$-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$;

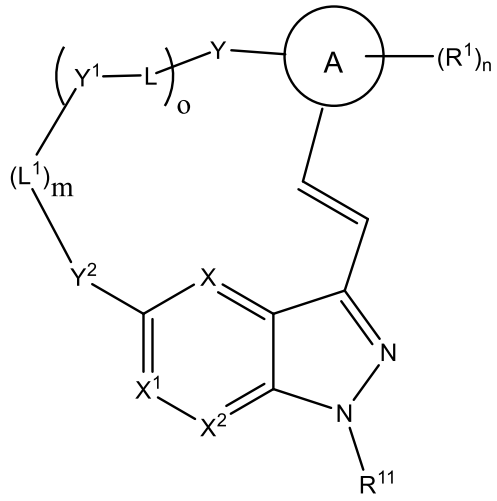
[022] each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from the group consisting of H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, C_1-C_6 alkylene-C_6-C_{10} aryl, and 5- to 10-membered heteroaryl;

[023] m is 0, 1, 2, 3, or 4;

[024] n is 0, 1, 2, 3, or 4, and

[025] o is 0, 1, 2, or 3.

[026] In another ~~aspect~~example, the disclosure relates to a compound of the formula Ia, or a pharmaceutically acceptable salt thereof,



Ia

[027] wherein

[028] A is a ring selected from 5- to 10-membered heteroarylene or C_6-C_{10} arylene;

[029] X is $C(R^2)$ or N;

[030] X^1 is $C(R^3)$ or N;

[031] X^2 is $C(R^4)$ or N;

[032] Y is O, $N(R^5)C(O)$, $C(O)N(R^5)$, $N(R^6)$, $N(R^5)S(O)$, $S(O)N(R^5)$, $N(R^5)S(O)_2$, $S(O)_2N(R^5)$, S, S(O), $S(O)_2$, or Y is absent;

[033] each Y^1 is independently O, $C(O)N(R^7)$, $N(R^7)C(O)$, $N(R^8)$, $N(R^7)S(O)$, $S(O)N(R^7)$, $N(R^7)S(O)_2$, $S(O)_2N(R^7)$, S, S(O), $S(O)_2$, or absent;

[034] Y^2 is O, $C(O)N(R^9)$, $N(R^9)C(O)$, $N(R^{10})$, $N(R^9)S(O)$, $S(O)N(R^9)$, $N(R^9)S(O)_2$, $S(O)_2N(R^9)$, S, S(O), $S(O)_2$, or Y^2 is absent;

[035] each L is independently a C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5-

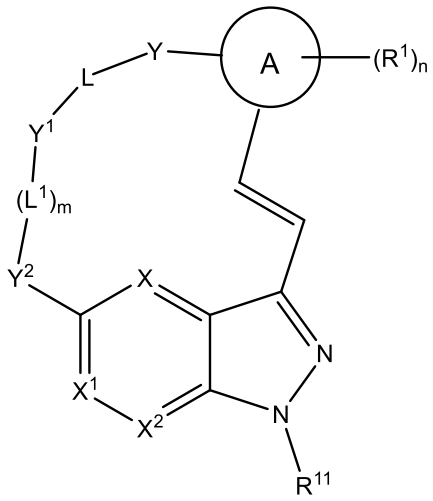
to 7-membered heterocycloalkyl, C_6-C_{10} aryl, C_1-C_6 alkylene-C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or C_1-C_6 alkylene-5- to 10-membered heteroaryl is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OH, -OC_1-C_6 alkyl, -OC(O)-(H or C_1-C_6 alkyl), -OC(O)N(H or C_1-C_6 alkyl)$_2$, -OC(O)N(C_2-C_6 alkylene), -OS(O)-(H or C_1-C_6 alkyl), -OS(O)$_2$-(H or C_1-C_6 alkyl), -OS(O)N(H or C_1-C_6 alkyl)$_2$, -OS(O)N(C_2-C_6 alkylene), -OS(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -OS(O)$_2$N(C_2-C_6 alkylene), -S(H or C_1-C_6 alkyl), -S(O)(H or C_1-C_6 alkyl), -S(O)$_2$(H or C_1-C_6 alkyl), -S(O)N(H or C_1-C_6 alkyl)$_2$, -S(O)N(C_2-C_6 alkylene), -S(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)$_2$, -N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)C(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)O(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)C(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)$_2$(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)$_2$N(C_2-C_6 alkylene), -C(O)-(H or C_1-C_6 alkyl), -C(O)O(H or C_1-C_6 alkyl), -C(O)N(C_2-C_6 alkylene), -P(H or C_1-C_6 alkyl)$_2$, -P(C_2-C_6 alkylene), -P(O)(H or C_1-C_6 alkyl)$_2$, -P(O)(C_2-C_6 alkylene), -P(O)$_2$(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$(C_2-C_6 alkylene), -P(O)N(H or C_1-C_6 alkyl)$_2$, -P(O)N(C_2-C_6 alkylene), -P(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$N(C_2-C_6 alkylene), -P(O)O(H or C_1-C_6 alkyl), -P(O)$_2$O(H or C_1-C_6 alkyl), -CN, or -NO_2;

[041] m is 0, 1, 2, 3, or 4;

[042] n is 0, 1, 2, 3, or 4; and

[043] o is 0, 1, 2, or 3.

[044] In another ~~aspect~~example, the disclosure relates to a compound of the formula I, or a pharmaceutically acceptable salt thereof,

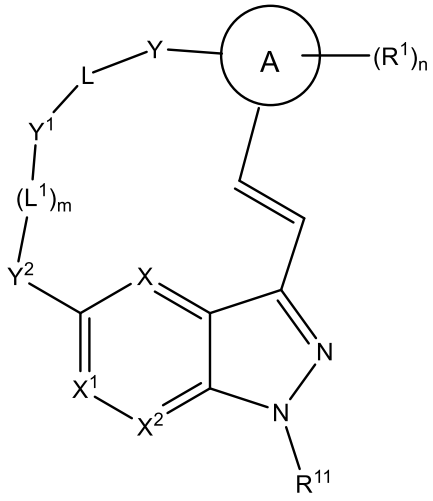


I

[045] wherein

[060] n is 0, 1, 2, 3, or 4.

[061] In another ~~aspect~~example, the disclosure relates to a compound of the formula I, or a pharmaceutically acceptable salt thereof,



I

[062] wherein

[063] A is a ring selected from 5- to 10-membered heteroarylene or C_6-C_{10} arylene;

[064] X is $C(R^2)$ or N;

[065] X^1 is $C(R^3)$ or N;

[066] X^2 is $C(R^4)$ or N;

[067] Y is O, $N(R^5)C(O)$, $N(R^5)$, $N(R^6)$, S, S(O), $S(O)_2$, or Y is absent;

[068] Y^1 is O, $C(O)N(R^7)$, $N(R^8)$, S, S(O), $S(O)_2$, or Y^1 is absent;

[069] Y^2 is O, $C(O)N(R^9)$, $N(R^{10})$, S, S(O), $S(O)_2$, or Y^2 is absent;

[070] L is a C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^aR^b$, $-S(O)_2NR^aR^b$, $-OS(O)NR^aR^b$, $-OS(O)_2NR^aR^b$, $-NR^aR^b$, $-NR^aC(O)R^b$, $-NR^aC(O)OR^b$, $-NR^aC(O)NR^aR^b$, $-NR^aS(O)R^b$, $-NR^aS(O)_2R^b$, $-NR^aS(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-PR^aR^b$, $-P(O)R^aR^b$, $-P(O)_2R^aR^b$, $-P(O)NR^aR^b$, $-P(O)_2NR^aR^b$, $-P(O)OR^a$, $-P(O)_2OR^a$, -CN, or $-NO_2$;

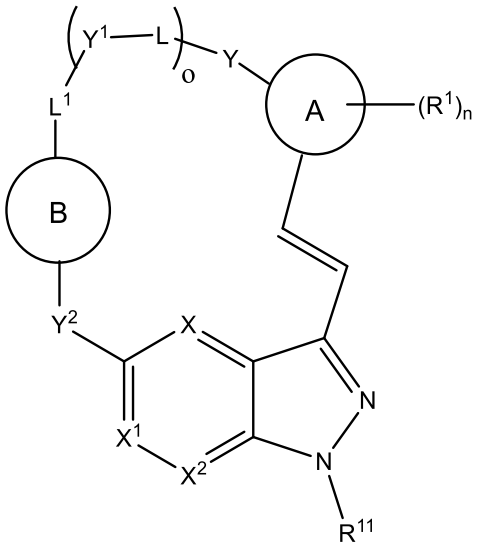
[071] each L^1, when present, is independently C_1-C_6 alkylene or a ring B selected from the group consisting of 5- to 10-membered heteroarylene, 3- to 10-membered heterocycloalkylene, 3- to 6-membered cycloalkylene, and C_6-C_{10} arylene, wherein each hydrogen atom in 5- to 10-membered heteroarylene, 3- to 10-membered heterocycloalkylene, C_6-C_{10} arylene, and C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-

alkyl)$_2$, -P(O)N(C_2-C_6 alkylene), -P(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$N(C_2-C_6 alkylene), -P(O)O(H or C_1-C_6 alkyl), -P(O)$_2$O(H or C_1-C_6 alkyl), -CN, or -NO_2;

[076] m is 0, 1, 2, 3, or 4; and

[077] n is 0, 1, 2, 3, or 4.

[078] In another ~~aspect~~example, the disclosure provides a compound of the formula IIa, or a pharmaceutically acceptable salt thereof,



IIa

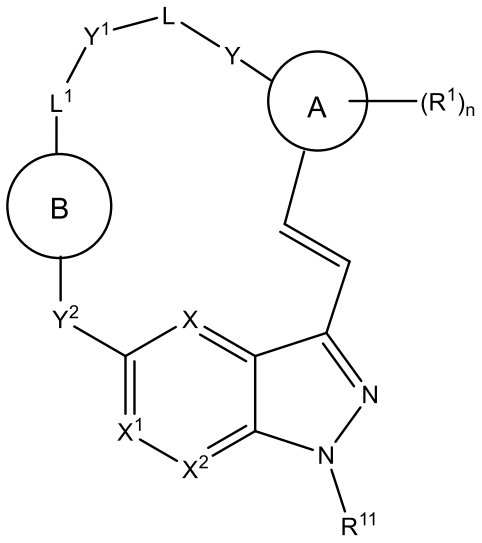
[079] wherein R^1, R^{11}, A, L, X, X^1, X^2, Y, Y^1, Y^2, n, and o are as described herein;

[080] ring B is a 5- to 10-membered heteroarylene, 3- to 10-membered heterocycloalkylene, or C_6-C_{10} arylene, wherein each hydrogen atom in 3- to 10-membered heteroarylene, 5- to 10-membered heterocycloalkylene, and C_6-C_{10} arylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^c, -$OC(O)R^c$, -$OC(O)NR^cR^d$, -$OC(=N)NR^cR^d$, -$OS(O)R^c$, -$OS(O)_2R^c$, -$OS(O)NR^cR^d$, -$OS(O)_2NR^cR^d$, -SR^c, -$S(O)R^c$, -$S(O)_2R^c$, -$S(O)NR^cR^d$, -$S(O)_2NR^cR^d$, -NR^cR^d, -$NR^cC(O)R^d$, -$N(C(O)R^c)(C(O)R^d)$, -$NR^cC(O)OR^d$, -$NR^cC(O)NR^cR^d$, -$NR^cC(=N)NR^cR^d$, -$NR^cS(O)R^d$, -$NR^cS(O)_2R^d$, -$NR^cS(O)NR^cR^d$, -$NR^cS(O)_2NR^cR^d$, -$C(O)R^c$, -$C(O)OR^c$, -$C(O)NR^cR^d$, -$C(=N)NR^cR^d$, -PR^cR^d, -$P(O)R^cR^d$, -$P(O)_2R^cR^d$, -$P(O)NR^cR^d$, -$P(O)_2NR^cR^d$, -$P(O)OR^c$, -$P(O)_2OR^c$, -CN, or -NO_2; and

[081] L^1 is C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^c, -$OC(O)R^c$, -$OC(O)NR^cR^d$, -$OC(=N)NR^cR^d$, -$OS(O)R^c$, -$OS(O)_2R^c$, -$OS(O)NR^cR^d$, -$OS(O)_2NR^cR^d$, -SR^c, -$S(O)R^c$, -$S(O)_2R^c$, -$S(O)NR^cR^d$, -$S(O)_2NR^cR^d$, -NR^cR^d, -$NR^cC(O)R^d$,

-N(C(O)R^c)(C(O)R^d), -NR^{c}C(O)OR^d, -NR^{c}C(O)NR^{c}R^d, -NR^{c}C(=N)NR^{c}R^d, -NR^{c}S(O)R^d, -NR^{c}S(O)$_2$R^d, -NR^{c}S(O)NR^{c}R^d, -NR^{c}S(O)$_2$NR^{c}R^d, -C(O)R^c, -C(O)OR^c, -C(O)NR^{c}R^d, -C(=N)NR^{c}R^d, -PR^{c}R^d, -P(O)R^{c}R^d, -P(O)$_2$R^{c}R^d, -P(O)NR^{c}R^d, -P(O)$_2$NR^{c}R^d, -P(O)OR^c, -P(O)$_2$OR^c, -CN, or -NO$_2$.

[082] In another ~~aspect~~example, the disclosure provides a compound of the formula II, or a pharmaceutically acceptable salt thereof,



II

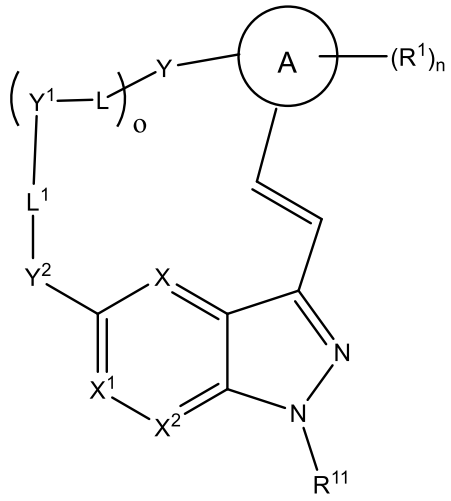
[083] wherein R^1, R^{11}, A, L, X, X^1, X^2, Y, Y^1, Y^2, and n are as described herein;

[084] ring B is a 5- to 10-membered heteroarylene, 3- to 10-membered heterocycloalkylene, or C$_6$-C$_{10}$ arylene, wherein each hydrogen atom in 3- to 10-membered heteroarylene, 5- to 10-membered heterocycloalkylene, and C$_6$-C$_{10}$ arylene is independently optionally substituted by deuterium, halogen, C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, C$_3$-C$_6$ cycloalkyl, 3- to 7-membered heterocycloalkyl, C$_6$-C$_{10}$ aryl, 5- to 10-membered heteroaryl, -OR^c, -OC(O)R^c, -OC(O)NR^{c}R^d, -OC(=N)NR^{c}R^d, -OS(O)R^c, -OS(O)$_2$R^c, -OS(O)NR^{c}R^d, -OS(O)$_2$NR^{c}R^d, -SR^c, -S(O)R^c, -S(O)$_2$R^c, -S(O)NR^{c}R^d, -S(O)$_2$NR^{c}R^d, -NR^{c}R^d, -NR^{c}C(O)R^d, -N(C(O)R^c)(C(O)R^d), -NR^{c}C(O)OR^d, -NR^{c}C(O)NR^{c}R^d, -NR^{c}C(=N)NR^{c}R^d, -NR^{c}S(O)R^d, -NR^{c}S(O)$_2$R^d, -NR^{c}S(O)NR^{c}R^d, -NR^{c}S(O)$_2$NR^{c}R^d, -C(O)R^c, -C(O)OR^c, -C(O)NR^{c}R^d, -C(=N)NR^{c}R^d, -PR^{c}R^d, -P(O)R^{c}R^d, -P(O)$_2$R^{c}R^d, -P(O)NR^{c}R^d, -P(O)$_2$NR^{c}R^d, -P(O)OR^c, -P(O)$_2$OR^c, -CN, or -NO$_2$; and

[085] L^1 is C$_1$-C$_6$ alkylene, wherein each hydrogen atom in C$_1$-C$_6$ alkylene is independently optionally substituted by deuterium, halogen, C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, C$_3$-C$_6$ cycloalkyl, 3- to 7-membered heterocycloalkyl, C$_6$-C$_{10}$ aryl, 5- to 10-membered heteroaryl, -OR^c, -OC(O)R^c, -OC(O)NR^{c}R^d, -OC(=N)NR^{c}R^d, -OS(O)R^c, -OS(O)$_2$R^c, -OS(O)NR^{c}R^d,

$-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$.

