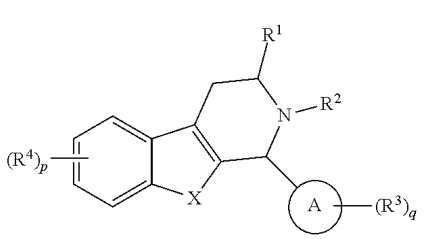
What is claimed is:

1. A compound of formula (I):



(I)

or a tautomer, stereoisomer, mixture of stereoisomers, isotopically enriched analog, or pharmaceutically acceptable salt thereof, wherein:

ring A is C_4-C_{10}cycloalkyl, heterocyclyl, aryl, or heteroaryl;

X is NR^5, O, or S;

p is 0, 1, 2, or 3;

q is 0, 1, 2, or 3;

R^1 is C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6haloalkyl, C_3-C_{10}cycloalkyl, —CN, —OH, —$C(O)OR^6$, —$C(O)N(R^7)_2$, —$OC(O)R^6$, —$S(O)_2R^8$, —$S(O)_2N(R^7)_2$, —$S(O)N(R^7)_2$, —$S(O)R^8$, —NH_2, —NHR^8, —$N(R^8)_2$, —NO_2, —OR^8, —C_1-C_6alkyl-OH, —C_1-C_6alkyl-OR^8, or —$Si(R^{15})_3$;

R^2 is —$C(O)R^9$;

each R^3 is independently halo, —CN, —OH, —OR^8, —NH_2, —NHR^8, —$N(R)_2$, —$S(O)_2R^8$, —$S(O)R^8$, —$S(O)_2N(R^7)_2$, —$S(O)N(R^7)_2$, —NO_2, —$Si(R^{12})_3$, —SF_5, —$C(O)OR^6$, —$C(O)N(R^7)_2$, —$NR^{12}C(O)R^8$, —$NR^{12}C(O)OR^8$, —$OC(O)N(R^7)_2$, —$OC(O)R^8$, —$C(O)R^6$, —$OC(O)CHR^8N(R^{12})_2$, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, heteroaryl, —C_1-C_6alkylC_3-C_{10}cycloalkyl, —C_2-C_6alkenylC_3-C_{10}cycloalkyl, —C_1-C_6alkylheterocyclyl, —C_2-C_6alkenylheterocyclyl, —C_1-C_6alkylaryl, —C_2-C_6alkenylaryl, C_1-C_6alkylheteroaryl, or —C_2-C_6alkenylheteroaryl, wherein each C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, heteroaryl, —C_1-C_6alkylC_3-C_{10}cycloalkyl, —C_2-C_6alkenylC_3-C_{10}cycloalkyl, —C_1-C_6alkylheterocyclyl, —C_2-C_6alkenylheterocyclyl, —C_1-C_6alkylaryl, —C_2-C_6alkenylaryl, C_1-C_6alkylheteroaryl, or —C_2-C_6alkenylheteroaryl of R^3 is independently optionally substituted with one to three R^{10};

each R^4 is independently halo, —CN, —OH, —OR^8, —NH_2, —NHR^8, —$N(R)_2$, —$S(O)_2R^8$, —$S(O)R^8$, —$S(O)_2N(R^7)_2$, —$S(O)N(R^7)_2$, —NO_2, —$Si(R^{15})_3$, —$C(O)OR^6$, —$C(O)N(R^7)_2$, —$NR^{12}C(O)R^8$, —$OC(O)R^8$, —$C(O)R^6$, —$NR^{12}C(O)OR^8$, —$OC(O)N(R^7)_2$, —$OC(O)CHR^8N(R^{12})_2$, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, heteroaryl, —C_1-C_6alkylC_3-C_{10}cycloalkyl, —C_2-C_6alkenylC_3-C_{10}cycloalkyl, —C_1-C_6alkylheterocyclyl, —C_2-C_6alkenylheterocyclyl, —C_1-C_6alkylaryl, —C_2-C_6alkenylaryl, C_1-C_6alkylheteroaryl, or —C_2-C_6alkenylheteroaryl, wherein each C_1-C_6alkyl, C_2-C_6alkenyl, C_2-

C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, heteroaryl, —C_1-C_6alkylC_3-C_{10}cycloalkyl, —C_2-C_6alkenylC_3-C_{10}cycloalkyl, —C_1-C_6alkylheterocyclyl, —C_2-C_6alkenylheterocyclyl, —C_1-C_6alkylaryl, —C_2-C_6alkenylaryl, C_1-C_6alkylheteroaryl, or —C_2-C_6alkenylheteroaryl of R^4 is independently optionally substituted with one to three R^{10};

R^5 is hydrogen or C_1-C_6alkyl;

each R^6 is independently hydrogen, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, heteroaryl, —C_1-C_6alkylC_3-C_{10}cycloalkyl, —C_2-C_6alkenylC_3-C_{10}cycloalkyl, —C_1-C_6alkylheterocyclyl, —C_2-C_6alkenylheterocyclyl, —C_1-C_6alkylaryl, —C_2-C_6alkenylaryl, C_1-C_6alkylheteroaryl, or —C_2-C_6alkenylheteroaryl; wherein each R^6 is optionally independently further substituted with one to three R^{11};

each R^7 is independently hydrogen, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, heteroaryl, —C_1-C_6alkylC_3-C_6cycloalkyl, —C_2-C_6alkenylC_3-C_6cycloalkyl, —C_1-C_6alkylheterocyclyl, —C_2-C_6alkenylheterocyclyl, —C_1-C_6alkylaryl, —C_2-C_6alkenylaryl, —C_1-C_6alkylheteroaryl, or —C_2-C_6alkenylheteroaryl, or two R^7 together with the nitrogen atom to which they are attached form a 4- to 7- membered heterocyclyl, wherein each R^7 or ring formed thereby is optionally independently further substituted with one to three R^{11};

each R^8 is independently C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, heteroaryl, —C_1-C_6alkylC_3-C_{10}cycloalkyl, —C_2-C_6alkenylC_3-C_{10}cycloalkyl, —C_1-C_6alkylheterocyclyl, —C_2-C_6alkenylheterocyclyl, —C_1-C_6alkylaryl, —C_2-C_6alkenylaryl, —C_1-C_6alkylheteroaryl, or —C_2-C_6alkenylheteroaryl, wherein each R^8 is optionally independently further substituted with one to three R^{11};

R^9 is C_2alkynyl optionally substituted with one —CH_3;

each R^{10} is independently halo, —CN, —OR^{12}, —NO_2, —$N(R^{12})_2$, —$S(O)R^{13}$, —$S(O)_2R^{13}$, —$S(O)N(R^{12})_2$, —$S(O)_2N(R^{12})_2$, —$Si(R^{12})_3$, —$C(O)R^{12}$, —$C(O)OR^{12}$, —$C(O)N(R^{12})_2$, —$NR^{12}C(O)R^{12}$, —$OC(O)R^{12}$, —$OC(O)OR^{12}$, —$OC(O)N(R^{12})_2$, —$NR^{12}C(O)OR^{12}$, —$OC(O)CHR^{12}N(R^{12})_2$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each C_1-C_6alkyl, C_1-C_6haloalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, or heteroaryl of R^{10} is optionally independently substituted with one to three R^{11};

each R^{11} is independently halo, —CN, —OR^{12}, —NO_2, —$N(R^{12})_2$, —$S(O)R^{13}$, —$S(O)_2R^{13}$, —$S(O)N(R^{12})_2$, —$S(O)_2N(R^{12})_2$, —$Si(R^{12})_3$, —$C(O)R^{12}$, —$C(O)OR^{12}$, —$C(O)N(R^{12})_2$, —$NR^{12}C(O)R^{12}$, —$OC(O)R^{12}$, —$OC(O)OR^{12}$, —$OC(O)N(R^{12})_2$, —$NR^{12}C(O)OR^{12}$, —$OC(O)CHR^{12}N(R^{12})_2$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_{10}cycloalkyl, heterocyclyl, aryl, or heteroaryl;

