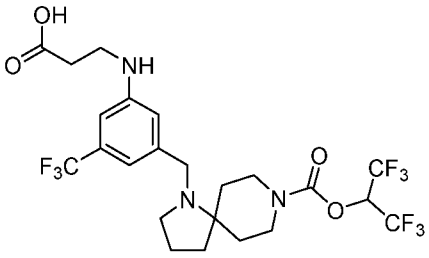
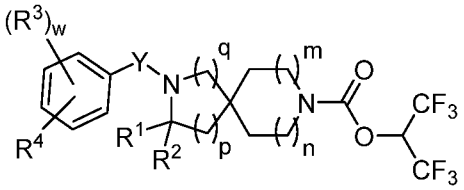


; or a pharmaceutically acceptable salt or solvate thereof.

[00351] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (IX):



Formula (IX);

wherein:

Y is $-CH_2-$ or -C(O)-;

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-SF_5$, and $-OR^7$;

R^4 is selected from $-C\equiv C-C_{1-6}alkyl-CO_2H$ and $-C_{3-8}cycloalkyl-CO_2H$;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, and $-C_{1-6}alkyl-C_{3-8}cycloalkyl$;

w is 0, 1, 2, 3, or 4;

n is 0 or 1;

m is 0 or 1;

p is 0, 1, or 2; and

q is 0, 1, or 2; provided that when q is 0, then p is 2;

or a pharmaceutically acceptable salt or solvate thereof.

[00352] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (IX), wherein the dyskinesia is levodopa-induced dyskinesia.

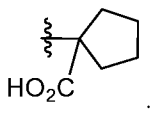
[00353] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), m is 0, n is 0, p is 1, and q is 2. In some embodiments of the methods

for treating dyskinesia with a compound of Formula (IX), m is 0, n is 1, p is 1, and q is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), m is 1, n is 0, p is 1, and q is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), m is 1, n is 1, p is 0, and q is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), m is 1, n is 1, p is 1, and q is 1. In another embodiment is a compound of Formula (IX), m is 1, n is 1, p is 2 and q is 0.

[00354] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), Y is $-CH_2-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), Y is -C(O)-.

[00355] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^1 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^2 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^1 and R^2 are both H.

[00356] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), w is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), w is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), w is 1 or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), w is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), w is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), w is 2.

[00357] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is $-C{\equiv}C-C_{1\text{-}6}$alkyl-$CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is $-C_{3\text{-}8}$cycloalkyl-CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is 

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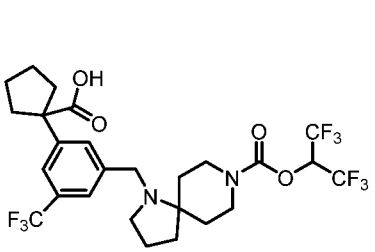
[00358] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is $-C{\equiv}C-C_{1\text{-}6}$alkyl-$CO_2H$, w is 1, and R^3 is selected from $C_{1\text{-}6}$alkyl, halogen, $C_{1\text{-}6}$haloalkyl, $-SF_5$, and $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is $-C{\equiv}C-C_{1\text{-}6}$alkyl-$CO_2H$, w is 1, and R^3 is selected from halogen, $C_{1\text{-}6}$haloalkyl, and $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is $-C{\equiv}C-C_{1\text{-}6}$alkyl-$CO_2H$, w is 1, and R^3 is selected from halogen and $C_{1\text{-}6}$haloalkyl. In some

embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C≡C-C_{1-6}alkyl-CO_2H, w is 1, and R^3 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C≡C-C_{1-6}alkyl-CO_2H, w is 1, and R^3 is -CH_3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C≡C-C_{1-6}alkyl-CO_2H, w is 1, and R^3 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C≡C-C_{1-6}alkyl-CO_2H, w is 1, and R^3 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C≡C-C_{1-6}alkyl-CO_2H, w is 1, and R^3 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C≡C-C_{1-6}alkyl-CO_2H, w is 1, and R^3 is -CF_3.

[00359] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is selected from C_{1-6}alkyl, halogen, C_{1-6}haloalkyl, -SF_5, and -OR^7. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is selected from halogen, C_{1-6}haloalkyl, and -OR^7. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is selected from halogen and C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is -CH_3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), R^4 is -C_{3-8}cycloalkyl-CO_2H, w is 1, and R^3 is -CF_3.

[00360] In some embodiments of the methods for treating dyskinesia with a compound of Formula (IX), the compound is selected from:



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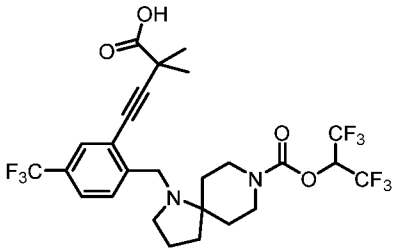
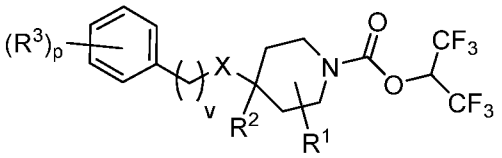


; or a pharmaceutically acceptable salt or solvate thereof.

[00361] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (X):



Formula (X);

wherein:

X is -O- or -N(R^{11})-;

R^1 is H or C_{1-6}alkyl;

R^2 is C_{1-6}alkyl;

each R^3 is independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, -C≡C-C_{1-6}alkyl-CO_2H, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), C_{1-9}heteroaryl, -SF_5, -NR^5R^6, -OR^7, -CO_2R^8, and -$C(O)NR^8R^9$, wherein C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{1-9}heteroaryl are optionally substituted with one or two R^4; or two adjacent R^3 form a C_{2-9}heterocycloalkyl ring, wherein the C_{2-9}heterocycloalkyl ring is optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{1-6}haloalkyl, halogen, oxo, -CN, -CO_2R^8, -$C(O)R^8$, -$C(O)NR^8R^9$, -SO_2R^8, -$NR^9C(O)R^8$, and -$NR^9SO_2R^8$;

each R^5 and R^6 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-C(O)(C_{2-9}heterocycloalkyl), C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl; or R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-C(O)(C_{2-9}heterocycloalkyl), -C_{1-6}alkyl-CO_2H, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl, wherein C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl are

optionally substituted with one or two groups selected from oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and CO_2NH_2;

each R^8 and R^9 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one or two groups selected from C_{1-6}alkyl, C_{1-6}haloalkyl, CO_2H, and CO_2NH_2;

each R^{10} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, oxo, -CN, $-CO_2R^8$, $-C(O)R^8$, $-C(O)NR^8R^9$, $-SO_2R^8$, $-NR^9C(O)R^8$, and $-NR^9SO_2R^8$;

R^{11} is H, C_{1-6}alkyl, $-C(O)-C_{1-6}$alkyl, or $-CH_2CO_2H$;

p is 0, 1, 2, 3, 4, or 5; and

v is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00362] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (X), wherein the dyskinesia is levodopa-induced dyskinesia.

[00363] In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), X is -O-. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), X is $-N(R^{11})-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), X is $-N(R^{11})-$ and R^{11} is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), X is $-N(R^{11})-$ and R^{11} is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), X is $-N(R^{11})-$ and R^{11} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), X is $-N(R^{11})-$ and R^{11} is $-C(O)-C_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), X is $-N(R^{11})-$ and R^{11} is $-CH_2CO_2H$.

[00364] In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), R^1 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), R^1 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), R^2 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), R^1 and R^2 are both $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), R^1 is H and R^2 is $-CH_3$.

[00365] In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 0, 1, or 2. In some embodiments of the methods for

treating dyskinesia with a compound of Formula (X), p is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2.

[00366] In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2 and each R^3 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, -C_{1-6}alkyl(heterocycloalkyl), -SF_5, -NR^5R^6, and -OR^7; wherein -C_{1-6}alkyl(heterocycloalkyl) is optionally substituted with one or two groups selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, and oxo. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2 and each R^3 is independently selected halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), -NR^5R^6, -OR^7, -CO_2R^8, and -$C(O)NR^8R^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2 and each R^3 is independently selected from C_{1-6}alkyl, halogen, C_{1-6}haloalkyl, -NR^5R^6, and -OR^7. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2 and each R^3 is independently selected from halogen, C_{1-6}haloalkyl, -NR^5R^6, and -OR^7. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2 and each R^3 is independently selected from halogen, -NR^5R^6, and C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is halogen and one R^3 is -NR^5R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is halogen and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is halogen and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted C_{2-9}heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is halogen and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is halogen and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-}

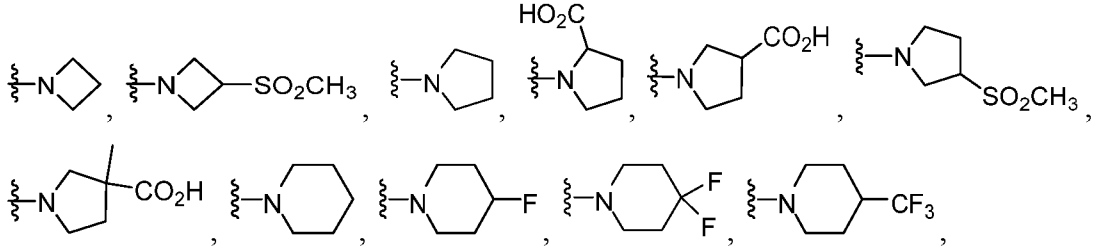
$_{9}$heterocycloalkyl ring substituted with one or two R^{10} selected from C_{1-6}alkyl and -CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is halogen and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with -CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is -Cl and one R^3 is -NR^5R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is -Cl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is -Cl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted C_{2-9}heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is -Cl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is -Cl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10} selected from C_{1-6}alkyl and -CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is -Cl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with -CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is C_{1-6}haloalkyl and one R^3 is -NR^5R^6. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is C_{1-6}haloalkyl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is C_{1-6}haloalkyl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted C_{2-9}heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is C_{1-6}haloalkyl and one R^3 is -NR^5R^6 wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is C_{1-}

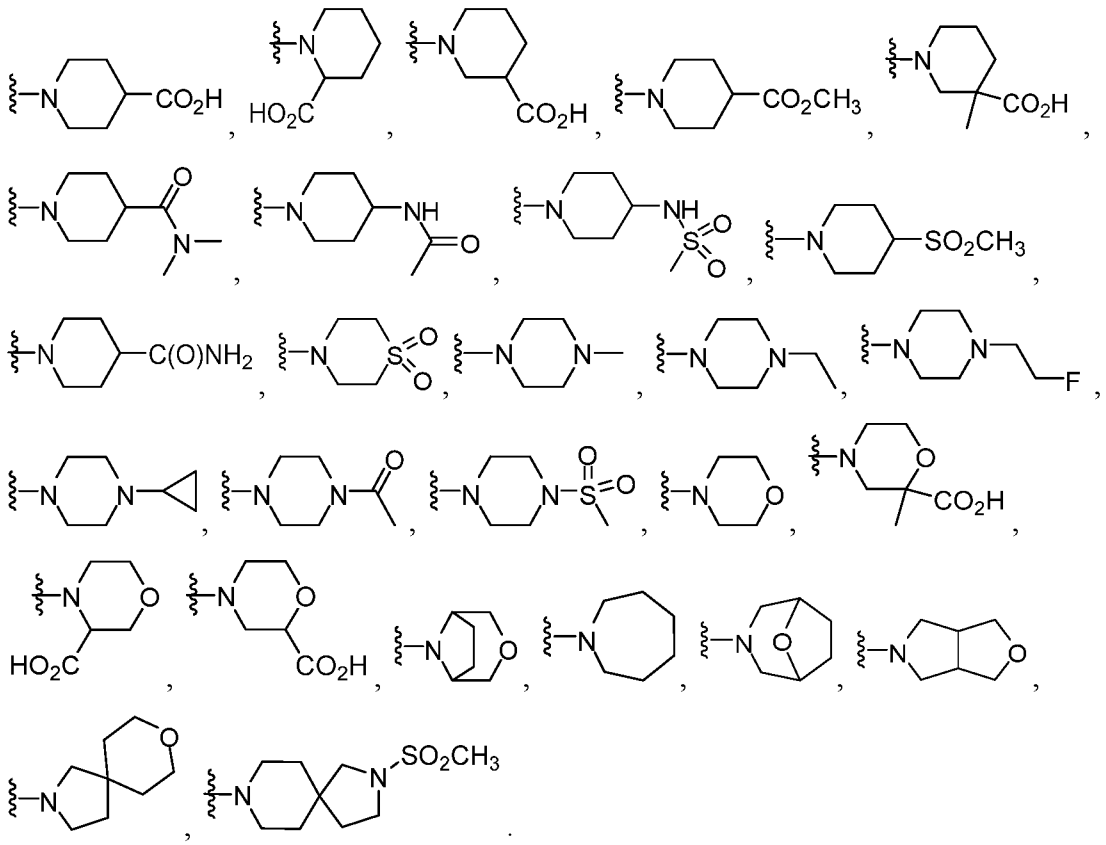
$_{6}$haloalkyl and one R^3 is $-NR^5R^6$ wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10} selected from C_{1-6}alkyl and $-CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is C_{1-6}haloalkyl and one R^3 is $-NR^5R^6$ wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with $-CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is $-CF_3$ and one R^3 is $-NR^5R^6$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is $-CF_3$ and one R^3 is $-NR^5R^6$ wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is $-CF_3$ and one R^3 is $-NR^5R^6$ wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted C_{2-9}heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is $-CF_3$ and one R^3 is $-NR^5R^6$ wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is $-CF_3$ and one R^3 is $-NR^5R^6$ wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10} selected from C_{1-6}alkyl and $-CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 2, one R^3 is $-CF_3$ and one R^3 is $-NR^5R^6$ wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with $-CO_2H$.

[00367] In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{1-6}aminoalkyl, -C_{1-6}alkyl(heterocycloalkyl), $-SF_5$, $-NR^5R^6$, and $-OR^7$; wherein -C_{1-6}alkyl(heterocycloalkyl) is optionally substituted with one or two groups selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, and oxo. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is selected halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), $-NR^5R^6$, $-OR^7$, $-CO_2R^8$, and $-C(O)NR^8R^9$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is selected from C_{1-6}alkyl, halogen, C_{1-6}haloalkyl, $-NR^5R^6$, and $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is selected from

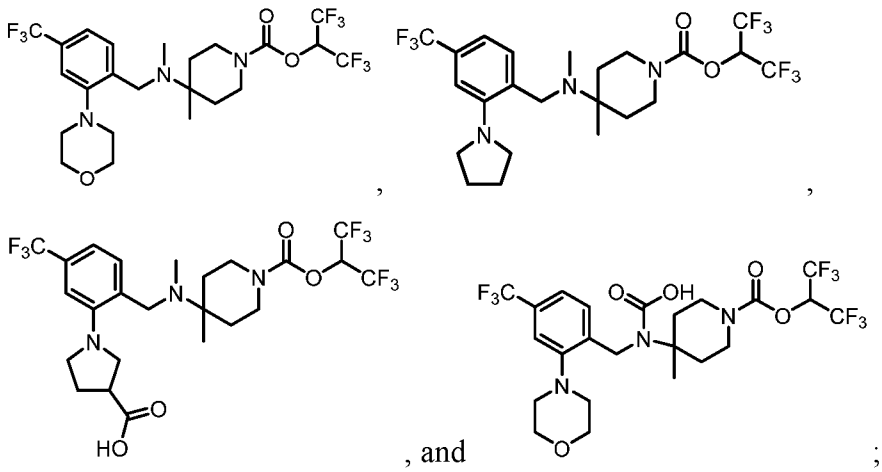
halogen, C_{1-6}haloalkyl, $-NR^5R^6$, and $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is selected from halogen, $-NR^5R^6$, and C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is $-NR^5R^6$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is $-NR^5R^6$, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring optionally substituted with one, two, or three R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is $-NR^5R^6$, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted C_{2-9}heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is $-NR^5R^6$, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10}. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is $-NR^5R^6$, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with one or two R^{10} selected from C_{1-6}alkyl and $-CO_2H$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), p is 1 and R^3 is $-NR^5R^6$, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring substituted with $-CO_2H$.

[00368] In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), R^5 and R^6, together with the nitrogen to which they are attached, form a C_{2-9}heterocycloalkyl ring selected from:



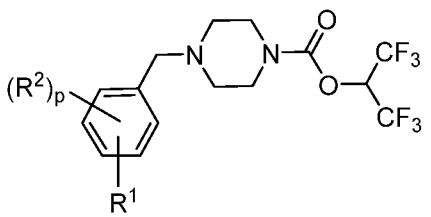


[00369] In some embodiments of the methods for treating dyskinesia with a compound of Formula (X), the compound is selected from:



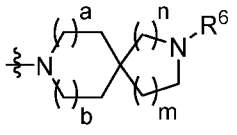
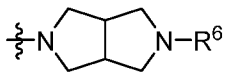
; or a solvate, hydrate, tautomer, *N*-oxide, stereoisomer, or pharmaceutically acceptable salt thereof.

[00370] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XI):



Formula (XI);

wherein:

R^1 is selected from  and  ;

each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, $-SF_5$, $-OR^3$, and $-C(O)NR^4R^5$;

each R^3 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, and -C_{1-6}alkyl-C_{3-8}cycloalkyl;

each R^4 and R^5 is independently selected from H, C_{1-6}alkyl, and C_{3-8}cycloalkyl;

R^6 is selected from C_{1-6}alkyl, -C(O)-C_{1-6}alkyl, and $-S(O)_2$-C_{1-6}alkyl;

a is 0 or 1;

b is 0 or 1;

m is 0, 1, or 2;

n is 0, 1, or 2; provided that when n is 0, then m is 2; and

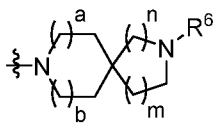
p is 0, 1, 2, 3, or 4;

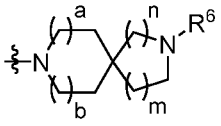
or a pharmaceutically acceptable salt or solvate thereof.

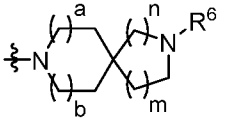
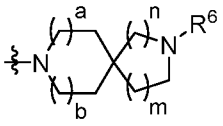
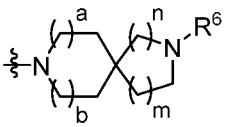
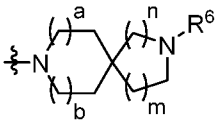
[00371] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XI), wherein the dyskinesia is levodopa-induced dyskinesia.

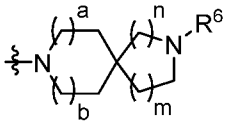
[00372] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^2 is $-NR^5R^6$.

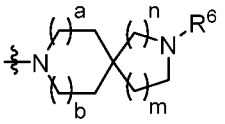
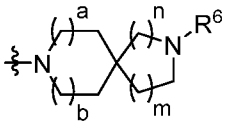
[00373] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 0 or 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 2.

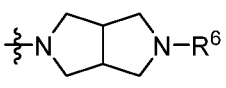
[00374] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is



, a is 1, b is 1, m is 1, and n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  , a is 1, b is 1, m is 0, and n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  , a is 1, b is 1, m is 2, and n is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  , a is 0, b is 1, m is 1, and n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  , a is 0, b is 1, m is 1, and n is 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is



, a is 0, b is 1, m is 0, and n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  , a is 0, b is 0, m is 1, and n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  , a is 0, b is 0, m is 1, and n is 2.

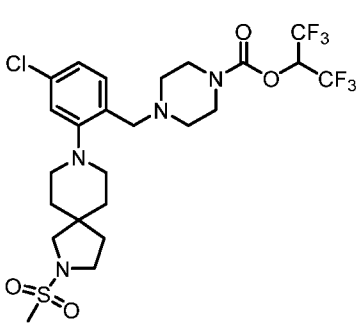
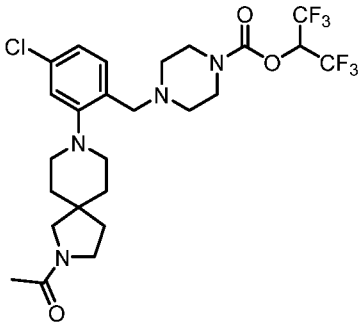
[00375] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^1 is  .

[00376] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^6 is $C_{1\text{-}6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^6 is -CH_3. In some embodiments

of the methods for treating dyskinesia with a compound of Formula (XI), R^6 is $-CH_2CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^6 is $-C(O)-C_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^6 is $-C(O)CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^6 is $-S(O)_2-C_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), R^6 is $-S(O)_2CH_3$.

