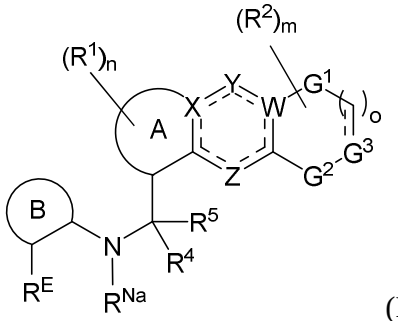
CLAIMS

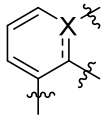
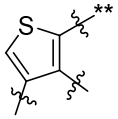
1. A compound of Formula (I'):



(I'),

or a pharmaceutically acceptable salt thereof, wherein:

⚌⚌⚌ is a single bond or a double bond as valency permits;

Ring A is  or , wherein ** is the attachment point to Y;

(i) when W is C and Y is N or CR^{Z1}, then X is C, and Z is N or CR^{Z1};

(ii) when W is C and Y is C(O), then X is C or N, and Z is CR^{Z1}, N, NR^{N1}, or O;

(iii) when W is N, then Y is C(O), X is C, and Z is N or CR^{Z1};

G^1, G^2, and G^3 are each, independently, $C(R^{G2})_2$, NR^{N2}, or O;

n is 0, 1, 2, or 3;

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

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

R^{Na} is H;

R^{N1} is H, C_{1-6}alkyl, C_{1-6}haloalkyl, $-C(O)R^{1a}$, C_{3-6}cycloalkyl, phenyl, or 5-to 6-membered heteroaryl, wherein the phenyl and 5-to 6-membered heteroaryl represented by R^{N1} are each optionally substituted with one to three substituents selected from halo, C_{1-3}alkyl, and C_{1-3}haloalkyl;

R^{Z1} is H, halo, cyano, NO_2,C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, $NR^{N1a}R^{N1b}$, $-C(O)R^{1a}$, $-C(O)OR^{O1a}$, $-C(O)NR^{N1a}R^{N1b}$, $-OR^{O1a}$, 3-12 membered carbocyclyl, phenyl, 5- or 6-membered heteroaryl, or 4-12 membered heterocyclyl, wherein the carbocyclyl, phenyl, 5- or 6-membered heteroaryl, or 4-12 membered heterocyclyl represented by R^{Z1} are each optionally substituted by one to four R^{1b};

each R^1 is, independently, halo, cyano, NO_2, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, C_{2-6}alkenyl, C_{2-6}alkynyl, $NR^{N1a}R^{N1b}$,

-C(O)R^{1a}, -C(O)OR^{O1a}, -C(O)$NR^{N1a}R^{N1b}$, -OR^{O1a}, –$(CH_2)_{0\text{ or }1}$-3-12 membered carbocyclyl, –$(CH_2)_{0\text{ or }1}$-4-12 membered heterocyclyl, –$(CH_2)_{0\text{ or }1}$-6-10 membered aryl, or –$(CH_2)_{0\text{ or }1}$-5-10 membered heteroaryl, wherein the C_{2-6} alkenyl, C_{2-6} alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl represented by R^1 are each optionally substituted by one to four R^{1b};

R^{1a}, R^{O1a}, R^{N1a}, and R^{N1b} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or 4-6 membered heterocyclyl;

each R^{1b} is independently halo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{1-6}hydroxyalkoxy, -C(O)R^{1a}, -C(O)OR^{O1a}, -C(O)$NR^{N1a}R^{N1b}$, -SO_2R^{1a}, - $NR^{N1a}R^{N1b}$, -NR^{N1a}C(O)R^{1a}, -NR^{N1a}C(O)OR^{1a}, -$NR^{N1a}SO_2R^{1a}$, -$NR^{N1a}SO_2NR^{N1a}R^{N1b}$, cyano, NO_2, or OR^{O1a};

R^{N2} is H, C_{1-6}alkyl, C_{1-6}haloalkyl, -C(O)R^{2a}, C_{3-6}cycloalkyl, phenyl, or 5-to 6-membered heteroaryl, wherein the phenyl and 5-to 6-membered heteroaryl represented by R^{N2} are each optionally substituted with one to three substituents selected from halo, C_{1-3}alkyl, and C_{1-3}haloalkyl;

each R^{G2} is, independently, H, halo, cyano, oxo (as appropriate), NO_2, C_{1-6}alkyl, C_{1-6}haloalkyl, *=CH-R^7 (as appropriate), C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, -C(O)R^{2a}, -C(O)OR^{O2a}, -C(O)$NR^{N2a}R^{N2b}$, OR^{O2a}, $NR^{N2a}R^{N2b}$, SO_2R^{2a}, -NR^{N2a}C(O)R^{2a}, -NR^{N2a}C(O)OR^{2a}, -$NR^{N2a}SO_3R^{2a}$, -$NR^{N2a}SO_3NR^{N2a}R^{N2a}$, –$(CH_2)_{0\text{ or }1}$-3-12 membered carbocyclyl, –$(CH_2)_{0\text{ or }1}$-4-12 membered heterocyclyl, –$(CH_2)_{0\text{ or }1}$-6-10 membered aryl, or –$(CH_2)_{0\text{ or }1}$-5-10 membered heteroaryl, wherein the carbocyclyl, heterocyclyl, aryl, or heteroaryl represented by R^{G2} are each optionally substituted by one to four halo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{1-6}hydroxyalkoxy, -C(O)R^{2a}, -C(O)OR^{O2a}, -C(O)$NR^{N2a}R^{N2b}$, cyano, NO_2, OR^{O2a}, $NR^{N2a}R^{N2b}$, SO_3R^{2a}, -NR^{N2a}C(O)R^{2a}, -NR^{N2a}C(O)OR^{2a}, -$NR^{N2a}SO_3R^{2a}$, or -$NR^{N2a}SO_3NR^{N2a}R^{N2a}$, and wherein the C_2alkenyl is optionally substituted with phenyl or 5- to 6-membered heteroaryl;

each R^2 is independently halo, cyano, oxo (as appropriate), NO_2, C_{1-6}alkyl, C_{1-6}haloalkyl, *=CH-R^7 (as appropriate), C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, -C(O)R^{2a}, -C(O)OR^{O2a}, -C(O)$NR^{N2a}R^{N2b}$, OR^{O2a}, $NR^{N2a}R^{N2b}$, SO_2R^{2a}, -NR^{N2a}C(O)R^{2a}, -NR^{N2a}C(O)OR^{2a}, -$NR^{N2a}SO_3R^{2a}$, -$NR^{N2a}SO_3NR^{N2a}R^{N2a}$, –$(CH_2)_{0\text{ or }1}$-3-12 membered carbocyclyl, –$(CH_2)_{0\text{ or }1}$-4-12 membered heterocyclyl, –$(CH_2)_{0\text{ or }1}$-6-10 membered aryl, or –$(CH_2)_{0\text{ or }1}$-5-10 membered heteroaryl, wherein the carbocyclyl, heterocyclyl, aryl, or heteroaryl represented by R^2 are each optionally substituted

by one to four halo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{1-6}hydroxyalkoxy, -C(O)R^{2a}, -C(O)OR^{O2a}, -C(O)$NR^{N2a}R^{N2b}$, cyano, NO_2, OR^{O2a}, $NR^{N2a}R^{N2b}$, SO_3R^{2a}, -NR^{N2a}C(O)R^{2a}, -NR^{N2a}C(O)OR^{2a}, -$NR^{N2a}SO_3R^{2a}$, or -$NR^{N2a}SO_3NR^{N2a}R^{N2a}$, and wherein the C_2alkenyl is optionally substituted with phenyl or 5- to 6-membered heteroaryl; or

two R^2, two R^{G2}, one R^2 and one R^{N2}, one R^2 and one R^{G2}, or one R^{G2} and one R^{N2}, together with the atoms to which they are connected, form 3- to 12 membered carbocyclyl, 4- to 12 membered heterocyclyl, phenyl, naphthyl or 5- to 10-membered heteroaryl, each of which is optionally substituted by one to four R^6;

R^{2a} and R^{O2a} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or 4-6 membered heterocyclyl;

R^{N2a} and R^{N2b} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, OR^{O2a}, or C_{3-6}cycloalkyl;

* is the connection point to the tricyclic core ring;

