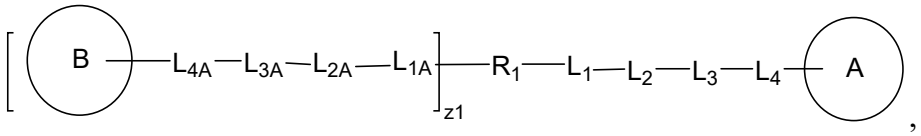
CLAIMS

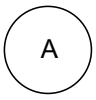
1. A compound, or a stereoisomer, tautomer, prodrug, or salt thereof, comprising the structure of Formula (I'):

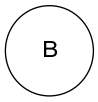


,

Formula (I')

wherein:

each of 

and 

is independently a cannabinoid receptor type 1 (CB_1) ligand;

each of L_1, L_2, L_3, L_4, L_{1A}, L_{2A}, L_{3A}, and L_{4A} is independently a linker, a bond, or absent, wherein at least one of L_1, L_2, L_3, and L_4 comprises a linker or a bond;

R^1 comprises one or more oligonucleotides, protecting groups, small molecules, proteins, antibodies, and/or peptides; and

z1 is 0 or 1.

2. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 1, wherein the compound comprises the structure of Formula (I''):



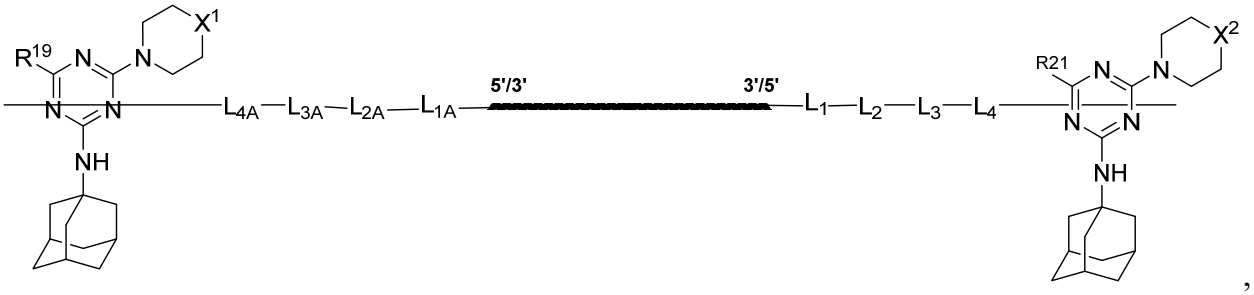
,

Formula (I'')

wherein:

 is an oligonucleotide.

3. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 2, wherein the compound comprises the structure of Formula (I"-a):



,

Formula (I"-a)

wherein:

X^1 is NR^{10} or $CR^{11}R^{12}$;

X^2 is NR^{13} or $CR^{14}R^{15}$;

R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently hydrogen, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

R^{19} is hydrogen, $–SO_{n19}R^{19A}$, $–SO_{v19}NR^{19B}R^{19C}$, $–NHNR^{19B}R^{19C}$, $–ONR^{19B}R^{19C}$, $–NHC(O)NHNR^{19B}R^{19C}$, $–NHC(O)NR^{19B}R^{19C}$, $–NR^{19B}R^{19C}$, $–C(O)R^{19D}$, $–C(O)OR^{19D}$, $–C(O)NR^{19B}R^{19C}$, $–OR^{19A}$, $-NR^{19B}SO_2R^{19A}$, $-NR^{19B}C(O)R^{19D}$; $-NR^{19B}C(O)OR^{19D}$, $–NR^{19B}OR^{19D}$, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

R^{21} is hydrogen, $–SO_{n21}R^{21A}$, $–SO_{v21}NR^{21B}R^{21C}$, $–NHNR^{21B}R^{21C}$, $–ONR^{21B}R^{21C}$, $–NHC(O)NHNR^{21B}R^{21C}$, $–NHC(O)NR^{21B}R^{21C}$, $–NR^{21B}R^{21C}$, $–C(O)R^{21D}$, $–C(O)OR^{21D}$, $–C(O)NR^{21B}R^{21C}$, $–OR^{21A}$, $-NR^{21B}SO_2R^{21A}$, $-NR^{21B}C(O)R^{21D}$; $-NR^{21B}C(O)OR^{21D}$, $–NR^{21B}OR^{21D}$, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

