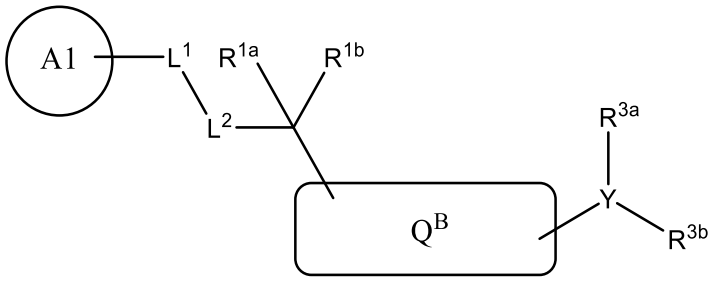
That which is claimed is:

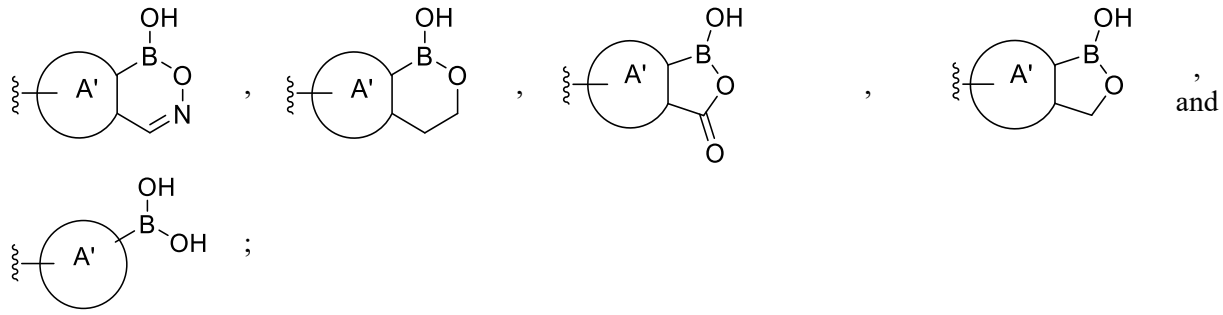
1. A compound of Formula (A):



(A),

or a tautomer, enantiomer, diastereomer, mixture, salt, hydrate, solvate, or deuterated form thereof, wherein

A1 is selected from the group consisting of:



, , , , and ;

each  represents the point of attachment to the depicted L^1;

each depicted A' independently is selected from cycloalkyl, heterocyclyl, aryl, and heteroaryl;

wherein each of heterocyclyl and heteroaryl may contain one or more heteroatoms selected from N, O, and S;

each A1 is optionally substituted;

L^1 is selected from the group consisting of (i) a direct bond, (ii) optionally substituted arylene, and (iii) optionally substituted heteroarylene;

L^2 is selected from the group consisting of O and NH;

each of R^{1a} and R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

Q^B an optionally substituted 8- to 14-membered fused ring system optionally containing one or more heteroatoms selected from the group consisting of O, N, and S; and

Y is H, CR^{3c}, N, O, or S;

a) when Y is H, each of R^{3a} and R^{3b} is absent;

b) when Y is N,

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an N atom, combines with R^{3a} and R^{3b} to form a heterocyclic or heteroaromatic mono ring or spiro or fused ring system, which may contain one or more additional heteroatoms selected from the group consisting of N, O, and S, and wherein the ring or ring system is optionally substituted;

c) when Y is CR^{3c}

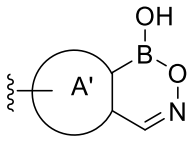
R^{3c} is absent or is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl;

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an C atom, combines with R^{3a} and R^{3b} to form a cycloalkyl, aryl, heterocyclic, or heteroaromatic mono ring or spiro or fused ring system, where the heterocyclic and heteroaromatic rings contain one or more heteroatoms selected from the group consisting of N, O, and S, and wherein the Y-containing ring or ring system is optionally substituted; or

d) when Y is O or S, R^{3a} is absent and R^{3b} is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl.

2. The compound of claim 1, wherein A1 is selected from the group consisting of:



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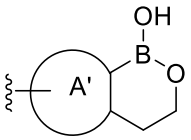

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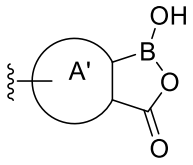

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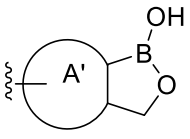


;

wherein each ≀ represents the point of attachment to the depicted L^1;

each depicted A' independently is selected from cycloalkyl, heterocyclyl, aryl, and heteroaryl;

wherein each of heterocyclyl and heteroaryl may contain one or more heteroatoms selected from N, O, and S;

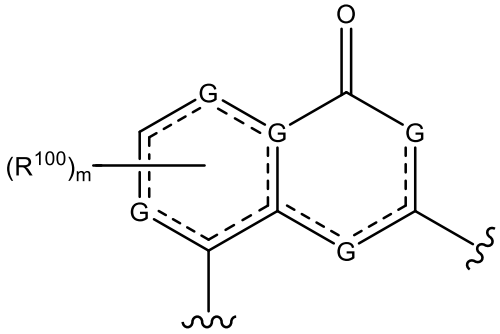
each A1 is optionally substituted;

L^1 is selected from the group consisting of (i) a direct bond, (ii) optionally substituted arylene, and (iii) optionally substituted heteroarylene;

L^2 is selected from the group consisting of O and NH;

each of R^{1a} and R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

Q^B is selected from the group consisting of;



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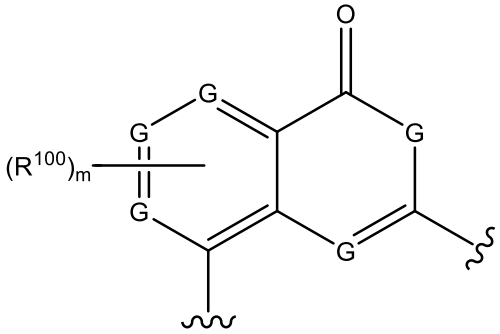

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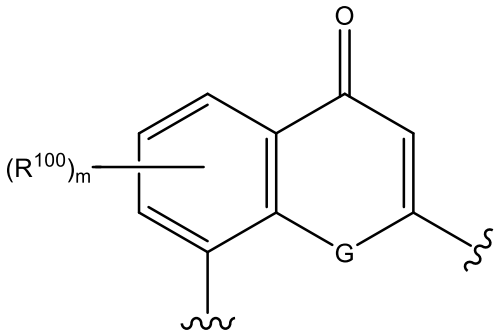

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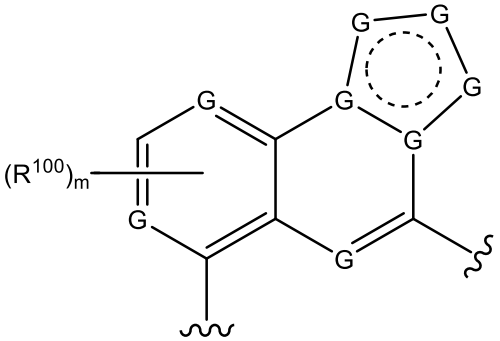

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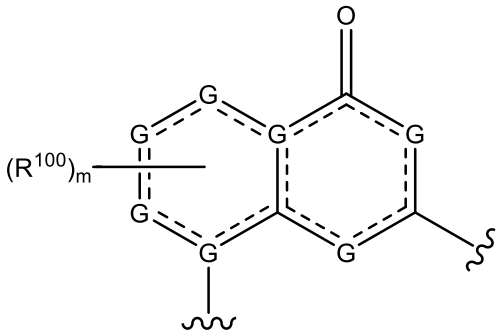

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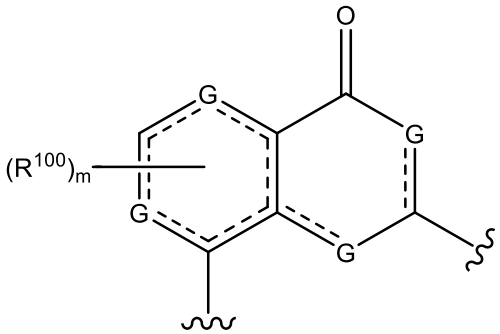

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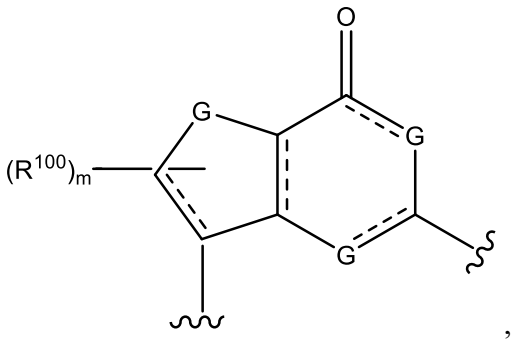
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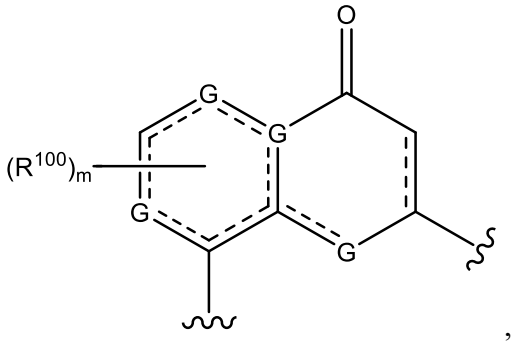
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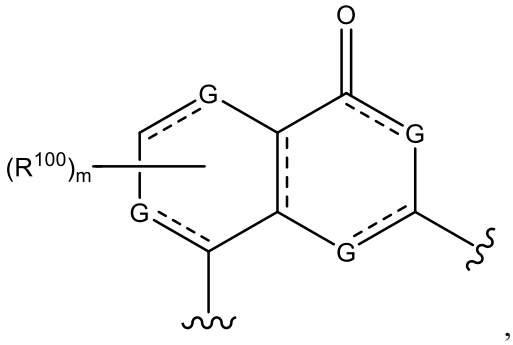
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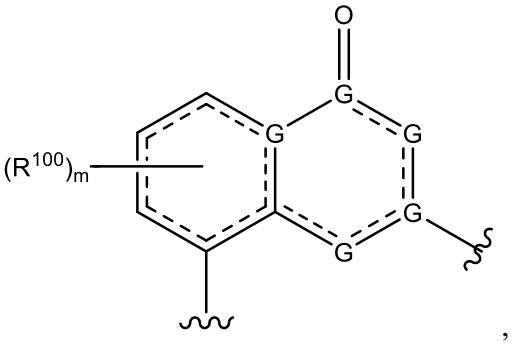
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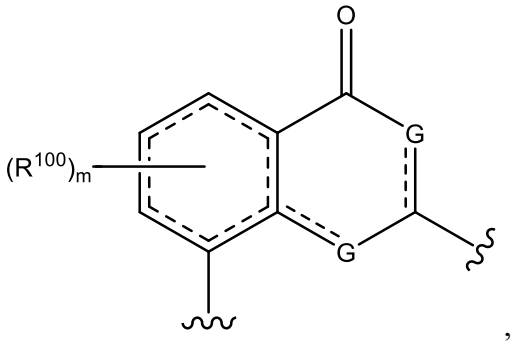
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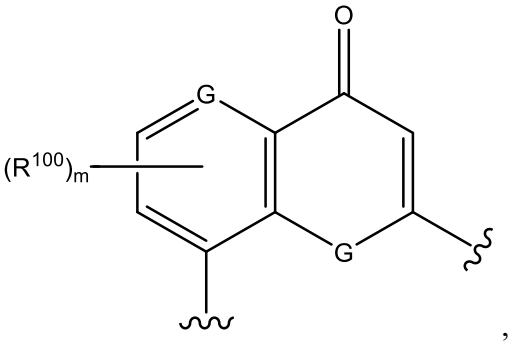
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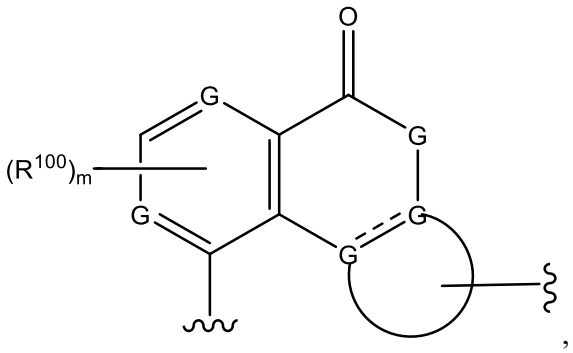
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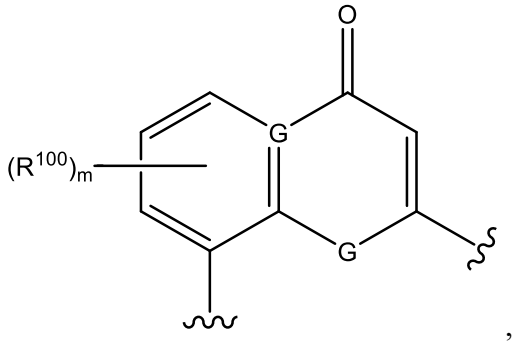

,

wherein

each G is, at each occurrence, independently selected from carbon or a heteroatom selected from O, N, or S;

each m is, at each occurrence, independently selected from 0, 1, 2, 3, 4, 5, and 6;

when m is not 0, each R^{100} may be substituted from any depicted ring; and

when present, each R^{100} independently is selected from the group consisting of halogen, OH, oxo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $(CH_2)_q$-N(H or C_{1-6}alkyl), $(CH_2)_q$-O-C(O)-$(CH_2)_r$-R^{140}, $(CH_2)_q$-NH-C(O)-$(CH_2)_r$-R^{140}, $(CH_2)_q$-O-C(O)-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-NH-C(O)-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-O-$(CH_2)_r$-R^{140}, $(CH_2)_q$-NH-$(CH_2)_r$-R^{140}, $(CH_2)_q$-O-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-NH-$(CH_2)_r$-OR^{140}, C_{3-10} cycloalkyl, $(CH_2)_q$-heterocycle, $(CH_2)_q$-aryl, and $(CH_2)_q$-heteroaryl, wherein each of the cycloalkyl, heterocycle, aryl, and heteroaryl is optionally substituted with one or more halogen, OH, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

R^{140} is an E3 ligase binding ligand; and

each of q and r, independently is, at each occurrence, selected from 0, 1, 2, 3, 4, or 5;

and

Y is H, CR^{3c}, N, O, or S;

a) when Y is H, each of R^{3a} and R^{3b} is absent;

b) when Y is N,

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an N atom, combines with R^{3a} and R^{3b} to form a heterocyclic or heteroaromatic mono ring or spiro or fused ring system, which may contain one or more additional heteroatoms selected from the group consisting of N, O, and S, and wherein the ring or ring system is optionally substituted;

c) when Y is CR^{3c}

R^{3c} is absent or is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl;

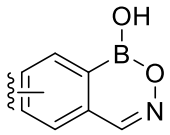
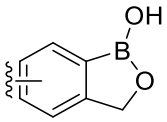
each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as a C atom, combines with R^{3a} and R^{3b} to form a cycloalkyl, aryl, heterocyclic, or heteroaromatic mono ring or spiro or fused ring system, wherein the heterocyclic and heteroaromatic rings contain one or more heteroatoms selected from the group consisting of N, O, and S, and wherein the Y-containing ring or ring system is optionally substituted; or

d) when Y is O or S, R^{3a} is absent and R^{3b} is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl.

3. The compound of claim 1, wherein:

(i) A1 is selected from:

 and  , wherein

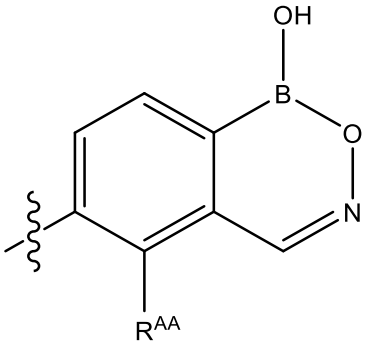
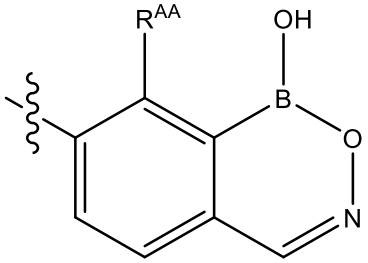
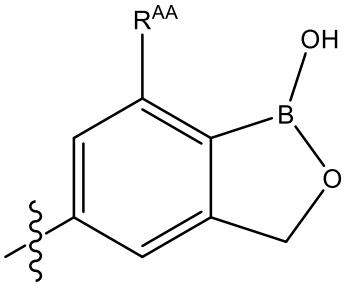
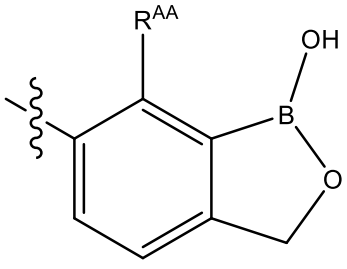
each A1 is optionally substituted from either depicted ring,

optionally, wherein

each A1 is optionally substituted with one or more R^{A1}, wherein

each R^{A1} independently is selected from halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, $(CH_2)_{0-6}CN$, $(CH_2)_{1-6}OH$, $(CH_2)_{0-6}O$-C_{1-6} alkyl, $(CH_2)_{0-6}O$-C_{2-6} alkenyl, $(CH_2)_{0-6}O$-C_{2-6} alkynyl, $(CH_2)_{0-6}C(O)H$, $(CH_2)_{0-6}C(O)(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{1-6} alkynyl), $(CH_2)_{0-6}C(O)OH$, $(CH_2)_{0-6}C(O)O(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}NH_2$, $(CH_2)_{0-6}NH(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}N(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}C(O)NH_2$, $(CH_2)_{0-6}C(O)NH(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}C(O)N(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}NHC(O)H$, $(CH_2)_{0-6}NHC(O)(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), and $(CH_2)_{0-6}N(C_{1-6}$ alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl)$C(O)(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), or an isotopic form of R^{A1}, and/or

(ii) A1 is selected from the group consisting of:

 ,  ,  , and  and

each A1 is optionally further substituted,

optionally, wherein:

(i) each R^{AA} is independently selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, OH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, and O-C_{2-6} alkynyl, or

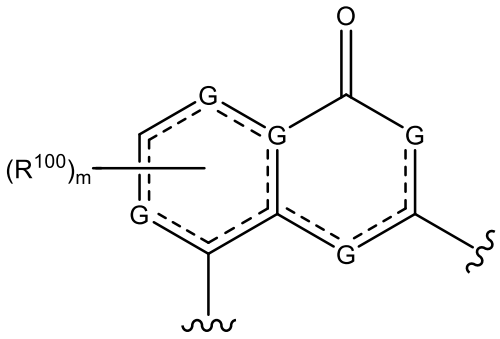
(ii) R^{AA} is selected from the group consisting of C_{1-6} alkyl, O-C_{1-6} alkyl, C_{1-6} haloalkyl, deuterated C_{1-6} alkyl, deuterated O-C_{1-6} alkyl, deuterated C_{1-6} haloalkyl, halogen, and CN, or

(iii) R^{AA} is F, Cl, CH_3, OCH_3, or CD_3.

4. The compound of any one of claims 1 to 3, wherein one or more atom is an isotopic form, optionally, wherein the isotope is deuterium,
wherein R^{AA} is deuterated.

