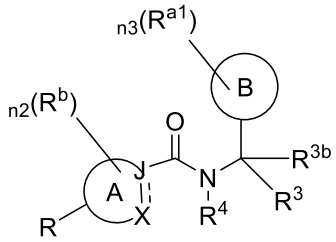
WHAT IS CLAIMED IS:

1. A compound of Formula A:



Formula A,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein:

ring B is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

n3 is an integer from 0 to 5, as valency permits;

R^{a1} at each occurrence is independently deuterium, halogen, CN, OH, NH_2, SH, optionally substituted C_{1-4} alkyl, optionally substituted C_{1-4} heteroalkyl, or optionally substituted 3- to 6-membered ring; or

two adjacent or germinal R^{a1} together with the atom(s) they are attached to form an optionally substituted 3- to 6-membered ring;

R^3 is an optionally substituted C_6-C_{10} aryl, optionally substituted 5- to 10-membered heteroaryl, optionally substituted C_3-C_8 cycloalkyl, or optionally substituted 3- to 10-membered heterocyclyl;

R^{3b} is hydrogen, deuterium, or optionally substituted C_{1-4} alkyl;

R^4 is hydrogen;

ring A is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

$\overline{\quad}$ is a single bond or a double bond;

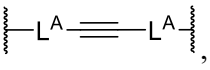
J is C, CH, C(C_{1-4} alkyl), or N;

X is N, NH, N(C_{1-4} alkyl), CH, C(C_{1-4} alkyl), CF, CCl, C(OH), CH_2, CH(C_{1-4} alkyl), C(C_{1-4} alkyl)$_2$, or C(=O);

n2 is an integer from 0 to 5, as valency permits;

R^b at each occurrence is independently deuterium, halogen, CN, OH, $CONH_2$, $CONHR^6$, $CONR^6R^7$, $NHC(O)R^6$, $NR^6C(O)R^7$, $S(O)R^6$, $S(O)_2R^6$, $S(O)_2NHR^6$, $S(O)_2NR^6R^7$, $NHS(O)_2R^6$, $NR^6S(O)_2R^7$, optionally substituted C_{1-4} alkyl, optionally substituted C_{1-4} alkoxy, optionally substituted C_{2-4} alkenyl, optionally substituted C_{2-4} alkynyl, optionally substituted C_{1-4} heteroalkyl, or an optionally substituted 3- to 6-membered ring;

R is R^5 or $-L^1-R^5$;

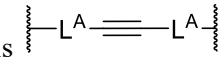
L^1 is  , $-L^A$-(optionally substituted C_6-C_{10} arylene)-L^A-, $-L^A$-(optionally substituted 5- to 10-membered heteroarylene)-L^A-;

L^A at each occurrence is independently absent, O, NH, $N(C_{1-4}$ alkyl), optionally substituted C_{1-4} alkylene, or optionally substituted C_{1-4} heteroalkylene;

R^5 is hydrogen, deuterium, halogen, CN, OH, OR^6, NH_2, NHR^6, NR^6R^7, $NHC(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $S(O)_2R^6$, $P(O)R^6R^7$, CO_2H, $CONH_2$, $CONHR^6$, CO_2R^6, $S(O)_2NH_2$, $S(O)_2NHR^6$, $S(O)_2NR^6R^7$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, an optionally substituted C_6-C_{10} aryl, optionally substituted 5- to 10-membered heteroaryl, optionally substituted C_3-C_8 cycloalkyl, or optionally substituted 3- to 10-membered heterocyclyl;

wherein each of R^6 and R^7 at each occurrence is independently optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} heteroalkyl, an optionally substituted C_6-C_{10} aryl, optionally substituted 5- to 10-membered heteroaryl, optionally substituted C_3-C_8 cycloalkyl, or optionally substituted 3- to 10-membered heterocyclyl; or R^6 and R^7 together with the nitrogen they are attached to form an optionally substituted 3- to 10-membered heterocyclyl; and

provided one or more of the following conditions are met:

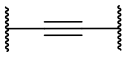
(i) R is $-L^1-R^5$, and L^1 is  ;

(ii) ring A is 5- or 6-membered heteroaryl, and X is N; or ring A is phenyl, and X is CF, CCl, or C(OH);

(iii) ring A is 8- to 10-membered fused bicyclic heteroaryl or 8- to 10-membered fused bicyclic heterocyclyl;

(iv) ring B is 8- to 10-membered fused bicyclic heteroaryl; and

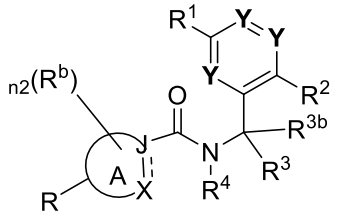
(v) R^3 is para-substituted phenyl.

2. The compound of claim 1, wherein in condition (i): L^1 is  ;

wherein in condition (i): ring A is phenyl or 6-membered heteroaryl, and R is at the para-position to X; or ring A is 5-membered heteroaryl, and R is at the position that is not adjacent to either J or X; or

wherein in condition (iv): ring B is a 5- or 6-membered heteroaryl fused to a 5- or 6-membered non-aromatic ring.

3. The compound of claim 1 or 2, which is a compound of Formula A-1:



Formula A-1,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein:

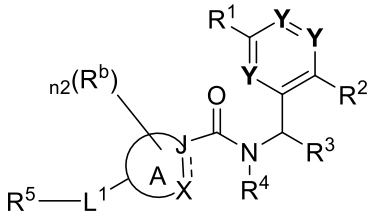
R^1 is hydrogen, halogen, OH, optionally substituted C_{1-4} alkyl, or optionally substituted C_{1-4} alkoxy;

R^2 is hydrogen, halogen, OH, NH_2, SH, optionally substituted C_{1-4} alkyl, or optionally substituted C_{1-4} alkoxy;

each Y is independently CH, CR^a, or N; and

R^a at each occurrence is independently halogen, deuterium, CN, OH, NH_2, SH, optionally substituted C_{1-4} alkyl, or optionally substituted C_{1-4} heteroalkyl.

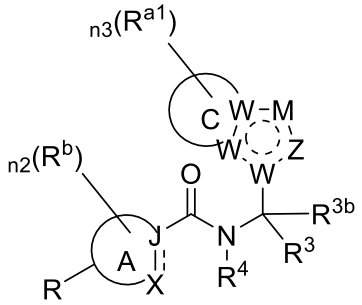
4. The compound of claim 3, which is a compound of Formula I:



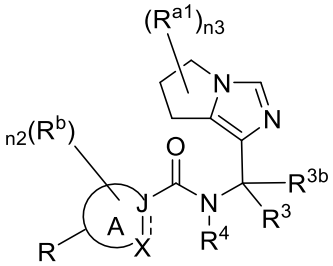
Formula I,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof.

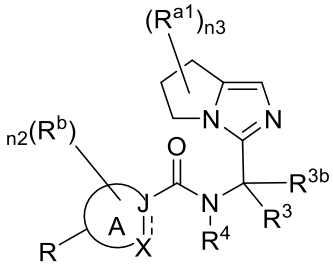
5. The compound of claim 1 or 2, which is a compound of Formula A-2, A-2-a, or A-2-b:



Formula A-2,



Formula A-2-a, or



Formula A-2-b,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein:

ring C is a 4- to 7-membered ring;



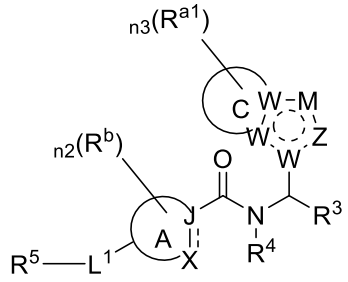
is a 5-membered heteroaryl fused to ring C; wherein M and Z are each independently CH, CD, S, N or NH; and each W is independently C or N; and

n3 is an integer from 0 to 5, as valency permits;

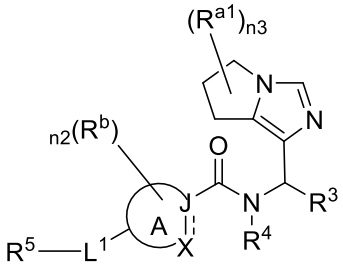
R^{a1} at each occurrence is independently halogen, deuterium, CN, OH, NH_2, SH, optionally substituted C_{1-4} alkyl, or optionally substituted C_{1-4} heteroalkyl; or

two adjacent or germinal R^{a1} together with the atom(s) they are attached to form an optionally substituted 3- to 6-membered ring.

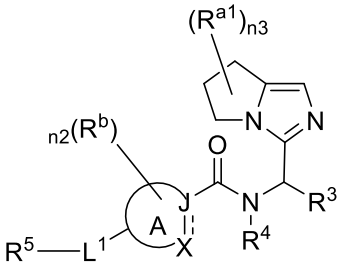
6. The compound of claim 5, which is a compound of Formula II, II-a, or II-b:



Formula II,



Formula II-a, or



Formula II-b,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof; optionally

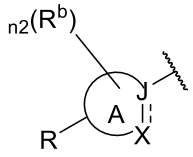
wherein ring C is a 5-membered non-aromatic ring.

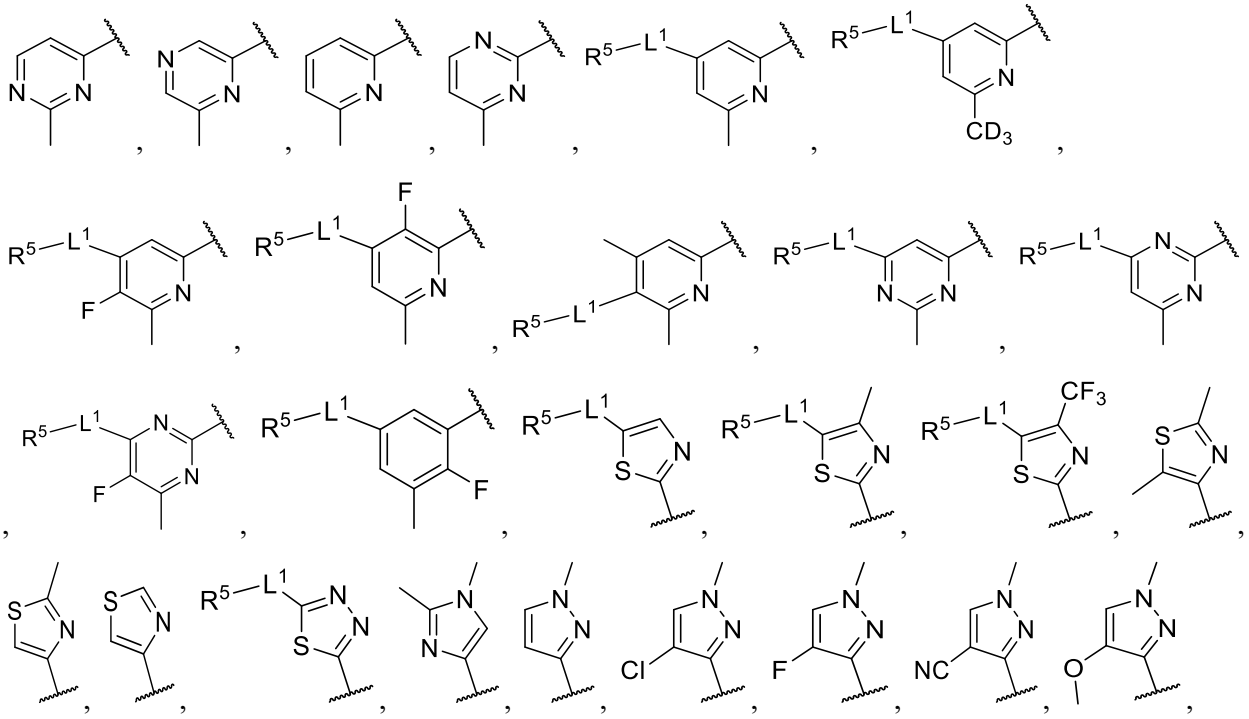
7. The compound of any one of claims 1 to 6,

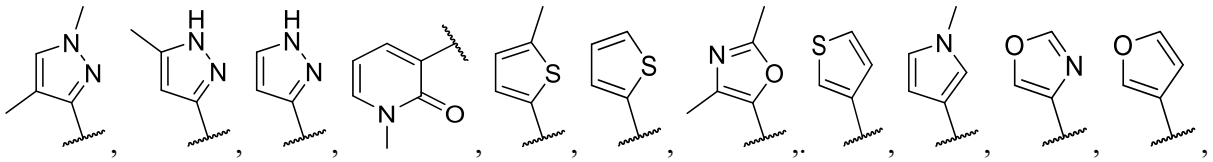
(i) wherein X is N;

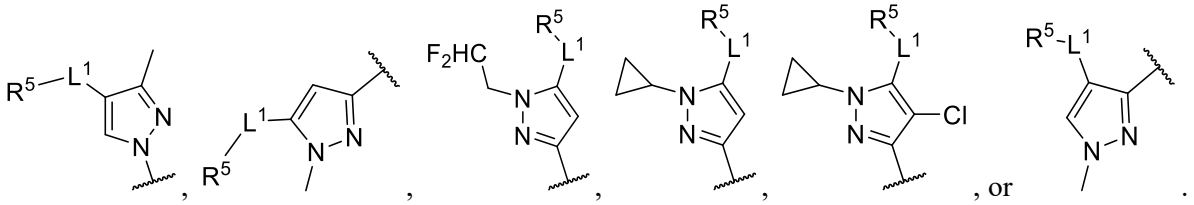
(ii) wherein ring A is a 5-membered heteroaryl; optionally wherein the 5-membered heteroaryl is thiazole, oxazole, pyrazole, isothiazole, isoxazole, imidazole, thiophene, thiadiazole, or furan; or

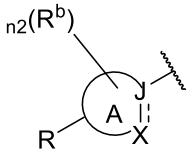
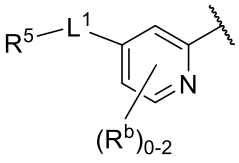
(iii) wherein ring A is a 6-membered heteroaryl; optionally wherein the 6-membered heteroaryl is pyridine, pyridone, pyrazine, pyridazine, or pyrimidine.

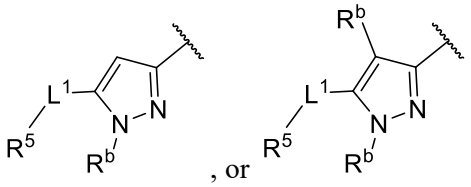
8. The compound of any one of claims 1 to 6, wherein  is:





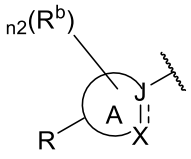


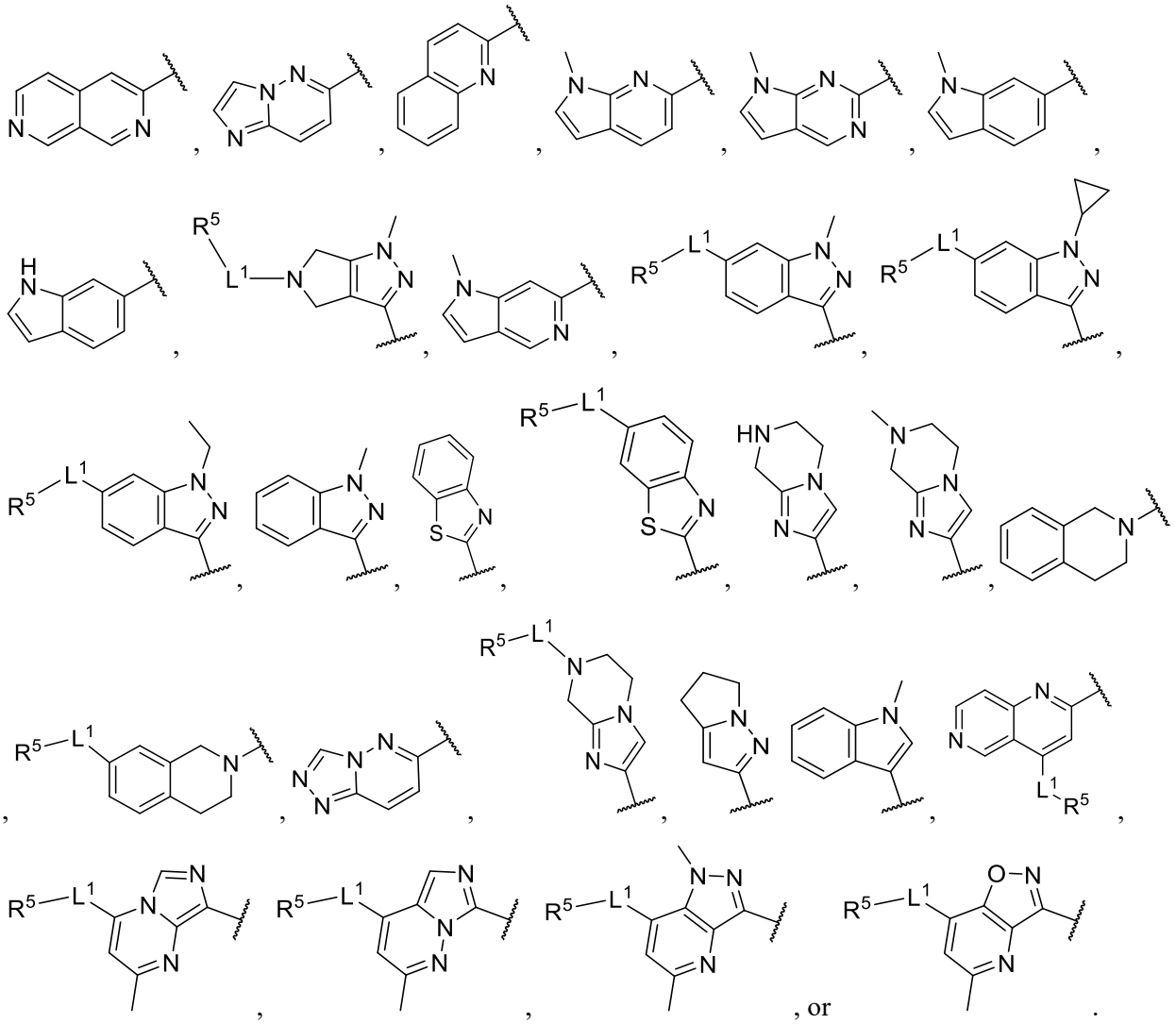
9. The compound of any one of claims 1 to 6, wherein  is  ,



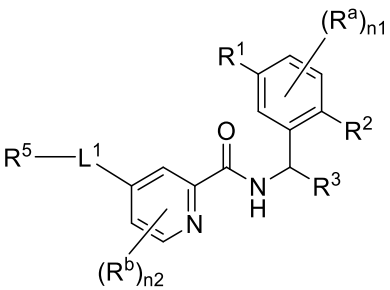
wherein ring A is a 8- to 10-membered fused bicyclic heteroaryl, or ring A is a 8- to 10-membered fused bicyclic ring in which one of the fused rings is a phenyl or heteroaryl, optionally

wherein ring A is indole, azaindole, indazole, benzimidazole, imidazopyridazine, imidazopyridine, benzothiazole, benzoxazole, thienopyridine, benzodiazine, naphthyridine, quinoline, or isoquinoline.