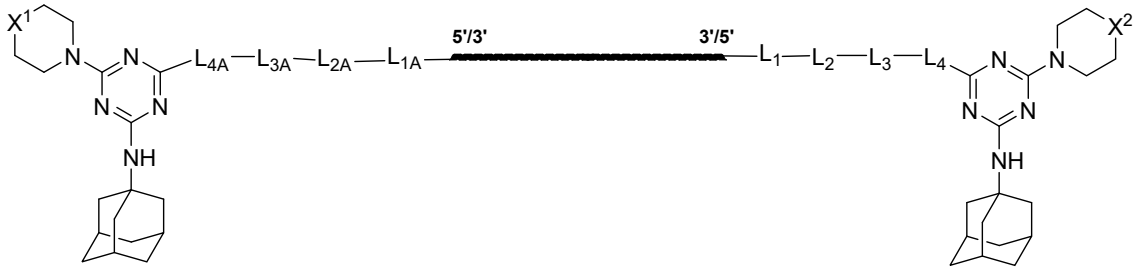
R^{19A}, R^{19B}, R^{19C}, R^{19D}, R^{21A}, R^{21B}, R^{21C}, and R^{21D} are each independently hydrogen, halogen, $–CF_3$, $–CCl_3$, $–CBr_3$, $–CI_3$, –COOH, $–CONH_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or

unsubstituted heteroaryl; wherein R^{19B} and R^{19C}; and R^{21B} and R^{21C} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

n19 and n21 are each independently 0, 1, 2, 3, or 4; and

v19 and v21 are each independently 1 or 2.

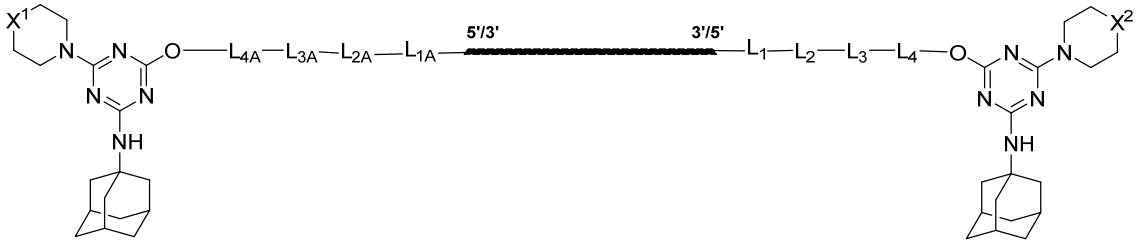
4. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 3, wherein the compound comprises the structure of Formula (I"-a-1):



[[.]]

Formula (I"-a-1)

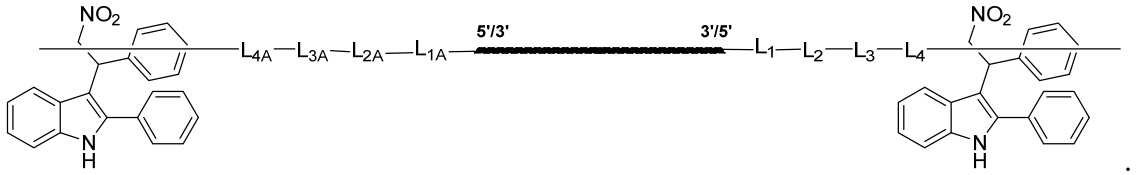
or the structure of Formula (I"-a-2):



.

Formula (I"-a-2)

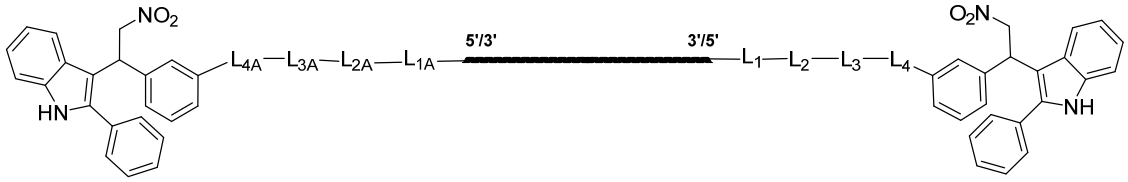
5. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 2, wherein the compound comprises the structure of Formula (I"-b):



.