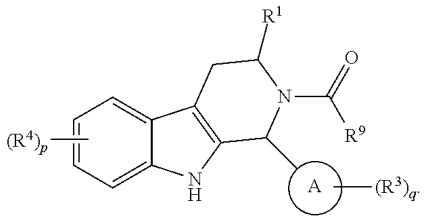
each R^{12} is independently hydrogen, C_1-C_6alkyl or C_3-C_{10}cycloalkyl;

each R^{13} is independently C_1-C_6alkyl, or C_3-C_{10}cycloalkyl; and

each R^{15} is independently C_1-C_6alkyl, C_2-C_6alkenyl, aryl, heteroaryl, arylC_1-C_6alkyl-, arylC_2-C_6alkenyl-, heteroarylC_1-C_6alkyl-, and heteroarylC_2-C_6alkenyl-.

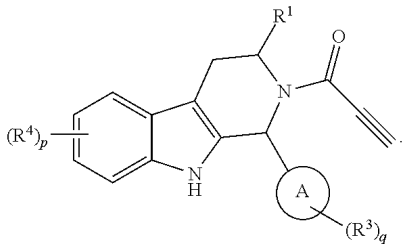
2. The compound of claim 1, or a tautomer, stereoisomer, mixture of stereoisomers, isotopically enriched analog, or pharmaceutically acceptable salt thereof, represented by formula (II):

(II)



3. The compound of claim 1, or a tautomer, stereoisomer, mixture of stereoisomers, isotopically enriched analog, or pharmaceutically acceptable salt thereof, represented by formula (III):

(III)



4. The compound of claim 1, wherein ring A is C_4-C_{10}cycloalkyl.

5. The compound of claim 1, wherein ring A is heterocyclyl.

6. The compound of claim 1, wherein ring A is aryl.

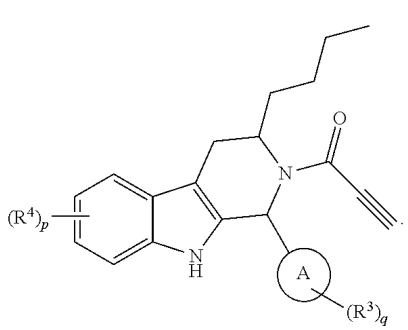
7. The compound of claim 1, wherein ring A is heteroaryl.

8. The compound of claim 1, wherein R^1 is C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6haloalkyl, C_3-C_{10}cycloalkyl, —CN, —C(O)OR^6, —C(O)$N(R^7)_2$, —NH_2, —NHR^8, —$N(R^8)_2$, —OH, —OR^8, —C_1-C_6alkyl-OH, or —C_1-C_6alkyl-OR^8.

9. The compound of claim 1, wherein R^1 is C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6haloalkyl, C_3-C_{10}cycloalkyl, —NH_2, —NHR^8, —$N(R^8)_2$, —OH, —OR^8, —C_1-C_6alkyl-OH, or —C_1-C_6alkyl-OR^8.

10. The compound of claim 1, wherein R^1 is C_1-C_6alkyl.

11. The compound of claim 1, or a tautomer, stereoisomer, mixture of stereoisomers, isotopically enriched analog, or pharmaceutically acceptable salt thereof, represented by formula (IV):



12. The compound of claim 1, wherein each R^4 is independently halo, —CN, —OH, —OR^8, —NH_2, —NHR^8, —$N(R)_2$, —$S(O)_2R^8$, —$S(O)R^8$, —$S(O)_2N(R^7)_2$, —$S(O)N(R^7)_2$, —NO_2, —$Si(R^{15})_3$, —$C(O)OR^6$, —$C(O)N(R^7)_2$, —$NR^{12}C(O)R^8$, —$OC(O)R^8$, —$C(O)R^6$, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, or C_3-C_{10}cycloalkyl, wherein each C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, or C_3-C_{10}cycloalkyl of R^4 is independently optionally substituted with one to three R^{10}.

13. The compound of claim 1, wherein each R^4 is independently halo, —CN, —OH, —OR^8, C_1-C_6alkyl, C_2-C_6alkynyl, or C_3-C_{10}cycloalkyl, wherein each C_1-C_6alkyl, C_2-C_6alkynyl, or C_3-C_{10}cycloalkyl of R^4 is independently optionally substituted with one to three R^{10}.

14. The compound of claim 1, wherein p is 0.

15. The compound of claim 1, wherein q is 0.

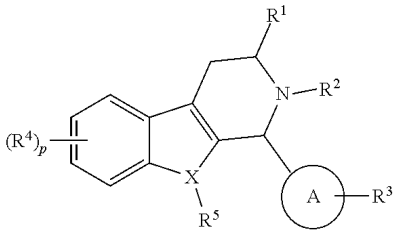
16. The compound of claim 1, wherein p is 1, 2, or 3.

17. The compound of claim 1, wherein q is 2 or 3.

18. A pharmaceutical composition comprising a compound, or a tautomer, stereoisomer, mixture of stereoisomers, isotopically enriched analog, or pharmaceutically acceptable salt thereof, of claim 1, and a pharmaceutically acceptable carrier.

19. A compound of formula (V):

(V)



or an enantiomer or pharmaceutically acceptable salt thereof, wherein:

X is N, O, or S;

A is a 4- to 7-membered cycloalkyl, 4- to 7-membered heterocyclyl, aryl, heteroaryl, or bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^1 is H, C_1—C_6alkyl, —C_1—C_6alkylhalo, —C(O)OR^6, —C(O)$N(R^7)_2$, —OC(O)R^6, —SO_2R^8, —SOR^8, NO_2, —OR^8, —C_1—C_6alkyl—OR^{12}, or —$Si(R^{15})_3$;

R^2 is —C(O)R^9;

R^3 is H, halo, —C(O)OR^{10}, —C(O)$N(R^{11})_2$, —OC(O)R^{10}, —C_0—C_6alkylC_3—C_8cycloalkyl, —C_0-C_6alkylheterocyclyl, —$N(R^{11})_2$, —SO_2R^8, —SOR^8, —NO_2, or —$Si(R^{15})_3$;

R^4 is independently halo, CN, —NH_2, —SO_2, C_1—C_8alkyl, —OR^{12},—C_1—C_6alkyl-OR^{12}, —C_1—C_6alkyl—NR^{12}, or —OC(O)R^{12};

