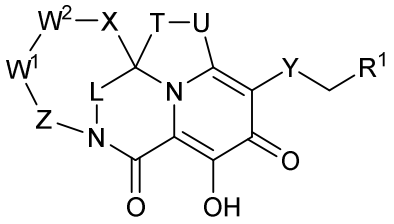
CLAIMS

We claim:

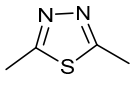
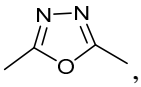
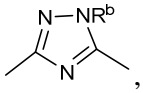
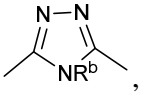
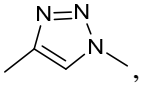
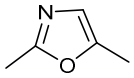
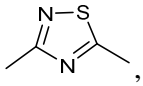
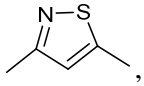
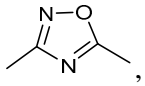
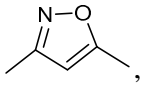
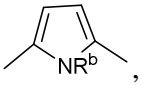
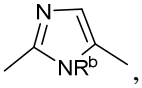
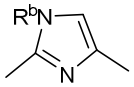
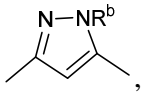
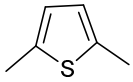
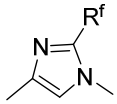
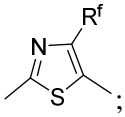
1. A compound of Formula I:



Formula I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is H, C_{6-10}aryl or C_{6-10}heteroaryl, wherein the C_{6-10}aryl or C_{6-10}heteroaryl are optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, cyano, –O–C_{1-4}alkyl, –O–C_{3-6}cycloalkyl, or C_{1-4}alkyl–O–C_{1-4}alkyl;

Y is selected from the group consisting of –C(O)NH–, , , , , , , , , , , , , , , , , and ;

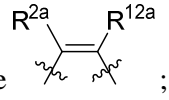
L is $–CR^{3a}R^{3b}–$, –C(O)–, $–SO_2–$, $–CR^{3a}R^{3b}–CR^{3c}R^{3d}–$, or $–N(R^a)–$;

W^1 is a bond or $–CR^{4a}R^{4b}–$;

W^2 is $–CR^{5a}R^{5b}–$, $–CR^{5a}R^{5b}CR^{5c}R^{5d}–$, $–CR^{6a}=CR^{6b}–$, $–N(R^7)–$, $–O–$, $–S(O)_n–$, $–C(O)NR^e–$, $–CR^{5a}R^{5b}–N(R^7)–$, $–CR^{5a}R^{5b}–O–$, $–CR^{5a}R^{5b}–S(O)_n–$, $-CR^{5a}R^{5b}–C(O)NR^e–$, $–CR^{5a}R^{5b}–NR^e–C(O)–$, $–S(O)_nN(R^e)–CR^{5a}R^{5b}–$, or $–N(R^e)–S(O)_n–CR^{5a}R^{5b}–$;

X is a bond or $–CR^{8a}R^{8b}–$;

Z is $–CR^{9a}R^{9b}–$, $–CR^{9a}R^{9b}CR^{9c}R^{9d}–$, or $–CR^{10a}=CR^{10b}–$;

T is $–CR^{2a}R^{2b}–$ or $—CR^{2a}R^{2b}–CR^{2c}R^{2d}$; U is $–NR^{11}–$, $–CR^{12a}R^{12b}–$, $–S(O)_n–$, $–C(O)–$, or $–O–$; or T and U together are ;

R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{12a}, and R^{12b} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, $–CH_2R^a–$, $–CH_2OR^a$, $–CH_2–S(O)_nR^a–$, $–OR^a$, $–O–C(O)–NHR^a$, $–NHR^a–$, $–C(O)–NH(R^a)–$, $–NR^e–C(O)R^a–$, $–NR^e–S(O)_nR^a–$, $–S(O)_n–NH(R^a)–$, or $–S(O)_n–R^a–$; ~~or~~

~~any one of (i) R^{2a} and R^{2b}, (ii) R^{2c} and R^{2d} or (iii) R^{12a} and R^{12b} together with the carbon atom to which they are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or OR^e;~~

R^{3a}, R^{3b}, R^{3c}, and R^{3d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or $–O–C_{1-4}$alkyl; ~~or~~

~~any one of (i) R^{3a} and R^{3b} or (ii) R^{3c} and R^{3d} together with the carbon atom to which they are attached form (i) a 3 to 7 membered carbocyclic ring or (ii) a 3 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 3 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or OR^e;~~

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{5c}, R^{5d}, R^{8a}, R^{8b}, R^{9a}, R^{9b}, R^{9c}, and R^{9d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, hydroxyl, cyano, –O–C_{1-4}alkyl, or C_{1-4}alkylene–O–C_{1-4}alkyl; ~~or~~

~~any one of (i) R^{4a} and R^{4b}, (ii) R^{5a} and R^{5b}, (iii) R^{5c} and R^{5d}, (iv) R^{5a} and R^{5c}, (v) R^{5b} and R^{5d}, (vi) R^{8a} and R^{8b}, (vii) R^{9a} and R^{9b}, (viii) R^{9c} and R^{9d}, (ix) R^{9a} and R^{9c}, (x) R^{9b} and R^{9d}, (xi) R^{8b} and one of R^{5a}, R^{5b}, R^{5c}, R^{5d}, and R^{7}, or (x) one of R^{9a}, R^{9b}, R^{9c}, and R^{9d} and one of R^{4a}, R^{4b}, R^{5a}, R^{5b}, and R^{7} together with the carbon atom to which they are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 to 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A3}, wherein each R^{A3} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or –OR^{e};~~

each R^{6a}, R^{6b}, R^{10a}, and R^{10b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl; ~~or~~

~~any one of (i) R^{6a} and R^{6b} or (ii) R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a 5 to 10 membered carbocyclic ring, (ii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (iii) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S, wherein the 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, the 6 to 10 membered aromatic ring, or the 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or –OR^{e};~~

R^{7} is H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $C(O)R^{c}$, or SO_2R^{c};

R^{11} is H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, –$C(O)$–R^{a}, –$S(O)_n$–R^{a}, –CH_2–R^{a};

each R^{a} is independently (i) H, (ii) C_{1-6}alkyl, (iii) C_{3-6}cycloalkyl, (iv) a 5 to 10 membered carbocyclic ring, (v) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (vi) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S;

wherein the C_{1-6}alkyl, C_{3-6}cycloalkyl, 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring or 5 to 10 membered

heteroaromatic ring is optionally substituted with 0 to 4 substituents independently selected from the group consisting of (i) oxo (ii) halo, (iii) cyano, (iv) –O–C_{1-4}alkyl, (v) C_{1-6}alkyl, (vi) –OR^e (vii) 3 to 10 membered carbocyclic ring, (viii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (ix) 6 to 10 membered aromatic ring, or (x) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S; wherein the 3 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring, or 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or –OR^e;

R^b is H, C_{1-4}alkyl, C_{1-4}haloalkyl or C_{3-6}cycloalkyl;

R^f is H, halo, C_{1-4}alkyl, or C_{1-4}haloalkyl;

each R^c is independently, H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl; C(O)R^d, or –SO_2R^d;

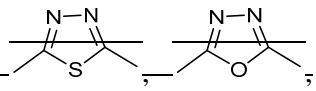
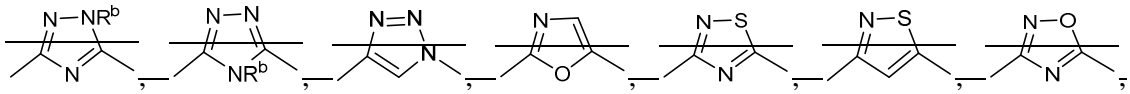
each R^d is independently C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, –NR^e_2, or –OR^e;

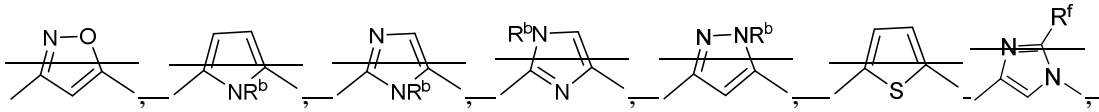
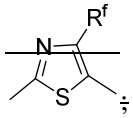
each R^e is independently H, C_{1-4}alkyl or C_{3-6}cycloalkyl wherein each C_{1-4}alkyl or C_{3-6}cycloalkyl is optionally substituted by a halo or a cyano; and

each n is 0, 1, or 2.

~~2. The compound of claim 1, or the pharmaceutically acceptable salt thereof, wherein:~~

~~R^1 is H, C_{6-10}aryl or C_{6-10}heteroaryl, wherein the C_{6-10}aryl or C_{6-10}heteroaryl are optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, cyano, –O–C_{1-4}alkyl, –O–C_{3-6}cycloalkyl, or C_{1-4}alkyl–O–C_{1-4}alkyl;~~

~~Y is selected from the group consisting of –C(O)NH–,~~  

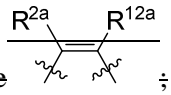
L is $CR^{3a}R^{3b}$, C(O), SO_2, $CR^{3a}R^{3b}CR^{3c}R^{3d}$, or $N(R^a)$;

W^1 is a bond or $-CR^{4a}R^{4b}-$;

W^2 is $CR^{5a}R^{5b}$, $CR^{5a}R^{5b}CR^{5c}R^{5d}$, $CR^{6a}=CR^{6b}$, $N(R^7)$, O, $S(O)_n$, $C(O)NR^e$, $CR^{5a}R^{5b}N(R^7)$, $CR^{5a}R^{5b}O$, $CR^{5a}R^{5b}S(O)_n$, $CR^{5a}R^{5b}C(O)NR^e$, $CR^{5a}R^{5b}NR^eC(O)$, $S(O)_nN(R^e)CR^{5a}R^{5b}$, or $N(R^e)S(O)_nCR^{5a}R^{5b}$;

X is a bond or $CR^{8a}R^{8b}$;

Z is $CR^{9a}R^{9b}$, $CR^{9a}R^{9b}CR^{9c}R^{9d}$, or $CR^{10a}=CR^{10b}$;

T is $CR^{2a}R^{2b}$ or $CR^{2a}R^{2b}CR^{2c}R^{2d}$; U is NR^{11}, $CR^{12a}R^{12b}$, $S(O)_n$, C(O), or O; or T and U together are ;

R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{12a}, and R^{12b} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, CH_2R^a, CH_2OR^a, $CH_2S(O)_nR^a$, OR^a, $OC(O)NHR^a$, NHR^a, $C(O)NH(R^a)$, $NR^eC(O)R^a$, $NR^eS(O)_nR^a$, $S(O)_nNH(R^a)$, or $S(O)_nR^a$; or

any one of (i) R^{2a} and R^{2b}, (ii) R^{2c} and R^{2d} or (iii) R^{12a} and R^{12b} together with the carbon atom to which they are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^e$;

R^{3a}, R^{3b}, R^{3c}, and R^{3d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or OC_{1-4}alkyl;