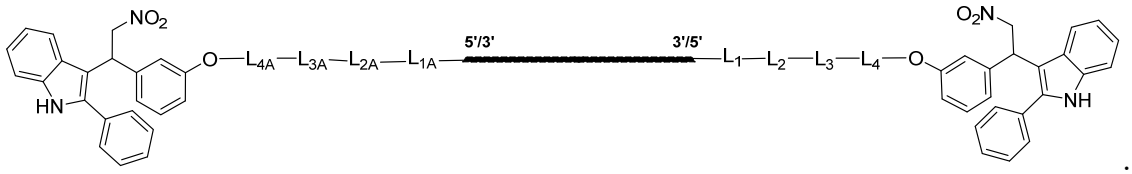
Formula (I"-b)

6. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 5, wherein the compound comprises the structure of Formula (I"-b-1):



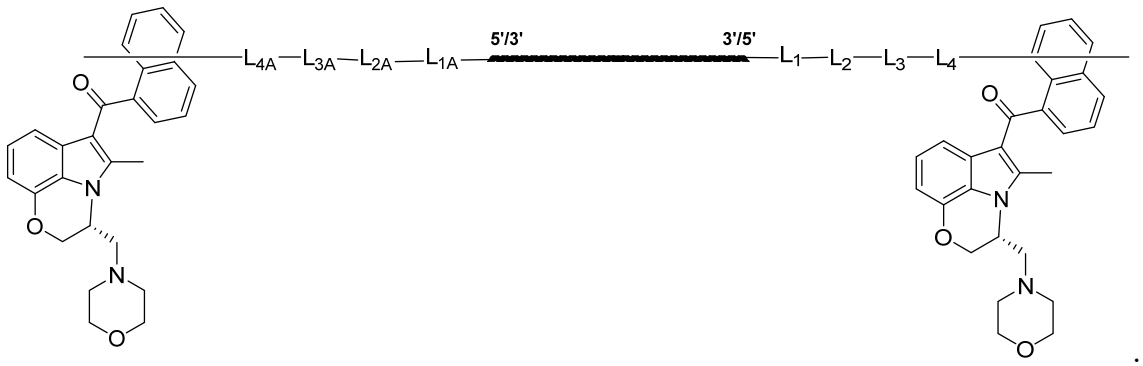
Formula (I"-b-1)

or the structure of Formula (I"-b-2):



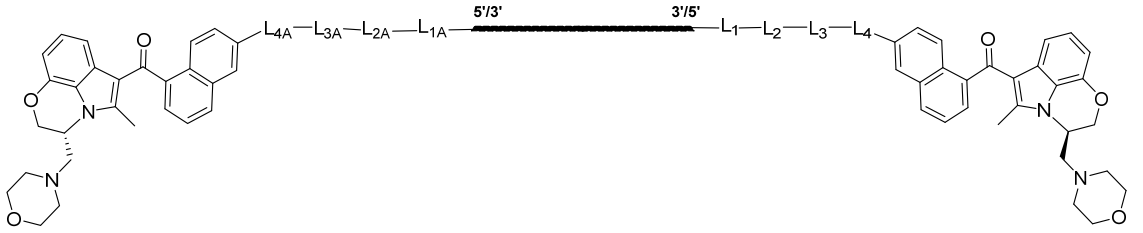
Formula (I"-b-2)

7. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 2, wherein the compound comprises the structure of Formula (I"-c):



Formula (I"-c)

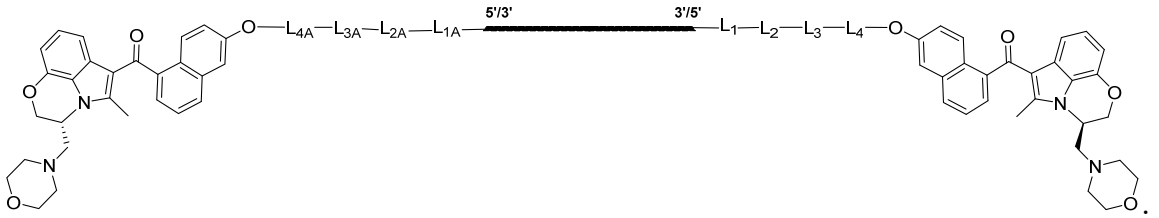
8. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 7, wherein the compound comprises the structure of:



[[.]]