[086] In another ~~aspect~~example, the disclosure provides a compound of the formula IIIa, or a pharmaceutically acceptable salt thereof,

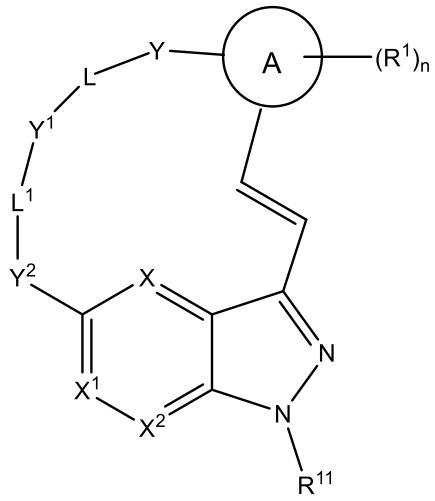


IIIa

[087] wherein R^1, R^{11}, A, L, X, X^1, X^2, Y, Y^1, Y^2, n, and o are as described herein; and.

[088] L^1 is C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^c$, $-OC(O)R^c$, $-OC(O)NR^cR^d$, $-OC(=N)NR^cR^d$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)NR^cR^d$, $-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$.

[089] In another ~~aspect~~example, the disclosure provides a compound of the formula III, or a pharmaceutically acceptable salt thereof,

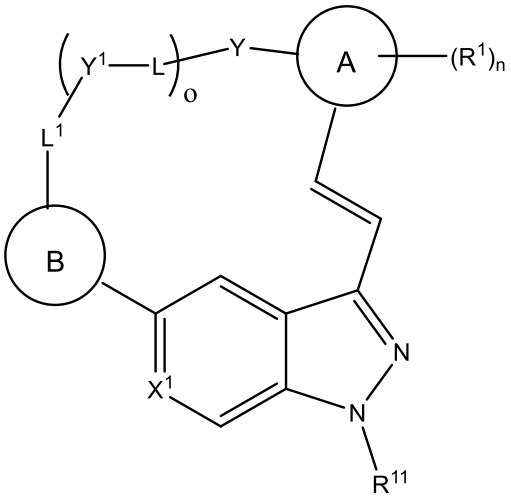


III

[090] wherein R^1, R^{11}, A, L, X, X^1, X^2, Y, Y^1, Y^2, and n are as described herein; and.

[091] L^1 is C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^c$, $-OC(O)R^c$, $-OC(O)NR^cR^d$, $-OC(=N)NR^cR^d$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)NR^cR^d$, $-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$.

[092] In another ~~aspect~~example, the disclosure relates to a compound of the formula IVa, or a pharmaceutically acceptable salt thereof,



IVa

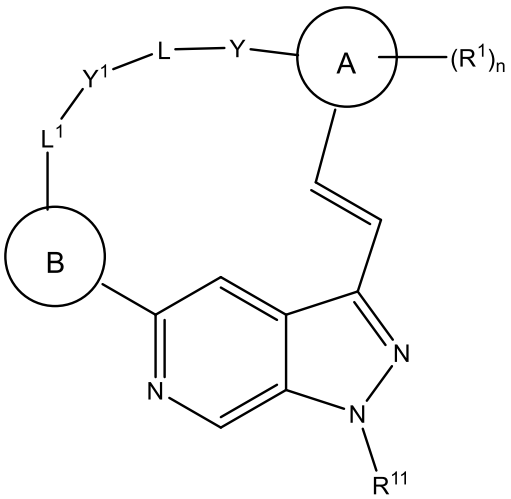
[093] wherein

alkyl)C(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)$_2$(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)$_2$N(C_2-C_6 alkylene), -C(O)-(H or C_1-C_6 alkyl), -C(O)O(H or C_1-C_6 alkyl), -C(O)N(C_2-C_6 alkylene), -P(H or C_1-C_6 alkyl)$_2$, -P(C_2-C_6 alkylene), -P(O)(H or C_1-C_6 alkyl)$_2$, -P(O)(C_2-C_6 alkylene), -P(O)$_2$(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$(C_2-C_6 alkylene), -P(O)N(H or C_1-C_6 alkyl)$_2$, -P(O)N(C_2-C_6 alkylene), -P(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$N(C_2-C_6 alkylene), -P(O)O(H or C_1-C_6 alkyl), -P(O)$_2$O(H or C_1-C_6 alkyl), -CN, or -NO_2;

[0105] n is 0, 1, 2, 3, or 4; and

[0106] o is 0, 1, 2, or 3.

[0107] In another ~~aspect~~example, the disclosure relates to a compound of the formula IV, or a pharmaceutically acceptable salt thereof,



IV

[0108] wherein

[0109] ring A is a ring selected from 5- to 10-membered heteroarylene or C_6-C_{10} arylene;

[0110] Y is O, N(R^5)C(O), S, S(O), or S(O)$_2$;

[0111] Y^1 is O, S, S(O), or S(O)$_2$;

[0112] L is a C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium;

[0113] L^1 is absent, or L^1 is C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium or C_1-C_6 alkyl;

[0114] ring B is a 5- to 10-membered heteroarylene or C_6-C_{10} arylene, wherein each hydrogen atom in 3- to 10-membered heteroarylene or C_6-C_{10} arylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^c,

substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OH, -OC_1-C_6 alkyl, -OC(O)-(H or C_1-C_6 alkyl), -OC(O)N(H or C_1-C_6 alkyl)$_2$, -OC(O)N(C_2-C_6 alkylene), -OS(O)-(H or C_1-C_6 alkyl), -OS(O)$_2$-(H or C_1-C_6 alkyl), -OS(O)N(H or C_1-C_6 alkyl)$_2$, -OS(O)N(C_2-C_6 alkylene), -OS(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -OS(O)$_2$N(C_2-C_6 alkylene), -S(H or C_1-C_6 alkyl), -S(O)(H or C_1-C_6 alkyl), -S(O)$_2$(H or C_1-C_6 alkyl), -S(O)N(H or C_1-C_6 alkyl)$_2$, -S(O)N(C_2-C_6 alkylene), -S(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)$_2$, -N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)C(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)O(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)C(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)$_2$(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)$_2$N(C_2-C_6 alkylene), -C(O)-(H or C_1-C_6 alkyl), -C(O)O(H or C_1-C_6 alkyl), -C(O)N(C_2-C_6 alkylene), -P(H or C_1-C_6 alkyl)$_2$, -P(C_2-C_6 alkylene), -P(O)(H or C_1-C_6 alkyl)$_2$, -P(O)(C_2-C_6 alkylene), -P(O)$_2$(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$(C_2-C_6 alkylene), -P(O)N(H or C_1-C_6 alkyl)$_2$, -P(O)N(C_2-C_6 alkylene), -P(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$N(C_2-C_6 alkylene), -P(O)O(H or C_1-C_6 alkyl), -P(O)$_2$O(H or C_1-C_6 alkyl), -CN, or -NO_2; and

[0118] n is 0, 1, 2, 3, or 4.

[0119] In certain ~~embodiments of the above aspects~~examples, the compound of Formula (Ia)-(IXa) or (I)-(IX) is a compound selected from those species described or exemplified in the detailed description below.

[0120a] In another aspect, there is provided a pharmaceutical composition comprising a compound of any one of the preceding claims, and optionally one or more excipients.

[0120] In further ~~aspects~~examples, the disclosure relates to a pharmaceutical composition comprising at least one compound of Formula (Ia)-(IXa) or (I)-(IX) or a pharmaceutically acceptable salt thereof. Pharmaceutical compositions according to the disclosure may further comprise a pharmaceutically acceptable excipient.

[0121] In further ~~aspects~~examples, the disclosure relates to a compound of Formula (Ia)-(IXa) or (I)-(IX), or a pharmaceutically acceptable salt thereof, for use as a medicament.

[0122] In further ~~aspects~~examples, the disclosure relates to a method of treating disease, such as cancer comprising administering to a subject in need of such treatment an effective amount of at least one compound of Formula (Ia)-(IXa) or (I)-(IX), or a pharmaceutically acceptable salt thereof.

[0122a] In another aspect, there is provided the use of a compound as defined above in the manufacture of a medicament for the treatment of disease in a subject.

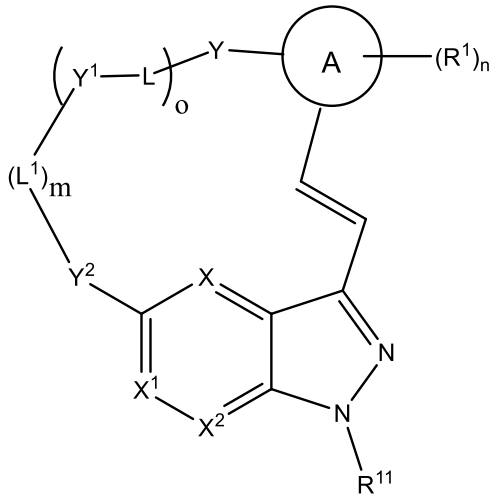
[0123] In further ~~aspects~~examples, the disclosure relates to use of a compound of Formula (Ia)-(IXa) or (I)-(IX), or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of disease, such as cancer, and the use of such compounds and salts for treatment of such diseases.

[0124] In further ~~aspects~~examples, the disclosure relates to a method of inhibiting a tyrosine kinase, such as EGFR, comprising contacting a cell comprising one or more of kinase with an effective

amount of at least one compound of Formula (Ia)-(IXa) or (I)-(IX), or a pharmaceutically acceptable salt thereof, and/or with at least one pharmaceutical composition of the disclosure, wherein the contacting is *in vitro, ex vivo,* or *in vivo*.

[0125] Additional ~~embodiments~~examples, features, and advantages of the disclosure will be apparent from the following detailed description and through practice of the disclosure. The compounds of the present disclosure can be described as ~~embodiments~~examples in any of the following enumerated clauses. It will be understood that any of the examples~~embodiments~~ described herein can be used in connection with any other ~~embodiments~~ examples described herein to the extent that the embodiments do not contradict one another.

[0126] 1. A compound of the formula Ia, or a pharmaceutically acceptable salt thereof,



Ia

[0127] wherein

[0128] A is a ring selected from 5- to 10-membered heteroarylene or C_6-C_{10} arylene;

[0129] X is $C(R^2)$ or N;

[0130] X^1 is $C(R^3)$ or N;

[0131] X^2 is $C(R^4)$ or N;

[0132] Y is O, $N(R^5)C(O)$, $C(O)N(R^5)$, $N(R^6)$, $N(R^5)S(O)$, $S(O)N(R^5)$, $N(R^5)S(O)_2$, $S(O)_2N(R^5)$, S, S(O), $S(O)_2$, or Y is absent;

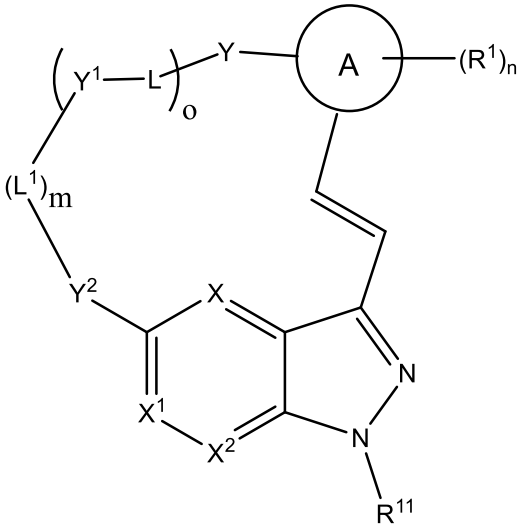
[0133] each Y^1 is independently O, $C(O)N(R^7)$, $N(R^7)C(O)$, $N(R^8)$, $N(R^7)S(O)$, $S(O)N(R^7)$, $N(R^7)S(O)_2$, $S(O)_2N(R^7)$, S, S(O), $S(O)_2$, or absent;

[0134] Y^2 is O, $C(O)N(R^9)$, $N(R^9)C(O)$, $N(R^{10})$, $N(R^9)S(O)$, $S(O)N(R^9)$, $N(R^9)S(O)_2$, $S(O)_2N(R^9)$, S, S(O), $S(O)_2$, or Y^2 is absent;

[0135] each L is independently a C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5-

WHAT IS CLAIMED IS:

1. A compound of the formula Ia



Ia

wherein

A is a ring selected from 5- to 10-membered heteroarylene or C_6-C_{10} arylene;

X is $C(R^2)$ or N;

X^1 is $C(R^3)$ or N;

X^2 is $C(R^4)$ or N;

Y is O, $N(R^5)C(O)$, $C(O)N(R^5)$, $N(R^6)$, $N(R^5)S(O)$, $S(O)N(R^5)$, $N(R^5)S(O)_2$, $S(O)_2N(R^5)$, S, S(O), $S(O)_2$, or Y is absent;

each Y^1 is independently O, $C(O)N(R^7)$, $N(R^7)C(O)$, $N(R^8)$, $N(R^7)S(O)$, $S(O)N(R^7)$, $N(R^7)S(O)_2$, $S(O)_2N(R^7)$, S, S(O), $S(O)_2$, or absent;