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{5c}, R^{5d}, R^{8a}, R^{8b}, R^{9a}, R^{9b}, R^{9c}, and R^{9d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, hydroxyl, cyano, –O–C_{1-4}alkyl, or C_{1-4}alkylene–O–C_{1-4}alkyl;

each R^{6a}, R^{6b}, R^{10a}, and R^{10b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl;

R^{7} is H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, C(O)R^{e}, or SO_2R^{e};

R^{11} is H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, –C(O)–R^{a}, –$S(O)_n$–R^{a}, –CH_2–R^{a};

each R^{a} is independently (i) H, (ii) C_{1-6}alkyl, (iii) C_{3-6}cycloalkyl, (iv) a 5 to 10 membered carbocyclic ring, (v) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (vi) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S;

wherein the C_{1-6}alkyl, C_{3-6}cycloalkyl, 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring or 5 to 10 membered heteroaromatic ring is optionally substituted with 0 to 4 substituents independently selected from the group consisting of (i) oxo (ii) halo, (iii) cyano, (iv) –O–C_{1-4}alkyl, (v) C_{1-6}alkyl, (vi) –OR^{e} (vii) 3 to 10 membered carbocyclic ring, (viii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (ix) 6 to 10 membered aromatic ring, or (x) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S; wherein the 3 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring, or 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or –OR^{e};

R^{b} is H, C_{1-4}alkyl, C_{1-4}haloalkyl or C_{3-6}cycloalkyl;

R^{f} is H, halo, C_{1-4}alkyl, or C_{1-4}haloalkyl;

each R^{e} is independently, H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl; C(O)R^{d}, or SO_2R^{d};

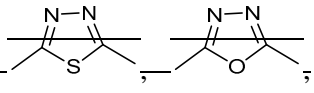
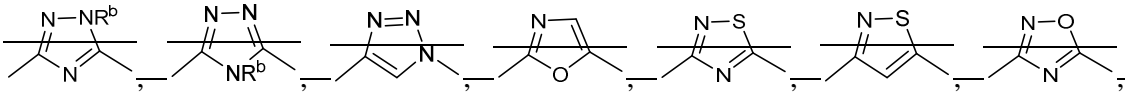
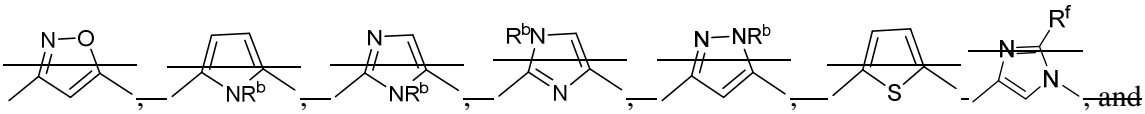
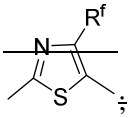
each R^{d} is independently C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, NR^{e}_2, or –OR^{e};

each R^e is independently H, C_{1-4}alkyl or C_{3-6}cycloalkyl wherein each C_{1-4}alkyl or C_{3-6}cycloalkyl is optionally substituted by a halo or a cyano; and

each n is 0, 1, or 2.

3. The compound of claim 1, or the pharmaceutically acceptable salt thereof, wherein:

R^1 is H, C_{6-10}aryl or C_{6-10}heteroaryl, wherein the C_{6-10}aryl or C_{6-10}heteroaryl are optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, cyano, -O-C_{1-4}alkyl, -O-C_{3-6}cycloalkyl, or C_{1-4}alkyl-O-C_{1-4}alkyl;

Y is selected from the group consisting of -C(O)NH-, , , , and ;

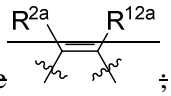
L is $CR^{3a}R^{3b}$, C(O), SO_2, $CR^{3a}R^{3b}-CR^{3c}R^{3d}$, or $N(R^a)$;

W^1 is a bond or $CR^{4a}R^{4b}$;

W^2 is $CR^{5a}R^{5b}$, $CR^{5a}R^{5b}CR^{5c}R^{5d}$, $CR^{6a}=CR^{6b}$, $N(R^7)$, O, $S(O)_n$, $C(O)NR^e$, $CR^{5a}R^{5b}-N(R^7)$, $CR^{5a}R^{5b}-O$, $CR^{5a}R^{5b}-S(O)_n$, $CR^{5a}R^{5b}-C(O)NR^e$, $CR^{5a}R^{5b}-NR^e-C(O)$, $S(O)_nN(R^e)$, $CR^{5a}R^{5b}$, or $N(R^e)-S(O)_n-CR^{5a}R^{5b}$;

X is a bond or $CR^{8a}R^{8b}$;

Z is $CR^{9a}R^{9b}$, $CR^{9a}R^{9b}CR^{9c}R^{9d}$, or $CR^{10a}=CR^{10b}$;

T is $CR^{2a}R^{2b}$ or $CR^{2a}R^{2b}-CR^{2c}R^{2d}$; U is NR^{11}, $CR^{12a}R^{12b}$, $S(O)_n$, C(O), or -O-; or T and U together are ;

R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{12a}, and R^{12b} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, $-CH_2R^a$, $-CH_2OR^a$, $-CH_2-S(O)_nR^a$, $-OR^a$, $-O-C(O)-NHR^a$, $-NHR^a$, $-C(O)-NH(R^a)$, $-NR^e-C(O)R^a$, $-NR^e-S(O)_nR^a$, $-S(O)_n-NH(R^a)$, or $-S(O)_n-R^a$;

R^{3a}, R^{3b}, R^{3c}, and R^{3d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or $-O-C_{1-4}$alkyl; or

any one of (i) R^{3a} and R^{3b} or (ii) R^{3c} and R^{3d} together with the carbon atom to which they are attached form (i) a 3 to 7 membered carbocyclic ring or (ii) a 3 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 3 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^e$;

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{5c}, R^{5d}, R^{8a}, R^{8b}, R^{9a}, R^{9b}, R^{9c}, and R^{9d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, hydroxyl, cyano, $-O-C_{1-4}$alkyl, or C_{1-4}alkylene$-O-C_{1-4}$alkyl;

each R^{6a}, R^{6b}, R^{10a}, and R^{10b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $C(O)R^e$, or SO_2R^e;

R^{11} is H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $-C(O)-R^a$, $-S(O)_n-R^a$, $-CH_2-R^a$;

each R^a is independently (i) H, (ii) C_{1-6}alkyl, (iii) C_{3-6}cycloalkyl, (iv) a 5 to 10 membered carbocyclic ring, (v) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (vi) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S;

wherein the C_{1-6}alkyl, C_{3-6}cycloalkyl, 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring or 5 to 10 membered heteroaromatic ring is optionally substituted with 0 to 4 substituents independently selected from the group consisting of (i) oxo (ii) halo, (iii) cyano, (iv) $-O-C_{1-4}$alkyl, (v) C_{1-6}alkyl, (vi) $-OR^e$ (vii) 3 to 10 membered carbocyclic ring, (viii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (ix) 6 to 10 membered aromatic ring, or (x) a 5 to 10

membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S; wherein the 3 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring, or 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^{e}$;

R^{b} is H, C_{1-4}alkyl, C_{1-4}haloalkyl or C_{3-6}cycloalkyl;

R^{f} is H, halo, C_{1-4}alkyl, or C_{1-4}haloalkyl;

each R^{e} is independently, H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl; $C(O)R^{d}$, or $-SO_2R^{d}$;

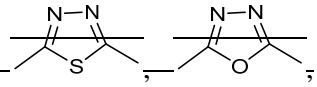
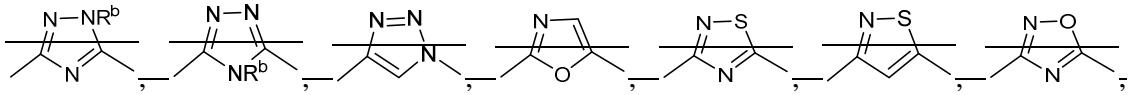
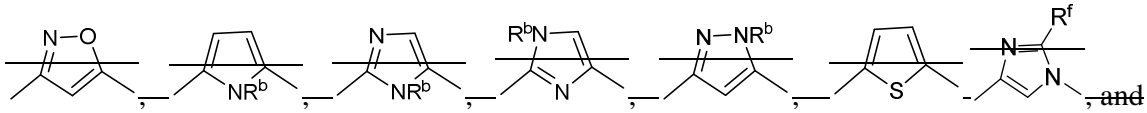
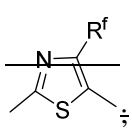
each R^{d} is independently C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $-NR^{e}_2$, or $-OR^{e}$;

each R^{e} is independently H, C_{1-4}alkyl or C_{3-6}cycloalkyl wherein each C_{1-4}alkyl or C_{3-6}cycloalkyl is optionally substituted by a halo or a cyano; and

each n is 0, 1, or 2.

4. A compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^{1} is H, C_{6-10}aryl or C_{6-10}heteroaryl, wherein the C_{6-10}aryl or C_{6-10}heteroaryl are optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, cyano, $-O-C_{1-4}$alkyl, $-O-C_{3-6}$cycloalkyl, or C_{1-4}alkyl-O-C_{1-4}alkyl;

Y is selected from the group consisting of $-C(O)NH-$, , , , , , and ;

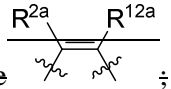
L is $-CR^{3a}R^{3b}-$, $-C(O)-$, $-SO_2-$, $-CR^{3a}R^{3b}-CR^{3c}R^{3d}-$, or $-N(R^a)-$;

W^1 is a bond or $-CR^{4a}R^{4b}-$;

W^2 is $-CR^{5a}R^{5b}-$, $-CR^{5a}R^{5b}CR^{5c}R^{5d}-$, $-CR^{6a}=CR^{6b}-$, $-N(R^7)-$, $-O-$, $-S(O)_n-$, $-C(O)NR^e-$, $-CR^{5a}R^{5b}-N(R^7)-$, $-CR^{5a}R^{5b}-O-$, $-CR^{5a}R^{5b}-S(O)_n-$, $-CR^{5a}R^{5b}-C(O)NR^e-$, $-CR^{5a}R^{5b}-NR^e-C(O)-$, $-S(O)_nN(R^e)-CR^{5a}R^{5b}-$, or $-N(R^e)-S(O)_n-CR^{5a}R^{5b}-$;

X is a bond or $-CR^{8a}R^{8b}-$;

Z is $-CR^{9a}R^{9b}-$, $-CR^{9a}R^{9b}CR^{9c}R^{9d}-$, or $-CR^{10a}=CR^{10b}-$;

T is $-CR^{2a}R^{2b}-$ or $-CR^{2a}R^{2b}-CR^{2c}R^{2d}-$; U is $-NR^{11}-$, $-CR^{12a}R^{12b}-$, $-S(O)_n-$, $-C(O)-$, or $-O-$; or T and U together are 

;

R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{12a}, and R^{12b} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, $-CH_2R^a$, $-CH_2OR^a$, $-CH_2-S(O)_nR^a$, $-OR^a$, $-O-C(O)-NHR^a$, $-NHR^a$, $-C(O)-NH(R^a)$, $-NR^e-C(O)R^a$, $-NR^e-S(O)_nR^a$, $-S(O)_n-NH(R^a)$, or $-S(O)_n-R^a$; or