R^7 is C_{1-4}alkyl, 3- to 12 membered carbocyclyl, 4- to 12 membered heterocyclyl, phenyl, naphthyl, or 5- to 10-membered heteroaryl, each of which is optionally substituted by one to four halo, -OH, $-NH_2$, cyano, NO_2, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl;

each R^6 is independently halo, cyano, oxo (as appropriate), NO_2, C_{1-6}alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, -C(O)R^{6a}, -C(O)OR^{O6a}, -C(O)$NR^{N6a}R^{N6b}$, OR^{O6a}, $NR^{N6a}R^{N6b}$, SO_2R^{6a}, -NR^{N6a}C(O)R^{6a}, -NR^{N6a}C(O)OR^{6a}, -$NR^{N6a}SO_3R^{6a}$, -$NR^{N6a}SO_3NR^{N6a}R^{N6a}$, $–(CH_2)_{0\text{ or }1}$-3-12 membered carbocyclyl, $–(CH_2)_{0\text{ or }1}$-4-12 membered heterocyclyl, $–(CH_2)_{0\text{ or }1}$-6-10 membered aryl, or $–(CH_2)_{0\text{ or }1}$-5-10 membered heteroaryl, wherein the carbocyclyl, heterocyclyl, aryl, or heteroaryl represented by R^6 are each optionally substituted by one to four halo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{1-6}hydroxyalkoxy, -C(O)R^{6a}, -C(O)OR^{O6a}, -C(O)$NR^{N6a}R^{N6b}$, cyano, NO_2, OR^{O6a}, $NR^{N6a}R^{N6b}$, SO_3R^{6a}, -NR^{N6a}C(O)R^{6a}, -NR^{N6a}C(O)OR^{6a}, -$NR^{N6a}SO_3R^{6a}$, or -$NR^{N6a}SO_3NR^{N6a}R^{N6a}$;

or two R^6, together with the atoms to which they are attached, form C_{3-6}cycloalkyl;

R^{6a} and R^{O6a} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or 4-6 membered heterocyclyl;

R^{N6a} and R^{N6b} are each independently H, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, OR^{O6a}, or C_{3-6}cycloalkyl;

Ring B is phenyl or 5- to 10-membered monocyclic or bicyclic heteroaryl, each of which is substituted with R^E ortho to the N(R^{Na}) substituent, and optionally substituted with one to four R^3;

each R^3 is independently halo, cyano, NO_2, C_{1-6}alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, -C(O)R^{3a}, -C(O)OR^{O3a}, -C(O)N$R^{N3a}R^{N3b}$, OR^{O3a}, N$R^{N3a}R^{N3b}$, SO_2R^{3a}, -NR^{N3a}C(O)R^{3a}, -NR^{N3a}C(O)OR^{3a}, -N$R^{N3a}SO_3R^{3a}$, -N$R^{N3a}SO_3NR^{N3a}R^{N3a}$, –$(CH_2)_{0 \text{ or } 1}$-3-12 membered carbocyclyl, –$(CH_2)_{0 \text{ or } 1}$-4-12 membered heterocyclyl, –$(CH_2)_{0 \text{ or } 1}$-6-10 membered aryl, or –$(CH_2)_{0 \text{ or } 1}$-5-10 membered heteroaryl, wherein the carbocyclyl, heterocyclyl, aryl, or heteroaryl represented by R^3 are each optionally substituted by one to four halo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, -C(O)R^{3a}, -C(O)OR^{O3a}, -C(O)N$R^{N3a}R^{N3b}$, cyano, NO_2, OR^{O3a}, N$R^{N3a}R^{N3b}$, SO_3R^{3a}, -NR^{N3a}C(O)R^{3a}, -NR^{N3a}C(O)OR^{3a}, -N$R^{N3a}SO_3R^{3a}$, or -N$R^{N3a}SO_3NR^{N3a}R^{N3a}$;

R^E is H, cyano, C_{1-4}alkyl, -C(O)R^8, -C(NH)N$R^{N3E}R^{N3E}$, -S(O_2)N$R^{N3E}R^{N3E}$, -C(O)OR^{O3a}, -C(O)N$R^{N3a}R^{N3b}$, phenyl, 5- to 10-membered heteroaryl, or 4- to 12-membered heterocyclyl, wherein the C_{1-4}alkyl is optionally substituted by one to four R^{Ea}, and the phenyl, 5- to 10-membered heteroaryl, and 4- to 12-membered heterocyclyl are each optionally substituted with one or two R^{Eb};

or R^E and R^3, together with the atoms to which they are attached, form a 5- to 6-membered monocyclic heterocyclyl;

R^8 is H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{1-4}thioalkyl, C_{1-4}thiohaloalkyl, or SH;

each R^{Ea} is, independently halo, cyano, OH, or N$R^{N3E}R^{N3E}$;

each R^{Eb} is, independently, oxo, =S, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, cyano, C_{1-3}alkoxy, -OH, or -C(O)N$R^{N3E}R^{N3E}$, wherein the C_{1-3}alkyl represented by R^{Eb} is optionally substituted by 4- to 6-membered heterocyclyl optionally substituted with C_{1-3}alkyl;

each R^{N3E} is, independently, H, OH or C_{1-3}alkyl;

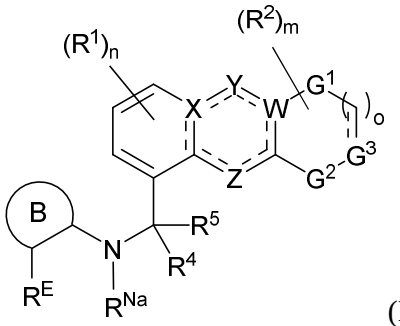
R^{3a} and R^{O3a} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or 4-6 membered heterocyclyl, wherein the C_{1-6}alkyl represented by R^{3a} or R^{O3a} is optionally substituted by a 4-6 membered heterocyclyl;

R^{N3a} and R^{N3b} are each independently H, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, OR^{O3a}, -SO_2C_{1-4}alkyl, or C_{3-6}cycloalkyl, wherein the C_{1-6}alkyl represented by R^{N3a} or R^{N3b} is optionally substituted by C_{1-3}alkoxy or a 5- to 6-membered heteroaryl;

R^4 is C_{1-3}alkyl and

R^5 is H.

2. The compound of claim 1, wherein the compound is of Formula (I):



(I),

a pharmaceutically acceptable salt, wherein:

each R^6 is independently halo, cyano, oxo (as appropriate), NO_2, C_{1-6}alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}hydroxyalkoxy, -C(O)R^{6a}, -C(O)OR^{O6a}, -C(O)$NR^{N6a}R^{N6b}$, OR^{O6a}, $NR^{N6a}R^{N6b}$, SO_2R^{6a}, -NR^{N6a}C(O)R^{6a}, -NR^{N6a}C(O)OR^{6a}, -$NR^{N6a}SO_3R^{6a}$, -$NR^{N6a}SO_3NR^{N6a}R^{N6a}$, –$(CH_2)_{0 \text{ or } 1}$-3-12 membered carbocyclyl, –$(CH_2)_{0 \text{ or } 1}$-4-12 membered heterocyclyl, –$(CH_2)_{0 \text{ or } 1}$-6-10 membered aryl, or –$(CH_2)_{0 \text{ or } 1}$-5-10 membered heteroaryl, wherein the carbocyclyl, heterocyclyl, aryl, or heteroaryl represented by R^6 are each optionally substituted by one to four halo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}hydroxylalkyl, C_{1-6}alkoxylalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{1-6}hydroxyalkoxy, -C(O)R^{6a}, -C(O)OR^{O6a}, -C(O)$NR^{N6a}R^{N6b}$, cyano, NO_2, OR^{O6a}, $NR^{N6a}R^{N6b}$, SO_3R^{6a}, -NR^{N6a}C(O)R^{6a}, -NR^{N6a}C(O)OR^{6a}, -$NR^{N6a}SO_3R^{6a}$, or -$NR^{N6a}SO_3NR^{N6a}R^{N6a}$;

R^7 is 3- to 12 membered carbocyclyl, 4- to 12 membered heterocyclyl, phenyl, naphthyl, or
5- to 10-membered heteroaryl, each of which is optionally substituted by one to four halo, -OH, $-NH_2$, cyano, NO_2, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl;