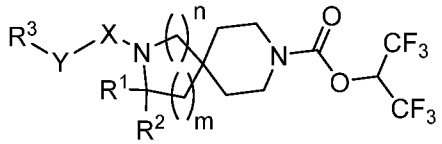
[00377] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is selected from C_{1-6}alkyl, halogen, C_{1-6}haloalkyl, $-SF_5$, and $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is selected from halogen, C_{1-6}haloalkyl, and $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is selected from halogen and C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is -CN. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is $-SF_5$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), p is 1 and R^3 is $-OCH_3$.

[00378] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XI), the compound is selected from:

and ; or a pharmaceutically acceptable salt or solvate thereof.

[00379] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XII):



Formula (XII);

wherein:

X is $-CH_2-$ or -C(O)-;

Y is a bond, C_{1-6}alkyl, C_{1-6}haloalkyl, or C_{3-8}cycloalkyl;

R^1 is H or C_{1-6}alkyl;

R^2 is H or C_{1-6}alkyl;

R^3 is a 5- to 6-membered heteroaryl ring or a 9- to 10-membered bicyclic heteroaryl ring; wherein the 5- to 6-membered heteroaryl ring and the 9- to 10-membered bicyclic heteroaryl ring are optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl-(C_{2-9}heterocycloalkyl), phenyl, $-CH_2-$phenyl, C_{1-9}heteroaryl, $-OR^7$, $-CO_2R^6$, $-CH_2CO_2R^6$, and $-CH_2C(O)N(H)SO_2R^8$; wherein C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), phenyl, and C_{1-9}heteroaryl are optionally substituted with one or two R^5; or two adjacent R^4 form a 6-membered cycloalkyl or 6-membered heterocycloalkyl ring, wherein the cycloalkyl and heterocycloalkyl ring are optionally substituted with one or two R^5;

each R^5 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}heteroalkyl, C_{1-6}alkoxy, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, $-CO_2R^6$, $-CH_2CO_2R^6$, and -C_{1-6}alkyl(C_{2-9}heterocycloalkyl) optionally substituted with C_{1-6}alkyl;

each R^6 is independently selected from H and C_{1-6}alkyl;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;
each R^8 is independently selected from C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;
n is 0 or 1; and
m is 1 or 2; provided that when n is 0, then m is 2; and when n is 1, then m is 1;
or a pharmaceutically acceptable salt or solvate thereof.

[00380] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XII), wherein the dyskinesia is levodopa-induced dyskinesia.

[00381] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), n is 0 and m is 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), n is 1 and m is 1.

[00382] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^1 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^2 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^1 is H and R^2 is H.

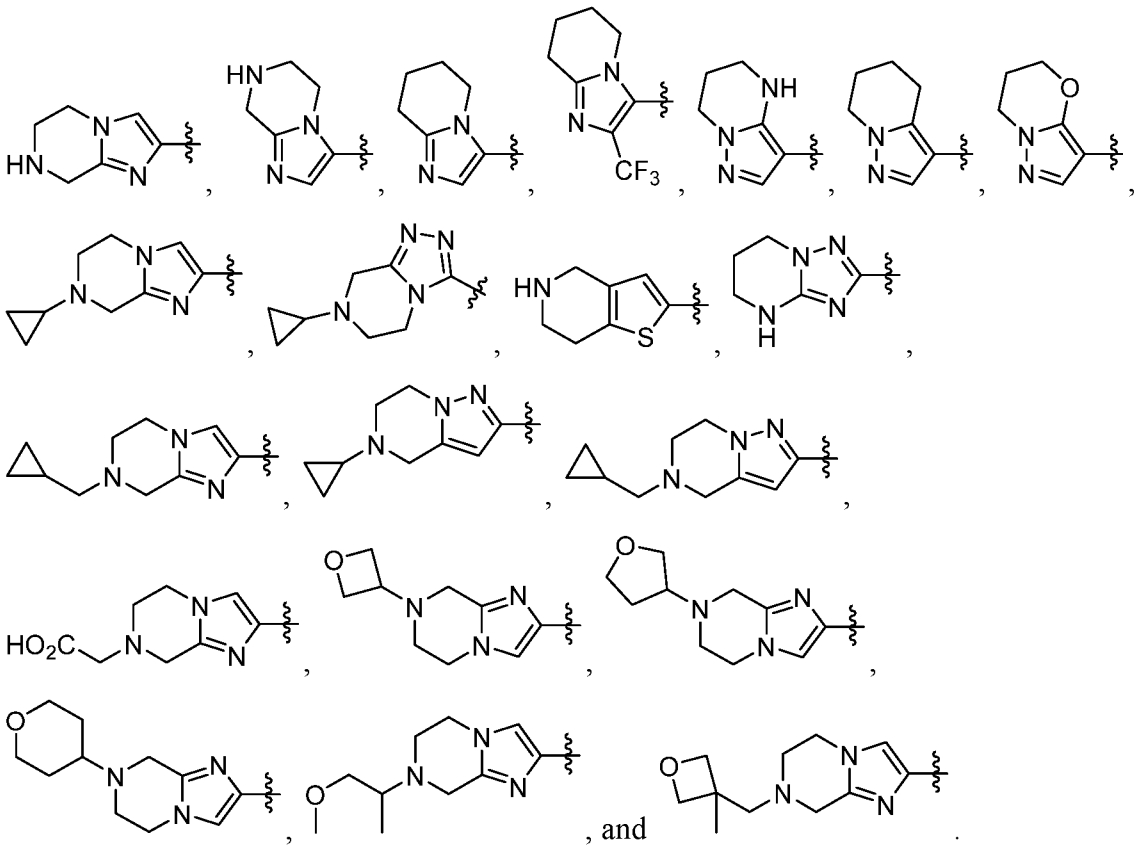
[00383] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), X is $-CH_2-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), X is -C(O)-.

[00384] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), Y is a bond. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), Y is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), Y is $-CH_2-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), Y is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), Y is $-CF_2-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), Y is C_{3-8}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), Y is cyclopropyl.

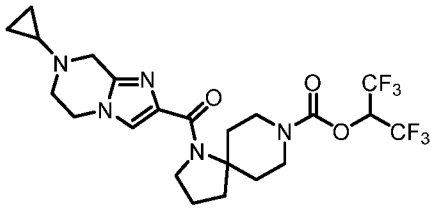
[00385] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5- to 6-membered heteroaryl ring optionally substituted with one, two, or three R^4. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring optionally substituted with one, two, or three R^4. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is an unsubstituted 5-membered heteroaryl ring. In some embodiments of the methods for treating dyskinesia with a compound of

Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with one, two, or three R^4. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two or three R^4, wherein two adjacent R^4 form a 6-membered heterocycloalkyl ring optionally substituted with one or two R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form an unsubstituted 6-membered heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is selected from C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, and -CH_2CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{1-6}heteroalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{3-8}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is -C_{1-6}alkyl(C_{3-8}cycloalkyl). In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{2-9}heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is -CH_2CO_2H. In some

embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two or three R^4, wherein two adjacent R^4 form a 6-membered cycloalkyl ring optionally substituted with one or two R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form an unsubstituted 6-membered cycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered cycloalkyl ring substituted with one R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), R^3 is selected from:

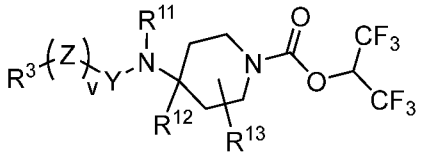


[00386] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XII), the compound is:



; or a pharmaceutically acceptable salt or solvate thereof.

[00387] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XIII):



Formula (XIII);

wherein:

Y is $-CH_2-$ or $-C(O)-$;

Z is C_{3-6}cycloalkyl;

R^3 is a 5- to 6-membered heteroaryl ring or a 9- to 10-membered bicyclic heteroaryl ring; wherein the 5- to 6-membered heteroaryl ring and the 9- to 10-membered bicyclic heteroaryl ring are optionally substituted with one, two, or three R^4;

each R^4 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl-(C_{2-9}heterocycloalkyl), phenyl, $-CH_2-$phenyl, C_{1-9}heteroaryl, $-OR^7$, $-CO_2R^6$, and $-CH_2CO_2R^6$; wherein C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), phenyl, and C_{1-9}heteroaryl are optionally substituted with one or two R^5; or two adjacent R^4 form a 6-membered cycloalkyl or 6-membered heterocycloalkyl ring, wherein the cycloalkyl and heterocycloalkyl ring are optionally substituted with one or two R^5;

each R^5 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}heteroalkyl, C_{1-6}alkoxy, C_{3-8}cycloalkyl, -C_{1-6}alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, $-CO_2R^6$, $-CH_2CO_2R^6$, and -C_{1-6}alkyl(C_{2-9}heterocycloalkyl) optionally substituted with C_{1-6}alkyl;

each R^6 is independently selected from H and C_{1-6}alkyl;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-8}cycloalkyl;

R^{11} is H, C_{1-6}alkyl, or -C_{1-6}alkyl-O-C_{1-6}alkyl;

R^{12} is C_{1-6}alkyl;

R^{13} is H or C_{1-6}alkyl; and

v is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00388] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient in need thereof a therapeutically effective amount of a compound of Formula (XIII), wherein the dyskinesia is levodopa-induced dyskinesia.

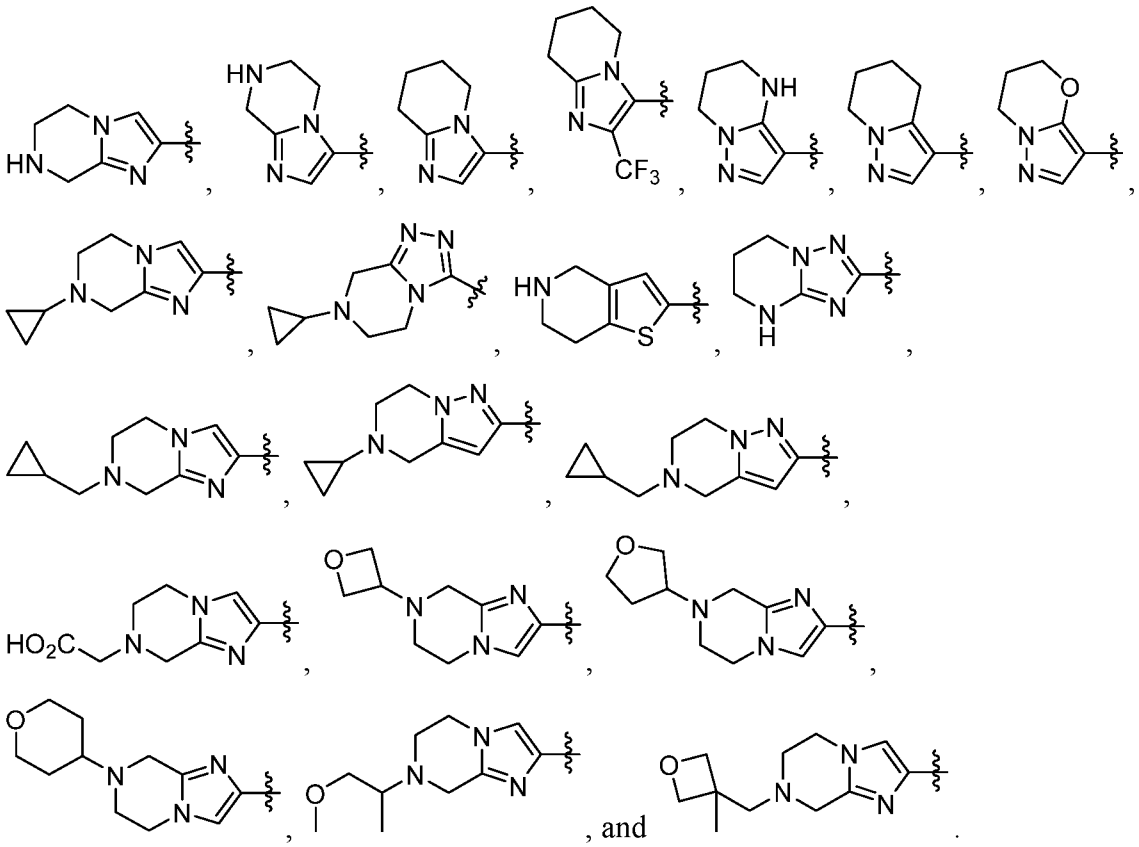
[00389] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^{11} is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^{11} is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^{11} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^{12} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^{13} is H.

[00390] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), Y is $-CH_2-$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), Y is -C(O)-.

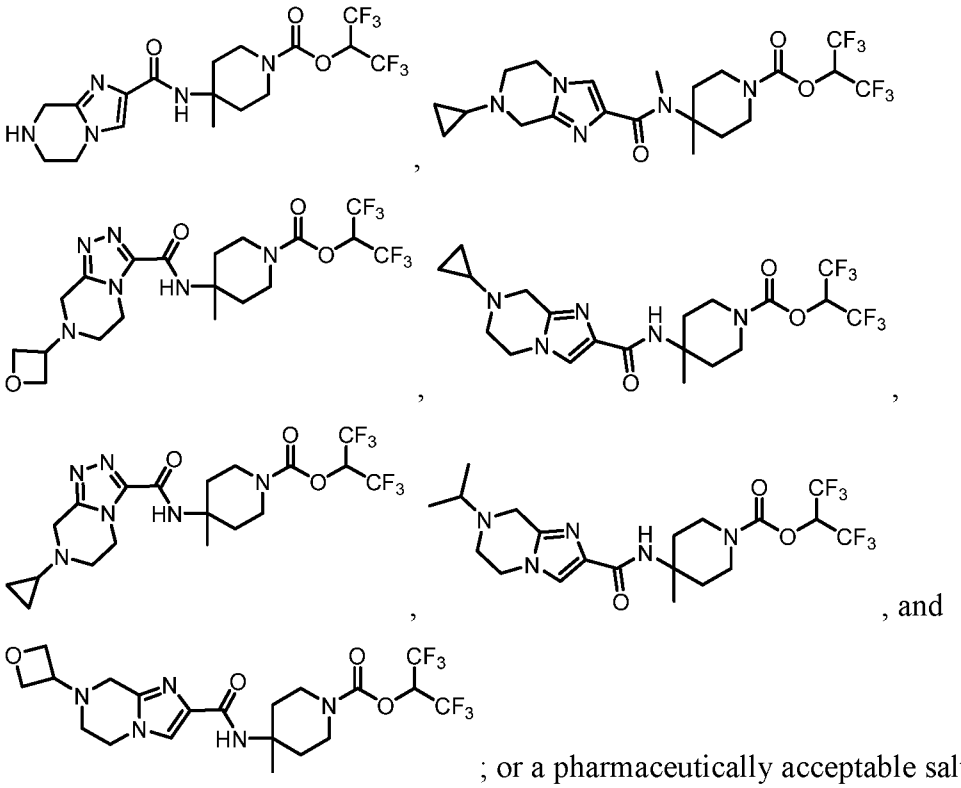
[00391] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), v is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), v is 1.

[00392] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5- to 6-membered heteroaryl ring optionally substituted with one, two, or three R^4. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring optionally substituted with one, two, or three R^4. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is an unsubstituted 5-membered heteroaryl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with one, two, or three R^4. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two or three R^4, wherein two adjacent R^4 form a 6-membered heterocycloalkyl ring optionally substituted with one or two R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form an unsubstituted 6-membered heterocycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is selected from C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-8}cycloalkyl, $-C_{1-6}$alkyl(C_{3-8}cycloalkyl), C_{2-9}heterocycloalkyl, and $-CH_2CO_2H$. In some embodiments

of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{1-6}heteroalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{3-8}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is -C_{1-6}alkyl(C_{3-8}cycloalkyl). In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is C_{2-9}heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered heterocycloalkyl ring substituted with one R^5 and R^5 is -CH_2CO_2H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two or three R^4, wherein two adjacent R^4 form a 6-membered cycloalkyl ring optionally substituted with one or two R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form an unsubstituted 6-membered cycloalkyl ring. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is a 5-membered heteroaryl ring substituted with two adjacent R^4, wherein the two adjacent R^4 form a 6-membered cycloalkyl ring substituted with one R^5. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), R^3 is selected from:

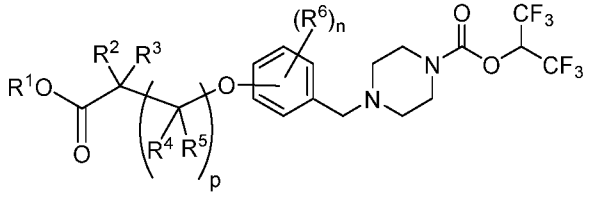


[00393] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIII), the compound is selected from:



; or a pharmaceutically acceptable salt or solvate thereof.

[00394] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XIV):



Formula (XIV);

wherein:

R^1 is H or C_{1-6}alkyl;

R^2 is C_{1-6}alkyl;

R^3 is H or C_{1-6}alkyl;

R^4 and R^5 are independently selected from H and C_{1-6}alkyl;

each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, -OR^7, -$C(O)NR^8R^9$, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{2-9}heteroaryl, wherein C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, -C_{1-6}alkyl(C_{2-9}heterocycloalkyl), and C_{2-9}heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

each R^7 is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-6}cycloalkyl;

each R^8 and R^9 is each independently selected from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, aryl, and heteroaryl; or R^8 and R^9, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{10};

each R^{10} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

n is 0, 1, 2, 3, or 4; and

p is 0 or 1;

or a pharmaceutically acceptable salt or solvate thereof.

[00395] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XIV), wherein the dyskinesia is levodopa-induced dyskinesia.

[00396] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), p is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), p is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), p is 1 and R^4 and R^5 are H. In

some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^3 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^3 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^3 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^3 is H and R^2 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^3 is C_{1-6}alkyl and R^2 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^3 is $-CH_3$ and R^2 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^1 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^1 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), R^1 is $-CH_3$.

[00397] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 0. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 2.

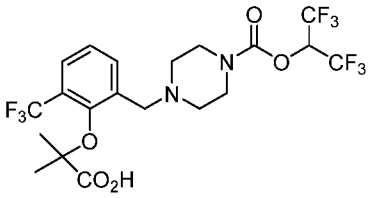
[00398] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-OR^7$, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl, wherein C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl are optionally substituted with one or two groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-OR^7$, and C_{3-6}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-OR^7$, and C_{3-6}cycloalkyl, wherein each R^7 is independently selected from C_{1-6}alkyl and C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), each R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, and C_{1-6}haloalkyl.

[00399] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-OR^7$, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl, wherein C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, and C_{2-9}heteroaryl are optionally substituted with one or two groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound

of Formula (XIV), n is 1 and R^6 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is -CN. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is $-OR^7$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1, R^6 is $-OR^7$, and R^7 is selected from C_{1-6}alkyl and C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1, R^6 is $-OR^7$, and R^7 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1, R^6 is $-OR^7$, and R^7 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1, R^6 is $-OR^7$, and R^7 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1, R^6 is $-OR^7$, and R^7 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1, R^6 is $-OR^7$, and R^7 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1, R^6 is $-OR^7$, and R^7 is C_{3-6}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is C_{3-6}cycloalkyl optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is C_{3-6}cycloalkyl substituted with one or two groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is unsubstituted C_{3-6}cycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is C_{2-9}heterocycloalkyl optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula

(XIV), n is 1 and R^6 is C_{2-9}heterocycloalkyl substituted with one or two groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is unsubstituted C_{2-9}heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is C_{2-9}heteroaryl optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is C_{2-9}heteroaryl substituted with one or two groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), n is 1 and R^6 is unsubstituted C_{2-9}heteroaryl.