5. The compound of any one of claims 1 to 4, wherein:

(i) Q^B is selected from the group consisting of:



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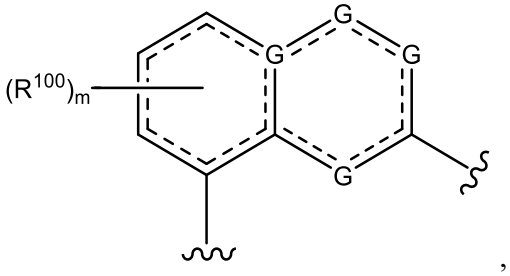

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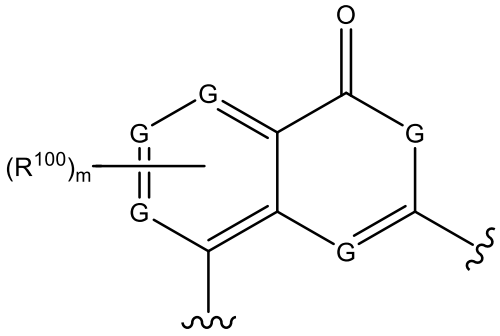

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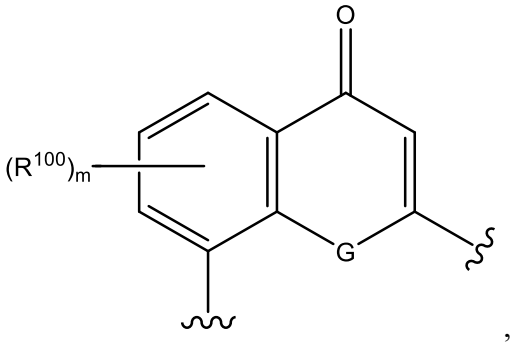

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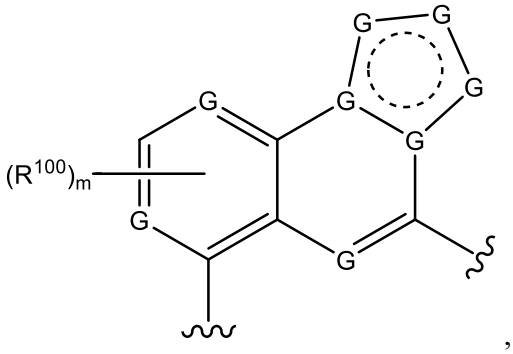
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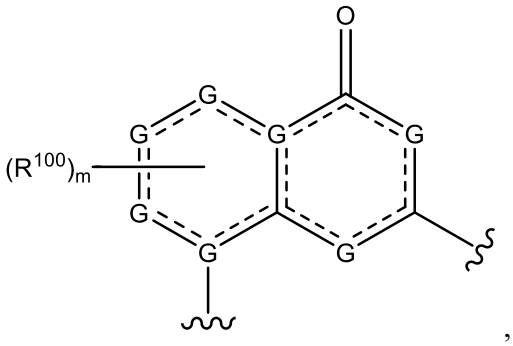
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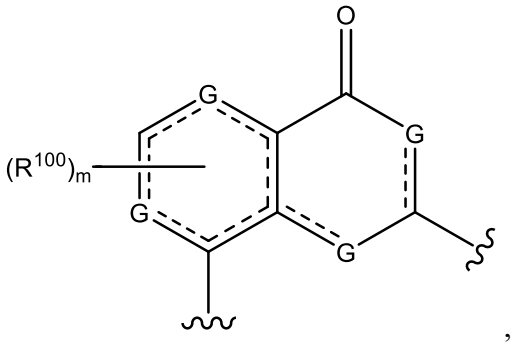
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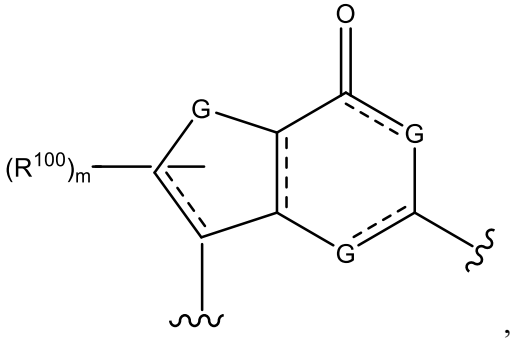
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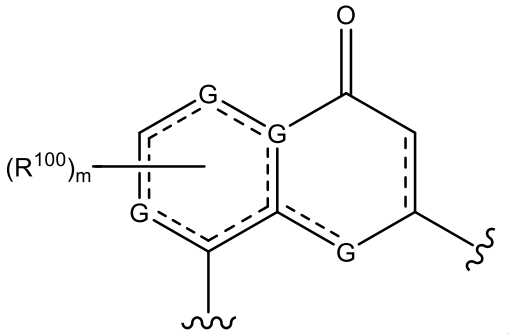
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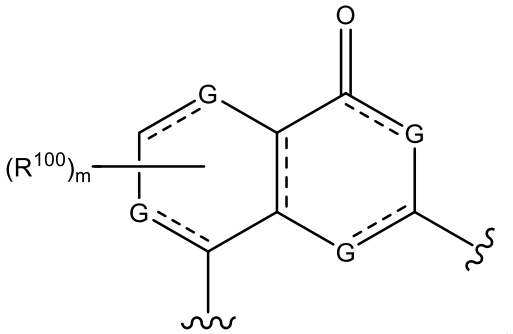
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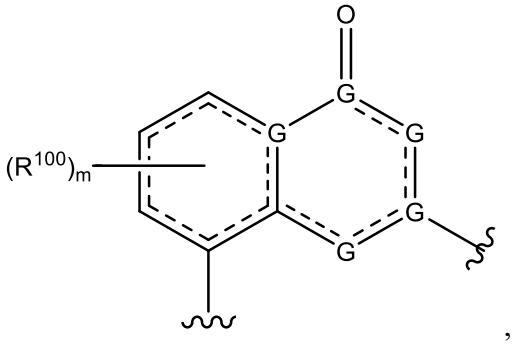
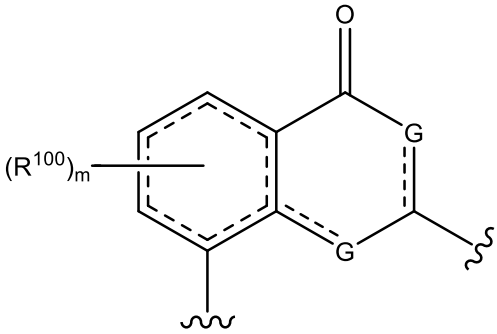

,

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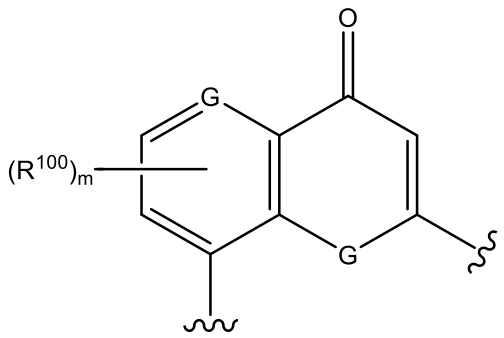

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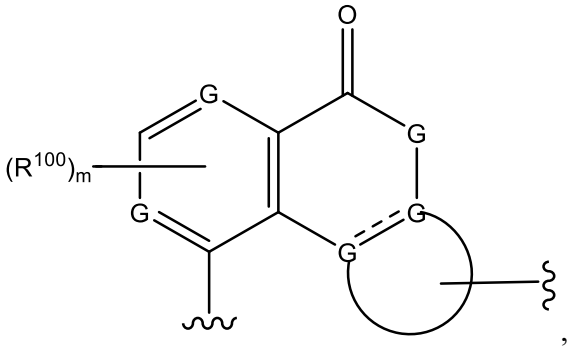

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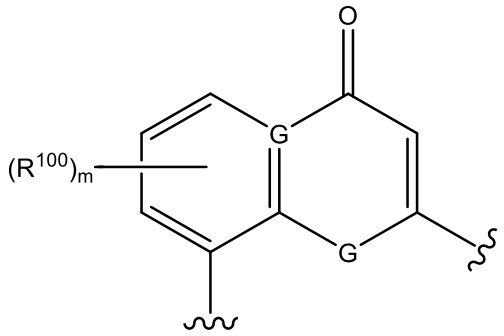

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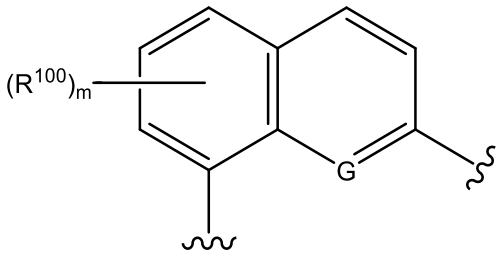


,

wherein

each G is, at each occurrence, independently selected from carbon or a heteroatom selected from O, N, or S;

each m is, at each occurrence, independently selected from 0, 1, 2, 3, 4, 5, and 6;

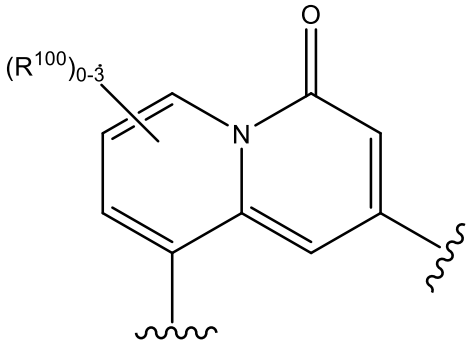
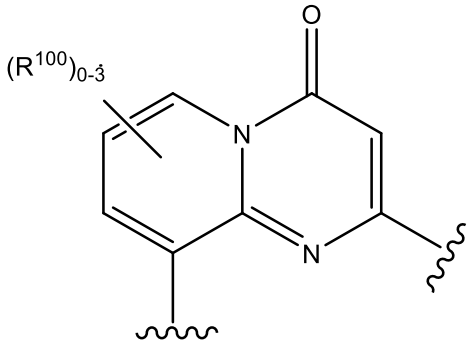
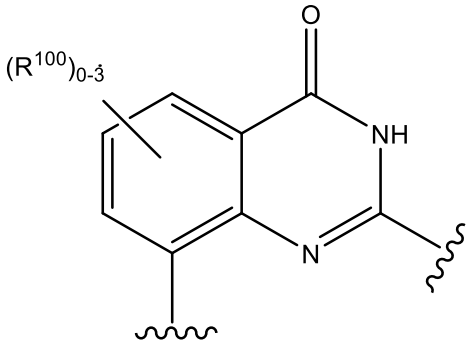
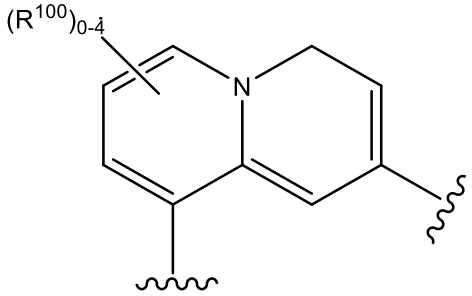
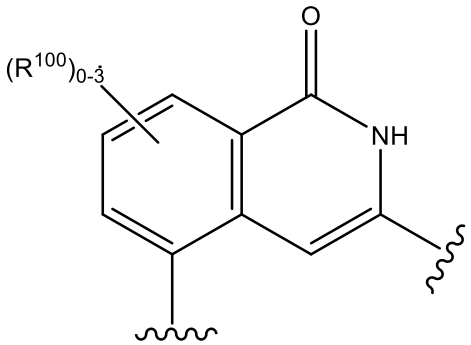
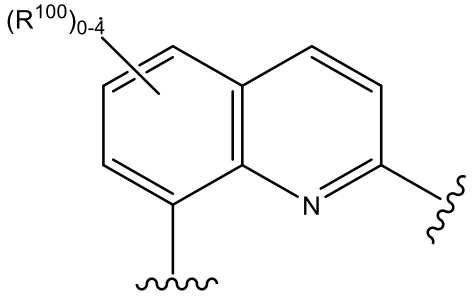
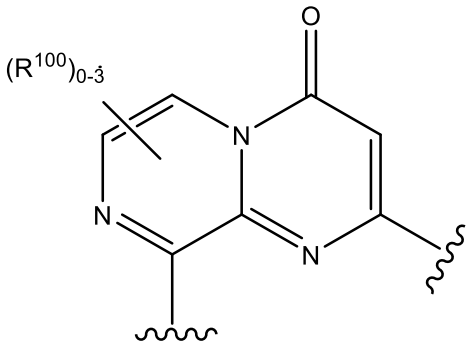
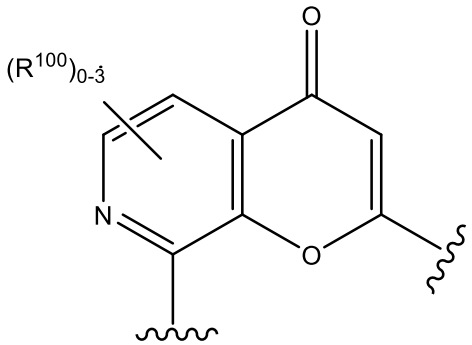
when m is not 0, each R^{100} may be substituted from any depicted ring; and

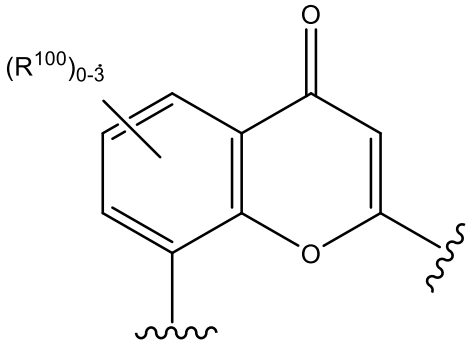
when present, each R^{100} independently is selected from the group consisting of halogen, OH, oxo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $(CH_2)_q$-N(H or C_{1-6}alkyl), $(CH_2)_q$-O-C(O)-$(CH_2)_r$-R^{140}, $(CH_2)_q$-NH-C(O)-$(CH_2)_r$-R^{140}, $(CH_2)_q$-O-C(O)-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-NH-C(O)-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-O-$(CH_2)_r$-R^{140}, $(CH_2)_q$-NH-$(CH_2)_r$-R^{140}, $(CH_2)_q$-O-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-NH-$(CH_2)_r$-OR^{140}, C_{3-10} cycloalkyl, $(CH_2)_q$-heterocycle, $(CH_2)_q$-aryl, and $(CH_2)_q$-heteroaryl, wherein each of the cycloalkyl, heterocycle, aryl, and heteroaryl is optionally substituted with one or more halogen, OH, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

R^{140} is an E3 ligase binding ligand; and

each of q and r, independently is, at each occurrence, selected from 0, 1, 2, 3, 4, 5, and 6; or

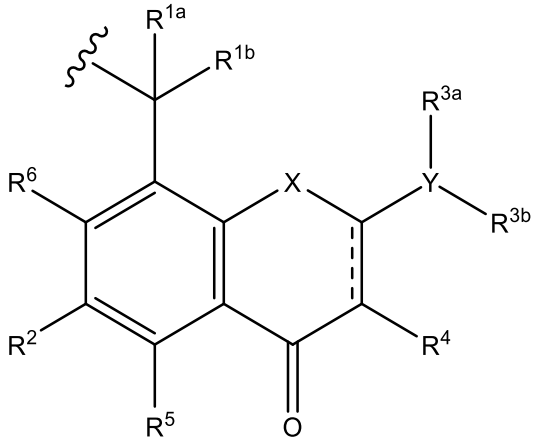
(ii) Q^B is selected from the group consisting of:


(R100)0-3
O
N
,

(R100)0-3
O
N
N
,

(R100)0-3
O
NH
N
,

(R100)0-4
N
,

(R100)0-3
O
NH
,

(R100)0-4
N
,

(R100)0-3
O
N
N
N
,

(R100)0-3
O
N
O
, and



; or

(iii) Q^B is:



(Q^B1),

wherein

X is $C(R^x)_2$, O, NR^x, or S;

each R^x independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

R^2 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{QB1}, $(CH_2)_{0-6}$-OR^{QB1}, $(CH_2)_{0-6}$-$N(R^{QB1})_2$, $(CH_2)_{0-6}$-$C(O)R^{QB1}$, $(CH_2)_{0-6}$-$C(O)OR^{QB1}$, $(CH_2)_{0-6}$-$C(O)N(R^{QB1})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^4 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{QB1}, $(CH_2)_{0-6}$-OR^{QB1}, $(CH_2)_{0-6}$-$N(R^{QB1})_2$, $(CH_2)_{0-6}$-$C(O)R^{QB1}$, $(CH_2)_{0-6}$-$C(O)OR^{QB1}$, $(CH_2)_{0-6}$-$C(O)N(R^{QB1})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^5 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{QB1}, $(CH_2)_{0-6}$-OR^{QB1}, $(CH_2)_{0-6}$-

$N(R^{QB1})_2$, $(CH_2)_{0-6}$-$C(O)R^{QB1}$, $(CH_2)_{0-6}$-$C(O)OR^{QB1}$, $(CH_2)_{0-6}$-$C(O)N(R^{QB1})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^6 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{QB1}, $(CH_2)_{0-6}$-OR^{QB1}, $(CH_2)_{0-6}$-$N(R^{QB1})_2$, $(CH_2)_{0-6}$-$C(O)R^{QB1}$, $(CH_2)_{0-6}$-$C(O)OR^{QB1}$, $(CH_2)_{0-6}$-$C(O)N(R^{QB1})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl; and

each R^{QB1} is independently H, halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{2-6} alkenoxy, C_{2-6} alkynoxy, C_{1-6} haloalkoxy, C_{2-6} haloalkenoxy, and C_{2-6} alkynoxy,

optionally, wherein each of R^2, R^4, R^5, and R^6 independently is H, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_3-C_6 cycloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, or C_{1-6} haloalkyl,

optionally, wherein R^4 is H or CH_3,

optionally, wherein R^2 is H, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl,

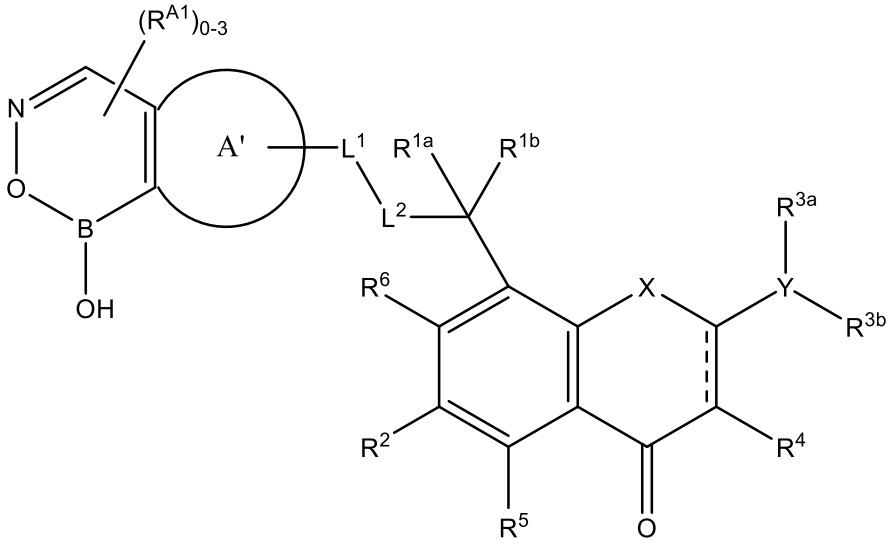
optionally, wherein R^4 is CH_3,

optionally, wherein R^5 is H,

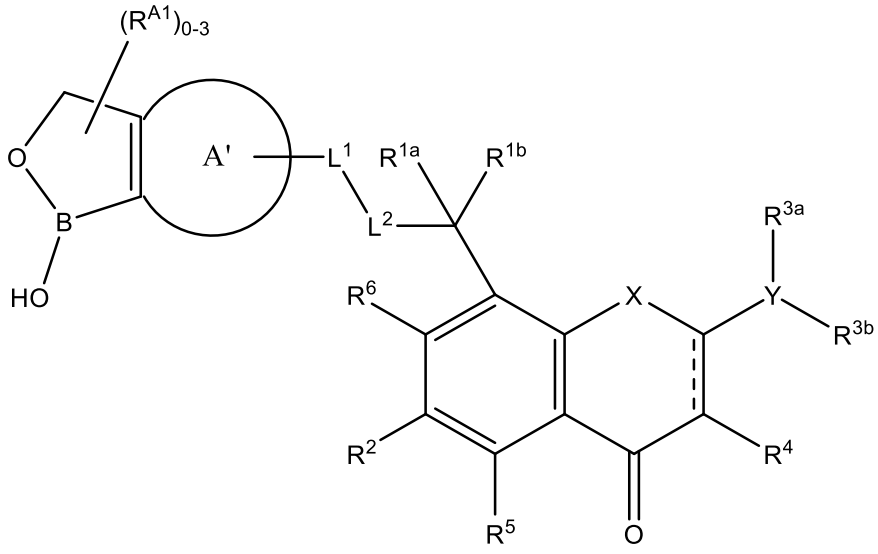
optionally, wherein R^6 is H,

optionally, wherein the depicted dashed bond is a double bond.

6. The compound of any one of claims 1 to 5, wherein the compound is a compound of Formula A(Ia) or A(Ib):



A(Ia), or



A(Ib),

optionally, wherein A' is fused aryl or heteroaryl,

optionally, wherein A' is selected from optionally substituted phenyl, or

optionally, wherein A' is substituted phenyl.

7. The compound of any one of claims 1 to 6, wherein L^1 is selected from the group consisting of a direct bond, optionally substituted heteroarylene, or optionally substituted arylene,

(i) optionally, wherein the optionally substituted arylene is optionally substituted phenylene, or wherein the optionally substituted heteroarylene is optionally substituted pyridylene; or

(ii) optionally, wherein each of optionally substituted arylene and optionally substituted heteroarylene is unsubstituted; or

(iii) optionally, wherein each of optionally substituted arylene and optionally substituted heteroarylene is substituted with one or two substituents selected from the group consisting of halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_2-C_3 alkenyl, C_2-C_3 haloalkenyl, C_2-C_3 alkynyl, C_2-C_3 haloalkynyl, OH, O-(C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl), NH_2, NH(C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl), N(C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl)$_2$, C_3 cycloalkyl, and C_3 halocycloalkyl, or

optionally, wherein each of optionally substituted arylene and optionally substituted heteroarylene is substituted with one or two substituents selected from the group consisting of halogen and C_1-C_3 alkyl.

8. The compound of any one of claims 1 to 7, wherein L^2 is NH.

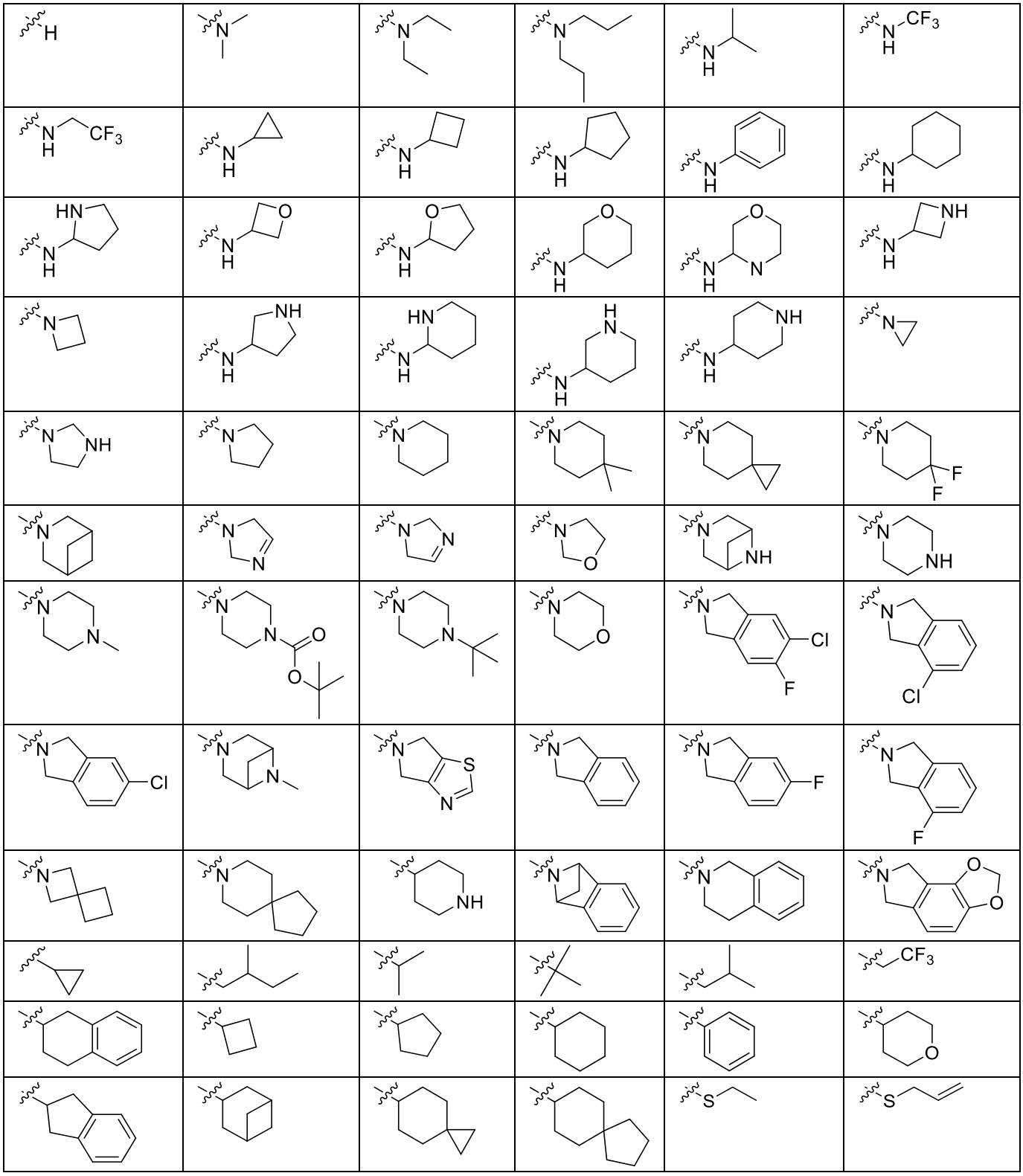
9. The compound of any one of claims 1 to 8, wherein each of R^{1a} and R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-3} haloalkyl, and C_{1-3} alkyl,

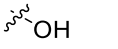
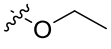
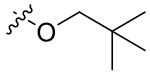
optionally, wherein each of R^{1a} and R^{1b} independently is selected from the group consisting of H and CH_3.