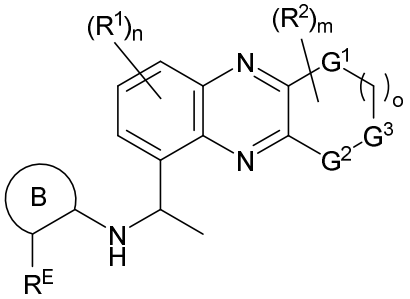
R^E is -C(O)OR^{O3a} or -C(O)$NR^{N3a}R^{N3b}$;

R^{3a} and R^{O3a} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or 4-6 membered heterocyclyl; and

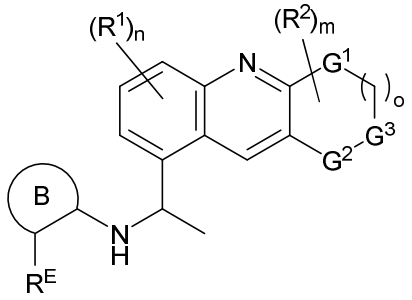
R^{N3a} and R^{N3b} are each independently H, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, OR^{O3a}, or C_{3-6}cycloalkyl.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:

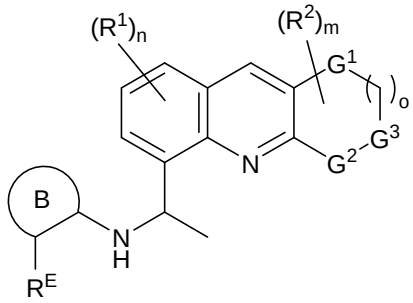
(a) the compound is represented by Formula (VI), (VII), or (VII’):



(VI),



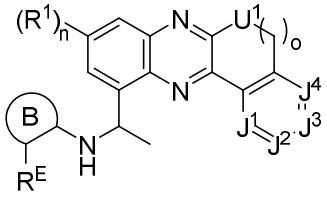
(VII), or



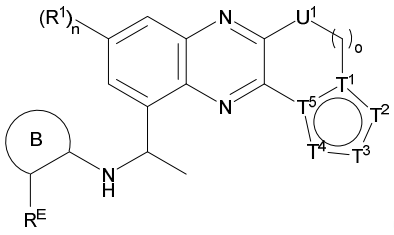
(VII'),

wherein m and n are each, independently, 0, 1 or 2; and o is 0 or 1; or

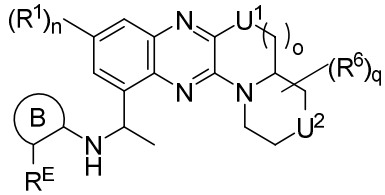
(b) the compound is represented by Formula (VIa), (VIb), (VIc), (VId), (VIe), (VIIa), (VIIb), (VIIc), or (VIIa'):



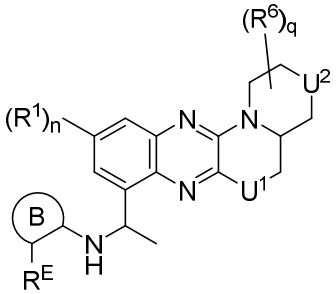
(VIa),



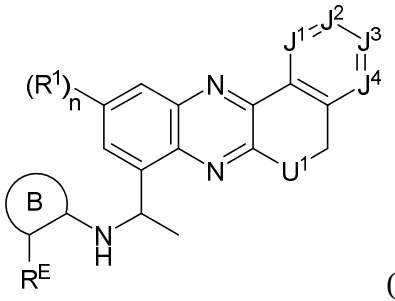
(VIb),



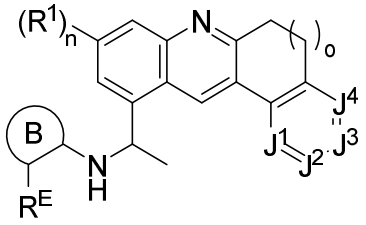
(VIc),



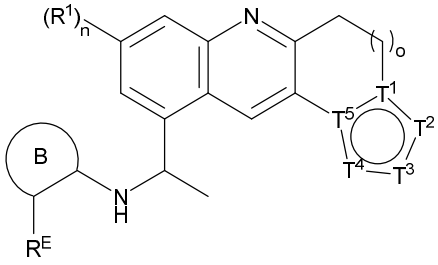
(VId),



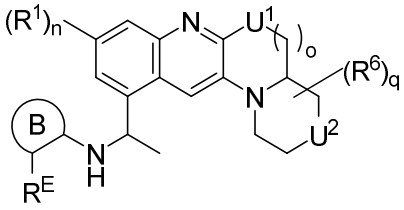
(VIe),



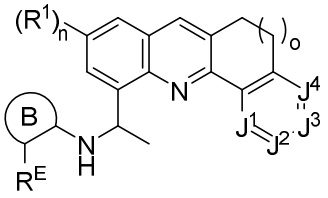
(VIIa),



(VIIb),



(VIIc), or



(VIIa'),

wherein:

n and o, are each, independently 0 or 1;

q is 0, 1, or 2;

J^1, J^2, J^3, and J^4, are each, independently, N, CH, or CR^6;

T^1 and T^5, are each, independently, N or C;

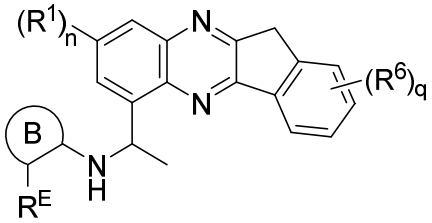
T^2, T^3, and T^4, are each, independently, N, NR^{N6}, O, S, CH, or CR^6;

R^{N6} is H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, phenyl, or 5- to 6-membered heteroaryl, wherein the phenyl and 5- to 6-membered heteroaryl represented by R^{N6} are each optionally substituted by one to three halo, C_{1-3}alkyl, C_{1-3}haloalkyl, cyano, OH, C_{1-3}alkoxy, or C_{1-3}haloalkoxy;

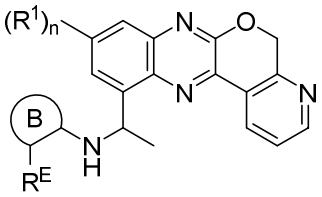
U^1 is NR^{N2}, CH_2, or O;

U^2 is absent, NR^{N6}, CH_2, or O; or

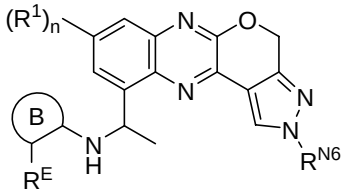
(c) the compound is represented by Formula (VIa-1), (VIa-2), (VIa-3), (VIb-1), (VIc-1), (VIc-2), (VIc-3), (VIc-4), (VId-1), (VId-2), (VIe-1), or (VIIc-1):



