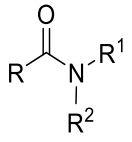
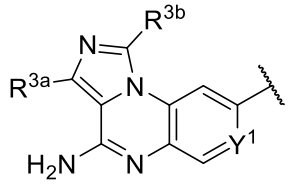
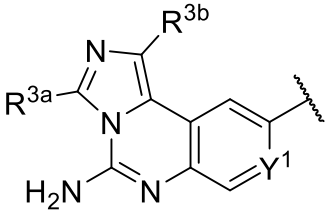
CLAIMS

1. A compound of Formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein

R is  or ;

each R^{3a} is independently H, -CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{3-4} cycloalkyl, or halo;

each R^{3b} is independently H, -CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{3-4} cycloalkyl, or halo;

Y^1 is N, or CR^{Y1}; wherein R^{Y1} is H, F, Cl, Br, CN, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, $-CH_2OCH_3$, or C_{1-3} haloalkoxy;

R^1 and R^2 together with the N to which they are attached form a heterocyclyl; wherein the heterocyclyl formed from R^1 and R^2 together with the N to which they are attached is optionally substituted with one to four Z^6, which may be the same or different; wherein the heterocyclyl formed from R^1 and R^2 is 10 to 20 membered heterocyclyl having 0 to 3 additional heteroatoms each independently N, O, or S; wherein the heterocyclyl formed from R^1 and R^2 together with the N to which they are attached is tricycle or tetracycle;

each Z^6 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, $-N_3$, -CN, $-O-R^{12a}$, $-C(O)-R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)-N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})C(O)-R^{12b}$, $-N(R^{12a})C(O)O-R^{12b}$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-NR^{12a}S(O)_2N(R^{12b})(R^{12c})$, $-NR^{12a}S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, $-OC(O)-N(R^{12a})(R^{12b})$, $-S-R^{12a}$, $-SF_5$, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, or $-S(O)(NR^{12a})R^{12b}$; wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl of each Z^6, is each optionally substituted with 1 to 4 Z^{1a}, which may be the same or different;

each Z^{1a} is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), or -S(O)(N$R^{12a}$)$R^{12b}$; wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl of Z^{1a} is each optionally substituted with 1 to 4 Z^{1b}, which may be the same or different;

each Z^{1b} is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -OH, -CN, -NO_2, -NH_2, -N_3, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{2-6} alkenyl), -O(C_{2-6} alkynyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(C_{6-10} aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{2-6} alkenyl), -NH(C_{2-6} alkynyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(C_{6-10} aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$, -N(C_{2-6} alkenyl)$_2$, -N(C_{2-6} alkynyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -N(heterocyclyl)$_2$, -N(C_{6-10} aryl)$_2$, -N(heteroaryl)$_2$, -N(C_{1-9} alkyl)(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)(C_{2-6} alkenyl), -N(C_{1-9} alkyl)(C_{2-6} alkynyl), -N(C_{1-9} alkyl)(C_{3-15} cycloalkyl), -N(C_{1-9} alkyl)(heterocyclyl), -N(C_{1-9} alkyl)(C_{6-10} aryl), -N(C_{1-9} alkyl)(heteroaryl), -C(O)(C_{1-9} alkyl), -C(O)(C_{1-8} haloalkyl), -C(O)(C_{2-6} alkenyl), -C(O)(C_{2-6} alkynyl), -C(O)(C_{3-15} cycloalkyl), -C(O)(heterocyclyl), -C(O)(C_{6-10} aryl), -C(O)(heteroaryl), -C(O)O(C_{1-9} alkyl), -C(O)O(C_{1-8} haloalkyl), -C(O)O(C_{2-6} alkenyl), -C(O)O(C_{2-6} alkynyl), -C(O)O(C_{3-15} cycloalkyl), -C(O)O(heterocyclyl), -C(O)O(C_{6-10} aryl), -C(O)O(heteroaryl), -C(O)NH_2, -C(O)NH(C_{1-9} alkyl), -C(O)NH(C_{1-8} haloalkyl), -C(O)NH(C_{2-6} alkenyl), -C(O)NH(C_{2-6} alkynyl), -C(O)NH(C_{3-15} cycloalkyl), -C(O)NH(heterocyclyl), -C(O)NH(C_{6-10} aryl), -C(O)NH(heteroaryl), -C(O)N(C_{1-9} alkyl)$_2$, -C(O)N(C_{1-8} haloalkyl)$_2$, -C(O)N(C_{2-6} alkenyl)$_2$, -C(O)N(C_{2-6} alkynyl)$_2$, -C(O)N(C_{3-15} cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, -C(O)N(C_{6-10} aryl)$_2$, -C(O)N(heteroaryl)$_2$, -NHC(O)(C_{1-9} alkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{2-6} alkenyl), -NHC(O)(C_{2-6} alkynyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(C_{6-10} aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkenyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl),-NHC(O)O(C_{6-10} aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), -NHC(O)NH(C_{1-8} haloalkyl), -NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), -NHC(O)NH(heteroaryl), -