R^{3a}, R^{3b}, R^{3c}, and R^{3d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or $-O-C_{1-4}$alkyl; or

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{5c}, R^{5d}, R^{8a}, R^{8b}, R^{9a}, R^{9b}, R^{9c}, and R^{9d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, hydroxyl, cyano, $-O-C_{1-4}$alkyl, or C_{1-4}alkylene$-O-C_{1-4}$alkyl; or

any one of (i) R^{4a} and R^{4b}, (ii) R^{5a} and R^{5b}, (iii) R^{5c} and R^{5d}, (iv) R^{5a} and R^{5c}, (v) R^{5b} and R^{5d}, (vi) R^{8a} and R^{8b}, (vii) R^{9a} and R^{9b}, (viii) R^{9c} and R^{9d}, (ix) R^{9a} and R^{9c}, (x) R^{9b} and R^{9d}, (xi) R^{8b} and one of R^{5a}, R^{5b}, R^{5c}, R^{5d}, and R^7, or (x) one of R^{9a}, R^{9b}, R^{9c}, and R^{9d} and one of R^{4a}, R^{4b}, R^{5a}, R^{5b}, and R^7 together with the carbon atom to which they are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 to 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A3}, wherein each R^{A3} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^e$;

each R^{6a}, R^{6b}, R^{10a}, and R^{10b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl;

~~R^7 is H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, C(O)R^e, or SO_2R^e;~~

~~R^{11} is H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, –C(O)–R^a, –$S(O)_n$–R^a, –CH_2–R^a;~~

~~each R^a is independently (i) H, (ii) C_{1-6}alkyl, (iii) C_{3-6}cycloalkyl, (iv) a 5 to 10 membered carbocyclic ring, (v) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (vi) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S;~~

~~wherein the C_{1-6}alkyl, C_{3-6}cycloalkyl, 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring or 5 to 10 membered heteroaromatic ring is optionally substituted with 0 to 4 substituents independently selected from the group consisting of (i) oxo (ii) halo, (iii) cyano, (iv) –O–C_{1-4}alkyl, (v) C_{1-6}alkyl, (vi) –OR^e (vii) 3 to 10 membered carbocyclic ring, (viii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (ix) 6 to 10 membered aromatic ring, or (x) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S; wherein the 3 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring, or 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or –OR^e;~~

~~R^b is H, C_{1-4}alkyl, C_{1-4}haloalkyl or C_{3-6}cycloalkyl;~~

~~R^f is H, halo, C_{1-4}alkyl, or C_{1-4}haloalkyl;~~

~~each R^e is independently, H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl; C(O)R^d, or –SO_2R^d;~~

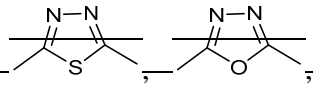
~~each R^d is independently C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, –NR^e_2, or –OR^e;~~

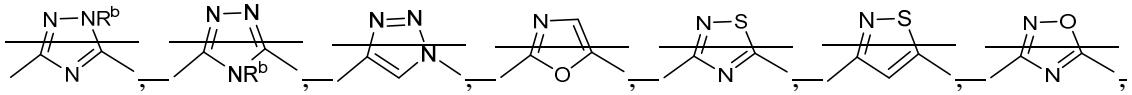
~~each R^e is independently H, C_{1-4}alkyl or C_{3-6}cycloalkyl wherein each C_{1-4}alkyl or C_{3-6}cycloalkyl is optionally substituted by a halo or a cyano; and~~

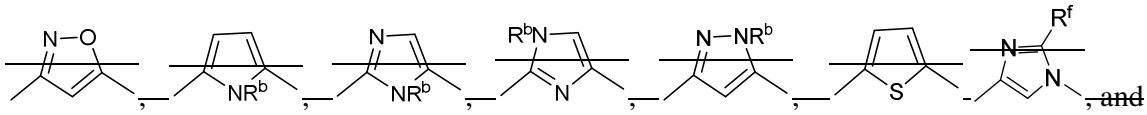
~~each n is 0, 1, or 2.~~

~~5. The compound of claim 1, or the pharmaceutically acceptable salt thereof, wherein:~~

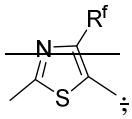
~~R^1 is H, C_{6-10}aryl or C_{6-10}heteroaryl, wherein the C_{6-10}aryl or C_{6-10}heteroaryl are optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, cyano, –O–C_{1-4}alkyl, –O–C_{3-6}cycloalkyl, or C_{1-4}alkyl–O–C_{1-4}alkyl;~~

~~Y is selected from the group consisting of –C(O)NH–,~~  ~~;~~





~~, and~~

 ~~;~~

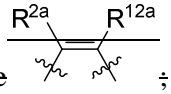
~~L is –$CR^{3a}R^{3b}$–, –C(O)–, –SO_2–, –$CR^{3a}R^{3b}$–$CR^{3c}R^{3d}$–, or –$N(R^a)$–;~~

~~W^1 is a bond or –$CR^{4a}R^{4b}$–;~~

~~W^2 is –$CR^{5a}R^{5b}$–, –$CR^{5a}R^{5b}CR^{5c}R^{5d}$–, –$CR^{6a}$=$CR^{6b}$–, –$N(R^7)$–, –O–, –$S(O)_n$–, –C(O)$NR^e$–, –$CR^{5a}R^{5b}$–$N(R^7)$–, –$CR^{5a}R^{5b}$–O–, –$CR^{5a}R^{5b}$–$S(O)_n$–, –$CR^{5a}R^{5b}$–C(O)$NR^e$–, –$CR^{5a}R^{5b}$–$NR^e$–C(O)–, –$S(O)_n N(R^e)$–$CR^{5a}R^{5b}$–, or –$N(R^e)$–$S(O)_n$–$CR^{5a}R^{5b}$–;~~

~~X is a bond or –$CR^{8a}R^{8b}$–;~~

~~Z is –$CR^{9a}R^{9b}$–, –$CR^{9a}R^{9b}CR^{9c}R^{9d}$–, or –$CR^{10a}$=$CR^{10b}$–;~~

~~T is –$CR^{2a}R^{2b}$– or –$CR^{2a}R^{2b}$–$CR^{2c}R^{2d}$–; U is –NR^{11}–, –$CR^{12a}R^{12b}$–, –$S(O)_n$–, –C(O)–, or –O–; or T and U together are~~  ~~;~~

~~R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{12a}, and R^{12b} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, –CH_2R^a–, –CH_2OR^a, –CH_2–$S(O)_nR^a$–, –OR^a, –O–C(O)–NHR^a, –NHR^a–, –C(O)–$NH(R^a)$–, –NR^e–C(O)R^a–, –NR^e–$S(O)_nR^a$–, –$S(O)_n$–$NH(R^a)$–, or –$S(O)_n$–R^a–;~~

R^{3a}, R^{3b}, R^{3c}, and R^{3d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or $-O-C_{1-4}$alkyl;

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{5c}, R^{5d}, R^{8a}, R^{8b}, R^{9a}, R^{9b}, R^{9c}, and R^{9d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, hydroxyl, cyano, $-O-C_{1-4}$alkyl, or C_{1-4}alkylene$-O-C_{1-4}$alkyl;

each R^{6a}, R^{6b}, R^{10a}, and R^{10b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl; or

any one of (i) R^{6a} and R^{6b} or (ii) R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a 5 to 10 membered carbocyclic ring, (ii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (iii) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S, wherein the 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, the 6 to 10 membered aromatic ring, or the 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^{e}$;

R^{7} is H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $C(O)R^{e}$, or SO_2R^{e};

R^{11} is H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $-C(O)-R^{a}$, $-S(O)_n-R^{a}$, $-CH_2-R^{a}$;

each R^{a} is independently (i) H, (ii) C_{1-6}alkyl, (iii) C_{3-6}cycloalkyl, (iv) a 5 to 10 membered carbocyclic ring, (v) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (vi) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S;

wherein the C_{1-6}alkyl, C_{3-6}cycloalkyl, 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring or 5 to 10 membered heteroaromatic ring is optionally substituted with 0 to 4 substituents independently selected from the group consisting of (i) oxo (ii) halo, (iii) cyano, (iv) $-O-C_{1-4}$alkyl, (v) C_{1-6}alkyl, (vi) $-OR^{e}$ (vii) 3 to 10 membered carbocyclic ring, (viii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (ix) 6 to 10 membered aromatic ring, or (x) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S; wherein the 3 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring, or 5 to 10 membered heteroaromatic ring is optionally substituted with

~~one to four R^{A5}, wherein each R^{A5} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^{e}$;~~

~~R^{b} is H, C_{1-4}alkyl, C_{1-4}haloalkyl or C_{3-6}cycloalkyl;~~

~~R^{f} is H, halo, C_{1-4}alkyl, or C_{1-4}haloalkyl;~~

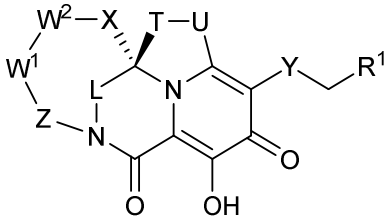
~~each R^{e} is independently, H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $C(O)R^{d}$, or $-SO_2R^{d}$;~~

~~each R^{d} is independently C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, NR^{e}_2, or $-OR^{e}$;~~

~~each R^{e} is independently H, C_{1-4}alkyl or C_{3-6}cycloalkyl wherein each C_{1-4}alkyl or C_{3-6}cycloalkyl is optionally substituted by a halo or a cyano; and~~

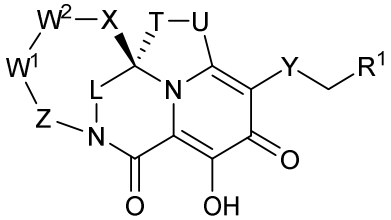
~~each n is 0, 1, or 2.~~

~~6.~~2. The compound of ~~any one of~~ claims 1~~-5~~, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula Ia or Formula Ib:

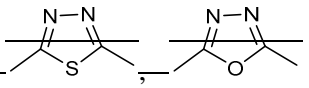
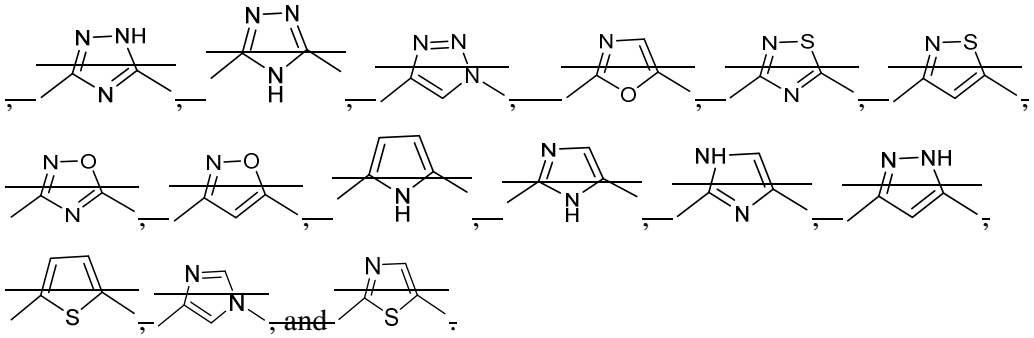


Formula Ia~~.~~

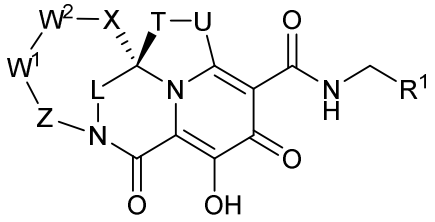
~~7. The compound of any of claims 1-5, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula Ib:~~



Formula Ib.