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

(i) Y is N or CR^3; or

(ii) Y is selected from the group consisting of substituted or unsubstituted:

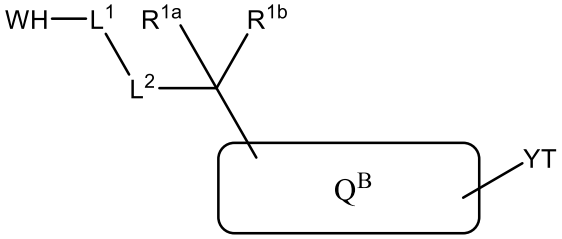


			and		; or

(iii) Y is CR^{3c} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl,

optionally, wherein each of R^{3a} and R^{3b} is independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3- to 6-membered heterocyclyl.

11. A compound of Formula (AWH):



(AWH),

or a tautomer, enantiomer, diastereomer, mixture, salt, hydrate, solvate, or deuterated form thereof, wherein

WH is a warhead moiety;

L^1 is selected from the group consisting of a direct bond, optionally substituted cycloalkylene, optionally substituted heterocyclylene, optionally substituted arylene, and optionally substituted heteroarylene;

L^2 is selected from the group consisting of $(CH_2)_{1-6}$, O, C(O), S, and NH;

each of R^{1a} and R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

or L^2-$C(R^{1a})(R^{1b})$ combines to form NHC(S), C(S)NH, NHC(O), C(O)NH, $NHS(O)_2$, $S(O)_2NH$, NHC(NH), or C(NH)NH;

Q^B an optionally substituted 8- to 14-membered spiro or fused ring system optionally containing one or more heteroatoms selected from the group consisting of O, N, and S;

YT is any moiety that provides desired physicochemical properties; and

an optional E3 ligase binding ligand.

12. The compound of claim 11, wherein:

(i) WH is a ring system:

Q1-Q2,

wherein:

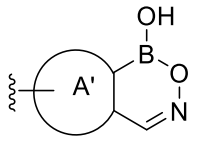
the ring system is attached to the depicted L^1 through either the Q1 or Q2 portion; and

a) Q1 is an optionally substituted 5- or 6-membered ring, having one or more degrees of unsaturation, and optionally having one or more heteroatom selected from B, N, O, or S; and
Q2 is fused to Q1 and is an optionally substituted 5- or 6-membered ring, having one or more degrees of unsaturation, and optionally having one or more heteroatom selected from B, N, O, or S;

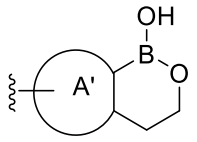
or

b) Q1 does not exist; and
Q2 is an optionally substituted 5- or 6-membered ring, having one or more degrees of unsaturation, and optionally having one or more heteroatom selected from B, N, O, or S,

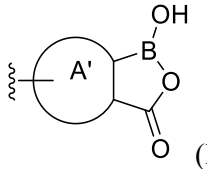
optionally, wherein Q1-Q2 is selected from:



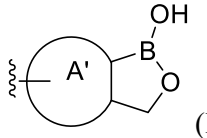
(I^{X1})



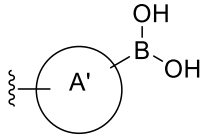
(I^{X2})



(I^{X3});



(I^{X4});



(I^{X5});

where each  represents the point of attachment to the depicted L^1;
each depicted A' is a cycloalkyl, heterocyclyl, aryl, or heteroaryl, mono-ring;
wherein each of the heterocyclyl or heteroaryl rings contain one or more heteroatoms selected from N, O, and S; and
each is optionally substituted with one or more R^{A1}, where each R^{A1} independently is selected from halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, $(CH_2)_{0-6}CN$, $(CH_2)_{1-6}OH$, $(CH_2)_{0-6}O$-C_{1-6} alkyl, $(CH_2)_{0-6}O$-

C_{2-6} alkenyl, $(CH_2)_{0-6}O$-C_{2-6} alkynyl, $(CH_2)_{0-6}C(O)H$, $(CH_2)_{0-6}C(O)(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{1-6} alkynyl), $(CH_2)_{0-6}C(O)OH$, $(CH_2)_{0-6}C(O)O(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}NH_2$, $(CH_2)_{0-6}NH(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}N(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}C(O)NH_2$, $(CH_2)_{0-6}C(O)NH(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}C(O)N(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}NHC(O)H$, $(CH_2)_{0-6}NHC(O)(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), and $(CH_2)_{0-6}N(C_{1-6}$ alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl)$C(O)(C_{1-6}$ alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), or an isotopic form of R^A,

optionally, wherein A' is aryl,

optionally, wherein A' is phenyl,

optionally, wherien A' is heterocyclyl,

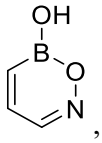
optionally, wherein A' is heteroaryl,

optionally, wherein the heteroaryl is a 5- or 6-membered heteroaryl, containing one or two heteroatoms selected from N, O, and S; or

(ii) WH is selected from an optionally substituted:

Group (a): a cyclohexenone derivative, an alkyl halide derivative, a sulfonyl derivative, an α-cyanoenone derivative, and an epoxide or spiro-epoxide derivative;

Group (b)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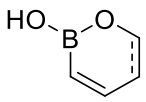
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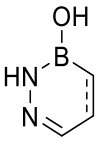
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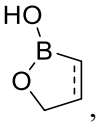
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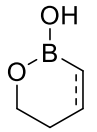
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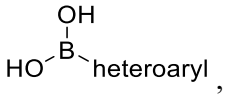
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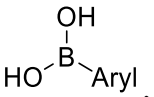
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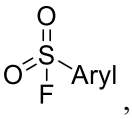
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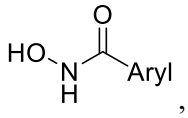
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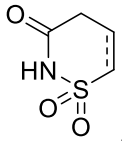
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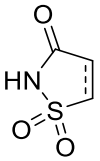
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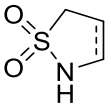
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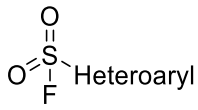
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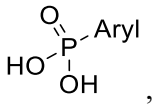
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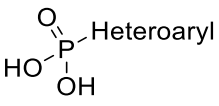

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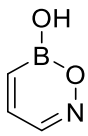
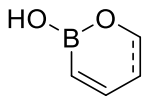
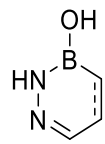
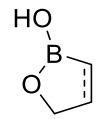
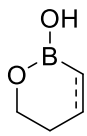
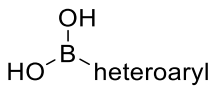
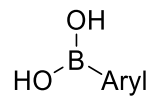
 ,  ,  ,  ,

 ,  , and  ; or

(iii) WH provides chemical capture of a solvent accessible surface area of a protein,

optionally, wherein the chemical capture is a binding interaction,

optionally, wherein the binding interaction is covalent binding, or

optionally, wherein the binding interaction is hydrogen binding,

optionally, wherein the solvent accessible surface area of a protein is an accessible amino acid,

optionally, wherein the amino acid is arginine, histidine, lysine, glutamic acid, serine, threonin, or glutamine,

optionally, wherein the amino acid is histidine; or

(iv) WH is a boron-containing warhead; or

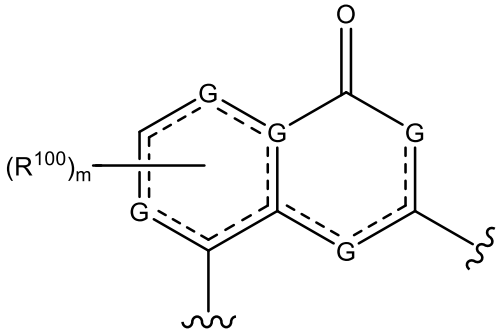
(v) WH is a non-boron-containing warhead.

13. The compound of claims 11 or 12, wherein optionally substituted is substituted with one or more substituents selected from the group consisting of: deuterium, halogen, haloalkyl, R', OR', OH, SH, SR', NO_2, CN, C(O)R', NH_2, C(O)OR', OC(O)R', $CON(R')_2$, $OC(O)N(R')_2$, NH_2, NHR', $N(R')_2$, NHCOR', NHCOH, $NHCONH_2$, NHCONHR', $NHCON(R')_2$, NRCOR', NRCOH, $NHCO_2H$, $NHCO_2R'$, $NHC(S)NH_2$, NHC(S)NHR', $NHC(S)N(R')_2$, CO_2R', CO_2H, CHO, $CONH_2$, CONHR', $CON(R')_2$, $S(O)_2H$, $S(O)_2R'$, SO_2NH_2, S(O)H, S(O)R', SO_2NHR', $SO_2N(R')_2$, $NHS(O)_2H$, $NR'S(O)_2H$, $NHS(O)_2R'$, $NR'S(O)_2R'$, $Si(R')_3$, =O, =S, =NNHR', $=NNH_2$, $=NN(R')_2$, =N-OR', =N-OH, =NNHCOR', =NNHCOH, $=NNHCO_2R'$, $=NNHCO_2H$, $=NNHSO_2R'$, $=NNHSO_2H$, =N-CN, =NH, =NR', where each of the preceding may be linked through a divalent alkylene linker, $(CH_2)_x$, where x is 1, 2, or 3, and where each occurrence of R' is the same or different and represents hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, or heteroaryl, or when two R' are each attached to a nitrogen atom, they may form a saturated or unsaturated heterocyclic ring containing from 4 to 6 ring atoms.

14. The compound of any one of claims 11 to 13, wherein:

(i) Q^B is an oxo-substituted 6,6 fused ring containing one or more heteroatom selected from O, N, or S; or

(ii) Q^B is selected from:



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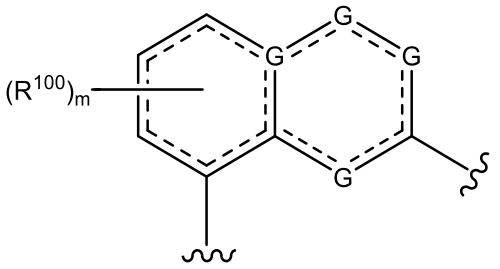

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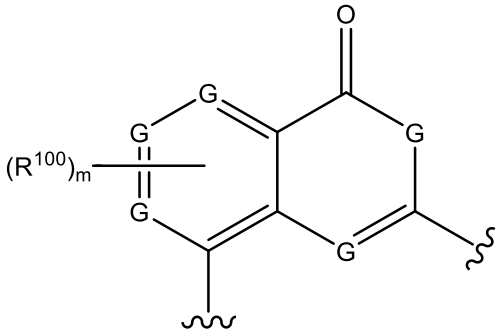

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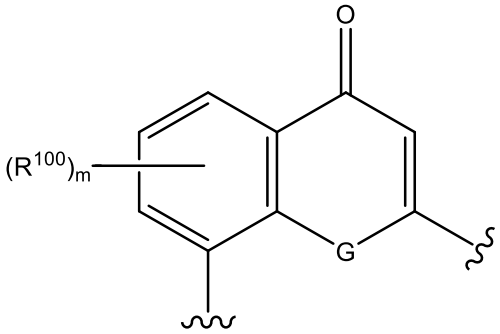

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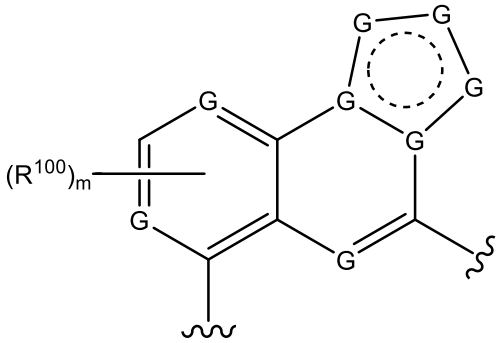

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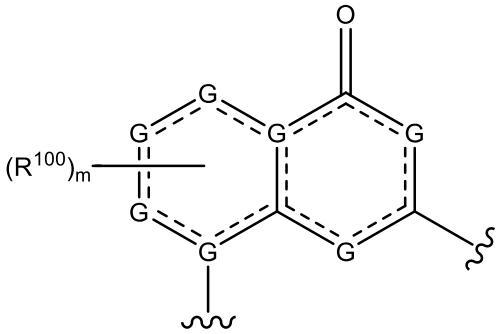

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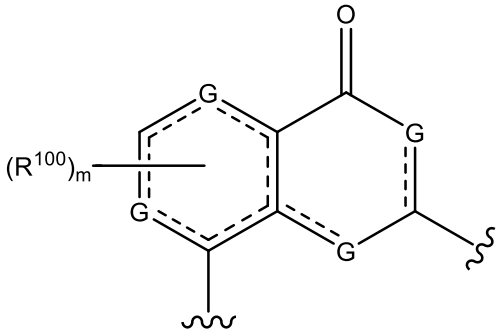

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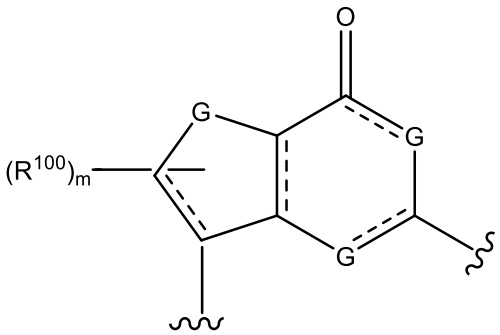

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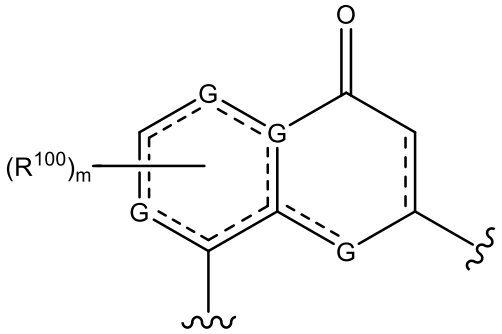
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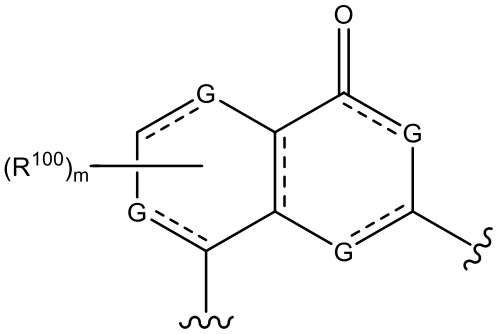
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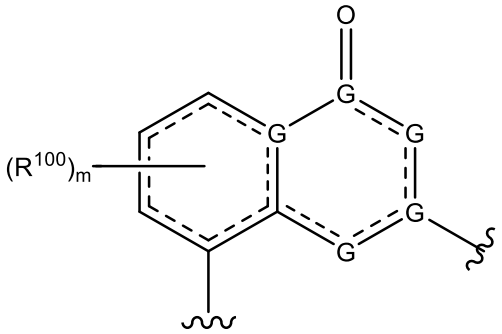
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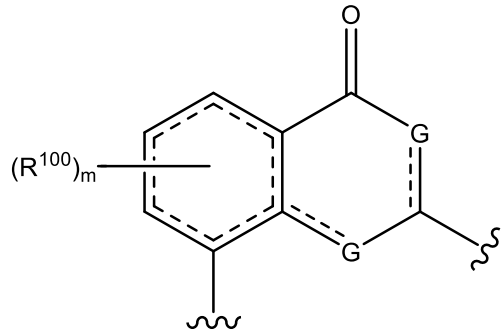
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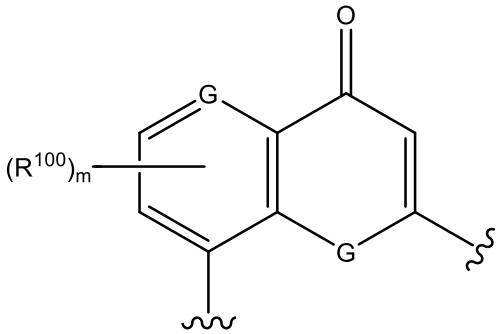
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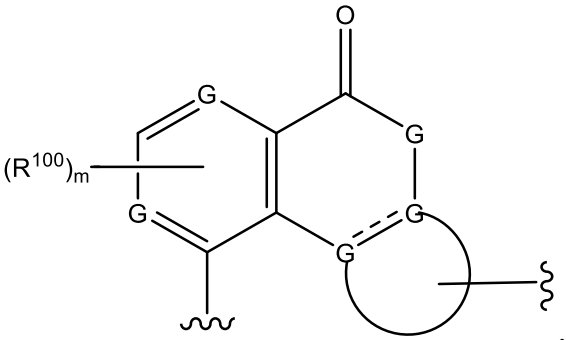
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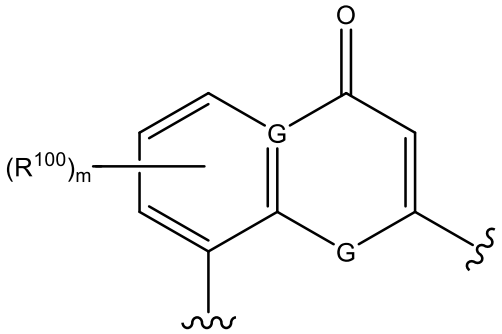
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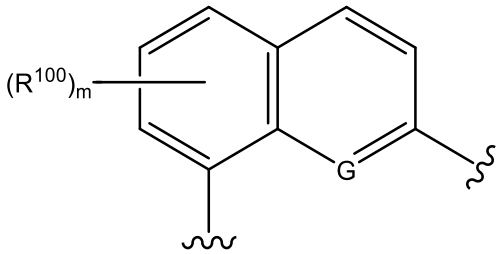
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wherein

each G is, at each occurrence, independently selected from carbon or a heteroatom selected from O, N, or S;

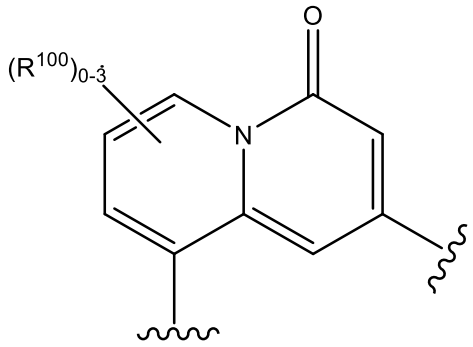
each m is, at each occurrence, independently selected from 0, 1, 2, 3, 4, 5, and 6; and

each R^{100} independently is selected from the group consisting of halogen, OH, oxo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_q$-N(H or C_{1-6}alkyl), $(CH_2)_q$-O-C(O)-$(CH_2)_r$-R^{140}, $(CH_2)_q$-NH-C(O)-$(CH_2)_r$-R^{140}, $(CH_2)_q$-O-C(O)-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-NH-C(O)-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-O-$(CH_2)_r$-R^{140}, $(CH_2)_q$-NH-$(CH_2)_r$-R^{140}, $(CH_2)_q$-O-$(CH_2)_r$-OR^{140}, $(CH_2)_q$-NH-$(CH_2)_r$-OR^{140}, C_{3-10} cycloalkyl, $(CH_2)_q$-heterocycle, $(CH_2)_q$-aryl, and $(CH_2)_q$-heteroaryl, wherein each of the cycloalkyl, heterocycle, aryl, and heteroaryl is optionally substituted with one or more halogen, OH, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, and C_{1-6} haloalkoxy;

R^{140} is an E3 ligase binding ligand; and

each of q and r, independently is, at each occurrence, selected from 0, 1, 2, 3, 4, 5, and 6; or.