Y^2 is O, $C(O)N(R^9)$, $N(R^9)C(O)$, $N(R^{10})$, $N(R^9)S(O)$, $S(O)N(R^9)$, $N(R^9)S(O)_2$, $S(O)_2N(R^9)$, S, S(O), $S(O)_2$, or Y^2 is absent;

each L is independently a C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^aR^b$, $-S(O)_2NR^aR^b$, $-OS(O)NR^aR^b$, $-OS(O)_2NR^aR^b$, $-NR^aR^b$, $-NR^aC(O)R^b$, $-NR^aC(O)OR^b$, $-NR^aC(O)NR^aR^b$, $-NR^aS(O)R^b$, $-NR^aS(O)_2R^b$, $-NR^aS(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-PR^aR^b$, $-P(O)R^aR^b$, $-P(O)_2R^aR^b$, $-P(O)NR^aR^b$, $-P(O)_2NR^aR^b$, $-P(O)OR^a$, $-P(O)_2OR^a$, -CN, or $-NO_2$; or optionally two hydrogen atoms on one carbon atom in C_1-C_6 alkylene are optionally substituted by a C_2-C_5 alkylene to provide a C_3-C_6 cycloalkylene; or optionally two hydrogen atoms on two carbon atoms in C_1-C_6 alkylene are optionally substituted by a C_1-C_4 alkylene to provide a C_3-C_6 cycloalkylene;

or optionally one hydrogen atom on one carbon atom in C_1-C_6 alkylene and one of R^5, R^6, R^7, or R^8 taken together with the atoms to which they are attached combine to form a 3- to 7-membered heterocycloalkylene;

each L^1, when present, is independently C_1-C_6 alkylene or a ring B selected from the group consisting of 5- to 10-membered heteroarylene, 3- to 10-membered heterocycloalkylene, 3- to 6-membered cycloalkylene, and C_6-C_{10} arylene, wherein each hydrogen atom in 5- to 10-membered heteroarylene, 3- to 10-membered heterocycloalkylene, C_6-C_{10} arylene, and C_1-C_6 alkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^c$, $-OC(O)R^c$, $-OC(O)NR^cR^d$, $-OC(=N)NR^cR^d$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)NR^cR^d$, $-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$;

each R^1 is independently deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^aR^b$, $-S(O)_2NR^aR^b$, $-OS(O)NR^aR^b$, $-OS(O)_2NR^aR^b$, $-NR^aR^b$, $-NR^aC(O)R^b$, $-NR^aC(O)OR^b$, $-NR^aC(O)NR^aR^b$, $-NR^aS(O)R^b$, $-NR^aS(O)_2R^b$, $-NR^aS(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-PR^aR^b$, $-P(O)R^aR^b$, $-P(O)_2R^aR^b$, $-P(O)NR^aR^b$, $-P(O)_2NR^aR^b$, $-P(O)OR^a$, $-P(O)_2OR^a$, -CN, or $-NO_2$, wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl, is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^e$, $-OC(O)R^e$, $-OC(O)NR^eR^f$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)NR^eR^f$, $-OS(O)_2NR^eR^f$, $-SR^e$, $-S(O)R^e$, $-S(O)_2R^e$, $-S(O)NR^eR^f$, $-S(O)_2NR^eR^f$, $-NR^eR^f$, $-NR^eC(O)R^f$, $-NR^eC(O)OR^f$, $-NR^eC(O)NR^eR^f$, $-NR^eS(O)R^f$, $-NR^eS(O)_2R^f$, $-NR^eS(O)NR^eR^f$, $-NR^eS(O)_2NR^eR^f$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)NR^eR^f$, $-PR^eR^f$, $-P(O)R^eR^f$, $-P(O)_2R^eR^f$, $-P(O)NR^eR^f$, $-P(O)_2NR^eR^f$, $-P(O)OR^e$, $-P(O)_2OR^e$, -CN, or $-NO_2$;

each of R^2, R^3, and R^4, when present, is independently H, deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^aR^b$, $-S(O)_2NR^aR^b$, $-OS(O)NR^aR^b$, $-OS(O)_2NR^aR^b$, $-NR^aR^b$, $-NR^aC(O)R^b$, $-NR^aC(O)OR^b$, $-NR^aC(O)NR^aR^b$, $-NR^aS(O)R^b$,

$-NR^aS(O)_2R^b$, $-NR^aS(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-PR^aR^b$, $-P(O)R^aR^b$, $-P(O)_2R^aR^b$, $-P(O)NR^aR^b$, $-P(O)_2NR^aR^b$, $-P(O)OR^a$, $-P(O)_2OR^a$, -CN, or $-NO_2$, wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, and 5- to 10-membered heteroaryl, is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^e$, $-OC(O)R^e$, $-OC(O)NR^eR^f$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)NR^eR^f$, $-OS(O)_2NR^eR^f$, $-SR^e$, $-S(O)R^e$, $-S(O)_2R^e$, $-S(O)NR^eR^f$, $-S(O)_2NR^eR^f$, $-NR^eR^f$, $-NR^eC(O)R^f$, $-NR^eC(O)OR^f$, $-NR^eC(O)NR^eR^f$, $-NR^eS(O)R^f$, $-NR^eS(O)_2R^f$, $-NR^eS(O)NR^eR^f$, $-NR^eS(O)_2NR^eR^f$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)NR^eR^f$, $-PR^eR^f$, $-P(O)R^eR^f$, $-P(O)_2R^eR^f$, $-P(O)NR^eR^f$, $-P(O)_2NR^eR^f$, $-P(O)OR^e$, $-P(O)_2OR^e$, -CN, or $-NO_2$;

each of R^5, R^6, R^7, R^8, R^9, R^{10}, and R^{11}, when present, is independently H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl, wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl is independently optionally substituted by $-OR^c$, $-OC(O)R^c$, $-OC(O)NR^cR^d$, $-OC(=N)NR^cR^d$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)NR^cR^d$, $-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from the group consisting of H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, C_1-C_6 alkylene-C_6-C_{10} aryl, 5- to 10-membered heteroaryl, and C_1-C_6 alkylene-5- to 10-membered heteroaryl, or R^a and R^b or R^c and R^d or R^e and R^f, taken together with the atom to which they are attached, form a a 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, C_1-C_6 alkylene-C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or C_1-C_6 alkylene-5- to 10-membered heteroaryl is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OH, -OC_1-C_6 alkyl, -OC(O)-(H or C_1-C_6 alkyl), -OC(O)N(H or C_1-C_6 alkyl)$_2$, -OC(O)N(C_2-C_6 alkylene), -OS(O)-(H or C_1-C_6 alkyl), -OS(O)$_2$-(H or C_1-C_6 alkyl), -OS(O)N(H or C_1-C_6 alkyl)$_2$, -OS(O)N(C_2-C_6 alkylene), -OS(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -OS(O)$_2$N(C_2-C_6 alkylene), -S(H or C_1-C_6 alkyl), -S(O)(H or C_1-C_6 alkyl), -S(O)$_2$(H or C_1-C_6 alkyl), -S(O)N(H or C_1-C_6 alkyl)$_2$, -S(O)N(C_2-C_6 alkylene), -S(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)$_2$,

-N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)C(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)O(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)C(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)$_2$(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)$_2$N(C_2-C_6 alkylene), -C(O)-(H or C_1-C_6 alkyl), -C(O)O(H or C_1-C_6 alkyl), -C(O)N(C_2-C_6 alkylene), -P(H or C_1-C_6 alkyl)$_2$, -P(C_2-C_6 alkylene), -P(O)(H or C_1-C_6 alkyl)$_2$, -P(O)(C_2-C_6 alkylene), -P(O)$_2$(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$(C_2-C_6 alkylene), -P(O)N(H or C_1-C_6 alkyl)$_2$, -P(O)N(C_2-C_6 alkylene), -P(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$N(C_2-C_6 alkylene), -P(O)O(H or C_1-C_6 alkyl), -P(O)$_2$O(H or C_1-C_6 alkyl), -CN, or -NO_2;

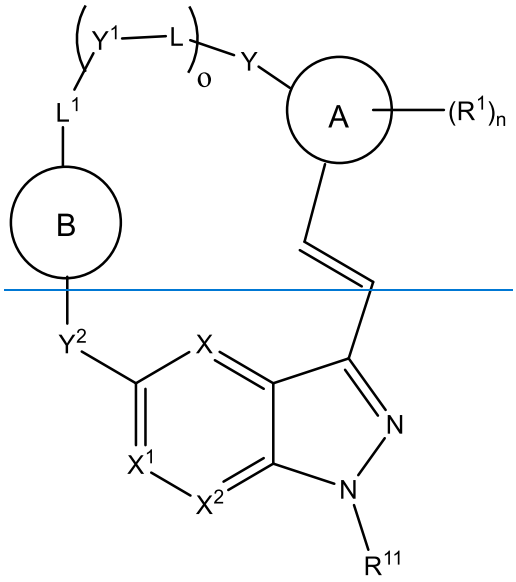
m is 0, 1, 2, 3, or 4;

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

o is 0, 1, 2, or 3;

or a pharmaceutically acceptable salt thereof.

~~2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having the formula IIa~~



~~IIa~~

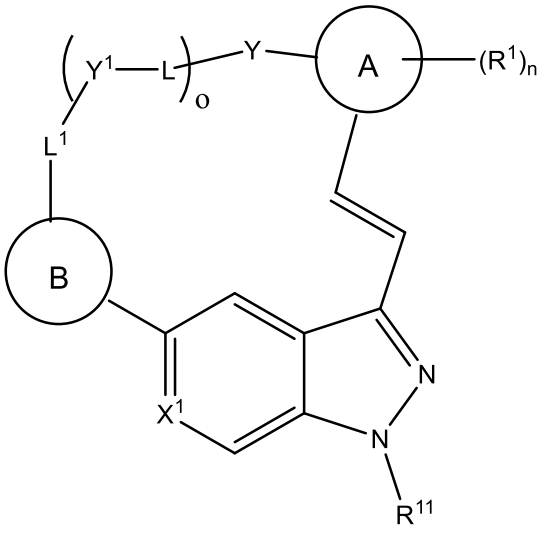
~~wherein~~

~~ring B is a 5- to 10-membered heteroarylene, 3- to 10-membered heterocycloalkylene, or C_6-C_{10} arylene, wherein each hydrogen atom in 3- to 10-membered heteroarylene, 5- to 10-membered heterocycloalkylene, and C_6-C_{10} arylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^e, -$OC(O)R^e$,~~

~~-OC(O)NR^{e}R^d, -OC(=N)NR^{e}R^d, -OS(O)R^e, -OS(O)$_2$R^e, -OS(O)NR^{e}R^d, -OS(O)$_2$NR^{e}R^d, -SR^e, -S(O)R^e, -S(O)$_2$R^e, -S(O)NR^{e}R^d, -S(O)$_2$NR^{e}R^d, -NR^{e}R^d, -NR^{e}C(O)R^d, -N(C(O)R^e)(C(O)R^d), -NR^{e}C(O)OR^d, -NR^{e}C(O)NR^{e}R^d, -NR^{e}C(=N)NR^{e}R^d, -NR^{e}S(O)R^d, -NR^{e}S(O)$_2$R^d, -NR^{e}S(O)NR^{e}R^d, -NR^{e}S(O)$_2$NR^{e}R^d, -C(O)R^e, -C(O)OR^e, -C(O)NR^{e}R^d, -C(=N)NR^{e}R^d, -PR^{e}R^d, -P(O)R^{e}R^d, -P(O)$_2$R^{e}R^d, -P(O)NR^{e}R^d, -P(O)$_2$NR^{e}R^d, -P(O)OR^e, -P(O)$_2$OR^e, -CN, or -NO$_2$; and~~

~~L^1 is C$_1$-C$_6$ alkylene, wherein each hydrogen atom in C$_1$-C$_6$ alkylene is independently optionally substituted by deuterium, halogen, C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, C$_3$-C$_6$ cycloalkyl, 3- to 7-membered heterocycloalkyl, C$_6$-C$_{10}$ aryl, 5- to 10-membered heteroaryl, -OR^e, -OC(O)R^e, -OC(O)NR^{e}R^d, -OC(=N)NR^{e}R^d, -OS(O)R^e, -OS(O)$_2$R^e, -OS(O)NR^{e}R^d, -OS(O)$_2$NR^{e}R^d, -SR^e, -S(O)R^e, -S(O)$_2$R^e, -S(O)NR^{e}R^d, -S(O)$_2$NR^{e}R^d, -NR^{e}R^d, -NR^{e}C(O)R^d, -N(C(O)R^e)(C(O)R^d), -NR^{e}C(O)OR^d, -NR^{e}C(O)NR^{e}R^d, -NR^{e}C(=N)NR^{e}R^d, -NR^{e}S(O)R^d, -NR^{e}S(O)$_2$R^d, -NR^{e}S(O)NR^{e}R^d, -NR^{e}S(O)$_2$NR^{e}R^d, -C(O)R^e, -C(O)OR^e, -C(O)NR^{e}R^d, -C(=N)NR^{e}R^d, -PR^{e}R^d, -P(O)R^{e}R^d, -P(O)$_2$R^{e}R^d, -P(O)NR^{e}R^d, -P(O)$_2$NR^{e}R^d, -P(O)OR^e, -P(O)$_2$OR^e, -CN, or -NO$_2$.~~

~~3~~2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having the formula IVa



IVa

wherein

ring A is a ring selected from 5- to 10-membered heteroarylene or C$_6$-C$_{10}$ arylene;

X^1 is C(R^3) or N;

Y is O, N(R^5)C(O), S, S(O), or S(O)$_2$;

each Y^1 is indepedently O, S, S(O), or S(O)$_2$;

each L is independently a C$_1$-C$_6$ alkylene, wherein each hydrogen atom in C$_1$-C$_6$

alkylene is independently optionally substituted by deuterium;

L^1 is absent, or L^1 is C_1-C_6 alkylene, wherein each hydrogen atom in C_1-C_6 alkylene is independently optionally substituted by deuterium or C_1-C_6 alkyl;

ring B is a 5- to 10-membered heteroarylene or C_6-C_{10} arylene, wherein each hydrogen atom in 5- to 10-membered heteroarylene or C_6-C_{10} arylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^c$, $-OC(O)R^c$, $-OC(O)NR^cR^d$, $-OC(=N)NR^cR^d$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)NR^cR^d$, $-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$;

each R^1 is independently deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^aR^b$, $-S(O)_2NR^aR^b$, $-OS(O)NR^aR^b$, $-OS(O)_2NR^aR^b$, $-NR^aC(O)R^b$, $-NR^aC(O)OR^b$, $-NR^aC(O)NR^aR^b$, $-NR^aS(O)R^b$, $-NR^aS(O)_2R^b$, $-NR^aS(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-PR^aR^b$, $-P(O)R^aR^b$, $-P(O)_2R^aR^b$, $-P(O)NR^aR^b$, $-P(O)_2NR^aR^b$, $-P(O)OR^a$, $-P(O)_2OR^a$, -CN, or $-NO_2$, wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl, is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^e$, $-OC(O)R^e$, $-OC(O)NR^eR^f$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)NR^eR^f$, $-OS(O)_2NR^eR^f$, $-SR^e$, $-S(O)R^e$, $-S(O)_2R^e$, $-S(O)NR^eR^f$, $-S(O)_2NR^eR^f$, $-NR^eC(O)R^f$, $-NR^eC(O)OR^f$, $-NR^eC(O)NR^eR^f$, $-NR^eS(O)R^f$, $-NR^eS(O)_2R^f$, $-NR^eS(O)NR^eR^f$, $-NR^eS(O)_2NR^eR^f$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)NR^eR^f$, $-PR^eR^f$, $-P(O)R^eR^f$, $-P(O)_2R^eR^f$, $-P(O)NR^eR^f$, $-P(O)_2NR^eR^f$, $-P(O)OR^e$, $-P(O)_2OR^e$, -CN, or $-NO_2$;

R^3, when present, is independently H, deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^aR^b$, $-S(O)_2NR^aR^b$, $-OS(O)NR^aR^b$, $-OS(O)_2NR^aR^b$, $-NR^aR^b$, $-NR^aC(O)R^b$, $-NR^aC(O)OR^b$, $-NR^aC(O)NR^aR^b$, $-NR^aS(O)R^b$, $-NR^aS(O)_2R^b$, $-NR^aS(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-PR^aR^b$, $-P(O)R^aR^b$, $-P(O)_2R^aR^b$, $-P(O)NR^aR^b$, $-P(O)_2NR^aR^b$, $-P(O)OR^a$, $-P(O)_2OR^a$, -CN, or $-NO_2$, wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, and 5- to 10-membered heteroaryl, is independently optionally

substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^e, -$OC(O)R^e$, -$OC(O)NR^eR^f$, -$OS(O)R^e$, -$OS(O)_2R^e$, -$OS(O)NR^eR^f$, -$OS(O)_2NR^eR^f$, -SR^e, -$S(O)R^e$, -$S(O)_2R^e$, -$S(O)NR^eR^f$, -$S(O)_2NR^eR^f$, -NR^eR^f, -$NR^eC(O)R^f$, -$NR^eC(O)OR^f$, -$NR^eC(O)NR^eR^f$, -$NR^eS(O)R^f$, -$NR^eS(O)_2R^f$, -$NR^eS(O)NR^eR^f$, -$NR^eS(O)_2NR^eR^f$, -$C(O)R^e$, -$C(O)OR^e$, -$C(O)NR^eR^f$, -PR^eR^f, -$P(O)R^eR^f$, -$P(O)_2R^eR^f$, -$P(O)NR^eR^f$, -$P(O)_2NR^eR^f$, -$P(O)OR^e$, -$P(O)_2OR^e$, -CN, or -NO_2;