[00400] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XIV), the compound is selected from: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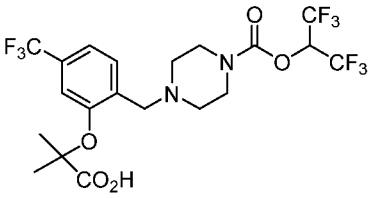
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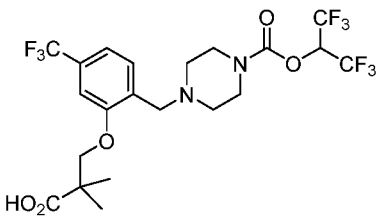
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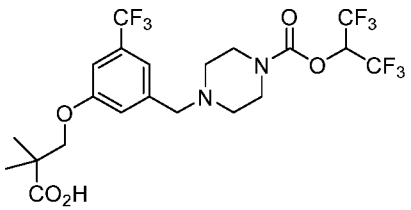
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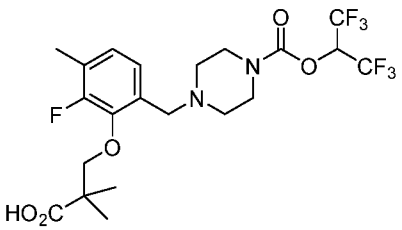
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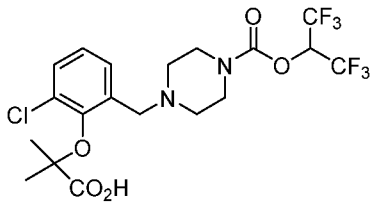
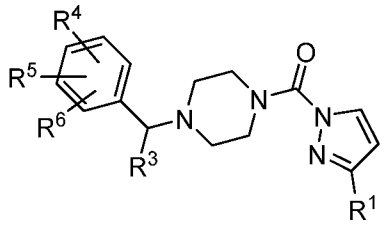

; or a pharmaceutically acceptable salt or solvate thereof.

[00401] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XV):



Formula (XV);

wherein:

R^1 is $-N(R^2)C(O)R^{15}$ or $-N(H)SO_2R^{15}$;

R^2 is H or C_{1-6}alkyl;

R^3 is H or optionally substituted phenyl;

R^4 is H, halogen, $-OR^7$, C_{1-6}alkyl, C_{1-6}haloalkyl, optionally substituted heterocycloalkyl, optionally substituted C_{1-6}alkyl-heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, $-CO_2H$, or $-C(O)NR^8R^9$;

R^5 is H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or phenyl; or

R^4 and R^5 are combined to form a heterocycloalkyl ring;

R^6 is H, halogen or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, optionally substituted phenyl, optionally substituted C_{1-6}alkyl-phenyl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, or $-C_{1-6}$alkyl$C(O)NR^{10}R^{11}$;

R^8 and R^9 are each independently H, or C_{1-6}alkyl; or R^8 and R^9 together with the nitrogen to which they are attached are combined to form an optionally substituted heterocycloalkyl ring;

R^{10} and R^{11} are each independently H, or C_{1-6}alkyl; or R^{10} and R^{11} together with the nitrogen to which they are attached are combined to form a heterocycloalkyl ring; and

R^{15} is optionally substituted C_{1-6}alkyl;

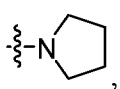
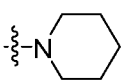
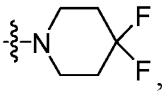
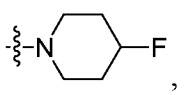
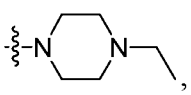
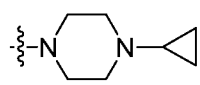
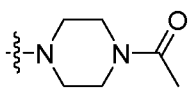
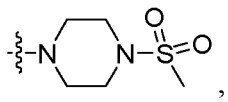
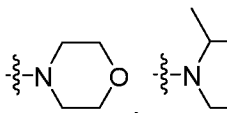
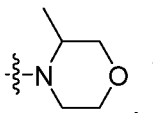
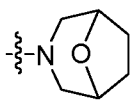
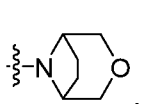
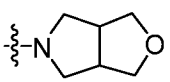
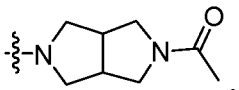
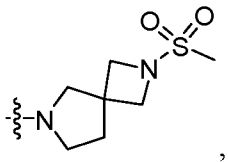
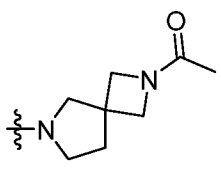
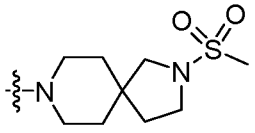
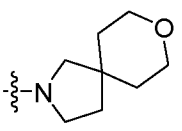
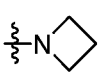
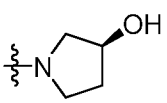
or a pharmaceutically acceptable salt or solvate thereof.

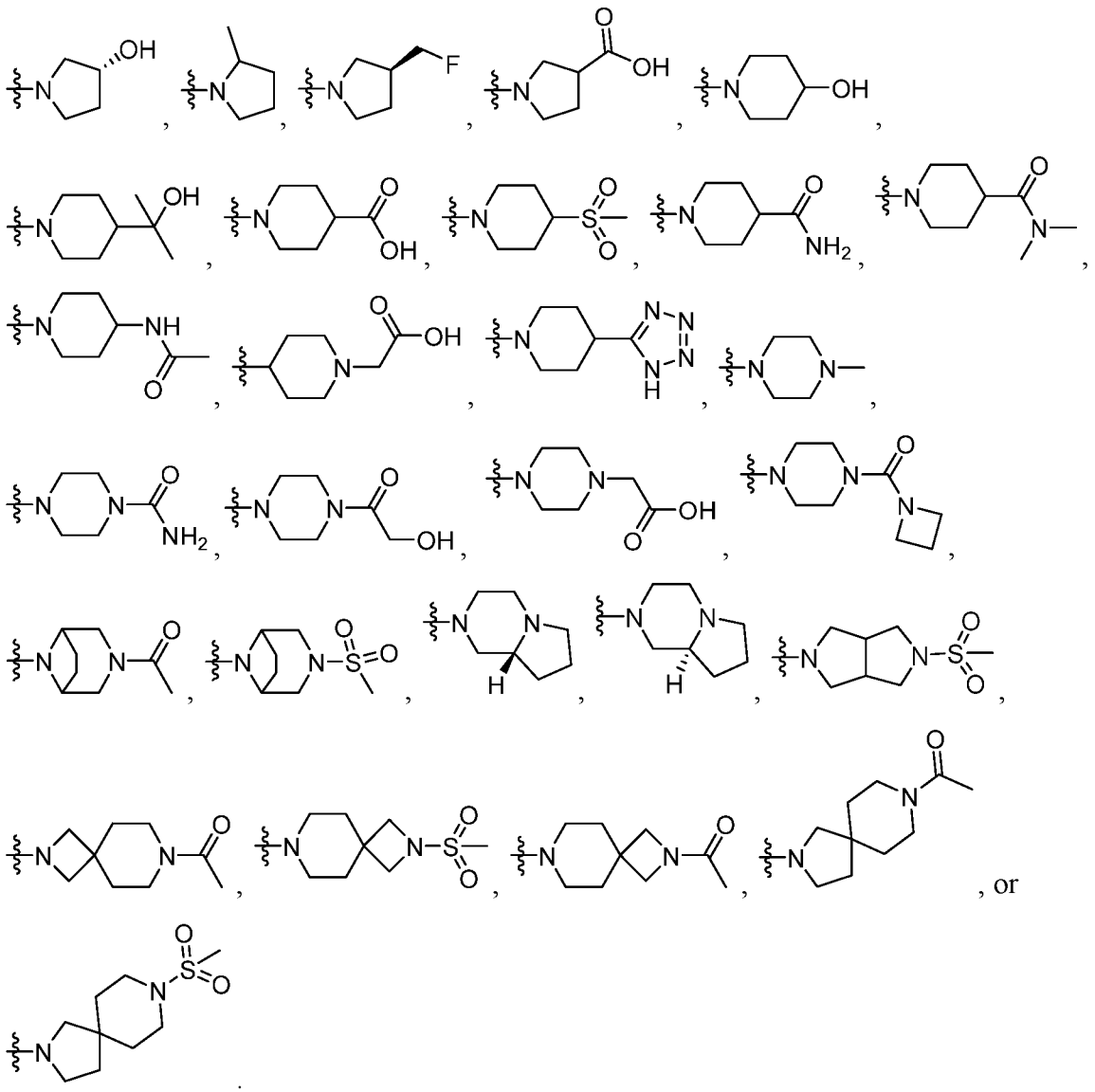
[00402] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XV), wherein the dyskinesia is levodopa-induced dyskinesia.

[00403] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$ and R^2 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$ and R^2 is C_{1-6}alkyl. In some embodiments of the

methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$ and R^2 is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$, R^2 is H, and R^{15} is unsubstituted C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$, R^2 is H, R^{15} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$, R^2 is C_{1-6}alkyl, R^{15} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$, R^2 is $-CH_3$, and R^{15} is unsubstituted C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(R^2)C(O)R^{15}$, R^2 is $-CH_3$, R^{15} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 $-N(H)SO_2R^{15}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(H)SO_2R^{15}$ and R^{15} is unsubstituted C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^1 is $-N(H)SO_2R^{15}$ and R^{15} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^3 is H.

[00404] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is optionally substituted C_{1-6}alkyl-heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is optionally substituted heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is heterocycloalkyl optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-6}alkyl, -C_{1-6}alkyl-OH, C_{1-6}fluoroalkyl, C_{3-6}cycloalkyl, heteroaryl, $-CO_2H$, -C_{1-6}alkyl-CO_2H, -$C(O)C_{1-6}$alkyl, -$C(O)C_{1-6}$alkyl-OH, -$N(H)C(O)C_{1-6}$alkyl, $-C(O)NH_2$, -$C(O)N(H)(C_{1-6}$alkyl), -$C(O)N(C_{1-6}alkyl)_2$, -$C(O)C_{2-7}$heterocycloalkyl, and -$S(O)_2C_{1-6}$alkyl. In some

embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is heterocycloalkyl optionally substituted with one or two groups selected from halogen, hydroxy, C_{1-6}alkyl, -C_{1-6}alkyl-OH, C_{1-6}fluoroalkyl, C_{3-6}cycloalkyl, heteroaryl, -CO_2H, -C_{1-6}alkyl-CO_2H, -C(O)C_{1-6}alkyl, -C(O)C_{1-6}alkyl-OH, -N(H)C(O)C_{1-6}alkyl, -$C(O)NH_2$, -C(O)N(H)(C_{1-6}alkyl), -C(O)N(C_{1-6}alkyl)$_2$, -C(O)C_{2-7}heterocycloalkyl, and -$S(O)_2C_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is optionally substituted heterocycloalkyl and the heterocycloalkyl is a 4-6 membered monocyclic heterocycloalkyl, a 8-9 membered bicyclic heterocycloalkyl, a 7-8 membered bridged heterocycloalkyl, a 5,5 fused heterocycloalkyl, or an 8-11 membered spirocyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is an optionally substituted 4-6 membered monocyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is an optionally substituted 8-9 membered bicyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is an optionally substituted 7-8 membered bridged heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is an optionally substituted 5,5 fused heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is an optionally substituted 8-11 membered spirocyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is optionally substituted heterocycloalkyl selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  . In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^4 is optionally substituted heterocycloalkyl selected from  ,  ,

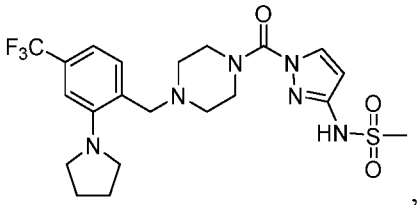


[00405] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is $C_{1\text{-}6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is $C_{1\text{-}6}$haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^5 is phenyl.

[00406] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^6 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^6 is halogen. In some embodiments of the methods

for treating dyskinesia with a compound of Formula (XV), R^6 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^6 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), R^6 is C_{1-6}alkyl.

[00407] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XV), the compound is selected from: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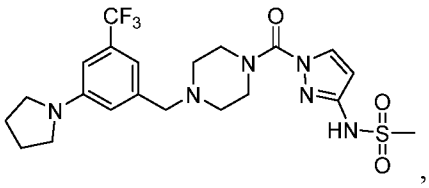
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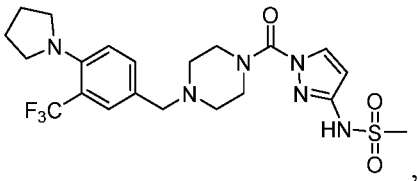
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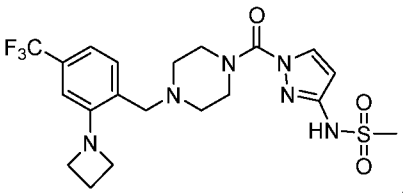
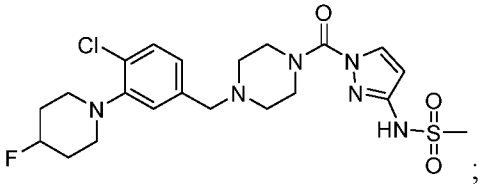
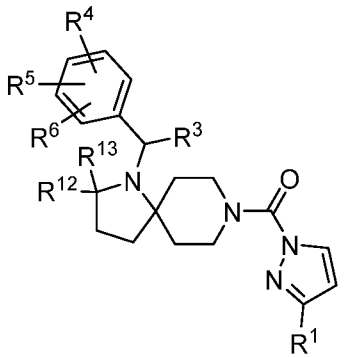

, and

; or a pharmaceutically acceptable salt or solvate thereof.

[00408] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XVI):



Formula (XVI);

wherein:

R^1 is $-N(R^2)C(O)R^{15}$ or $-N(H)SO_2R^{15}$;

R^2 is H or C_{1-6}alkyl;

R^3 is H or optionally substituted phenyl;

R^4 is H, halogen, -OR^7, C_{1-6}alkyl, C_{1-6}haloalkyl, optionally substituted heterocycloalkyl, optionally substituted C_{1-6}alkyl-heterocycloalkyl, optionally substituted phenyl, optionally substituted heteroaryl, -CO_2H, or -$C(O)NR^8R^9$;

R^5 is H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, or phenyl; or

R^4 and R^5 are combined to form a heterocycloalkyl ring;

R^6 is H, halogen or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, optionally substituted phenyl, optionally substituted C_{1-6}alkyl-phenyl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, or -C_{1-6}alkyl$C(O)NR^{10}R^{11}$;

R^8 and R^9 are each independently H, or C_{1-6}alkyl; or R^8 and R^9 together with the nitrogen to which they are attached are combined to form an optionally substituted heterocycloalkyl ring;

R^{10} and R^{11} are each independently H, or C_{1-6}alkyl; or R^{10} and R^{11} together with the nitrogen to which they are attached are combined to form a heterocycloalkyl ring;

R^{12} is H or C_{1-6}alkyl;

R^{13} is H or C_{1-6}alkyl; and

R^{15} is optionally substituted C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

[00409] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XVI), wherein the dyskinesia is levodopa-induced dyskinesia.

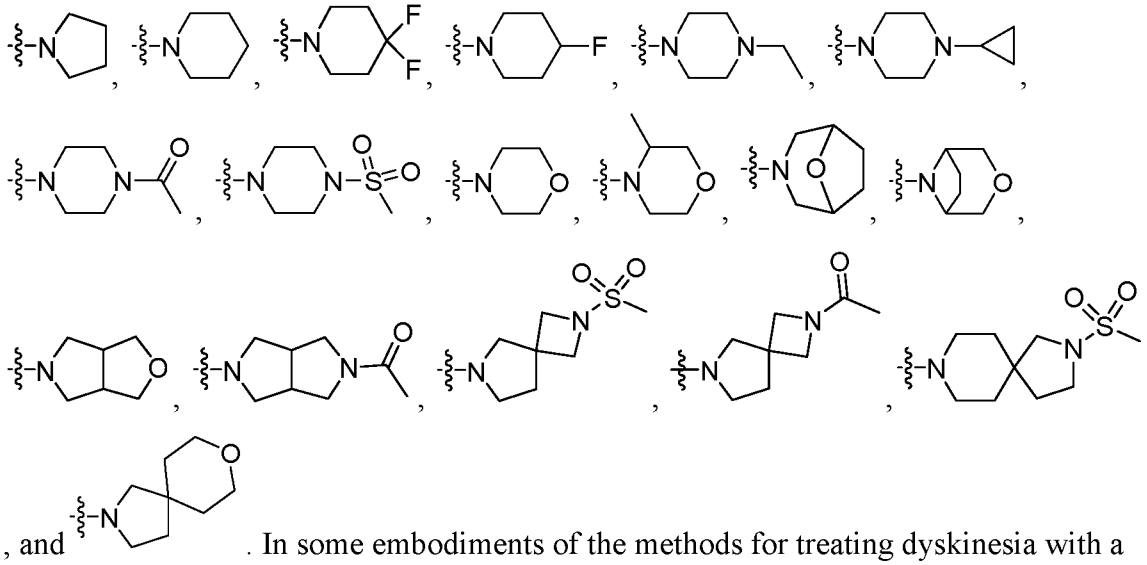
[00410] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^{12} and R^{13} are H.

[00411] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is -$N(R^2)C(O)R^{15}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is -$N(R^2)C(O)R^{15}$ and R^2 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is -$N(R^2)C(O)R^{15}$ and R^2 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is -$N(R^2)C(O)R^{15}$ and R^2 is -CH_3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is -$N(R^2)C(O)R^{15}$, R^2 is H, and R^{15} is unsubstituted C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is -$N(R^2)C(O)R^{15}$, R^2 is H, R^{15} is -CH_3. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is -$N(R^2)C(O)R^{15}$, R^2 is C_{1-6}alkyl, R^{15} is -CH_3. In some embodiments of the methods

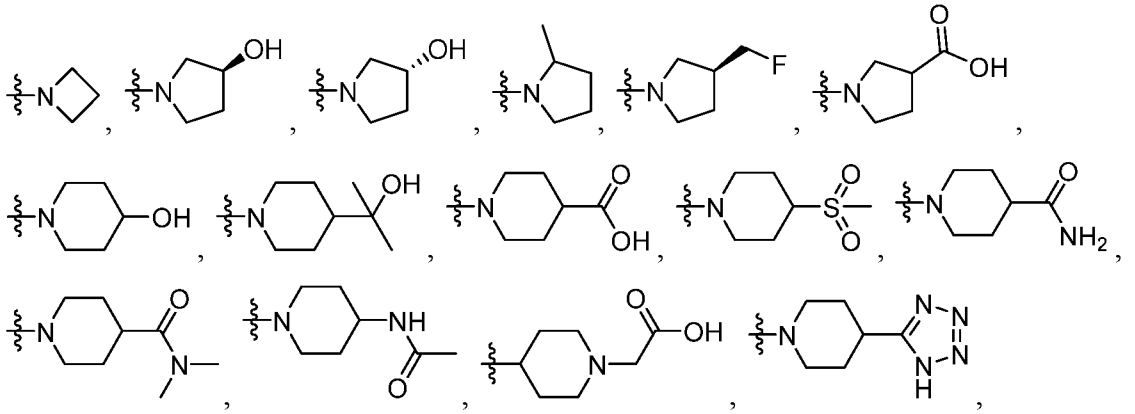
for treating dyskinesia with a compound of Formula (XVI), R^1 is $-N(R^2)C(O)R^{15}$, R^2 is $-CH_3$, and R^{15} is unsubstituted C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is $-N(R^2)C(O)R^{15}$, R^2 is $-CH_3$, R^{15} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 $-N(H)SO_2R^{15}$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is $-N(H)SO_2R^{15}$ and R^{15} is unsubstituted C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^1 is $-N(H)SO_2R^{15}$ and R^{15} is $-CH_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^3 is H.