(iii) Q^B is selected from:



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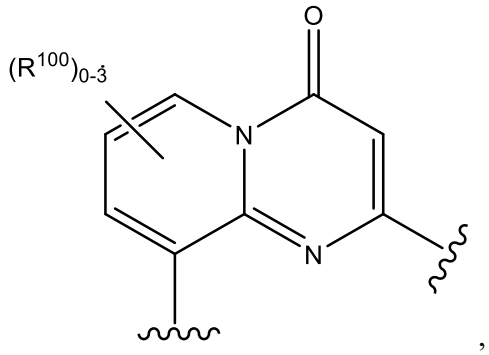

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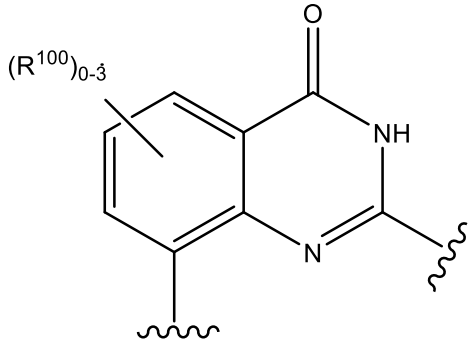

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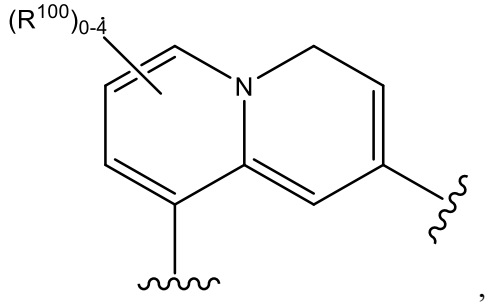

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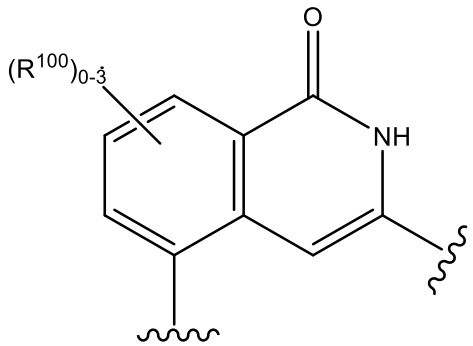

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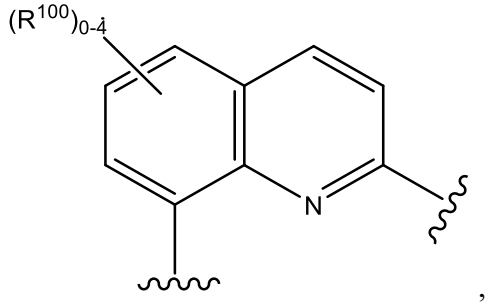

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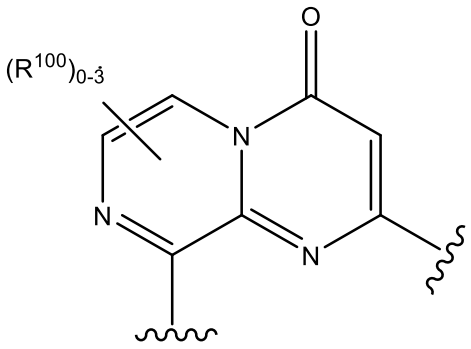

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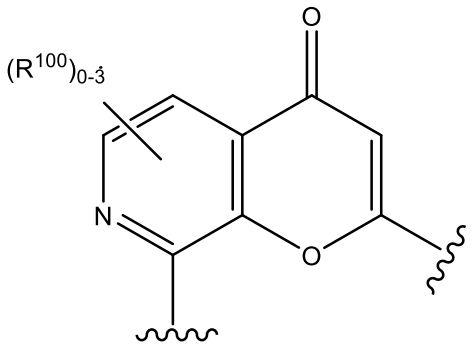

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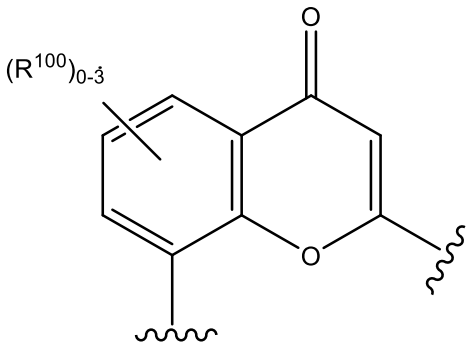

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optionally, wherein at least one R^{100} is substituted from a depicted N in Q^B.

15. The compound of any one of claims 11 to 14, wherein Y^T is $YR^{3a}R^{3b}$; and

Y is H, CR^{3c}, N, O, or S;

a) when Y is H, each of R^{3a} and R^{3b} is absent;

b) when Y is N,

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an N atom, combines with R^{3a} and R^{3b} to form a heterocyclic or heteroaromatic mono ring or spiro or fused ring system, which may contain one or more additional heteroatoms selected from the group consisting of N, O, and S, and wherein the ring or ring system is optionally substituted;

c) when Y is CR^{3c}

R^{3c} is absent or is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl;

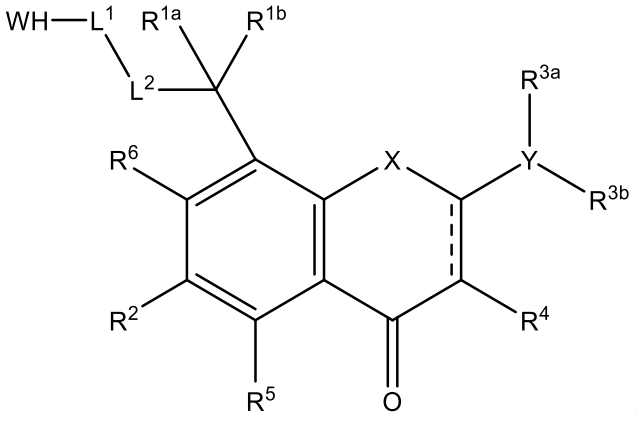
each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an C atom, combines with R^{3a} and R^{3b} to form a cycloalkyl, aryl, heterocyclic, or heteroaromatic mono ring or spiro or fused ring system, where the heterocyclic and heteroaromatic rings contain one or more heteroatoms selected from the group consisting of N, O, and S, and wherein the Y-containing ring or ring system is optionally substituted; or

d) when Y is O or S, R^{3a} is absent and R^{3b} is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl.

optionally, wherein when $YR^{3a}R^{3b}$ forms a ring, the ring is optionally substituted with one or more substituents selected from the group consisting of: deuterium, halogen, haloalkyl, R', OR', OH, SH, SR', NO_2, CN, C(O)R', NH_2, C(O)OR', OC(O)R', $CON(R')_2$, $OC(O)N(R')_2$, NH_2, NHR', $N(R')_2$, NHCOR', NHCOH, $NHCONH_2$, NHCONHR', $NHCON(R')_2$, NRCOR', NRCOH, $NHCO_2H$, $NHCO_2R'$, $NHC(S)NH_2$, NHC(S)NHR', $NHC(S)N(R')_2$, CO_2R', CO_2H, CHO, $CONH_2$, CONHR', $CON(R')_2$, $S(O)_2H$, $S(O)_2R'$, SO_2NH_2, S(O)H, S(O)R', SO_2NHR', $SO_2N(R')_2$, $NHS(O)_2H$, $NR'S(O)_2H$, $NHS(O)_2R'$, $NR'S(O)_2R'$, $Si(R')_3$, =O, =S, =NNHR', $=NNH_2$, $=NN(R')_2$, =N-OR', =N-OH, =NNHCOR', =NNHCOH, $=NNHCO_2R'$, $=NNHCO_2H$, $=NNHSO_2R'$, $=NNHSO_2H$, =N-CN, =NH, =NR', where each of the preceding may be linked through a divalent alkylene linker, $(CH_2)_x$, where x is 1, 2, or 3, and where each occurrence of R' is the same or different and represents hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, or heteroaryl, or when two R' are each attached to a nitrogen atom, they may form a saturated or unsaturated heterocyclic ring containing from 4 to 6 ring atoms.

16. The compound of any one of claims 11 to 15, comprising a compound of (AWH2):



(AWH2),

or a tautomer, enantiomer, diastereomer, mixture, salt, hydrate, solvate, or deuterated form thereof,

wherein

X is $C(R^x)_2$, O, NR^x, or S;

each R^x independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

R^2 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AWH2}, $(CH_2)_{0-6}$-OR^{AWH2}, $(CH_2)_{0-6}$-$N(R^{AWH2})_2$, $(CH_2)_{0-6}$-$C(O)R^{AWH2}$, $(CH_2)_{0-6}$-$C(O)OR^{AWH2}$, $(CH_2)_{0-6}$-$C(O)N(R^{AWH2})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^4 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AWH2}, $(CH_2)_{0-6}$-OR^{AWH2}, $(CH_2)_{0-6}$-$N(R^{AWH2})_2$, $(CH_2)_{0-6}$-$C(O)R^{AWH2}$, $(CH_2)_{0-6}$-$C(O)OR^{AWH2}$, $(CH_2)_{0-6}$-$C(O)N(R^{AWH2})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^5 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AWH2}, $(CH_2)_{0-6}$-OR^{AWH2}, $(CH_2)_{0-6}$-$N(R^{AWH2})_2$, $(CH_2)_{0-6}$-$C(O)R^{AWH2}$, $(CH_2)_{0-6}$-$C(O)OR^{AWH2}$, $(CH_2)_{0-6}$-$C(O)N(R^{AWH2})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^6 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AWH2}, $(CH_2)_{0-6}$-OR^{AWH2}, $(CH_2)_{0-6}$-$N(R^{AWH2})_2$, $(CH_2)_{0-6}$-$C(O)R^{AWH2}$, $(CH_2)_{0-6}$-$C(O)OR^{AWH2}$, $(CH_2)_{0-6}$-$C(O)N(R^{AWH2})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl; and

each R^{AWH2} is independently H, halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{2-6} alkenoxy, C_{2-6} alkynoxy, C_{1-6} haloalkoxy, C_{2-6} haloalkenoxy, and C_{2-6} alkynoxy.

17. The compound of claim 11 or 16, wherein:

(i) Y is N or CR^{3c},

optionally, wherein Y combines with R^{3a} and R^{3b} to form:

a) cycloalkyl substituted with $B(OH)_2$;

b) aryl substituted with $B(OH)_2$;

c) heterocyclyl, either

i) containing a B atom in the ring or ring system,

ii) substituted with $B(OH)_2$, or

iii) substituted with an optionally substituted 4- to 6-membered ring containing a B atom, one or more additional heteroatoms selected from O, N, or S, and one or more degrees of unsaturation; or

d) heteroaryl, either

i) containing a B atom in the ring or ring system, or

ii) substituted with $B(OH)_2$, or

iii) substituted with an optionally substituted 4- to 6-membered ring containing a B atom, one or more additional heteroatoms selected from O, N, or S, and one or more degrees of unsaturation;

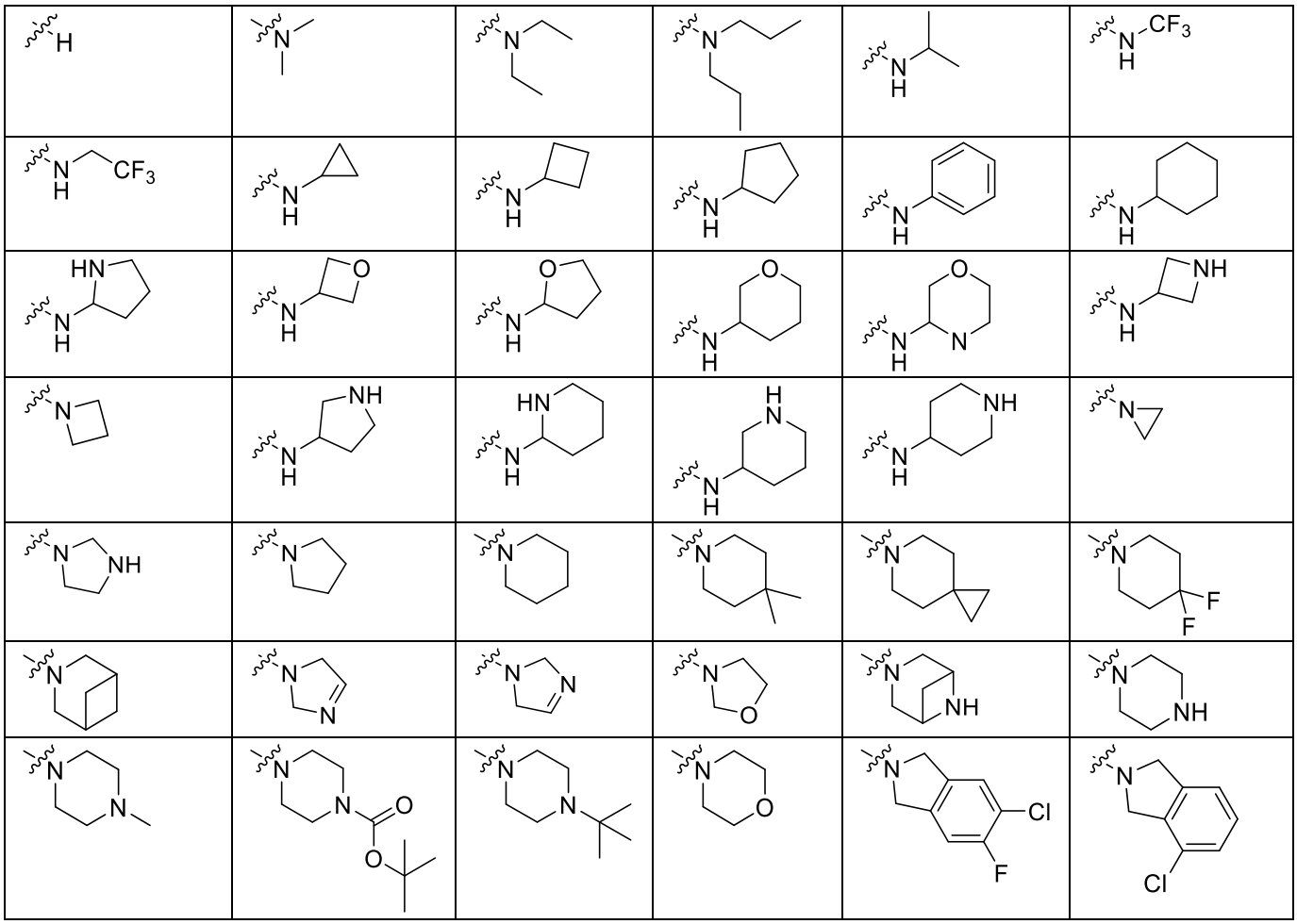
and

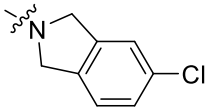
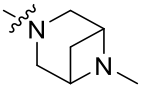
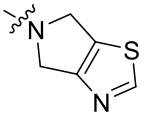
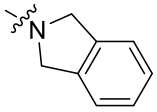
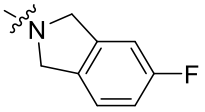
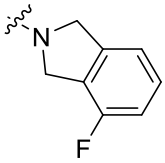
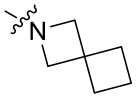
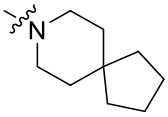
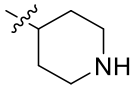
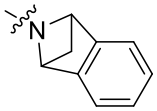
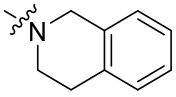
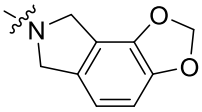
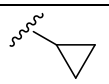
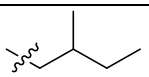
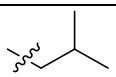
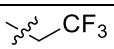
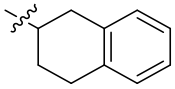
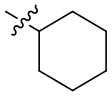
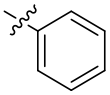
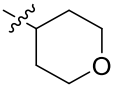
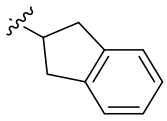
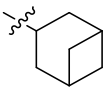
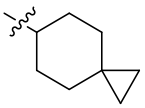
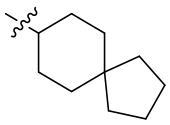
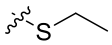
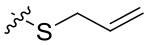
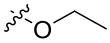
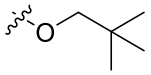
wherein each Y-ring or ring system is optionally substituted; or

(ii) Y is CR^{3c}, R^{3c} is absent or H, and each of R^{3a} and R^{3b} is independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3- to 6-membered heterocyclyl.

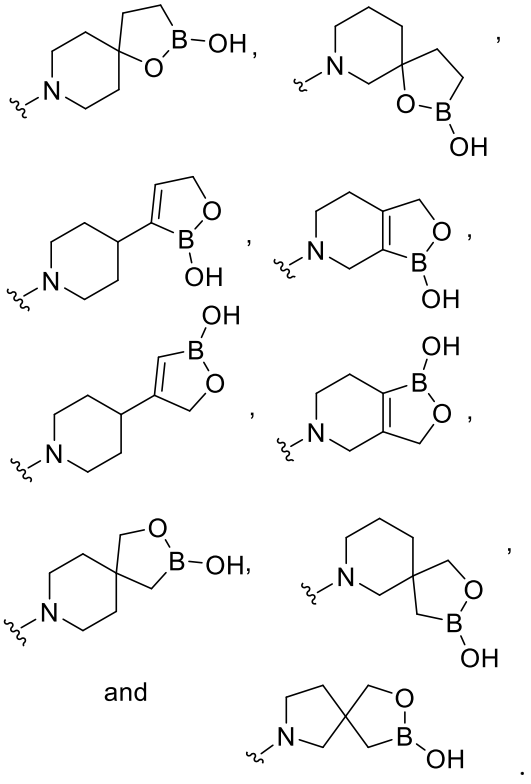
18. The compound of any one of claims 11 to 16, wherein:

(i) Y^T is selected from the group consisting of substituted or unsubstituted:

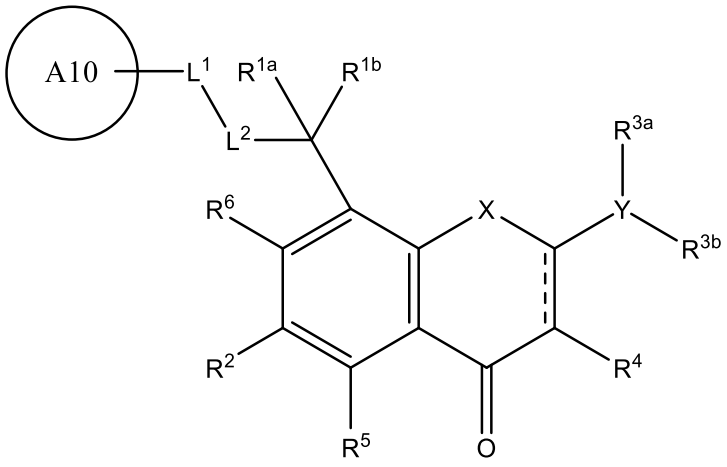


					
					
					
					
					
			and		; or

(ii) Y^T is selected from the group consisting of:



19. A compound of Formula (AX):



(AX)

or a tautomer, enantiomer, diastereomer, mixture, salt, hydrate, solvate, or deuterated form thereof, wherein

A10 is a 5- to 14-membered mono- or fused-ring system comprising one or more of cycloalkyl, heterocyclyl, aryl, and heteroaryl,

each of heterocyclyl or heteroaryl rings may contain one or more heteroatoms selected from N, O, S, and B;

A10 is optionally substituted with one or more R^{A10};

each R^{A10} independently is selected from halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, oxo, $(CH_2)_{0-6}CN$, $(CH_2)_{1-6}OH$, $(CH_2)_{0-6}O$-C_{1-6} alkyl, $(CH_2)_{0-6}O$-C_{2-6} alkenyl, $(CH_2)_{0-6}O$-C_{2-6} alkynyl, $(CH_2)_{0-6}C(O)H$, $(CH_2)_{0-6}C(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{1-6} alkynyl), $(CH_2)_{0-6}C(O)OH$, $(CH_2)_{0-6}C(O)O$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}NH_2$, $(CH_2)_{0-6}NH$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}N$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}C(O)NH_2$, $(CH_2)_{0-6}C(O)NH$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}C(O)N$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}NHC(O)H$, $(CH_2)_{0-6}NHC(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}N$(C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl)$C(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $B(OH)_2$, SO_2-halogen, and O-SO_2-halogen;

L^1 is selected from the group consisting of a direct bond, optionally substituted arylene, and optionally substituted heteroarylene;

L^2 is selected from the group consisting of O and NH;

each of R^{1a} and R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

or L^2-$C(R^{1a})(R^{1b})$ combines to form NHC(O), C(O)NH, $NHS(O)_2$, $S(O)_2NH$, or $C(NH)NH_2$;

X is $C(R^x)_2$, O, NR^x, or S;

each R^x independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

Y is H, CR^{3c}, N, O, or S;

a) when Y is H, each of R^{3a} and R^{3b} is absent;

b) when Y is N,

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an N atom, combines with R^{3a} and R^{3b} to form a heterocyclic or heteroaromatic mono ring or spiro or fused ring system, which may contain one or more additional heteroatoms selected from the group consisting of N, O, and S, and wherein the ring or ring system is optionally substituted;

c) when Y is CR^{3c}

R^{3c} is absent or is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl;

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an C atom, combines with R^{3a} and R^{3b} to form a cycloalkyl, aryl, heterocyclic, or heteroaromatic mono ring or spiro or fused ring system, where the heterocyclic and heteroaromatic rings contain one or more heteroatoms selected from the group consisting of N, O, and S, and wherein the Y-containing ring or ring system is optionally substituted; or

d) when Y is O or S, R^{3a} is absent and R^{3b} is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

R^2 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^4 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

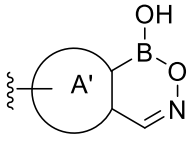
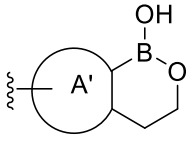
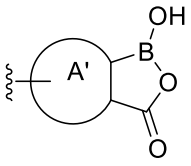
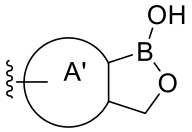
R^5 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^6 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl; and

each R^{AX} is independently H, halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{2-6} alkenoxy, C_{2-6} alkynoxy, C_{1-6} haloalkoxy, C_{2-6} haloalkenoxy, and C_{2-6} alkynoxy,

optionally, wherein the depicted dashed bond is a double bond.