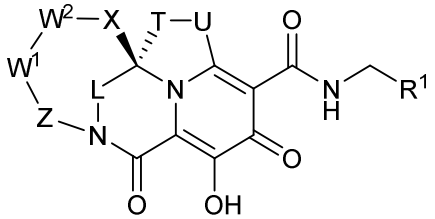
~~8. The compound of any one of claims 1-7, or the pharmaceutically acceptable salt thereof, wherein Y is selected from the group consisting of –C(O)NH–,~~  

~~12.~~5. The compound of ~~any one of~~ claim~~s 1-11~~4, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIa or Formula IIb:



Formula IIa.

~~13. The compound of any one of claims 1-11, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIb:~~



Formula IIb.

~~14. The compound of any one of claims 1-13, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, CH_2R^a, CH_2OR^a, $CH_2S(O)_nR^a$, OR^a, $OC(O)NHR^a$, NHR^a, $C(O)NHR^a$, $NR^eC(O)R^a$, $NR^eS(O)_nR^a$, $S(O)_nNHR^a$, or $S(O)_nR^a$.~~

~~15. The compound of any one of claims 1-14, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, CH_2R^a, CH_2OR^a, OR^a or NHR^a.~~

~~16. The compound of any one of claims 1-15, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, CH_2R^a, CH_2OR^a, or OR^a.~~

~~17. The compound of any one of claims 1-16, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, halo, or OR^a.~~

~~18.~~6. The compound of any one of claims 1-~~17~~5, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, halo, C_{1-6}alkyl, $-CH_2OR^a$ or $-OR^a$; and wherein each R^a is independently ~~H or R^a is independently~~ H or C_{1-6}alkyl.

~~19. The compound of any one of claims 1-18, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, halo, or $-OR^a$; and wherein R^a is H or R^a is independently H or C_{1-3}alkyl.~~

~~20. The compound of any one of claims 1-18, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, halo, or $-OR^a$; and wherein R^a is H or R^a is independently H or methyl.~~

~~21. The compound of any one of claims 1-16, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, or halo.~~

~~22. The compound of any one of claims 1-16, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, C_{1-6}alkyl, C_{3-6}cycloalkyl, or halo.~~

~~23. The compound of any one of claims 1-22, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H or halo.~~

~~24. The compound of any one of claims 1-14, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, $-C(O)-NH(R^a)$, $-NR^e-C(O)R^a$, $-NR^e-S(O)_nR^a$, $-S(O)_n-NH(R^a)$, $-S(O)_n-R^a$, or $-O-C(O)-NHR^a$.~~

~~25. The compound of any one of claims 1-14, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, $-OR^a$, $-NHR^a$, $-C(O)-NH(R^a)$, $-NR^e-C(O)R^a$, or $-NR^e-S(O)_nR^a$.~~

~~26. The compound of any one of claims 1-14, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, $-OR^a$, or $-O-C(O)-NHR^a$.~~

~~27. The compound of any one of claims 1-14, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, $-S(O)_n-NH(R^a)$, or $-S(O)_n-R^a$.~~

28. The compound of any one of claims 1-14, or the pharmaceutically acceptable salt thereof, R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, halo, cyano, $-NHR^a$ or $-OR^a$.

29. The compound of any one of claims 1-14 and 28, or the pharmaceutically acceptable salt thereof, R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H or $-NHR^a$.

30. The compound of any one of claims 1-16, or the pharmaceutically acceptable salt thereof, R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently is H, halo, cyano, or $-OR^a$.

31. The compound of any one of claims 1-16 and 30, or the pharmaceutically acceptable salt thereof, R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H or cyano.

32. The compound of any one of claims 1-16 and 30, or the pharmaceutically acceptable salt thereof, R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H or $-OR^a$.

33. The compound of any one of claims 1-13, wherein, any one of (i) R^{2a} and R^{2b} or (ii) R^{2c} and R^{2d} together with the carbon to which they are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_1-C_6alkyl, C_3-C_6cycloloalkyl or $-OR^e$.

34. The compound of any one of claims 1-33, or the pharmaceutically acceptable salt thereof, wherein R^a is independently H, C_{1-6}alkyl, or C_{3-6}cycloalkyl; wherein each C_{1-6}alkyl or C_{3-6}cycloalkyl is optionally substituted with 0 to 4 substituents independently selected from the group consisting of halo, cyano, $-O-C_{1-4}$alkyl, a 5 to 10 membered carbocyclic ring, a 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, a 6 to 10 membered aromatic ring, or a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S, wherein the 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, the 6 to 10 membered aromatic ring, or the 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^e$.

35. The compound of any one of claims 1-34, or the pharmaceutically acceptable salt thereof, wherein each R^a is independently H, C_1-C_6 alkyl, or C_3-C_6 cycloalkyl optionally

~~substituted with 1 to 2 substituents independently selected from the group consisting of halo, cyano, –O–C_1-C_4 alkyl, 5 to 10 membered carbocyclic ring, and 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O and S.~~

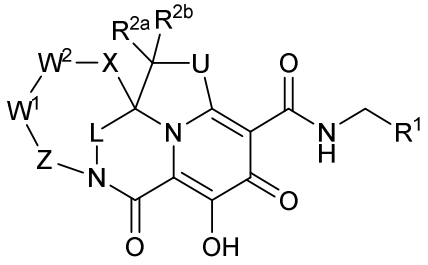
~~36. The compound of any one of claims 1-35, or the pharmaceutically acceptable salt thereof, wherein R^a is H, C_1-C_4 alkyl, or C_3-C_6 cycloalkyl optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, cyano, and –O–C_1-C_4 alkyl.~~

~~37. The compound of any one of claims 1-36, or the pharmaceutically acceptable salt thereof, wherein R^a is C_3-C_6 cycloalkyl optionally substituted optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, cyano, and –O–C_1-C_4alkyl.~~

~~38. The compound of any one of claims 1-36, or the pharmaceutically acceptable salt thereof, wherein R^a is C_1-C_6 alkyl optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, cyano, –O–C_1-C_4 alkyl.~~

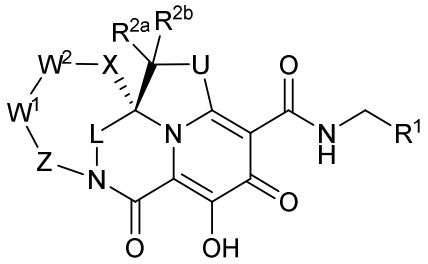
~~39. The compound of any one of claims 1-36, or the pharmaceutically acceptable salt thereof, wherein R^a is C_{1-6}alkyl optionally substituted with a –O–C_{1-4}alkyl or halo.~~

~~40.~~7. The compound of any one of claims 1-~~39~~6, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula III:



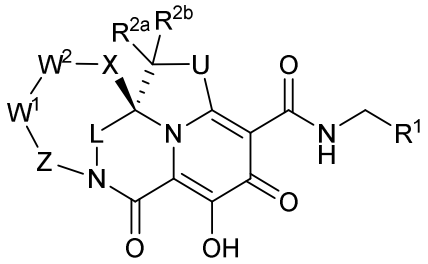
Formula III.

~~41.~~8. The compound of ~~any one of~~ claim~~s 1-40~~7, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIIa or Formula IIIb:



Formula IIIa.

~~42. The compound of any one of claims 1-40, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIIb:~~



Formula IIIb.

~~43. The compound of any one of claims 1-42, or the pharmaceutically acceptable salt thereof, wherein U is NR^{11}, CR^{12a}R^{12b}, C(O) or O.~~

~~44. The compound of any one of claims 1-43, or the pharmaceutically acceptable salt thereof, wherein U is NR^{11}, CR^{12a}R^{12b}, or O.~~

~~45. The compound of any one of claims 1-44, or the pharmaceutically acceptable salt thereof, wherein U is NR^{11} or CR^{12a}R^{12b}.~~

~~46. The compound of any one of claims 1-45, or the pharmaceutically acceptable salt thereof, wherein U is NR^{11}.~~

~~47. The compound of any one of claims 1-46, or the pharmaceutically acceptable salt thereof, wherein R^{11} is H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6cycloalkyl, or C_3-C_6halocycloalkyl.~~

~~48. The compound of any one of claims 1-47, or the pharmaceutically acceptable salt thereof, wherein R^{11} is H, C_3-C_6cycloalkyl, or C_3-C_6halocycloalkyl.~~

~~49. The compound of any one of claims 1-46, or the pharmaceutically acceptable salt thereof, wherein R^{11} is $-C(O)-R^a$, $-S(O)_n-R^a$, $-CH_2-R^a$.~~

~~50. The compound of any one of claims 1-42, or the pharmaceutically acceptable salt thereof, wherein U is $-S-$, $-S(O)-$, or $-S(O)_2-$.~~

~~51. The compound of any one of claims 1-42 and 50, or the pharmaceutically acceptable salt thereof, wherein U is $-S-$.~~

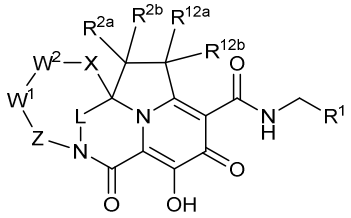
~~52. The compound of any one of claims 1-42 and 50, or the pharmaceutically acceptable salt thereof, wherein U is $-S(O)-$.~~

~~53. The compound of any one of claims 1-42 and 50, or the pharmaceutically acceptable salt thereof, wherein U is $-S(O)_2-$.~~

~~54. The compound of any one of claims 1-43, or the pharmaceutically acceptable salt thereof, wherein U is $-C(O)-$.~~

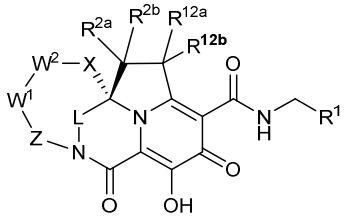
~~55. The compound of any one of claims 1-44, or the pharmaceutically acceptable salt thereof, wherein U is $-O-$.~~

~~56.~~9. The compound of any one of claims 1-~~45~~8, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IV:



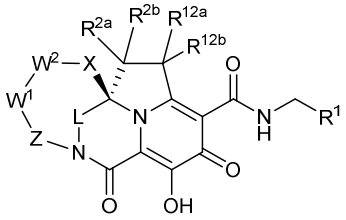
Formula IV.

~~57.~~10. The compound of ~~any one of~~ claim~~s 1-45 and 56~~9, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula ~~Iva~~IVa or Formula IVb:



Formula IVa~~.~~

~~58. The compound of any one of claims 1-45 and 56, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IVb:~~



Formula IVb.