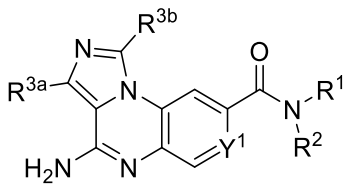
NHS(O)(C_{1-9} alkyl), -N(C_{1-9} alkyl)(S(O)(C_{1-9} alkyl), -S(C_{1-9} alkyl), -S(C_{1-8} haloalkyl), -S(C_{2-6} alkenyl), -S(C_{2-6} alkynyl), -S(C_{3-15} cycloalkyl), -S(heterocyclyl), -S(C_{6-10} aryl), -S(heteroaryl), -S(O)N(C_{1-9} alkyl)$_2$, -S(O)(C_{1-9} alkyl), -S(O)(C_{1-8} haloalkyl), -S(O)(C_{2-6} alkenyl), -S(O)(C_{2-6} alkynyl), -S(O)(C_{3-15} cycloalkyl), -S(O)(heterocyclyl), -S(O)(C_{6-10} aryl), -S(O)(heteroaryl), -S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{2-6} alkenyl), -S(O)$_2$(C_{2-6} alkynyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(C_{6-10} aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl of Z^{1b} is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH$_2$, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(aryl), -NH(heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(heteroaryl), -NHC(O)NH(C_{1-9} alkyl), S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(aryl), -S(O)$_2$(heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$; and

each R^{2a1}, R^{2b1}, R^{12a}, R^{12b}, or R^{12c} is independently H, C_{1-6} alkyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or heteroaryl; wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl of each of R^{2a1}, R^{2b1}, R^{12a}, R^{12b}, or R^{12c} is each optionally substituted 1 to 4 Z^{1b}, which may be the same or different;

wherein each heteroaryl of the compound of Formula (I) unless otherwise specified is 5 to 14 membered heteroaryl having one to four heteroatoms each independently N, O, or S;

wherein each heterocyclyl of the compound of Formula (I) unless otherwise specified is 3 to 20 membered heterocyclyl having one to four heteroatoms each independently N, O or S.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having the structure of Formula (Ia)



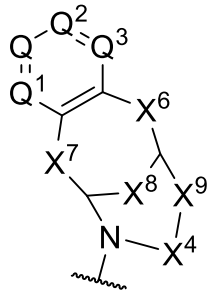
(Ia),

wherein R^{3a} is H, CH_3, F, or Cl; and

R^{3b} is H, CH_3, F, Cl, OCH_3, CF_2H, or CF_3.

3. The compound of any one of claims 1-2, or a pharmaceutically acceptable salt thereof, wherein R^1 and R^2 together with the N to which they are attached form a heterocyclyl; the heterocyclyl formed from R^1 and R^2 is 13-18 membered tricycle; wherein the heterocyclyl formed from R^1 and R^2 may be optionally substituted with 1 to 4 Z^6.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein

$-NR^1R^2$ is ;

each of Q, Q^1, Q^2, and Q^3, is independently N, or C optionally substituted with Z^6, provided that not more than two of Q, Q^1, Q^2, and Q^3 are N;

X^4 is CH_2 optionally substituted with one or two Z^6;

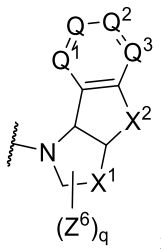
X^6 is a bond, O, CH_2, CH_2O, CH_2CH_2, or OCH_2, wherein each of CH_2, CH_2O, CH_2CH_2, and OCH_2 of X^6 is optionally substituted with one or two Z^6;

X^7 is a bond or CH_2 optionally substituted with one or two Z^6;

X^8 is a bond, CH_2, or CH_2O, wherein each of CH_2 and CH_2O of X^8 is optionally substituted with one or two Z^6; and

X^9 is CH_2, CH_2O, or CH_2CH_2, wherein each of CH_2, CH_2O, and CH_2CH_2 of X^9 is optionally substituted with one or two Z^6.