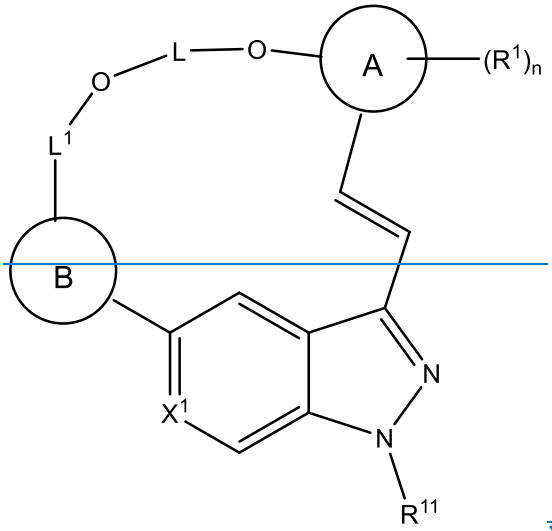
each of R^5, and R^{11}, when present, is independently H, deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^c, -$OC(O)R^c$, -$OC(O)NR^cR^d$, -$OC(=N)NR^cR^d$, -$OS(O)R^c$, -$OS(O)_2R^c$, -$OS(O)NR^cR^d$, -$OS(O)_2NR^cR^d$, -SR^c, -$S(O)R^c$, -$S(O)_2R^c$, -$S(O)NR^cR^d$, -$S(O)_2NR^cR^d$, -NR^cR^d, -$NR^cC(O)R^d$, -$N(C(O)R^c)(C(O)R^d)$, -$NR^cC(O)OR^d$, -$NR^cC(O)NR^cR^d$, -$NR^cC(=N)NR^cR^d$, -$NR^cS(O)R^d$, -$NR^cS(O)_2R^d$, -$NR^cS(O)NR^cR^d$, -$NR^cS(O)_2NR^cR^d$, -$C(O)R^c$, -$C(O)OR^c$, -$C(O)NR^cR^d$, -$C(=N)NR^cR^d$, -PR^cR^d, -$P(O)R^cR^d$, -$P(O)_2R^cR^d$, -$P(O)NR^cR^d$, -$P(O)_2NR^cR^d$, -$P(O)OR^c$, -$P(O)_2OR^c$, -CN, or -NO_2;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from the group consisting of H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, C_1-C_6 alkylene-C_6-C_{10} aryl, 5- to 10-membered heteroaryl, and C_1-C_6 alkylene-5- to 10-membered heteroaryl, or R^a and R^b or R^c and R^d or R^e and R^f, taken together with the atom to which they are attached, form a a 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, C_1-C_6 alkylene-C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or C_1-C_6 alkylene-5- to 10-membered heteroaryl is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OH, -OC_1-C_6 alkyl, -OC(O)-(H or C_1-C_6 alkyl), -OC(O)N(H or C_1-C_6 alkyl)$_2$, -OC(O)N(C_2-C_6 alkylene), -OS(O)-(H or C_1-C_6 alkyl), -$OS(O)_2$-(H or C_1-C_6 alkyl), -OS(O)N(H or C_1-C_6 alkyl)$_2$, -OS(O)N(C_2-C_6 alkylene), -$OS(O)_2$N(H or C_1-C_6 alkyl)$_2$, -$OS(O)_2$N(C_2-C_6 alkylene), -S(H or C_1-C_6 alkyl), -S(O)(H or C_1-C_6 alkyl), -$S(O)_2$(H or C_1-C_6 alkyl), -S(O)N(H or C_1-C_6 alkyl)$_2$, -S(O)N(C_2-C_6 alkylene), -$S(O)_2$N(H or C_1-C_6 alkyl)$_2$, -$S(O)_2$N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)$_2$, -N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)C(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)O(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)C(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)C(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)S(O)-(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)$S(O)_2$(H or C_1-C_6 alkyl), -N(H or C_1-C_6 alkyl)S(O)N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)S(O)N(C_2-C_6 alkylene), -N(H or C_1-C_6 alkyl)$S(O)_2$N(H or C_1-C_6 alkyl)$_2$, -N(H or C_1-C_6 alkyl)$S(O)_2$N(C_2-C_6 alkylene), -C(O)-(H or C_1-C_6 alkyl), -C(O)O(H or C_1-C_6 alkyl), -C(O)N(C_2-C_6 alkylene), -P(H or C_1-C_6 alkyl)$_2$, -P(C_2-C_6 alkylene), -P(O)(H or C_1-C_6 alkyl)$_2$,

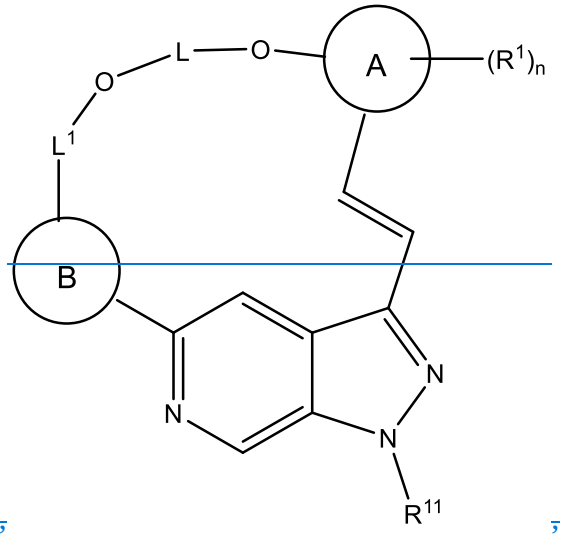
-P(O)(C_2-C_6 alkylene), -P(O)$_2$(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$(C_2-C_6 alkylene), -P(O)N(H or C_1-C_6 alkyl)$_2$, -P(O)N(C_2-C_6 alkylene), -P(O)$_2$N(H or C_1-C_6 alkyl)$_2$, -P(O)$_2$N(C_2-C_6 alkylene), -P(O)O(H or C_1-C_6 alkyl), -P(O)$_2$O(H or C_1-C_6 alkyl), -CN, or -NO$_2$; and

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

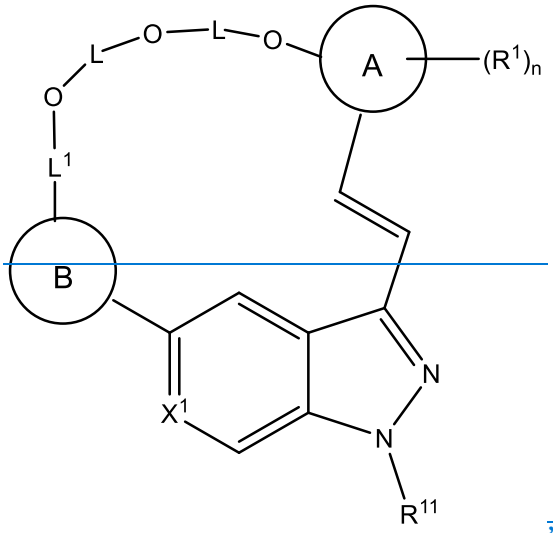
~~4. The compound of claim 1, having the formula Va, V, Via, VI, VIIa, VII, VIIIa, VIII, IXa, or IX~~



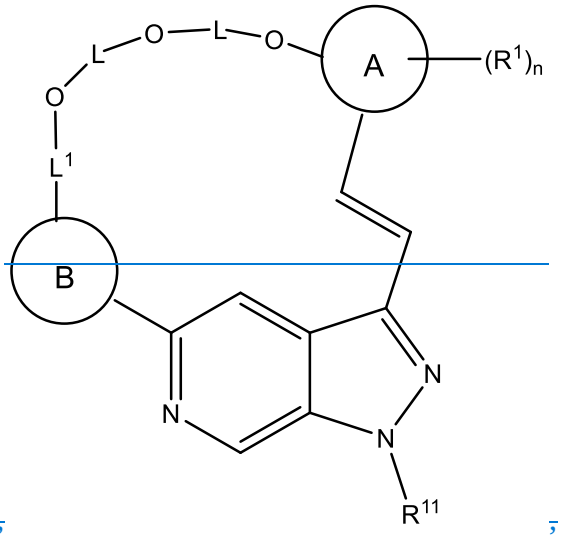
~~Va~~



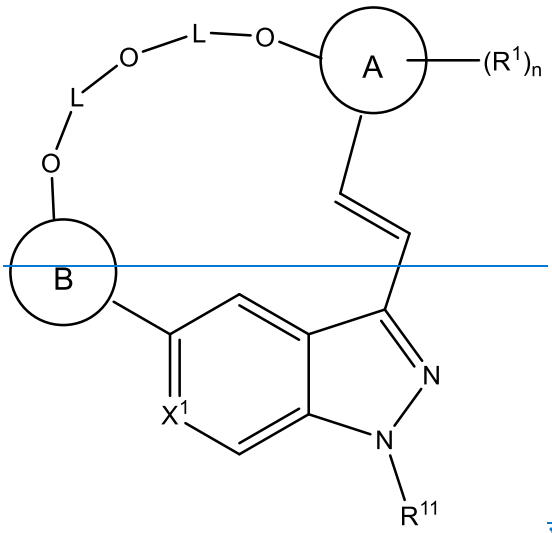
~~V~~



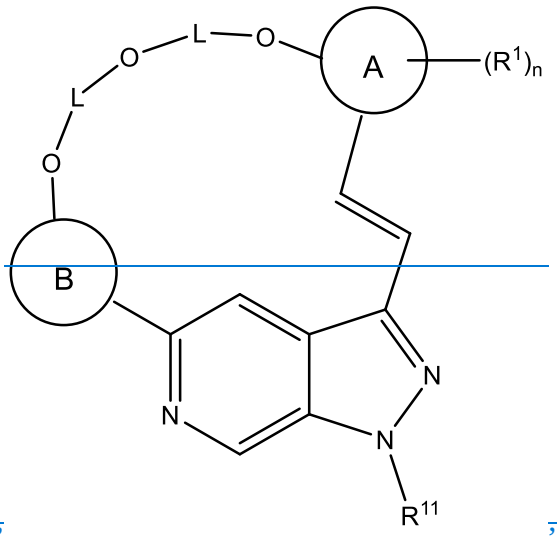
~~VIa~~



~~VI~~

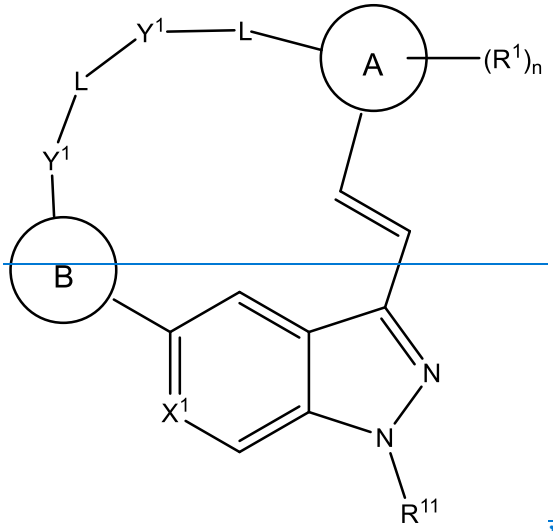


,

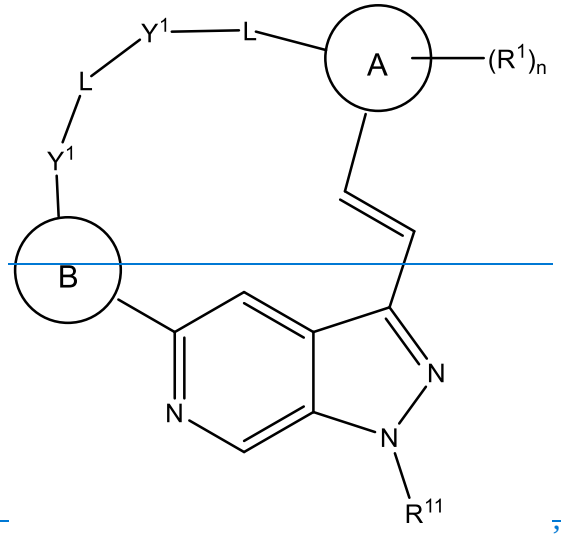


,

VIIa VII

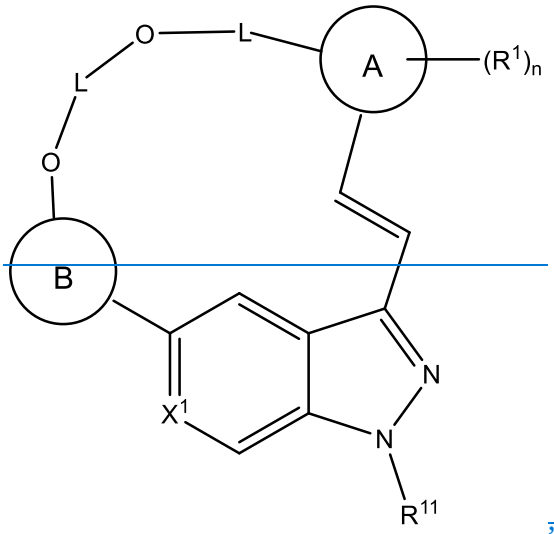


,

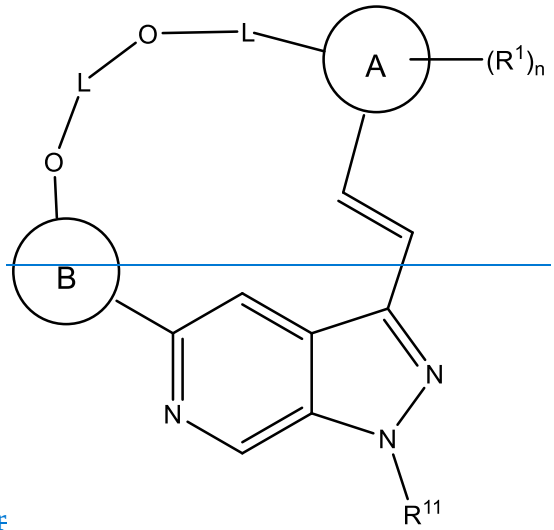


,

VIIIa VIII



, or

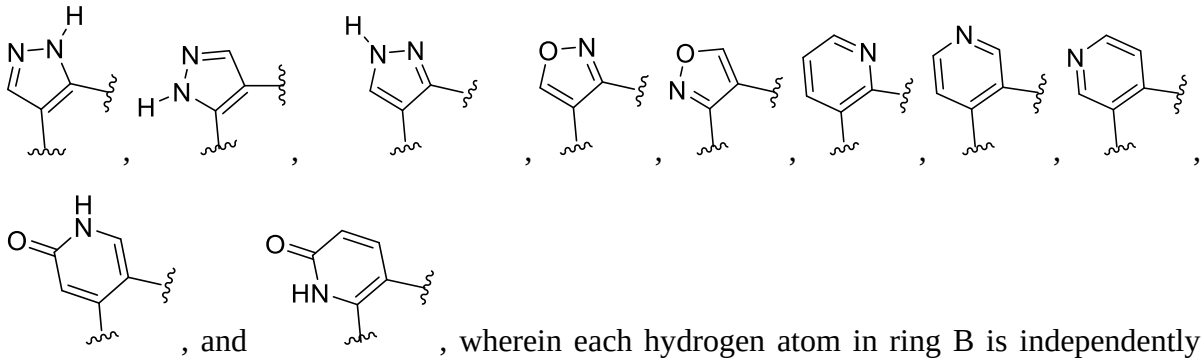


IXa IX

or a pharmaceutically acceptable salt thereof.