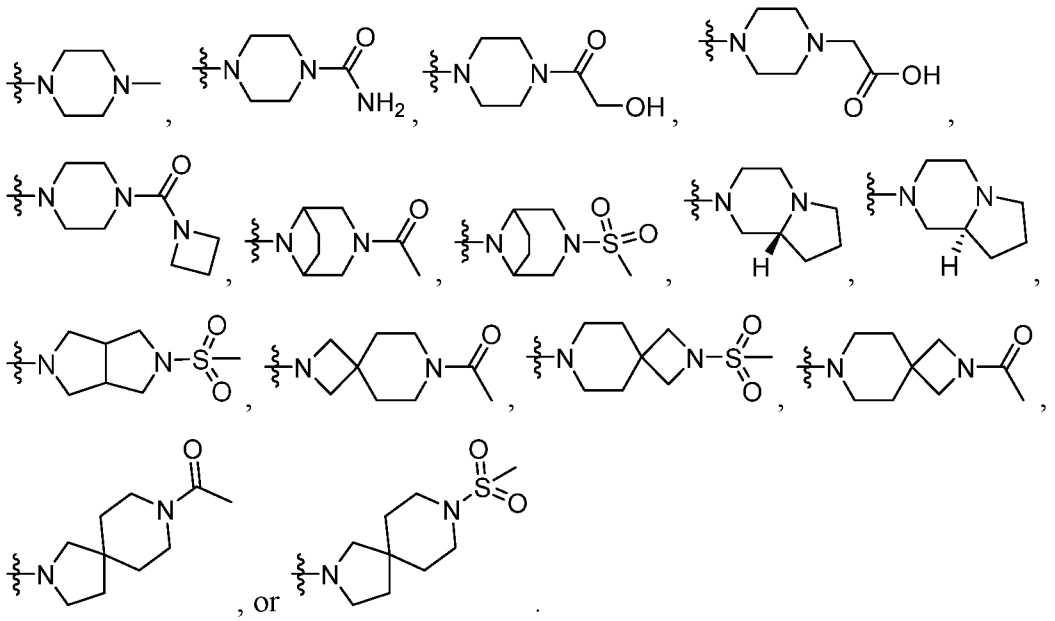
[00412] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is C_{1-6}alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is C_{1-6}haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is optionally substituted C_{1-6}alkyl-heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is optionally substituted heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is heterocycloalkyl optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-6}alkyl, $-C_{1-6}$alkyl-OH, C_{1-6}fluoroalkyl, C_{3-6}cycloalkyl, heteroaryl, $-CO_2H$, $-C_{1-6}$alkyl-CO_2H, $-C(O)C_{1-6}$alkyl, $-C(O)C_{1-6}$alkyl-OH, $-N(H)C(O)C_{1-6}$alkyl, $-C(O)NH_2$, $-C(O)N(H)(C_{1-6}$alkyl), $-C(O)N(C_{1-6}$alkyl$)_2$, $-C(O)C_{2-7}$heterocycloalkyl, and $-S(O)_2C_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is heterocycloalkyl optionally substituted with one or two groups selected from halogen, hydroxy, C_{1-6}alkyl, $-C_{1-6}$alkyl-OH, C_{1-6}fluoroalkyl, C_{3-6}cycloalkyl, heteroaryl, $-CO_2H$, $-C_{1-6}$alkyl-CO_2H, $-C(O)C_{1-6}$alkyl, $-C(O)C_{1-6}$alkyl-OH, $-N(H)C(O)C_{1-6}$alkyl, $-C(O)NH_2$, $-C(O)N(H)(C_{1-6}$alkyl), $-C(O)N(C_{1-6}$alkyl$)_2$, $-C(O)C_{2-7}$heterocycloalkyl, and $-S(O)_2C_{1-6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is optionally substituted

heterocycloalkyl and the heterocycloalkyl is a 4-6 membered monocyclic heterocycloalkyl, a 8-9 membered bicyclic heterocycloalkyl, a 7-8 membered bridged heterocycloalkyl, a 5,5 fused heterocycloalkyl, or an 8-11 membered spirocyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is an optionally substituted 4-6 membered monocyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is an optionally substituted 8-9 membered bicyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is an optionally substituted 7-8 membered bridged heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is an optionally substituted 5,5 fused heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is an optionally substituted 8-11 membered spirocyclic heterocycloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is optionally substituted heterocycloalkyl selected from



, and . In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^4 is optionally substituted heterocycloalkyl selected from

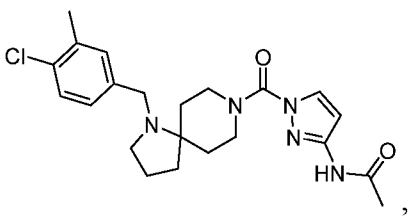




[00413] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is $C_{1\text{-}6}$alkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is $C_{1\text{-}6}$haloalkyl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is $-CF_3$. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^5 is phenyl.

[00414] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^6 is H. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^6 is halogen. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^6 is -Cl. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^6 is -F. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), R^6 is $C_{1\text{-}6}$alkyl.

[00415] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVI), the compound is selected from: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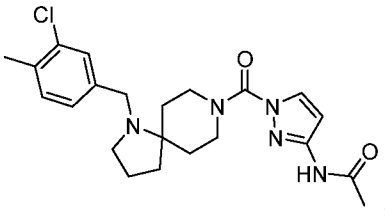
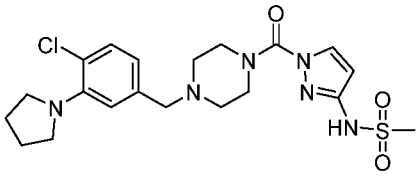
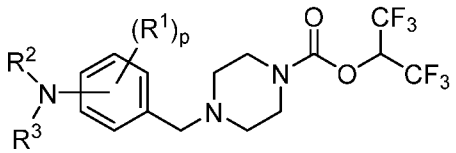

, and

; or a pharmaceutically acceptable salt or solvate thereof.

[00416] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XVII):



Formula (XVII);

wherein:

each R^1 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-8}cycloalkyl, -OH, and -CN;

R^2 and R^3, together with the carbon to which they are attached, form

(iii) a C_2-C_7heterocycloalkyl; or

(iv) a C_2-C_9heteroaryl;

wherein the C_2-C_7heterocycloalkyl or the C_2-C_9heteroaryl is substituted with one R^4 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^4 is -CO_2H or -C_{1-6}alkyl-CO_2H; and

p is 0, 1, 2, 3, or 4;

or a pharmaceutically acceptable salt or solvate thereof.

[00417] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (XVII), wherein the dyskinesia is levodopa-induced dyskinesia.

[00418] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_7heterocycloalkyl substituted with one R^4 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-}

$_{6}$alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_7heterocycloalkyl substituted with -CO_2H and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_7heterocycloalkyl substituted with -CO_2H and optionally substituted with no additional substituents. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_7heterocycloalkyl substituted with -C_{1-6}alkyl-CO_2H and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_7heterocycloalkyl substituted with -C_{1-6}alkyl-CO_2H and optionally substituted with no additional substituents. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a piperidine substituted with -CO_2H and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a piperidine substituted with -CO_2H and optionally substituted with no additional substituents. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a piperidine substituted with -C_{1-6}alkyl-CO_2H and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a piperidine substituted with -C_{1-6}alkyl-CO_2H and optionally substituted with no additional substituents.

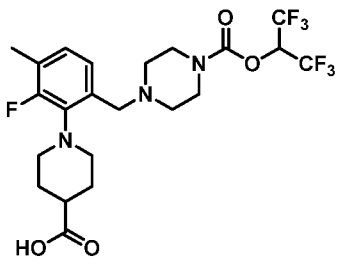
[00419] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_9heteroaryl substituted with one R^4 and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-

C_9heteroaryl substituted with -CO_2H and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_9heteroaryl substituted with -CO_2H and optionally substituted with no additional substituents. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_9heteroaryl substituted with -C_{1-6}alkyl-CO_2H and optionally substituted with one or two additional substituents selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), R^2 and R^3, together with the carbon to which they are attached, form a C_2-C_9heteroaryl substituted with -C_{1-6}alkyl-CO_2H and optionally substituted with no additional substituents.

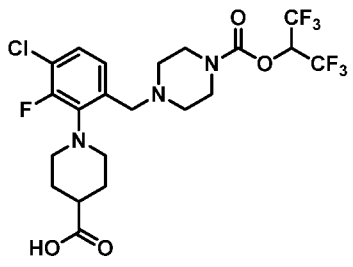
[00420] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), each R^1 is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, and C_{1-6}haloalkoxy. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), each R^1 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl.

[00421] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), p is 0, 1, or 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), p is 2. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), p is 1. In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), p is 0.

[00422] In some embodiments of the methods for treating dyskinesia with a compound of Formula (XVII), the compound is selected from:



and



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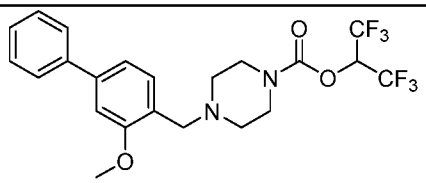
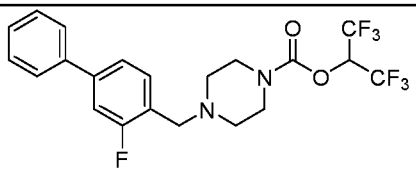
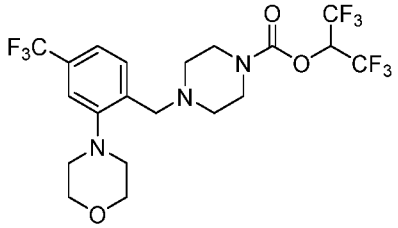
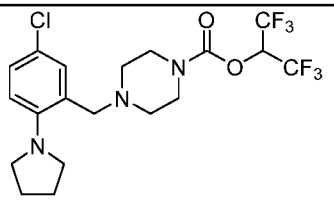
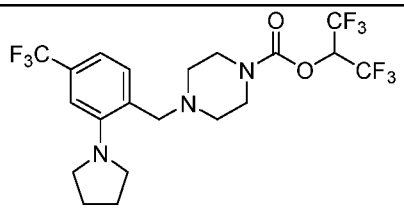
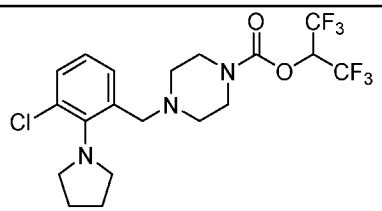
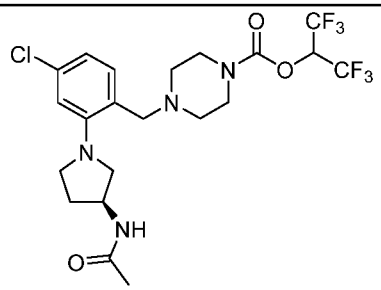
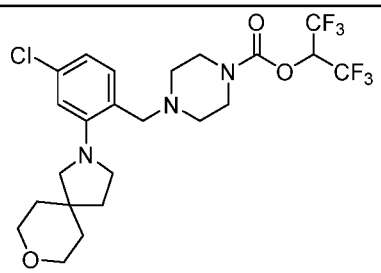
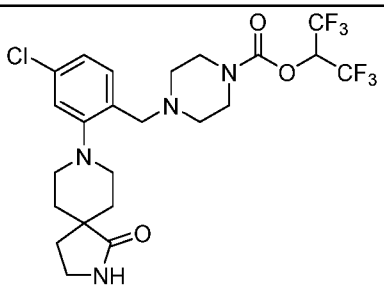
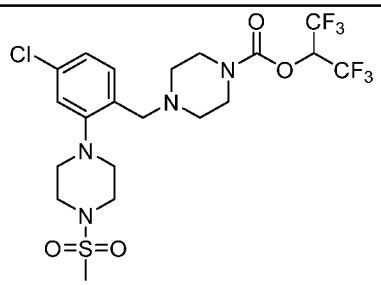
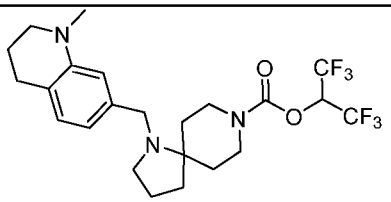
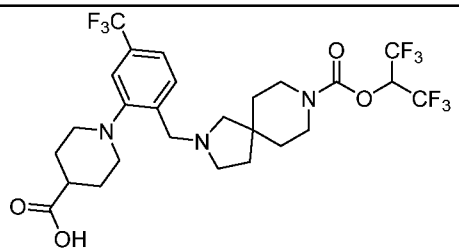
[00423] Further embodiments provided herein include combinations of one or more of the particular embodiments set forth above.

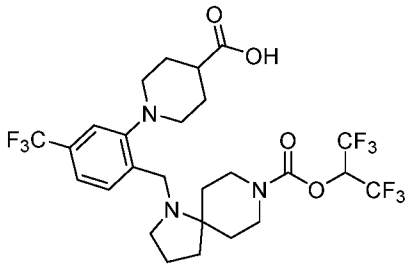
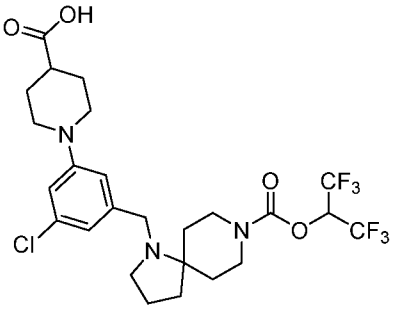
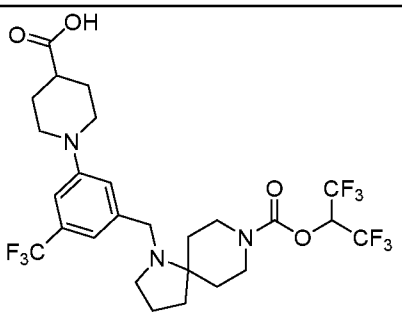
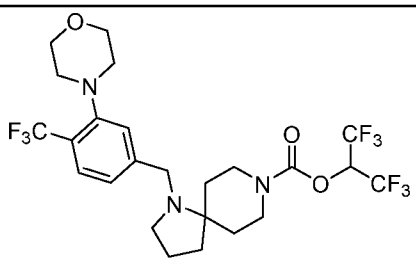
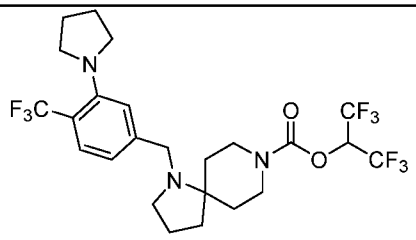
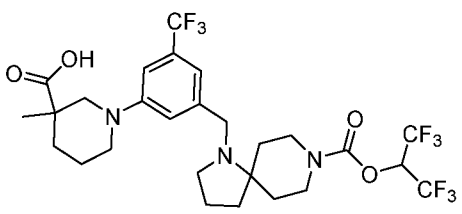
[00424] In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a

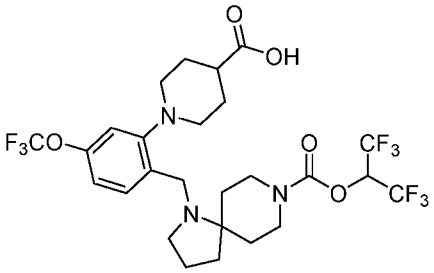
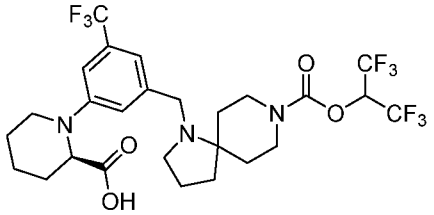
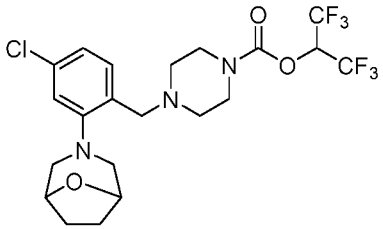
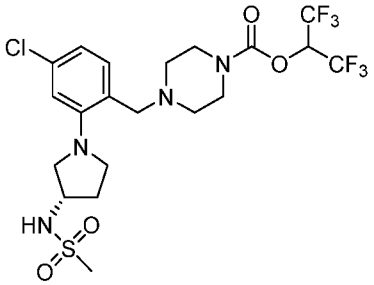
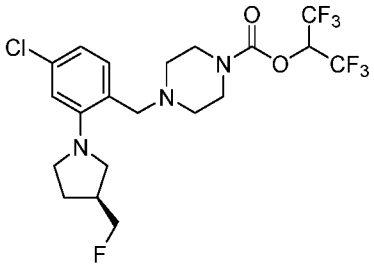
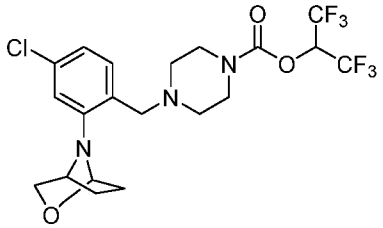
compound having the structure provided in Table 1. In some embodiments is a method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound having the structure provided in Table 1; wherein the dyskinesia is levodopa-induced dyskinesia.

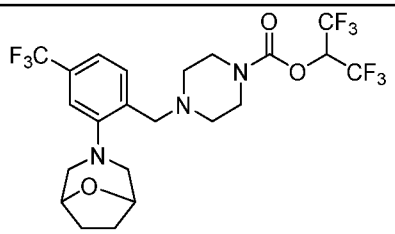
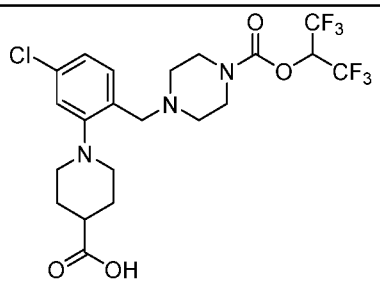
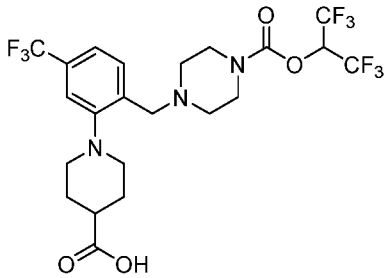
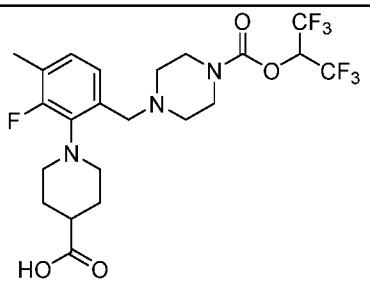
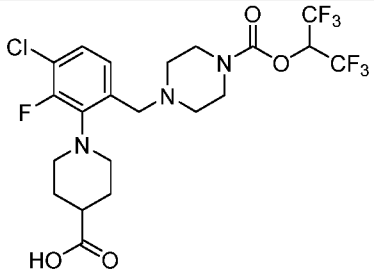
TABLE 1

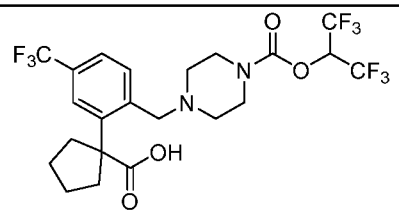
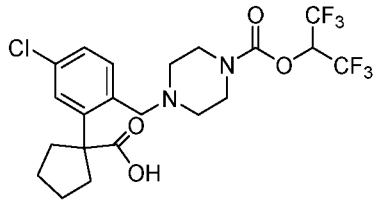
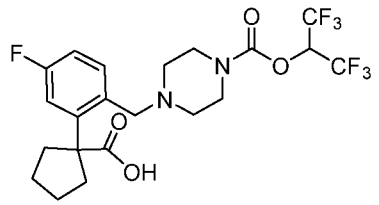
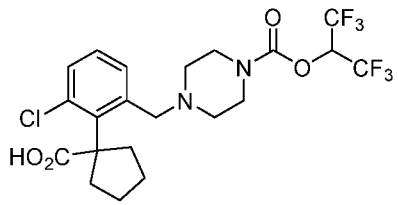
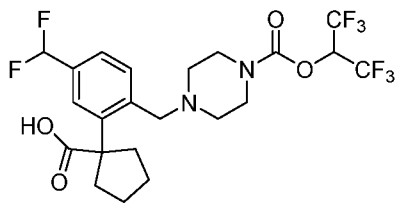
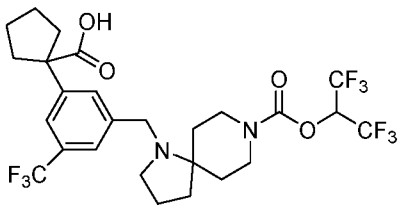
Compound Number	Structure	Name
1		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-((3-methoxy-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate
2		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-((3-fluoro-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate
3		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(2-morpholino-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate
4		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(5-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate
5		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate
6		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(3-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