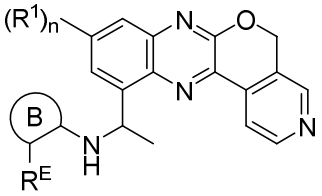
(VIa-1),



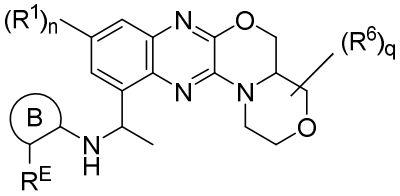
(VIa-2),



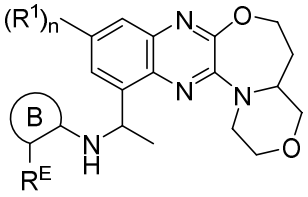
(VIb-1),



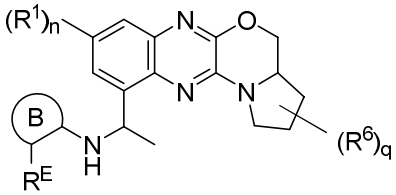
(VIa-3),



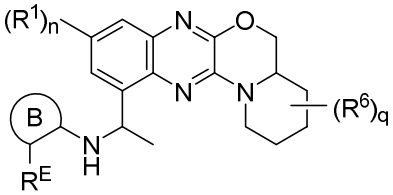
(VIc-1),



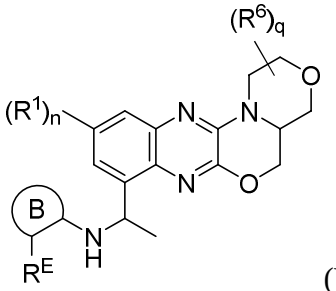
(VIc-2),



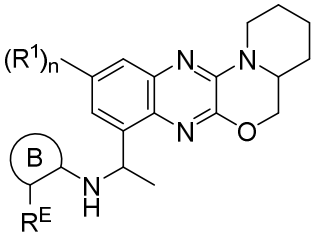
(VIc-3),



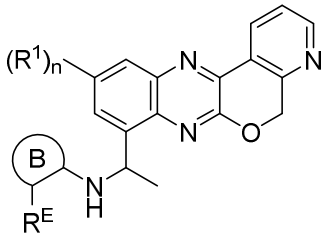
(VIc-4),



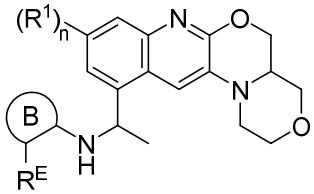
(VId-1),



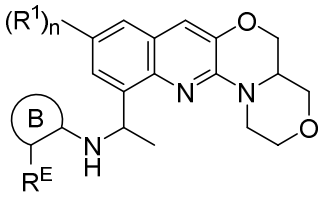
(VId-2),



(VIe-1),



(VIIc-1), or

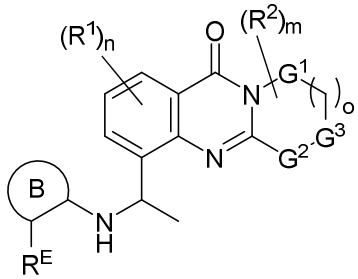


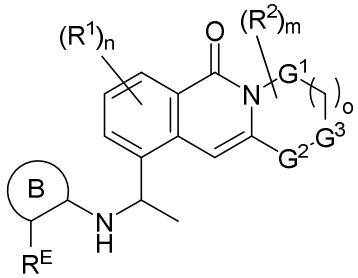
(VIIa'-1);

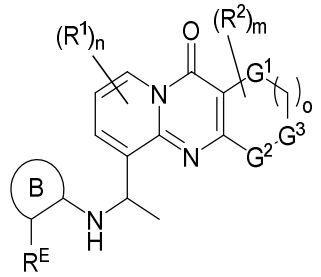
wherein n is 0 or 1 and q is 0, 1, or 2..

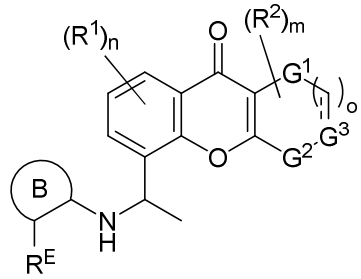
4. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:

(a) the compound is represented by Formula (II), (III), (IV), or (V):


(II),

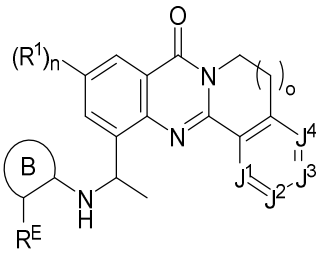

(III),

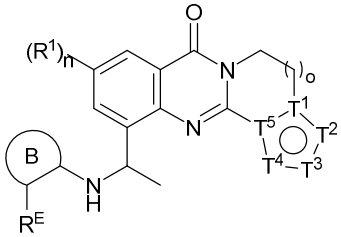

(IV), or

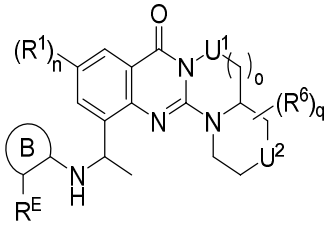

(V);

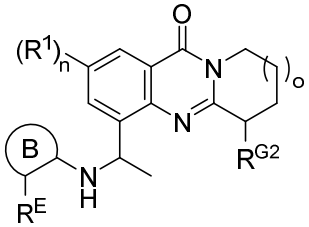
wherein m and n are each, independently, 0, 1, or 2; o is 0 or 1; or

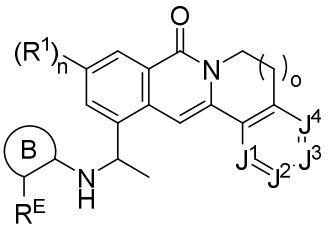
(b) the compound is represented by Formula (IIa), (IIb), (IIc), (IId), (IIIa), (IIIb), (IIIc), (IVa), (IVb), (IVc), (Va), (Vb), (Vc), or (Vd):


(IIa),

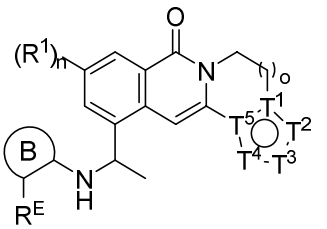

(IIb),


(IIc),

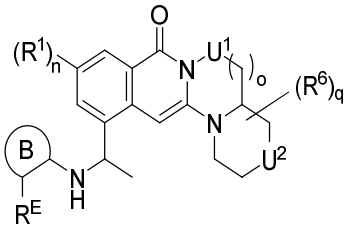

(IId),



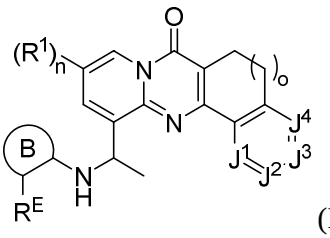
(IIIa),



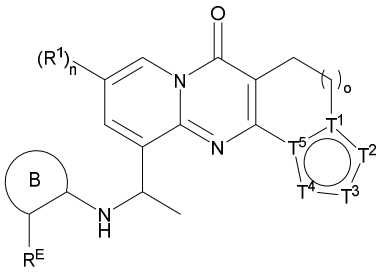
(IIIb),



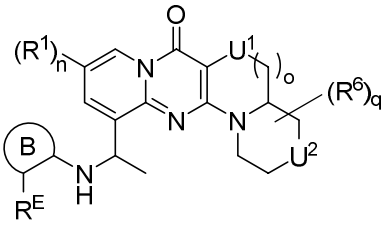
(IIIc),



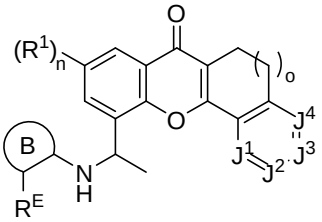
(IVa),



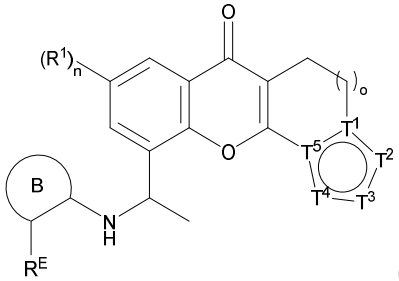
(IVb),



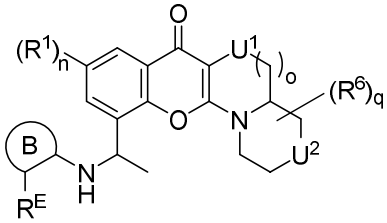
(IVc),



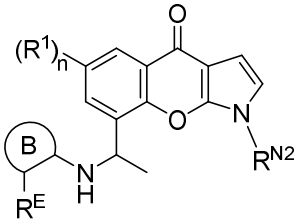
(Va),



(Vb),



(Vc) or



(Vd);

wherein:

n and o, are each, independently, 0 or 1;

q is 0, 1, or 2;

J^1, J^2, J^3, and J^4, are each, independently, N, CH, or CR^6;

T^1 and T^5, are each, independently, N or C;