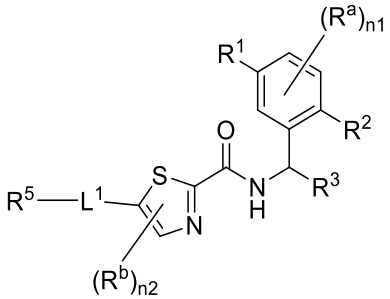
10. The compound of any one of claims 1 to 6, wherein  is:



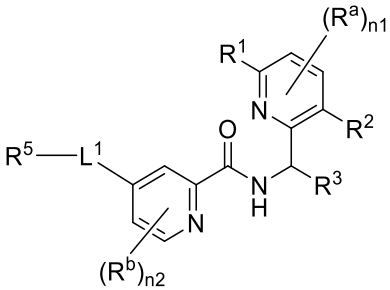
11. The compound of any one of claims 1 to 6, which is a compound of Formula I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, II-1, II-2, II-3, II-4, II-5, III-1, or III-2:



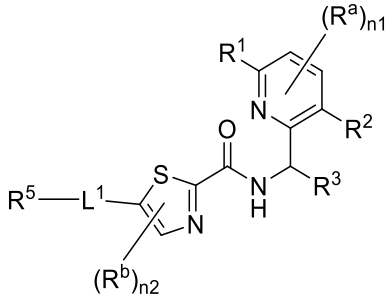
Formula I-1,



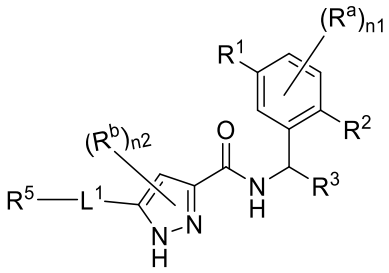
Formula I-2,



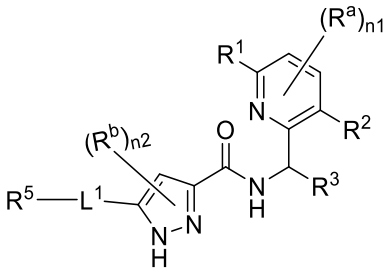
Formula I-3,



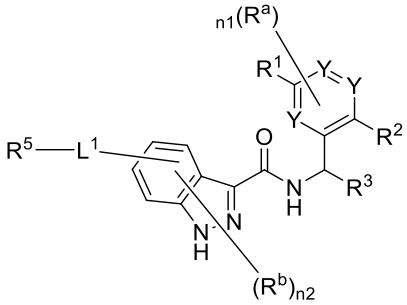
Formula I-4,



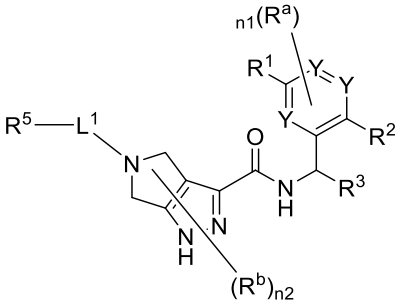
Formula I-5,



Formula I-6,



Formula I-7,



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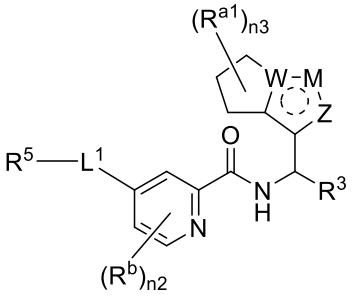
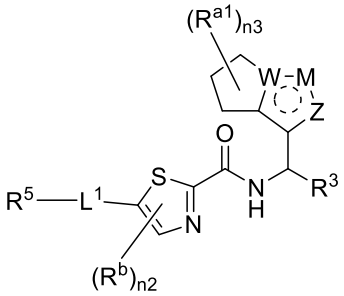
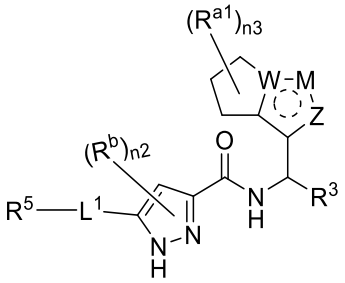


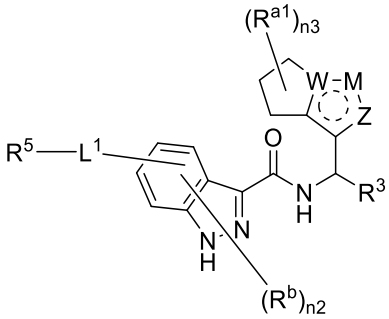
Formula II-1,



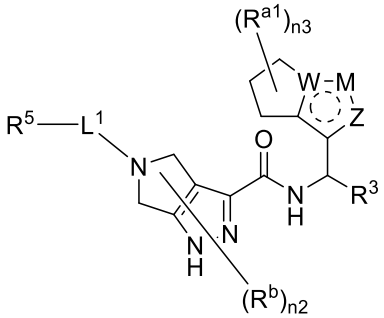
Formula II-2,



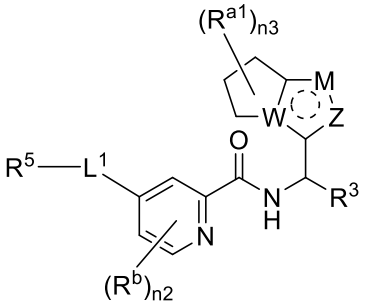
Formula II-3,



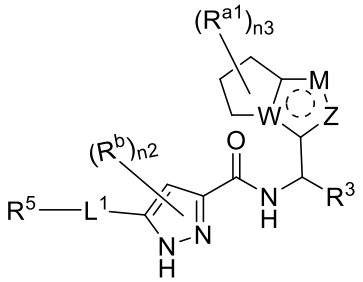
Formula II-4,



Formula II-5,



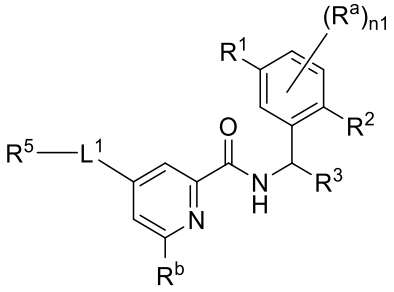
Formula III-1, or



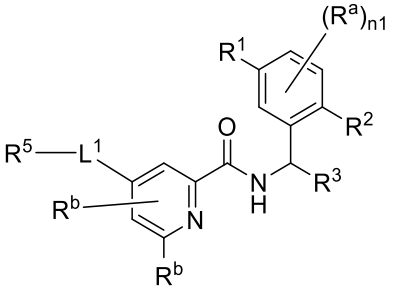
Formula III-2,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein n1 is an integer from 0 to 3, as valency permits, and W is C or N.

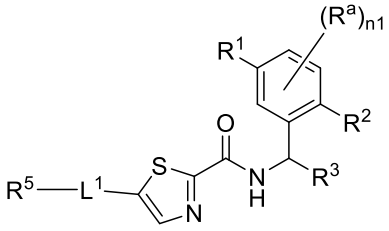
12. The compound of claim 11, which is a compound of Formula I-1a, I-1b, I-2a, I-2b, I-5a, I-5b, I-7a, I-7b, I-8a, II-1a, II-1b, II-2a, II-2b, II-3a, II-3b, II-4a, II-4b, II-5a, II-6a, III-1a, III-1b, III-2a, or III-2b:



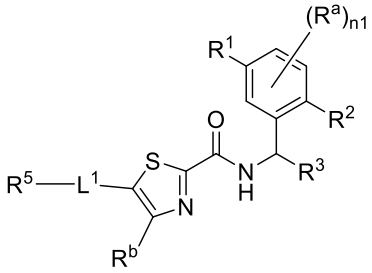
Formula I-1a,



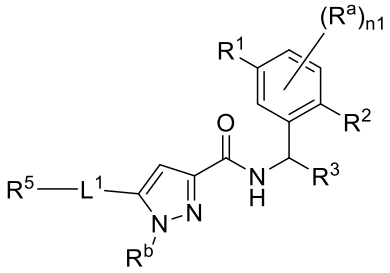
Formula I-1b,



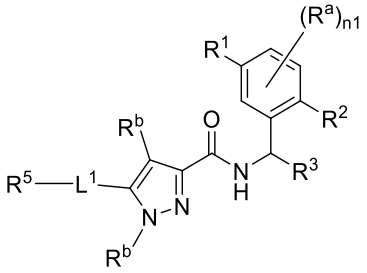
Formula I-2a,



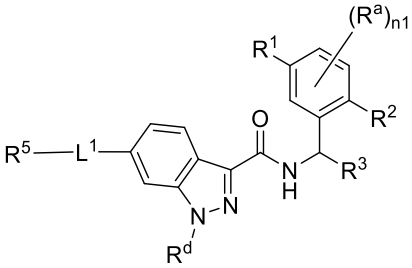
Formula I-2b,



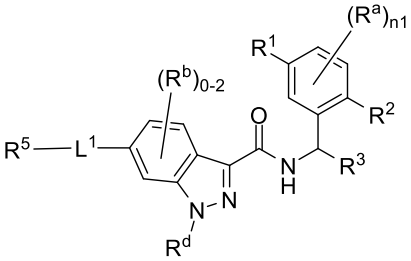
Formula I-5a,



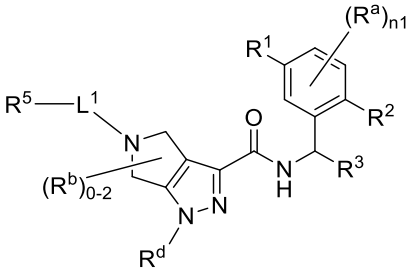
Formula I-5b,



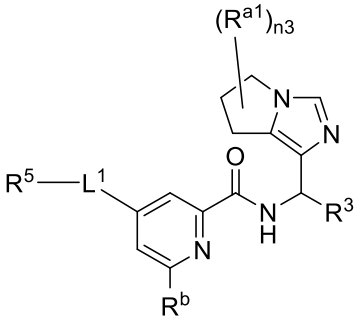
Formula I-7a,



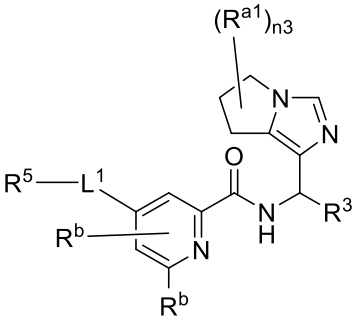
Formula I-7b,



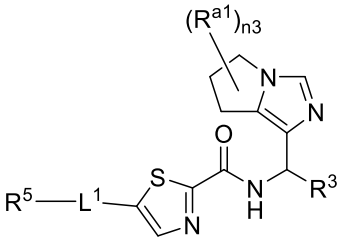
Formula I-8a,



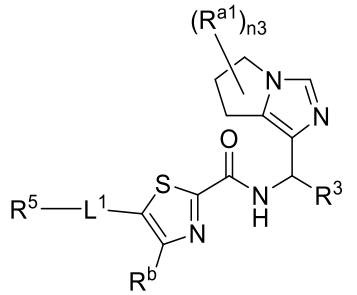
Formula II-1a,



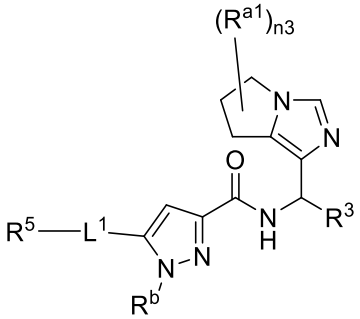
Formula II-1b,



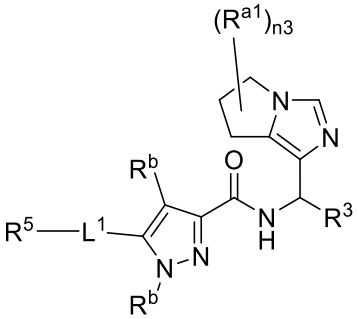
Formula II-2a,



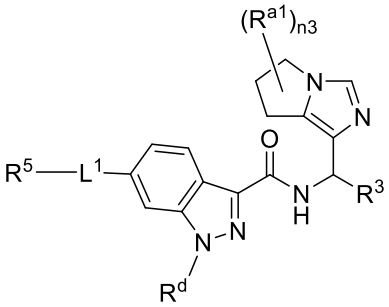
Formula II-2b,



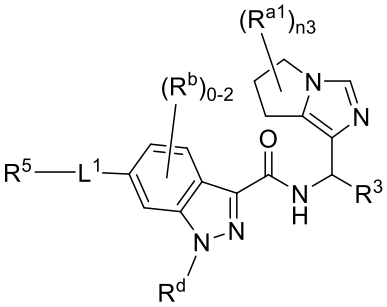
Formula II-3a,



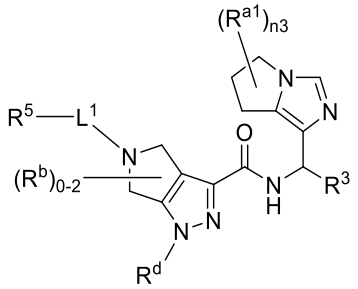
Formula II-3b,



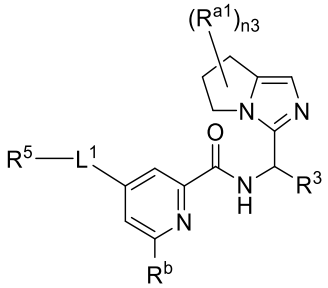
Formula II-4a,



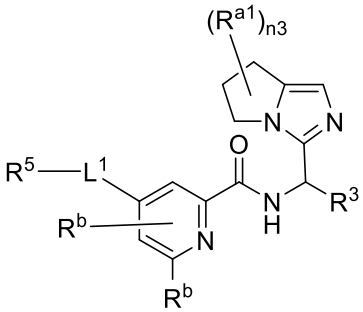
Formula II-4b,



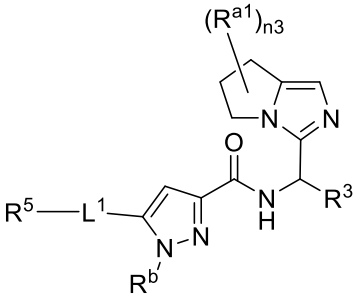
Formula II-5a,



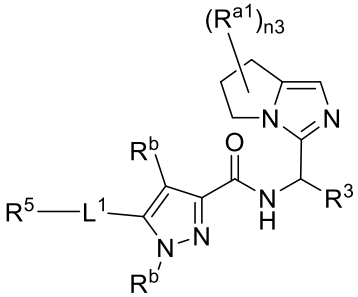
Formula III-1a,



Formula III-1b,



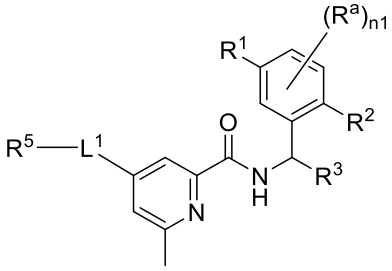
Formula III-2a, or



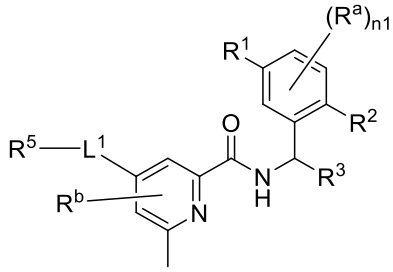
Formula III-2b,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein R^d is hydrogen or an optionally substituted C_{1-4} alkyl.