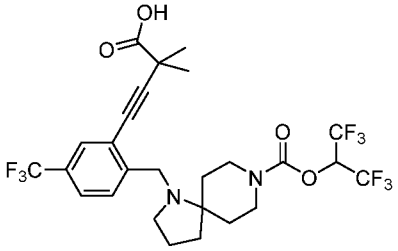
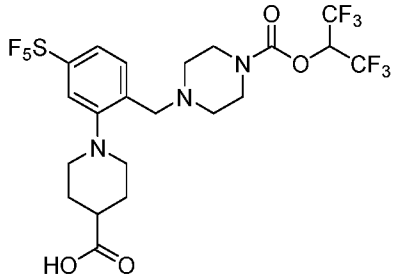
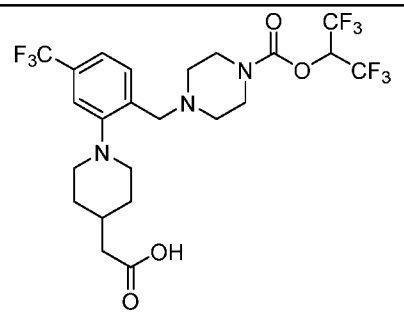
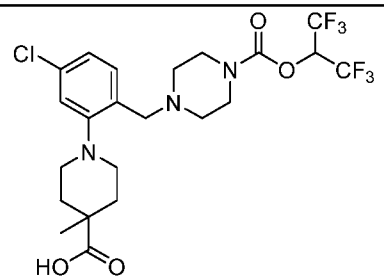
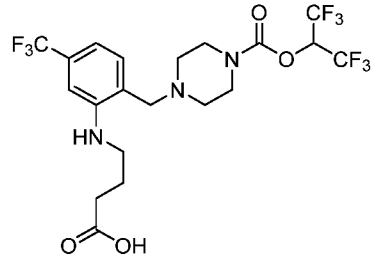
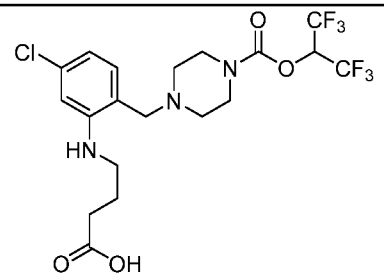
Compound Number	Structure	Name
7		1,1,1,3,3,3-Hexafluoropropan-2-yl (S)-4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate
8		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(4-chloro-2-(8-oxa-2-azaspiro[4.5]decan-2-yl)benzyl)piperazine-1-carboxylate
9		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(4-chloro-2-(1-oxo-2,8-diazaspiro[4.5]decan-8-yl)benzyl)piperazine-1-carboxylate
10		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(4-chloro-2-(4-(methylsulfonyl)piperazin-1-yl)benzyl)piperazine-1-carboxylate
11		1,1,1,3,3,3-Hexafluoropropan-2-yl 1-((1-methyl-1,2,3,4-tetrahydroquinolin-7-yl)methyl)-1,8-diazaspiro[4.5]decane-8-carboxylate
12		1-(2-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-2,8-diazaspiro[4.5]decan-2-yl)methyl)-5-(trifluoromethyl)phenyl)piperidine-4-carboxylic acid

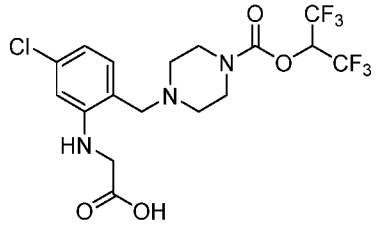
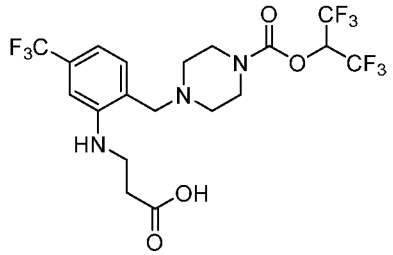
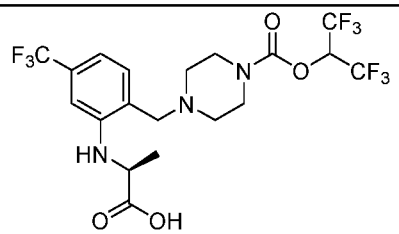
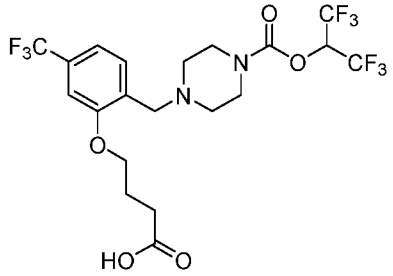
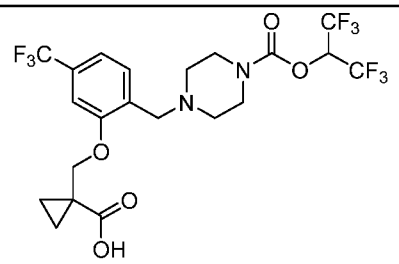
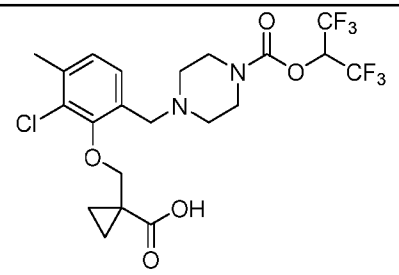
Compound Number	Structure	Name
13		1-(2-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)piperidine-4-carboxylic acid
14		1-(3-Chloro-5-((8-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)phenyl)piperidine-4-carboxylic acid
15		1-(3-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)piperidine-4-carboxylic acid
16		1,1,1,3,3,3-Hexafluoropropan-2-yl 1-(3-morpholino-4-(trifluoromethyl)benzyl)-1,8-diazaspiro[4.5]decane-8-carboxylate
17		1,1,1,3,3,3-Hexafluoropropan-2-yl 1-(3-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)-1,8-diazaspiro[4.5]decane-8-carboxylate
18		1-(3-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)-3-methylpiperidine-3-carboxylic acid

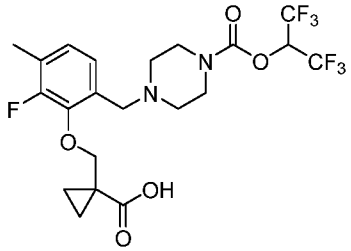
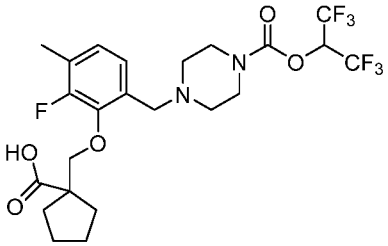
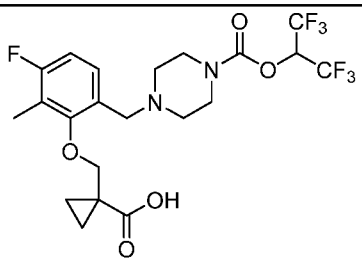
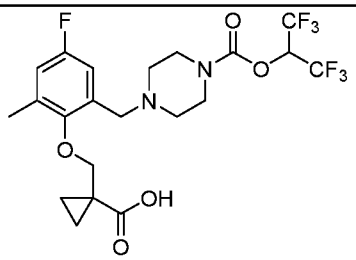
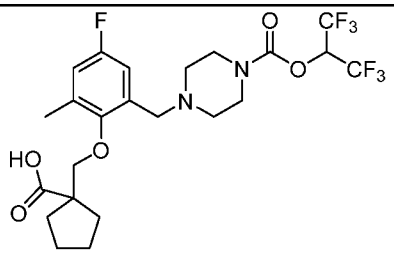
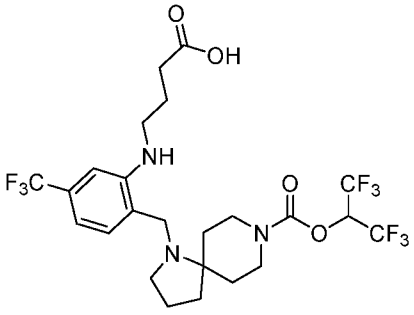
Compound Number	Structure	Name
19		1-(2-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethoxy)phenyl)piperidine-4-carboxylic acid
20		(*R*)-1-(3-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)piperidine-2-carboxylic acid
21		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(2-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-4-chlorobenzyl)piperazine-1-carboxylate
22		1,1,1,3,3,3-Hexafluoropropan-2-yl (*S*)-4-(4-chloro-2-(3-(methylsulfonamido)pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate
23		1,1,1,3,3,3-Hexafluoropropan-2-yl (*S*)-4-(4-chloro-2-(3-(fluoromethyl)pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate
24		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(2-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-4-chlorobenzyl)piperazine-1-carboxylate

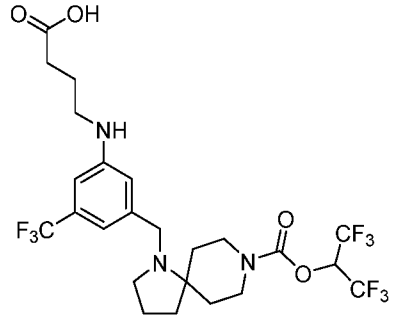
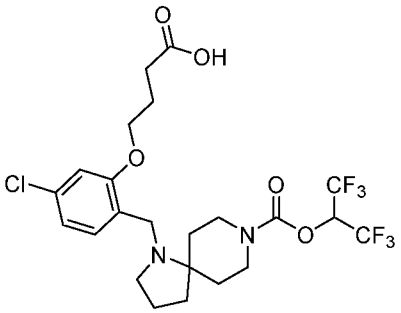
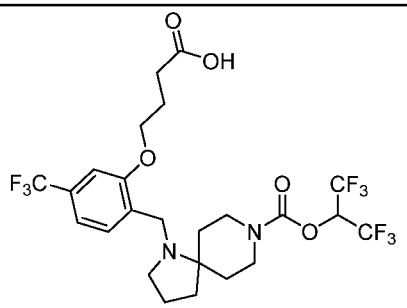
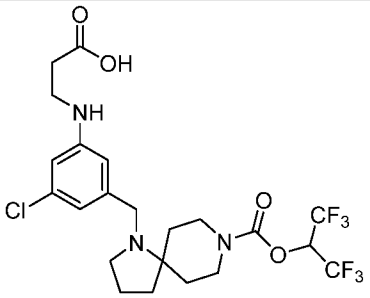
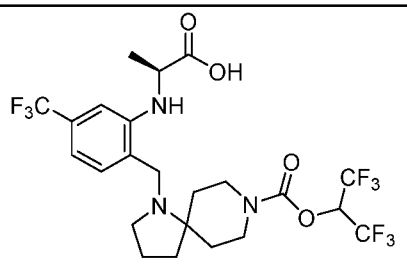
Compound Number	Structure	Name
25		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(2-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate
26		1-(5-Chloro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)piperidine-4-carboxylic acid
27		1-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenyl)piperidine-4-carboxylic acid
28		1-(2-Fluoro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-3-methylphenyl)piperidine-4-carboxylic acid
29		1-(3-Chloro-2-fluoro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)piperidine-4-carboxylic acid

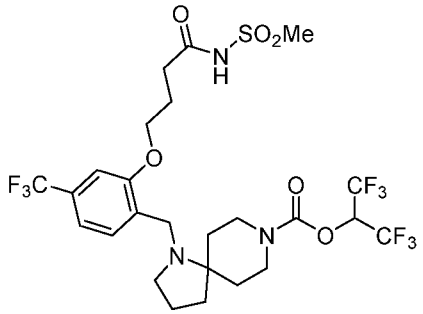
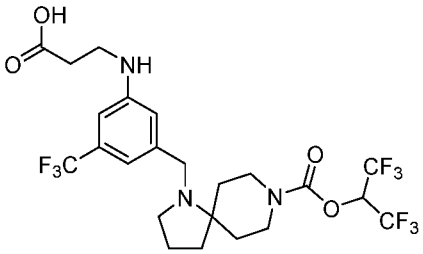
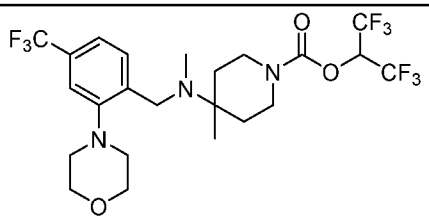
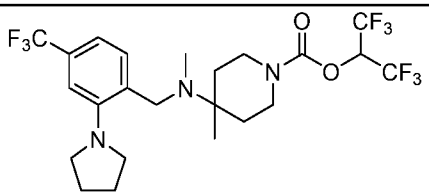
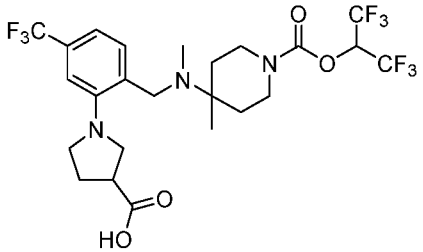
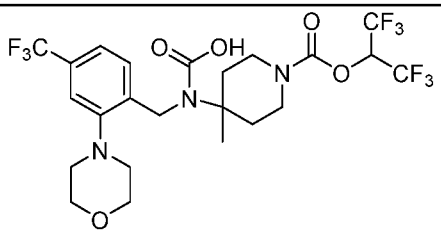
Compound Number	Structure	Name
30		1-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenyl)cyclopentane-1-carboxylic acid
31		1-(5-Chloro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)cyclopentane-1-carboxylic acid
32		1-(5-Fluoro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)cyclopentane-1-carboxylic acid
33		1-(2-Chloro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)cyclopentane-1-carboxylic acid
34		1-(5-(Difluoromethyl)-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)cyclopentane-1-carboxylic acid
35		1-(3-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)cyclopentane-1-carboxylic acid

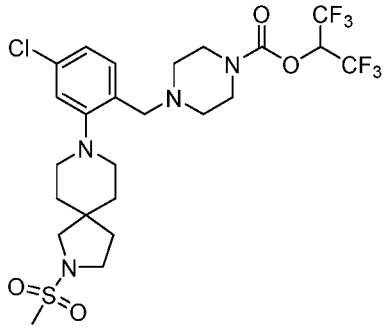
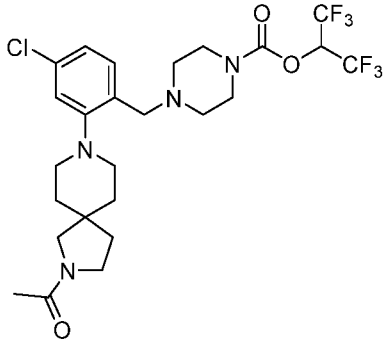
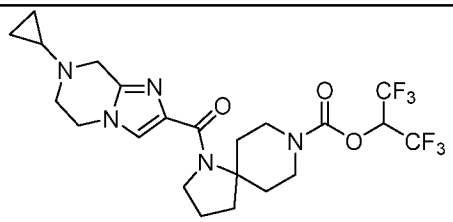
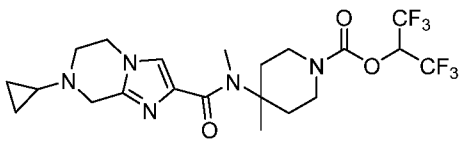
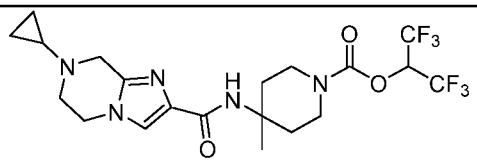
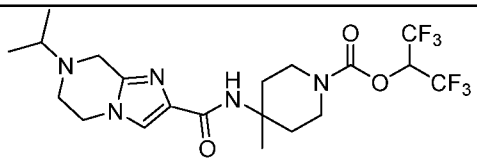
Compound Number	Structure	Name
36		4-(2-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)-2,2-dimethylbut-3-ynoic acid
37		1-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(pentafluoro-l6-sulfaneyl)phenyl)piperidine-4-carboxylic acid
38		2-(1-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenyl)piperidin-4-yl)acetic acid
39		1-(5-Chloro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)-4-methylpiperidine-4-carboxylic acid
40		4-((2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenyl)amino)butanoic acid
41		4-((5-Chloro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)amino)butanoic acid

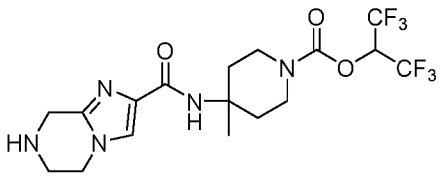
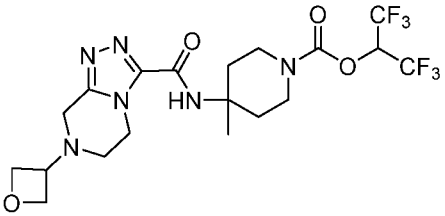
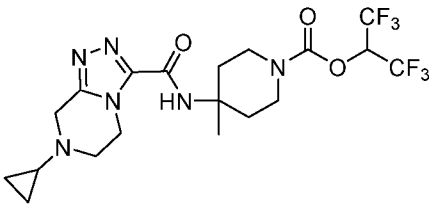
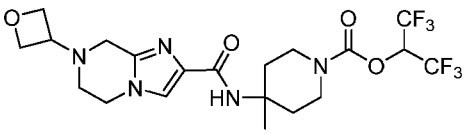
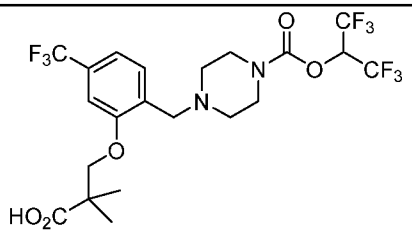
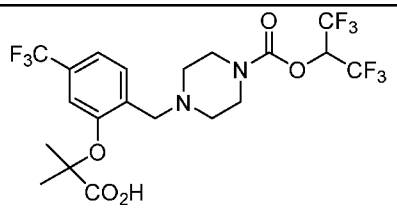
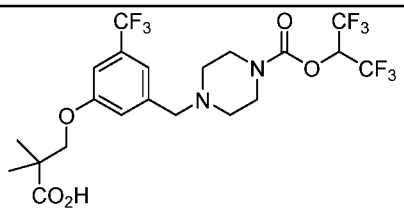
Compound Number	Structure	Name
42		(5-Chloro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenyl)glycine
43		3-((2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenyl)amino)propanoic acid
44		(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenyl)-L-alanine
45		4-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenoxy)butanoic acid
46		1-((2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenoxy)methyl)cyclopropane-1-carboxylic acid
47		1-((2-Chloro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-3-methylphenoxy)methyl)cyclopropane-1-carboxylic acid

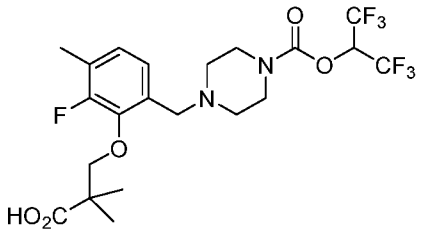
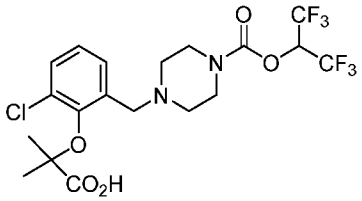
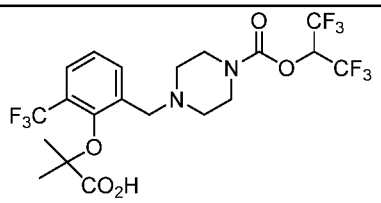
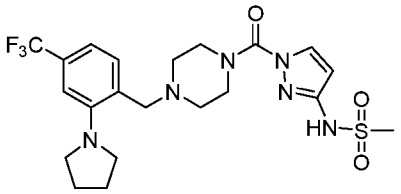
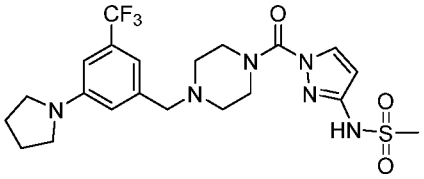
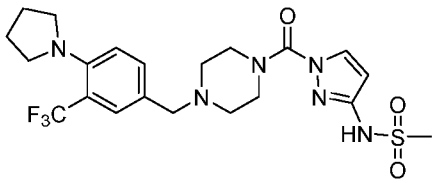
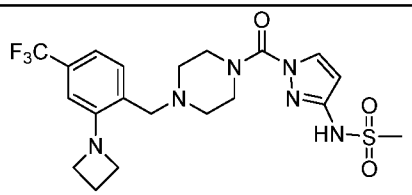
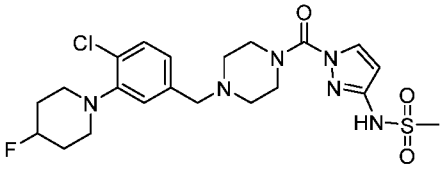
Compound Number	Structure	Name
48		1-((2-Fluoro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-3-methylphenoxy)methyl)cyclopropane-1-carboxylic acid
49		1-((2-Fluoro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-3-methylphenoxy)methyl)cyclopentane-1-carboxylic acid
50		1-((3-Fluoro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-2-methylphenoxy)methyl)cyclopropane-1-carboxylic acid
51		1-((4-Fluoro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-6-methylphenoxy)methyl)cyclopropane-1-carboxylic acid
52		1-((4-Fluoro-2-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-6-methylphenoxy)methyl)cyclopentane-1-carboxylic acid
53		4-((2-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)amino)butanoic acid