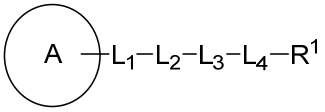
Formula (I"-c-1)

or the structure of Formula (I"-c-2):



Formula (I"-c-2)

9. A compound, or a stereoisomer, tautomer, prodrug, or salt thereof, comprising the structure of Formula (I):



,

Formula (I)

wherein

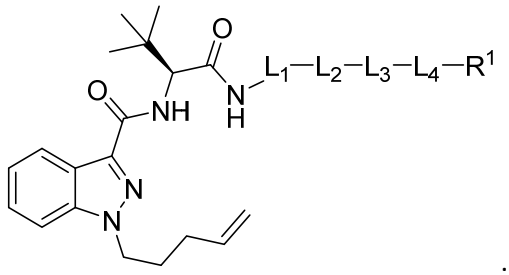


is a cannabinoid receptor type 1 (CB_1) ligand;

each of L_1, L_2, L_3, and L_4 is independently a linker, a bond, or absent, wherein at least one of L_1, L_2, L_3, and L_4 comprises a linker or a bond; and

R^1 comprises one or more oligonucleotides, protecting groups, small molecules, proteins, antibodies, and/or peptides.

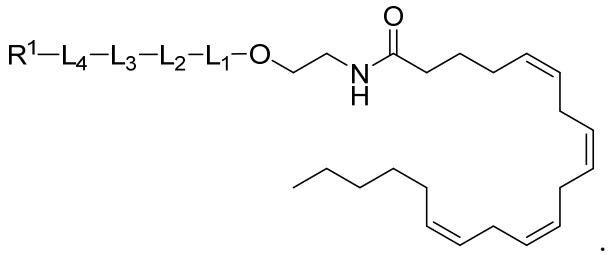
10. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 9, wherein the compound comprises the structure of Formula (II-a):



.

Formula (II-a)

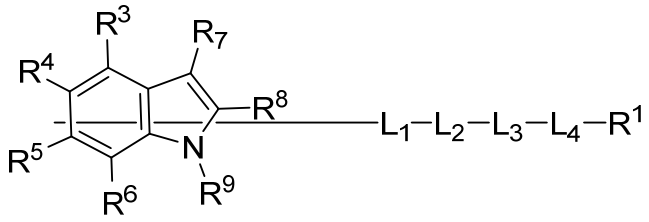
11. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 9, wherein the compound comprises the structure of Formula (III-a):



.

Formula (III-a)

12. A compound, or a stereoisomer, tautomer, prodrug, or salt thereof, comprising the structure of Formula (VIII):



,

Formula (VIII)

wherein:

each of L_1, L_2, L_3, and L_4 is independently a linker, a bond, or absent, wherein at least one of L_1, L_2, L_3, and L_4 comprises a linker or a bond;

R^1 comprises one or more oligonucleotides, protecting groups, small molecules, proteins, antibodies, and/or peptides;

R^3, R^4, R^5, R^6, and R^8 are each independently hydrogen, halogen, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

R^9 is hydrogen, optionally substituted alkyl, or optionally substituted heteroalkyl; or R^6 and R^9 substituents may be joined together form an optionally substituted heterocycloalkyl or optionally substituted heteroaryl; and

R^7 is hydrogen, $–SO_{n7}R^{7A}$, $–SO_{v7}NR^{7B}R^{7C}$, $–NHNR^{7B}R^{7C}$, $–ONR^{7B}R^{7C}$, $–NHC(O)NHNR^{7B}R^{7C}$, $–NHC(O)NR^{7B}R^{7C}$, $–NR^{7B}R^{7C}$, $–C(O)R^{7D}$, $–C(O)OR^{7D}$, $–C(O)NR^{7B}R^{7C}$, $–OR^{7A}$, $–NR^{7B}SO_2R^{7A}$, $–NR^{7B}C(O)R^{7D}$;