R^5 is H, C_1—C_6alkyl, or is absent when X is S or O;

p is 0, 1, 2, or 3;

each R^6 is independently C_1—C_6alkyl, C_3—C_6alkyl, C_2—C_6alkynyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, $(R^{11})_2NC_1$—C_6alkyl—, or $(R^{11})_2NC_2$—C_6alkenyl-;

each R^7 is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O$—C_1—C_6alkyl-, or $R^{12}O(O)C$—C_1—C_6alkyl-, or two R^7 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^7 groups is optionally substituted with OH, halo, C_1—C_6alkyl, a 4- to 6-membered heterocyclyl, or $(R^{11})_2N$-, wherein the 4- to 6-membered heterocyclyl when containing 2 or more N atoms is optionally substituted with an N-protecting group;

each R^8 is independently C_1—C_6alkyl, C_3—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—

C_6cycloalkylC_2–C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, or $(R^{11})_2N$-;

R^9 is C_2alkynyl;

R^{10} is C_1—C_6alkyl, C_2—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{13}(NH_2)CH$-, $R^{14}C_0$—C_6alkyl-, or $(R^{15})_3SiC_0$—C_6alkyl-;

each R^{11} is independently H, C_1—C_6alkyl, C_2C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1–C_6aliphatic-, $R^{12}O$—C_1—C_6alkyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O(O)C$—C_1—C_6alkyl—, $R^{13}(NH_2)CH$—, $R^{14}C_0$—C_6alkyl—, $(R^{15})_3SiC_0$—C_6alkyl-, or an N-protecting group, or two R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^{11} groups has optionally 0, 1, or 2 additional heteroatoms selected from nitrogen, oxygen, and sulfur, and the heterocyclyl is optionally substituted with OH, halo, C_1C_6alkyl, C_1—C_6alkyl-O(O)C—, $(R^{11})_2N$—, or a 4- to 6-membered heterocyclyl, wherein the 4- to 6-membered heterocyclyl is optionally substituted with OH, halo, —NH_2, or C_1—C_6alkyl, or when containing 2 or more N atoms is optionally substituted with an N- protecting group;

each R^{12} is independently H or C_1—C_6alkyl;

each R^{13} is independently H, C_1—C_6alkyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, or an N protecting group;

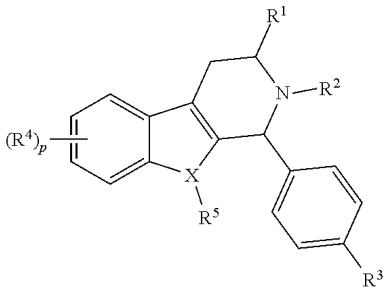
R^{14} is a bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

each R^{15} is independently C_1—C_6alkyl, C_2—C_6alkenyl, aryl, heteroaryl, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, or heteroarylC_2—C_6alkenyl-;

wherein each C_1—C_6alkyl, —C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, or bridged bicyclic ring, by itself or attached to another moiety, are independently optionally substituted with 1-3 substituents selected from the group consisting of OH, halo, —NH_2, C_1—C_6alkyl, C_1—C_6alkyl—O—, $R^{12}O$—C_1—C_6alkyl(O)C—, and $R^{12}O(O)C$—.

20. The compound of claim 19, having the structure formula (Va):

(Va)



or an enantiomer or pharmaceutically acceptable salt thereof,

wherein:

X is N, O, or S;

R^1 is C_1—C_6alkyl, —C_1—C_6alkylhalo, —C(O)OR^6, —C(O)N(R^7)$_2$, —OC(O)R^6, —SO_2R^8, —SOR^8, NO_2, —OR^8, —C_1—C_6alkyl—OR^{12}, or —Si(R^{15})$_3$;

R^2 is —C(O)R^9;

R^3 is —C(O)OR^{10}, —C(O)N(R^{11})$_2$, —OC(O)R^{10}, —C_0—C_6alkylC_3—C_8cycloalkyl, —C_0—C_6alkylheterocyclyl, —N(R^{11})$_2$, —SO_2R^8, —SOR^8, —NO_2, or —Si(R^{15})$_3$;

R^4 is independently halo, CN, —NH_2, —SO_2, C_1—C_8alkyl, —$OR^{12,}$ —C_1—C_6alkyl—OR^{12}, —C_1—C_6alkyl—NR^{12}, or —OC(O)R^{12};

R^5 is H, C_1—C_6alkyl, or is absent when X is S or O;

p is 0, 1, 2, or 3;

each R^6 is independently C_1—C_6alkyl, C_3—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2-C_6alkenyl-, (R^{11})$_2$NC_1—C_6alkyl-, or (R^{11})$_2$NC_2—C_6alkenyl-;

each R^7 is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, (R^{11})$_2$NC_1—C_6alkyl-, (R^{11})$_2$NC_2—C_6alkenyl-, R^{12}O—C_1—C_6alkyl-, or R^{12}O(O)C—C_1—C_6alkyl-, or two R^7 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^7 groups is optionally substituted with OH, halo, C_1—C_6alkyl, a 4- to 6-membered heterocyclyl, or (R^{11})$_2$N—, wherein the 4- to 6-membered heterocyclyl when containing 2 or more N atoms is optionally substituted with an N-protecting group;

each R^8 is independently C_1—C_6alkyl, C_3—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—

C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, or $(R^{11})_2N$-;

R^9 is C_2alkynyl;

R^{10} is C_1—C_6alkyl, C_2—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{13}(NH_2)CH$-, $R^{14}C_0$–C_6alkyl-, or $(R^{15})_3Si$ C_0—C_6alkyl-;

each R^{11} is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $R^{12}O$—C_1—C_6alkyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O(O)C$—C_1—C_6alkyl- , $R^{13}(NH_2)CH$—, $R^{14}C_0$—C_6alkyl-, $(R^{15})_3SiC_0$—C_6alkyl-, or an N-protecting group, or two R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^{11} groups has optionally 0, 1, or 2 additional heteroatoms selected from nitrogen, oxygen, and sulfur, and the heterocyclyl is optionally substituted with OH, halo, C_1—C_6alkyl, C_1—C_6alkyl—O(O)C-, $(R^{11})_2N$-, or a 4- to 6-membered heterocyclyl, wherein the 4- to 6-membered heterocyclyl is optionally substituted with OH, halo, —NH_2, or C_1—C_6alkyl, or when containing 2 or more N atoms is optionally substituted with an N-protecting group;

each R^{12} is independently H or C_1—C_6alkyl;

each R^{13} is independently H, C_1—C_6alkyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, or an N protecting group;

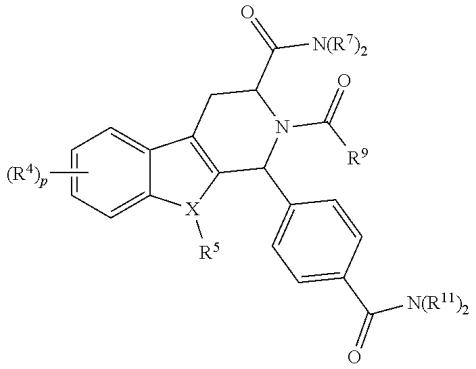
R^{14} is a bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

each R^{15} is independently C_1—C_6alkyl, C_2—C_6alkenyl, aryl heteroaryl, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, or heteroarylC_2—C_6alkenyl-;

wherein each C_1—C_6alkyl, —C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, or bridged bicyclic ring, by itself or attached to another moiety, are independently optionally substituted with 1-3 substituents selected from the group consisting of OH, halo, —NH_2, C_1—C_6alkyl, C_1—C_6alkyl—O—, $R^{12}O$—C_1—C_6alkyl(O)C—, and $R^{12}O(O)C$—.