~~59.~~11. The compound of ~~any one of~~ claim~~s 56-58~~9 or 10, or the pharmaceutically acceptable salt thereof, wherein:

X is $–CR^{8a}R^{8b}–$;

W^1 is a bond or $–CR^{4a}R^{4b}–$;

W^2 is $–CR^{5a}R^{5b}–$ or $–CR^{6a}=CR^{6b}–$;

Z is $–CR^{9a}R^{9b}–$;

L is $–CH_2–$;

R^{2a}, R^{2b}, R^{12a}, and R^{12b} are independently H, C_{1-6}alkyl, halo, $–OR^a–$, or $–CH_2OR^a$;

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

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a}, R^{9b} are independently H, hydroxyl, C_{1-6}alkyl, or $–O–C_{1-4}$alkyl;

both R^{6a} and R^{6b} are H; and

R^1 is C_{6-10}aryl optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently fluoro or chloro.

~~60. The compound of any one of claims 1-58, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H, –OR^a, or –O–C(O)–NHR^a.~~

~~61. The compound of any one of claims 1-58, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H, –NHR^a, –C(O)–$NH(R^a)$, –NR^e–C(O)R^a, –NR^e–$S(O)_nR^a$.~~

~~62. The compound of any one of claims 1-58, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H, –$S(O)_n$–$NH(R^a)$, or –$S(O)_n$–R^a–.~~

~~63. The compound of any one of claims 1-58, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H, halo, cyano, –NHR^a– or –OR^a.~~

~~64. The compound of any one of claims 1-60, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or –NHR^a.~~

~~65. The compound of any one of claims 1-58, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H, halo, cyano, or –OR^a.~~

~~66. The compound of any one of claims 1-58 and 65, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or cyano.~~

~~67. The compound of any one of claims 1-58 and 65, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or –OR^a.~~

~~68.~~12. The compound of ~~any one of~~ claim~~s~~ 1~~-58, 65, and 67~~, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H, halo, C_{1-6}alkyl, -CH_2OR^a, or –OR^a; and wherein each R^a is H or C_{1-6}alkyl.

~~69. The compound of any one of claims 1-58, 65, 67, and 68, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or –OR^a; and wherein each R^a is H or C_{1-3}alkyl.~~

~~70. The compound of any one of claims 1-58, 65, and 67-69, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or –OR^a; and wherein each R^a is H or methyl.~~

71. The compound of any one of claims 1-58, 65, and 67, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or $-OR^a$, and R^a is C_{3-6}cycloalkyl.

72. The compound of any one of claims 1-58, 65, and 67, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or $-OR^a$, and R^a is C_{1-4}haloalkyl.

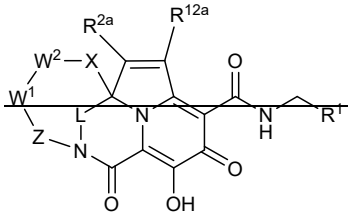
73. The compound of any one of claims 1-58, 65, and 67, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H or $-OR^a$, and R^a is C_{1-4}alkyl optionally substituted with $-O-C_{1-4}$alkyl.

74. The compound of any one of claims 1-58, wherein R^{12a} and R^{12b} together with the carbon atom to which they are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{1-6}cycloloalkyl or $-OR^e$.

75. The compound of any one of claims 1-58 and 74, wherein R^{12a} and R^{12b} together with the carbon atom to which they are attached form a (i) 3 to 7 membered carbocyclic ring, wherein the 3 to 7 membered carbocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{1-6}cycloloalkyl or $-OR^e$.

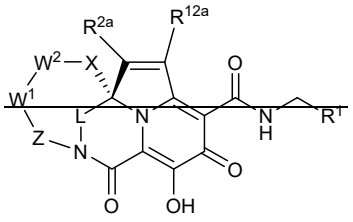
76. The compound of any one of claims 1-58 and 74, wherein R^{12a} and R^{12b} together with the carbon atom to which they are attached form a 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 4 to7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{1-6}cycloloalkyl or $-OR^e$.

~~77. The compound of any one of claims 1-13, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula V:~~



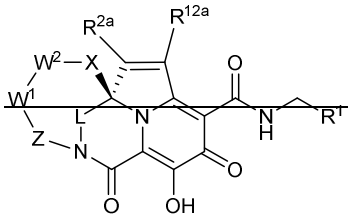
~~Formula V.~~

~~78. The compound of any one of claims 1-13 and 77, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula Va:~~



~~Formula Va.~~

~~79. The compound of any one of claims 1-13, and 78, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula Vb:~~



~~Formula Vb.~~

~~80.~~13. The compound of any one of claims 1-~~79~~12, or the pharmaceutically acceptable salt thereof, wherein W^1 is a bond.

~~81.~~14. The compound of any one of claims 1-~~79~~12, or the pharmaceutically acceptable salt thereof, wherein W^1 is $–CR^{4a}R^{4b}–$.

~~82.~~15. The compound of any one of claims 1-~~81~~14, or the pharmaceutically acceptable salt thereof, wherein W^2 is $–CR^{5a}R^{5b}–$ or $–CR^{6a}=CR^{6b}–$.

~~83.~~16. The compound of any one of claims 1-~~82~~15, or the pharmaceutically acceptable salt thereof, wherein W^2 is $–CR^{5a}R^{5b}–$.

~~84. The compound of any one of claims 1-82, or the pharmaceutically acceptable salt thereof, wherein W^2 is $–CR^{6a}=CR^{6b}–$; wherein R^{6a} and R^{6b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl.~~

~~85. The compound of any one of claims 1-82, or the pharmaceutically acceptable salt thereof, wherein W^2 is $–CR^{6a}=CR^{6b}–$; wherein each R^{6a} and R^{6b} together with the carbon atoms to which each is attached form (i) a 5 to 10 membered carbocyclic ring, (ii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (iii) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S, wherein the 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring, or 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl.~~

~~86. The compound of any one of claims 1-82, or the pharmaceutically acceptable salt thereof, wherein W2 is $–CR^{6a}=CR^{6b}–$; wherein each R^{6a} and R^{6b} together with the carbon atoms to which each is attached form (i) a 6 to 10 membered aromatic ring, or (ii) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S, wherein the 6 to 10 membered aromatic ring or the 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl.~~

~~87. The compound of any one of claims 1-82 and 85, or the pharmaceutically acceptable salt thereof, wherein W^2 is $–CR^{6a}=CR^{6b}–$; wherein each R^{6a} and R^{6b} together with the carbon atoms to which each is attached form (i) a 5 to 10 membered carbocyclic ring or (ii) a 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, wherein the 5 to 10 membered carbocyclic ring or the 5 to 10 membered heterocyclic ring, is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl.~~

~~88.~~17. The compound of any one of claims 1-~~87~~16, or the pharmaceutically acceptable salt thereof, wherein X is a bond.

~~89.~~18. The compound of any one of claims 1-~~87~~16, or the pharmaceutically acceptable salt thereof, wherein X is –$CR^{8a}R^{8b}$–.

~~90.~~19. The compound of any one of claims 1-~~89~~18, or the pharmaceutically acceptable salt thereof, wherein Z is –$CR^{9a}R^{9b}$–.

~~91. The compound of any one of claims 1-90, or the pharmaceutically acceptable salt thereof, wherein Z is –CR^{10a}=CR^{10b}–; wherein each R^{10a} and R^{10b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl.~~

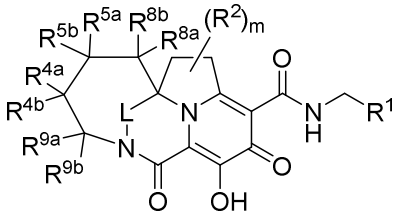
~~92. The compound of any one of claims 1-90, or the pharmaceutically acceptable salt thereof, wherein Z is –CR^{10a}=CR^{10b}–; wherein each R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a 5-to-10 membered carbocyclic ring, (ii) 5-to-10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (iii) a 6-to-10 membered aromatic ring, or (iv) a 5-to-10 membered heteroaromatic ring containing 1-to-3 heteroatoms selected from N, O and S, wherein the 5-to-10 membered carbocyclic ring, 5-to-10 membered heterocyclic ring, 6-to-10 membered aromatic ring, or 5-to-10 membered heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo, oxo, cyano, or C_{1-4}alkyl.~~

~~93. The compound of any one of claims 1-92, or the pharmaceutically acceptable salt thereof, wherein Z is –CR^{10a}=CR^{10b}–; wherein each R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a 6-to-10 membered aromatic ring, or (ii) a 5-to-10 membered heteroaromatic ring containing 1-to-3 heteroatoms selected from N, O and S, wherein the 6-to-10 membered aromatic ring or the 5-to-10 membered heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl.~~

~~94. The compound of any one of claims 1-90, or the pharmaceutically acceptable salt thereof, wherein Z is –CR^{10a}=CR^{10b}–; wherein each R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a 5-to-10 membered carbocyclic ring or (ii) a 5-to-10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, wherein the 5-to-10 membered carbocyclic ring or the 5-to-10 membered~~

~~heterocyclic ring, is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl.~~

~~95.~~20. The compound of any one of claims 1-~~94~~19, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VI:

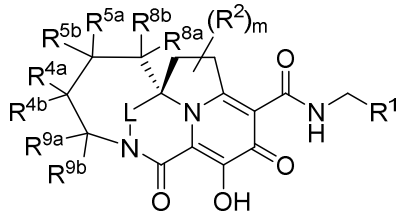


Formula VI;

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

each R^2 is independently C_{1-6}alkyl, ~~or~~ C_{3-6}cycloalkyl, halo, cyano, $–CH_2R^a–$, $–CH_2OR^a$, $–CH_2–S(O)_nR^a–$, $–OR^a$, $–O–C(O)–NHR^a$, $–NHR^a–$, $–C(O)–NH(R^a)–$, $–NR^e–C(O)R^a–$ $–NR^e–S(O)_nR^a–$, $–S(O)_n–NH(R^a)–$, or $–S(O)_n–R^a–$; or two R^2 on same carbon atom, together with the carbon atom to which they both are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $–OR^e$.

~~96.~~21. The compound of ~~any one of~~ claim~~s~~ ~~1-95~~20, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula ~~Via~~VIa or Formula VIb:

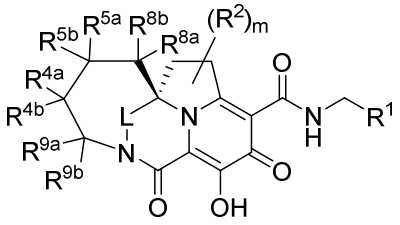


Formula VIa;

~~wherein m is 0, 1, 2, 3, or 4; and~~

~~each R^2 is independently C_{1-6}alkyl, or C_{3-6}cycloalkyl, halo, cyano, $-CH_2R^a-$, $-CH_2OR^a$, $-CH_2-S(O)_nR^a$, $-OR^a$, $-O-C(O)-NHR^a$, $-NHR^a$, $-C(O)-NH(R^a)$, $-NR^e-C(O)R^a$ $-NR^e-S(O)_nR^a$, $-S(O)_n-NH(R^a)$, or $-S(O)_n-R^a$; or two R^2 on same carbon atom, together with the carbon atom to which they both are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $-OR^e$.~~

~~97. The compound of any one of claims 1-95, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIb:~~



Formula VIb;

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

each R^2 is independently C_{1-6}alkyl, ~~or~~ C_{3-6}cycloalkyl, halo, cyano, $–CH_2R^a–$, $–CH_2OR^a$, $–CH_2–S(O)_nR^a–$, $–OR^a$, $–O–C(O)–NHR^a$, $–NHR^a–$, $–C(O)–NH(R^a)–$, $–NR^e–C(O)R^a–$ $–NR^e–S(O)_nR^a–$, $–S(O)_n–NH(R^a)–$, or $–S(O)_n–R^a–$; or two R^2 on same carbon atom, together with the carbon atom to which they both are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $–OR^e$.