5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein

$-NR^1R^2$ is a heterocyclyl of ;

each of Q, Q^1, Q^2, and Q^3, is independently N, or C optionally substituted with Z^6, provided that not more than two of Q, Q^1, Q^2, and Q^3 are N;

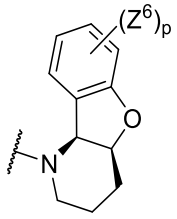
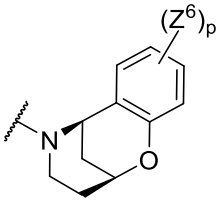
X^1 is $-OCF_2-$, $-OCH_2-$, $-CH_2-$, $-CH_2CH_2-$, $-OCH_2CH_2-$, $-CF_2-$, or $-CH_2NR^{1b}-$; wherein R^{1b} is C_{1-6} alkyl, C_{1-6} haloalkyl, oxetanyl, $-C(O)-R^{12a}$, $-S(O)R^{12a}$, or C_{3-6} cycloalkyl;

X^2 is O, $-OCH_2-$, $-CF_2-$, or $-CH_2-$; and

q is 0, 1, or 2.

6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein each Z^6 is independently -OH, CN, C_{1-6} alkyl, halo, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, phenyl, or 5 to 6 membered heteroaryl, wherein the phenyl or heteroaryl of Z^6 is optionally substituted with 1 to 3 Z^{1a}, which may be the same or different; each Z^{1a} is independently halo or C_{1-6} haloalkyl.

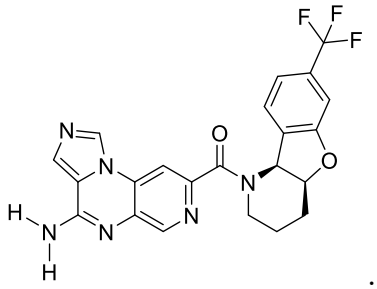
7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein

$-NR^1R^2$ is  or  ; and

p is 1 or 2.

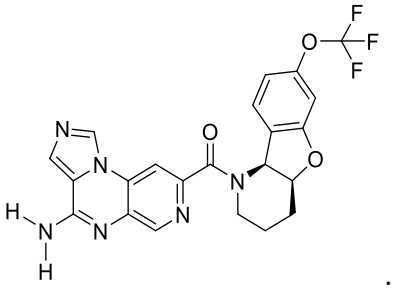
8. A compound as shown in Table 1D, or a pharmaceutically acceptable salt thereof.

9. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



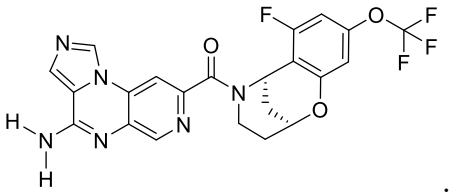
.

10. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



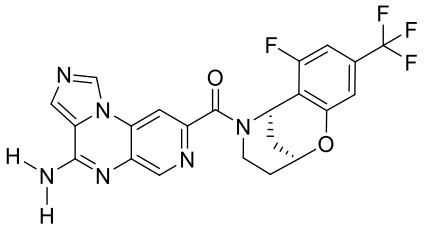
.

11. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



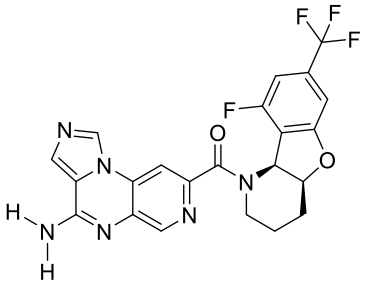
.

12. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



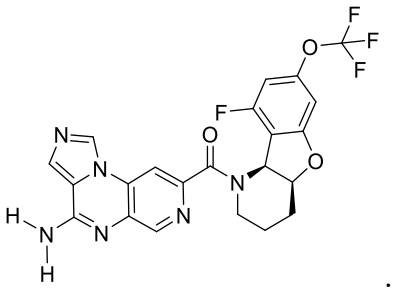
.

13. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



.

14. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



.

15. A pharmaceutical composition comprising a therapeutically effective amount of the compound of any one of claims 1-14, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.