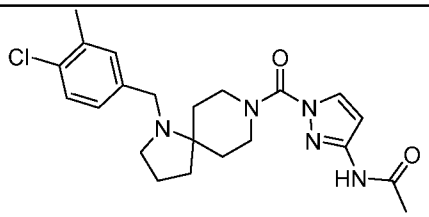
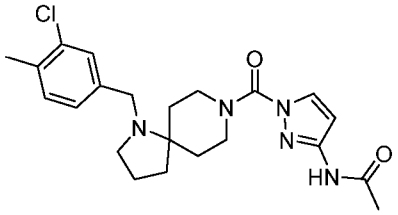
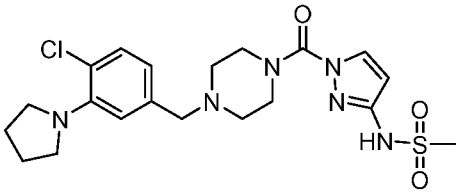
Compound Number	Structure	Name
54		4-((3-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)amino)butanoic acid
55		4-(5-Chloro-2-((8-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)phenoxy)butanoic acid
56		4-(2-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenoxy)butanoic acid
57		3-((3-Chloro-5-((8-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)phenyl)amino)propanoic acid
58		(2-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)-L-alanine

Compound Number	Structure	Name
59		1,1,1,3,3,3-Hexafluoropropan-2-yl 1-(2-(4-(methylsulfonamido)-4-oxobutoxy)-4-(trifluoromethyl)benzyl)-1,8-diazaspiro[4.5]decane-8-carboxylate
60		3-((3-((8-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-1,8-diazaspiro[4.5]decan-1-yl)methyl)-5-(trifluoromethyl)phenyl)amino)propanoic acid
61		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-methyl-4-(methyl(2-morpholino-4-(trifluoromethyl)benzyl)amino)piperidine-1-carboxylate
62		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-methyl-4-(methyl(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)amino)piperidine-1-carboxylate
63		1-(2-(((1-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-4-methylpiperidin-4-yl)(methyl)amino)methyl)-5-(trifluoromethyl)phenyl)pyrrolidine-3-carboxylic acid
64		(1-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)-4-methylpiperidin-4-yl)(2-morpholino-4-(trifluoromethyl)benzyl)carbamic acid

Compound Number	Structure	Name
65		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(4-chloro-2-(2-(methylsulfonyl)-2,8-diazaspiro[4.5]decan-8-yl)benzyl)piperazine-1-carboxylate
66		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(2-(2-acetyl-2,8-diazaspiro[4.5]decan-8-yl)-4-chlorobenzyl)piperazine-1-carboxylate
67		1,1,1,3,3,3-Hexafluoropropan-2-yl 1-(7-cyclopropyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carbonyl)-1,8-diazaspiro[4.5]decane-8-carboxylate
68		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(7-cyclopropyl-N-methyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)-4-methylpiperidine-1-carboxylate
69		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(7-cyclopropyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)-4-methylpiperidine-1-carboxylate
70		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(7-isopropyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)-4-methylpiperidine-1-carboxylate

Compound Number	Structure	Name
71		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-methyl-4-(5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)piperidine-1-carboxylate
72		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-methyl-4-(7-(oxetan-3-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-3-carboxamido)piperidine-1-carboxylate
73		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(7-cyclopropyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-3-carboxamido)-4-methylpiperidine-1-carboxylate
74		1,1,1,3,3,3-Hexafluoropropan-2-yl 4-methyl-4-(7-(oxetan-3-yl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)piperidine-1-carboxylate
75		3-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenoxy)-2,2-dimethylpropanoic acid
76		2-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenoxy)-2-methylpropanoic acid
77		3-(3-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-5-(trifluoromethyl)phenoxy)-2,2-dimethylpropanoic acid

Compound Number	Structure	Name
78		3-(2-Fluoro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-3-methylphenoxy)-2,2-dimethylpropanoic acid
79		2-(2-Chloro-6-((4-(((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)phenoxy)-2-methylpropanoic acid
80		2-(2-((4-(((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)carbonyl)piperazin-1-yl)methyl)-6-(trifluoromethyl)phenoxy)-2-methylpropanoic acid
81		N-(1-(4-(2-(Pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carbonyl)-1H-pyrazol-3-yl)methanesulfonamide
82		N-(1-(4-(3-(Pyrrolidin-1-yl)-5-(trifluoromethyl)benzyl)piperazine-1-carbonyl)-1H-pyrazol-3-yl)methanesulfnamide
83		N-(1-(4-(4-(Pyrrolidin-1-yl)-3-(trifluoromethyl)benzyl)piperazine-1-carbonyl)-1H-pyrazol-3-yl)methanesulfonamide
84		N-(1-(4-(2-(Azetidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carbonyl)-1H-pyrazol-3-yl)methanesulfonamide
85		N-(1-(4-(4-Chloro-3-(4-fluoropiperidin-1-yl)benzyl)piperazine-1-carbonyl)-1H-pyrazol-3-yl)methanesulfonamide

Compound Number	Structure	Name
86		N-(1-(1-(4-Chloro-3-methylbenzyl)-1,8-diazaspiro[4.5]decane-8-carbonyl)-1H-pyrazol-3-yl)acetamide
87		N-(1-(1-(3-Chloro-4-methylbenzyl)-1,8-diazaspiro[4.5]decane-8-carbonyl)-1H-pyrazol-3-yl)acetamide
88		N-(1-(4-(4-Chloro-3-(pyrrolidin-1-yl)benzyl)piperazine-1-carbonyl)-1H-pyrazol-3-yl)methanesulfonamide

Combination Therapies

[00425] Also contemplated herein are combination therapies, for example, co-administering a disclosed compound and an additional active agent, as part of a specific treatment regimen intended to provide the beneficial effect from the co-action of these therapeutic agents. The beneficial effect of the combination includes, but is not limited to, pharmacokinetic or pharmacodynamic co-action resulting from the combination of therapeutic agents. Administration of these therapeutic agents in combination typically is carried out over a defined time period (usually weeks, months or years depending upon the combination selected). Combination therapy is intended to embrace administration of multiple therapeutic agents in a sequential manner, that is, wherein each therapeutic agent is administered at a different time, as well as administration of these therapeutic agents, or at least two of the therapeutic agents, in a substantially simultaneous manner.

[00426] Substantially simultaneous administration is accomplished, for example, by administering to the subject a single formulation or composition, (*e.g.*, a tablet or capsule having a fixed ratio of each therapeutic agent or in multiple, single formulations (*e.g.*, capsules) for each of the therapeutic agents. Sequential or substantially simultaneous administration of each therapeutic agent is effected by any appropriate route including, but not limited to, oral routes, intravenous routes, intramuscular routes, and direct absorption through mucous membrane tissues. The therapeutic agents are administered

by the same route or by different routes. For example, a first therapeutic agent of the combination selected is administered by intravenous injection while the other therapeutic agents of the combination are administered orally. Alternatively, for example, all therapeutic agents are administered orally or all therapeutic agents are administered by intravenous injection.

[00427] Combination therapy also embraces the administration of the therapeutic agents as described above in further combination with other biologically active ingredients and non-drug therapies. Where the combination therapy further comprises a non-drug treatment, the non-drug treatment is conducted at any suitable time so long as a beneficial effect from the co-action of the combination of the therapeutic agents and non-drug treatment is achieved. For example, in appropriate cases, the beneficial effect is still achieved when the non-drug treatment is temporally removed from the administration of the therapeutic agents, perhaps by days or even weeks.

[00428] The components of the combination are administered to a patient simultaneously or sequentially. It will be appreciated that the components are present in the same pharmaceutically acceptable carrier and, therefore, are administered simultaneously. Alternatively, the active ingredients are present in separate pharmaceutical carriers, such as, conventional oral dosage forms, that are administered either simultaneously or sequentially.

[00429] In some embodiments, a compound of Formula (I)-(XVII) described herein, or a pharmaceutically acceptable salt or solvate thereof, is co-administered with dopamine replacement therapy, such as levodopa or carbidopa-levodopa. In some embodiments, a compound of Formula (I)-(XVII) described herein, or a pharmaceutically acceptable salt or solvate thereof, is co-administered with levodopa. In some embodiments, a compound of Formula (I)-(XVII) described herein, or a pharmaceutically acceptable salt or solvate thereof, is co-administered with carbidopa-levodopa. In some embodiments, a compound of Formula (I)-(XVII) described herein, or a pharmaceutically acceptable salt or solvate thereof, is co-administered with amantadine.

[00430] In certain embodiments, a disclosed compound utilized by one or more of the foregoing methods is one of the generic, subgeneric, or specific compounds described herein, such as a compound of Formula (I)-(XVII).

Preparation of the Compounds

[00431] The compounds used in the methods described herein are made according to procedures disclosed in US 9,133,148; US 10,030,020; US 9,771,341; WO 2018/053447; US 9,981,930; US 10,093,635; WO 2018/093949; PCT/US18/48388; PCT/US18/48372;

US 62/671,985; and WO 2017/087854; which are herein incorporated by reference in their entirety. In some embodiments, compounds used in the methods described herein are made by known organic synthesis techniques, starting from commercially available chemicals and/or from compounds described in the chemical literature. "Commercially available chemicals" are obtained from standard commercial sources including Acros Organics (Geel, Belgium), Aldrich Chemical (Milwaukee, WI, including Sigma Chemical and Fluka), Apin Chemicals Ltd. (Milton Park, UK), Ark Pharm, Inc. (Libertyville, IL), Avocado Research (Lancashire, U.K.), BDH Inc. (Toronto, Canada), Bionet (Cornwall, U.K.), Chemservice Inc. (West Chester, PA), Combi-blocks (San Diego, CA), Crescent Chemical Co. (Hauppauge, NY), eMolecules (San Diego, CA), Fisher Scientific Co. (Pittsburgh, PA), Fisons Chemicals (Leicestershire, UK), Frontier Scientific (Logan, UT), ICN Biomedicals, Inc. (Costa Mesa, CA), Key Organics (Cornwall, U.K.), Lancaster Synthesis (Windham, NH), Matrix Scientific, (Columbia, SC), Maybridge Chemical Co. Ltd. (Cornwall, U.K.), Parish Chemical Co. (Orem, UT), Pfaltz & Bauer, Inc. (Waterbury, CN), Polyorganix (Houston, TX), Pierce Chemical Co. (Rockford, IL), Riedel de Haen AG (Hanover, Germany), Ryan Scientific, Inc. (Mount Pleasant, SC), Spectrum Chemicals (Gardena, CA), Sundia Meditech, (Shanghai, China), TCI America (Portland, OR), Trans World Chemicals, Inc. (Rockville, MD), and WuXi (Shanghai, China).

[00432] Suitable reference books and treatises that detail the synthesis of reactants useful in the preparation of compounds described herein, or provide references to articles that describe the preparation, include for example, "Synthetic Organic Chemistry", John Wiley & Sons, Inc., New York; S. R. Sandler et al., "Organic Functional Group Preparations," 2nd Ed., Academic Press, New York, 1983; H. O. House, "Modern Synthetic Reactions", 2nd Ed., W. A. Benjamin, Inc. Menlo Park, Calif. 1972; T. L. Gilchrist, "Heterocyclic Chemistry", 2nd Ed., John Wiley & Sons, New York, 1992; J. March, "Advanced Organic Chemistry: Reactions, Mechanisms and Structure", 4th Ed., Wiley-Interscience, New York, 1992. Additional suitable reference books and treatises that detail the synthesis of reactants useful in the preparation of compounds described herein, or provide references to articles that describe the preparation, include for example, Fuhrhop, J. and Penzlin G. "Organic Synthesis: Concepts, Methods, Starting Materials", Second, Revised and Enlarged Edition (1994) John Wiley & Sons ISBN: 3-527-29074-5; Hoffman, R.V. "Organic Chemistry, An Intermediate Text" (1996) Oxford University Press, ISBN 0-19-509618-5; Larock, R. C. "Comprehensive Organic Transformations: A Guide to Functional Group Preparations" 2nd Edition (1999) Wiley-VCH, ISBN: 0-471-19031-4; March, J. "Advanced Organic Chemistry: Reactions,

Mechanisms, and Structure" 4th Edition (1992) John Wiley & Sons, ISBN: 0-471-60180-2; Otera, J. (editor) "Modern Carbonyl Chemistry" (2000) Wiley-VCH, ISBN: 3-527-29871-1; Patai, S. "Patai's 1992 Guide to the Chemistry of Functional Groups" (1992) Interscience ISBN: 0-471-93022-9; Solomons, T. W. G. "Organic Chemistry" 7th Edition (2000) John Wiley & Sons, ISBN: 0-471-19095-0; Stowell, J.C., "Intermediate Organic Chemistry" 2nd Edition (1993) Wiley-Interscience, ISBN: 0-471-57456-2; "Industrial Organic Chemicals: Starting Materials and Intermediates: An Ullmann's Encyclopedia" (1999) John Wiley & Sons, ISBN: 3-527-29645-X, in 8 volumes; "Organic Reactions" (1942-2000) John Wiley & Sons, in over 55 volumes; and "Chemistry of Functional Groups" John Wiley & Sons, in 73 volumes.

[00433] Specific and analogous reactants are also identified through the indices of known chemicals prepared by the Chemical Abstract Service of the American Chemical Society, which are available in most public and university libraries, as well as through on-line databases (the American Chemical Society, Washington, D.C., may be contacted for more details). Chemicals that are known but not commercially available in catalogs are optionally prepared by custom chemical synthesis houses, where many of the standard chemical supply houses (*e.g.*, those listed above) provide custom synthesis services. A reference for the preparation and selection of pharmaceutical salts of the compounds described herein is P. H. Stahl & C. G. Wermuth "Handbook of Pharmaceutical Salts", Verlag Helvetica Chimica Acta, Zurich, 2002.

Further Forms of Compounds Disclosed Herein

Isomers

[00434] Furthermore, in some embodiments, the compounds described herein exist as geometric isomers. In some embodiments, the compounds described herein possess one or more double bonds. The compounds presented herein include all cis, trans, syn, anti, entgegen (*E*), and zusammen (*Z*) isomers as well as the corresponding mixtures thereof. In some situations, compounds exist as tautomers. The compounds described herein include all possible tautomers within the formulas described herein. In some situations, the compounds described herein possess one or more chiral centers and each center exists in the R configuration, or S configuration. The compounds described herein include all diastereomeric, enantiomeric, and epimeric forms as well as the corresponding mixtures thereof. In additional embodiments of the compounds and methods provided herein, mixtures of enantiomers and/or diastereoisomers, resulting from a single preparative step, combination, or interconversion are useful for the applications described herein. In some embodiments, the compounds described herein

are prepared as their individual stereoisomers by reacting a racemic mixture of the compound with an optically active resolving agent to form a pair of diastereoisomeric compounds, separating the diastereomers and recovering the optically pure enantiomers. In some embodiments, dissociable complexes are preferred (e.g., crystalline diastereomeric salts). In some embodiments, the diastereomers have distinct physical properties (e.g., melting points, boiling points, solubilities, reactivity, etc.) and are separated by taking advantage of these dissimilarities. In some embodiments, the diastereomers are separated by chiral chromatography, or preferably, by separation/resolution techniques based upon differences in solubility. In some embodiments, the optically pure enantiomer is then recovered, along with the resolving agent, by any practical means that would not result in racemization.

Labeled compounds

[00435] In some embodiments, the compounds described herein exist in their isotopically-labeled forms. In some embodiments, the methods disclosed herein include methods of treating diseases by administering such isotopically-labeled compounds. In some embodiments, the methods disclosed herein include methods of treating diseases by administering such isotopically-labeled compounds as pharmaceutical compositions. Thus, in some embodiments, the compounds disclosed herein include isotopically-labeled compounds, which are identical to those recited herein, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that are incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, sulfur, fluorine and chloride, such as ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, and ^{36}Cl, respectively. Compounds described herein, and the pharmaceutically acceptable salts, esters, solvate, hydrates or derivatives thereof which contain the aforementioned isotopes and/or other isotopes of other atoms are within the scope of this invention. Certain isotopically-labeled compounds, for example those into which radioactive isotopes such as ^{3}H and ^{14}C are incorporated, are useful in drug and/or substrate tissue distribution assays. Tritiated, i. e., ^{3}H and carbon-14, i. e., ^{14}C, isotopes are particularly preferred for their ease of preparation and detectability. Further, substitution with heavy isotopes such as deuterium, *i.e.*, ^{2}H, produces certain therapeutic advantages resulting from greater metabolic stability, for example increased *in vivo* half-life or reduced dosage requirements. In some embodiments, the isotopically labeled compounds,

pharmaceutically acceptable salt, ester, solvate, hydrate or derivative thereof is prepared by any suitable method.

[00436] In some embodiments, the compounds described herein are labeled by other means, including, but not limited to, the use of chromophores or fluorescent moieties, bioluminescent labels, or chemiluminescent labels.

Pharmaceutically acceptable salts

[00437] In some embodiments, the compounds described herein exist as their pharmaceutically acceptable salts. In some embodiments, the methods disclosed herein include methods of treating diseases by administering such pharmaceutically acceptable salts. In some embodiments, the methods disclosed herein include methods of treating diseases by administering such pharmaceutically acceptable salts as pharmaceutical compositions.

[00438] In some embodiments, the compounds described herein possess acidic or basic groups and therefore react with any of a number of inorganic or organic bases, and inorganic and organic acids, to form a pharmaceutically acceptable salt. In some embodiments, these salts are prepared *in situ* during the final isolation and purification of the compounds of the invention, or by separately reacting a purified compound in its free form with a suitable acid or base, and isolating the salt thus formed.

Solvates

[00439] In some embodiments, the compounds described herein exist as solvates. The invention provides for methods of treating diseases by administering such solvates. The invention further provides for methods of treating diseases by administering such solvates as pharmaceutical compositions.

[00440] Solvates contain either stoichiometric or non-stoichiometric amounts of a solvent, and, in some embodiments, are formed during the process of crystallization with pharmaceutically acceptable solvents such as water, ethanol, and the like. Hydrates are formed when the solvent is water, or alcoholates are formed when the solvent is alcohol. Solvates of the compounds described herein are conveniently prepared or formed during the processes described herein. By way of example only, hydrates of the compounds described herein are conveniently prepared by recrystallization from an aqueous/organic solvent mixture, using organic solvents including, but not limited to, dioxane, tetrahydrofuran or methanol. In addition, the compounds provided herein exist in unsolvated as well as solvated forms. In general, the solvated forms are considered equivalent to the unsolvated forms for the purposes of the compounds and methods provided herein.

Pharmaceutical Compositions

[00441] In certain embodiments, the compounds described herein are administered as a pure chemical. In other embodiments, the compounds described herein are combined with a pharmaceutically suitable or acceptable carrier (also referred to herein as a pharmaceutically suitable (or acceptable) excipient, physiologically suitable (or acceptable) excipient, or physiologically suitable (or acceptable) carrier) selected on the basis of a chosen route of administration and standard pharmaceutical practice as described, for example, in *Remington: The Science and Practice of Pharmacy* (Gennaro, 21st Ed. Mack Pub. Co., Easton, PA (2005)).

[00442] Accordingly, provided herein is a pharmaceutical composition comprising at least one compound described herein, or a stereoisomer, pharmaceutically acceptable salt, hydrate, solvate, or N-oxide thereof, together with one or more pharmaceutically acceptable carriers. The carrier(s) (or excipient(s)) is acceptable or suitable if the carrier is compatible with the other ingredients of the composition and not deleterious to the recipient (*i.e.*, the subject) of the composition.

[00443] In certain embodiments, the compound as described herein is substantially pure, in that it contains less than about 5%, or less than about 1%, or less than about 0.1%, of other organic small molecules, such as contaminating intermediates or by-products that are created, for example, in one or more of the steps of a synthesis method.

[00444] These formulations include those suitable for oral, rectal, topical, buccal, parenteral (*e.g.*, subcutaneous, intramuscular, intradermal, or intravenous), vaginal, or aerosol administration.

[00445] Exemplary pharmaceutical compositions are used in the form of a pharmaceutical preparation, for example, in solid, semisolid or liquid form, which includes one or more of a disclosed compound, as an active ingredient, in a mixture with an organic or inorganic carrier or excipient suitable for external, enteral or parenteral applications. In some embodiments, the active ingredient is compounded, for example, with the usual non-toxic, pharmaceutically acceptable carriers for tablets, pellets, capsules, suppositories, solutions, emulsions, suspensions, and any other form suitable for use. The active object compound is included in the pharmaceutical composition in an amount sufficient to produce the desired effect upon the process or condition of the disease.