21. The compound of claim 19, having a structure of formula (Vg):

(Vg)



or an enantiomer or pharmaceutically acceptable salt thereof, wherein:

X is N, O, or S;

R^4 is independently halo, CN, —NH_2, —SO_2, C_1—C_8alkyl, —$OR^{12,}$ —C_1—C_6alkyl-OR^{12}, —C_1—C_6alkyl-NR^{12}, or —$OC(O)R^{12}$;

R^5 is H, C_1—C_6alkyl, or is absent when X is S or O;

p is 0, 1, 2, or 3;

each R^7 is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O$—C_1—C_6alkyl-, or $R^{12}O(O)C$—C_1—C_6alkyl-, or two R^7 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^7 groups is optionally substituted with OH, halo, C_1—C_6alkyl, a 4- to 6-membered heterocyclyl, or $(R^{11})_2N$—, wherein the 4- to 6-membered heterocyclyl when containing 2 or more N atoms is optionally substituted with an N-protecting group;

R^9 is C_2alkynyl;

each R^{11} is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $R^{12}O$—C_1—C_6alkyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O(O)C$—C_1—C_6alkyl- , $R^{13}(NH_2)CH$—, $R^{14}C_0$—C_6alkyl-, $(R^{15})_3SiC_0$—C_6alkyl-, or an N-protecting group, or two R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^{11} groups has optionally 0, 1, or 2 additional heteroatoms selected from nitrogen, oxygen, and sulfur, and the heterocyclyl is optionally substituted with OH, halo, C_1—C_6alkyl, C_1—C_6alkyl—O(O)C—, $(R^{11})_2N$—, or a 4- to 6-membered heterocyclyl, wherein the 4- to 6-membered heterocyclyl is optionally

substituted with OH, halo, —NH_2, or C_1—C_6alkyl, or when containing 2 or more N atoms is optionally substituted with an N-protecting group;

each R^{12} is independently H or C_1—C_6alkyl;

each R^{13} is independently H, C_1—C_6alkyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, or an N protecting group;

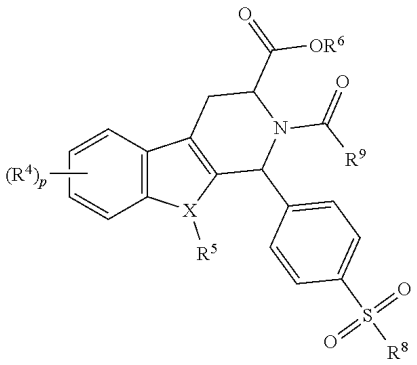
R^{14} is a bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

R^{15} is independently C_1—C_6alkyl, C_2—C_6alkenyl, aryl, heteroaryl, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, or heteroarylC_2—C_6alkenyl-;

wherein each C_1—C_6alkyl, —C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, or bridged bicyclic ring, by itself or attached to another moiety, are independently optionally substituted with 1-3 substituents selected from the group consisting of OH, halo, —NH_2, C_1—C_6alkyl, C_1—C_6alkyl—O—, R^{12}O—C_1—C_6alkyl(O)C—, and R^{12}O(O)C—.

22. The compound of claim 19, having as structure of formula (Vi):

(Vi)



or an enantiomer or pharmaceutically acceptable salt thereof, wherein:

X is N, O, or S;

R^4 is independently halo, CN, —NH_2, —SO_2, C_1—C_8alkyl, —$OR^{12,}$ —C_1—C_6alkyl-OR^{12}, —C_1—C_6alkyl-NR^{12}, or —OC(O)R^{12};

R^5 is H, C_1—C_6alkyl, or is absent when X is S or O;

p is 0, 1, 2, or 3;

R^6 is independently C_1—C_6alkyl, C_3—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, $(R^{11})_2NC_1$—C_6alkyl-, or $(R^{11})_2NC_2$—C_6alkenyl-;

R^8 is independently C_1—C_6alkyl, C_3—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, or $(R^{11})_2N$—;

R^9 is C_2alkynyl;

each R^{11} is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $R^{12}O$—C_1—C_6alkyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O(O)C$—C_1—C_6alkyl- , $R^{13}(NH_2)CH$—, $R^{14}C_0$—C_6alkyl-, $(R^{15})_3SiC_0$—C_6alkyl-, or an N-protecting group, or two R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^{11} groups has optionally 0, 1, or 2 additional heteroatoms selected from nitrogen, oxygen, and sulfur, and the heterocyclyl is optionally substituted with OH, halo, C_1—C_6alkyl, C_1—C_6alkyl-O(O)C—, $(R^{11})_2N$—, or a 4- to 6-membered heterocyclyl, wherein the 4- to 6-membered heterocyclyl is optionally substituted with OH, halo, —NH_2, or C_1—C_6alkyl, or when containing 2 or more N atoms is optionally substituted with an N-protecting group;

each R^{12} is independently H or C_1—C_6alkyl;

each R^{13} is independently H, C_1—C_6alkyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, or an N protecting group;

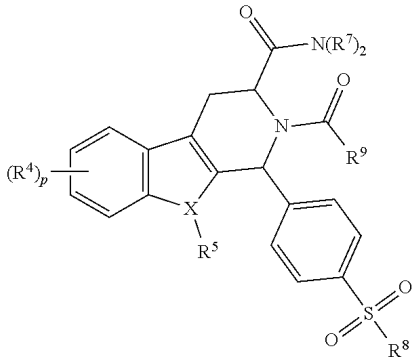
R^{14} is a bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

R^{15} is independently C_1—C_6alkyl, C_2—C_6alkenyl, aryl, heteroaryl, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, or heteroarylC_2—C_6alkenyl-;

wherein each C_1—C_6alkyl, —C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, or bridged bicyclic ring, by itself or attached to another moiety, are independently optionally substituted with 1-3 substituents selected from the group consisting of OH, halo, —NH_2, C_1—C_6alkyl, C_1—C_6alkyl—O—, $R^{12}O$—C_1—C_6alkyl(O)C—, and $R^{12}O(O)C$—.

23. The compound of claim 19, having a structure of formula (Vj):

(Vj)



or an enantiomer or pharmaceutically acceptable salt thereof, wherein:

X is N, O, or S;

R^4 is independently halo, CN, —NH_2, —SO_2, C_1—C_8alkyl, —$OR^{12,}$ —C_1—C_6alkyl-OR^{12}, —C_1—C_6alkyl-NR^{12}, or —$OC(O)R^{12}$;

R^5 is H, C_1—C_6alkyl, or is absent when X is S or O;

P is 0, 1, 2, or 3;

each R^7 is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O$—C_1—C_6alkyl-, or $R^{12}O(O)C$—C_1—C_6alkyl-, or two R^7 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^7 groups is optionally substituted with OH, halo, C_1—C_6alkyl, a 4- to 6-membered heterocyclyl, or $(R^{11})_2N$—, wherein the 4- to 6-membered heterocyclyl when containing 2 or more N atoms is optionally substituted with an N-protecting group;

R^8 is independently C_1—C_6alkyl, C_3—C_6, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, or $(R^{11})_2N$-;