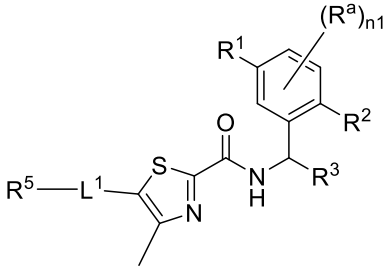
13. The compound of claim 12, which is a compound of Formula I-1a-1, I-1b-1, I-2b-1, I-5a-1, I-5b-1, I-7a-1, I-7b-1, I-8a-1, II-1a-1, II-1b-1, II-2b-1, II-4a-1, II-4b-1, II-5a-1, or III-1a-1:



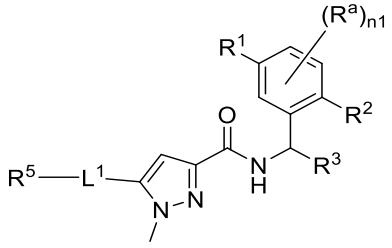
Formula I-1a-1,



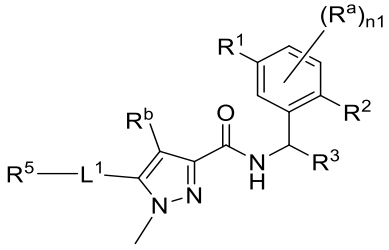
Formula I-1b-1,



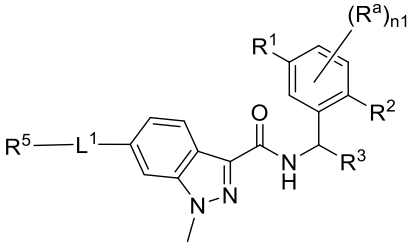
Formula I-2b-1,



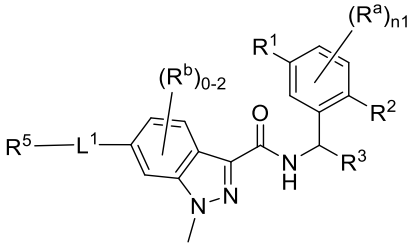
Formula I-5a-1,



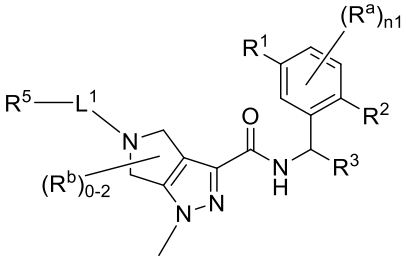
Formula I-5b-1,



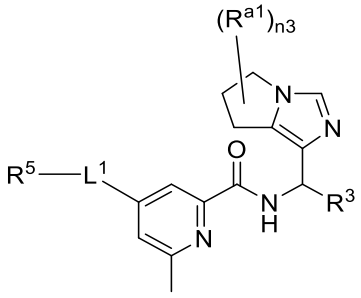
Formula I-7a-1,



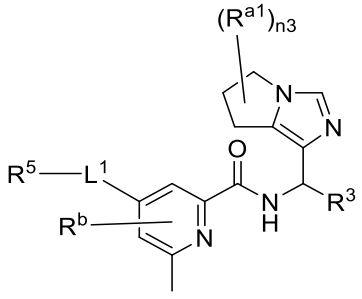
Formula I-7b-1,



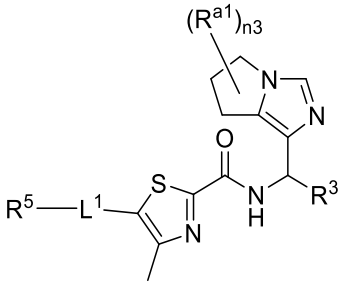
Formula I-8a-1,



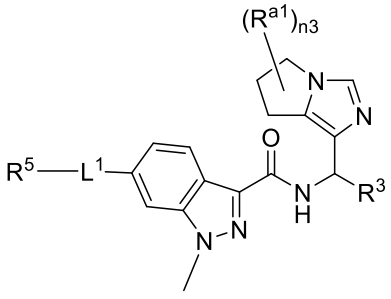
Formula II-1a-1,



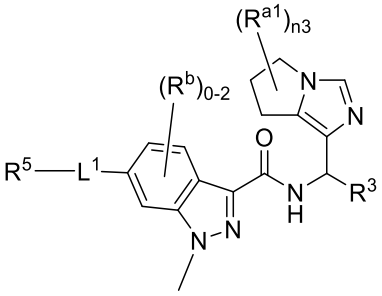
Formula II-1b-1,



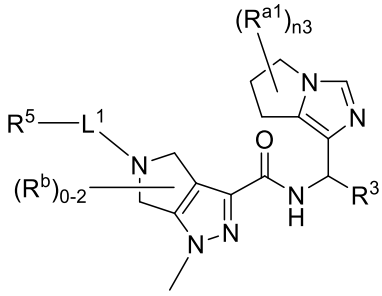
Formula II-2b-1,



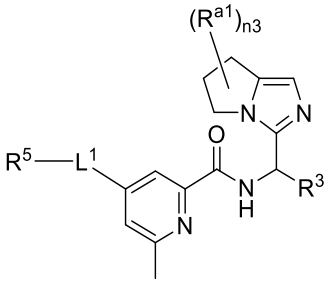
Formula II-4a-1,



Formula II-4b-1,

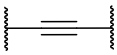


Formula II-5a-1, or

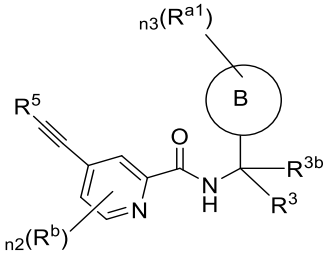


Formula III-1a-1,

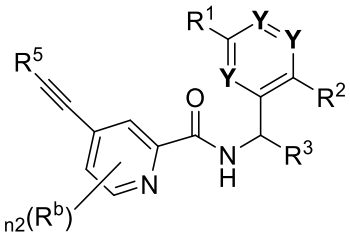
or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof.

14. The compound of any one of claims 1 to 13, wherein L^1 is  .

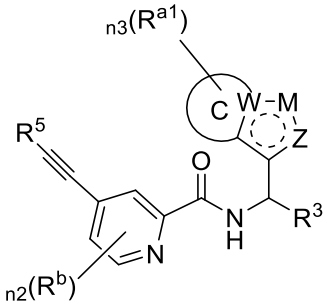
15. The compound of claim 14, which is a compound of formula A-X, I-X, II-X, or III-X:



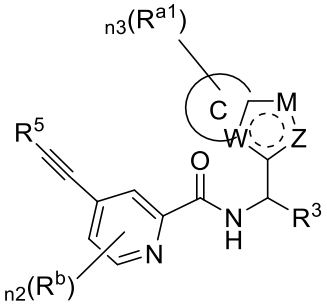
Formula A-X,



Formula I-X,



Formula II-X, or



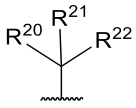
Formula III-X,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof.

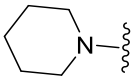
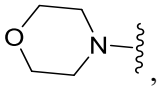
16. The compound of any one of claims 1 to 15, wherein R^5 is hydrogen, deuterium, $P(O)R^6R^7$, CO_2H, $C_{1\text{-}6}$ alkyl, $C_{2\text{-}6}$ alkynyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, C_3-C_8 cycloalkyl, or 3- to 10-membered heterocyclyl;

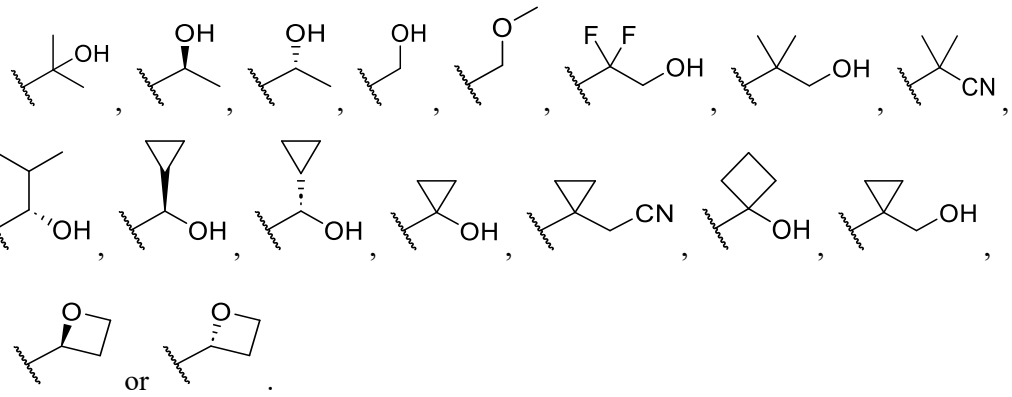
wherein the alkyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl is substituted with one or more substituents independently selected from: OH; oxo; halo; cyano; deuterium; NH_2; NHR^6; NR^6R^7; $NHC(O)R^6$; $NHCONH_2$; $NHS(O)_2R^6$; $NR^6S(O)_2R^6$; $S(O)_2R^6$; $P(O)R^6R^7$; CO_2H; $CONH_2$; $CONHR^6$;

$CONR^6R^7$; CO_2R^6; $C(O)R^6$; $S(O)_2NH_2$; $S(O)_2NHR^6$; $S(O)_2NR^6R^7$; $C_{1\text{-}6}$ alkyl optionally substituted with one or more OH, halo, cyano, or deterium; $C_{1\text{-}6}$ alkoxy optionally substituted with one or more OH, halo, cyano, or deterium; C_6-C_{10} aryl optionally substituted with one or more $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ haloalkyl, OH or halo; 5- to 10-membered heteroaryl optionally substituted with one or more $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ haloalkyl, OH or halo; C_3-C_8 cycloalkyl optionally substituted with one or more $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ haloalkyl, OH or halo; or 3- to 10-membered heterocyclyl optionally substituted with one or more $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ haloalkyl, OH or halo.

17. The compound of any one of claims 1 to 15, wherein R^5 is  , wherein:

each of R^{20} and R^{21} is independently hydrogen, deuterium, halo, cyano, $C_{1\text{-}6}$ alkyl optionally substituted with one or more OH, halo, cyano, deuterium, or C_3-C_8 cycloalkyl optionally substituted with one or more $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ haloalkyl, OH, halo, cyano, or deuterium; or R^{20} and R^{21} together with the carbon they are attached to form a C_3-C_8 cycloalkyl optionally substituted with one or more $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ haloalkyl, OH or halo, or form a 3- to 10-membered heterocyclyl optionally substituted with one or more $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ haloalkyl, OH,halo, cyano, or deuterium; and

R^{22} is hydrogen, deuterium, OH, halo, $C_{1\text{-}6}$ alkyl, or $C_{1\text{-}6}$ alkoxy, wherein the alkyl and alkoxy are optionally substituted with one or more OH, halo, cyano, deuterium, NH_2, $NH(C_{1\text{-}6}$ alkyl), $N(C_{1\text{-}6}$ alkyl)$_2$, C_3-C_8 cycloalkyl, 3- to 10-membered heterocyclyl, or 5- to 10-membered heteroaryl; optionally wherein R^5 is hydrogen; deuterium; halogen; COOH; $S(O)_2CH_3$; $P(O)(CH_3)_2$; or $C_{1\text{-}6}$ alkyl, which is optionally substituted with OH, OR^6, $O(CH_2)_{m1}OH$, $O(CH_2)_{m1}OR^6$, NH_2, $NH(CH_3)$, $N(CH_3)_2$,  ,  , or  , wherein m1 is 2 or 3; or optionally

wherein R^5 is  .

18. The compound of any one of claims 1 to 15,

(i) wherein R^5 is a 3-10 membered ring containing at least one ring heteroatom selected from N, O, and S, wherein the S atom is optionally oxidized, wherein the 3-10 membered ring is optionally substituted with 1-3 substituents each independently selected from oxo, deuterium, halo, G^1, OH, O-G^1, NH_2, $NH(G^1)$, $N(G^1)(G^1)$, $C(O)G^1$, C(O)H, COOH, COO-G^1, $C(O)NH_2$, $C(O)NH(G^1)$, $C(O)N(G^1)(G^1)$, $S(O)_2G^1$, $S(O)_3$-G^1, $S(O)_2NH_2$, $P(O)(G^1)(G^1)$, $S(O)_2NH(G^1)$, and $S(O)_2N(G^1)(G^1)$;

wherein G^1 at each occurrence is independently (1) a C_{1-4} alkyl optionally substituted with 1-3 substituents independently selected from deuterium, F, CN, OH, and C_{1-4} heteroalkyl, or (2) a 3- to 7-membered ring, such as C_{3-6} cycloalkyl, which is optionally substituted with 1-3 substituents independently selected from oxo, deuterium, F, CN, OH, C_{1-4} alkyl, and C_{1-4} heteroalkyl, preferably the C_{1-4} heteroalkyl has one or two heteroatoms selected from S, O, and N, wherein the S atom is optionally oxidized; or

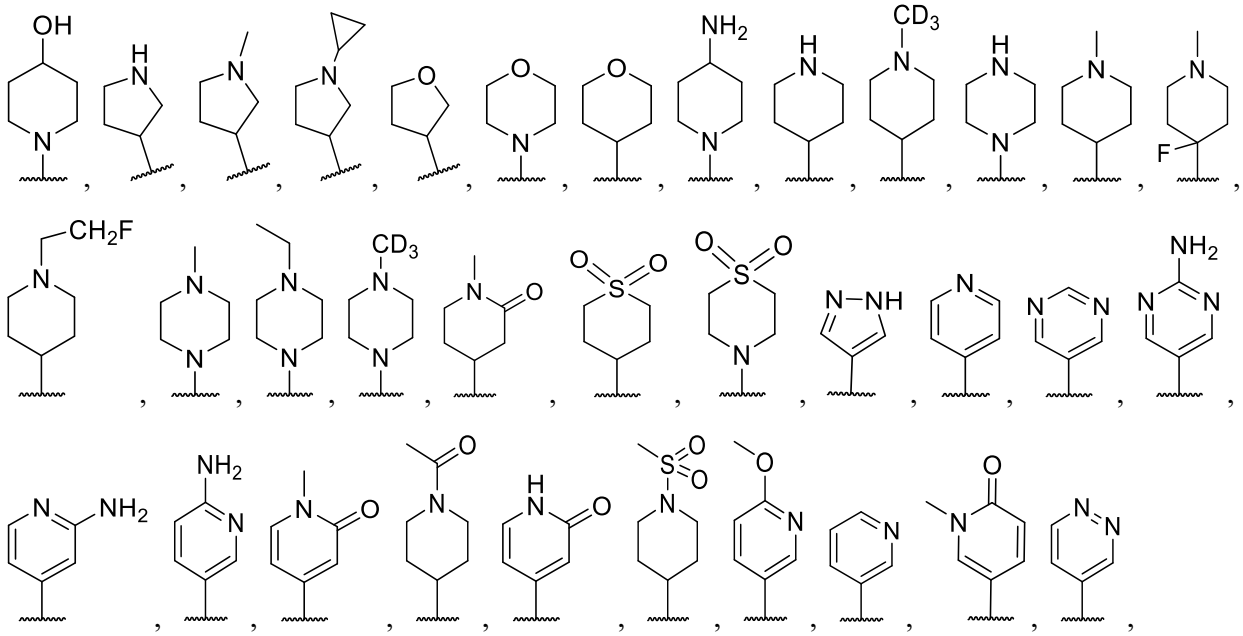
(ii) wherein R^5 is a 5- or 6-membered heteroaryl, 4- to 8-membered monocyclic or bicyclic heterocyclyl, wherein the heteroaryl or heterocyclyl is optionally substituted with 1-3 substituents each independently selected from oxo (as valency permits), deuterium, halo, G^1, OH, O-G^1, NH_2, $NH(G^1)$, $N(G^1)(G^1)$, $C(O)G^1$, C(O)H, COOH, COO-G^1, $C(O)NH_2$, $C(O)NH(G^1)$, $C(O)N(G^1)(G^1)$, $S(O)_2G^1$, $S(O)_3$-G^1, $S(O)_2NH_2$, $P(O)(G^1)(G^1)$, $S(O)_2NH(G^1)$, and $S(O)_2N(G^1)(G^1)$;