~~98. The compound of any one of claims 1-97, wherein L is $-C(O)-$.~~

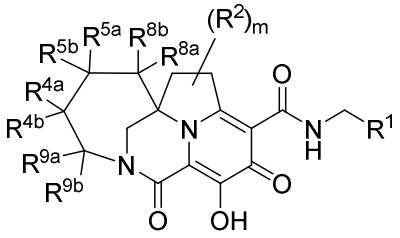
~~99. The compound of any one of claims 1-97, wherein L is $-SO_2-$.~~

~~100. The compound of any one of claims 1-97, wherein L is $-CH_2-CH_2-$.~~

~~101. The compound of any one of claims 1-97, wherein L is $-N(R^a)-$.~~

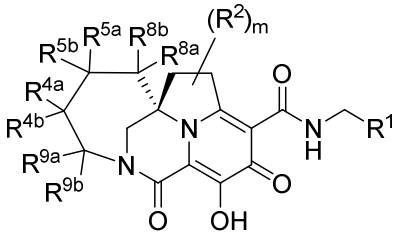
~~102. The compound of any one of claims 1-97, wherein L is $-CR^{3a}R^{3b}-$.~~

~~103.~~22. The compound of any one of claims 1-~~102~~21, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VII:



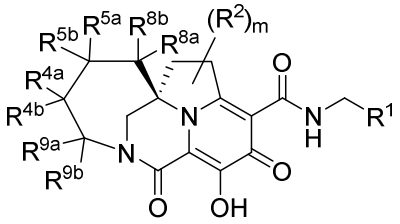
Formula VII.

~~104.~~23. The compound of ~~any one of~~ claim~~s~~ ~~1-102~~22, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIIa or Formula VIIb:



Formula VIIa~~.~~

~~105. The compound of any one of claims 1-102, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIIb:~~



Formula VIIb.

~~106. The compound of any one of claims 1-105, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl, pyridyl, pyridazine, pyrazine, or pyrimidine, wherein the phenyl, pyridyl, pyridazine, pyrazine, or pyrimidine is optionally substituted with one,~~

~~two, three, or four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, or –O–C_{1-4}alkyl.~~

~~107.~~24. The compound of any one of claims 1-~~106~~23, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl or pyridyl, wherein the phenyl or pyridyl is optionally substituted with one, two, three, or four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, or –O–C_{1-4}alkyl.

~~108.~~25. The compound of any one of claims 1-~~107~~24, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl or pyridyl, wherein the phenyl or pyridyl is substituted with one, two, three, or four halogens.

~~109. The compound of any one of claims 1-108 or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl or pyridyl, wherein the phenyl or pyridyl is substituted with two or three halogens selected from chloro and fluoro.~~

~~110. The compound of any one of claims 1-107, or the pharmaceutically acceptable salt thereof, wherein R^1 is pyridyl, wherein the pyridyl is optionally substituted with one, two, three, or four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, or –O–C_{1-4}alkyl.~~

~~111. The compound of any one of claims 1-107 and 110, or the pharmaceutically acceptable salt thereof, wherein R^1 is pyridyl, wherein the pyridyl is substituted with one, two, three, or four halogens.~~

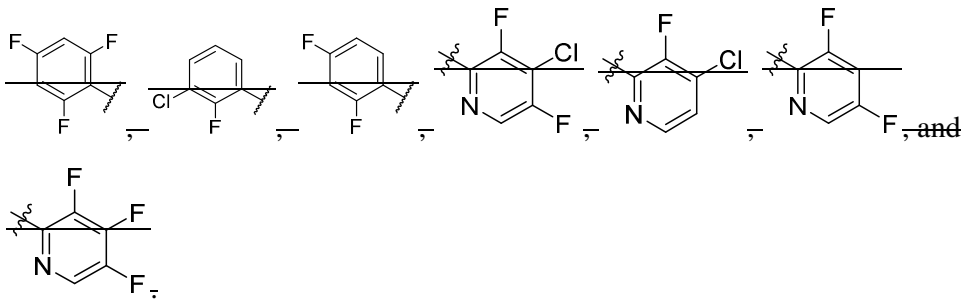
~~112. The compound of any one of claims 1-107 and 111, or the pharmaceutically acceptable salt thereof, wherein R^1 is pyridyl, wherein the pyridyl is substituted with two or three halogens selected from chloro and fluoro.~~

~~113.~~26. The compound of any one of claims 1-~~107~~24, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl, optionally substituted with one, two, three, or four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, or –O–C_{1-4}alkyl.

~~114. The compound of any one of claims 1-98 and 113, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl substituted with one, two, three, or four halogens.~~

~~115.~~27. The compound of any one of claims 1-~~98~~21, ~~113,~~ and ~~114~~26, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl substituted with two or three halogens selected from chloro and fluoro.

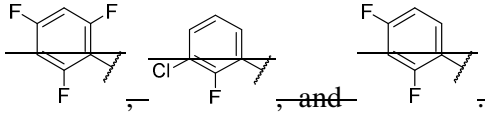
~~116. The compound of any one of claims 1-115, or the pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of:~~



~~, and~~

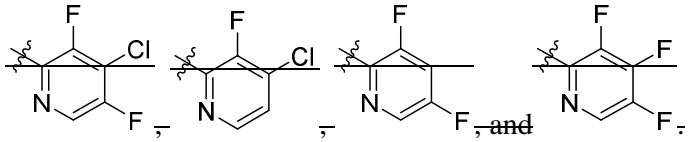
~~.~~

~~117. The compound of any one of claims 1-115, or the pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of:~~



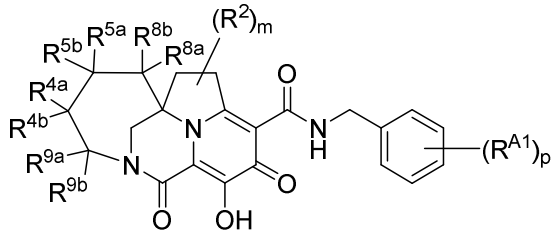
~~, and~~ ~~.~~

~~118. The compound of any one of claims 1-115, or the pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of:~~



~~, and~~ ~~.~~

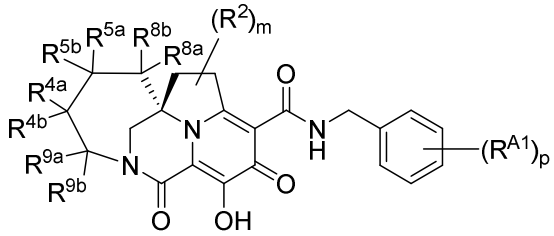
~~119.~~28. The compound of any one of claims 1-~~113~~26, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIII:



Formula VIII;

wherein p is 2 or 3.

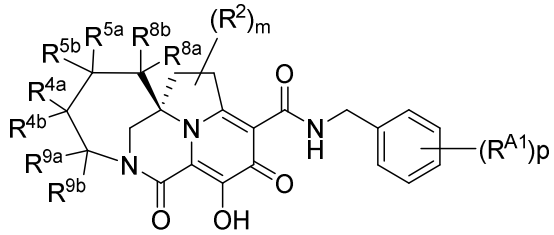
~~120.~~29.The compound of ~~any one of~~ claim~~s 1-119~~28, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIIIa or Formula VIIIb:



Formula VIIIa;

~~wherein p is 2 or 3.~~

~~121. The compound of any one of claims 1-119, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIIIb:~~



Formula VIIIb;

wherein p is 2 or 3.

~~122. The compound of any one of claims 1-121, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, halo, hydroxyl, cyano, –O–C_{1-4}alkyl, or C_{1-4}alkylene–O–C_{1-4}alkyl.~~

~~123.~~30.The compound of any one of claims 1-~~122~~29, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, C_1-C_6 alkyl, halo, or –O–C_{1-4}alkyl.

~~124. The compound of any one of claims 1-121, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, C_1-C_6 alkyl, halo, or cyano.~~

~~125. The compound of any one of claims 1-121, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, halo, or C_1-C_4 alkyl.~~

~~126. The compound of any one of claims 1-121, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, fluoro, chloro, or C_1-C_4 alkyl.~~

~~127. The compound of any one of claims 1-124, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, or cyano.~~

~~128. The compound of any one of claims 1-122, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, or C_1-C_{1-4}haloalkyl.~~

~~129. The compound of any one of claims 1-122 and 128, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, CH_3, CHF_2, or CH_2F.~~

~~130.~~31. The compound of any one of claims 1-~~122~~29, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, $-CH_3$, or $-OCH_3$.

~~131. The compound of claim 129, wherein R^{8a}, R^{8b}, R^{9a} or R^{9b} is H, CH_3, CHF_2, or CH_2F.~~

~~132. The compound of any one of claims 1-121, wherein any one of (i) R^{4a} and R^{4b}, (ii) R^{5a} and R^{5b}, (iii) R^{8a} and R^{8b}, or (iv) R^{9a} and R^{9b} together with the carbon atom to which they are attached form (i) a 3 to 7 membered carbocyclic ring or (ii) a 4 to 7 membered heterocyclic ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A3}, wherein each R^{A3} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or OR^e.~~

~~133. The compound of any one of claims 1-121, wherein any one of (i) R^{4a} and R^{4b}, (ii) R^{5a} and R^{5b}, (iii) R^{8a} and R^{8b}, or (iv) R^{9a} and R^{9b} together with the carbon atom to which they are attached form (i) a 3 to 7 membered carbocyclic ring.~~

~~134. The compound of any one of claims 1-121, wherein (i) R^{4a} and R^{4b}, (ii) R^{5a} and R^{5b}, (iii) R^{8a} and R^{8b}, or (iv) R^{9a} and R^{9b} together with the carbon atom to which they are attached form a 3 membered carbocyclic ring.~~

~~135.~~32. The compound of any one of claims ~~95~~20-~~126~~30, wherein m is 0, 1, or 2.