R^9 is C_2alkynyl;

each R^{11} is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $R^{12}O$—C_1—C_6alkyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O(O)C$—C_1—C_6alkyl- , $R^{13}(NH_2)CH$—, $R^{14}C_0$—C_6alkyl-, $(R^{15})_3SiC_0$—C_6alkyl-, or an N-protecting group, or two R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^{11} groups has optionally 0, 1, or 2

additional heteroatoms selected from nitrogen oxygen, and sulfur, and the heterocyclyl is optionally substituted with OH, halo, C_1—C_6alkyl, C_1—C_6alkyl-O(O)C—, $(R^{11})_2N$—, or a 4- to 6-membered heterocyclyl, wherein the 4- to 6-membered heterocyclyl is optionally substituted with OH, halo, —NH_2, or C_1—C_6alkyl, or when containing 2 or more N atoms is optionally substituted with an N-protecting group;

each R^{12} is independently H or C_1—C_6alkyl;

each R^{13} is independently H, C_1—C_6alkyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl—, adamantyl, adamantylC_1—C_6aliphatic-, or an N protecting group;

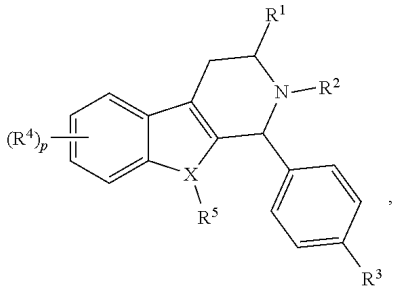
R^{14} is a bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

each R^{15} is independently C_1—C_6alkyl, C_2—C_6alkenyl, aryl, heteroaryl, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, or heteroarylC_2—C_6alkenyl-;

wherein each C_1—C_6alkyl, —C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, or bridged bicyclic ring, by itself or attached to another moiety, are independently optionally substituted with 1-3 substituents selected from the group consisting of OH, halo, —NH_2, C_1—C_6alkyl, C_1—C_6alkyl-O—, $R^{12}O$—C_1—C_6alkyl(O)C—, and $R^{12}O(O)C$—.

24. The compound of claim 19, having a structure of formula (Vn):

(Vn)



or an enantiomer or pharmaceutically acceptable salt thereof, wherein:

X is N, O, or S;

R^1 is C_1—C_6alkyl, —C_1—C_6alkylhalo, or —C_1—C_6alkyl-OR^{12};

R^2 is —$C(O)R^9$;

R^3 is —$C(O)OR^{10}$, —$C(O)N(R^{11})_2$, —$OC(O)R^{10}$, —C_0—C_6alkylC_3—C_8cycloalkyl, —C_0—C_6alkylheterocyclyl, —$N(R^{11})_2$, —SO_2R^8, —SOR^8, —NO_2, or —$Si(R^{15})_3$;

R^4 is independently halo, CN, —NH_2, —NH_2, —SO_2, C_1—C_8alkyl, —OR^{12}, —C_1—C_6alkyl-OR^{12}, —C_1—C_6alkyl-NR^{12}, or —$OC(O)R^{12}$;

R^5 is H, C_1—C_6alkyl, or is absent when X is S or O;

p is 0, 1, 2, or 3;

R^8 is independently C_1—C_6alkyl, C_3—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2N$—, or $R^{14}C_0$—C_6alkyl-;

R^9 is C_2alkynyl;

R^{10} is C_1—C_6alkyl, C_2—C_6alkyl, C_2—C_6alkenyl, C_2—C_6alkynyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{13}(NH_2)CH$—, $R^{14}C_0$—C_6alkyl-, or $(R^{15})_3SiC_0$—C_6alkyl-;

each R^{11} is independently H, C_1—C_6alkyl, C_2—C_6alkenyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, C_3—C_6cycloalkylC_1—C_6alkyl-, C_3—C_6cycloalkylC_3—C_6cycloalkylC_2—C_6alkenyl-, heterocyclylC_1—C_6alkyl-, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, $R^{12}O$—C_1—C_6alkyl-, $(R^{11})_2NC_1$—C_6alkyl-, $(R^{11})_2NC_2$—C_6alkenyl-, $R^{12}O(O)C$—C_1—C_6alkyl- , $R^{13}(NH_2)CH$—, $R^{14}C_0$—C_6alkyl-, $(R^{15})_3SiC_0$—C_6alkyl-, or an N-protecting group, or two R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclyl, wherein the heterocyclyl formed by the two R^{11} groups has optionally 0, 1, or 2 additional heteroatoms selected from nitrogen, oxygen, and sulfur, and the heterocyclyl is optionally substituted with OH, halo, C_1—C_6alkyl, C_1—C_6alkyl-O(O)C—, $(R^{11})_2N$—, or a 4- to 6-membered heterocyclyl, wherein the 4- to 6-membered heterocyclyl is optionally substituted with OH, halo, —NH_2, or C_1—C_6alkyl, or when containing 2 or more N atoms is optionally substituted with an N-protecting group;

each R^{12} is independently H or C_1—C_6alkyl;

each R^{13} is independently H, C $_3$—C_6alkyl, C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, heterocyclylC_2—C_6alkenyl-, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, heteroarylC_2—C_6alkenyl-, adamantyl, adamantylC_1—C_6aliphatic-, or an N protecting group;

R^{14} is a bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

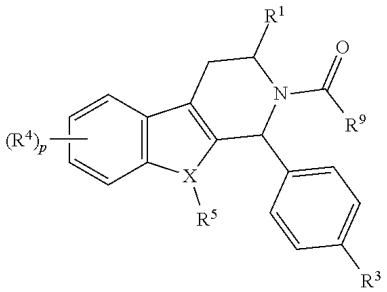
each R^{15} is independently C_1—C_6alkyl, C_2—C_6alkenyl, aryl, heteroaryl, arylC_1—C_6alkyl-, arylC_2—C_6alkenyl-, heteroarylC_1—C_6alkyl-, or heteroarylC_2—C_6alkenyl-;

wherein each C_1—C_6alkyl, —C_3—C_6cycloalkyl, heterocyclyl, aryl, heteroaryl, or bridged bicyclic ring, by itself or attached to another moiety, are independently optionally

substituted with 1-3 substituents selected from the group consisting of OH, halo, —NH_2, C_1—C_6alkyl, C_1—C_6alkyl-O—, $R^{12}O$—C_1—C_6alkyl(O)C—, and $R^{12}O(O)C$—.

25. The compound of claim 19, having a structure of formula (Vp):

(Vp)



or an enantiomer or pharmaceutically acceptable salt thereof, wherein:

X is N, O, or S;

R^1 is C_1—C_6alkyl, —C_1—C_6alkylhalo, or —C_1—C_6alkyl-OR^{12};

R^3 is —C_0—C_6alkylC_3—C_8cycloalkyl, or —C_0—C_6alkylheterocyclyl;

R^4 is independently halo, CN, —NH_2 , —SO_2, C_1—C_8alkyl, —$OR^{12,}$ —C_1—C_6alkyl-OR^{12}, —C_1—C_6alkyl-NR^{12}, or —$OC(O)R^{12}$;

R^5 is H, C_1—C_6alkyl, or is absent when X is S or O;

0, 1, 2, or 3;

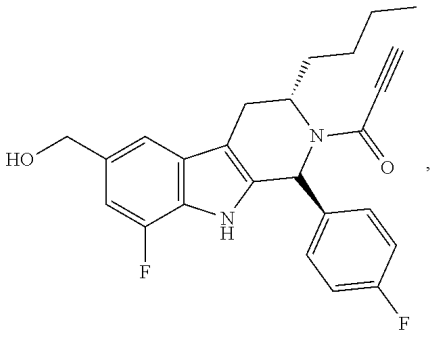
R^9 is C_2alkynyl;

R^{12} independently H or C_1—C_6alkyl;

wherein each C_0—C_6alkyl or —C_3—C_8cycloalkyl are independently optionally substituted with 1-3 substituents selected from the group consisting of OH, halo, —NH_2, C_1—C_6alkyl, C_1—C_6alkyl-O—, $R^{12}O$—C_1—C_6alkyl(O)C—, and $R^{12}O(O)C$—.