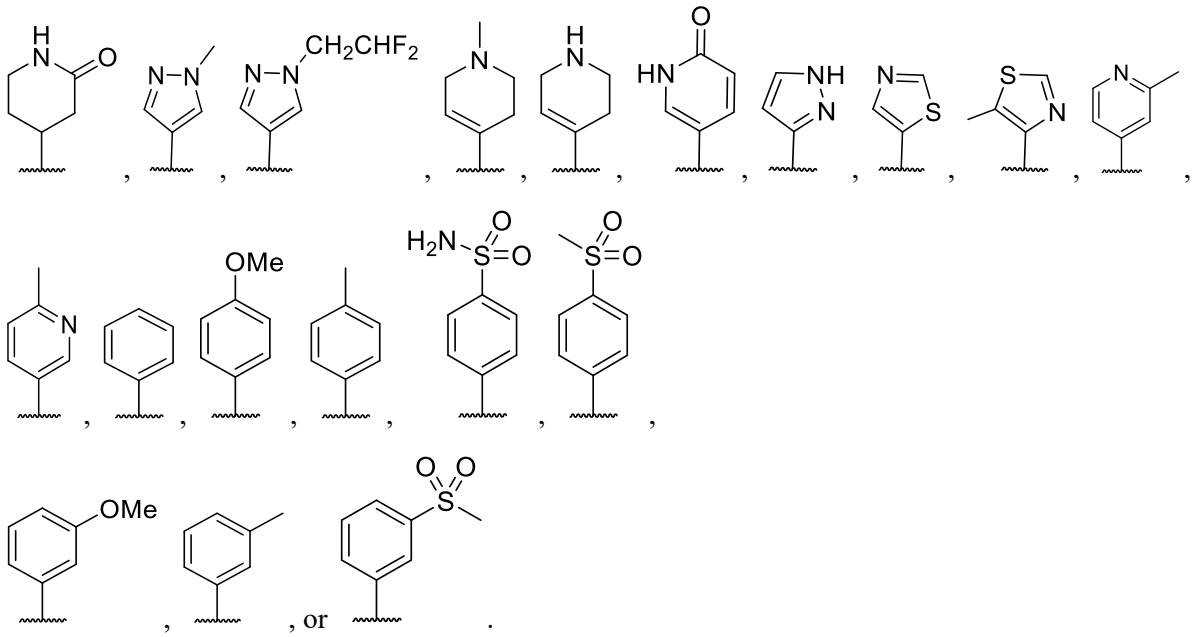
wherein G^1 at each occurrence is independently (1) a C_{1-4} alkyl optionally substituted with 1-3 substituents independently selected from deuterium, F, CN, OH, and C_{1-4} heteroalkyl, or (2) a 3- to 7-membered ring, such as C_{3-6} cycloalkyl, which is optionally substituted with 1-3 substituents independently selected from oxo, deuterium, F, CN, OH, C_{1-4} alkyl, and C_{1-4} heteroalkyl, preferably the

$C_{1\text{-}4}$ heteroalkyl has one or two heteroatoms selected from S, O, and N, wherein the S atom is optionally oxidized; optionally

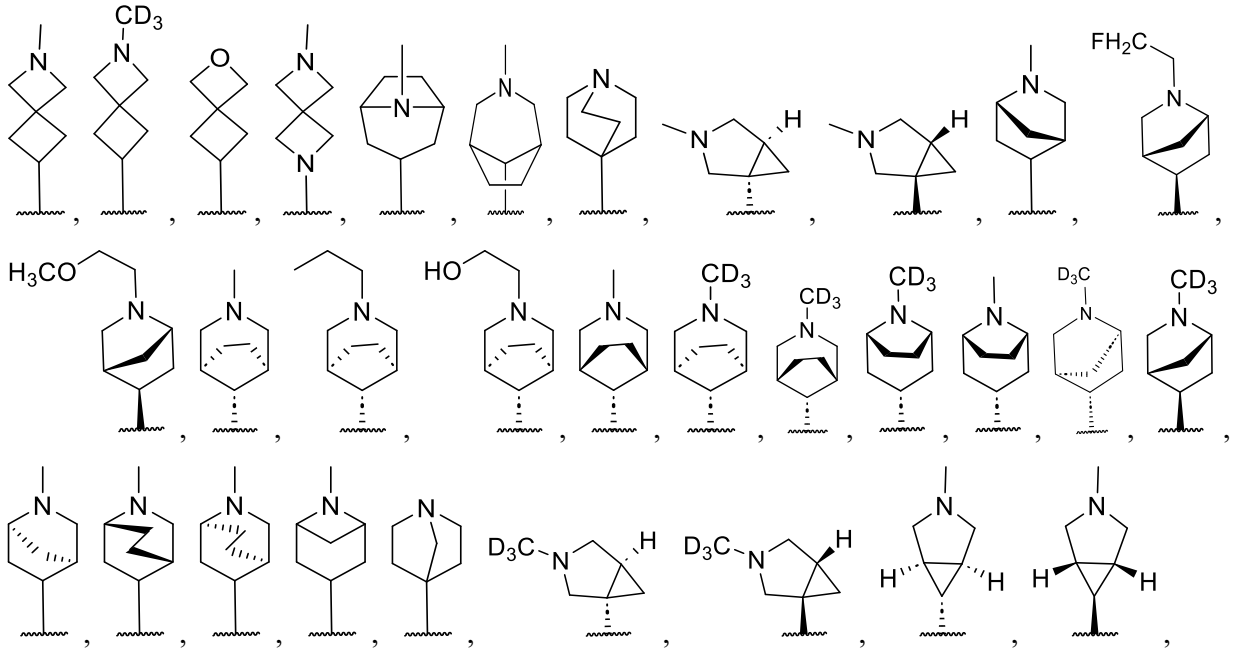
wherein the heteroaryl or heterocyclyl is an optionally substituted pyridine, optionally substituted pyridazine, optionally substituted pyrimidine, optionally substituted pyrazine, optionally substituted pyrazole, optionally substituted pyridone, optionally substituted oxetane, optionally substituted azetidine, optionally substituted pyrrolidine, optionally substituted piperidine, optionally substituted piperazine, optionally substituted morpholine, optionally substituted tetrahydropyran, or optionally substituted tetrahydrothiopyran dioxide.

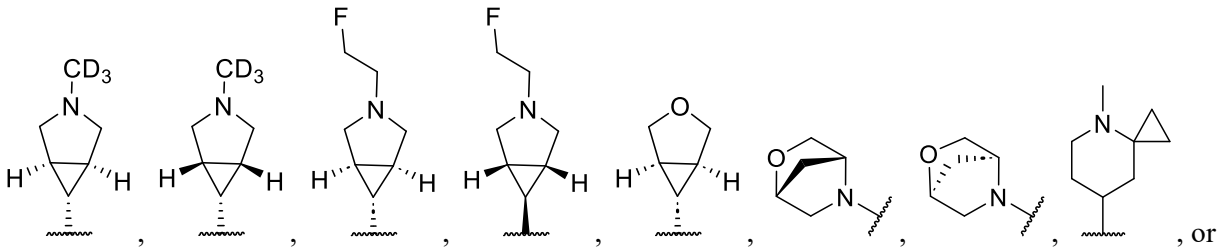
19. The compound of any one of claims 1 to 15, wherein R^5 is:



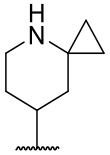


20. The compound of any one of claims 1 to 15, wherein R^5 is:



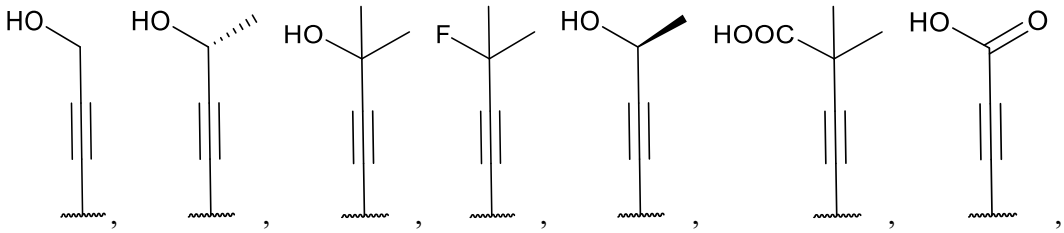


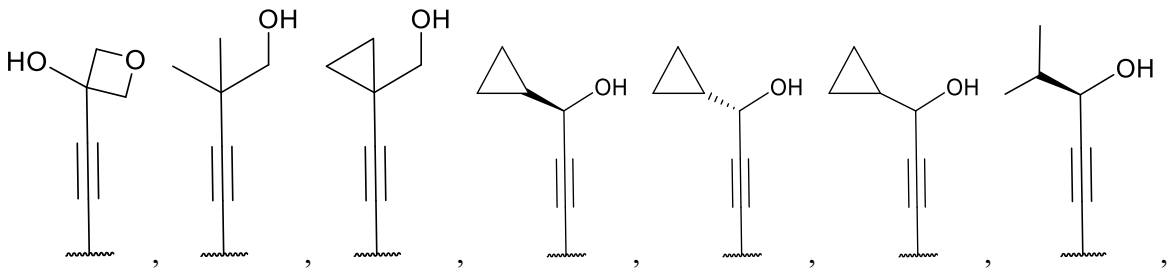
, or

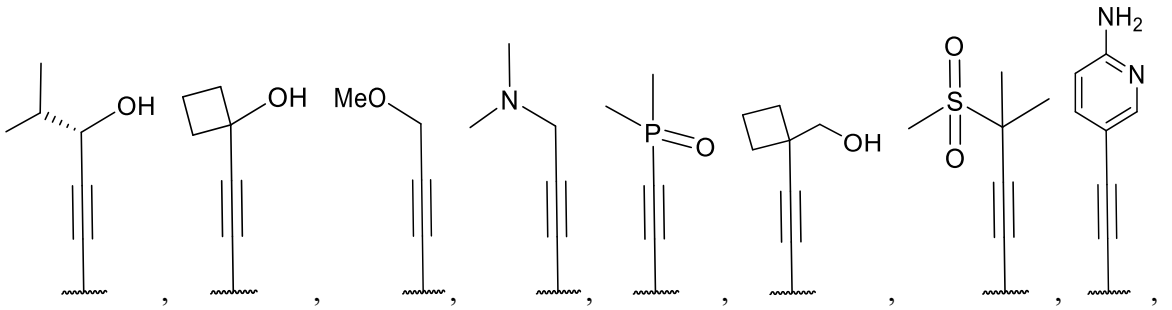


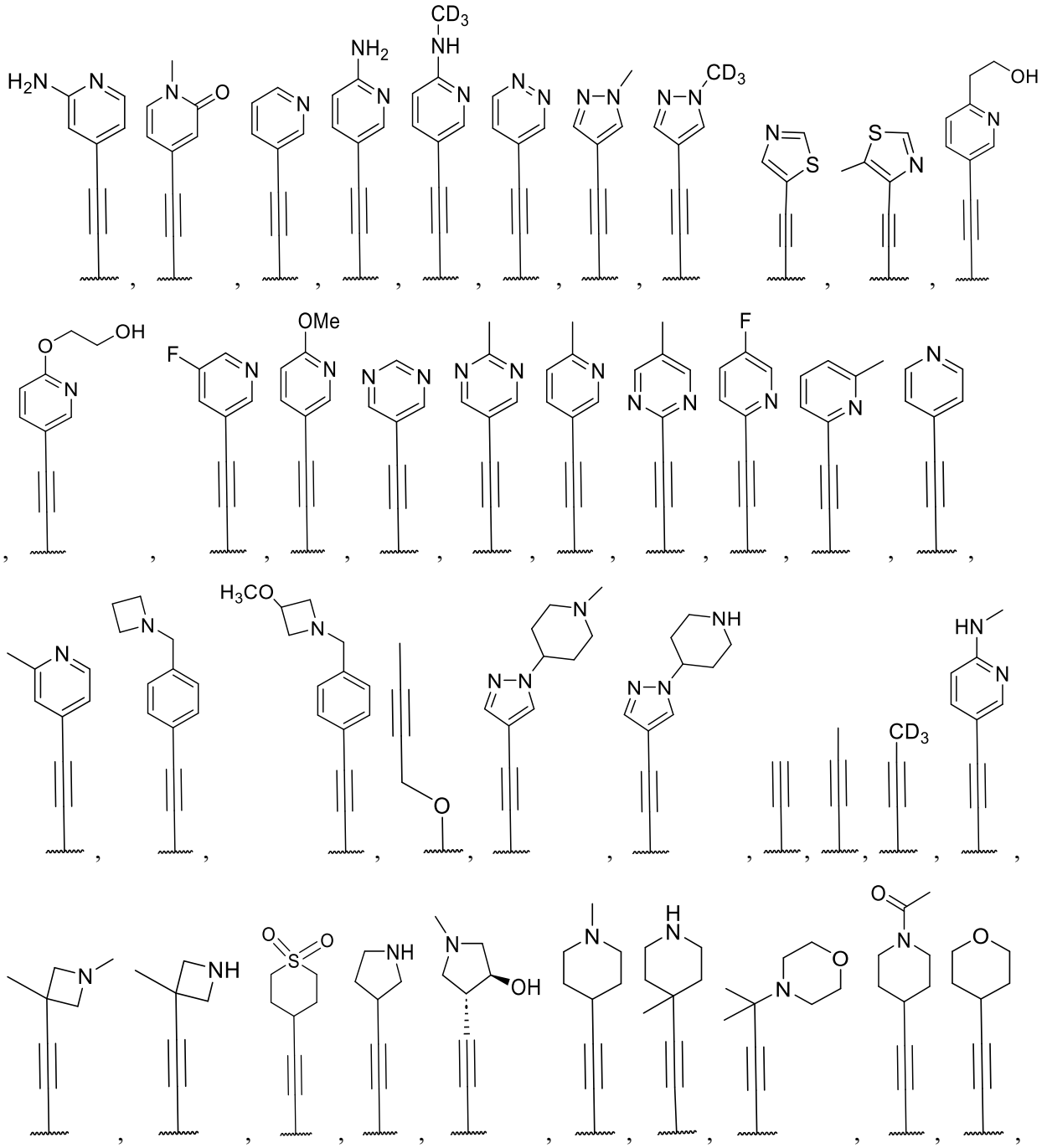
.

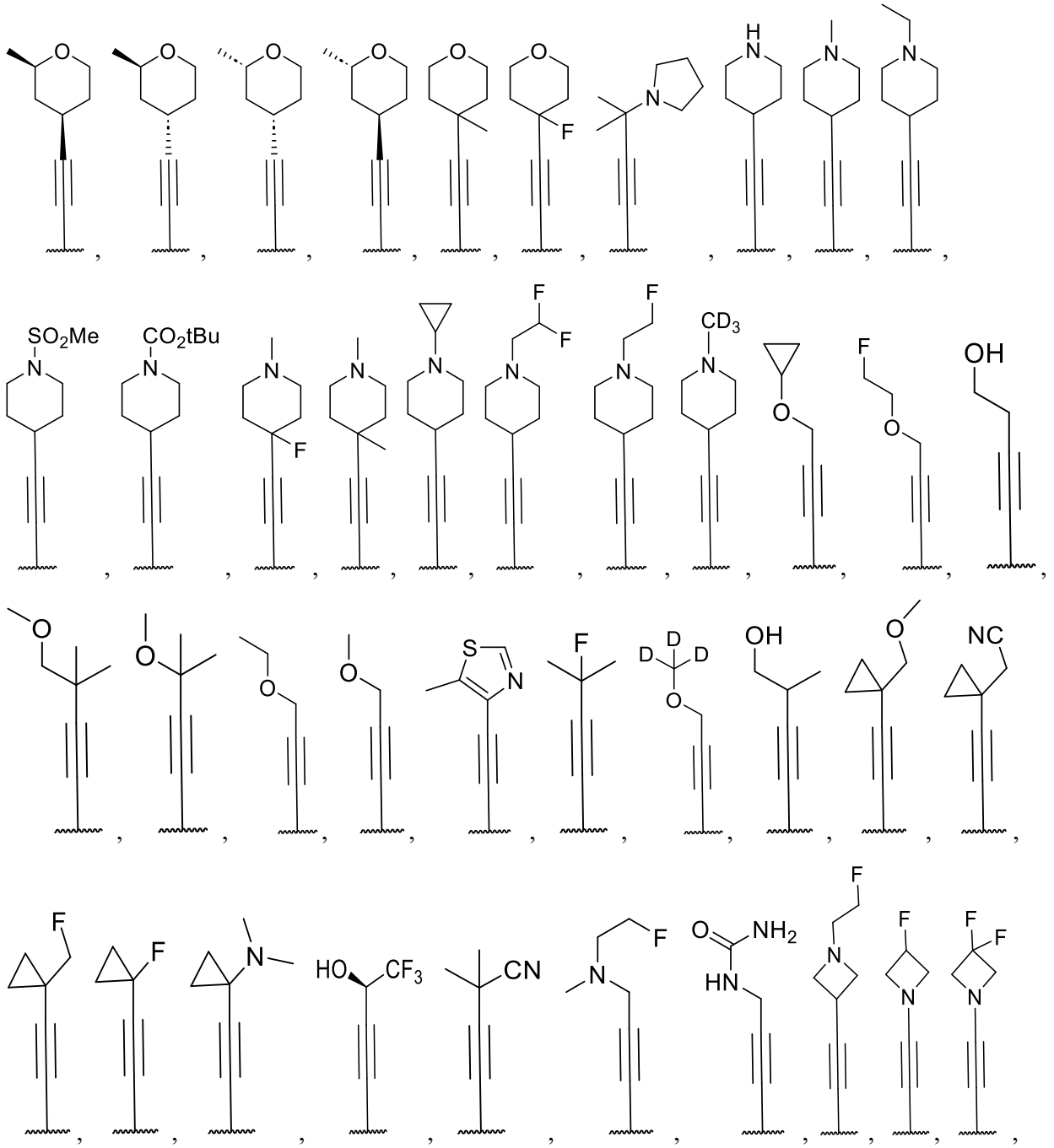
21. The compound of any one of claims 1 to 15, wherein -L^1-R^5 is:

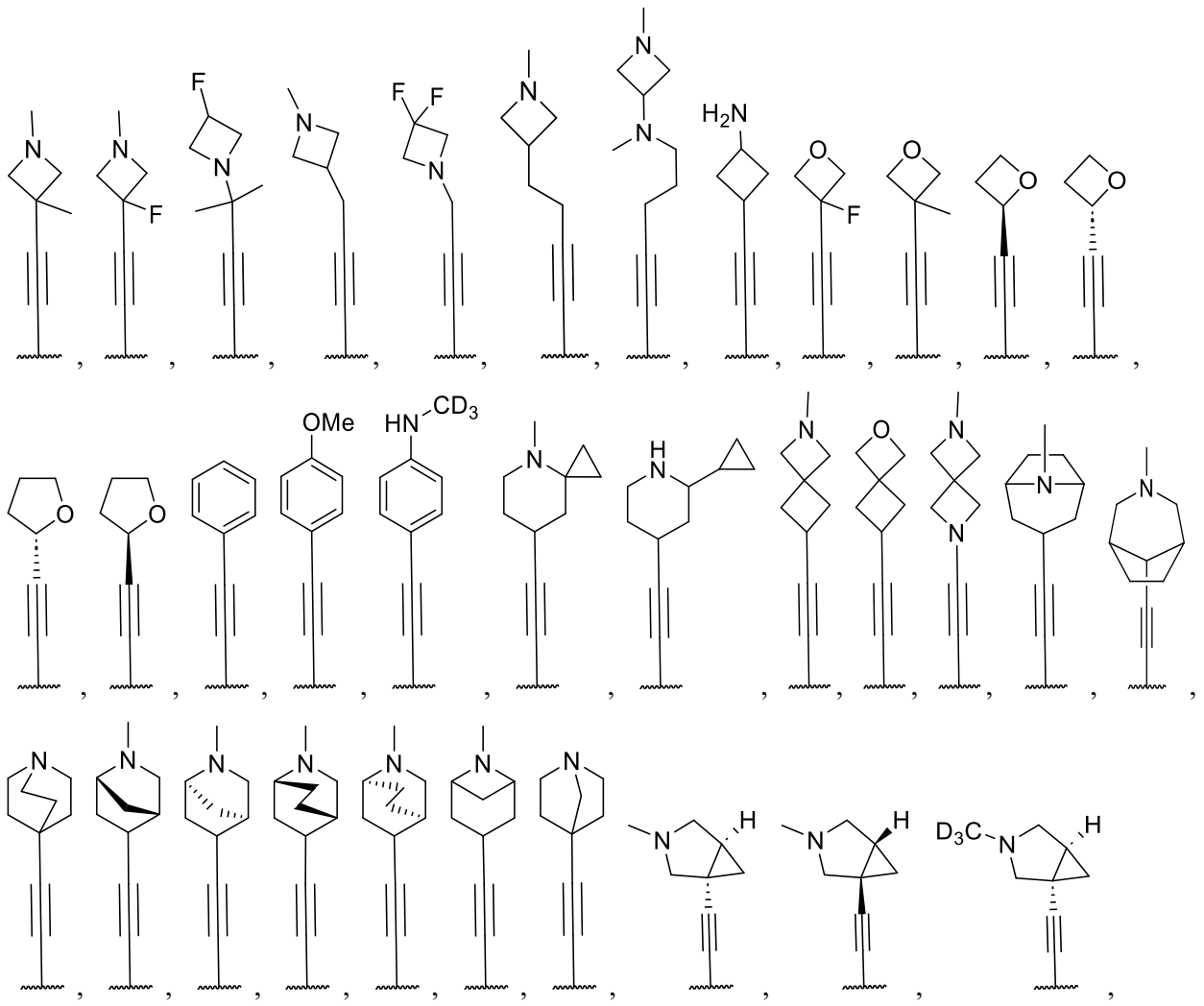


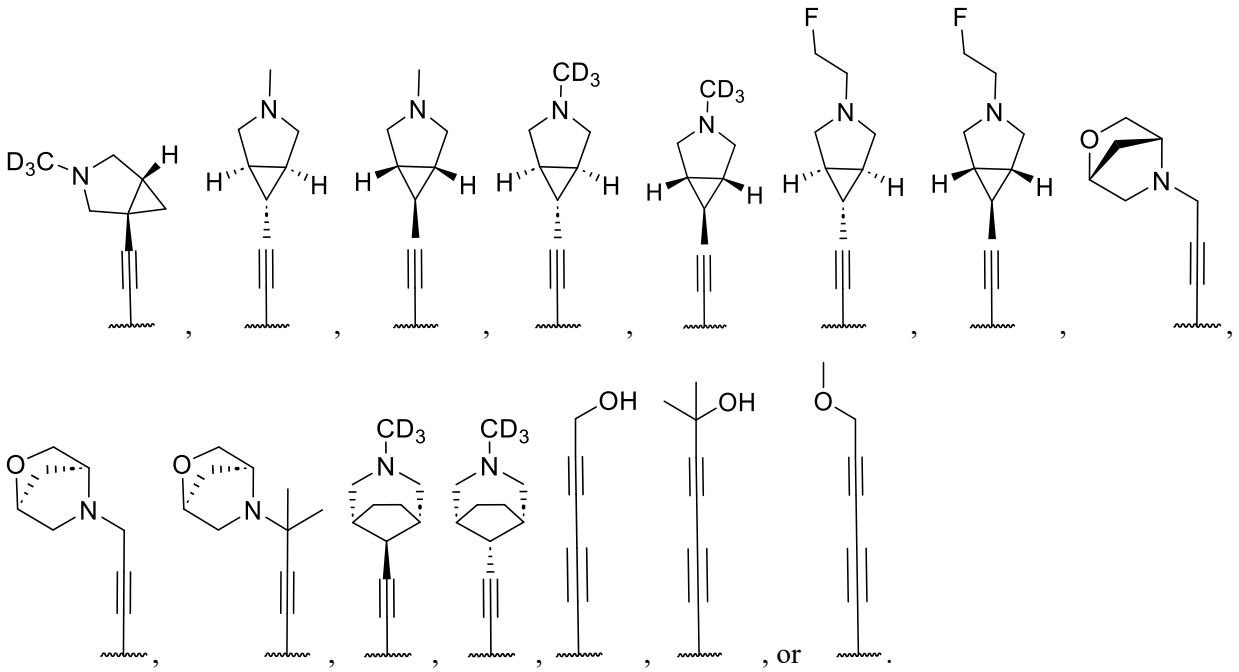




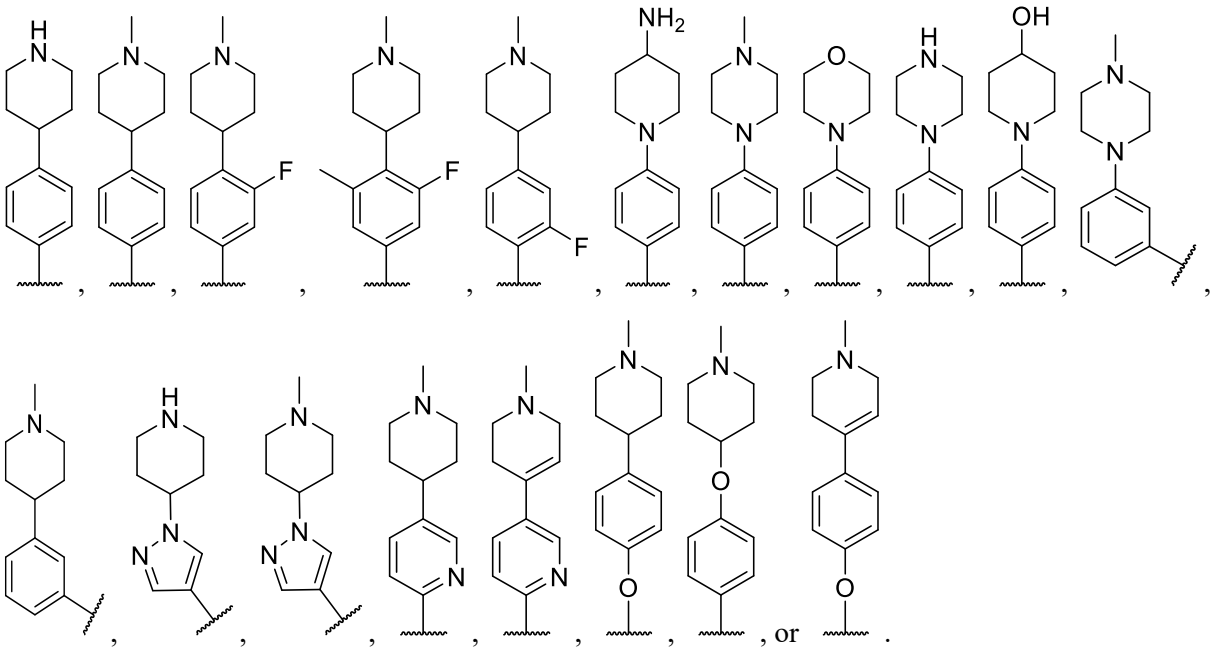






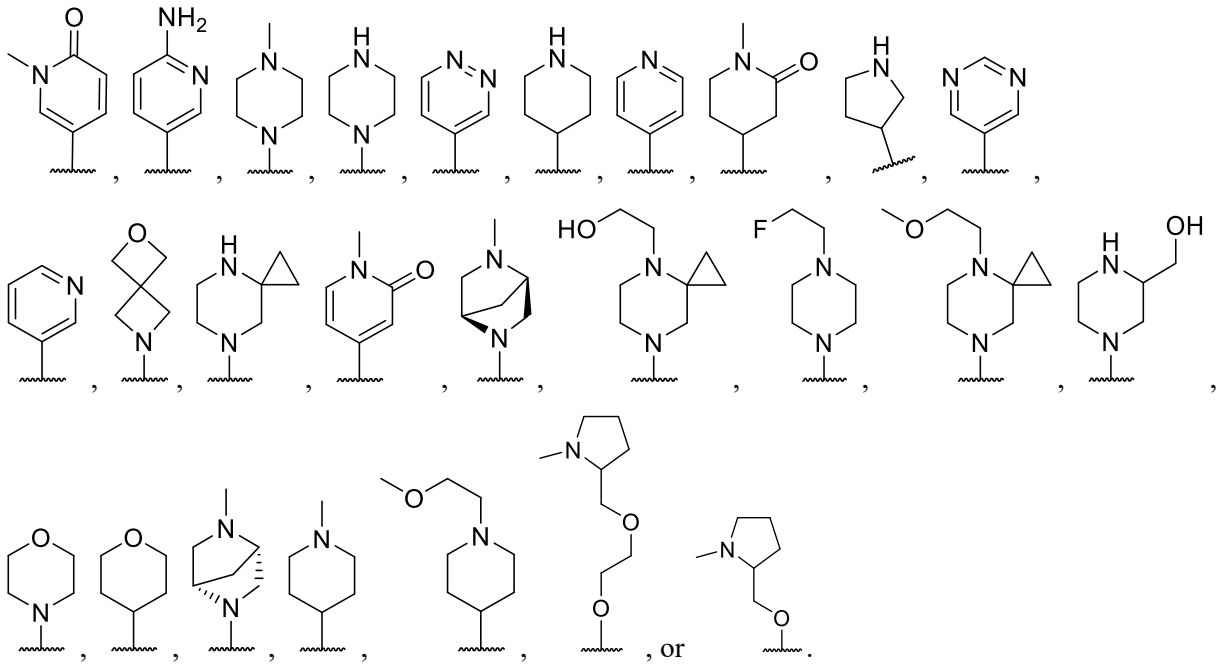


22. The compound of any one of claims 1 to 15, wherein $-L^1-R^5$ is:

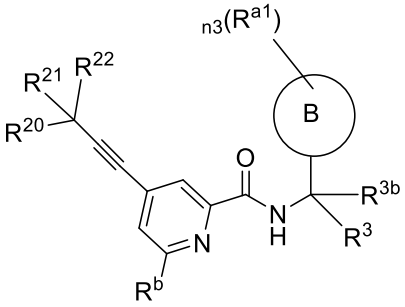


23. The compound of any one of claims 1 to 15, wherein R is hydrogen, OH, F, Cl, Br, CN, CO_2CH_3, COOH, NH-CH_2CH_2-OH, O-CH_2CH_2-OH, $CH_2CH_2CH_2$-OH, methoxy, methyl, NH-CH_2CH_2-OBn, $P(O)(CH_3)_2$, or CH_2-CH(F)-CH_2OH; or

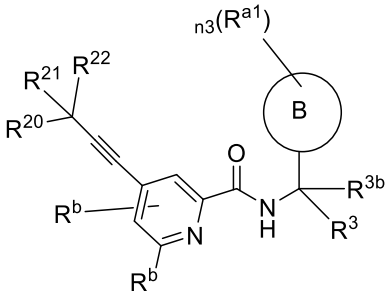
wherein R is:



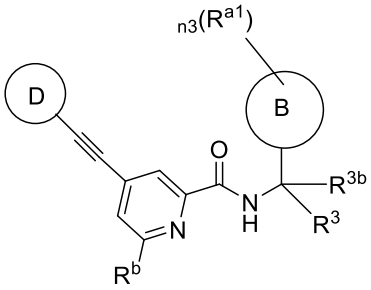
24. The compound of any one of claims 1 to 15, which is a compound of formula A-X-1, A-X-2, A-X-3, A-X-4, A-X-5, A-X-6, A-X-7, A-X-8, A-X-9, A-X-10, I-X-1, I-X-2, I-X-3, I-X-4, I-X-5, I-X-6, I-X-7, I-X-8, I-X-9, I-X-10, II-X-1, II-X-2, II-X-3, II-X-4, II-X-5, II-X-6, II-X-7, II-X-8, II-X-9, II-X-10, III-X-1, III-X-2, III-X-7, III-X-8, III-X-9, or III-X-10:



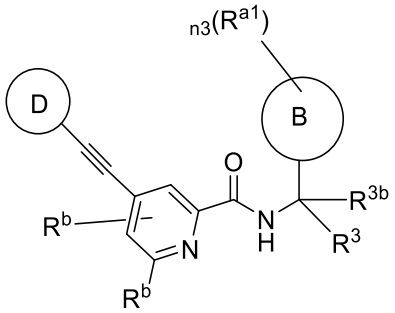
Formula A-X-1,



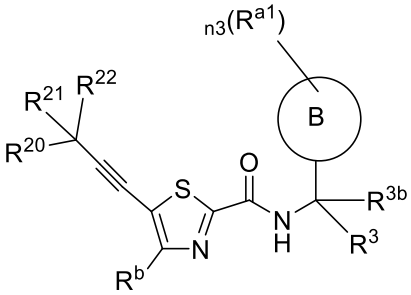
Formula A-X-2,



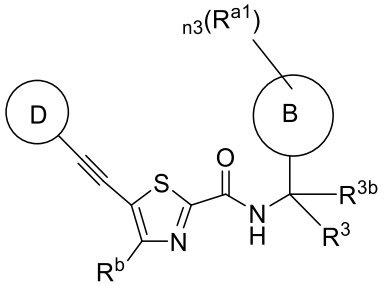
Formula A-X-3,



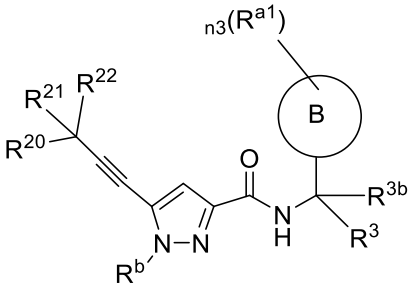
Formula A-X-4,



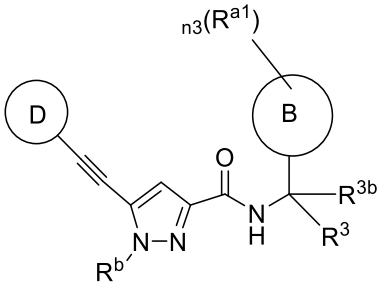
Formula A-X-5,



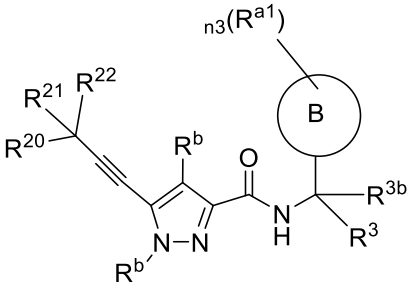
Formula A-X-6,



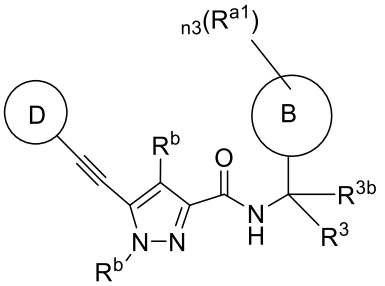
Formula A-X-7,



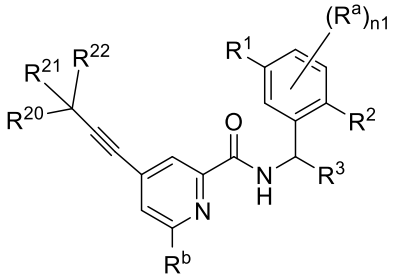
Formula A-X-8,



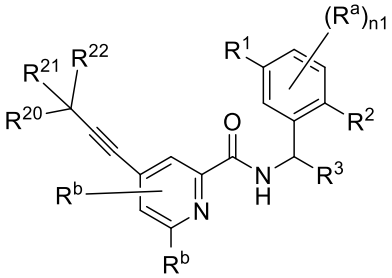
Formula A-X-9,



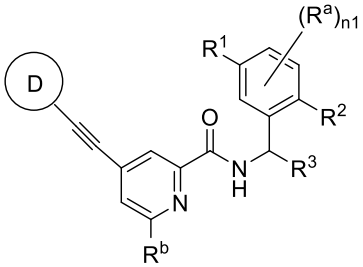
Formula A-X-10,



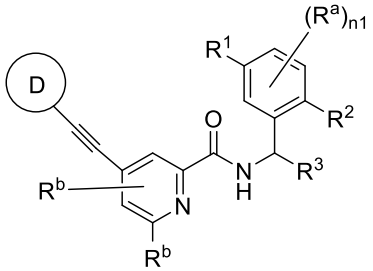
Formula I-X-1,



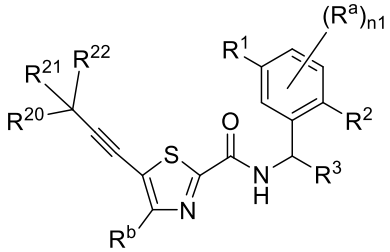
Formula I-X-2,



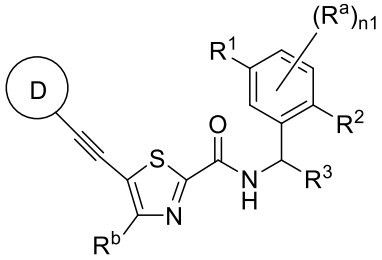
Formula I-X-3,



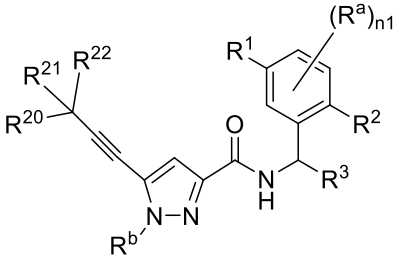
Formula I-X-4,



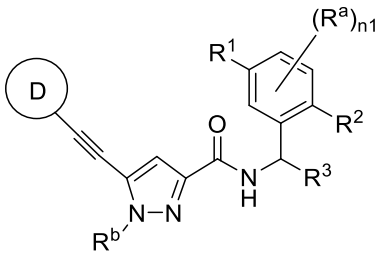
Formula I-X-5,



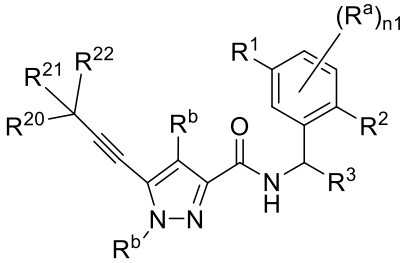
Formula I-X-6,



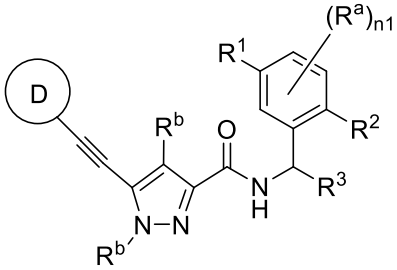
Formula I-X-7,



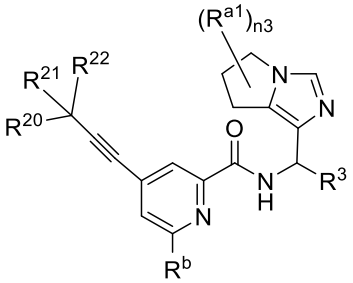
Formula I-X-8,



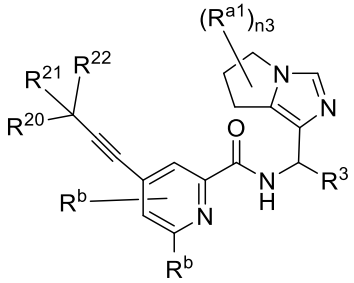
Formula I-X-9,



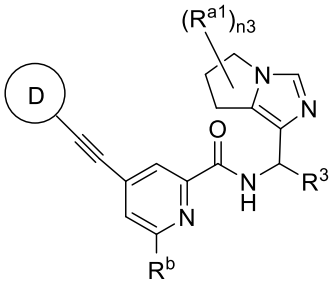
Formula I-X-10,



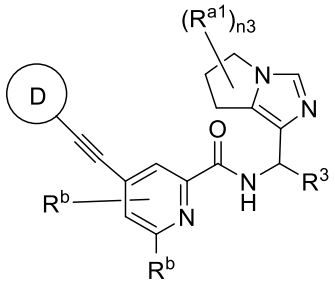
Formula II-X-1,



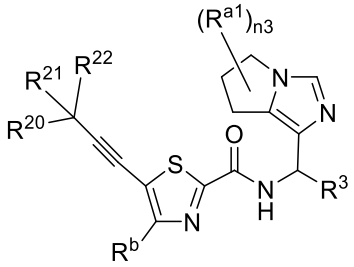
Formula II-X-2,



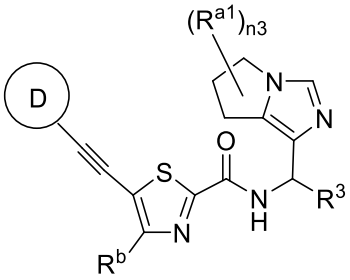
Formula II-X-3,



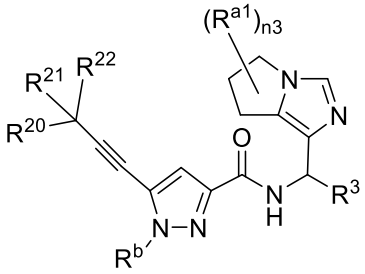
Formula II-X-4,



Formula II-X-5,



Formula II-X-6,



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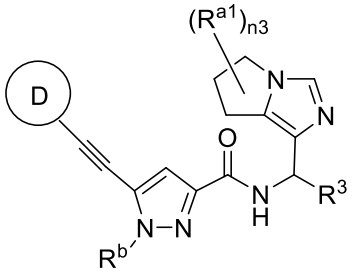
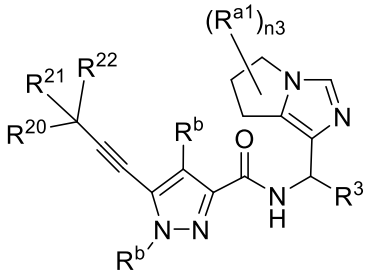


Formula II-X-8,



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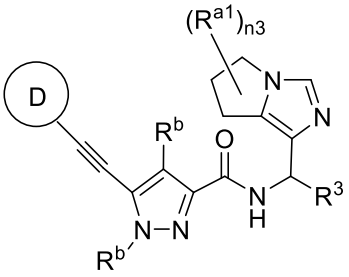

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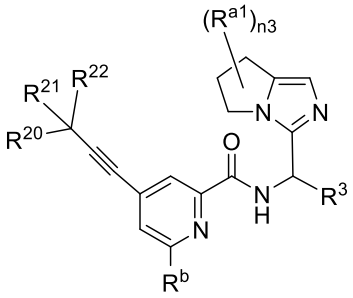
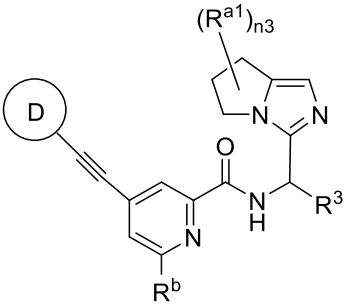
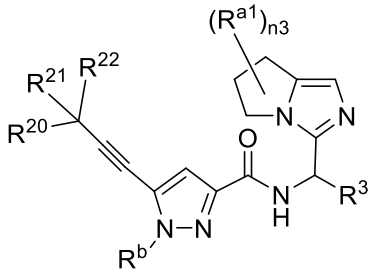


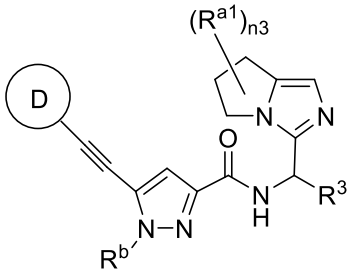
Formula III-X-1,



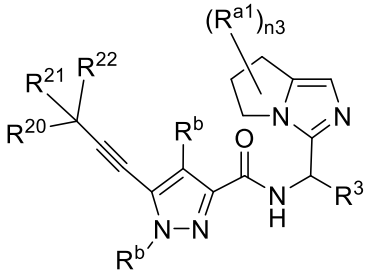
Formula III-X-2,



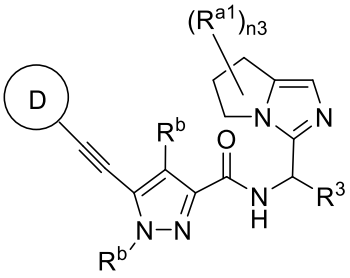
Formula III-X-7,



Formula III-X-8,



Formula III-X-9, or



Formula III-X-10,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein:

each of R^{20} and R^{21} is independently hydrogen, deuterium, halo, cyano, C_{1-6} alkyl optionally substituted with one or more OH, halo, cyano, or deuterium, or C_3-C_8 cycloalkyl optionally substituted with one or more C_{1-3} alkyl, C_{1-3} haloalkyl, OH, halo, cyano, or deuterium; or R^{20} and R^{21} together with the carbon they are attached to form a C_3-C_8 cycloalkyl optionally substituted with one or more C_{1-3} alkyl, C_{1-3} haloalkyl, OH or halo, or form a 3- to 10-membered heterocyclyl optionally substituted with one or more C_{1-3} alkyl, C_{1-3} haloalkyl, OH, halo, cyano, or deuterium; and

R^{22} is hydrogen, deuterium, OH, halo, C_{1-6} alkyl, or C_{1-6} alkoxy, wherein the alkyl and alkoxy are optionally substituted with one or more OH,halo, cyano, deuterium, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, C_3-C_8 cycloalkyl, 3- to 10-membered heterocyclyl, or 5- to 10-membered heteroaryl; and

ring D is phenyl, C_5-C_6 cycloalkyl, 5- or 6-membered heteroaryl, or 3- to 10-membered heterocyclyl, wherein the phenyl, cycloalkyl, heteroaryl, or heterocyclyl is optionally substituted with one or more substituents independently selected from: C_{1-3} alkyl, C_{1-3} haloalkyl, OH, oxo, halo, CN, NH_2, $NH(C_{1-3}$ alkyl), or $N(C_{1-3}$ alkyl$)_2$; and wherein the alkyl is optionally substituted with one or more OH, halo, cyano, or deuterium.

25. The compound of any one of claims 1 to 24, wherein R^3 is an optionally substituted C_6-C_{10} aryl or optionally substituted 5- to 10-membered heteroaryl; optionally

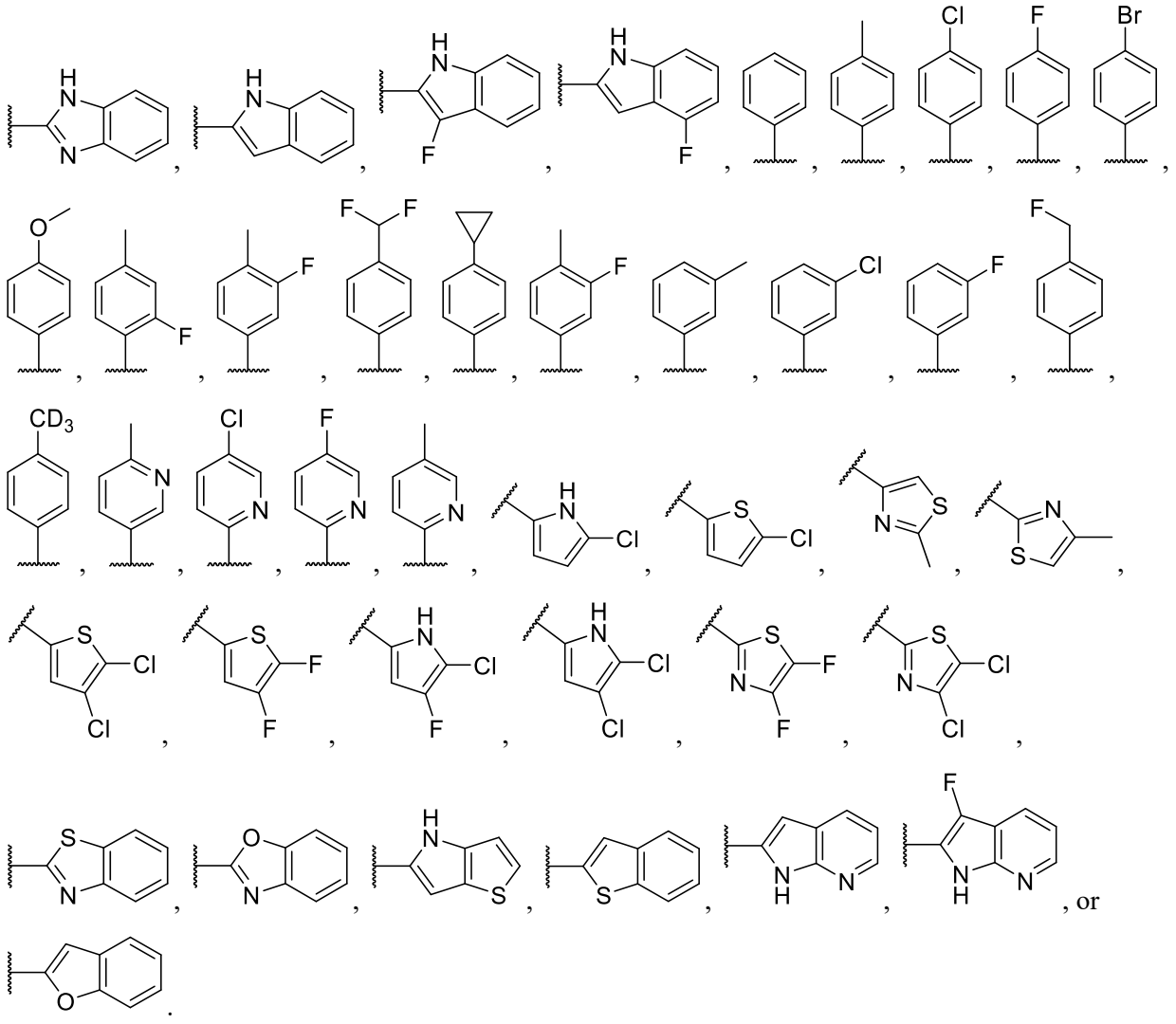
(i) wherein R^3 is phenyl, which is optionally substituted with 1-3 substituents independently selected from deuterium, halo, G^2, OH, O-G^2, or a 3- to 7-membered ring; wherein G^2 at each occurrence is independently a C_{1-4} alkyl optionally substituted with 1-3 deuterium and/or F; and wherein the 3- to 7-membered ring is optionally substituted with 1-3 substituents independently selected from oxo, deuterium, F, CN, OH, C_{1-4} alkyl, and C_{1-4} heteroalkyl;

(ii) wherein R^3 is phenyl, which is substituted at para-position with deuterium, halo, OH, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, wherein the alkyl and cycloalkyl are optionally substituted with 1-3 deuterium and/or F;