[00446] In some embodiments for preparing solid compositions such as tablets, the principal active ingredient is mixed with a pharmaceutical carrier, *e.g.*, conventional tableting ingredients such as corn starch, lactose, sucrose, sorbitol, talc, stearic acid,

magnesium stearate, dicalcium phosphate or gums, and other pharmaceutical diluents, *e.g.*, water, to form a solid preformulation composition containing a homogeneous mixture of a disclosed compound or a non-toxic pharmaceutically acceptable salt thereof. When referring to these preformulation compositions as homogeneous, it is meant that the active ingredient is dispersed evenly throughout the composition so that the composition is readily subdivided into equally effective unit dosage forms such as tablets, pills and capsules.

[00447] In solid dosage forms for oral administration (capsules, tablets, pills, dragees, powders, granules and the like), the subject composition is mixed with one or more pharmaceutically acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: (1) fillers or extenders, such as starches, cellulose, microcrystalline cellulose, silicified microcrystalline cellulose, lactose, sucrose, glucose, mannitol, and/or silicic acid; (2) binders, such as, for example, carboxymethylcellulose, hypromellose, alginates, gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; (3) humectants, such as glycerol; (4) disintegrating agents, such as crospovidone, croscarmellose sodium, sodium starch glycolate, agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; (5) solution retarding agents, such as paraffin; (6) absorption accelerators, such as quaternary ammonium compounds; (7) wetting agents, such as, for example, docusate sodium, cetyl alcohol and glycerol monostearate; (8) absorbents, such as kaolin and bentonite clay; (9) lubricants, such a talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof; and (10) coloring agents. In the case of capsules, tablets and pills, in some embodiments, the compositions comprise buffering agents. In some embodiments, solid compositions of a similar type are also employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like.

[00448] In some embodiments, a tablet is made by compression or molding, optionally with one or more accessory ingredients. In some embodiments, compressed tablets are prepared using binder (for example, gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. In some embodiments, molded tablets are made by molding in a suitable machine a mixture of the subject composition moistened with an inert liquid diluent. In some embodiments, tablets, and other solid dosage forms, such as dragees, capsules, pills and granules, are scored or prepared with coatings and shells, such as enteric coatings and other coatings.

[00449] Compositions for inhalation or insufflation include solutions and suspensions in pharmaceutically acceptable, aqueous or organic solvents, or mixtures thereof, and powders. Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the subject composition, in some embodiments, the liquid dosage forms contain inert diluents, such as, for example, water or other solvents, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, cyclodextrins and mixtures thereof.

[00450] In some embodiments, suspensions, in addition to the subject composition, contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, and mixtures thereof.

[00451] In some embodiments, formulations for rectal or vaginal administration are presented as a suppository, which are prepared by mixing a subject composition with one or more suitable non-irritating excipients or carriers comprising, for example, cocoa butter, polyethylene glycol, a suppository wax or a salicylate, and which is solid at room temperature, but liquid at body temperature and, therefore, will melt in the body cavity and release the active agent.

[00452] Dosage forms for transdermal administration of a subject composition include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. In some embodiments, the active component is mixed under sterile conditions with a pharmaceutically acceptable carrier, and with any preservatives, buffers, or propellants as required.

[00453] In some embodiments, the ointments, pastes, creams and gels contain, in addition to a subject composition, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

[00454] In some embodiments, powders and sprays contain, in addition to a subject composition, excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates and polyamide powder, or mixtures of these substances. In some embodiments, sprays additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

[00455] In some embodiments, the compounds described herein are formulated as eye drops for ophthalmic administration.

[00456] Compositions and compounds disclosed herein alternatively are administered by aerosol. This is accomplished by preparing an aqueous aerosol, liposomal preparation or solid particles containing the compound. In some embodiments, a non-aqueous (*e.g.*, fluorocarbon propellant) suspension is used. In some embodiments, sonic nebulizers are used because they minimize exposing the agent to shear, which results in degradation of the compounds contained in the subject compositions. Ordinarily, an aqueous aerosol is made by formulating an aqueous solution or suspension of a subject composition together with conventional pharmaceutically acceptable carriers and stabilizers. The carriers and stabilizers vary with the requirements of the particular subject composition, but typically include non-ionic surfactants (Tweens, Pluronics, or polyethylene glycol), innocuous proteins like serum albumin, sorbitan esters, oleic acid, lecithin, amino acids such as glycine, buffers, salts, sugars or sugar alcohols. Aerosols generally are prepared from isotonic solutions.

[00457] Pharmaceutical compositions suitable for parenteral administration comprise a subject composition in combination with one or more pharmaceutically-acceptable sterile isotonic aqueous or non-aqueous solutions, dispersions, suspensions or emulsions, or sterile powders which are reconstituted into sterile injectable solutions or dispersions just prior to use, which, in some embodiments, contain antioxidants, buffers, bacteriostats, solutes which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents.

[00458] Examples of suitable aqueous and non-aqueous carriers which are employed in the pharmaceutical compositions include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate and cyclodextrins. Proper fluidity is maintained, for example, by the use of coating materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants

[00459] Also contemplated are enteral pharmaceutical formulations including a disclosed compound and an enteric material; and a pharmaceutically acceptable carrier or excipient thereof. Enteric materials refer to polymers that are substantially insoluble in the acidic environment of the stomach, and that are predominantly soluble in intestinal fluids at specific pHs. The small intestine is the part of the gastrointestinal tract (gut) between the stomach and the large intestine, and includes the duodenum, jejunum, and

ileum. The pH of the duodenum is about 5.5, the pH of the jejunum is about 6.5 and the pH of the distal ileum is about 7.5. Accordingly, enteric materials are not soluble, for example, until a pH of about 5.0, of about 5.2, of about 5.4, of about 5.6, of about 5.8, of about 6.0, of about 6.2, of about 6.4, of about 6.6, of about 6.8, of about 7.0, of about 7.2, of about 7.4, of about 7.6, of about 7.8, of about 8.0, of about 8.2, of about 8.4, of about 8.6, of about 8.8, of about 9.0, of about 9.2, of about 9.4, of about 9.6, of about 9.8, or of about 10.0. Exemplary enteric materials include cellulose acetate phthalate (CAP), hydroxypropyl methylcellulose phthalate (HPMCP), polyvinyl acetate phthalate (PVAP), hydroxypropyl methylcellulose acetate succinate (HPMCAS), cellulose acetate trimellitate, hydroxypropyl methylcellulose succinate, cellulose acetate succinate, cellulose acetate hexahydrophthalate, cellulose propionate phthalate, cellulose acetate maleate, cellulose acetate butyrate, cellulose acetate propionate, copolymer of methylmethacrylic acid and methyl methacrylate, copolymer of methyl acrylate, methylmethacrylate and methacrylic acid, copolymer of methylvinyl ether and maleic anhydride (Gantrez ES series), ethyl methyacrylate-methylmethacrylate-chlorotrimethylammonium ethyl acrylate copolymer, natural resins such as zein, shellac and copal collophorium, and several commercially available enteric dispersion systems (*e.g.*, Eudragit L30D55, Eudragit FS30D, Eudragit L100, Eudragit S100, Kollicoat EMM30D, Estacryl 30D, Coateric, and Aquateric). The solubility of each of the above materials is either known or is readily determinable *in vitro*.

[00460] The dose of the composition comprising at least one compound described herein differs, depending upon the patient's (*e.g.,* human) condition, that is, stage of the disease, general health status, age, and other factors.

[00461] Pharmaceutical compositions are administered in a manner appropriate to the disease to be treated (or prevented). An appropriate dose and a suitable duration and frequency of administration will be determined by such factors as the condition of the patient, the type and severity of the patient's disease, the particular form of the active ingredient, and the method of administration. In general, an appropriate dose and treatment regimen provides the composition(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit (*e.g.,* an improved clinical outcome, such as more frequent complete or partial remissions, or longer disease-free and/or overall survival, or a lessening of symptom severity. Optimal doses are generally determined using experimental models and/or clinical trials. In some embodiments, the optimal dose depends upon the body mass, weight, or blood volume of the patient.

[00462] Oral doses typically range from about 1.0 mg to about 1000 mg, one to four times, or more, per day.

EXAMPLES

I. *In vitro* Biological Evaluation

[00463] Compounds were tested to assess their MAGL and serine hydrolase activity using the following *in vitro* assays.

***In vitro* competitive activity-based protein profiling**

[00464] Proteomes (mouse brain membrane fraction or cell lysates for mouse assays; human prefrontal cortex or cell membrane fractions for human assays) (50 μL, 1.0 mg/mL total protein concentration) were preincubated with varying concentrations of inhibitors at 37 °C. After 30 min, FP-Rh or HT-01 (1.0 μL, 50 μM in DMSO) was added and the mixture was incubated for another 30 min at 37 °C. Reactions were quenched with SDS loading buffer (15 μL - 4X) and run on SDS-PAGE. Following gel imaging, serine hydrolase activity was determined by measuring fluorescent intensity of gel bands corresponding to MAGL using ImageJ 1.43u software.

Preparation of Mouse Brain Proteomes from inhibitor treated mice

[00465] Inhibitors were administered to wild-type ICR mice by oral gavage in a vehicle of 7:2:1 polyethylene glycol 400 (PEG400)/ethanol/PBS (v/v/v). Each animal was sacrificed 4 h following administration, brains were removed and brain proteomes were prepared and analyzed according to previously established methods.

[00466] The compounds shown in Table 1 demonstrated MAGL inhibitory activity with an IC_{50} of less than 1 μM in the assays described herein.

II. *In vivo* Biological Evaluation

[00467] Compounds were tested to assess their MAGL and serine hydrolase activity using the following *in vivo* assay.

MPTP-lesioned macaque model of L-DOPA induced dyskinesia (LID)

[00468] The study utilized 8 female MPTP-lesioned cynomolgus macaques (10-15 years in age) that have received chronic repeat-treatment with L-DOPA and manifest stable and reproducible dyskinesia, of choreic and dystonic nature, in response to subsequent L-DOPA treatments.

[00469] A MGLL inhibitor, Compound 21, (3, 10 and 30 mg/kg), reference drug amantadine (10 mg/kg) and vehicle were administered by oral gavage as a single dose 2 h before a high-dose of L-DOPA (administered as Madopar™). The L-DOPA dose individualized for each animal is one that induced robust and reproducible anti-

parkinsonian effects lasting ~3-4 h but compromised by disabling dyskinesia. The animals were video-recorded for a 6 h period following L-DOPA administration and the effects of each treatment on dyskinesia, parkinsonian disability, duration and quality of anti-parkinsonian benefit (on-time) were scored blinded by a neurologist. Dyskinesia was scored using the non-human primate dyskinesia rating scale (NHPDysRS) and disability was scored using the monkey parkinsonian disability rating scale (mPDRS).

[00470] The study design was an ascending dose crossover with all animals receiving each treatment in the order of vehicle, 10 mg/kg amantadine, 3 mg/kg Compound 21, 10 mg/kg Compound 21, and 30 mg/kg Compound 21. An ascending dose design was chosen to avoid potential pharmacodynamic carryover between periods due to the long half-life of Compound 21 in MPTP-lesioned macaques (16-34 h) and the irreversible mechanism by which Compound 21 inhibits MGLL resulting pharmacodynamic effects that persist after the unbound compound is cleared from the body.

Results

[00471] L-DOPA administration induced antiparkinsonian effects with debilitating dyskinesia in 7/8 vehicle pre-treated animals. Based on pre-determined criteria, 1 animal was excluded from subsequent analysis as it did not demonstrate the level of dyskinesia required to evaluate anti-dyskinetic effects.

[00472] Amantadine (10 mg/kg, p.o.) was associated with a mean plasma exposure of 1,300 and 1,500 ng/mL 2 h and 8 h post-dose, respectively. The 10 mg/kg dose of amantadine produced a 29% reduction in median peak-dose dyskinesia after L-DOPA administration ($P < 0.05$, Fig. 1A and 1B), but was associated with a mild and statistically significant worsening of parkinsonian disability (0-2 h post L-DOPA administration totals, $P < 0.05$, Fig. 1E).

[00473] Compound 21 (3, 10 and 30 mg/kg, p.o.) dose-dependently reduced median peak dose dyskinesia induced by L-DOPA administration (0-2 h post L-DOPA totals, Fig. 1C and 1D). Following oral administration of 10 and 30 mg/kg Compound 21 median peak dose dyskinesia was reduced by 45% and 35%, respectively. Due to heterogeneity in animal response, the reduction in 0-2 hour total dyskinesia scores following Compound 21 administration did not reach statistical significance. However, a significant reduction in dyskinesia was observed for the 10 mg/kg group in the 1-2 h post L-DOPA interval (Fig. 1C). Although, dystonia is the predominant form of dyskinesia that presents in this model, evidence of benefit on both dystonia and chorea was observed following Compound 21 administration (data not shown). Importantly, Compound 21 (3, 10 and 30 mg/kg) did not affect the antiparkinsonian actions of L-DOPA (Fig. 1F).

[00474] Compound 21 produced robust anti-dyskinetic effects in the MPTP-lesioned macaque model of L-DOPA induced dyskinesia. The therapeutic effects of Compound 21 on median dyskinesia ratings were of greater magnitude than a therapeutically relevant dose of amantadine. Importantly, Compound 21 did not impact the antiparkinsonian effects of L-DOPA whereas amantadine was associated with a worsening of parkinsonian disability. These findings highlight a new and differentiated CNS mechanism for the treatment of L-DOPA induced dyskinesia in Parkinson's disease with a MAGL inhibitor.

III. A Randomized, Placebo-Controlled Phase II Study of a Test Compound (Compound of Formula (I)-(XVII)) in Patients with Parkinson's Disease and Dyskinesia

STUDY OBJECTIVE	1. To evaluate the efficacy of test compound in levodopa induced dyskinesia at 4 weeks compared to placebo, as measured using the change in UDysRS from baseline. 2. To evaluate the efficacy of test compound improve dyskinesia during an oral LD challenge compared to placebo measured using the change in LIDS from baseline. 3. To evaluate the efficacy of test compound on time without troublesome dyskinesia compared to placebo using PD diaries. 4. To evaluate the efficacy of test compound on motor symptoms (e.g. tremor, imbalance, freezing of gait) and NMS (e.g. pain, anxiety or sleep disruption) relative to placebo, measured using the change in appropriate endpoints. 5. To evaluate the safety and tolerability of test compound in patients with PD through analysis of adverse events (AE), serious adverse events (SAE), and Suspected Unexpected Serious Adverse Reactions (SUSAR).
STUDY POPULATION AND NUMBER OF SUBJECTS	40 eligible patients will be randomized at 1:1 Sequence A: Run-In Placebo, Period 1 test compound, Period 2 Placebo Sequence B: Run-In Placebo, Period 1 Placebo, Period 2 test compound
STUDY DESIGN	Double-blind, randomized, two period, multi-center crossover study. Eligible patients undergo a one-week single-blind placebo run-in to establish baseline symptoms. Patients continue with four weeks of double-blinded therapy, the first two weeks at a low dose of test compound /Placebo, then two weeks at a higher dose of test compound/Placebo. There is a 1-3 week washout period with no study therapy between treatment periods. The second treatment period is a four-week treatment with the alternative study treatment.
MAIN INCLUSION/ EXCLUSION CRITERIA	Diagnosis of PD according to the United Kingdom Parkinson's Disease Society Brain Bank criteria. Inclusion: Men or women 30-75 years of age (30-85 years of age after DSMB agreement).

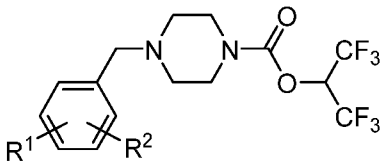
	LD responsive Parkinsonism Peak dose LD associated dyskinesia with a score of 1 (mild) or greater on the MDS-UPDRS question 4.2. Patients must be capable of recognizing LID Stable PD medication regimen for at least 30 days Willing to sign informed consent (and caregiver, if applicable). Exclusion: Diphasic dyskinesia Montreal Cognitive Assessment (MoCA) ≤ 25 History of psychosis or hallucination except hallucination with past use of amantadine Current use of amantadine (patients that discontinue amantadine for 30 days and are otherwise eligible may participate) Current use of cannabis or cannabinoid medications (e.g. Sativex, dronabinol, nabilone) Dopamine receptor blockers No strong 3A4 inhibitors or inducers Significant organ dysfunction
DOSAGE: ROUTE AND FORM	Test compound or matching placebo hard gelatin capsules will be administered orally in the morning with food. Study drug will be administered in the morning before the LD challenge at the usual time. Each 4 week double blind treatment period is dose-escalated in double-blind fashion: Week 1-2: 20 mg test compound or Placebo daily; (2 capsules) Week 3-4: 40 mg test compound or Placebo daily; (3 capsules) If 20 mg is not tolerated, then the dose should be reduced to 10 mg. If 40 mg is not tolerated, then the dose should be reduced to 30 mg. If dose reduction to 10 mg occurs during week 1-2, the dose in Week 3-4 will be 20 mg, if tolerated.
DURATION OF TREATMENT	Individual patients will participate for between 10-16 weeks. 4 weeks of double-blind therapy with test compound is adequate to understand its effects on dyskinesia.
PRIMARY OUTCOME MEASURE(S)	The **Unified Dyskinesia Rating Scale** (UDysRS) is a validated, FDA accepted, dyskinesia scale. Part 1 and 2 record patient perceptions of dyskinesia over the past week. Part 3 and 4 score impairment and disability from dyskinesia with 4 performance activities which are observed --communication, drinking from a cup, buttoning a lab coat, and rising from a chair, walking and returning to the chair. The objective parts of the UDysRS (Part 3 and 4) will also be separately reported. Scored by central raters from video record.
SECONDARY OUTCOME MEASURE(S)	**LIDS Performance Test**: The oral LD challenge paradigm measures ON-period dyskinesia. At 3 times after achieving full ON, the LIDS performance test is scored. Taking 5 minutes, the clinician scores 12 items (0=none; 4=severe) over 7 body regions, observing scoring patients at rest, and during a specified protocol of activities including speech, writing, walking, and limb movements. There are additional items to provide a global judgment of severity, impact and awareness of dyskinesia to generate a total score. In each body region, the highest severity of dyskinesia observed (even momentarily) is recorded as the rating. Scoring is performed by central raters from video record.

	PD Diaries: The distribution of time affected by dyskinesia using PD diaries. Diaries are completed for 48 hours before each visit and time (30 minute intervals) is allocated into 5 options: ON without dyskinesia, ON with dyskinesia, ON with troublesome dyskinesia, OFF, and asleep. PD diaries were a secondary endpoint for FDA review of extended release amantadine. **UPDRS:** The UPDRS measures general parkinsonian symptoms. Useful drugs for LID should reduce dyskinesia but not worsen core PD symptoms. **CGI-I:** Clinician's Global Impression of Change determines improvement in overall PD symptoms. It is a 7 point scale, graded by the investigator. **NMSS:** The Non-Motor Symptom Scale. Thirty items are scored by a clinician-rater for severity (0-3) and frequency (1-4). The NMSS will be modified to ask for symptoms over the last week instead of over the last month. The 30 items map to several domains (e.g. cardiovascular, sleep fatigue, mood and cognition, perception / hallucination, attention, memory etc). **PDSS-2:** Parkinson's Disease Sleep Scale consists of 15 items evaluating three domains (motor symptoms at night, PD symptoms at night, and disturbed sleep are rated by the patient using one of five categories, from 0 (never) to 4 (very frequent). Symptoms on each of 3 domains are scored 0–20 points. The questionnaire is filled out with regard to symptoms in the previous week. This scale is validated and responsive. **MPQ-2:** The McGill Pain Questionnaire-2 is responsive and validated in a large variety of pain conditions including muscular skeletal pain, neuropathic pain and cancer pain, and across a wide age range. It consists of 22 numeric rating scales of pain qualities (e.g. 'burning', 'aching') that the patient rates over the past week (0-10). The MPQ is considered a core endpoint in pain research. **GAI:** The Geriatric Anxiety Inventory consists of 20 "Agree/Disagree" items designed to assess typical common anxiety symptoms. The measurements of somatic symptoms with the instrument are limited in order to minimize confusion between symptoms common to anxiety and general medical conditions. The GAI is validated in PD. **Computerized Cognition Measure:** A validated computerized cognition measure (Cogstate) measures reaction time, discrimination, executive function and working memory.