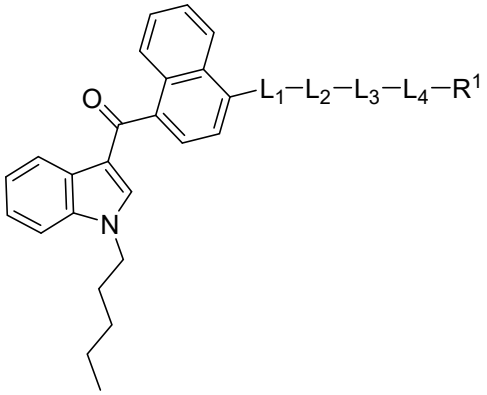
$–NR^{7B}C(O)OR^{7D}$, $–NR^{7B}OR^{7D}$, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

R^{7A}, R^{7B}, R^{7C}, R^{7D} are each independently hydrogen, halogen, $–CF_3$, $–CCl_3$, $–CBr_3$, $–CI_3$, –COOH, $–CONH_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl,substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; wherein R^{7B} and R^{7C} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

n7 is 0, 1, 2, 3, or 4; and

v7 is 1 or 2.

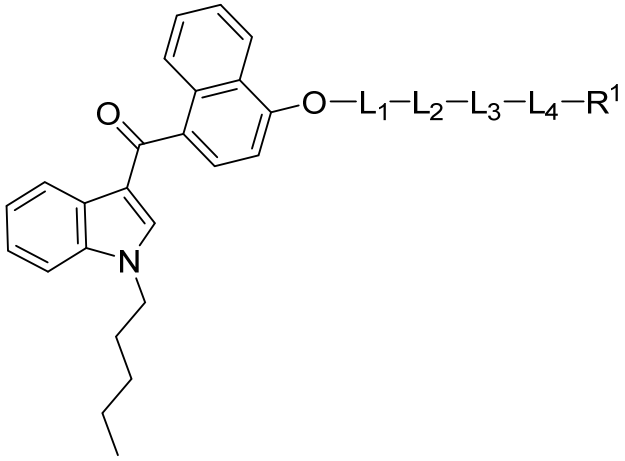
13. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 12, wherein the compound comprises the structure of Formula (VIII-a-1):



,

Formula (VIII-a-1)

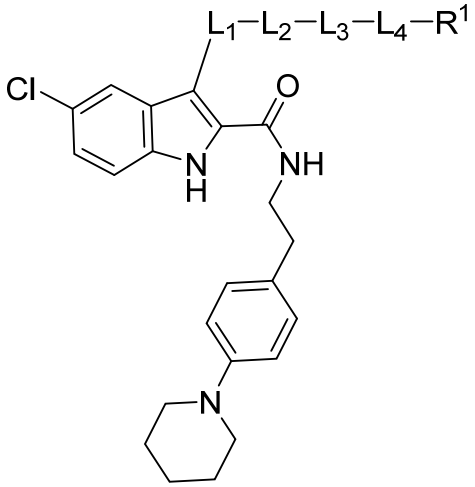
the structure of Formula (VIII-a-2):



,

Formula (VIII-a-2)

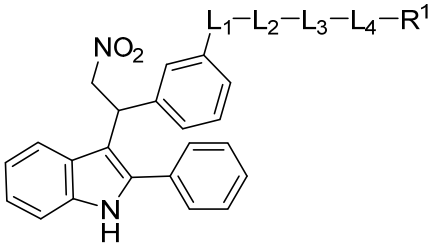
the structure of Formula (VIII-b-1):



,

Formula (VIII-b-1)

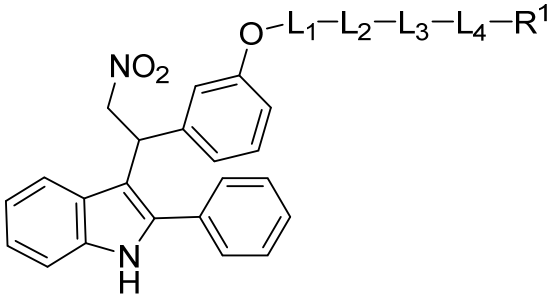
the structure of Formula (VIII-c-1):



,

Formula (VIII-c-2)