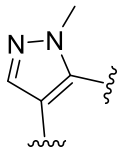
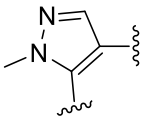
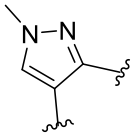
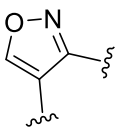
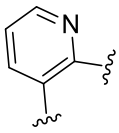
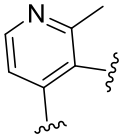
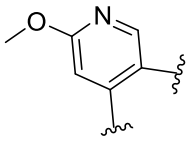
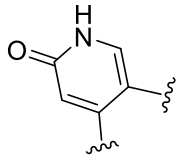
35. The compound of ~~any one of the preceding~~ claim~~s~~ 1 or 2, or a pharmaceutically acceptable salt thereof, wherein ring B is a 5- to 10-membered heteroarylene, wherein each hydrogen atom in 5- to 10-membered heteroarylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^c$, $-OC(O)R^c$, $-OC(O)NR^cR^d$, $-OC(=N)NR^cR^d$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)NR^cR^d$, $-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$.

~~6~~4. The compound of ~~any one of~~ claim~~s~~ 1 ~~to 4~~or 2, or a pharmaceutically acceptable salt thereof, wherein ring B is a 5- to 10-membered heteroarylene selected from the group consisting of



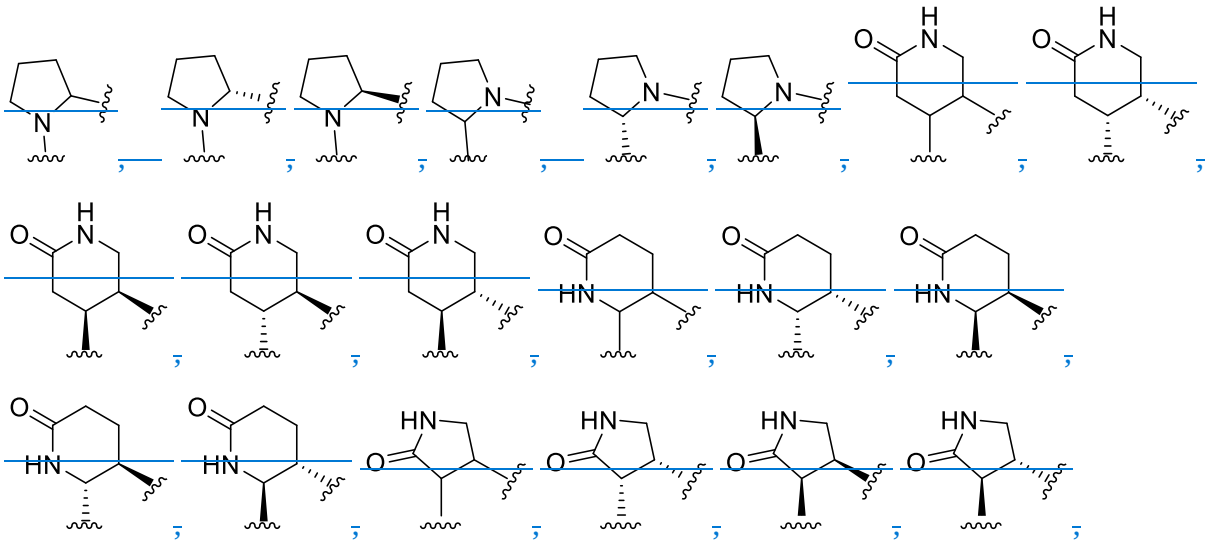
, and , wherein each hydrogen atom in ring B is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3-to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^c$, $-OC(O)R^c$, $-OC(O)NR^cR^d$, $-OC(=N)NR^cR^d$, $-OS(O)R^c$, $-OS(O)_2R^c$, $-OS(O)NR^cR^d$, $-OS(O)_2NR^cR^d$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, $-S(O)NR^cR^d$, $-S(O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cC(O)R^d$, $-N(C(O)R^c)(C(O)R^d)$, $-NR^cC(O)OR^d$, $-NR^cC(O)NR^cR^d$, $-NR^cC(=N)NR^cR^d$, $-NR^cS(O)R^d$, $-NR^cS(O)_2R^d$, $-NR^cS(O)NR^cR^d$, $-NR^cS(O)_2NR^cR^d$, $-C(O)R^c$, $-C(O)OR^c$, $-C(O)NR^cR^d$, $-C(=N)NR^cR^d$, $-PR^cR^d$, $-P(O)R^cR^d$, $-P(O)_2R^cR^d$, $-P(O)NR^cR^d$, $-P(O)_2NR^cR^d$, $-P(O)OR^c$, $-P(O)_2OR^c$, -CN, or $-NO_2$.

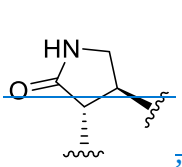
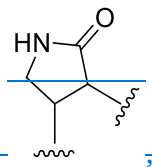
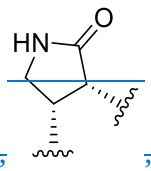
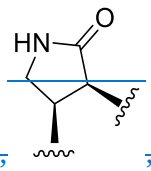
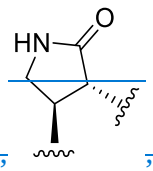
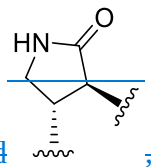
~~7~~5. The compound of ~~any one of~~ claim~~s~~ 1 ~~to 4~~or 2, or a pharmaceutically acceptable salt thereof, wherein ring B is


, 
, 
, 
, 
, 
, 
, or 
.

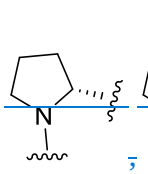
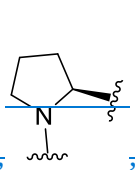
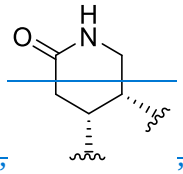
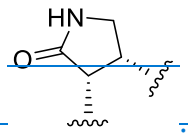
~~8. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein ring B is a 3- to 10-membered heterocycloalkylene, wherein each hydrogen atom in 3- to 10-membered heterocycloalkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^e$, $-OC(O)R^e$, $-OC(O)NR^eR^d$, $-OC(=N)NR^eR^d$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)NR^eR^d$, $-OS(O)_2NR^eR^d$, $-SR^e$, $-S(O)R^e$, $-S(O)_2R^e$, $-S(O)NR^eR^d$, $-S(O)_2NR^eR^d$, $-NR^eR^d$, $-NR^eC(O)R^d$, $-N(C(O)R^e)(C(O)R^d)$, $-NR^eC(O)OR^d$, $-NR^eC(O)NR^eR^d$, $-NR^eC(=N)NR^eR^d$, $-NR^eS(O)R^d$, $-NR^eS(O)_2R^d$, $-NR^eS(O)NR^eR^d$, $-NR^eS(O)_2NR^eR^d$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)NR^eR^d$, $-C(=N)NR^eR^d$, $-PR^eR^d$, $-P(O)R^eR^d$, $-P(O)_2R^eR^d$, $-P(O)NR^eR^d$, $-P(O)_2NR^eR^d$, $-P(O)OR^e$, $-P(O)_2OR^e$, $-CN$, or $-NO_2$.~~

~~9. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein ring B is a 3- to 10-membered heterocycloalkylene selected from the group consisting of~~









, , , , , and , wherein each hydrogen atom in 3- to 10-membered heterocycloalkylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^e, -$OC(O)R^e$, -$OC(O)NR^eR^d$, -$OC(=N)NR^eR^d$, -$OS(O)R^e$, -$OS(O)_2R^e$, -$OS(O)NR^eR^d$, -$OS(O)_2NR^eR^d$, -SR^e, -$S(O)R^e$, -$S(O)_2R^e$, -$S(O)NR^eR^d$, -$S(O)_2NR^eR^d$, -NR^eR^d, -$NR^eC(O)R^d$, -$N(C(O)R^e)(C(O)R^d)$, -$NR^eC(O)OR^d$, -$NR^eC(O)NR^eR^d$, -$NR^eC(=N)NR^eR^d$, -$NR^eS(O)R^d$, -$NR^eS(O)_2R^d$, -$NR^eS(O)NR^eR^d$, -$NR^eS(O)_2NR^eR^d$, -$C(O)R^e$, -$C(O)OR^e$, -$C(O)NR^eR^d$, -$C(=N)NR^eR^d$, -PR^eR^d, -$P(O)R^eR^d$, -$P(O)_2R^eR^d$, -$P(O)NR^eR^d$, -$P(O)_2NR^eR^d$, -$P(O)OR^e$, -$P(O)_2OR^e$, -CN, or -NO_2.

10. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein ring B is a 3- to 10-membered heterocycloalkylene selected from the group consisting of

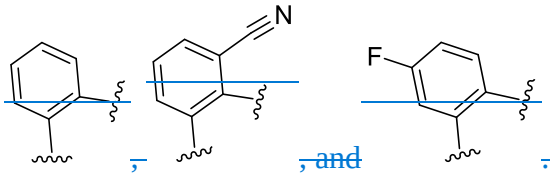



, , , and 
.

11. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein ring B is a C_6-C_{10} arylene, wherein each hydrogen atom in C_6-C_{10} arylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^e, -$OC(O)R^e$, -$OC(O)NR^eR^d$, -$OC(=N)NR^eR^d$, -$OS(O)R^e$, -$OS(O)_2R^e$, -$OS(O)NR^eR^d$, -$OS(O)_2NR^eR^d$, -SR^e, -$S(O)R^e$, -$S(O)_2R^e$, -$S(O)NR^eR^d$, -$S(O)_2NR^eR^d$, -NR^eR^d, -$NR^eC(O)R^d$, -$N(C(O)R^e)(C(O)R^d)$, -$NR^eC(O)OR^d$, -$NR^eC(O)NR^eR^d$, -$NR^eC(=N)NR^eR^d$, -$NR^eS(O)R^d$, -$NR^eS(O)_2R^d$, -$NR^eS(O)NR^eR^d$, -$NR^eS(O)_2NR^eR^d$, -$C(O)R^e$, -$C(O)OR^e$, -$C(O)NR^eR^d$, -$C(=N)NR^eR^d$, -PR^eR^d, -$P(O)R^eR^d$, -$P(O)_2R^eR^d$, -$P(O)NR^eR^d$, -$P(O)_2NR^eR^d$, -$P(O)OR^e$, -$P(O)_2OR^e$, -CN, or -NO_2.

12. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein ring B is a phenylene optionally substituted with one or more deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered

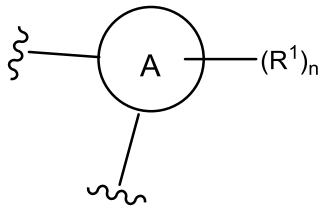
~~heterocycloalkyl, C6-C10 aryl, 5- to 10-membered heteroaryl, -OR^e, -OC(O)R^e, -OC(O)NR^{e}R^d, -OC(=N)NR^{e}R^d, -OS(O)R^e, -OS(O)$_2$R^e, -OS(O)NR^{e}R^d, -OS(O)$_2$NR^{e}R^d, -SR^e, -S(O)R^e, -S(O)$_2$R^e, -S(O)NR^{e}R^d, -S(O)$_2$NR^{e}R^d, -NR^{e}R^d, -NR^{e}C(O)R^d, -N(C(O)R^e)(C(O)R^d), -NR^{e}C(O)OR^d, -NR^{e}C(O)NR^{e}R^d, -NR^{e}C(=N)NR^{e}R^d, -NR^{e}S(O)R^d, -NR^{e}S(O)$_2$R^d, -NR^{e}S(O)NR^{e}R^d, -NR^{e}S(O)$_2$NR^{e}R^d, -C(O)R^e, -C(O)OR^e, -C(O)NR^{e}R^d, -C(=N)NR^{e}R^d, -PR^{e}R^d, -P(O)R^{e}R^d, -P(O)$_2$R^{e}R^d, -P(O)NR^{e}R^d, -P(O)$_2$NR^{e}R^d, -P(O)OR^e, -P(O)$_2$OR^e, -CN, or -NO$_2$.~~

~~13. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein ring B is selected from the group consisting of~~



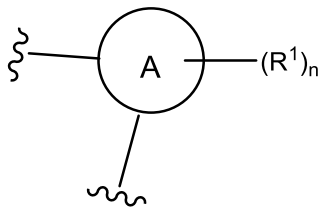
~~,~~ ~~, and~~ ~~.~~

~~14~~6. The compound of ~~any one of~~ claim~~s~~ 1 ~~to~~or ~~4~~2, or a pharmaceutically acceptable salt thereof, wherein

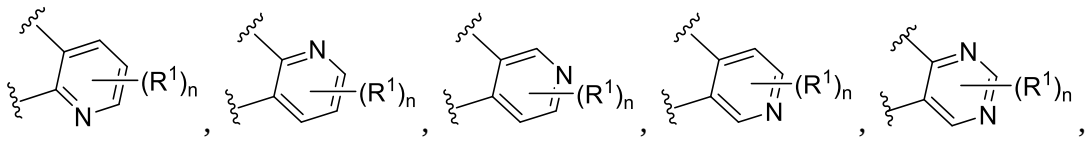


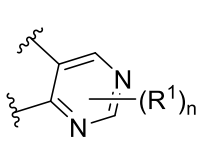
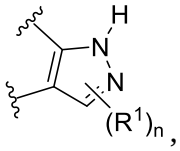
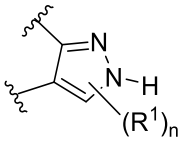
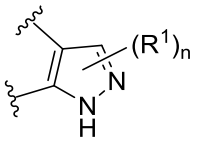
is a 5- to 10-membered heteroarylene, and n is 0, 1, 2, 3, or 4.

~~15~~7. The compound of ~~any one of~~ claim~~s~~ 1 ~~to~~or ~~4~~2, or a pharmaceutically acceptable salt thereof, wherein



is a 5- to 10-membered heteroarylene selected from the group consisting of



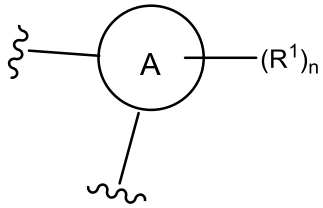



, and 
.

and n is 0, 1, or 2.