(iii) wherein R^3 is 5- or 6-membered heteroaryl, which is optionally substituted with 1-3 substituents independently selected from deuterium, halo, G^2, OH, O-G^2, or a 3- to 7-membered ring; wherein G^2 at each occurrence is independently a C_{1-4} alkyl optionally substituted with 1-3 deuterium and/or F; and wherein the 3- to 7-membered ring is optionally substituted with 1-3 substituents independently selected from oxo, deuterium, F, CN, OH, C_{1-4} alkyl, and C_{1-4} heteroalkyl;

(iv) wherein R^3 is 8- to 10-membered bicyclic heteroaryl, which is optionally substituted with 1-3 substituents independently selected from deuterium, halo, G^2, OH, O-G^2, or a 3- to 7-membered ring; wherein G^2 at each occurrence is independently a C_{1-4} alkyl optionally substituted with 1-3 deuterium and/or F; and wherein the 3- to 7-membered ring is optionally substituted with 1-3 substituents independently selected from oxo, deuterium, F, CN, OH, C_{1-4} alkyl, and C_{1-4} heteroalkyl; or

(v) wherein R^3 is:



26. The compound of any one of claims 1 to 25,

(i) wherein n1 is 0 or 1; or n3 is 0, 1, or 2;

(ii) wherein R^a at each occurrence is independently deuterium, F, Cl, OH, or C_{1-4} alkyl optionally substituted with 1-3 F; or R^{a1} at each occurrence is independently F, Cl, or C_{1-4} alkyl optionally substituted with 1-3 F, or two germinal R^{a1} together with the atom they are attached to form a cyclopropyl;

(iii) wherein one R^{a1} or R^1 is halogen;

(iv) wherein one R^{a1} or R^2 is OH;

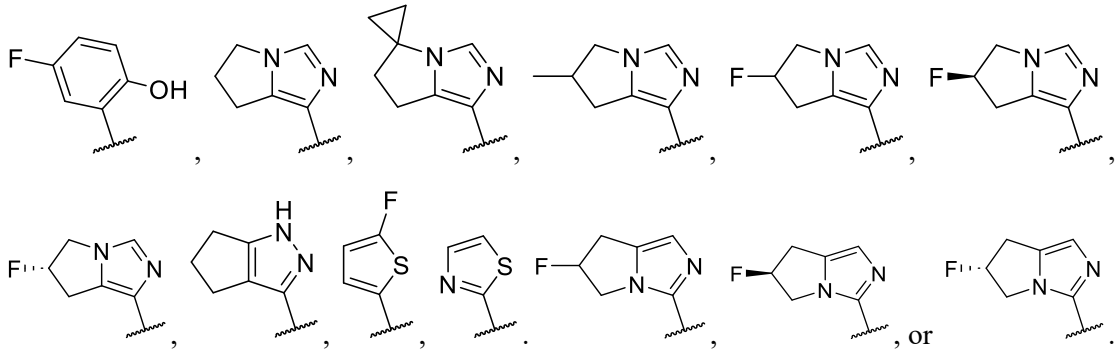
(v) wherein one R^{a1} or R^2 is hydrogen or a C_{1-4} alkyl optionally substituted with 1-3 F;

(vi) wherein n2 is 0, 1, or 2;

(vii) wherein R^b at each occurrence is independently deuterium, F, Cl, CN, OH, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl, or C_{1-4} alkyl optionally substituted with 1-3 F or 1-3 deuterium; or

(viii) wherein n2 is 2, one R^b is C_{1-4} alkyl optionally substituted with 1-3 F or 1-3 deuterium, C_{2-4} alkenyl, or C_{2-4} alkynyl, and the other R^b is F, Cl, OH, C_{1-4} alkyl optionally substituted with 1-3 F, C_{2-4} alkenyl, or C_{2-4} alkynyl.

27. The compound of any one of claims 1 to 26, wherein ring B including substituents is:



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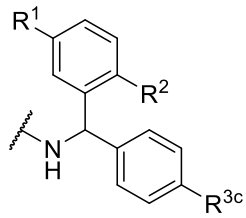
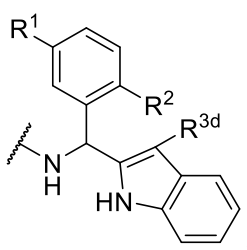
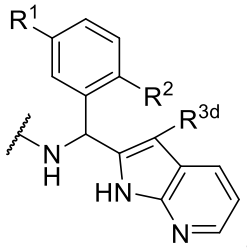
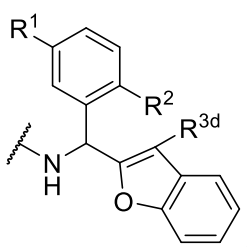
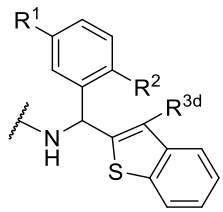
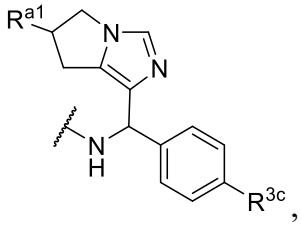
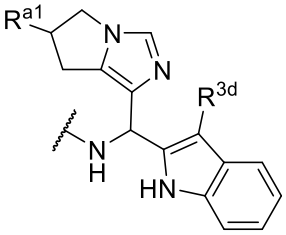
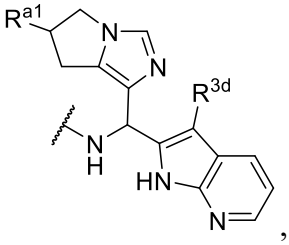
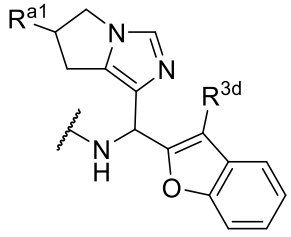
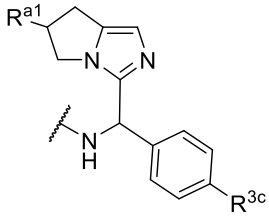
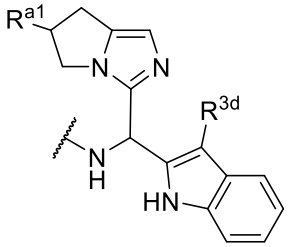
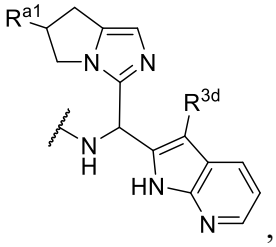
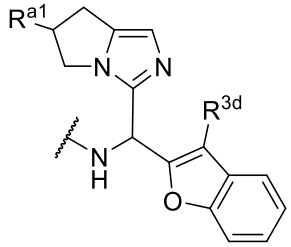
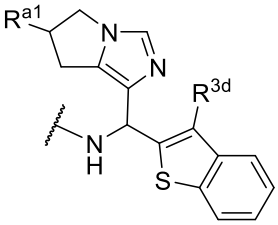
 ,  ,  ,  ,

 ,  ,  ,  ,

 ,  ,  ,  ,

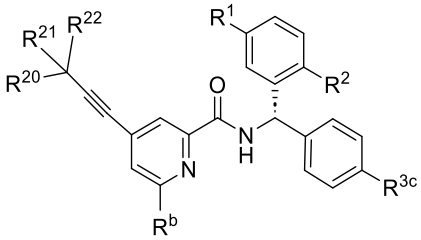
 , or  ,

wherein R^{3c} is hydrogen, deuterium, halogen, OH, cyano, C_{3-6} cycloalkyl, or C_{1-4} alkyl, wherein the alkyl and cycloalkyl are optionally substituted with 1-3 deuterium or halogen; and

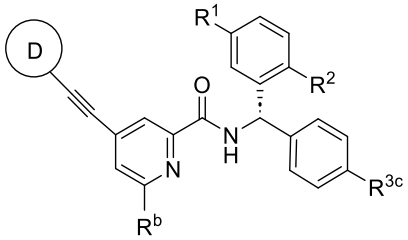
R^{3d} is hydrogen, deuterium, halogen, OH, cyano, or C_{1-4} alkyl optionally substituted with 1-3 deuterium or halogen.

29. The compound of any one of claims 1 to 28, which is a compound of formula Y1-1, Y1-2, Y1-3, Y1-4, Y1-5, Y1-6, Y1-7, Y1-8, Y1-9, Y1-10, Y1-11, Y1-12, Y1-13, Y1-14, Y1-15, Y1-16, Y1-17, Y1-18, Y1-19, Y1-20, Y1-21, Y1-22, Y1-23, Y1-24, Y1-25, Y1-26, Y1-27, Y1-28, Y2-1, Y2-2, Y2-3, Y2-4, Y2-5, Y2-6, Y2-7, Y2-8, Y2-9, Y2-10, Y2-11, Y2-12, Y2-13, Y2-14, Y2-15, Y2-16, Y2-17, Y2-18, Y2-

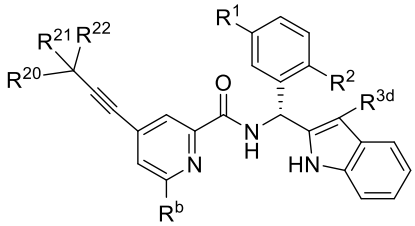
19, Y2-20, Y2-21, Y2-22, Y2-23, Y2-24, Y3-1, Y3-2, Y3-3, Y3-4, Y3-5, Y3-6, Y3-7, Y3-8, Y3-9, Y3-10, Y3-11, Y3-12, Y3-13, Y3-14, Y3-15, Y3-16, Y3-17, Y3-18, Y3-19, Y3-20, Y3-21, Y3-22, Y3-23, or Y3-24:



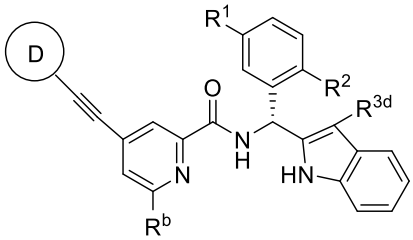
Formula Y1-1,



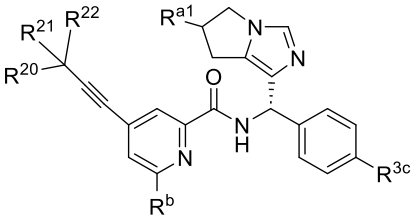
Formula Y1-2,



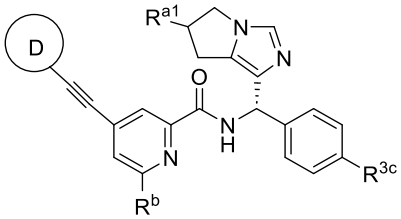
Formula Y1-3,



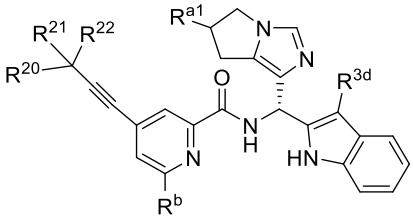
Formula Y1-4,



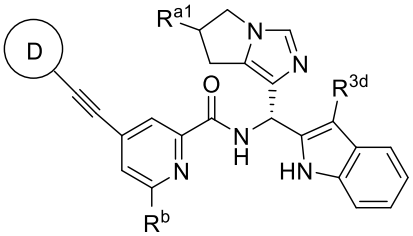
Formula Y1-5,



Formula Y1-6,



Formula Y1-7,



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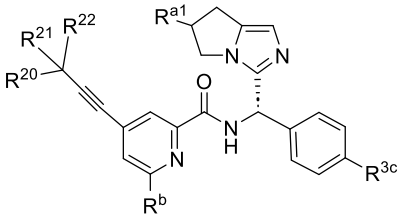
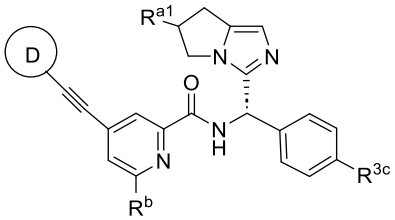
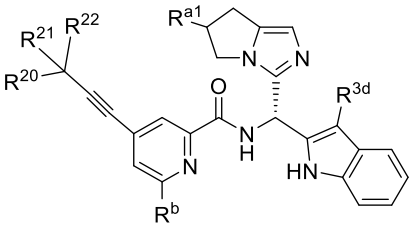


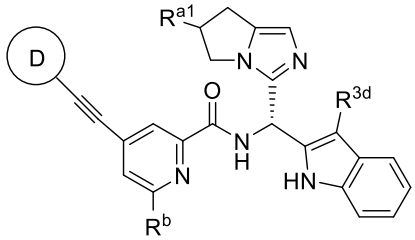
Formula Y1-9,



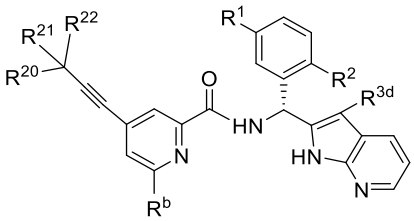
Formula Y1-10,



Formula Y1-11,



Formula Y1-12,



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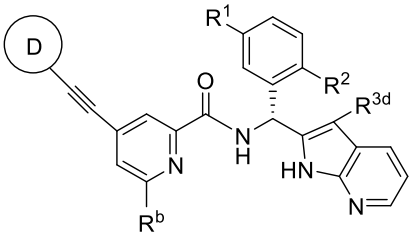

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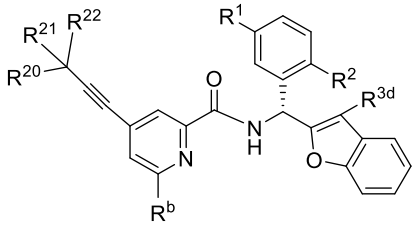

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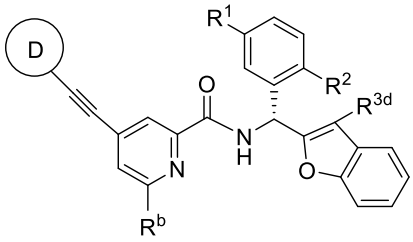

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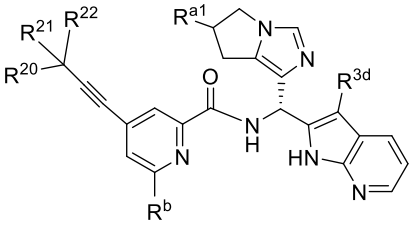

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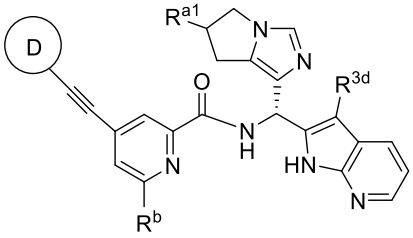

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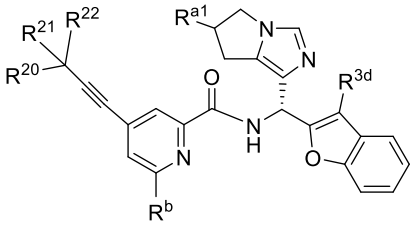

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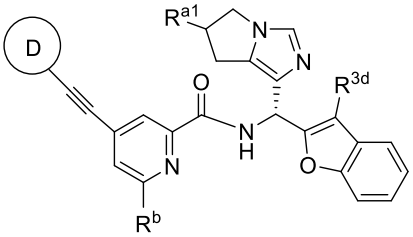

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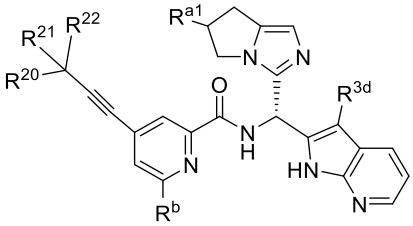

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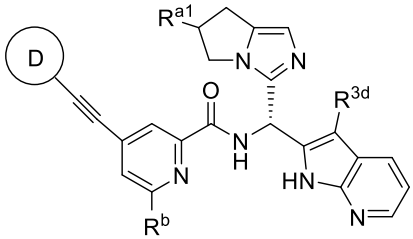

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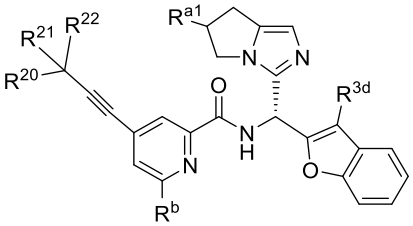

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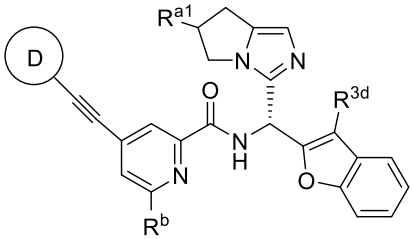

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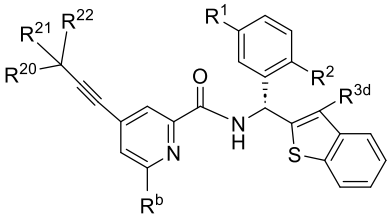

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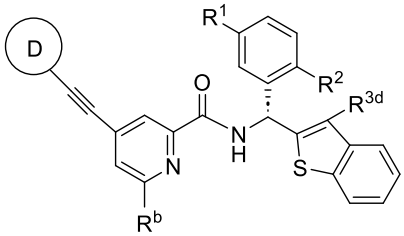