CLAIMS

We Claim:

1. A method for treating dyskinesia in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of Formula (I'):



Formula (I');

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is optionally substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

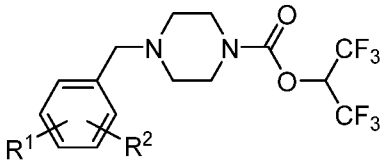
the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

each R^9 is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

2. The method of claim 1, wherein the compound of Formula (I') is a compound of Formula (III):



Formula (III);

wherein:

R^1 is halogen, $-OR^3$, $-SF_5$, -CN, C_{1-6}alkyl optionally substituted by halogen, or $-C(O)OR^9$;

R^2 is $-NR^5R^6$;

R^3 is selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}aminoalkyl;

R^5 and R^6, together with the nitrogen to which they are attached, form

(i) a 4-6 membered saturated monocyclic heterocycle; or

(ii) a 7-8 membered bridged heterocyclic ring optionally containing an additional O, N, or S;

wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one or two substituents independently selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S; and

the 7-8 membered bridged heterocyclic ring is optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl;

each R^8 is independently selected from C_{1-6}alkyl; and

each R^9 is independently selected from H and C_{1-6}alkyl;

or a pharmaceutically acceptable salt or solvate thereof.

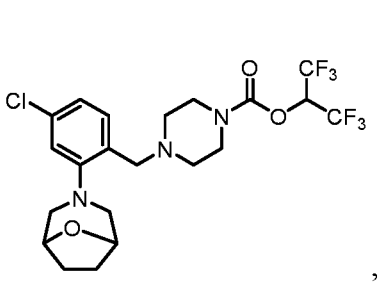
3. The method of claim 1 or 2, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$; and the 4-6 membered saturated monocyclic heterocycle optionally contains an additional O, N, or S.

4. The method of claim 3, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted with one substituent selected from C_{1-6}haloalkyl, $-C(O)OR^9$, and $-NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine.

5. The method of claim 4, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 4-6 membered saturated monocyclic heterocycle substituted

with one substituent selected from C_{1-6}haloalkyl, -C(O)OR^9, and -$NR^9SO_2R^8$, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine and piperidine.

6. The method of claim 1, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle.
7. The method of claim 6, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 4-6 membered saturated monocyclic heterocycle, wherein the 4-6 membered saturated monocyclic heterocycle is selected from pyrrolidine, piperidine, and morpholine.
8. The method of claim 1 or 2, wherein R^5 and R^6, together with the nitrogen to which they are attached, form a 7-8 membered bridged heterocyclic ring optionally substituted with one or two substituents independently selected from halogen, oxo, and C_{1-6}alkyl.
9. The method of claim 8, wherein R^5 and R^6, together with the nitrogen to which they are attached, form an unsubstituted 7-8 membered bridged heterocyclic ring.
10. The method of any one of claims 1-9, wherein R^1 is halogen, -SF_5, or optionally substituted C_{1-6}alkyl optionally substituted by halogen.
11. The method of claim any one of claims 1-10, wherein R^1 is halogen.
12. The method of claim any one of claims 1-10, wherein R^1 is C_{1-6}alkyl optionally substituted by halogen.
13. The method of claim 12, wherein R^1 is -CF_3.
14. The method of claim 1, wherein the compound is selected from: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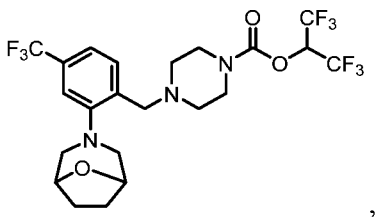
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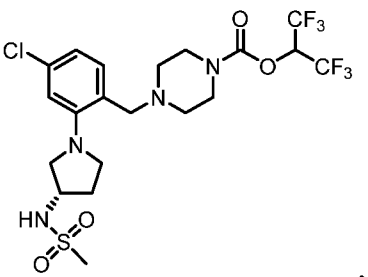
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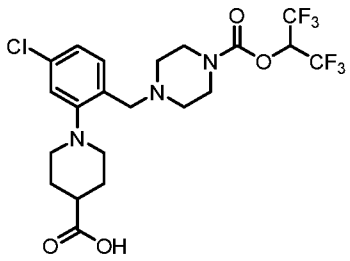
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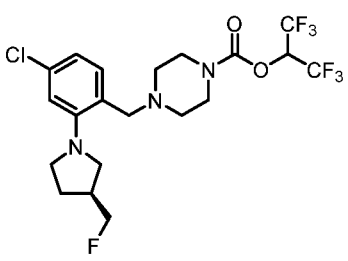
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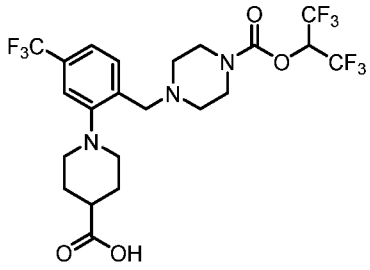
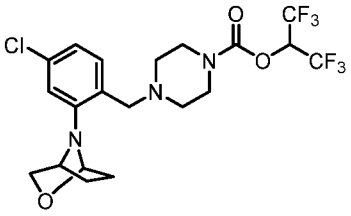
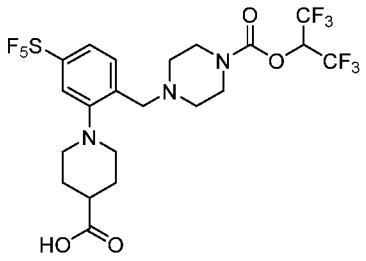
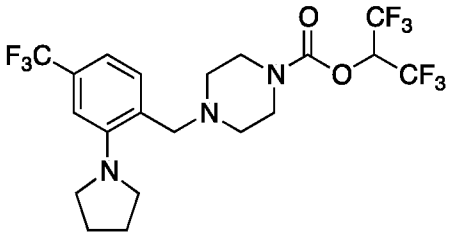

, 
, and 
; or a pharmaceutically acceptable salt or solvate thereof.

15. The method of claim 1, wherein the compound is:


; or a pharmaceutically acceptable salt or solvate thereof.

16. The method of any one of claims 1-15, wherein the dyskinesia is levodopa-induced dyskinesia.

FIG. 1A

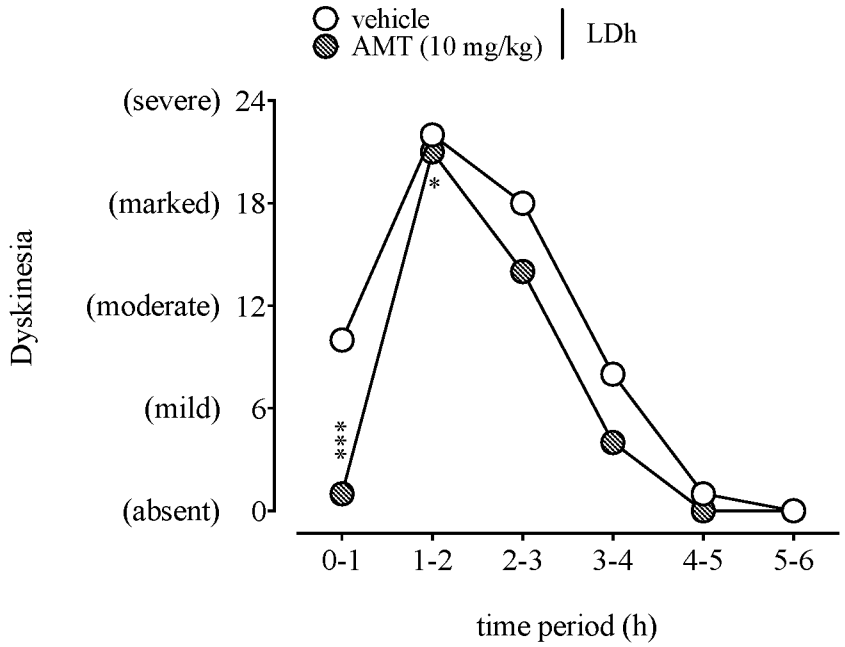

vehicle
AMT (10 mg/kg)
LDh
(severe) 24
(marked) 18
(moderate) 12
(mild) 6
(absent) 0
Dyskinesia
*
***
0-1
1-2
2-3
3-4
4-5
5-6
time period (h)

FIG. 1B

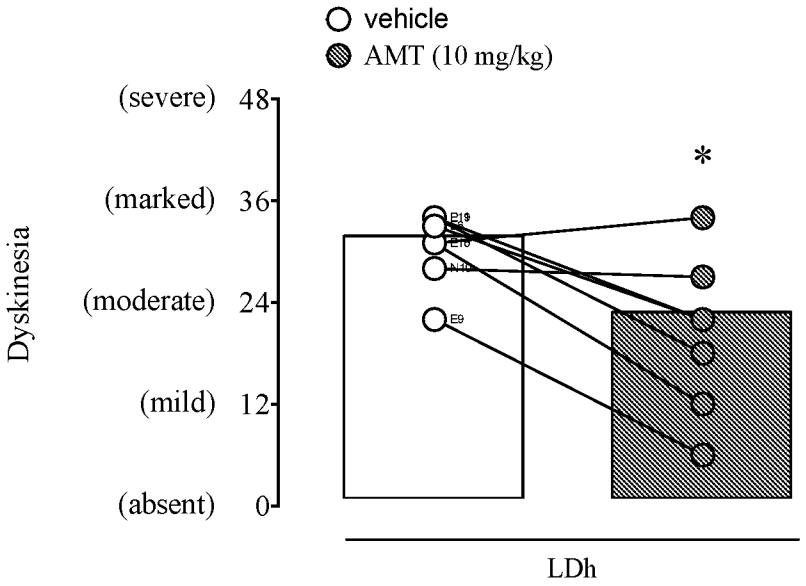

vehicle
AMT (10 mg/kg)
(severe) 48
(marked) 36
(moderate) 24
(mild) 12
(absent) 0
Dyskinesia
*
LDh

FIG. 1C

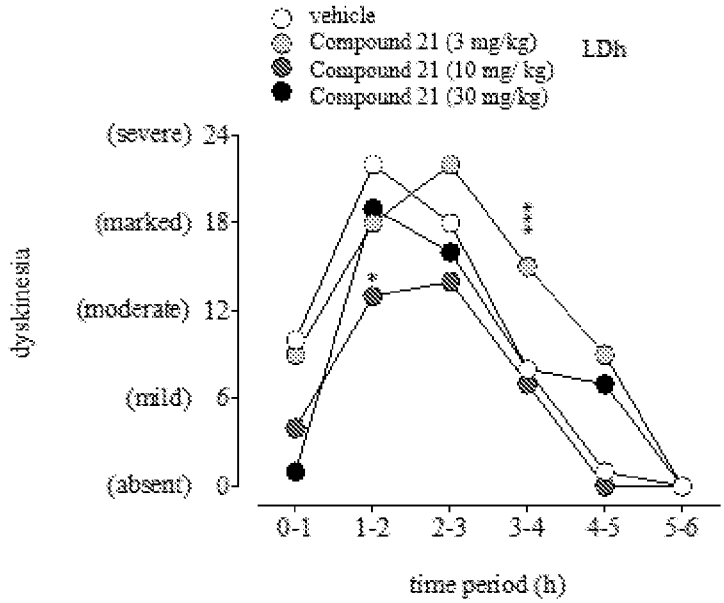

vehicle
Compound 21 (3 mg/kg)
Compound 21 (10 mg/ kg)
Compound 21 (30 mg/kg)
LDh
(severe) 24
(marked) 18
(moderate) 12
(mild) 6
(absent) 0
dyskinesia
*
***
0-1
1-2
2-3
3-4
4-5
5-6
time period (h)

FIG. 1D

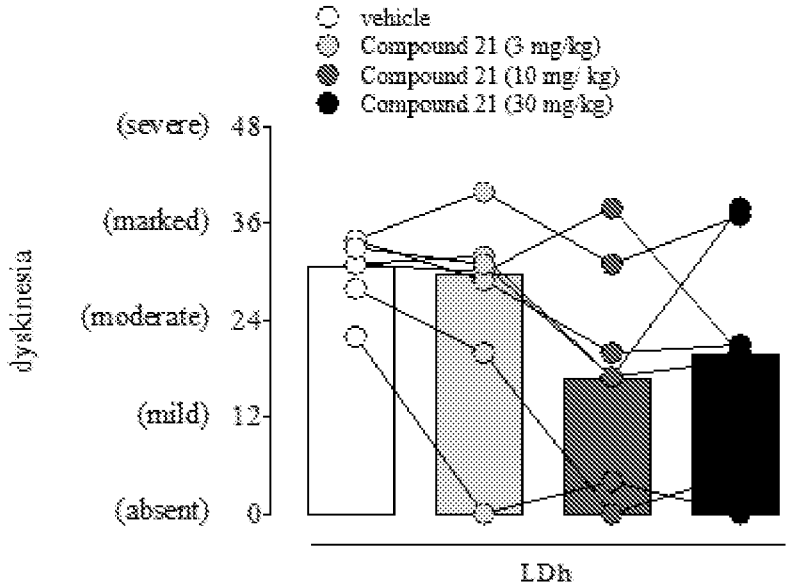

vehicle
Compound 21 (3 mg/kg)
Compound 21 (10 mg/ kg)
Compound 21 (30 mg/kg)
(severe) 48
(marked) 36
(moderate) 24
(mild) 12
(absent) 0
dyskinesia
*
LDh

FIG. 1E

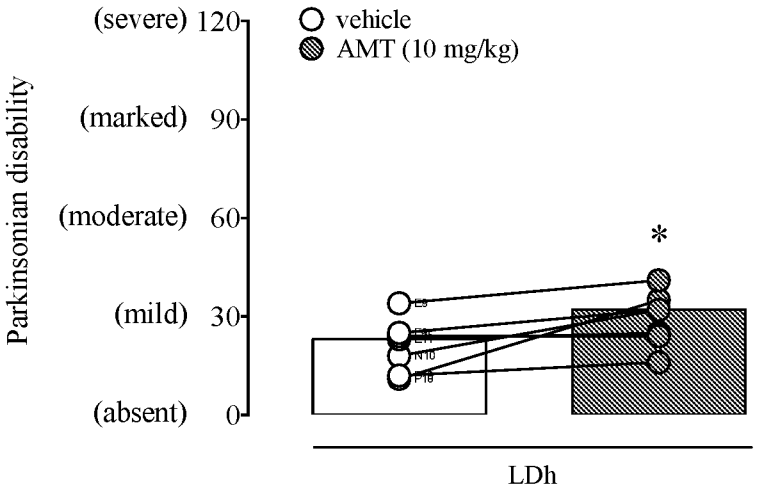

(severe) 120
(marked) 90
(moderate) 60
(mild) 30
(absent) 0
Parkinsonian disability
vehicle
AMT (10 mg/kg)
*
LDh

FIG. 1F

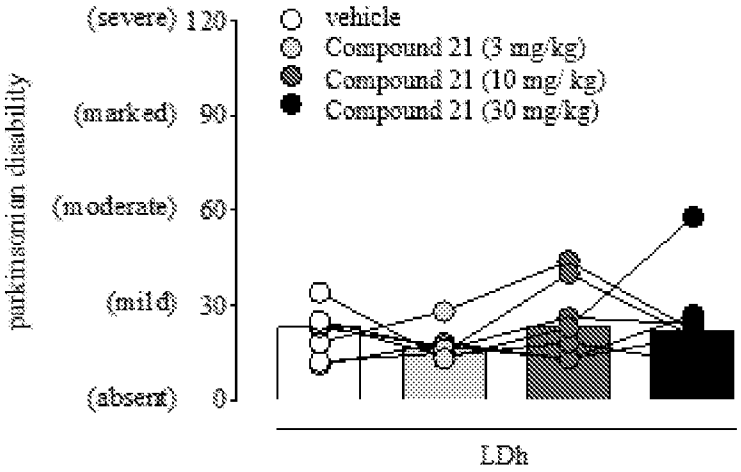
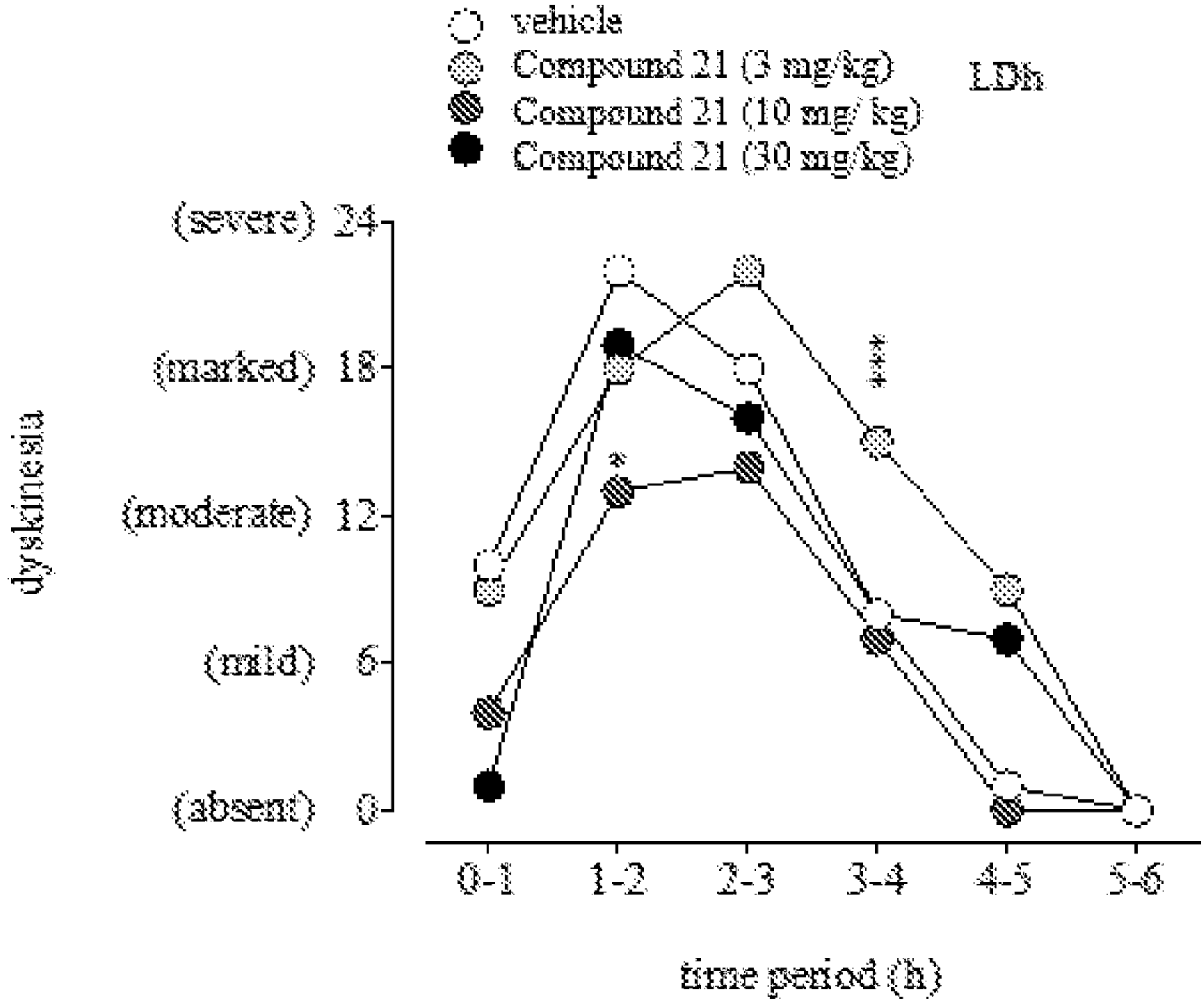

(severe) 120
(marked) 90
(moderate) 60
(mild) 30
(absent) 0
parkinsonian disability
vehicle
Compound 21 (3 mg/kg)
Compound 21 (10 mg/kg)
Compound 21 (30 mg/kg)
LDh

FIG. 1C


vehicle
Compound 21 (3 mg/kg)
Compound 21 (10 mg/ kg)
Compound 21 (30 mg/kg)
LDh
dyskinesia
(severe) 24
(marked) 18
(moderate) 12
(mild) 6
(absent) 0
***
*
0-1
1-2
2-3
3-4
4-5
5-6
time period (h)