26. A compound, or a tautomer, stereoisomer, mixture of stereoisomers, isotopically enriched analog, or pharmaceutically acceptable salt thereof, selected from:

Compound 134



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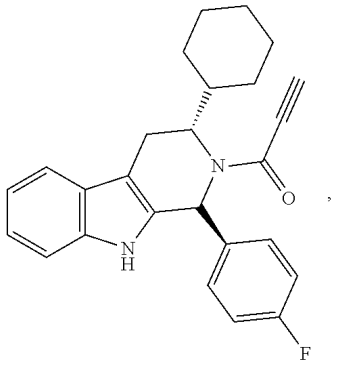

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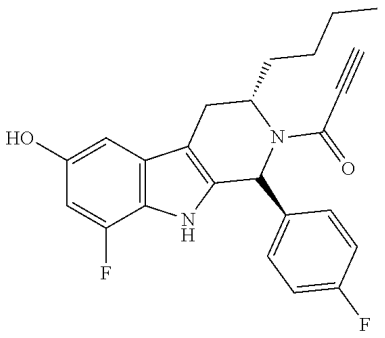

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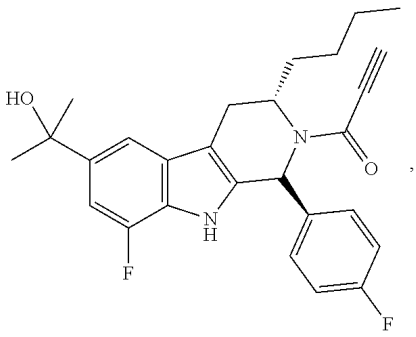

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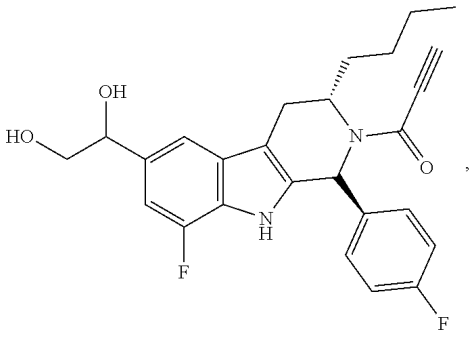
Compound 138



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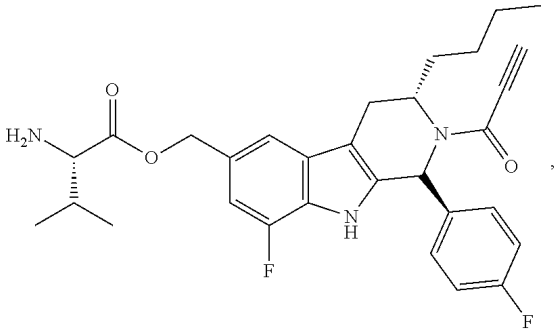

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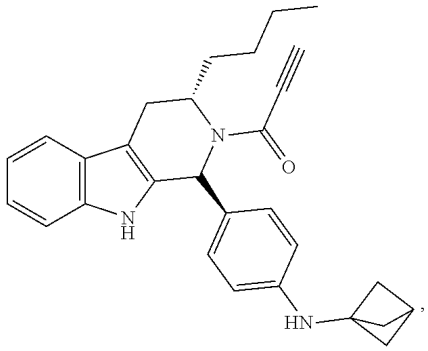

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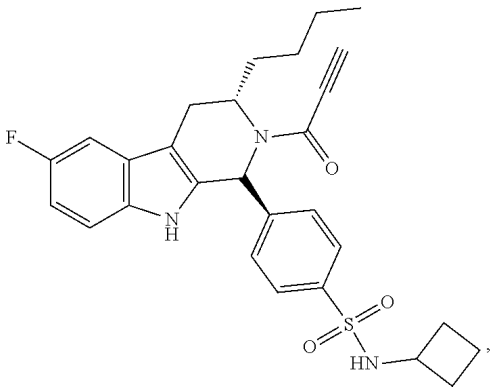
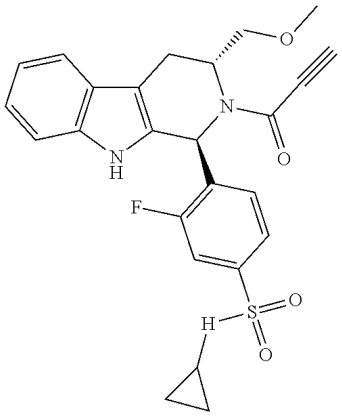


Compound 144



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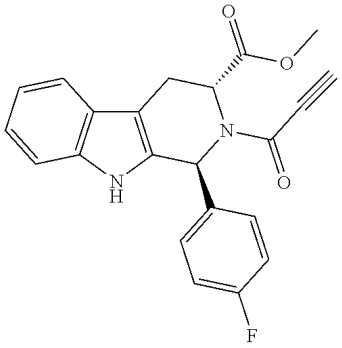

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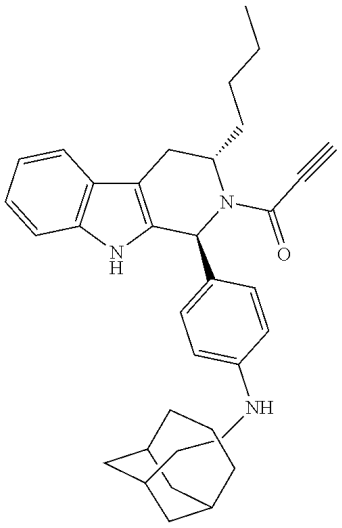

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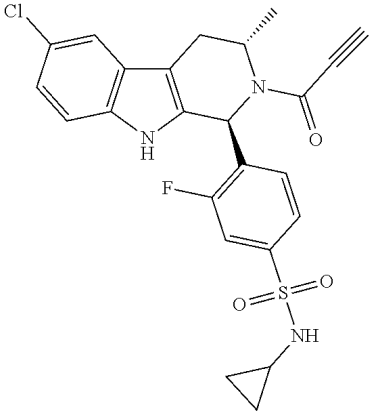

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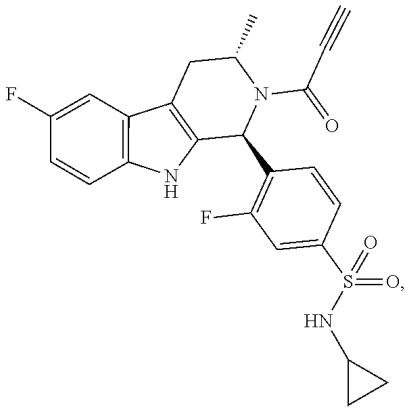