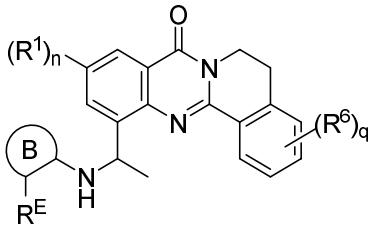
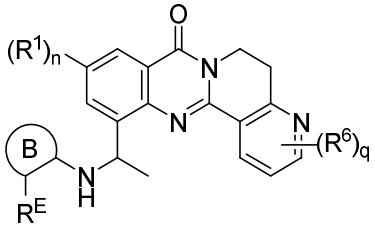
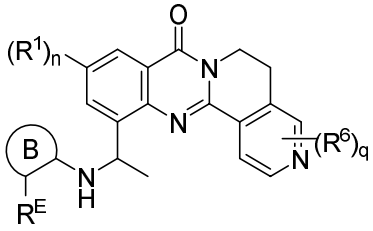
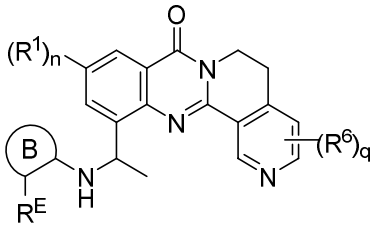
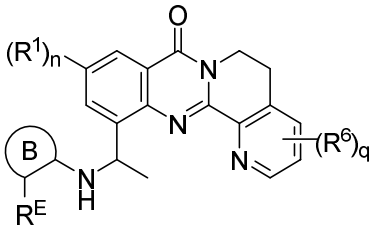
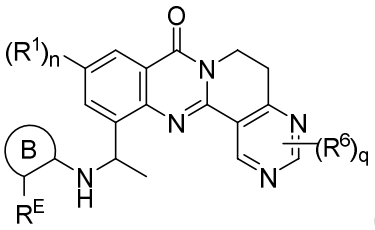
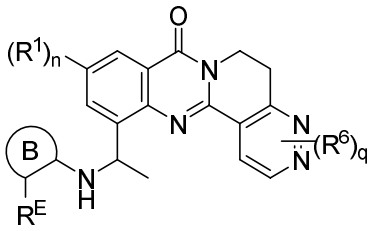
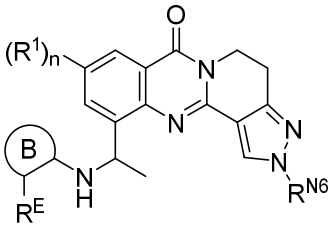
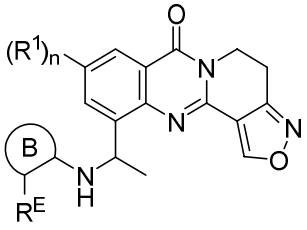
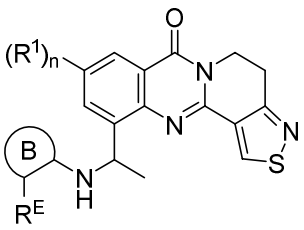
T^2, T^3, and T^4, are each, independently, N, NR^{N6}, O, S, CH, or CR^6;

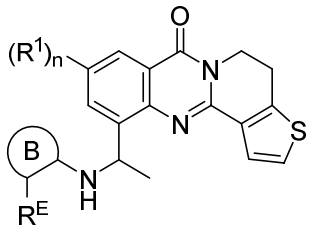
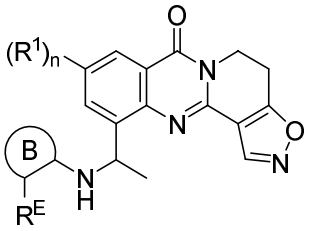
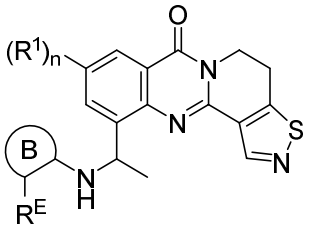
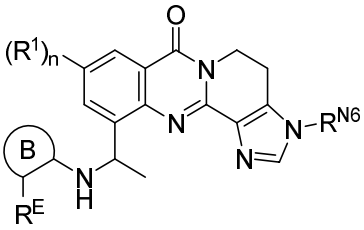
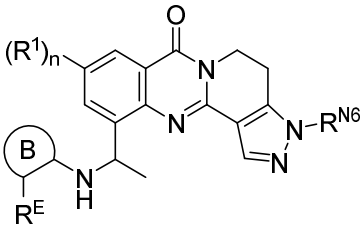
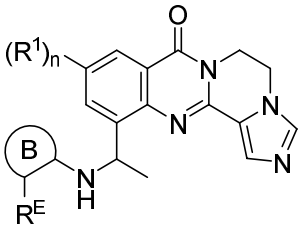
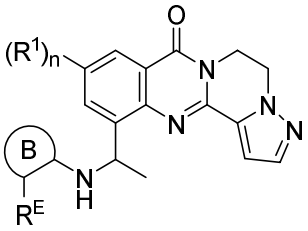
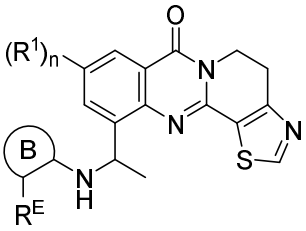
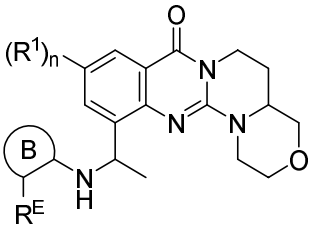
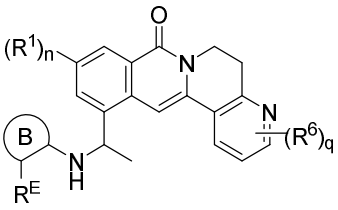
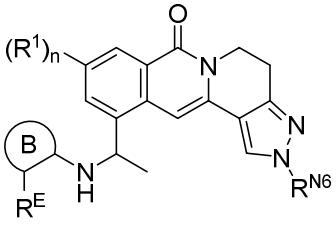
R^{N6} is H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, phenyl, naphthyl, or 5- to 6-membered heteroaryl, wherein the phenyl, naphthyl, and 5- to 6-membered heteroaryl represented by R^{N6} are each optionally substituted by one to three halo, C_{1-3}alkyl, C_{1-3}haloalkyl, cyano, OH, C_{1-3}alkoxy, or C_{1-3}haloalkoxy;

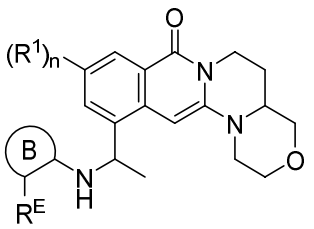
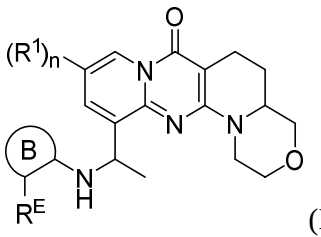
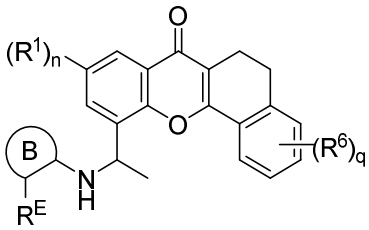
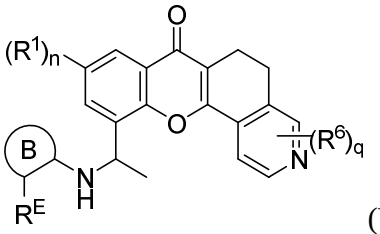
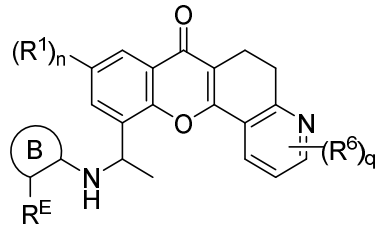
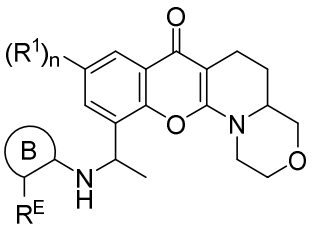
U^1 is NR^{N2}, CH_2, or O;