20. The compound of claim 19, wherein:

A10 is  (I^{X1}),  (I^{X2}),  (I^{X3}), or  (I^{X4});

wherein each  represents the point of attachment to the depicted L^1;

each depicted A' independently is a cycloalkyl, heterocyclyl, aryl, or heteroaryl; and

each A10 is optionally substituted with one or more R^{A10} on either depicted ring;

each R^{A10} independently is selected from halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, oxo, $(CH_2)_{0-6}CN$, $(CH_2)_{1-6}OH$, $(CH_2)_{0-6}O$-C_{1-6} alkyl, $(CH_2)_{0-6}O$-C_{2-6} alkenyl, $(CH_2)_{0-6}O$-C_{2-6} alkynyl, $(CH_2)_{0-6}C(O)H$, $(CH_2)_{0-6}C(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}C(O)OH$, $(CH_2)_{0-6}C(O)O$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}NH_2$, $(CH_2)_{0-6}NH$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}N$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}C(O)NH_2$, $(CH_2)_{0-6}C(O)NH$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}C(O)N$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}NHC(O)H$, $(CH_2)_{0-6}NHC(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}N$(C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl)$C(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $B(OH)_2$, SO_2-halogen, and O-SO_2-halogen;

L^1 is selected from the group consisting of a direct bond, optionally substituted arylene, and optionally substituted heteroarylene;

L^2 is selected from the group consisting of O and NH;

each of R^{1a} and R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

or L^2-$C(R^{1a})(R^{1b})$ combines to form NHC(O), C(O)NH, $NHS(O)_2$, $S(O)_2NH$, or $C(NH)NH_2$;

X is $C(R^x)_2$, O, NR^x, or S;

each R^x independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

Y is H, CR^{3c}, N, O, or S;

a) when Y is H, each of R^{3a} and R^{3b} is absent;

b) when Y is N,

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as an N atom, combines with R^{3a} and R^{3b} to form a heterocyclic or heteroaromatic mono ring or spiro or fused ring system, which may contain one or more additional heteroatoms selected from the group consisting of N, O, and S, and wherein the ring or ring system is optionally substituted;

c) when Y is CR^{3c}

R^{3c} is absent or is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl;

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y, as a C atom, combines with R^{3a} and R^{3b} to form a cycloalkyl, aryl, heterocyclic, or heteroaromatic mono ring or spiro or fused ring system, wherein the heterocyclic and heteroaromatic rings contain one or more heteroatoms selected from the group consisting of N, O, and S, and wherein the Y-containing ring or ring system is optionally substituted; or

d) when Y is O or S, R^{3a} is absent and R^{3b} is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

R^2 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

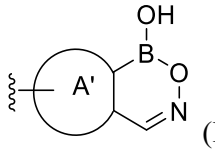
R^4 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

R^5 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl;

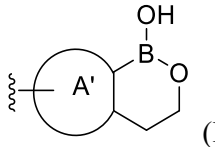
R^6 is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, $(CH_2)_{0-6}$-R^{AX}, $(CH_2)_{0-6}$-OR^{AX}, $(CH_2)_{0-6}$-$N(R^{AX})_2$, $(CH_2)_{0-6}$-$C(O)R^{AX}$, $(CH_2)_{0-6}$-$C(O)OR^{AX}$, $(CH_2)_{0-6}$-$C(O)N(R^{AX})_2$, $(CH_2)_{0-6}$-C_{3-10} cycloalkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heterocycle, and $(CH_2)_{0-6}$-heteroaryl; and

each R^{AX} is independently H, halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{2-6} alkenoxy, C_{2-6} alkynoxy, C_{1-6} haloalkoxy, C_{2-6} haloalkenoxy, and C_{2-6} alkynoxy.

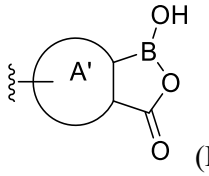
21. The compound of claim 20, wherein at least one of A10 or $Y(R^{3a})(R^{3b})$ has one or more of: (a) a B atom in the defined ring or ring sytem; (b) is substituted with a $B(OH)_2$; or carries a ring or ring system substituent that contains a B atom in the ring or ring system,
22. The compound of claim 20 or 21, wherein:
    (i) A10 is selected from the group consisting of:



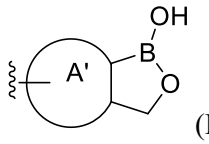
(I^{X1})



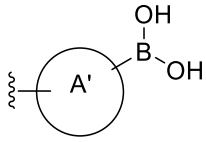
(I^{X2})



(I^{X3});



(I^{X4});



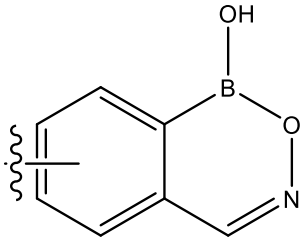
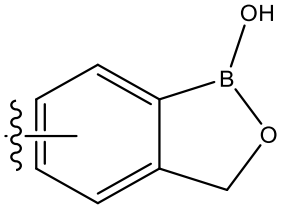
(I^{X5});

where each  represents the point of attachment to the depicted L^1;

each depicted A' independently is a cycloalkyl, heterocyclyl, aryl, or heteroaryl; and

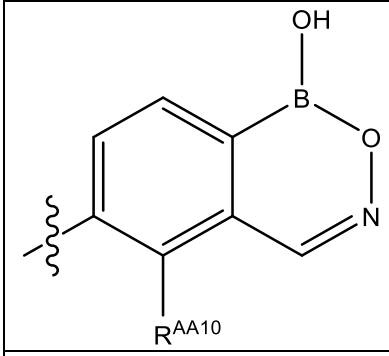
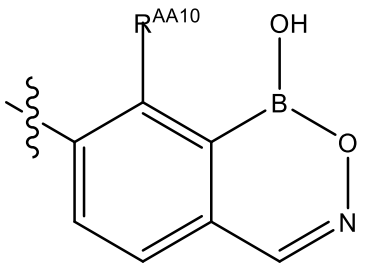
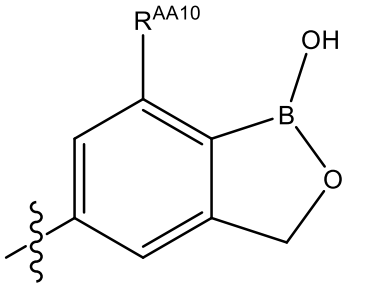
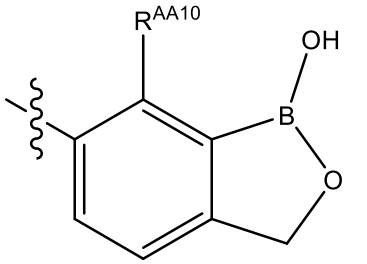
each A10 is optionally substituted with one or more R^{A10} on either depicted ring; or

(ii) A10 is:

	or	

each optionally substituted with one or more R^{A10} on either depicted ring; or

(iii) A10 is selected from the group consisting of:

	,		,
	, and		; and

each R^{AA10} is independently selected from the group consisting of: halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_3-C_6 cycloalkyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, OH, O-C_3-C_6 cycloalkyl, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, O-C_{2-6} alkynyl, and CN or a deuterated form thereof; and

each A10 may be further substituted with one or more R^{A10}.

optionally, wherein R^{AA10} is F, Cl, CH_3, OCH_3, or CD_3; or

(iv) A10 is not further substituted; or

(v) A10 is further substituted with one or more R^{A10}, each independently selected from the group consisting of: halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_3-C_6 cycloalkyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, OH, O-C_{1-6} alkyl, O-C_{2-6} alkenyl, and O-C_{2-6} alkynyl.

23. The compound of any one of claims 20 to 22, wherein:

(i) L^1 is:

substituted or unsubstituted arylene; or

substituted or unsubstituted heteroarylene; or

(ii) L^1 is

substituted or unsubstituted phenylene; or

substituted or unsubstituted 5- to 10-membered heteroarylene having one or more heteroatoms selected from N, O, and S; or

(iii) L^1 is

substituted or unsubstituted phenylene; or

substituted or unsubstituted pyridinylene; or

(iv) L^1 is substituted with one or more halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_2-C_3 alkenyl, C_2-C_3 haloalkenyl, C_2-C_3 alkynyl, C_2-C_3 haloalkynyl, OH, O-(C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl), NH_2, NH(C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl), N(C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl)$_2$, C_3 cycloalkyl, and C_3 halocycloalkyl,

optionally, wherein L^1 is substituted with one or more halogen or C_1-C_3 alkyl.

24. The compound of any one of claims 20 to 23, wherein X is oxygen.

25. The compound of any one of claims 20 to 24 wherein:

(i) Y is N or CR^{3c}.

(ii) Y is CR^{3c};

R^{3c} is H and each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

(iii) Y combines with R^{3a} and R^{3b} to form:

a) cycloalkyl substituted with $B(OH)_2$;

b) aryl substituted with $B(OH)_2$;

c) heterocyclyl, either

i) containing a B atom in the ring or ring system,

ii) substituted with $B(OH)_2$, or

iii) substituted with an optionally substituted 4- to 6-membered ring containing a B atom, one or more additional heteroatoms selected from O, N, or S, and one or more degrees of unsaturation; or

d) heteroaryl, either

iv) containing a B atom in the ring or ring system, or

v) substituted with $B(OH)_2$, or

vi) substituted with an optionally substituted 4- to 6-membered ring containing a B atom, one or more additional heteroatoms selected from O, N, or S, and one or more degrees of unsaturation; and

wherein each Y-ring or ring system is optionally substituted,

optionally, wherein Y is nitrogen.

26. The compound of any one of claims 20 to 25, wherein:

(i) R^{1a} is CH_3;

(ii) R^{1b} is H;

(iii) each of R^2, R^4, R^5, and R^6 independently is H, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_3-C_6 cycloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, or C_{1-6} haloalkyl;

(iv) R^2 is CH_3;

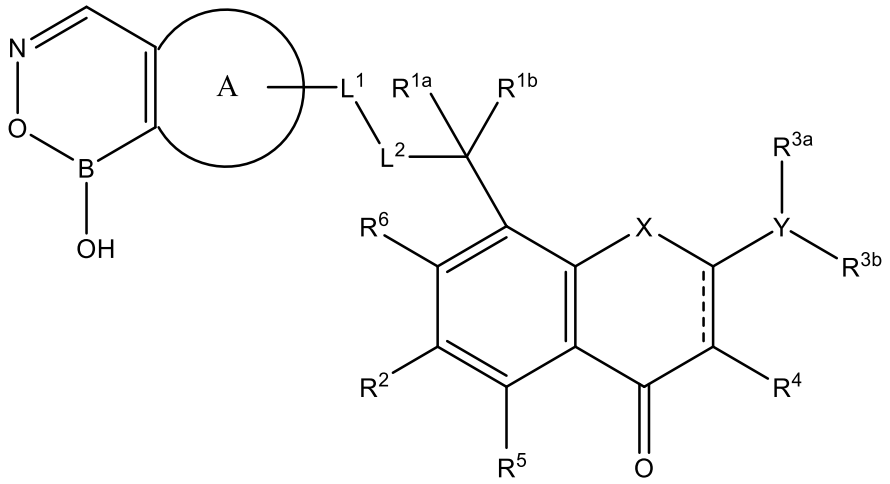
(v) R^4 is H, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl;

(vi) R^4 is H or CH_3;

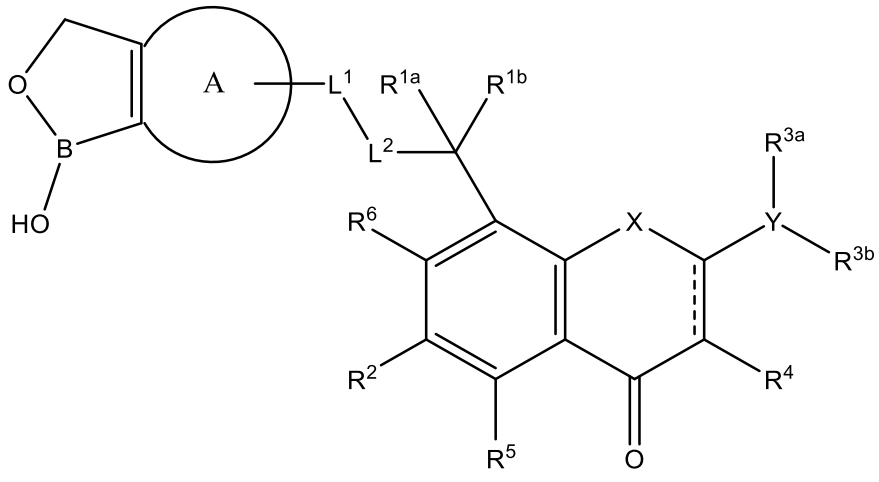
(vii) R^5 is H;

(viii) R^6 is H, or any combination of (i)-(viii).

27. A compound of Formula Ia or Ib:



(Ia),



(Ib)

or a tautomer, enantiomer, diastereomer, mixture, salt, hydrate, solvate, or deuterated form thereof,

A is an aryl or heteroaryl ring, and together with the depicted boron ring, creates a fused ring system that includes the depicted boron-containing ring, and which system is optionally substituted with one or more R^A;

each R^A independently is selected from halogen, OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, $(CH_2)_{0-6}CN$, $(CH_2)_{1-6}OH$, $(CH_2)_{0-6}O$-C_{1-6} alkyl, $(CH_2)_{0-6}O$-C_{2-6} alkenyl, $(CH_2)_{0-6}O$-C_{2-6} alkynyl, $(CH_2)_{0-6}C(O)H$, $(CH_2)_{0-6}C(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{1-6} alkynyl), $(CH_2)_{0-6}C(O)OH$, $(CH_2)_{0-6}C(O)O$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}NH_2$, $(CH_2)_{0-6}NH$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}N$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}C(O)NH_2$, $(CH_2)_{0-6}C(O)NH$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), $(CH_2)_{0-6}C(O)N$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl)$_2$, $(CH_2)_{0-6}NHC(O)H$, $(CH_2)_{0-6}NHC(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl), and $(CH_2)_{0-6}N$(C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl)$C(O)$(C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl) or a deuterated form thereof;

L^1 is selected from the group consisting of a direct bond, optionally substituted arylene, and optionally substituted heteroarylene;

L^2 is selected from the group consisting of O and NH;

each of R^{1a} and R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

X is $C(R^x)_2$, O, NR^x, or S;

each R^x independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

each of R^2, R^4, R^5, and R^6 independently is H, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_3-C_6 cycloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, or C_{1-6} haloalkyl; and

Y is N or CR^{3a}; and

a) when Y is N,

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

R^{3a} and R^{3b} combine with the N atom to form a heterocyclic or heteroaromatic mono ring or spiro or fused ring system, which may contain one or more additional heteroatoms selected from the group consisting of N, O, and S, and wherein the ring or ring system is optionally substituted;

b) when Y is CR^{3c},

R^{3c} is absent or is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl;

each of R^{3a} and R^{3b} independently is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

R^{3a} and R^{3b} combine with the C atom to form a cycloalkyl, aryl, heterocyclic, or heteroaromatic mono ring or spiro or fused ring system, where the heterocyclic and heteroaromatic rings contain one or more heteroatoms selected from the group consisting of N, O, and S, and wherein the Y-containing ring or ring system is optionally substituted,

optionally, wherein the depicted dashed bond is a double bond.

28. The compound of claim 27, wherein A is a phenyl ring.

29. The compound of claim 27 or 28, wherein:

(i) R^A is absent; or

(ii) the fused ring system is substituted with one or two R^A; or

(iii) each R^A is independently selected from the group consisting of C_{1-6} alkyl, O-C_{1-6} alkyl, C_{1-6} haloalkyl, and halogen, or a deuterated form thereof; or

(iv) each R^A is independently selected from the group consisting of halogen, CD_3, CH_3, OCH_3,and CF_3.

30. The compound of any one of claims 27 to 29, wherein:

(i) L^1 is optionally substituted phenylene,

optionally, wherein

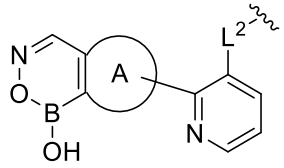
L^1 is phenylene substituted with one or more halogen or C_{1-6}alkyl; or

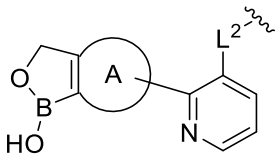
(ii) L^1 is optionally substituted heteroarylene; or

(iii) L^1 is optionally substituted pyridinylene,

optionally, wherein L^1 is pyridinylene substituted with one or more halogen or C_{1-6}alkyl; or

optionally, wherein the pyridinylene is attached as:



or


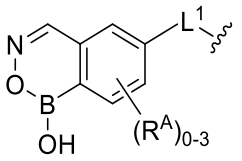
,

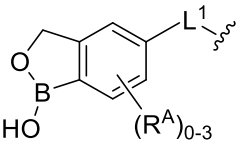
in either instance the depicted fused ring is optionally substituted with one or more R^A; or,

(iv) L^1 is substituted with one or two halogen

31. The compound of any one of claims 25 to 28, wherein:

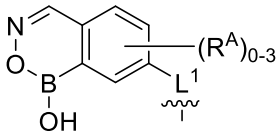
(i) the depicted L^1 moiety is substituted *para* to the depicted B atom in the fused ring system:

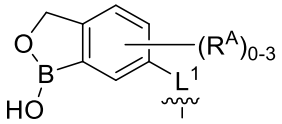


or


; or

(ii) the depicted L^1 moiety is substituted *meta* to the depicted B atom in the fused ring system.



or


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32. The compound of any one of claims 27 to 31, wherein L^2 is NH.
33. The compound of any one of claims 27 to 32, wherein:

R^{1a} is H; and

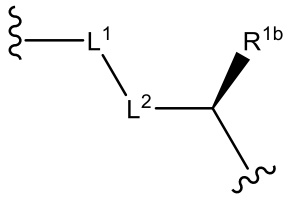
R^{1b} independently is selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy,

optionally, wherein

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

optionally, wherein R^{1b} is methyl.

34. The compound of claim 33, wherein the chiral center is in the R configuration, as depicted by:



35. The compound of any one of claims 27 to 34, wherein X is O.
36. The compound of any one of claims 27 to 35, wherein:

(i) Y is CH and each of R^{3a} and R^{3b} is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, C_{3-6} cycloalkyl, and 3 to 6 membered heterocyclyl; or

Y is CH and combines with R^{3a} and R^{3b} to form a cycloalkyl or heterocyclic mono ring system comprising one heteroatom selected from N and O; or

(ii) Y is CH and each of R^{3a} and R^{3b} is C_{1-3}alkyl,

optionally, wherein each of R^{3a} and R^{3b} is CH_3.

37. The compound of any one of claims 27 to 36, wherein:

(i) R^2 is CH_3;

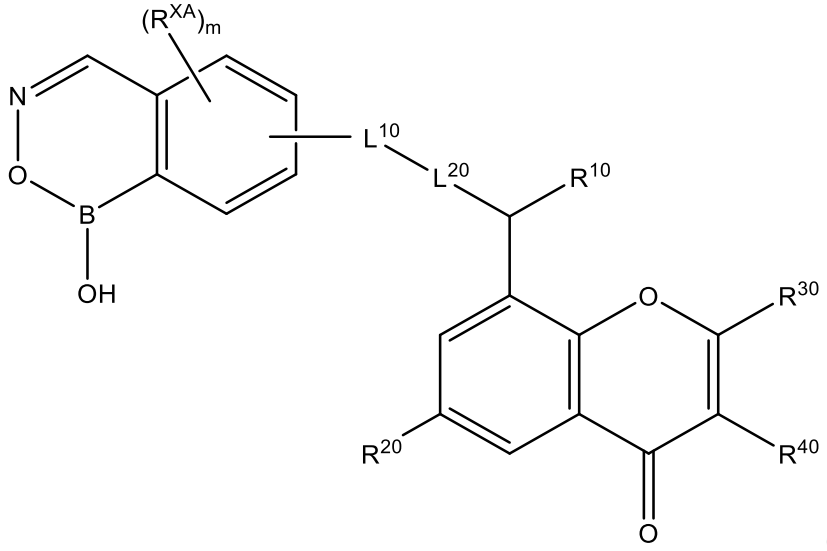
(ii) R^4 is H, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, optionally, wherein

R^4 is H or CH_3;

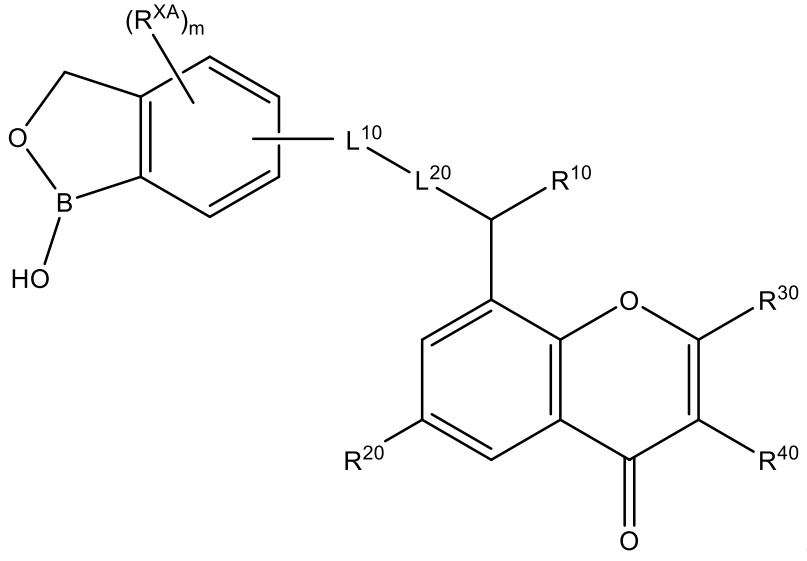
(iii) R^5 is H; or

(iv) R^6 is H, or any combination of (i)-(iv).

38. A compound of Formula Xa or Xb:



(Xa),



(Xb),

or a tautomer, enantiomer, diastereomer, mixture, salt, hydrate, solvate, or deuterated form thereof, wherein

each m is independently 0, 1, 2, 3, 4, or 5;

each R^{XA} independently is selected from halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, and C_{3-6} cycloalkyl, or a deuterated form thereof;

L^{10} is selected from the group consisting of a direct bond, optionally substituted arylene, or optionally susbstituted heteroarylene;

L^{20} is selected from the group consisting of O and NH;

R^{10} is selected from the group consisting of H and C_{1-6} alkyl;

R^{20} is selected from the group consisting of H, halogen, C_1-C_6 haloalkyl, and C_{1-6} alkyl;

R^{30} is selected from the group consisting of H or optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, N(C_1-C_6 alkyl), 6-membered aryl, 5- or 6-membered heteroaryl, or 3- to 10-membered heterocyclyl; and

R^{40} is selected from the group consisting of H and C_{1-6} alkyl.

39. The compound of claim 38, wherein:

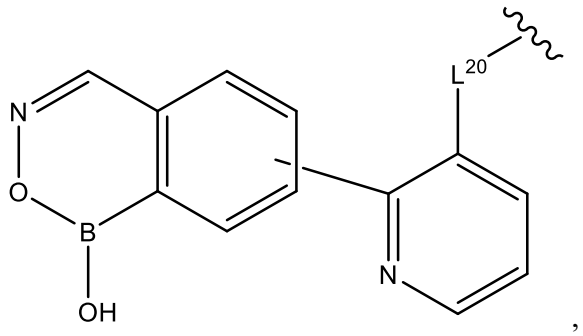
(i) L^{10} is an optionally substituted phenylene, optionally wherein

L^{10} is phenylene substituted with one or more halogen; or

(ii) L^{10} is optionally substituted heteroarylene, optionally

wherein L^{10} is optionally substituted pyridinylene; or

(iii) L^{10} is pyridinylene substituted with one or more halogen, optionally, as optionally substituted:



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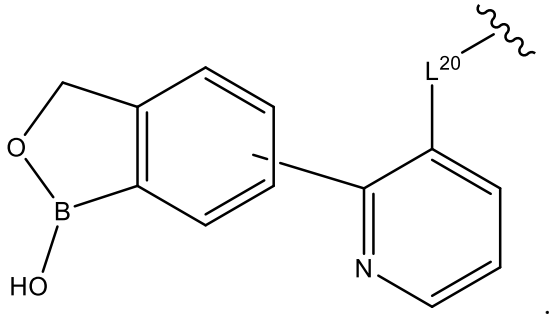
or



.