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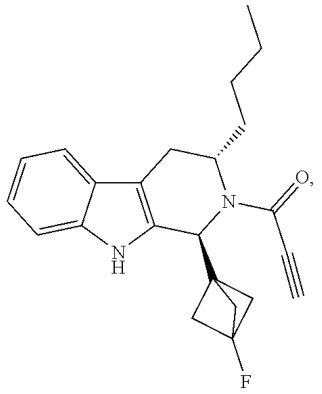

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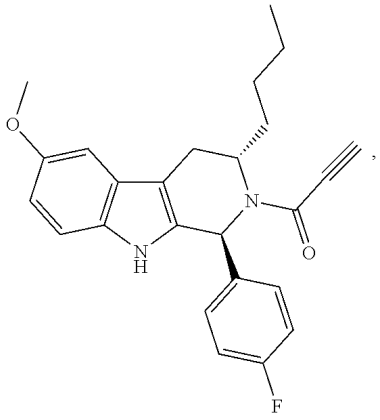

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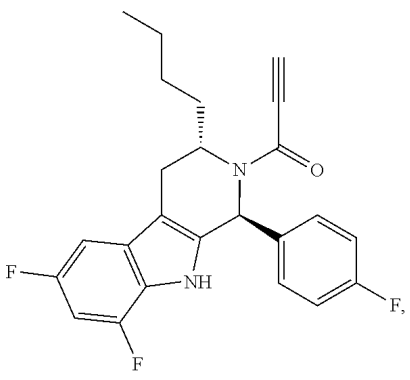

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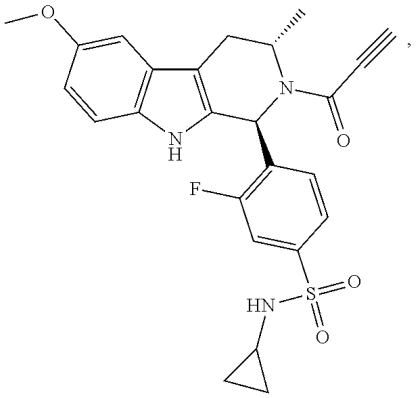

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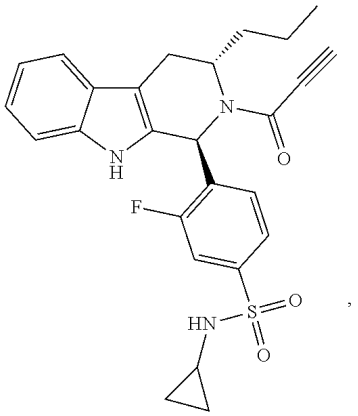

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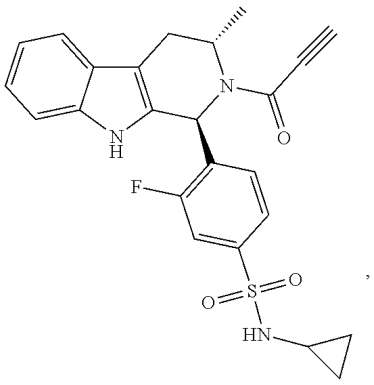

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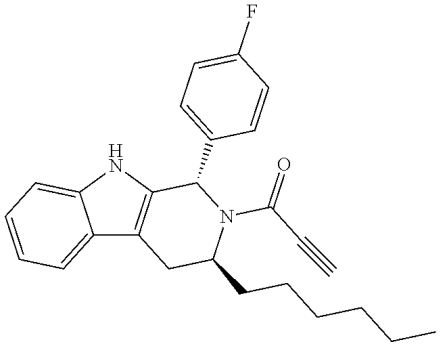

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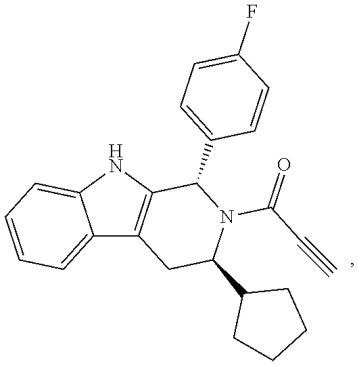

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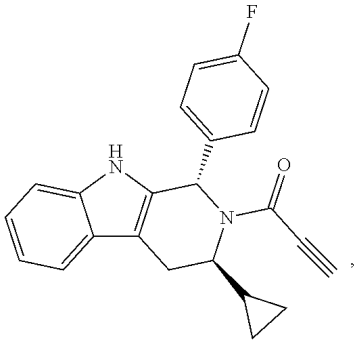

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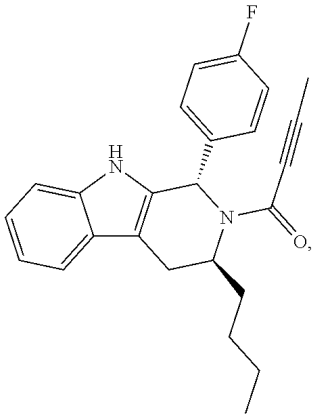

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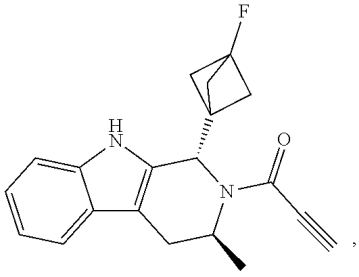

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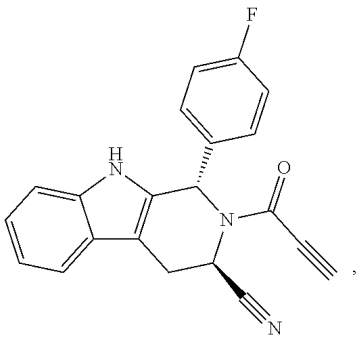

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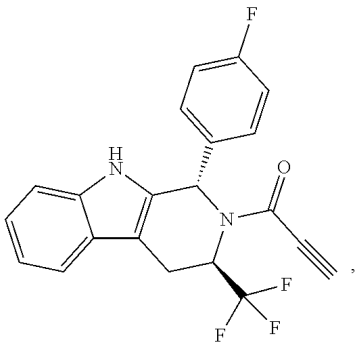

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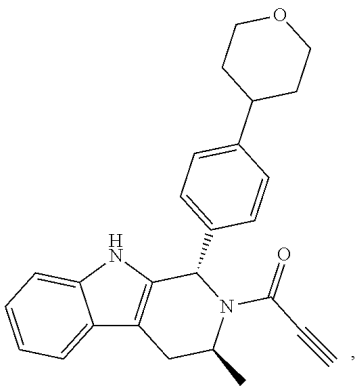

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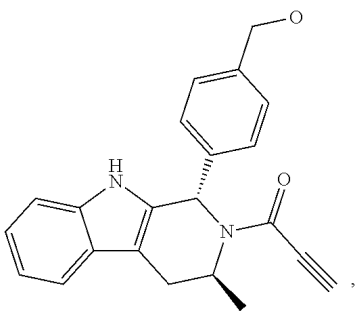

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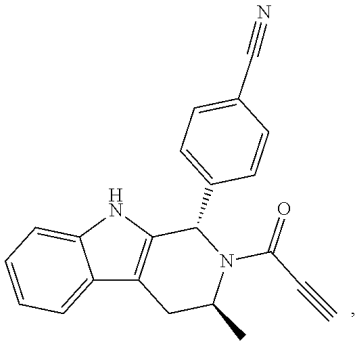