U^2 is NR^{N6}, CH_2, or O; or

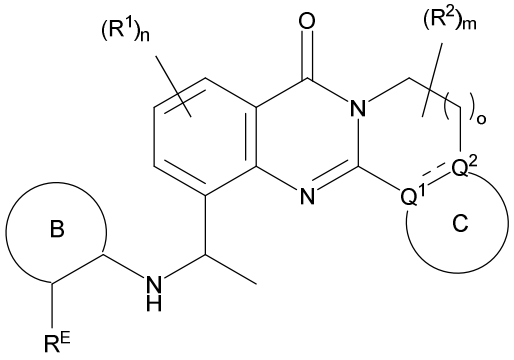
(c) the compound is represented by Formula (IIa-1), (IIa-2), (IIa-3), (IIa-4), (IIa-5), (IIa-6), (IIa-7), (IIb-1), (IIb-2), (IIb-3), (IIb-4), (IIb-5), (IIb-6), (IIb-7), (IIb-8), (IIb-9), (IIb-10), (IIb-11), (IIc-1), (IIIa-1), (IIIb-1), (IIIc-1), (IVc-1), (Va-1), (Va-2), (Va-3), or (Vc-1):


(IIa-1),

(IIa-2),

(IIa-3),

(IIa-4),

(IIa-5),

(IIa-6),

(IIa-7),

(IIb-1),

(IIb-2),

(IIb-3),


(IIb-4),

(IIb-5),

(IIb-6),

(IIb-7),

(IIb-8),

(IIb-9),

(IIb-10),

(IIb-11),

(IIc-1),

(IIIa-1),

(IIIb-1),


(IIIc-1),

(IVc-1),

(Va-1),

(Va-2),

(Va-3), or

(Vc-1); or

(d) the compound is represented by Formula (VIII):


(VIII);

or a pharmaceutically acceptable salt thereof, wherein:

n is 0, 1, or 2;

m is 0, 1, or 2;

o is 0 or 1;

each R^1 is, independently, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $-NR^{N1a}R^{N1b}$, $-C(O)R^{1a}$, $-C(O)OR^{O1a}$, $-C(O)NR^{N1a}R^{N1b}$, OR^{O1a}, C_{3-6}cycloalkyl, phenyl, or 5-to 6-membered monocyclic heteroaryl, wherein the C_{3-6}cycloalkyl, phenyl, and 5-to 6-membered monocyclic heteroaryl represented by R^1 are each optionally substituted by one to three halo, C_{1-3}alkyl, C_{1-3}haloalky, OH, C_{1-3}alkoxy, C_{1-3}haloalkoxy, $-C(O)R^{1a}$, $-C(O)OR^{O1a}$, or $-C(O)NR^{N1a}R^{N1b}$;

each R^2 is independently halo, oxo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, $-NR^{N2a}R^{N2b}$, $-C(O)R^{2a}$, $-C(O)OR^{O2a}$, $-C(O)NR^{N2a}R^{N2b}$, OR^{O2a}, C_{3-6}cycloalkyl, phenyl, or 5-to 6-membered monocyclic heteroaryl, wherein the C_{3-6}cycloalkyl, phenyl, and 5-to 6-membered monocyclic heteroaryl represented by R^2 are each optionally substituted by one to three halo, C_{1-3}alkyl, C_{1-3}haloalky, OH, C_{1-3}alkoxy, C_{1-3}haloalkoxy, $-C(O)R^{2a}$, $-C(O)OR^{O2a}$, or $-C(O)NR^{N2a}R^{N2b}$;

R^{2a}, R^{O2a}, R^{N2a}, and R^{N2b} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or 4-6 membered heterocyclyl;

Ring B is phenyl or 5- to 6-membered monocyclic heteroaryl, each of which is substituted with R^E ortho to the NH substituent, and one to three R^3;

each R^3 is independently halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, $-NR^{N3a}R^{N3b}$, $-C(O)R^{3a}$, $-C(O)OR^{O3a}$, $-C(O)NR^{N3a}R^{N3b}$, OR^{O3a}, C_{3-6}cycloalkyl, phenyl, or 5-to 6-membered monocyclic heteroaryl, wherein the C_{3-6}cycloalkyl, phenyl, and 5-to 6-membered monocyclic heteroaryl represented by R^3 are each optionally substituted by one to three halo, C_{3-3}alkyl, C_{3-3}haloalky, OH, C_{1-3}alkoxy, C_{1-3}haloalkoxy, $-C(O)R^{3a}$, $-C(O)OR^{O3a}$, or $-C(O)NR^{N3a}R^{N3b}$;

R^{3a}, R^{O3a}, R^{N3a}, and R^{N3b} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or 4-6 membered heterocyclyl;

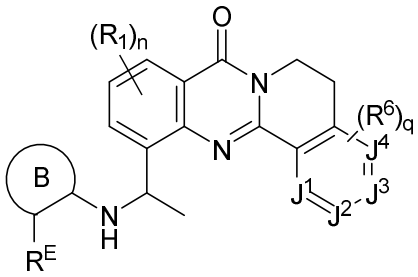
Ring C is 6-membered monocyclic heterocyclyl, phenyl, or 5- to 6-membered monocyclic heteroaryl, each of which is optionally substituted with one to three R^6;

Q^1 and Q^2 are each, independently, C, CH, or N, provided that at least one of Q^1 or Q^2 is C or CH;

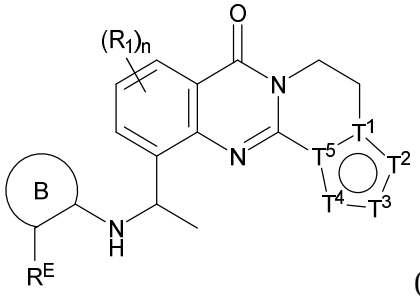
each R^6 is, independently, halo, oxo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, $-NR^{N6a}R^{N6b}$, $-C(O)R^{6a}$, $-C(O)OR^{O6a}$, $-C(O)NR^{N6a}R^{N6b}$, OR^{O6a}, C_{1-6}cycloalkyl, phenyl, or 5-to 6-membered monocyclic heteroaryl, wherein the C_{1-6}cycloalkyl, phenyl, and 5-to 6-membered monocyclic heteroaryl represented by R^6 are each independently substituted by one to three halo, OH, C_{1-6}alkyl, C_{1-6}haloalky, C_{1-6}alkoxy, C_{1-6}haloalkoxy, $-C(O)R^{6a}$, $-C(O)OR^{O6a}$, or $-C(O)NR^{N6a}R^{N6b}$;

R^{6a}, R^{O6a}, R^{N6a}, and R^{N6b} are each independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}cycloalkyl, or 4-6 membered heterocyclyl; or

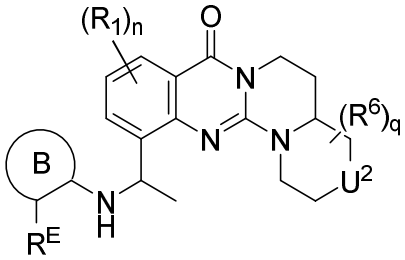
(e) the compound is represented by Formula (VIIIa), (VIIIb), or (VIIIc):



(VIIIa),



(VIIIb), or



(VIIIc);

wherein:

n is 0 or 1;

q is 0, 1, or 2;

U^2 is NR^{N6}, CH_2, or O;

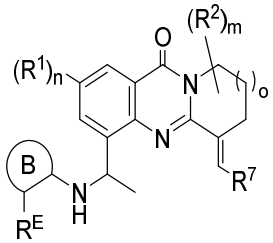
J^1, J^2, J^3, and J^4, are each, independently, N or CH, wherein at least one of J^1, J^2, J^3, and J^4 is CH;

T^1 and T^5, are each, independently, N or C;

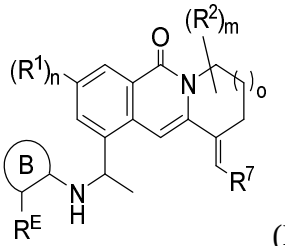
T^2, T^3, and T^4, are each, independently, N, NR^{N6}, O, S, or CH;

R^{N6} is H, $C_{1\text{-}3}$alkyl, $C_{1\text{-}3}$haloalkyl, $C_{3\text{-}6}$cycloalkyl, phenyl, or 5- to 6-membered heteroaryl, wherein the phenyl and 5- to 6-membered heteroaryl represented by R^{N6} are each optionally substituted by one to three halo, $C_{1\text{-}3}$alkyl, $C_{1\text{-}3}$haloalkyl, cyano, OH, $C_{1\text{-}3}$alkoxy, or $C_{1\text{-}3}$haloalkoxy; or