40. The compound of any one of claims 38 to 39, wherein:

(i) L^{20} is NH;

(ii) R^{10} is C_{1-6} alkyl,

optionally wherein R^{10} is CH_3;

(iii) R^{20} is C_{1-6} alkyl, optionally

wherein R^{20} is CH_3;

(iv) R^{40} is C_{1-6} alkyl, optionally

wherein R^{40} is CH_3;

(v) R^{30} is optionally substituted aryl, heteroaryl, or heterocyclyl, optionally

wherein the optionally substituted heterocyclyl comprises 3- to 6- ring atoms, with 1 or 2 of the ring atoms being independently selected from the group consisting of nitrogen and oxygen,

optionally, wherein the optionally substituted heterocyclyl is optionally substituted piperidinyl; or

optionally, wherein the optionally substituted piperidinyl is piperidinyl substituted with gem di-methyl; or

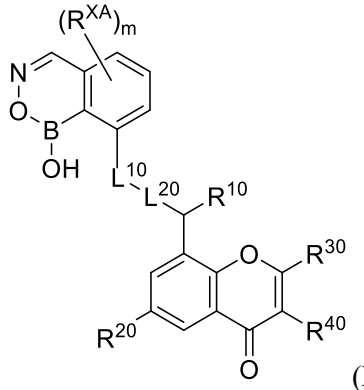
optionally, wherein the optionally substituted heterocyclyl is optionally substituted morpholinyl;

optionally, wherein the optionally substituted heterocyclyl comprises three to six ring atoms, wherein one atom is oxygen; or

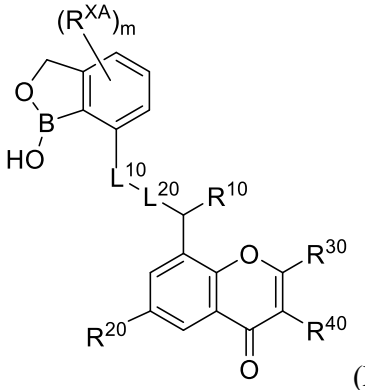
R^{30} is optionally substituted: C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl,

or any combination of (i)-(v).

41. The compound of any one of claims 38 to 40, wherein the compound is of formula XI:

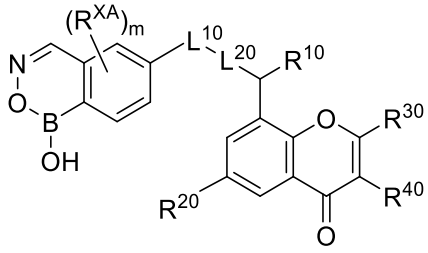


(XIa) or

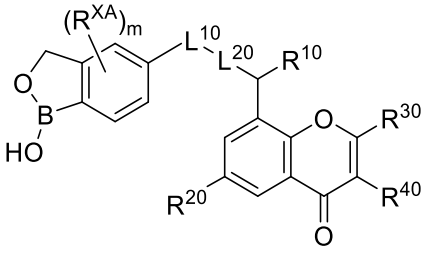


(XIb); or

the compound is of formula XII:

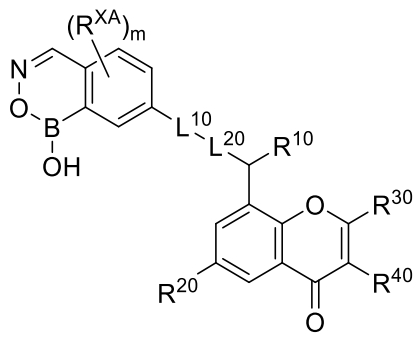


(XIIa) or

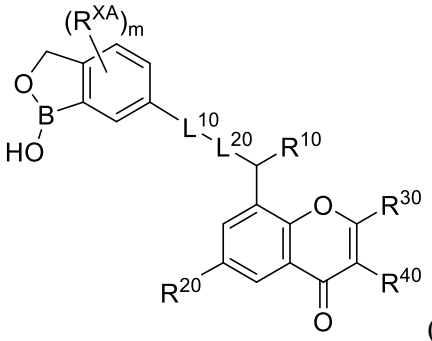


(XIIb); or

the compound is of formula XIII:

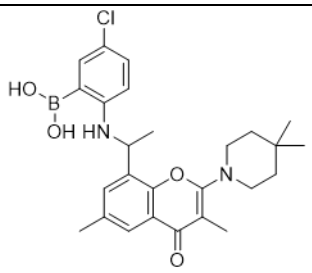
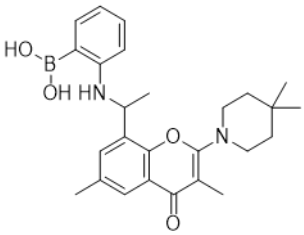
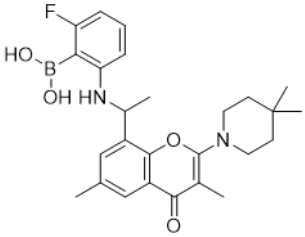
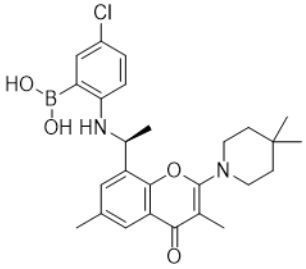
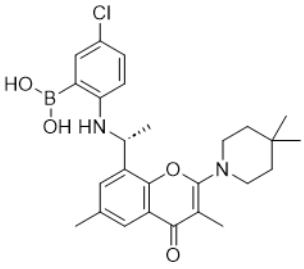
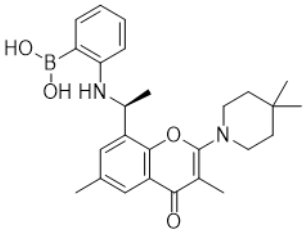
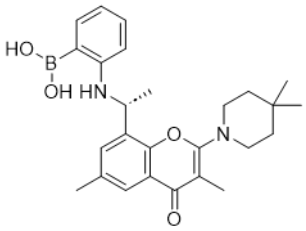
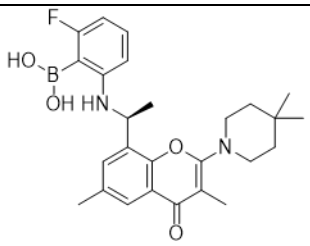
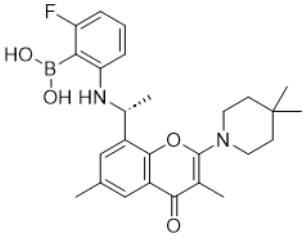
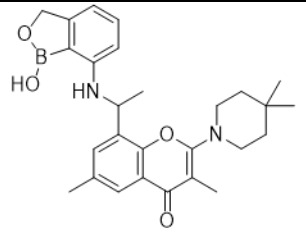
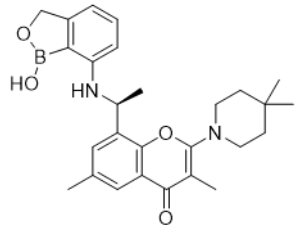
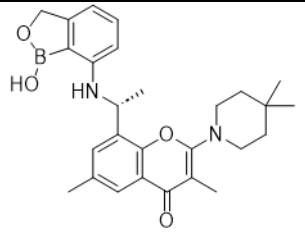
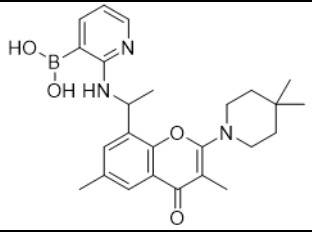
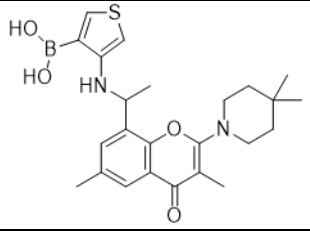
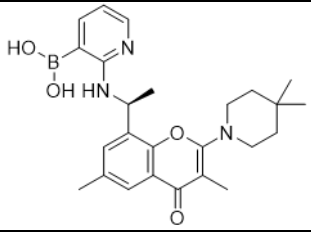


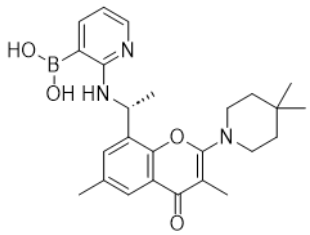
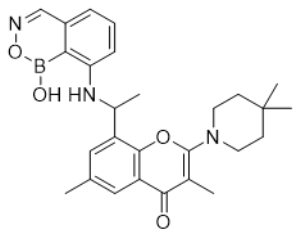
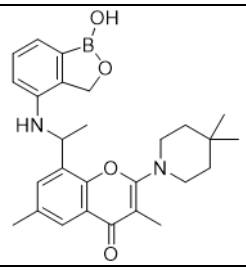
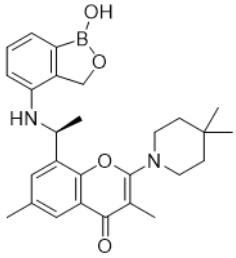
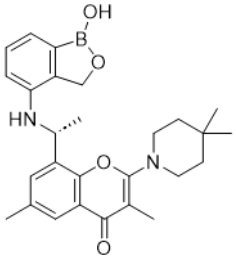
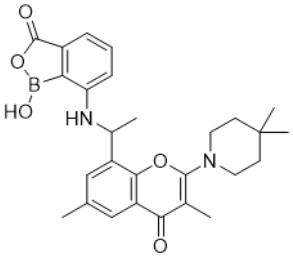
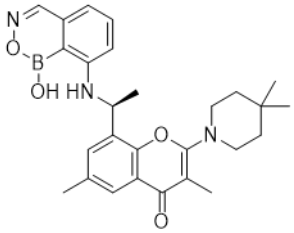
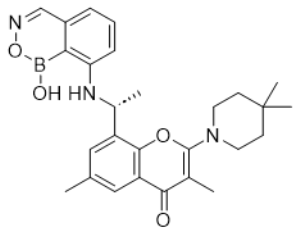
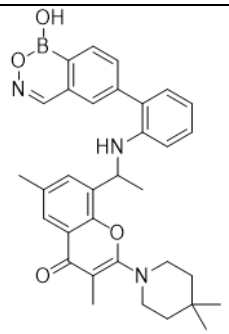
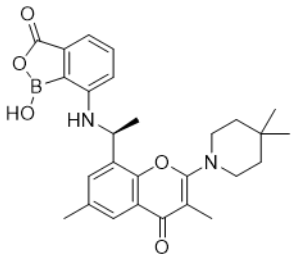
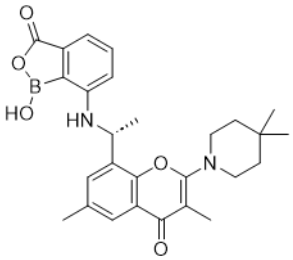
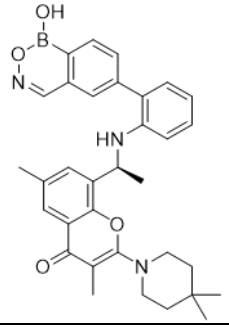
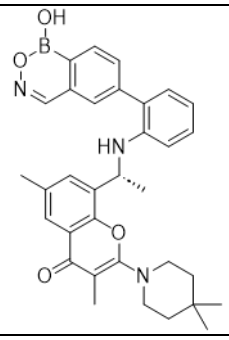
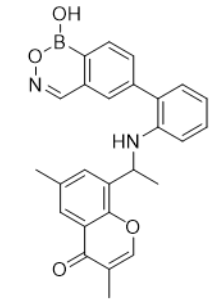
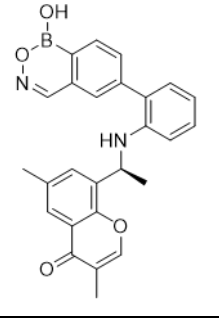
(XIIIa) or

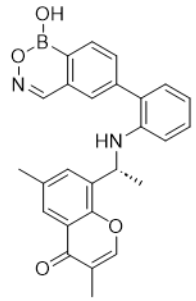
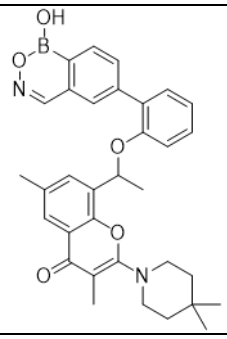
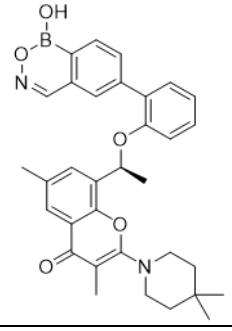
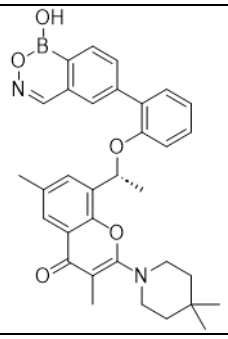
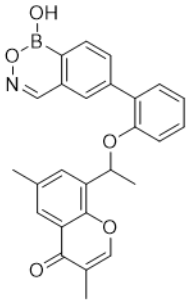
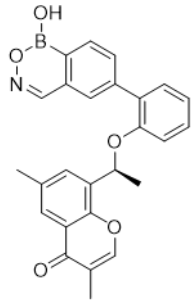
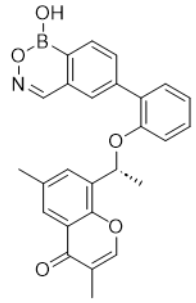
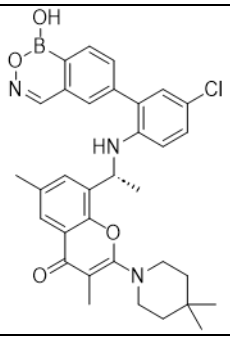
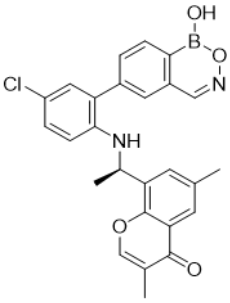
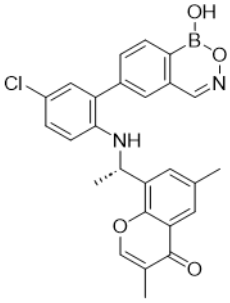
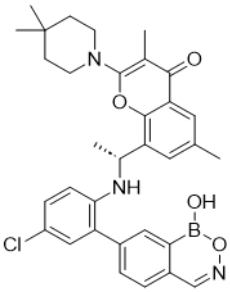
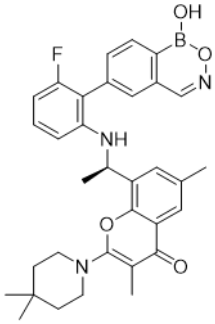
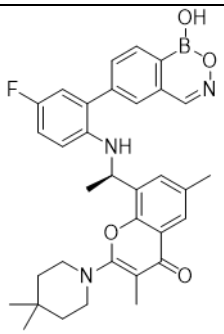
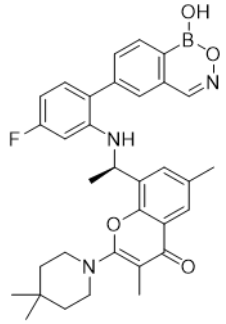


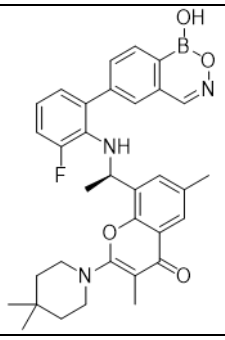
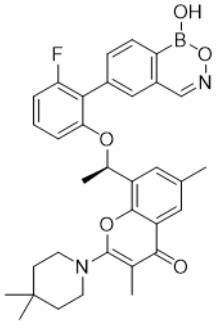
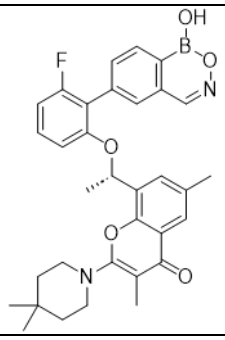
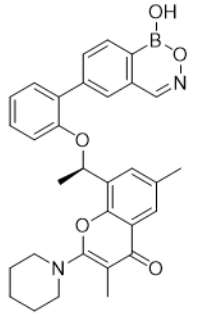
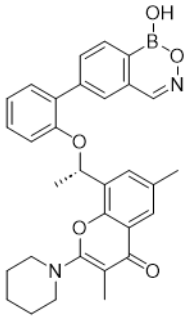
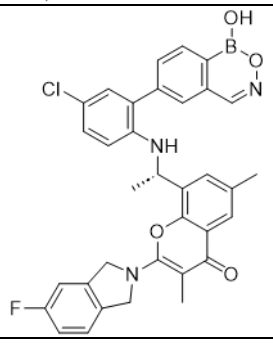
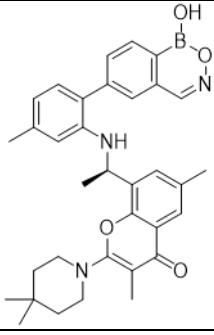
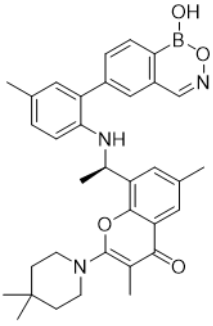
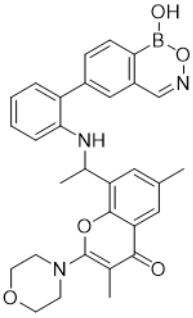
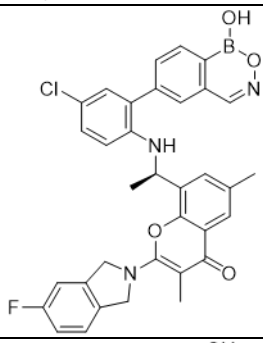
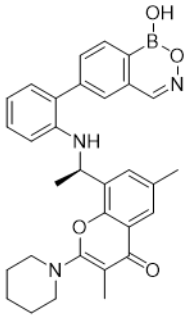
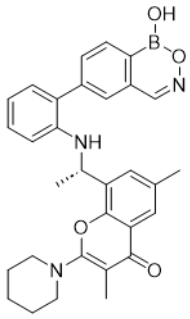
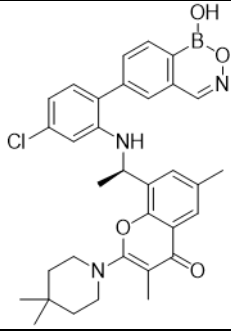
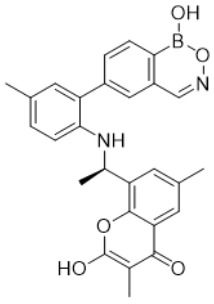
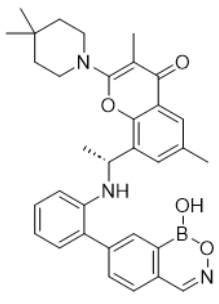
(XIIIb).