~~136. The compound of any one of claims 95-134, wherein m is 0.~~

~~137. The compound of any one of claims 95-134, wherein m is 1.~~

~~138. The compound of any one of claims 95-134, wherein m is 2.~~

~~139. The compound of any one of claims 95-138, wherein each R^2 is independently $-OR^a$ or $-O-C(O)-NHR^a$.~~

~~140. The compound of any one of claims 95-138, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently $-NHR^a$, $-C(O)-NH(R^a)$, $-NR^e-C(O)R^a$, $-NR^e-S(O)_nR^a$.~~

~~141. The compound of any one of claims 95-138, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently $-S(O)_n-NH(R^a)$, or $-S(O)_n-R^a$.~~

~~142. The compound of any one of claims 95-138, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, cyano, $-NHR^a$, or $-OR^a$.~~

~~143. The compound of any one of claims 95-138, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently $-NHR^a$.~~

~~144. The compound of any one of claims 95-138, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, cyano, or $-OR^a$.~~

~~145. The compound of any one of claims 1-138 and 144, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo or cyano.~~

~~146. The compound of any one of claims 95-138, or the pharmaceutically acceptable salt thereof, wherein R^2 is halo.~~

~~147. The compound of any one of claims 95-138, or the pharmaceutically acceptable salt thereof, wherein R^2 is cyano.~~

~~148. The compound of any one of claims 1-135, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo or –OR^a.~~

~~149.~~33. The compound of any one of claims 1-~~135~~ 32~~and 148~~, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, C_1-C_6 alkyl, -CH_2OR^a, or –OR^a; wherein each R^a is independently H or C_1-C_6 alkyl.

~~150. The compound of any one of claims 1-135, 148, and 149, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo or –OR^a; wherein each R^a is independently H or C_1-C_3 alkyl.~~

~~151.~~34. The compound of any one of claims 1-~~135~~33~~, and 148-150,~~ or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, C_1-C_6 alkyl, -CH_2OR^a, or –OR^a; wherein each R^a is independently H or methyl.

~~152. The compound of any one of claims 1-135, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently –OR^a.~~

~~153. The compound of any one of claims 95-135, or the pharmaceutically acceptable salt thereof, wherein R^2 is –OR^a and R^a is C_3-C_6 cycloalkyl optionally substituted optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, cyano, and –O-C_1-C_4alkyl.~~

~~154. The compound of any one of claims 95-135, or the pharmaceutically acceptable salt thereof, wherein R^2 is –OR^a; wherein R^a is C_1-C_6 alkyl optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, cyano, –O-C_1-C_4 alkyl.~~

~~155. The compound of any one of claims 95-135, or the pharmaceutically acceptable salt thereof, wherein R^2 is –OR^a; wherein R^a is C_1-C_6 alkyl optionally substituted with a –O-C_{1-4}alkyl or halo.~~

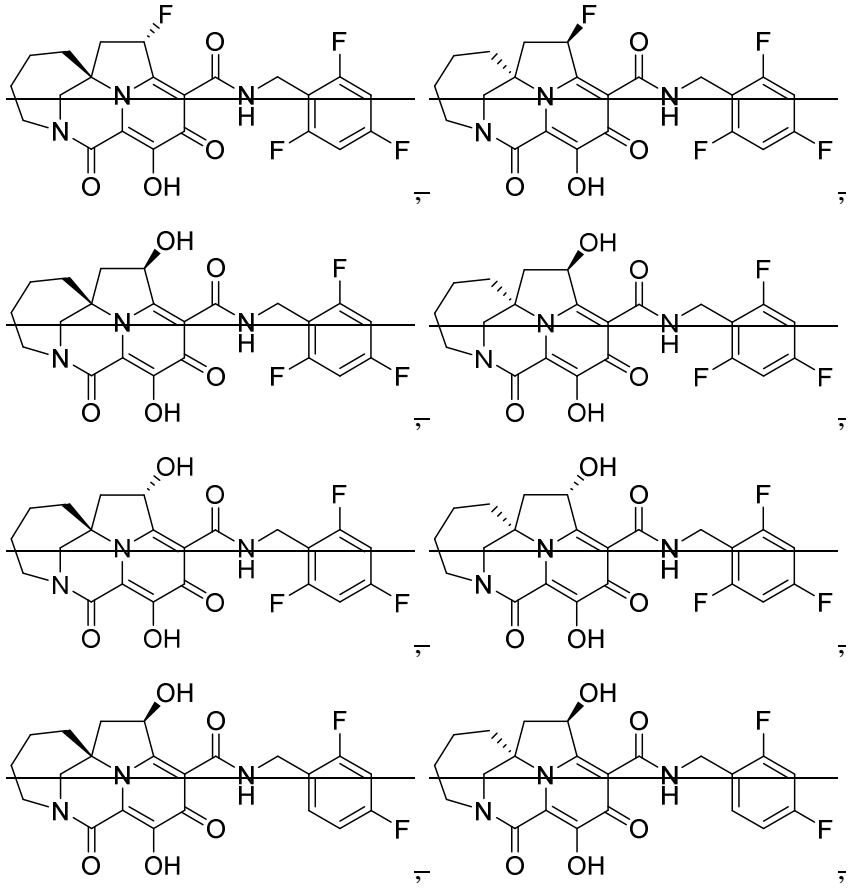
~~156. The compound of any one of claims 95-135 and 155, or the pharmaceutically acceptable salt thereof, wherein R^2 is $-OR^a$; wherein R^a is C_1-C_6 alkyl optionally substituted with a $-O-C_{1-4}$alkyl.~~

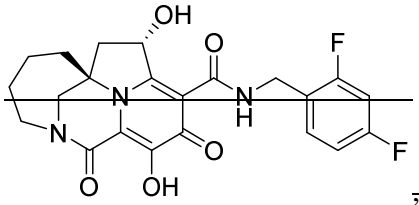
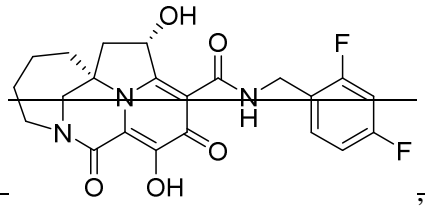
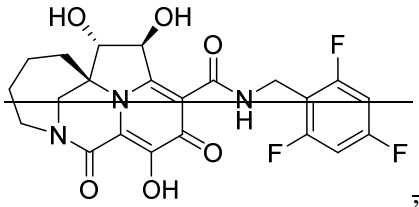
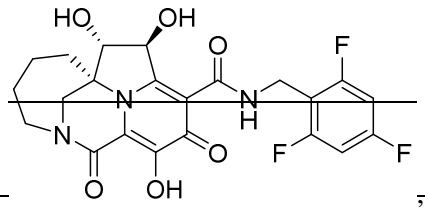
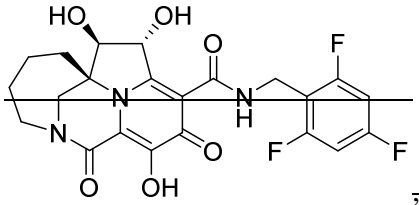
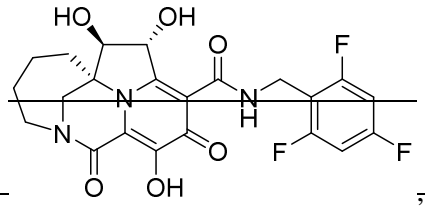
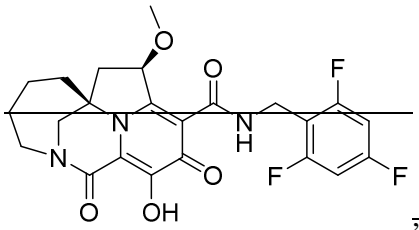
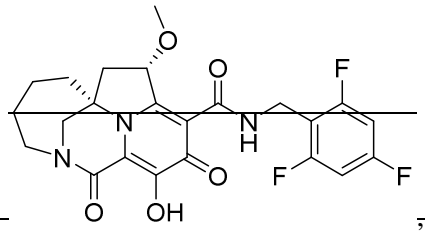
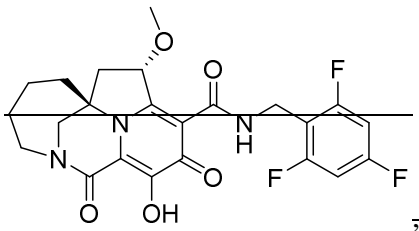
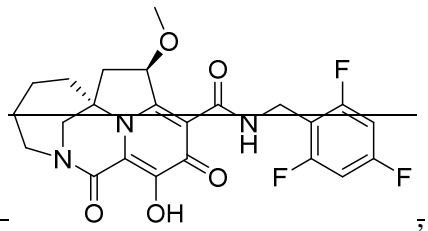
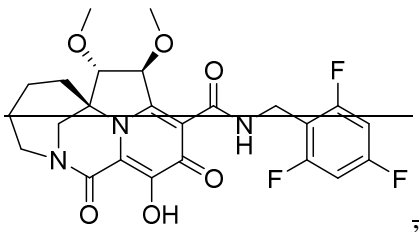
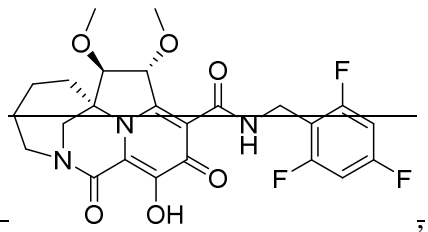
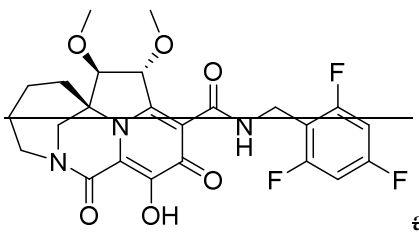
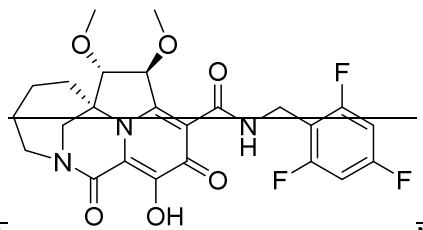
~~157.~~35. The compound of any one of claims ~~119~~28-~~155~~34, wherein ~~p is 3, and~~ each R^{A1} is independently a halo.

~~158. The compound of any one of claims 119-155, wherein p is 2, and each R^{A1} is independently a halo.~~

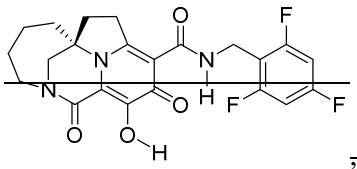
~~159. The compound of any one of claims 1-158, wherein each R^{A1} is independently a fluoro or a chloro.~~

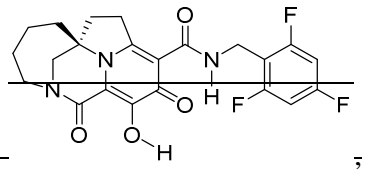
~~160. A compound selected from the group consisting of:~~

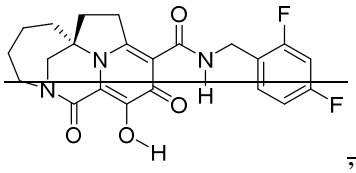


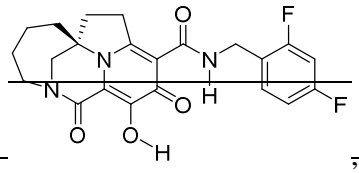

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and

, or a pharmaceutically acceptable salt thereof.