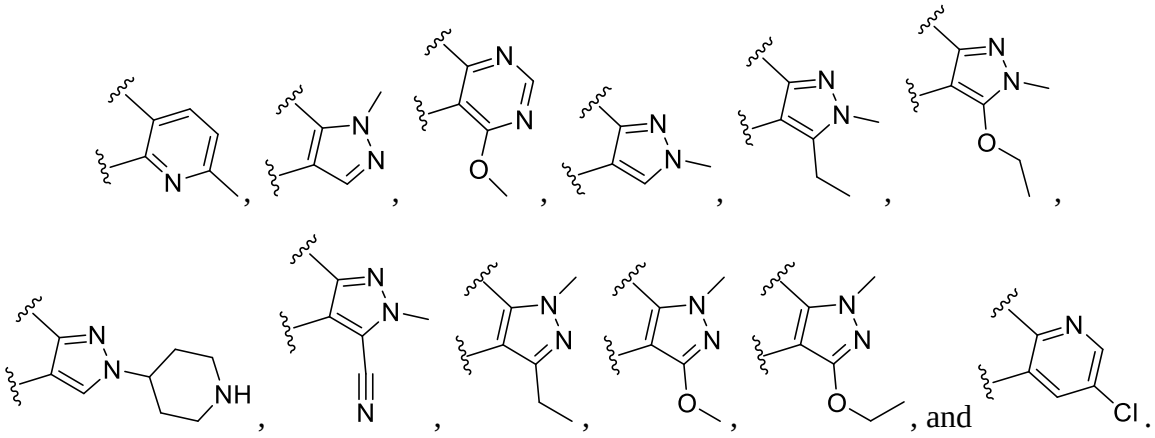
~~16~~8. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, and n is 0, 1, or 2.

~~17~~9. The compound of ~~any one of~~ claim~~s~~ 1 ~~to~~or ~~4~~2, or a pharmaceutically acceptable salt thereof, wherein each R^1, when present, is independently fluoro, chloro, methyl, ethyl, methoxy, ethoxy, -C(O)OR^a, -C(O)NR^aR^b, -CN, or 4-piperidinyl.

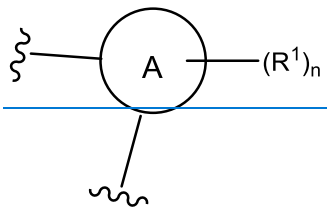
~~18~~10. The compound of ~~any one of~~ claim~~s~~ 1 or~~to~~ 2~~4~~, or a pharmaceutically acceptable salt thereof, wherein



is a 5- to 10-membered heteroarylene selected from the group consisting of

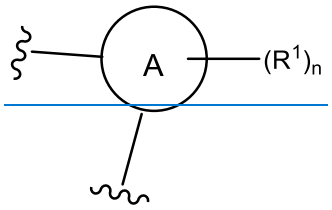


~~19. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein~~



~~is a C_6-C_{10} arylene, and n is 0, 1, 2, 3, or 4.~~

~~20. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein~~

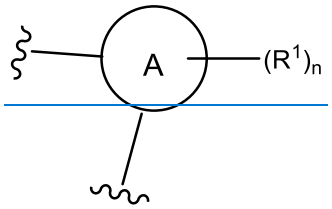


~~is a phenylene, and n is 0, 1, 2, 3, or 4.~~

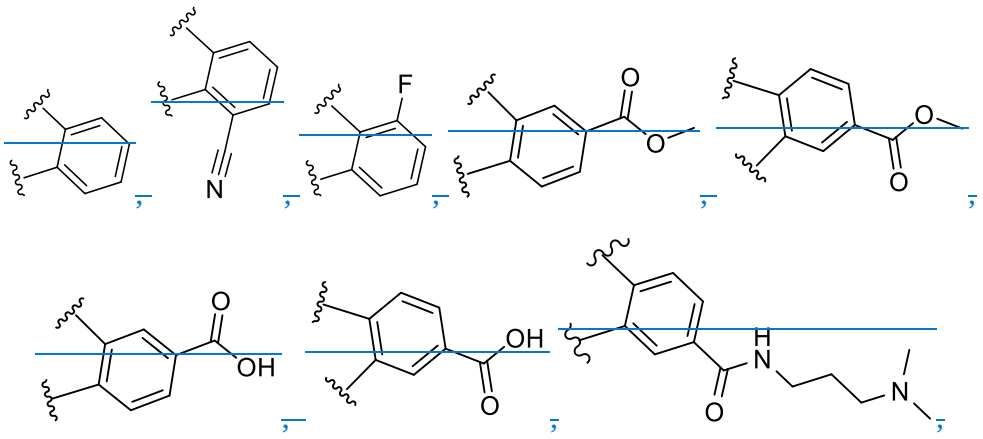
~~21. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein n is 0, 1, or 2.~~

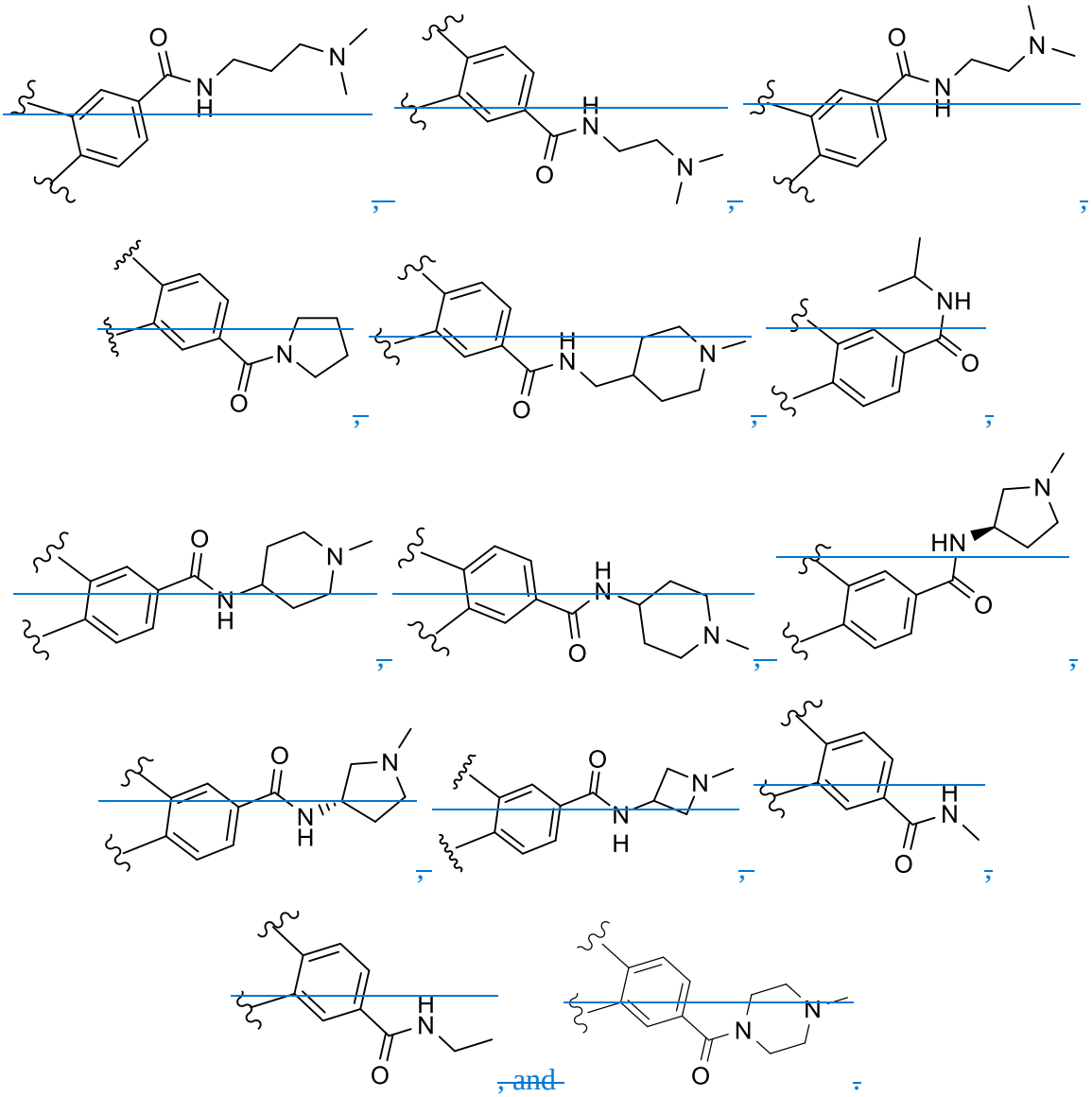
~~22. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein each R^1, when present, is independently fluoro, chloro, methyl, ethyl, methoxy, ethoxy, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-CN$, or 4-piperidinyl.~~

~~23. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein~~



~~is selected from the group consisting of~~





~~24~~11. The compound of ~~any one of~~ claim~~s~~ 1 ~~to~~or ~~4~~2, or a pharmaceutically acceptable salt thereof, wherein L is an ethylene, propylene, or butylene, wherein each hydrogen atom in ethylene, propylene, and butylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -$OS(O)R^a$, -$OS(O)_2R^a$, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)NR^aR^b$, -$S(O)_2NR^aR^b$, -$OS(O)NR^aR^b$, -$OS(O)_2NR^aR^b$, -NR^aR^b, -$NR^aC(O)R^b$, -$NR^aC(O)OR^b$, -$NR^aC(O)NR^aR^b$, -$NR^aS(O)R^b$, -$NR^aS(O)_2R^b$, -$NR^aS(O)NR^aR^b$, -$NR^aS(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$, -PR^aR^b, -$P(O)R^aR^b$, -$P(O)_2R^aR^b$, -$P(O)NR^aR^b$, -$P(O)_2NR^aR^b$, -$P(O)OR^a$, -$P(O)_2OR^a$, -CN, or -NO_2.

~~25~~12. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein L is an ethylene, propylene, or butylene, each of which is optionally

substituted by a C_1-C_6 alkyl.

~~26. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Y is O.~~

~~27~~13. The compound of any one of the preceding claims ~~1 to 25~~, or a pharmaceutically acceptable salt thereof, wherein Y is $N(R^5)C(O)$.

~~28~~14. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^5, when present, is H or methyl.

~~29~~15. The compound of any one of claims 1 to ~~25~~12, or a pharmaceutically acceptable salt thereof, wherein Y is absent.

~~30~~16. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Y^1 is O.

~~31. The compound of any one of claims 1 to 29, or a pharmaceutically acceptable salt thereof, wherein Y^1 is $C(O)N(R^7)$.~~

~~32. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^7, when present, is H or methyl.~~

~~33. The compound of any one of claims 1 to 29, or a pharmaceutically acceptable salt thereof, wherein Y^1 is $N(R^8)$.~~

~~34. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^8, when present, is H or methyl.~~

~~35. The compound of any one of claims 1 to 29, or a pharmaceutically acceptable salt thereof, wherein Y^1 is absent.~~

~~36. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Y^2 is O.~~

~~37. The compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, wherein Y^2 is $C(O)N(R^9)$.~~

~~38. The compound of claim 37, or a pharmaceutically acceptable salt thereof, wherein R^9 is H, methyl, ethyl, or cyclopropyl.~~

~~39. The compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, wherein Y^2 is $N(R^{10})$.~~

~~40. The compound of claim 39, or a pharmaceutically acceptable salt thereof, wherein R^{10} is H, methyl, or phenyl.~~

~~41. The compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, wherein Y^2 is $S(O)_2$.~~

~~42~~17. The compound of any one of the preceding claims ~~1 to 35~~, or a pharmaceutically acceptable salt thereof, wherein Y^2 is absent.

~~43~~18. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein m is 1.

~~44. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein m is 2.~~

~~45. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein at least one L^1 is methylene, ethylene, or propylene, wherein each hydrogen atom in methylene, ethylene, and propylene is independently optionally substituted by deuterium, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, $-OR^e$, $-OC(O)R^e$, $-OC(O)NR^eR^d$, $-OC(=N)NR^eR^d$, $-OS(O)R^e$, $-OS(O)_2R^e$, $-OS(O)NR^eR^d$, $-OS(O)_2NR^eR^d$, $-SR^e$, $-S(O)R^e$, $-S(O)_2R^e$, $-S(O)NR^eR^d$, $-S(O)_2NR^eR^d$, $-NR^eR^d$, $-NR^eC(O)R^d$, $-N(C(O)R^e)(C(O)R^d)$, $-NR^eC(O)OR^d$, $-NR^eC(O)NR^eR^d$, $-NR^eC(=N)NR^eR^d$, $-NR^eS(O)R^d$, $-NR^eS(O)_2R^d$, $-NR^eS(O)NR^eR^d$, $-NR^eS(O)_2NR^eR^d$, $-C(O)R^e$, $-C(O)OR^e$, $-C(O)NR^eR^d$, $-C(=N)NR^eR^d$, $-PR^eR^d$, $-P(O)R^eR^d$, $-P(O)_2R^eR^d$, $-P(O)NR^eR^d$, $-P(O)_2NR^eR^d$, $-P(O)OR^e$, $-P(O)_2OR^e$, $-CN$, or $-NO_2$.~~

~~46. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one L^1 is methylene, ethylene, or propylene, each of which is substituted with a C_1-C_6 alkyl or a $-C(O)NR^cR^d$.~~

~~47. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one L^1 is methylene, ethylene, or propylene, each of which is substituted with a methyl or a $-C(O)NR^cR^d$, wherein R^c and R^d are each H.~~

~~48. The compound of any one of claims 1 to 42, or a pharmaceutically acceptable salt thereof, wherein m is 0.~~

~~49~~19. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X is $C(R^2)$.

~~50~~20. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X^1 is CH or N.

~~51~~21. The compound of any one of claims 1 to ~~49~~19, or a pharmaceutically acceptable salt thereof, wherein X^1 is $C(R^3)$.

~~52~~22. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X^2 is $C(R^4)$.

~~53. The compound of any one of the claims 1 to 51, or a pharmaceutically acceptable salt thereof, wherein X^2 is N.~~

~~54. The compound of any one of claims 1 to 48, or a pharmaceutically acceptable salt thereof, wherein X is N.~~

~~55. The compound of any one of claims 1 to 48, or 54, or a pharmaceutically acceptable salt thereof, wherein X^1 is $C(R^3)$.~~

~~56. The compound of any one of claims 1 to 48, or 54, or a pharmaceutically acceptable salt thereof, wherein X^1 is N.~~

~~57. The compound of any one of claims 1 to 48, or 54 to 56, or a pharmaceutically acceptable salt thereof, wherein X^2 is $C(R^4)$.~~

~~58. The compound of any one of claims 1 to 48, or 54 to 56, or a pharmaceutically acceptable salt thereof, wherein X^2 is N.~~

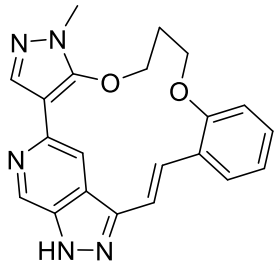
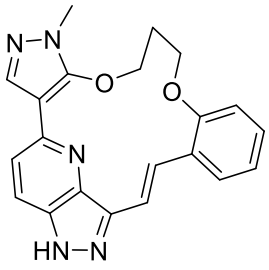
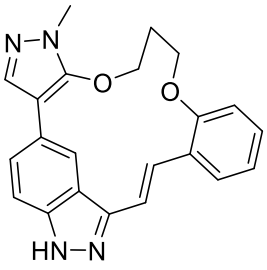
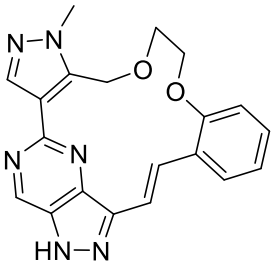
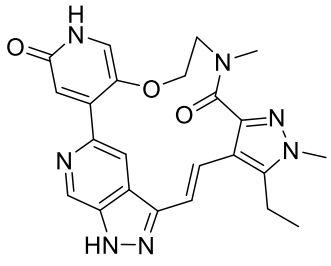
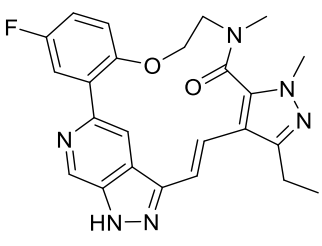
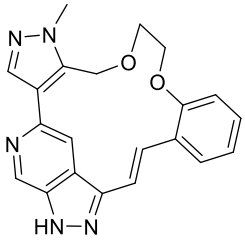
~~59~~23. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^2, when present, is H.