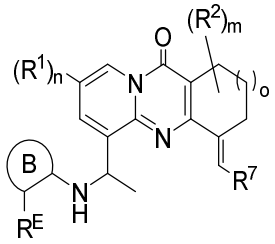
(f) the compound is represented by Formula (II-1), (III-1), (IV-1), (V-1), (VI-1), (VI-2), or (VII-1):



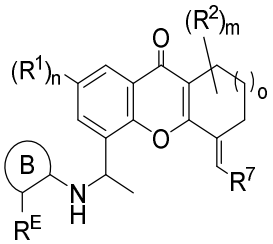
(II-1),



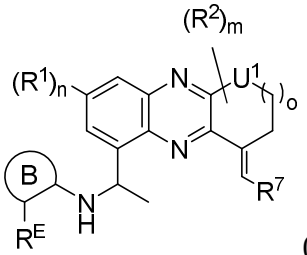
(III-1),



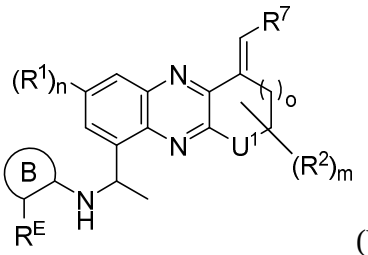
(IV-1),



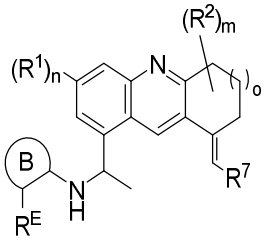
(V-1),



(VI-1),



(VI-2),or



(VII-1),

wherein

m, n, and o, are each, independently 0 or 1;

U^1 is NR^{N2}, CH_2, or O;

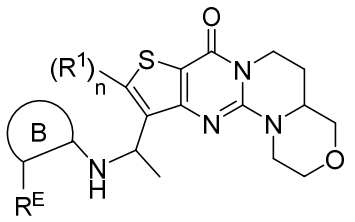
R^7 is;

(i) $C_{1\text{-}4}$alkyl, 5- or 6-membered heterocyclyl, phenyl, or 5- or 6-membered heteroaryl, wherein the 5- or 6-membered heterocyclyl, phenyl, or 5- or 6-membered heteroaryl are each optionally substituted by one to two halo, -OH, $-NH_2$, cyano, $C_{1\text{-}3}$alkyl, $C_{1\text{-}3}$alkyl-OR^{O7a}, $C_{3\text{-}6}$cycloalkyl, $C_{1\text{-}3}$haloalkyl, or 4-to 6 membered heterocyclyl; or

(ii) $C_{1\text{-}3}$alkyl, phenyl, pyridyl, isoxazolyl, pyrazolyl, imidazolyl, tetrahydrofuranyl, or tetrahydro-2H-pyranyl, wherein the phenyl, pyridyl, isoxazolyl, pyrazolyl, imidazolyl, tetrahydrofuranyl, and tetrahydro-2H-pyranyl are each optionally substituted by one to two halo, -OH, $C_{1\text{-}3}$alkoxy, $-NH_2$, cyano, $C_{1\text{-}3}$alkyl, $C_{1\text{-}3}$haloalkyl, $C_{1\text{-}3}$alkyl-OR^{O7a}, or cyclopropyl, or morpholinyl

R^{O7a} is H or $C_{1\text{-}3}$alkyl; or

(g) the compound is represented by Formula (IX):



(IX);

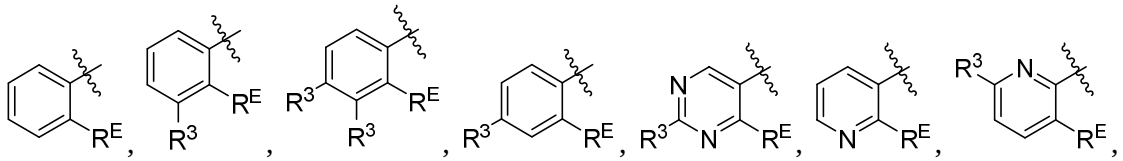
or a pharmaceutically acceptable salt thereof.

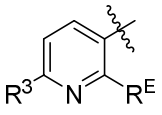
5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein:

(a) Ring B is phenyl or 6-membered monocyclic heteroaryl, each of which is substituted with R^E ortho to the NR^{Na} substituent, and further optionally substituted with one or two R^3;

(b) Ring B is phenyl, pyrimidinyl, or pyridinyl, each of which is substituted with R^E ortho to the NR^{Na} substituent, and further optionally substituted with one or two R^3;

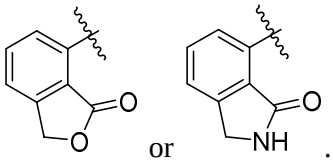
(c) Ring B and R^E, together with optionally substituted R^3, are represented by:



or 

; or

(d) Ring B and R^E, together with optionally substituted R^3, are represented by:



.

6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein:

(a) R^E is cyano, $C_{1\text{-}4}$alkyl, $-C(O)R^8$, $-C(NH)NR^{N3E}R^{N3E}$, $-S(O_2)NR^{N3E}R^{N3E}$, $-C(O)OR^{O3a}$, $-C(O)NR^{N3a}R^{N3b}$, phenyl, 5- to 6-membered heteroaryl, or 4- to 10-membered heterocyclyl, wherein the $C_{1\text{-}4}$alkyl is optionally substituted by one to four R^{Ea}, and the phenyl, 5- to 6-membered heteroaryl, and 4- to 10-membered heterocyclyl are each optionally substituted with one or two R^{Eb};

R^8 is H, C_{1-3}alkyl, C_{1-3}haloalkyl, or SH;

each R^{Ea} is, independently halo, cyano, OH, or $NR^{N3E}R^{N3E}$;

each R^{Eb} is, independently, oxo, =S, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, cyano, C_{1-3}alkoxy, -OH, or -C(O)N R^{N3E} R^{N3E}, wherein the C_{1-3}alkyl is optionally substituted by 4- to 6-membered heterocyclyl optionally substituted with C_{1-3}alkyl;

each R^{N3E} is, independently, H, OH or C_{1-3}alkyl;R^{O3a} is H, C_{1-3}alkyl, or 4- to 6-membered monocyclic heterocyclyl, wherein the C_{1-3}alkyl is optionally substituted by a 4- to 6-membered monocyclic heterocyclyl;

R^{N3a} and R^{N3b} are each independently H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{1-3}alkoxy, -OH, $-S(O)_2C_{1-3}$alkyl, or cyclopropyl, wherein the C_{1-3}alkyl is optionally substituted by C_{1-3}alkoxy or 6-membered heteroaryl;

(b) R^E is cyano, C_{1-4}alkyl, $-C(O)R^8$, $-C(NH)NR^{N3E}R^{N3E}$, $-S(O_2)NR^{N3E}R^{N3E}$, $-C(O)OR^{O3a}$ $-C(O)NR^{N3a}R^{N3b}$, phenyl, pyridinyl, pyrazolyl, oxadiazolyl, imidazolyl, thiazolyl, isothiazolyl, triazolyl, oxazolyl, thiophenyl, morpholinyl, piperdinyl, piperizinyl, or 7-oxa-2-azaspiro[3.5]nonanyl, wherein the C_{1-4}alkyl is optionally substituted by one to four R^{Ea}, and the phenyl, pyridinyl, pyrazolyl, oxadiazolyl, imidazolyl, thiazolyl, isothiazolyl, triazolyl, oxazolyl, thiophenyl, morpholinyl, piperdinyl, piperizinyl, and 7-oxa-2-azaspiro[3.5]nonanyl are each optionally substituted with one or two R^{Eb};

R^8 is H, C_{1-3}alkyl, C_{1-3}haloalkyl, or SH;

each R^{Ea} is, independently halo, cyano, OH, or $NR^{N3E}R^{N3E}$;

each R^{Eb} is, independently, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, cyano, C_{1-3}alkoxy, -OH, or $-C(O)NR^{N3E}R^{N3E}$, wherein the C_{1-3}alkyl is optionally substituted oxetanyl substituted with C_{1-3}alkyl;