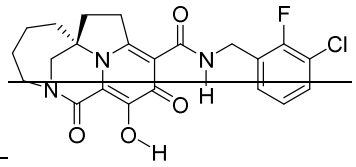
~~161. A compound selected from the group consisting of:~~

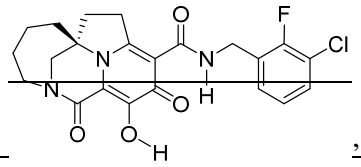

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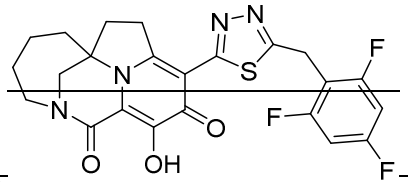

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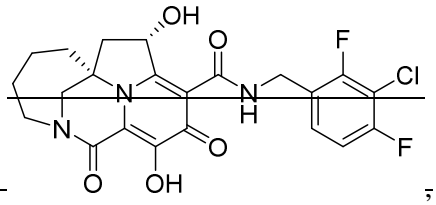

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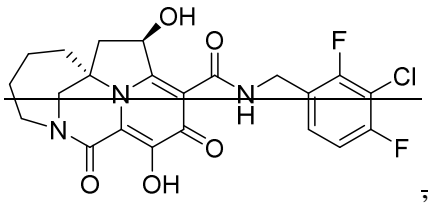

~~' and~~

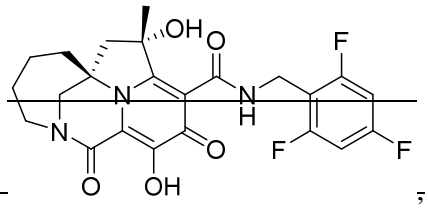
~~or a~~

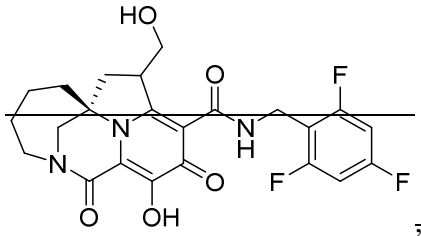
~~pharmaceutically acceptable salt thereof.~~

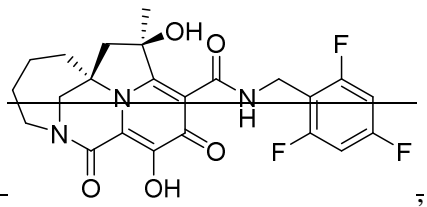

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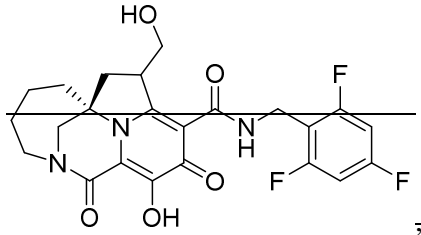
~~162. A compound selected from the group consisting of:~~

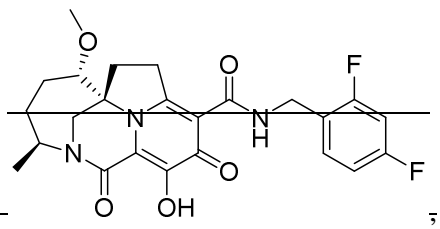

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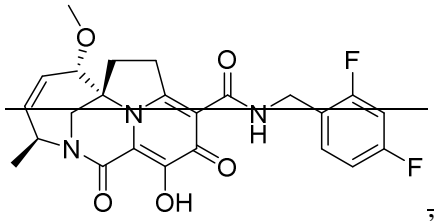
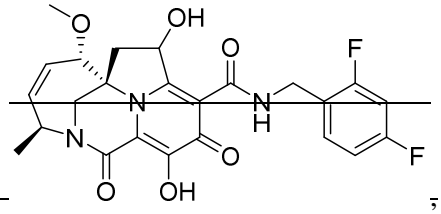
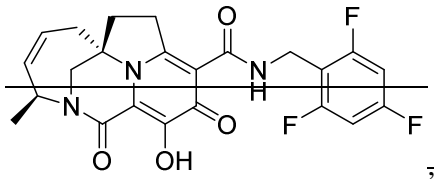
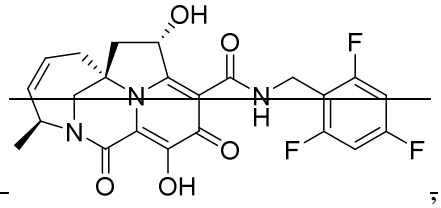
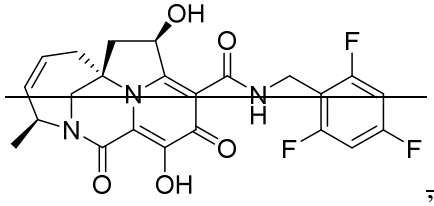
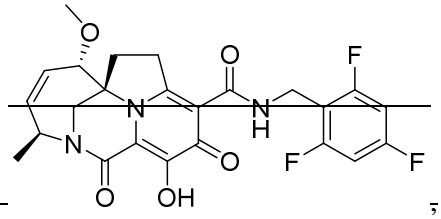
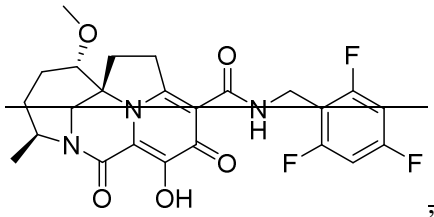
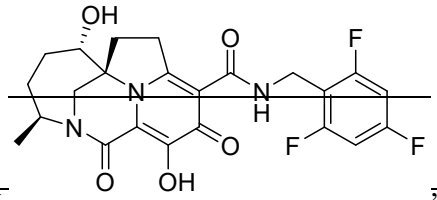

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~~, and~~ ~~, or a pharmaceutically acceptable salt thereof.~~

~~163.~~36. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-~~162~~35, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

~~164. The pharmaceutical composition of claim 163, further comprising one, two, three, or four additional therapeutic agents.~~

~~165. The pharmaceutical composition of claim 164, wherein the additional therapeutic agent or agents are anti-HIV agents.~~

~~166. The pharmaceutical composition of claim 164 or 165, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, latency reversing agents, capsid polymerization inhibitors,~~

HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof.

167. The pharmaceutical composition of any one of claims 164-166, wherein the additional therapeutic agent or agents comprise a HIV capsid inhibitor.

168. The pharmaceutical composition of any one of claims 164-167, wherein the additional therapeutic agent or agents comprise lenacapavir.

169. The pharmaceutical composition of any one of claims 164-166, wherein the additional therapeutic agent or agents comprise a nucleoside reverse transcriptase translocation inhibitor.

170. The pharmaceutical composition of any one of claims 164-166 and 169, wherein the additional therapeutic agent or agents comprise islatravir.

171. The pharmaceutical composition of any one of claims 164-166, wherein the additional therapeutic agent or agents comprise a HIV capsid inhibitor and a nucleoside reverse transcriptase translocation inhibitor.

172. The pharmaceutical composition of any one of claims 164-166 and 171, wherein the additional therapeutic agent or agents comprise lenacapavir and islatravir.

173. The pharmaceutical composition of any one of claims 164-166, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-1-(3-(4-chloro-3-(methylsulfonamido)-1-(2,2,2-trifluoroethyl)-1*H*-indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-1-yn-1-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-1*H*-cyclopropa[3,4]cyclopenta[1,2-*c*]pyrazol-1-yl)acetamide, or a pharmaceutically acceptable salt thereof.

174. The pharmaceutical composition of any one of claims 163-173, wherein the pharmaceutical composition is for oral or parenteral administration.

175. A kit comprising a compound of any one of claims 1-162, or a pharmaceutically acceptable salt thereof, and instructions for use.

176. The kit of claim 175, further comprising one, two, three, or four additional therapeutic agent or agents.

177. The kit of claim 176, wherein the additional therapeutic agent or agents are anti-HIV agents.

178. The kit of any one of claim 176 or 177, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, latency reversing agents, capsid polymerization inhibitors, HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof.

179. The kit of any one of claims 176-178, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-1-(3-(4-chloro-3-(methylsulfonamido)-1-(2,2,2-trifluoroethyl)-1*H*-indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-1-yn-1-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-1*H*-cyclopropa[3,4]cyclopenta[1,2-*c*]pyrazol-1-yl)acetamide, or a pharmaceutically acceptable salt thereof.

180. A method of treating an HIV infection in a human having or at risk of having the infection, comprising administering to the human a therapeutically effective amount of a compound of any one of claims 1-162, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 163-174.

181. The method of claim 180, further comprising administering to the human a therapeutically effective amount of one, two, three, or four additional therapeutic agents.

182. The method of claim 181, wherein the additional therapeutic agent or agents are anti-HIV agents.

183. The method of claim 181 or 182, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors,

latency reversing agents, capsid polymerization inhibitors, HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof.

184. The method of any one of claims 181-183, wherein the additional therapeutic agent or agents comprise a HIV capsid inhibitor or a nucleoside reverse transcriptase translocation inhibitor.

185. The method of any one of claims 181-184, wherein the additional therapeutic agent or agents comprise lenacapavir and islatravir.

186. The method of any one of claims 181-184, wherein the additional therapeutic agent or agents comprise a HIV capsid inhibitor.

187. The method of any one of claims 181-184 and 186, wherein the additional therapeutic agent or agents comprise lenacapavir.

188. The method of any one of claims 181-184, wherein the additional therapeutic agent or agents comprise a nucleoside reverse transcriptase translocation inhibitor.

189. The method of any one of claims 181-184 and 188, wherein the additional therapeutic agent or agents comprise islatravir.

190. The method of any one of claims 181-183, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-1-(3-(4-chloro-3-(methylsulfonamido)-1-(2,2,2-trifluoroethyl)-1*H*-indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-1-yn-1-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-1*H*-cyclopropa[3,4]cyclopenta[1,2-*c*]pyrazol-1-yl)acetamide, or a pharmaceutically acceptable salt thereof.

191. The method of any one of claim 180-190, wherein the administration is oral, intravenous, subcutaneous, or intramuscular.

192. Use of a compound of any one of claims 1-162, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 163-174, for treating an HIV infection in a human having or at risk of having the infection.

193. A compound of any one of claims 1-162, or pharmaceutically acceptable salt thereof, or

~~a pharmaceutical composition of any one of claims 163-174, for use in medical therapy.~~

~~194. A compound of any one of claims 1-162 or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 163-174, for use in treating an HIV infection.~~

~~195.~~37. Use of a compound of any one of claims 1-~~162~~ 35 or pharmaceutically acceptable salt thereof, ~~or a pharmaceutical composition of any one of claims 163-174,~~ in the

manufacture of a medicament for treating an HIV infection in a human having or at risk of having the infection.

38. The compound of claim 28, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, C_1-C_6 alkyl, halo, or –O-C_{1-4}alkyl.

39. The compound of claim 38, or the pharmaceutically acceptable salt thereof, wherein m is 0, 1, or 2.

40. The compound of claim 39, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, C_{1-6}alkyl, -CH_2OR^a or –OR^a; wherein each R^a is independently H or C_1-C_6 alkyl.

41. The compound of claim 40, or the pharmaceutically acceptable salt thereof, wherein each R^{A1} is independently a halo.

42. The compound of claim 41, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each H.

43. The compound of claim 42, or the pharmaceutically acceptable salt thereof, wherein m is 0.

44. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 42, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

45. Use of the compound of claim 42, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an HIV infection in a human having or at risk of having the infection.