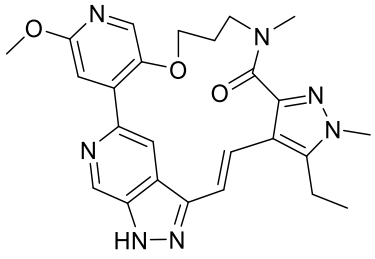
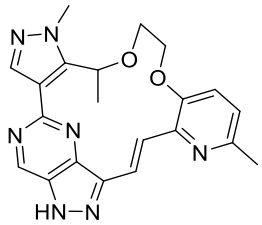
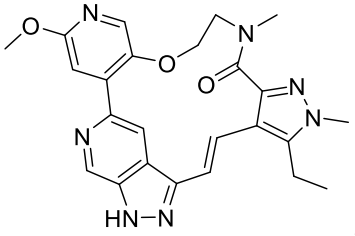
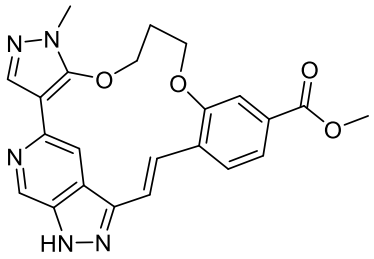
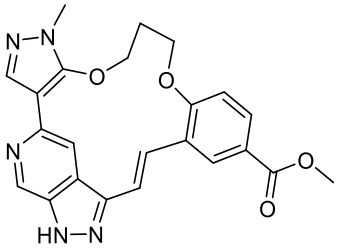
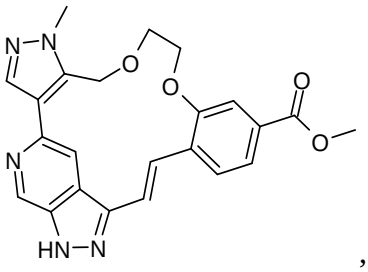
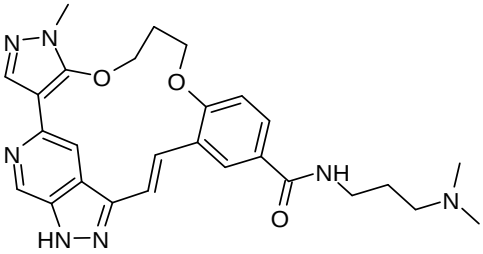
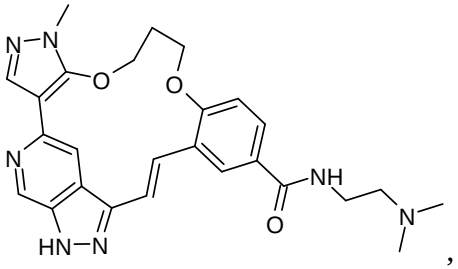
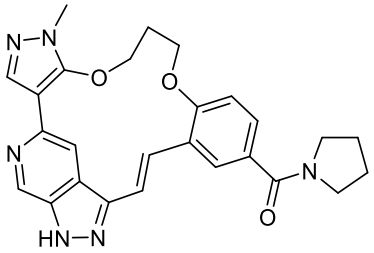
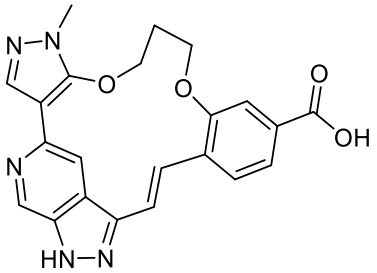
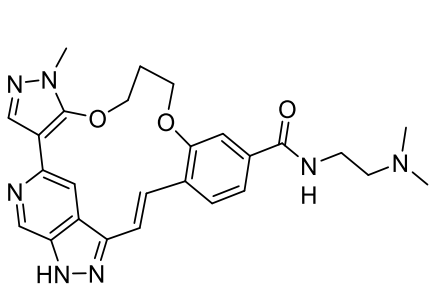
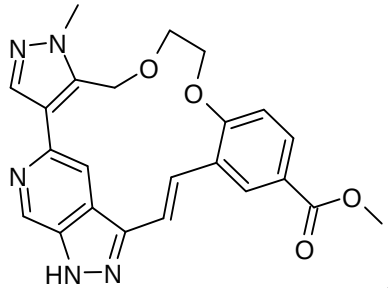
~~60~~24. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^3, when present, is H.

~~61~~25. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^4, when present, is H, fluoro, chloro, or methyl.

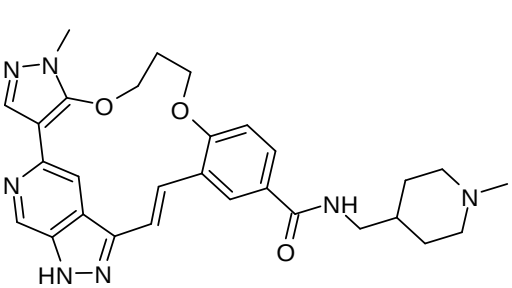
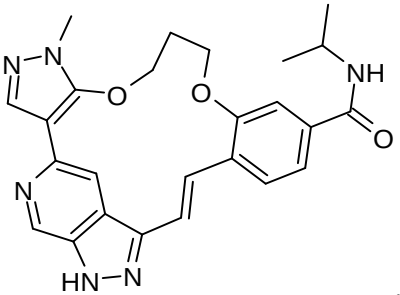
~~62~~26. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^{11} is H.

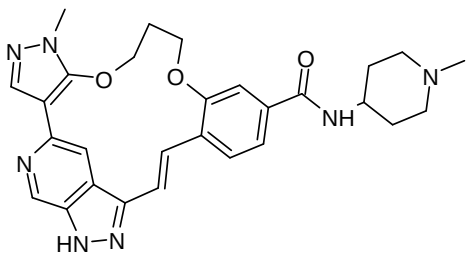
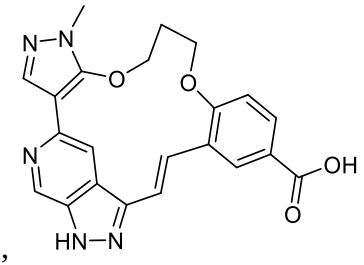
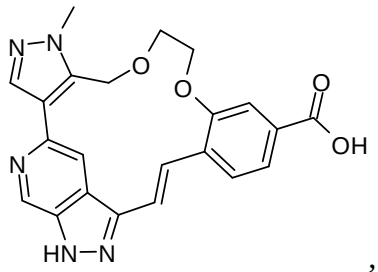
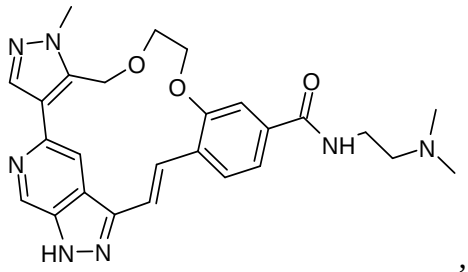
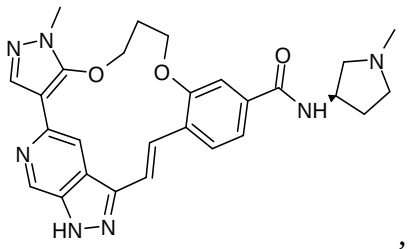
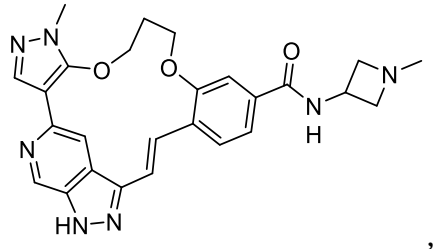
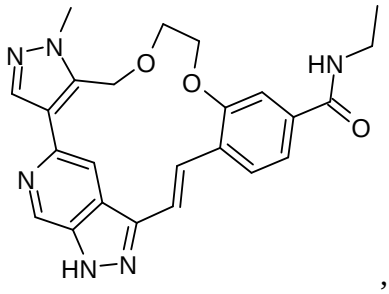
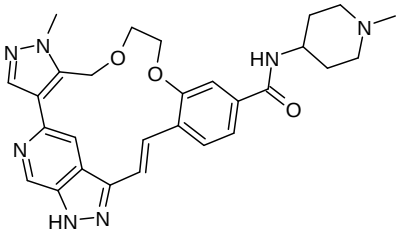
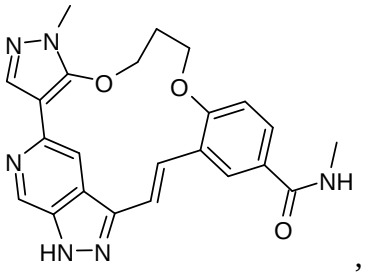
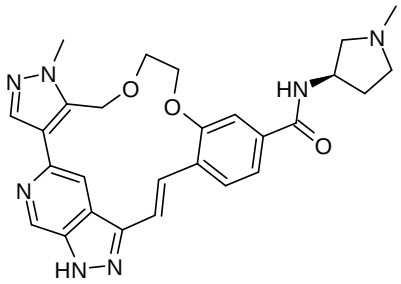
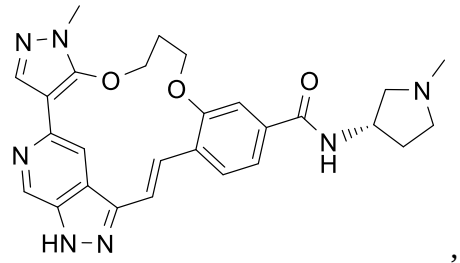
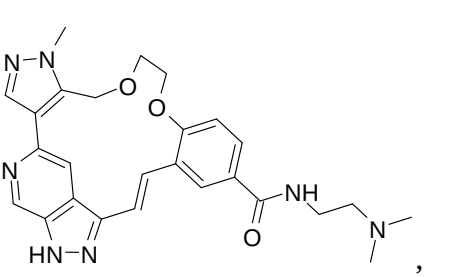
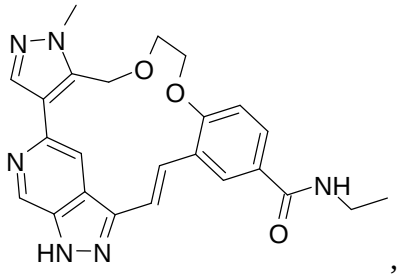
~~63~~27. The compound of claim 1, selected from the group consisting of


,

,

,

,

,

,

,


,

,

,

,

,

,

,

,

,

,

,

,

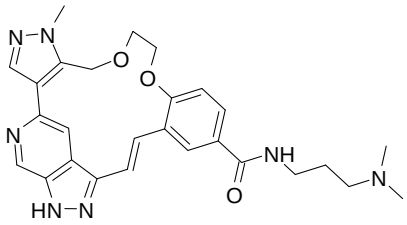
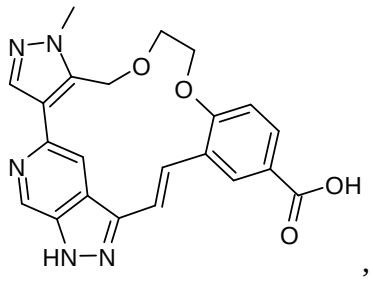
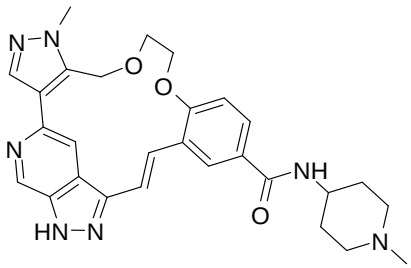
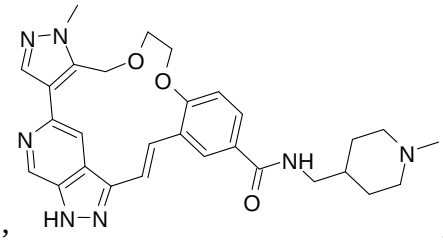
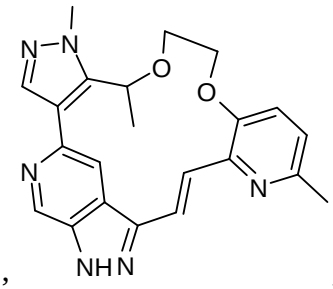
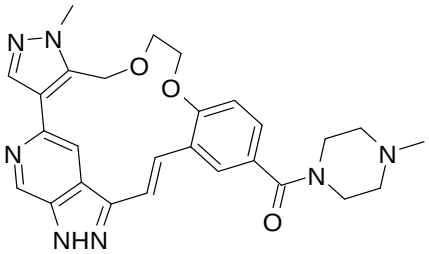
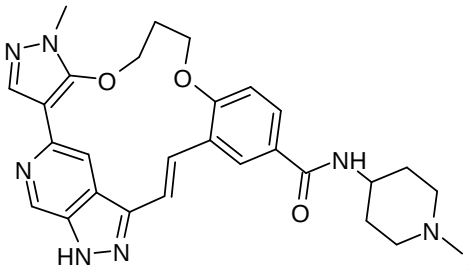
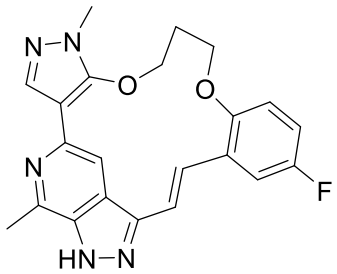
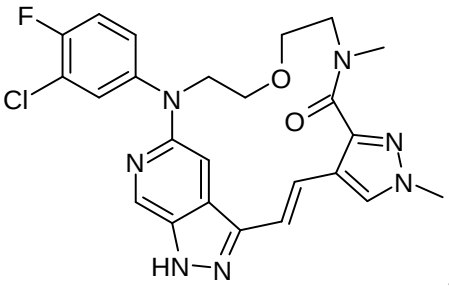
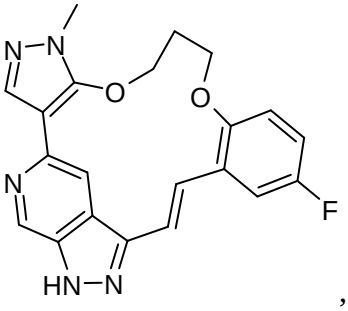
,

,

,

,

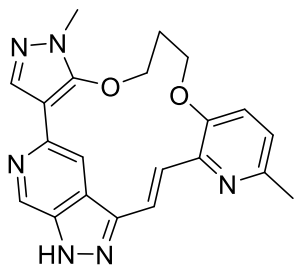
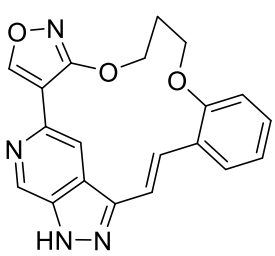
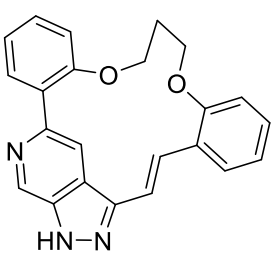
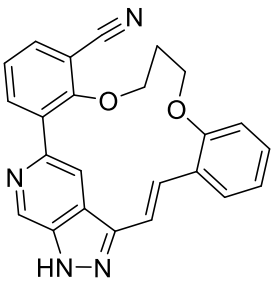