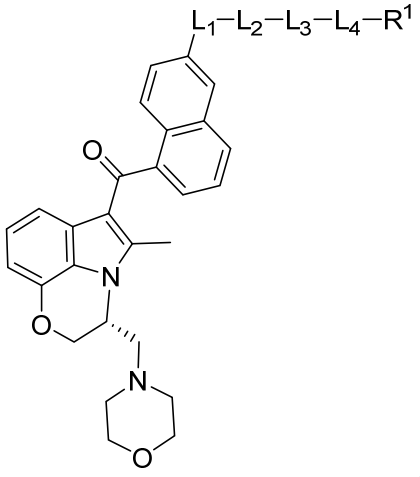
the structure of Formula (VIII-c-2):



,

Formula (VIII-c-2)

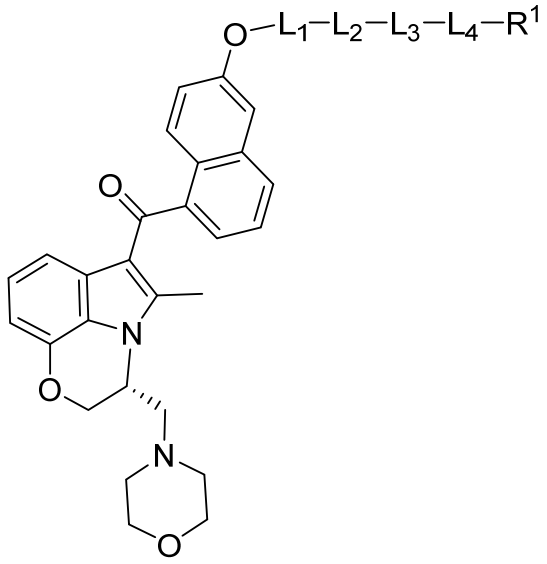
the structure of Formula (VIII-d-1):



,

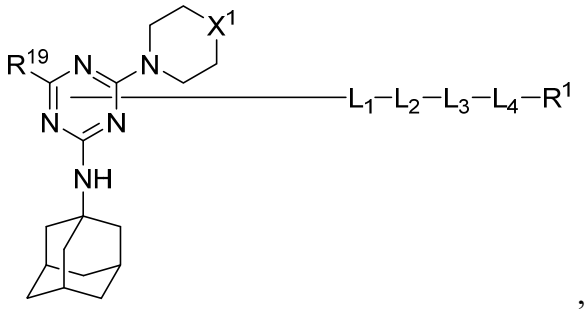
Formula (VIII-d-1)

or the structure of Formula (VIII-d-2):



Formula (VIII-d-2)

14. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 9, comprising the structure of Formula (IX):



Formula (IX)

wherein:

X^1 is NR^{10} or $CR^{11}R^{12}$;

R^{10}, R^{11}, and R^{12} are each independently hydrogen, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

R^{19} is hydrogen, $–SO_{n19}R^{19A}$, $–SO_{v19}NR^{19B}R^{19C}$, $–NHNR^{19B}R^{19C}$, $–ONR^{19B}R^{19C}$, $–NHC(O)NHNR^{19B}R^{19C}$, $–NHC(O)NR^{19B}R^{19C}$, $–NR^{19B}R^{19C}$, $–C(O)R^{19D}$, $–C(O)OR^{19D}$, $–C(O)NR^{19B}R^{19C}$, $–OR^{19A}$, $–NR^{19B}SO_2R^{19A}$, $–NR^{19B}C(O)R^{19D}$;

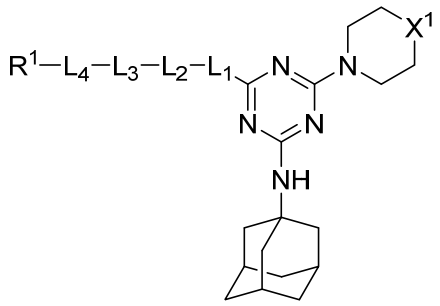
-$NR^{19B}C(O)OR^{19D}$, $–NR^{19B}OR^{19D}$, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