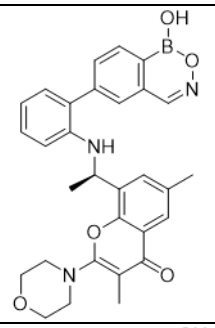
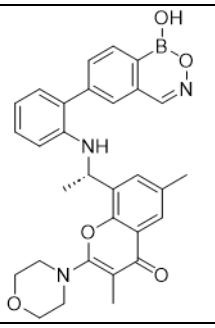
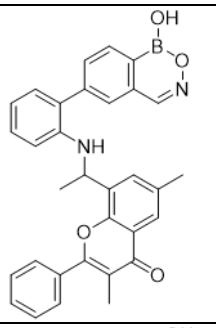
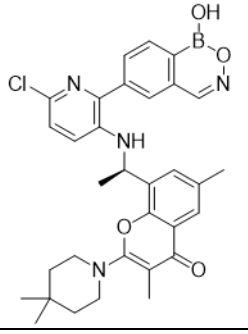
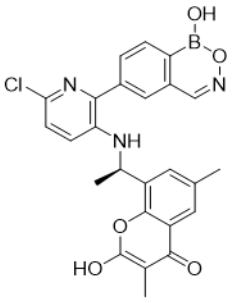
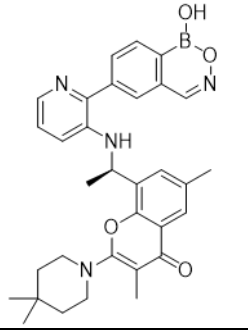
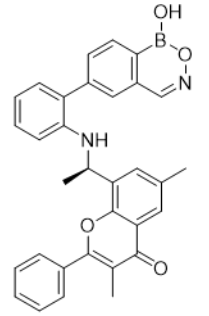
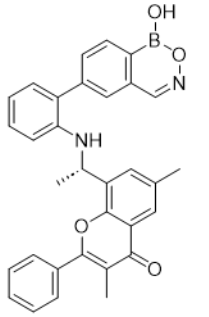
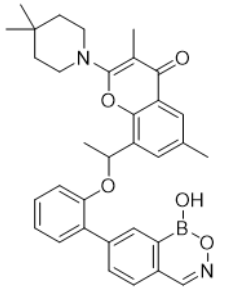
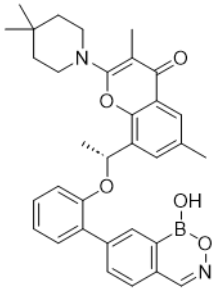
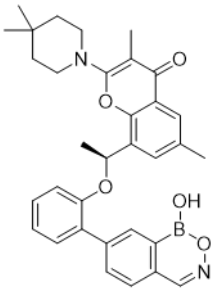
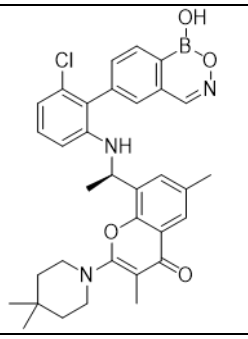
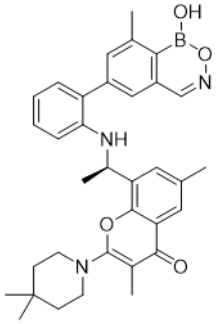
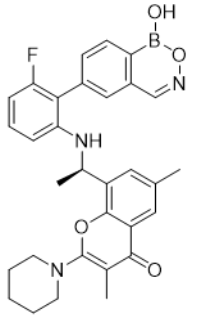
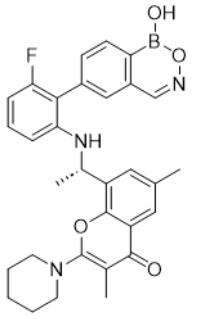
42. A compound selected from the group consisting of:

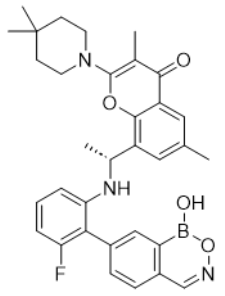
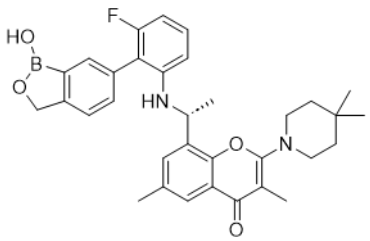
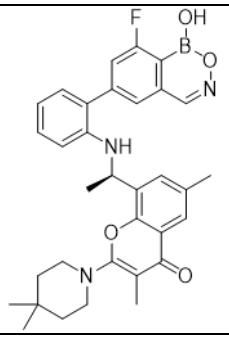
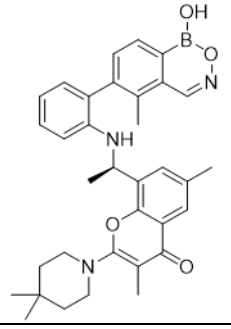
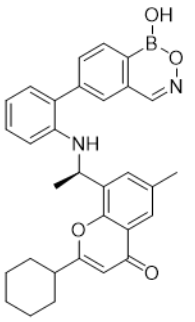
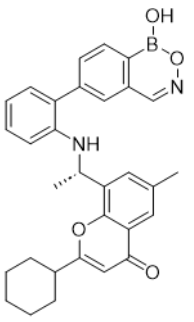
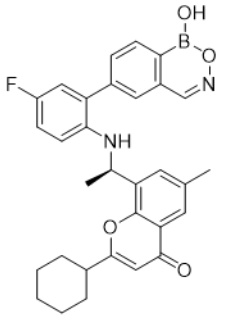
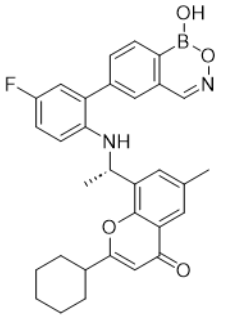
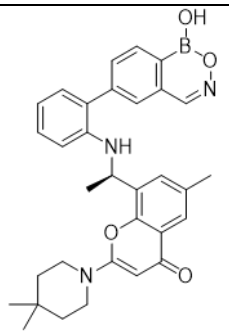
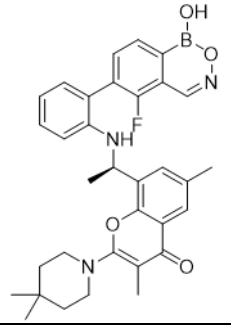
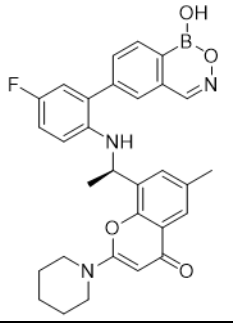
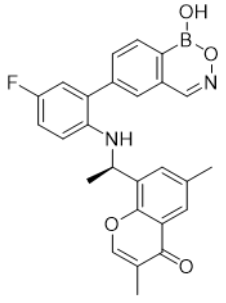
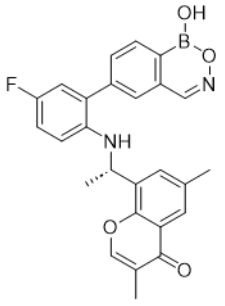
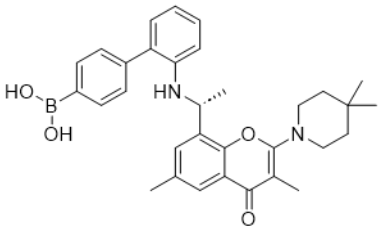
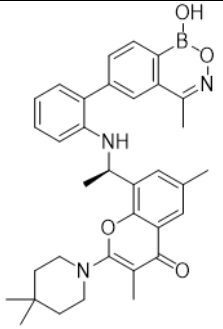
		
		
		
		
		

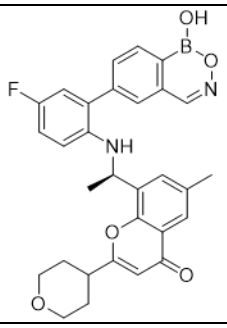
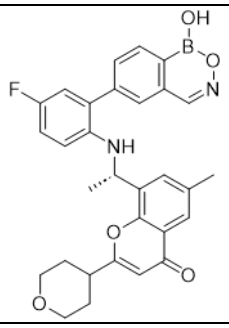
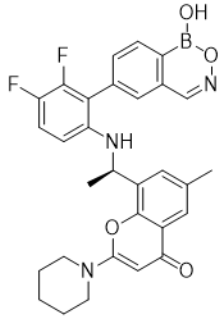
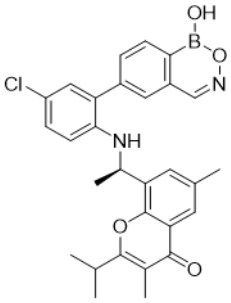
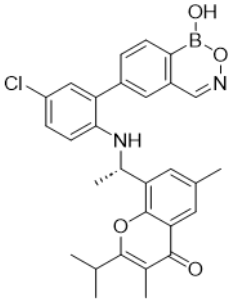
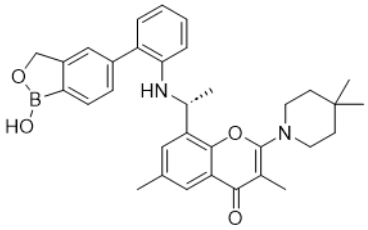
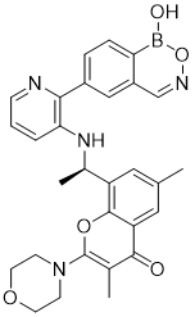
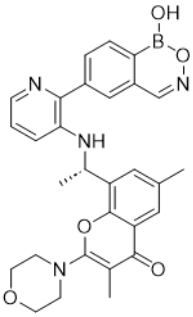
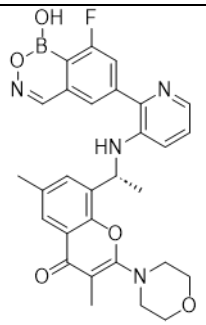
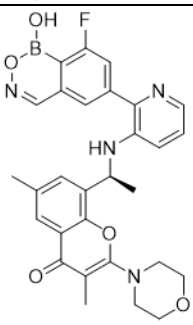
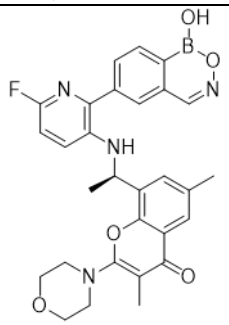
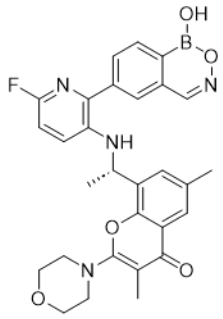
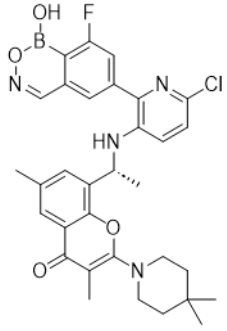
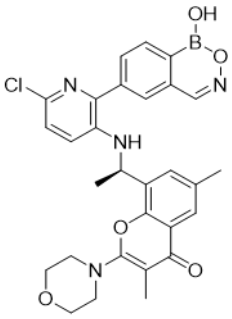
		
		
		
		
		

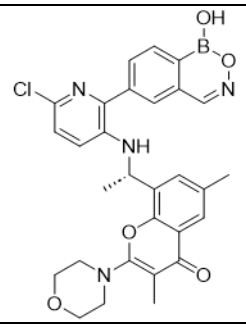
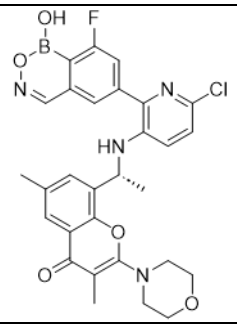
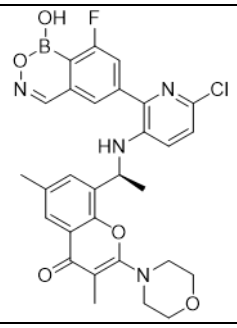
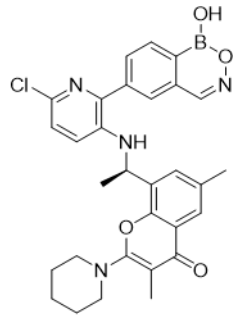
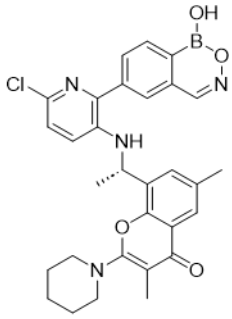
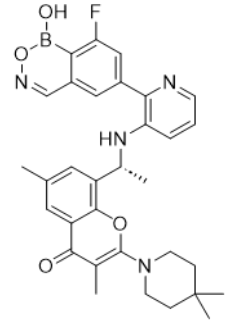
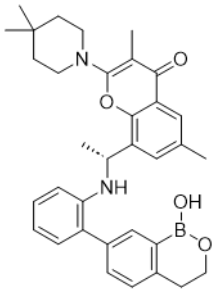
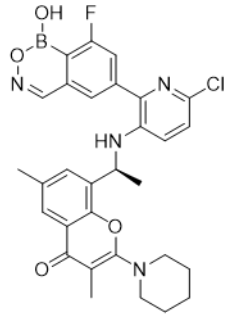
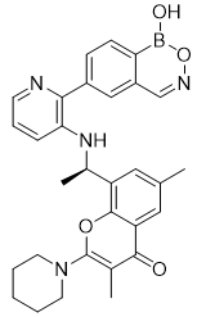
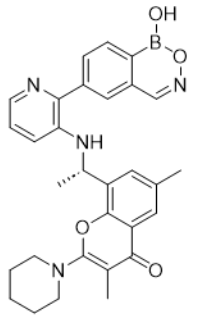
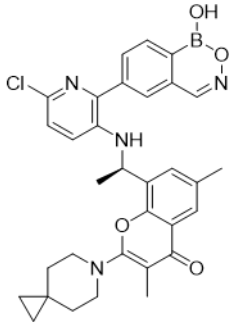
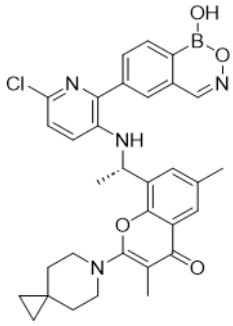
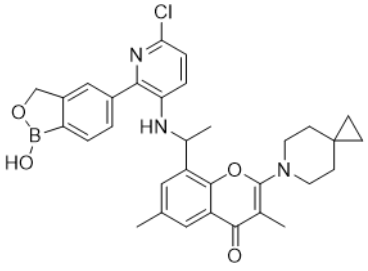
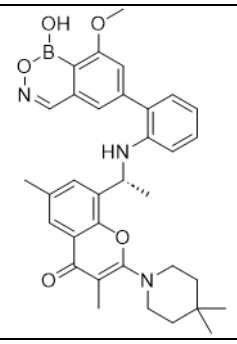
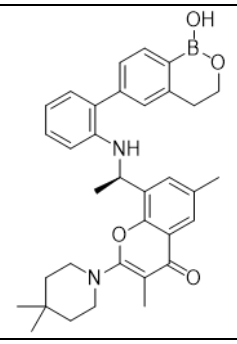
		
		
		
		
		

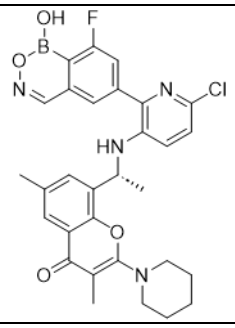
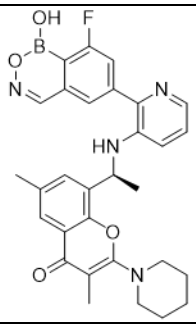
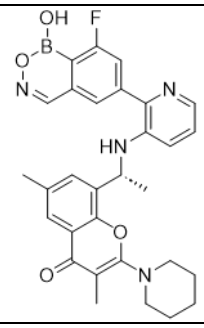
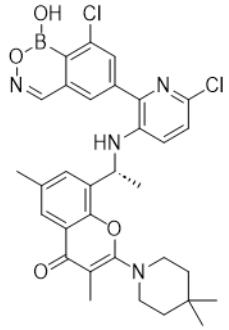
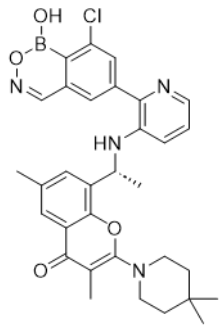
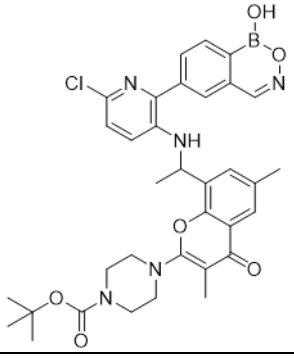
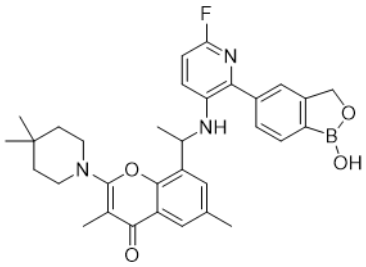
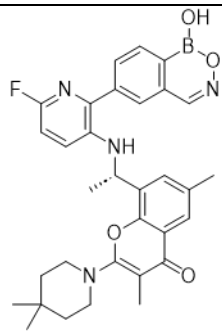
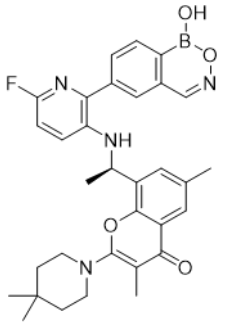
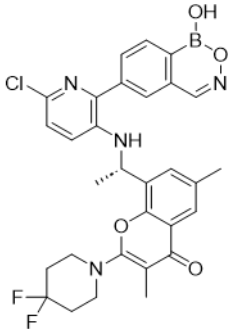
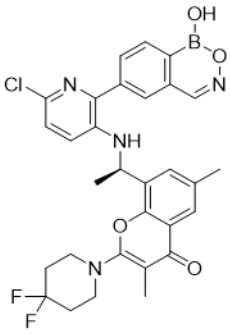
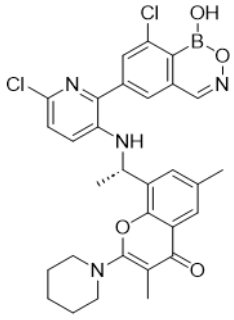
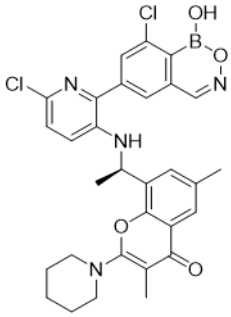
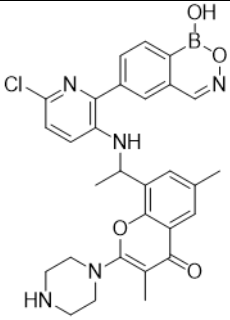
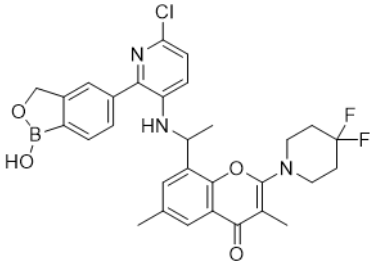
		
		
		
		
		

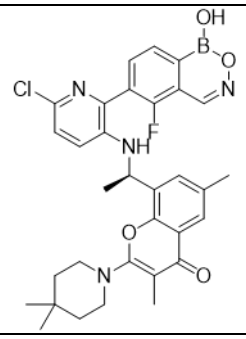
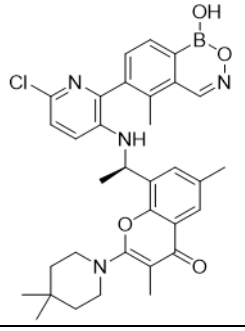
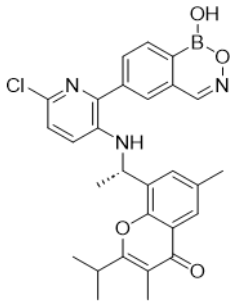
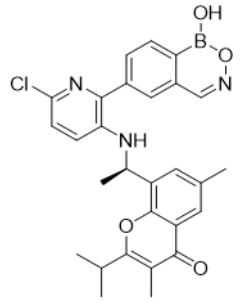
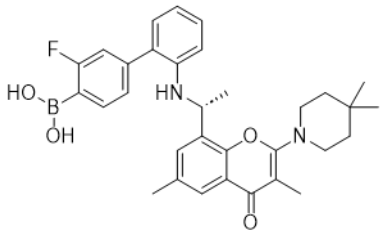
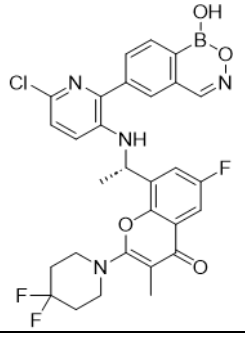
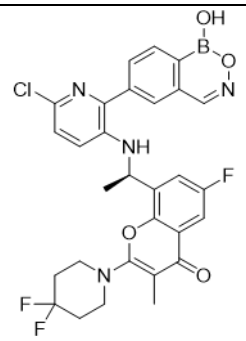
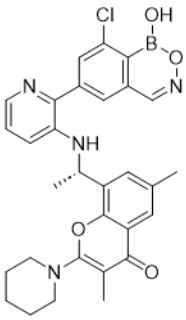
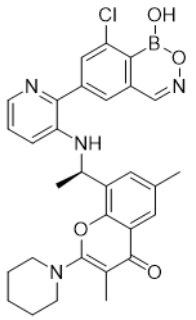
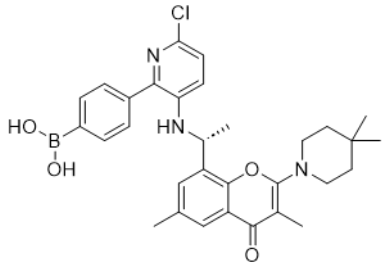
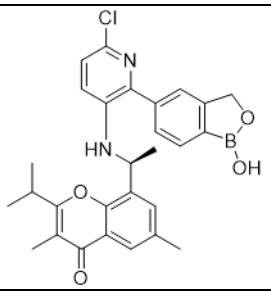
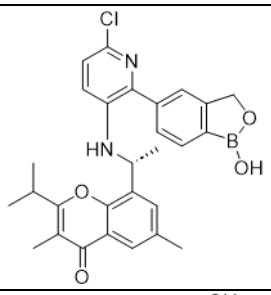
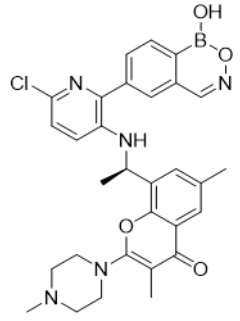
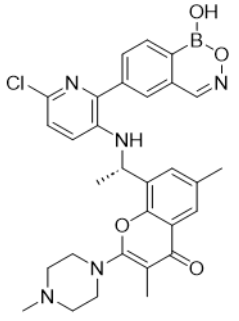
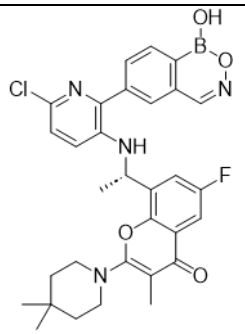
		
		
		
		
		