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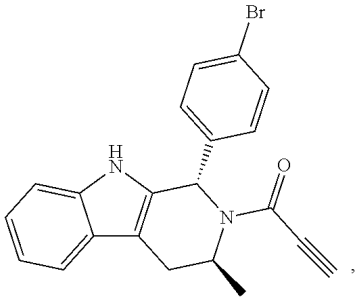

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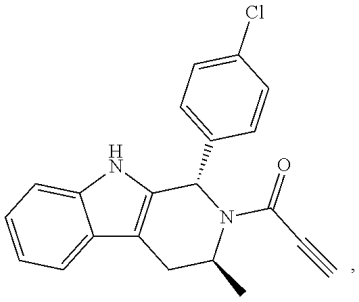

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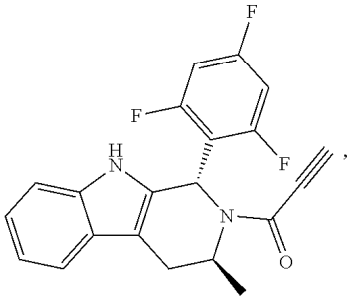

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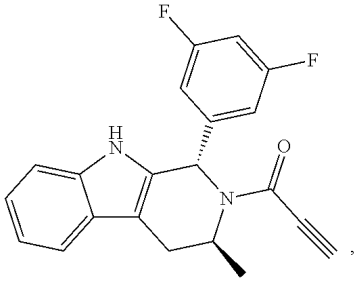

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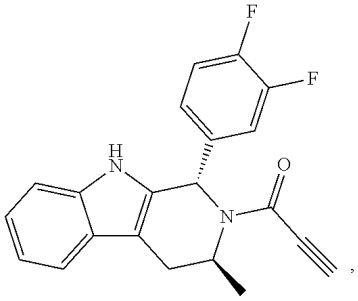

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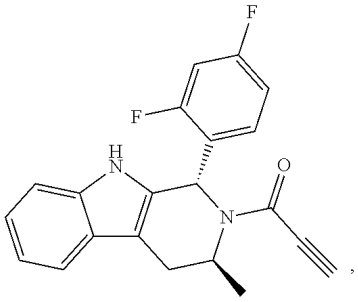

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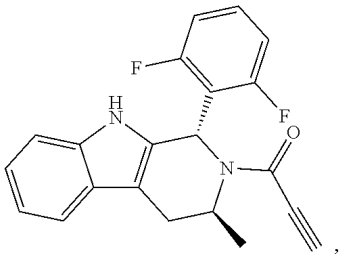

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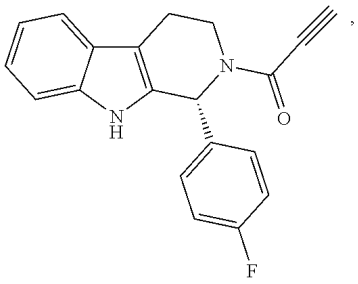

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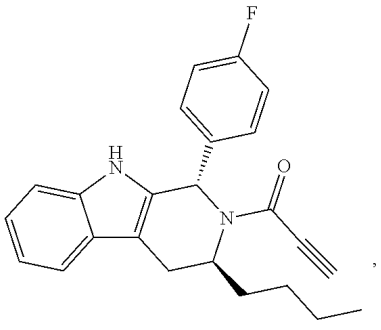

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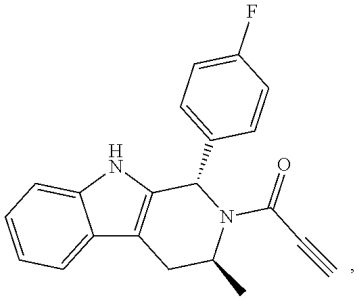

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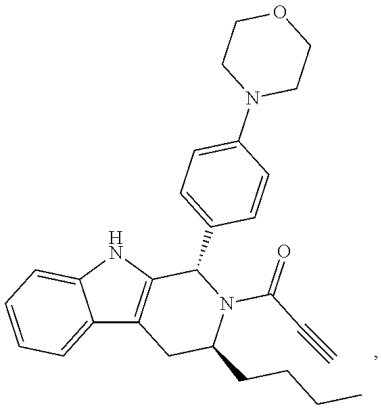

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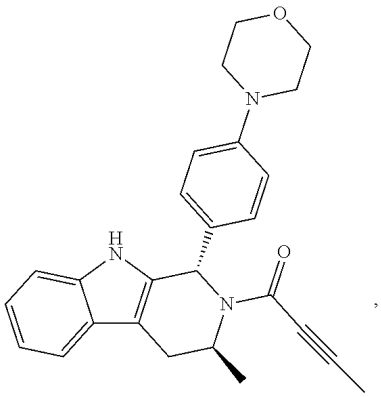

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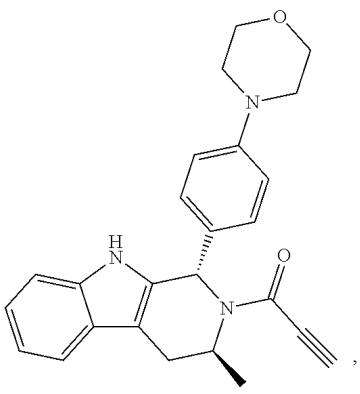

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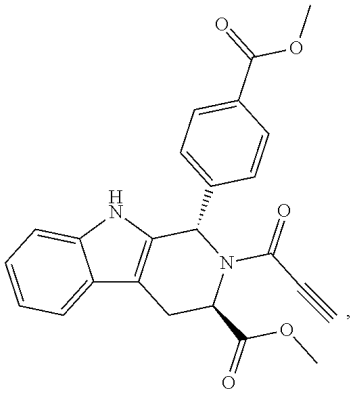

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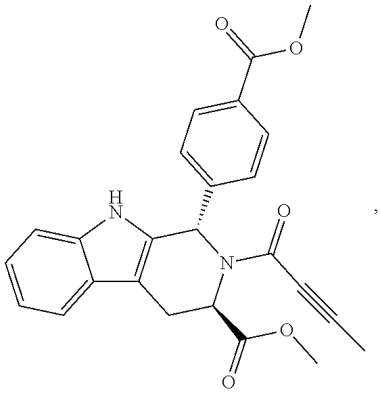

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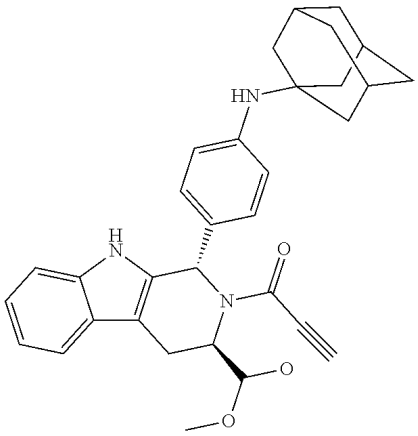
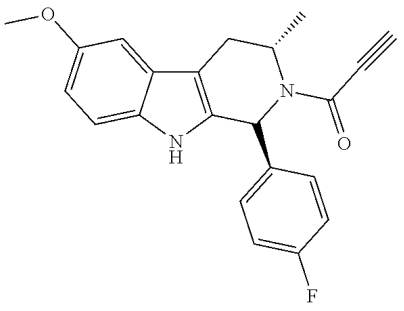


, and

Compound 282



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