R^{19A}, R^{19B}, R^{19C}, R^{19D} are each independently hydrogen, halogen, $–CF_3$, $–CCl_3$, $–CBr_3$, $–CI_3$, –COOH, $–CONH_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; wherein R^{19B} and R^{19C} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

n19 is 0, 1, 2, 3, or 4; and

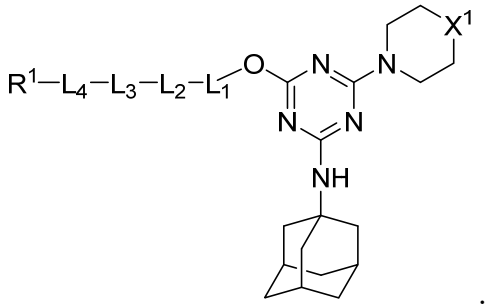
v19 is 1 or 2.

15. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 14, wherein the compound comprises the structure of Formula (IX-a-1):



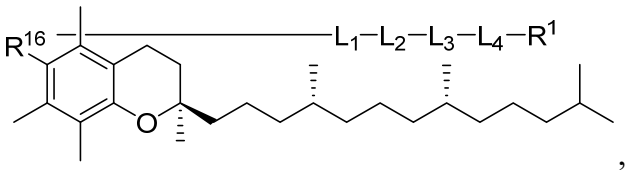
Formula (IX-a-1)

or the structure of Formula (IX-a-2):



Formula (IX-a-2)

16. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 9, comprising the structure of Formula (X):



,

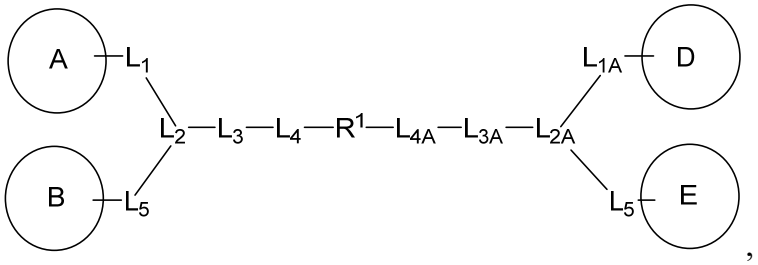
Formula (X)

wherein:

R^{16} is hydrogen, halogen, –CN, $–N_3$, $–NO_2$, $–NR^{16B}R^{16C}$, $–C(O)R^{16D}$, $–C(O)OR^{16D}$, $–C(O)NR^{16B}R^{16C}$, $–OR^{16A}$, $-NR^{16B}C(O)R^{16D}$, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl; and

R^{16A}, R^{16B}, R^{16C}, and R^{16D} are each independently hydrogen, halogen, $–CF_3$, $–CCl_3$, $–CBr_3$, $–CI_3$, –COOH, $–CONH_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; wherein R^{16B} and R^{16C} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl.

17. A compound, or a stereoisomer, tautomer, prodrug, or salt thereof, comprising the structure of Formula (IV'), or a salt thereof:



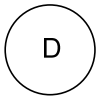
,

Formula (IV')

wherein:

each of 

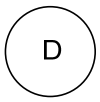
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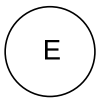
, 

, and 

is independently a ligand or a lipid, wherein at least one of 

, 

, 

and 

is a cannabinoid receptor type 1 (CB_1) ligand;

each of L_1 and L_2 is independently a linker or a bond;

each of L_3, L_4, L_5, L_{1A}, L_{2A}, L_{A3}, L_{A4}, and L_{A5} is independently a linker, a bond, or absent; and

R^1 comprises one or more oligonucleotides, protecting groups, small molecules, proteins, antibodies, and/or peptides.

18. The compound, or a stereoisomer, tautomer, prodrug, or salt thereof, of claim 2, wherein the CB1 ligand is conjugated to the oligonucleotide at an internucleoside linkage.

19. A composition comprising a compound, or a salt thereof, of any one of claims 1-18, and a pharmaceutically acceptable excipient.

20. Use of the compound, or a salt thereof, of any one of claims 1-18, or the composition of claim 19 in the manufacture of a medicament for treating or ameliorating a central nervous system (CNS) disease, disorder, or symptom thereof.

21. The use of claim 20, wherein the disease, disorder, or symptom thereof is Alzheimer's disease, or a symptom thereof.