,

,

,

,

,

,

,

,

,

,

,

,

,

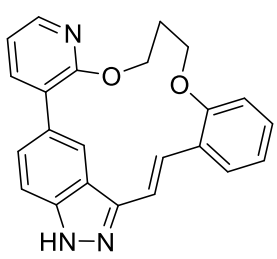
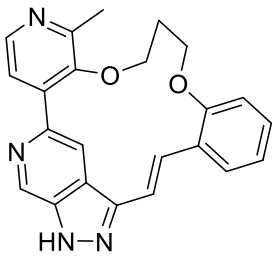
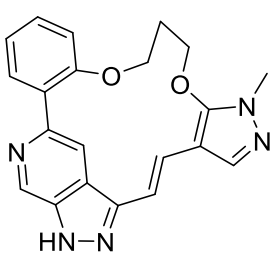
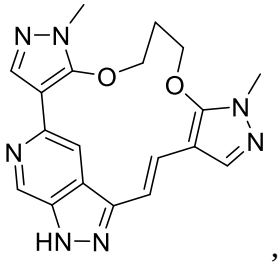
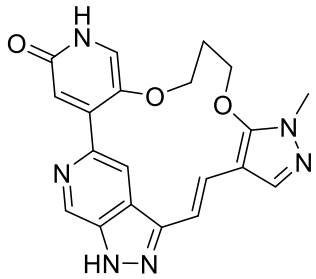
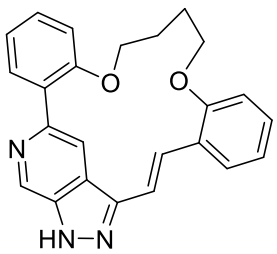
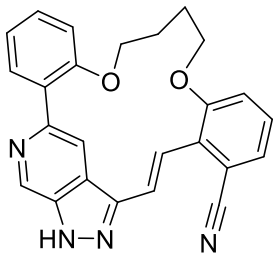
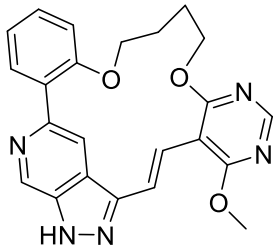
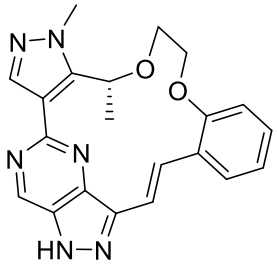
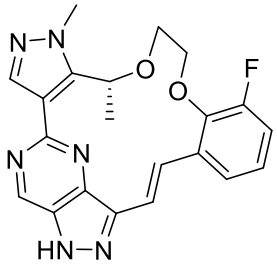
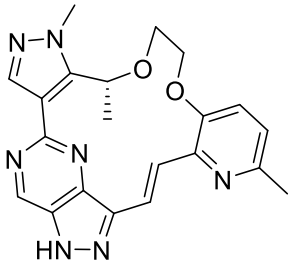
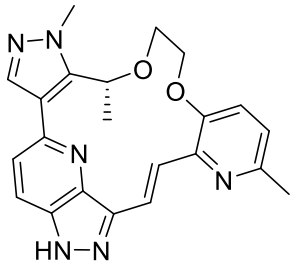
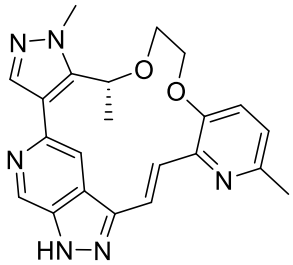
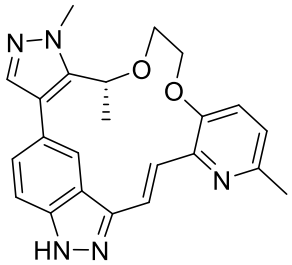
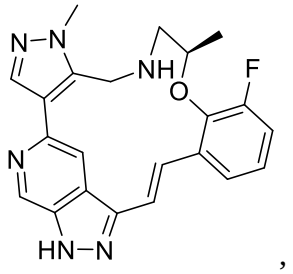
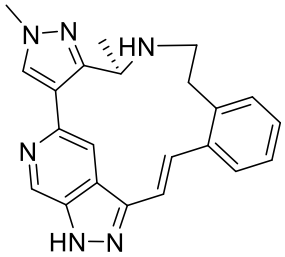
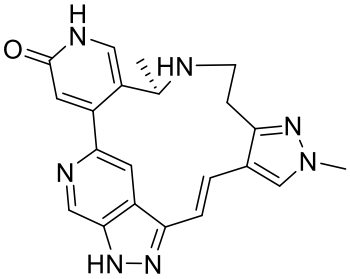
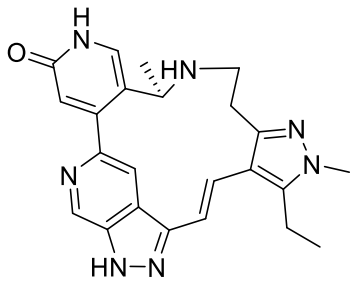
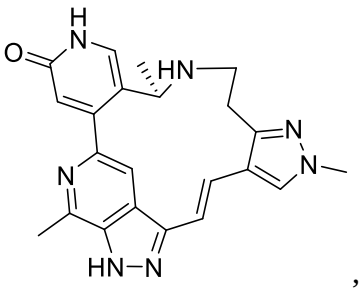
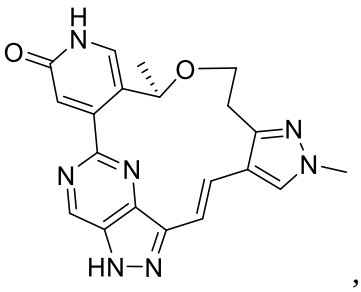
,

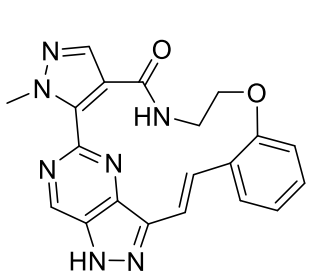
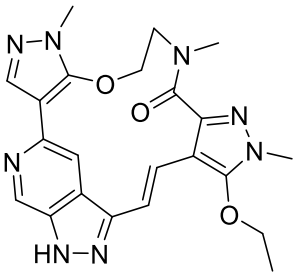
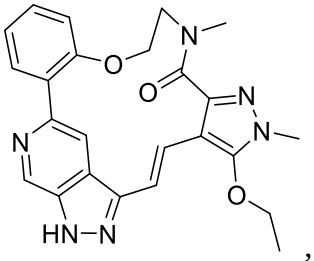
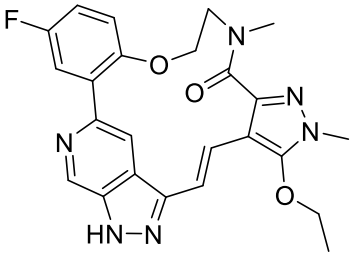
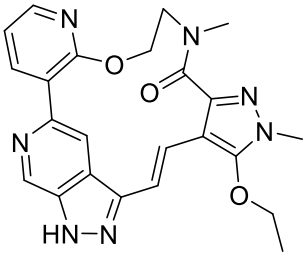
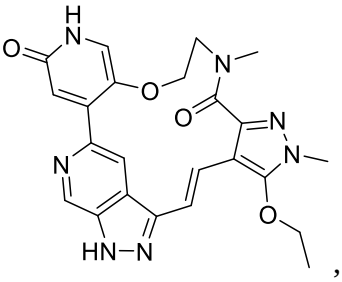
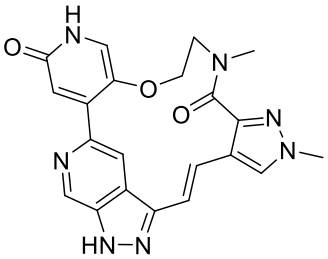
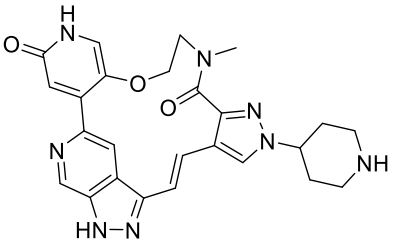
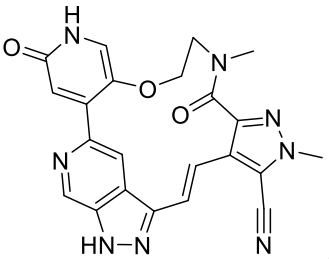
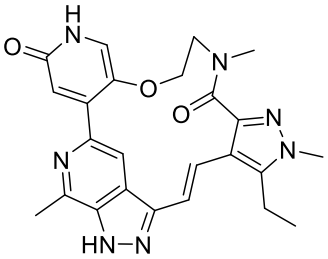
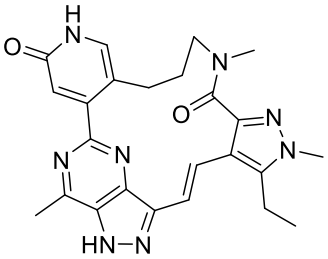
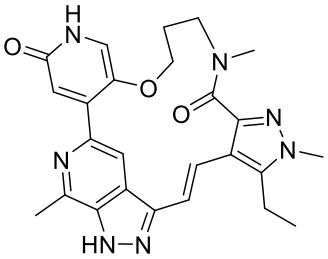
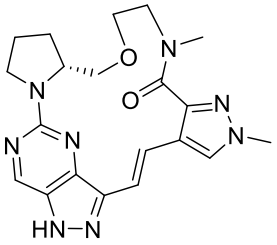
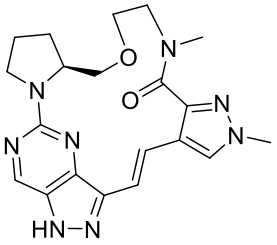
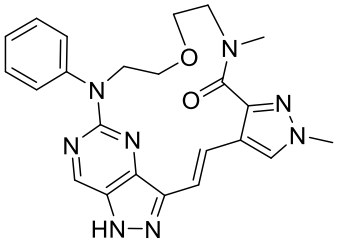
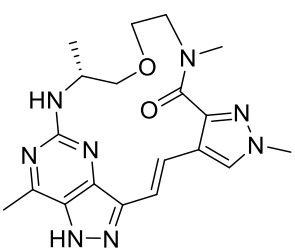
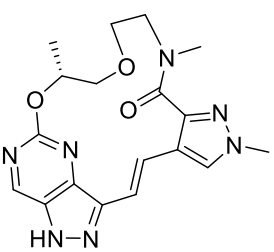
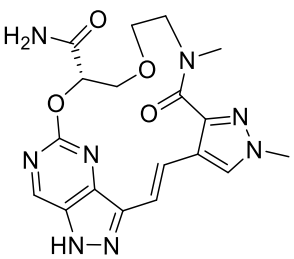
,


,

,

,

,

,

,

,

,

, ~~and~~

, ~~or a pharmaceutically acceptable salt thereof.~~

~~64. The compound of claim 1, selected from the group consisting of~~


,

,

,

,

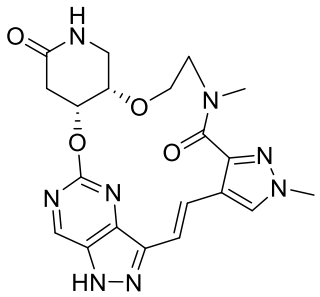
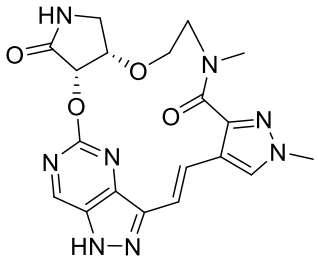
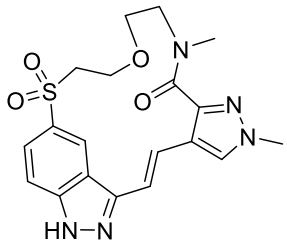

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

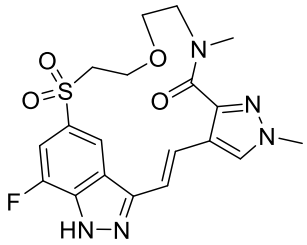
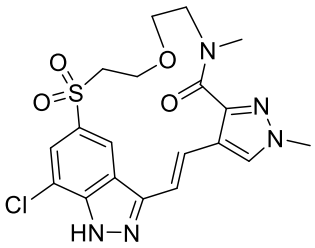
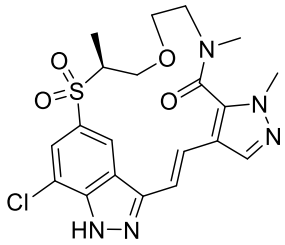

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

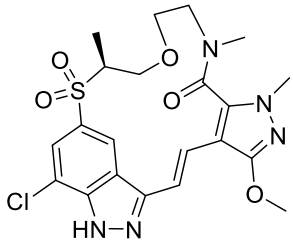
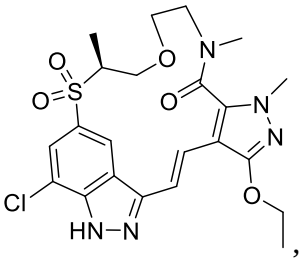
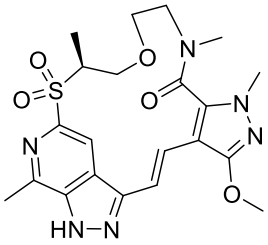
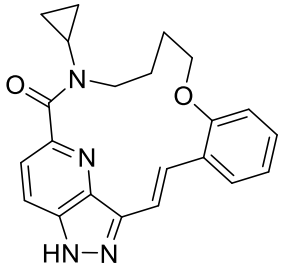
,

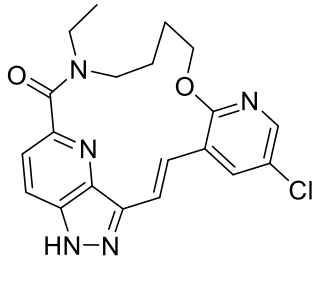
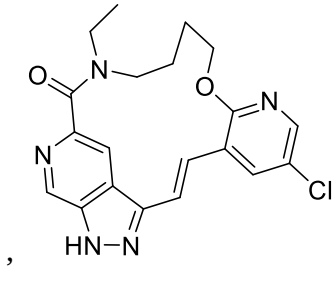
,

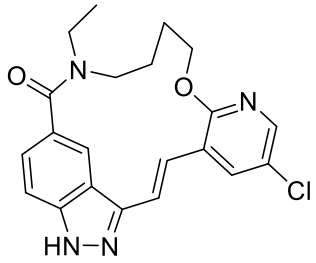
,

, , ,

, , ,

, , , ,

, , and

, or a pharmaceutical acceptable salt thereof.

~~65~~28. A pharmaceutical composition comprising a compound of any one of the preceding claims, and optionally one or more excipients.

~~66. A method of treating disease in a subject comprising, administering a therapeutically effective amount of a compound of any one of claims 1 to 64, or a pharmaceutical composition of claim 65.~~

~~67. A compound according to any one of claims 1 to 64, for use in a method of treating disease in a subject.~~

~~68~~29. Use of a compound according to any one of claims 1 to ~~64~~27 in the manufacture of a medicament for the treatment of disease in a subject.