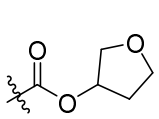
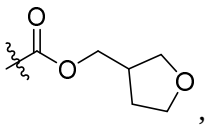
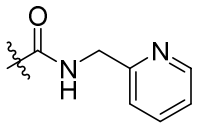
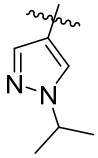
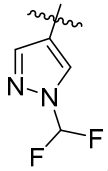
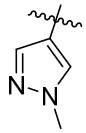
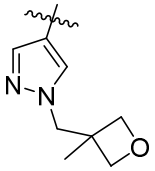
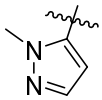
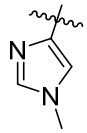
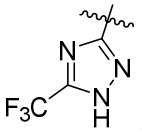
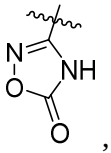
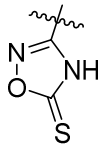
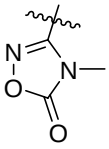
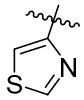
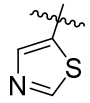
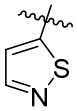
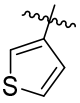
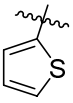
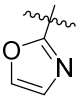
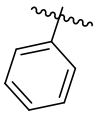
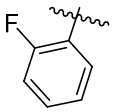
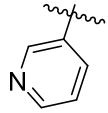
each R^{N3E} is, independently, H, OH or C_{1-3}alkyl;

R^{O3a} is H, C_{1-3}alkyl, or tetrahydrofuranyl, wherein the C_{1-3}alkyl is optionally substituted by tetrohydrofuranyl;

R^{N3a} and R^{N3b} are each independently H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{1-3}alkoxy, -OH, $-S(O)_2C_{1-3}$alkyl, or cyclopropyl, wherein the C_{1-3}alkyl is optionally substituted by C_{1-3}alkoxy or pyridinyl;

(c) R^E is $-C(O)OR^{O3a}$ or $-C(O)NR^{N3a}R^{N3b}$; R^{O3a} is H or C_{1-3}alkyl; and R^{N3a} and R^{N3b} are each independently H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{1-3}alkoxy, -OH, or cyclopropyl; or

(d) R^E is -C(O)OH, $-C(O)OCH_3$, $-C(O)OCH_2CH_3$, $-C(O)OC(CH_3)_3$, $-C(O)NH_2$, $-C(O)NHCH_3$, $-C(O)NHS(O)_2CH_3$, $-C(O)NHCH_2CH_2OCH_3$, $-C(O)N(CH_3)OCH_3$, cyano, -C(O)H, $-C(O)CH_3$, $-C(O)CF_3$, -C(O)SH, $-CH_3$, $-C(CH_2CN)_2OH$, -C(NH)NHOH, $-CH_2OH$,

-CH(OH)CF_3, -$S(O)_2NHC(CH_3)_3$, -$S(O)_2NH_2$, , , , , , , , , , , , , , , , , , , , , , , , , , or .

7. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^E is -C(O)OH.

8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein:

(a) each R^3 is, independently, halo, $C_{1\text{-}3}$alkyl, $C_{1\text{-}3}$haloalkyl, or 6-membered monocyclic heterocyclyl, wherein the 6-membered monocyclic heterocyclyl is optionally substituted with halo; or

(b) each R^3 is, independently, -Br, -Cl, -F, -CH_3, -CF_3, or pyridinyl, wherein the pyridinyl is optionally substituted with -F.

9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein:

(a) each R^1 is, independently, CN, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxylalkyl, or halo; or

(b) each R^1 is, independently, C_{1-3}alkyl, C_{1-3}haloalkyl, or halo, preferably wherein R^1 is $-CH_3$ or -F.

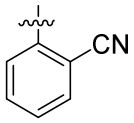
10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein:

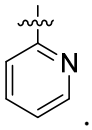
(a) each R^6 is, independently, oxo, halo, cyano, -OH, C_{1-3}alkyl, C_{1-3}alkoxy, $-C(O)NH_2$, or $-NH_2$;

or two R^6, together with the atoms to which they are attached, form cyclopropyl;

R^{N6} is H, C_{1-3}alkyl, phenyl, or pyridinyl, wherein the phenyl is optionally substituted with -CN; or

(b) each R^6 is, independently, oxo, -Cl, -F, -OH, $-CH_3$, $-OCH_3$, $-OCH(CH_3)_3$, CN, $-C(O)NH_2$, or $-NH_2$;

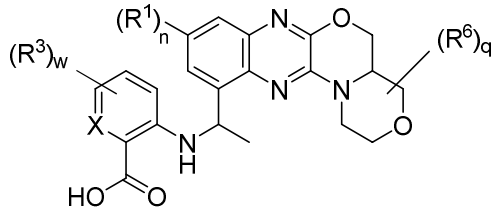
R^{N6} is H, $-CH_3$, 

, or 

.

11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, C_{1-3}alkyl, or C_{1-3}haloalkyl.

12. A compound of claim 1 or 2, wherein the compound is represented by Formula (VIc-1a):



(VIc-1a),

or a pharmaceutically acceptable salt thereof, wherein:

X is N or CH;

n is 0 or 1;

R^1 is halo or C_{1-3}alkyl;

w is 0, 1, or 2;

each R^3 is, independently, halo or C_{1-3}alkyl;

q is 0, 1, or 2; and

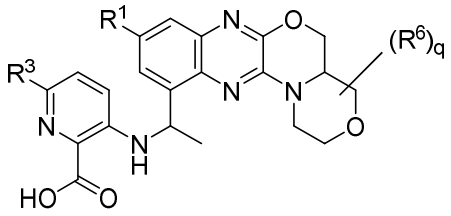
each R^6 is, independently, halo or $C_{1\text{-}3}$alkyl.

13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein:

(a) R^1 is -F or $-CH_3$; and/or

(b) each R^3 is, independently, -F, -Cl, -Br, or $-CH_3$.

14. The compound of claim 12 or 13, wherein the compound is represented by Formula (VIc-1aa):



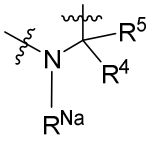
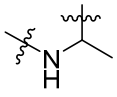
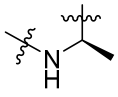
(VIc-1aa),

or a pharmaceutically acceptable salt thereof, wherein:

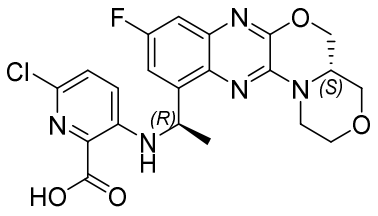
(a) each R^6 is, independently, $C_{1\text{-}3}$alkyl;

(b) each R^6 is $-CH_3$; and/or

(c) q is 0.

15. The compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein  or  is .

16. The compound of claim 1, wherein the compound is:



;

or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition comprising the compound of any one of claims 1 to 16, a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

18. Use of a therapeutically effective amount of a compound of any one of claims 1 to 16, a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 17, in the manufacture of a medicament for treating a disease or disorder associated with modulation of the alpha (α) isoform of phosphoinositide 3-kinase (PI3Kα).

19. The use of claim 18, wherein:

(a) the PI3Kα associated with the disease or disorder has or is characterized by a mutation;

(b) the PI3Kα associated with the disease or disorder has or is characterized by a H1047R or H1047L mutation;

(c) the disease or disorder is a cancer;

(d) the disease or disorder is selected from breast cancer, endometrial cancer, uterine cancer, gastric cancer, leukemia, lymphoma, sarcoma, colorectal cancer, lung cancer, ovarian cancer, skin cancer, head and neck cancer, brain cancer, or prostate cancer; or

(e) the disease or disorder is CLOVES syndrome (congenital lipomatous overgrowth, vascular malformations, epidermal naevi, scoliosis/skeletal and spinal syndrome), or PIK3CA-related overgrowth syndrome (PROS).

20. Use of a therapeutically effective amount of a compound of any one of claims 1 to 16, a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 17, in the manufacture of a medicament for treating cancer or a disorder.

21. The use of claim 20, wherein:

(a) the cancer is breast cancer, endometrial cancer, uterine cancer, gastric cancer, leukemia, lymphoma, sarcoma, colorectal cancer, lung cancer, ovarian cancer, skin cancer, head and neck cancer, brain cancer, or prostate cancer; or

(b) the disorder is CLOVES syndrome (congenital lipomatous overgrowth, vascular malformations, epidermal naevi, scoliosis/skeletal and spinal syndrome) or PIK3CA-related overgrowth syndrome (PROS).