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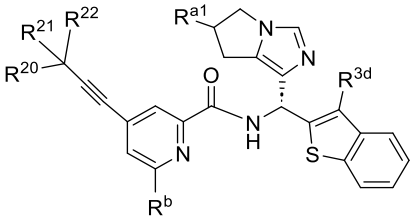

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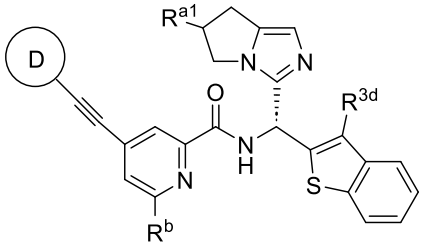

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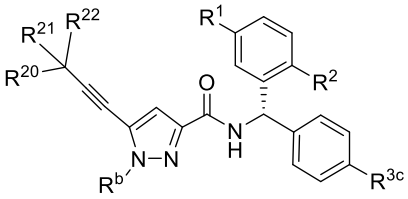

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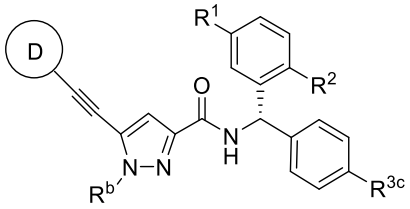

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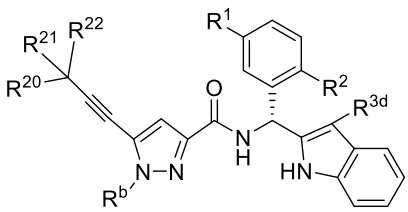

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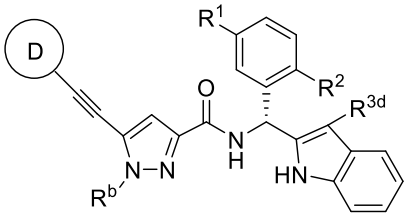

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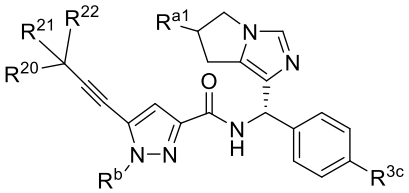
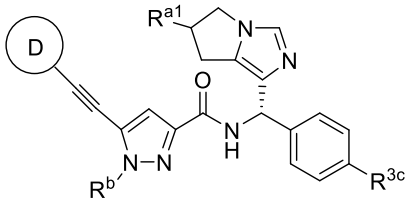


Formula Y2-5,



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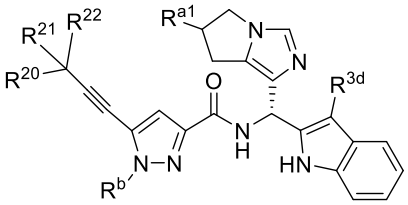

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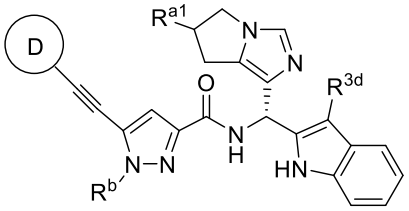

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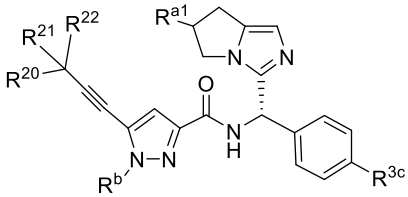

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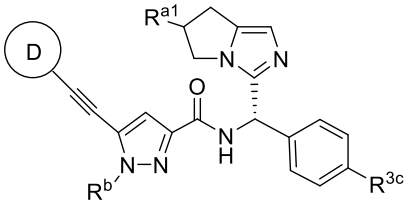

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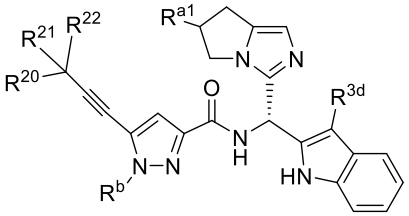

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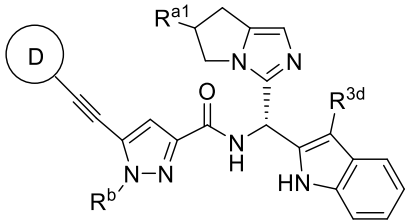

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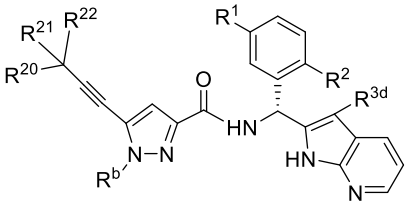

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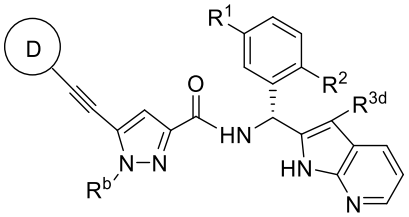

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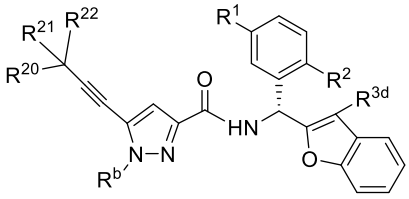

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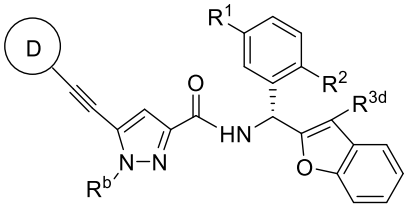

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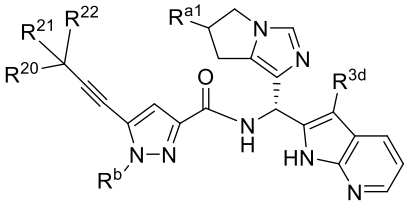

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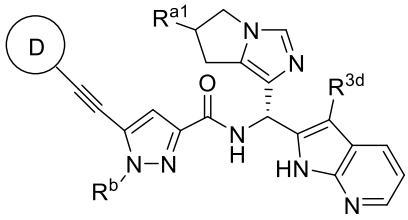

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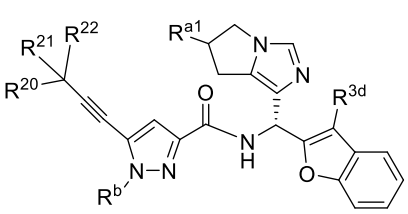

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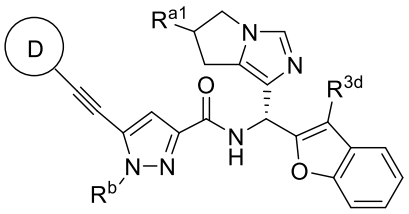

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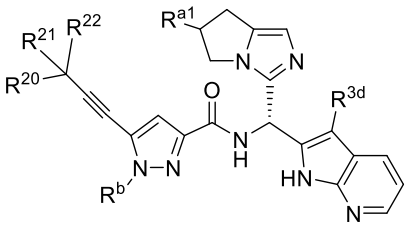

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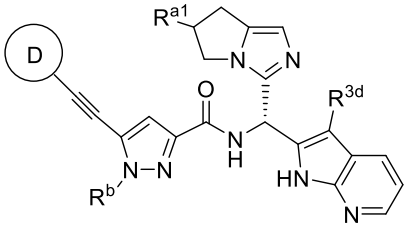

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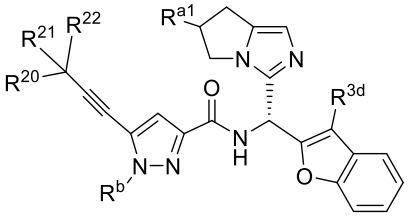

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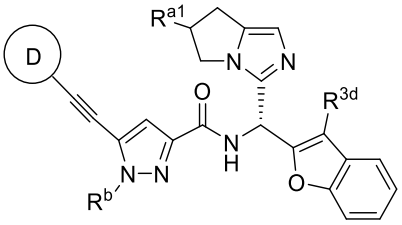

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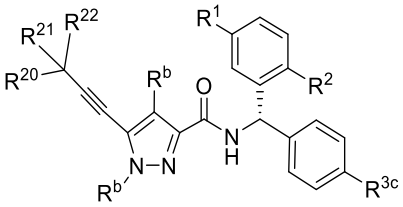

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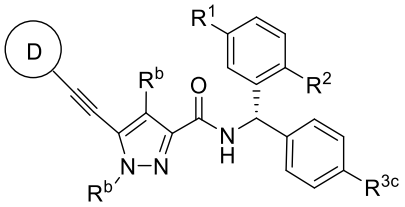

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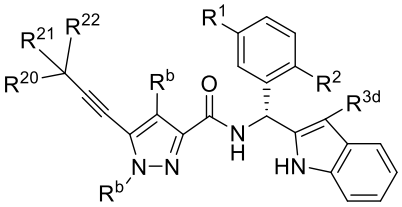

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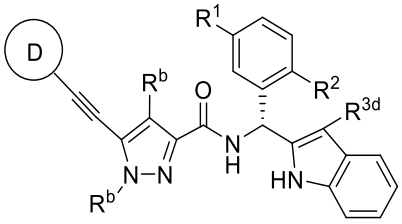

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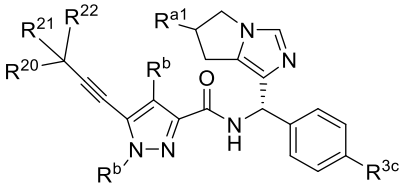

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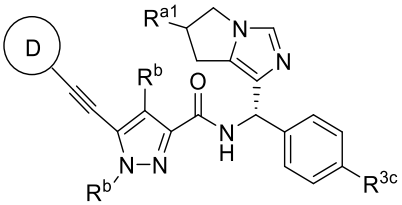

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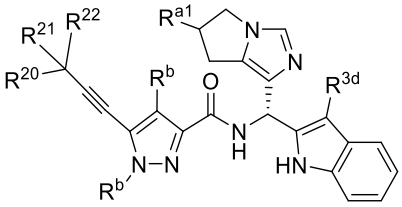

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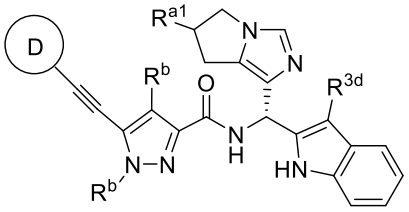

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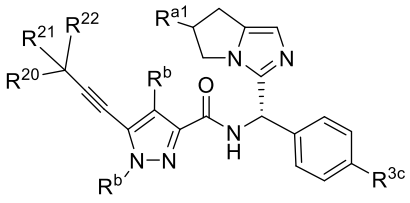

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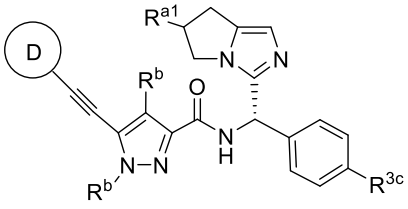

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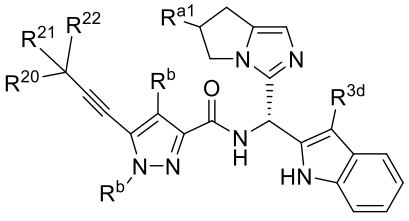

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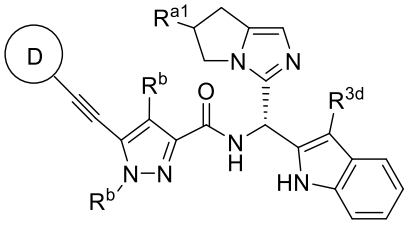

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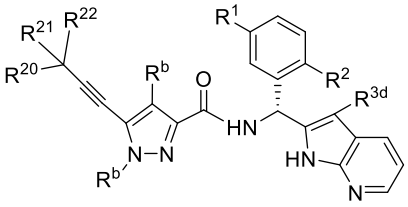

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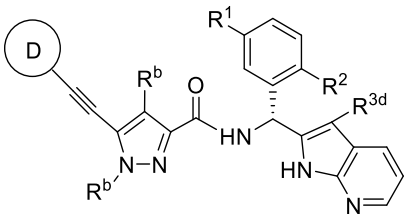

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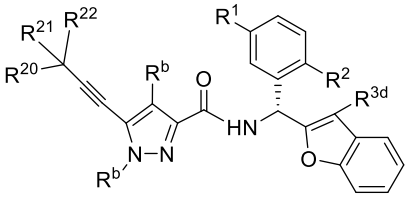

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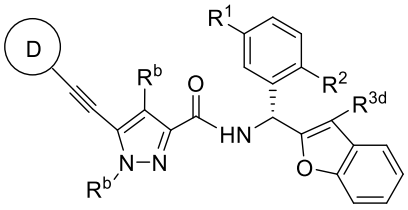

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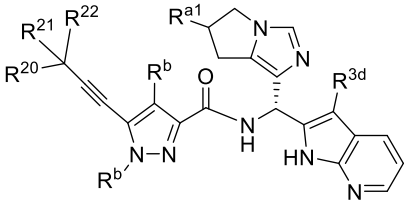

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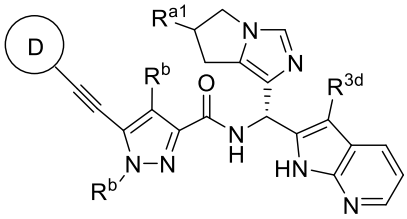

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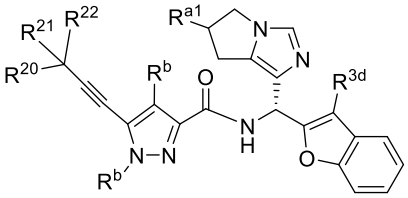

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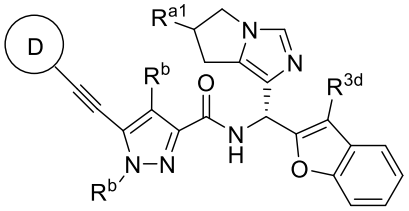

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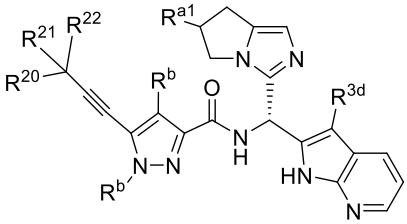

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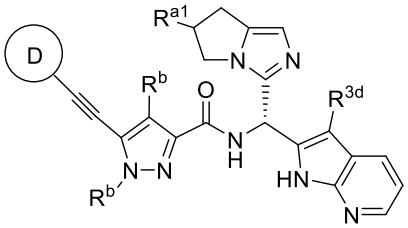

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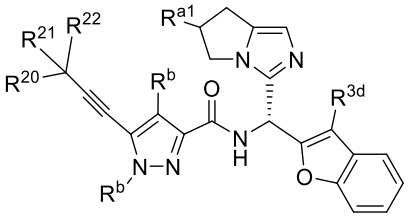

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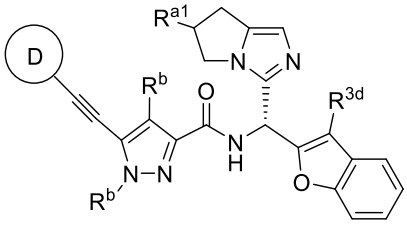

Formula Y3-24,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein R^{3c} is hydrogen, deuterium, halogen, OH, cyano, C_{3-6} cycloalkyl, or C_{1-4} alkyl, wherein the alkyl and cycloalkyl are optionally substituted with 1-3 deuterium or halogen; and

R^{3d} is hydrogen, deuterium, halogen, OH, cyano, or C_{1-4} alkyl optionally substituted with 1-3 deuterium or halogen; optionally

wherein R^{3d} is hydrogen or F.

30. A compound in Table 1, Table 1A, or Examples 1 to 1080, or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof.

31. A pharmaceutical composition comprising the compound of any one of claims 1 to 30, and a pharmaceutically acceptable excipient.

32. Use of the compound of any one of claims 1 to 30, or the pharmaceutical composition of claim 31 in the manufacture of medicament for treating cancer in a subject having the cancer; optionally

(i) wherein the cancer is lung cancer, colon cancer, breast cancer, endometrial cancer, thyroid cancer, glioma, squamous cell carcinoma, or prostate cancer;

(ii) wherein the cancer is non-small cell lung cancer (NSCLC);

(iii) wherein the cancer is characterized as having at least one EGFR mutation selected from L858R, T790M, and C797S;.

(iv) wherein the cancer is cancer with brain metastasis; or

(v) wherein the compound crosses blood-brain barrier (BBB) of the subject after administration.

33. Use of the compound of any one of claims 1 to 30, or the pharmaceutical composition of claim 31 in the manufacture of medicament for inhibiting a mutant EGFR in a subject in need thereof; optionally wherein the mutant EGFR has at least one EGFR mutation selected from L858R, T790M, and C797S.