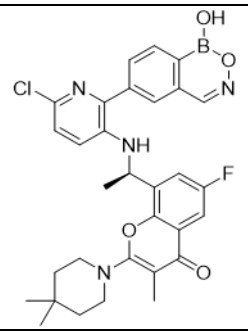
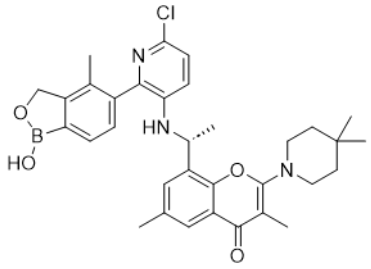
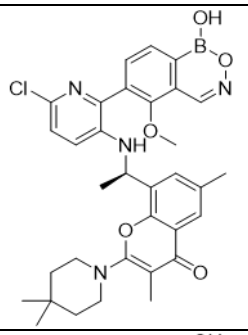
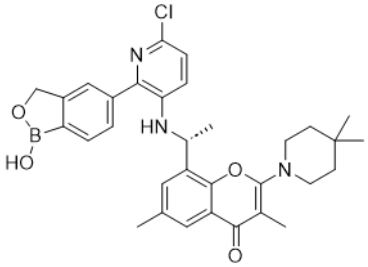
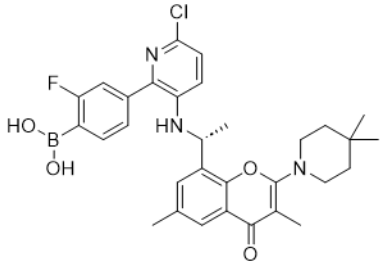
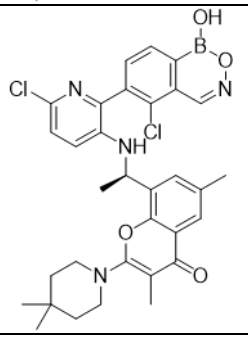
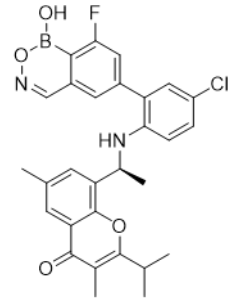
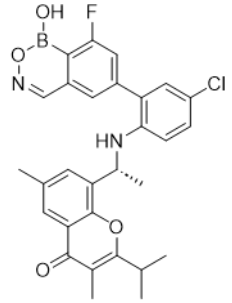
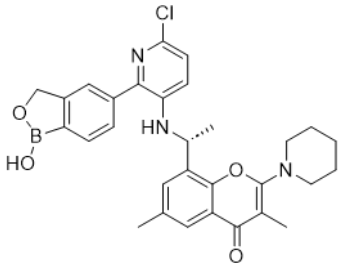
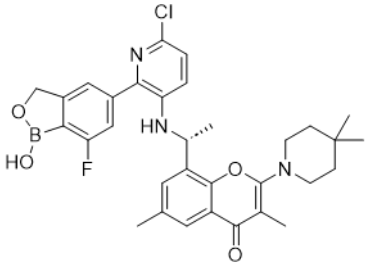
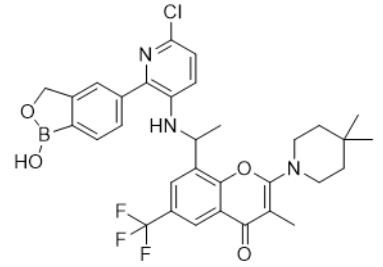
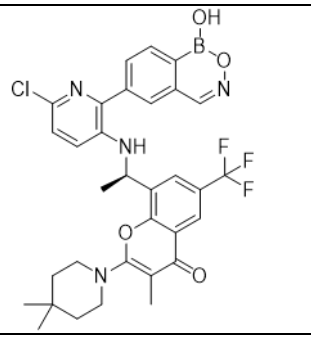
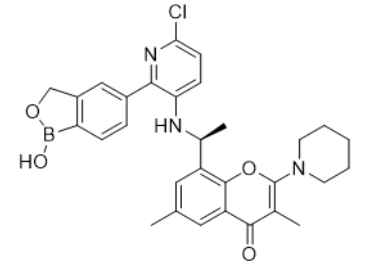
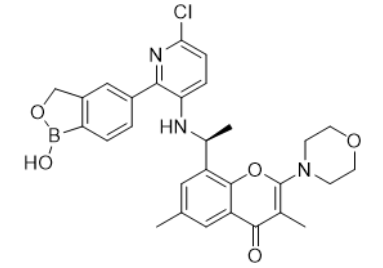
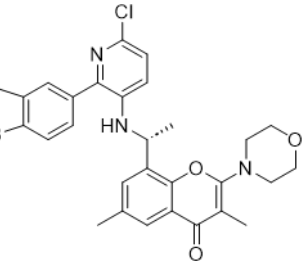
		
		
		
		
		

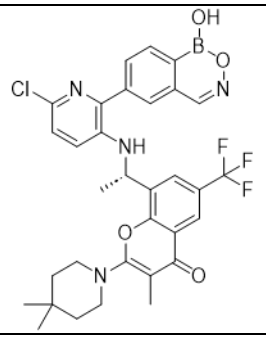
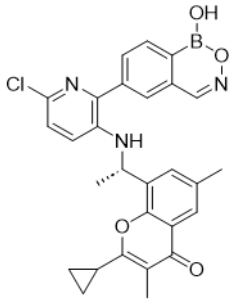
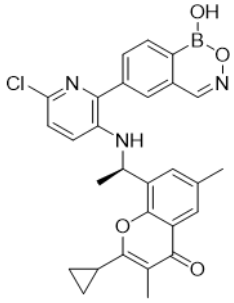
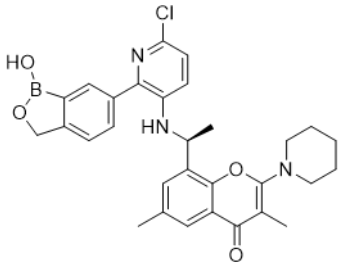
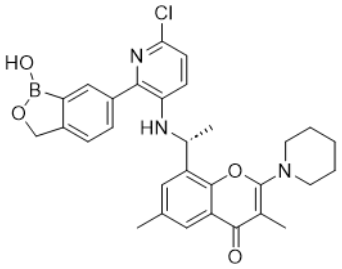
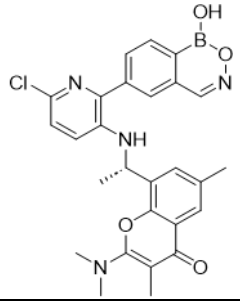
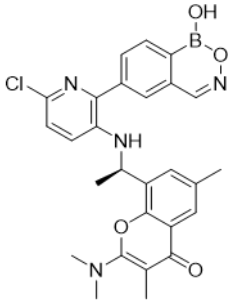
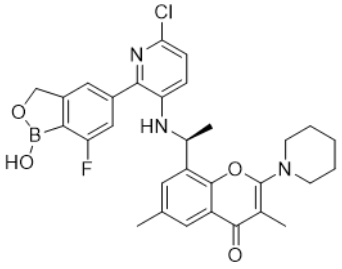
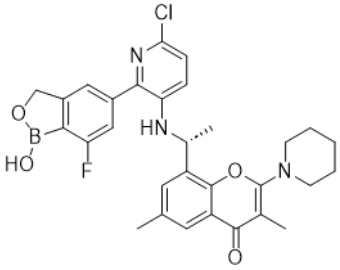
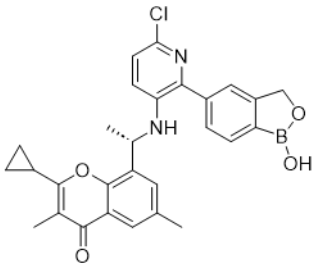
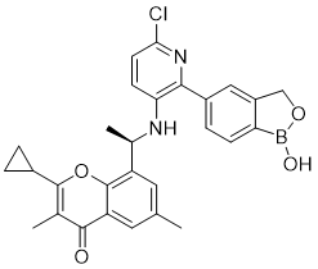
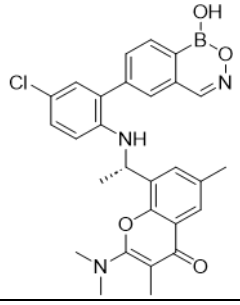
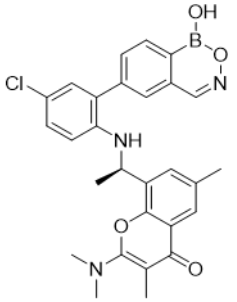
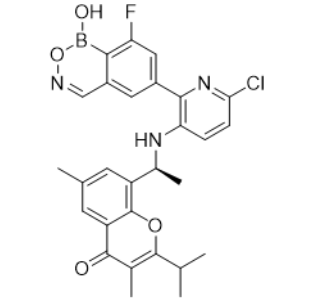
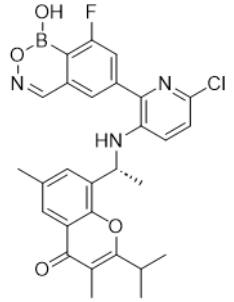
		
		
		
		
		

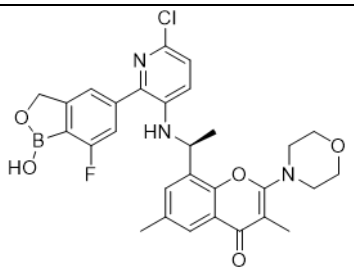
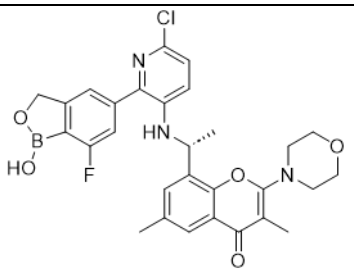
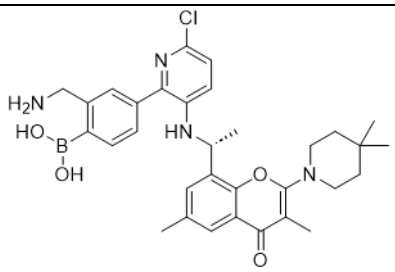
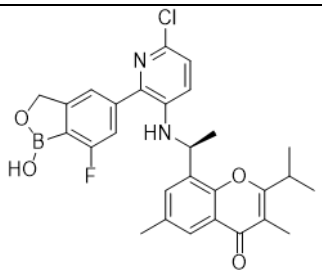
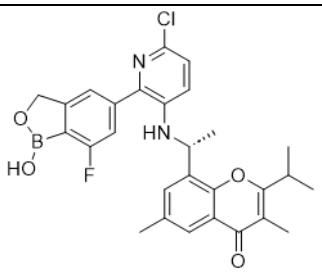
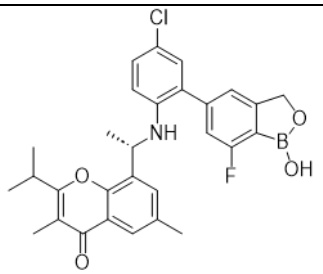
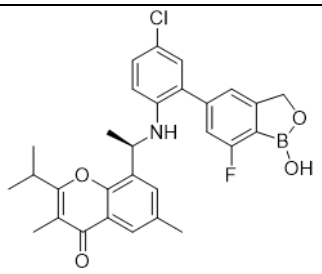
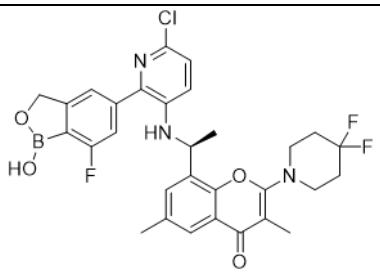
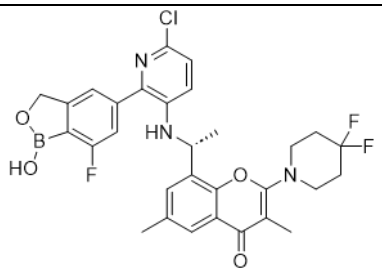
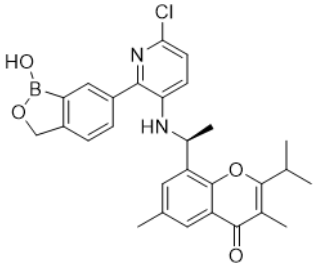
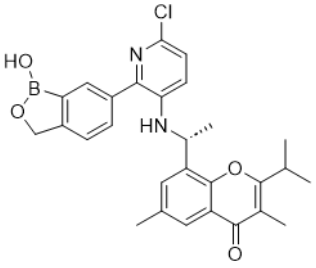
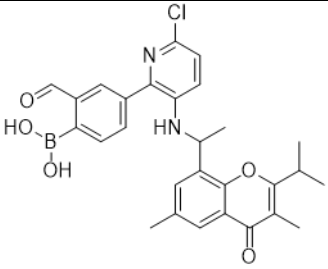
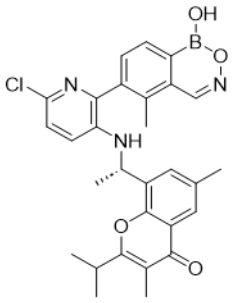
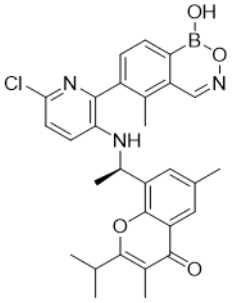
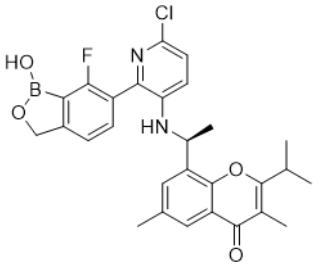
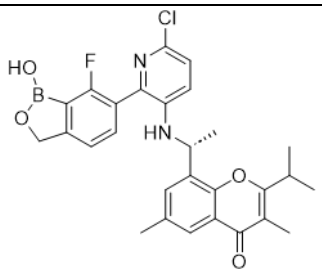
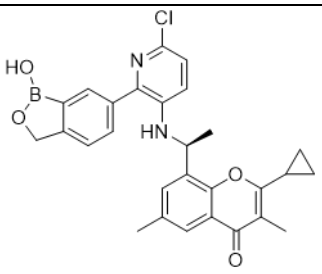
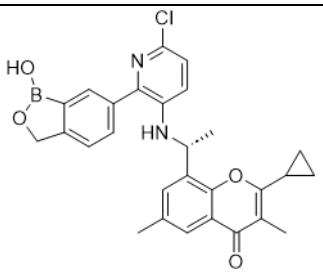
		
		
		
		
		

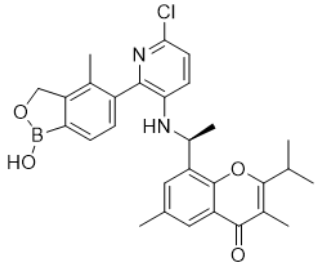
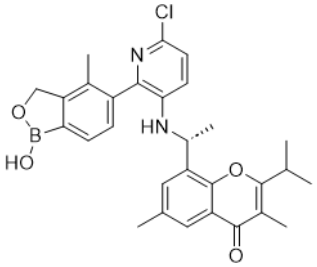
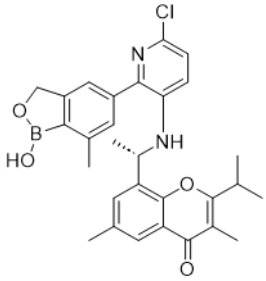
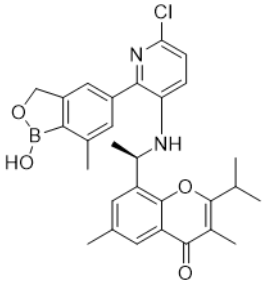
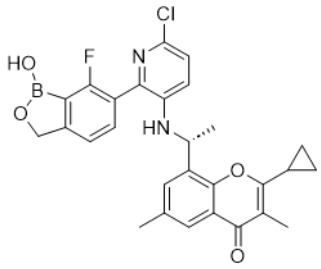
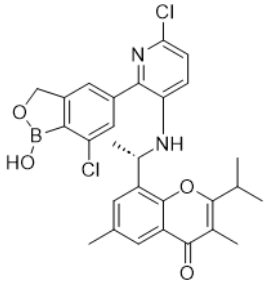
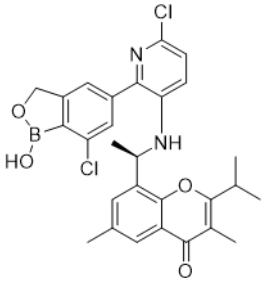
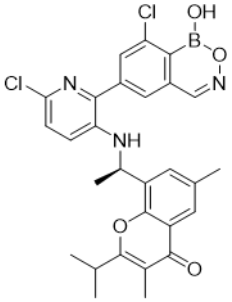
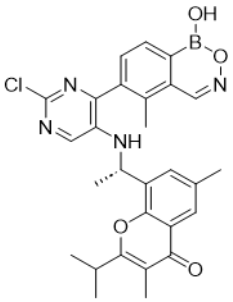
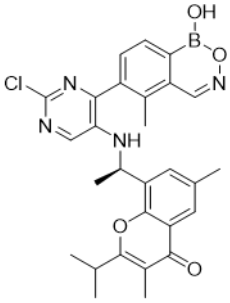
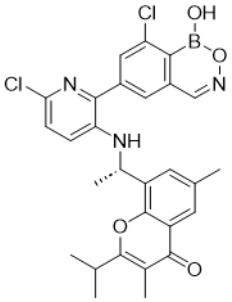
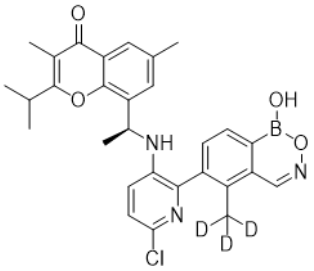
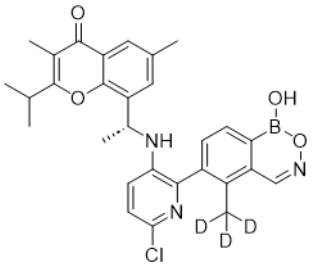
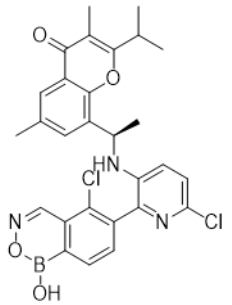
		
		
		
		
		

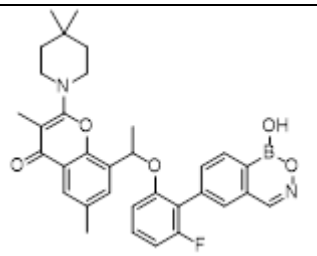
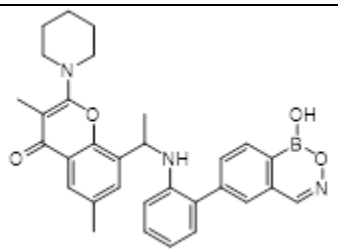
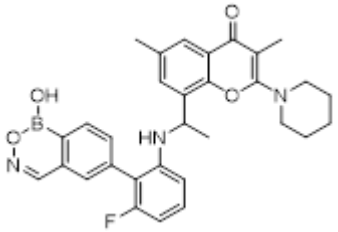
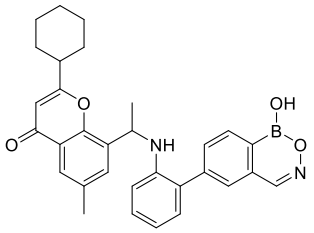
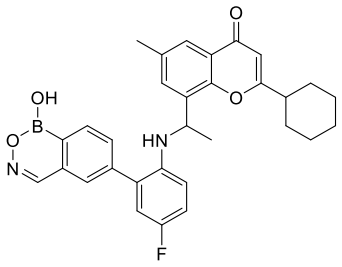
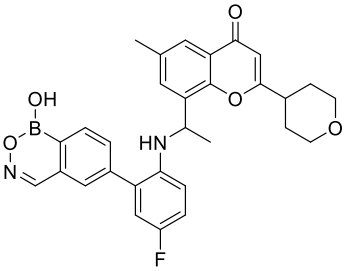
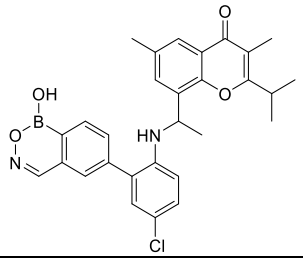
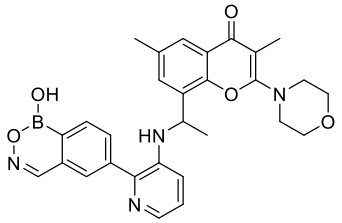
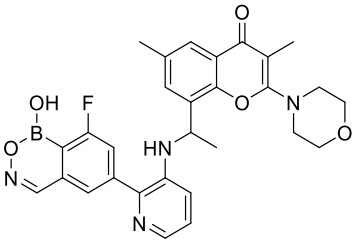
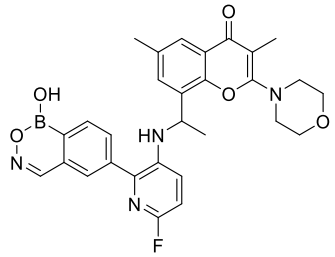
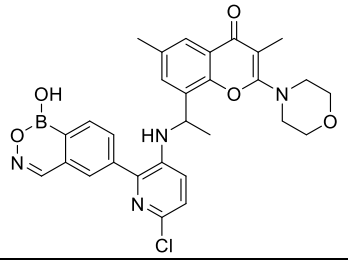
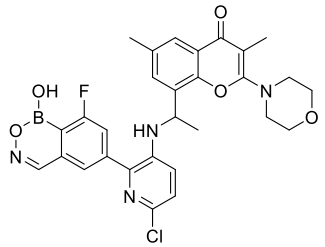
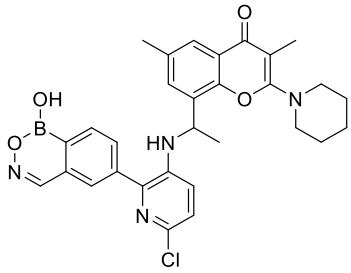
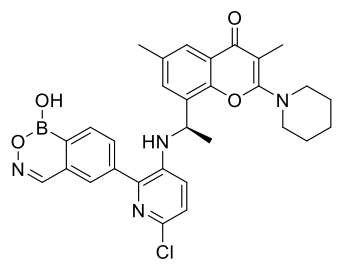
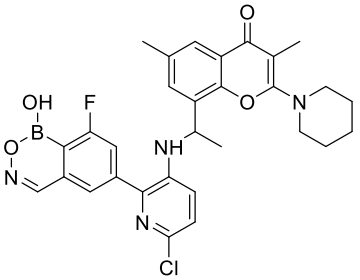
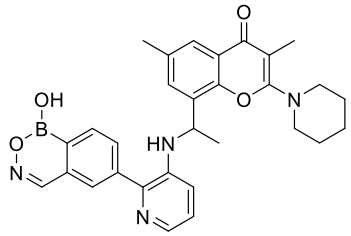
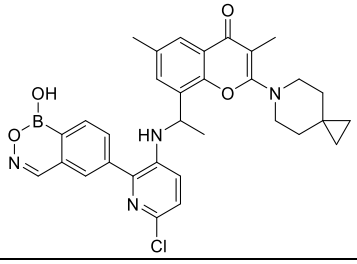
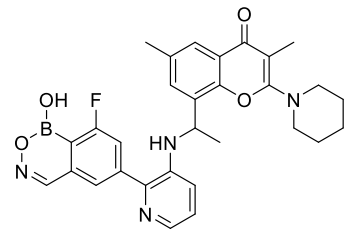
		
		
		
		
		

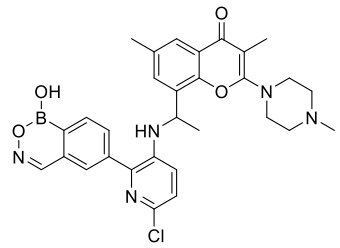
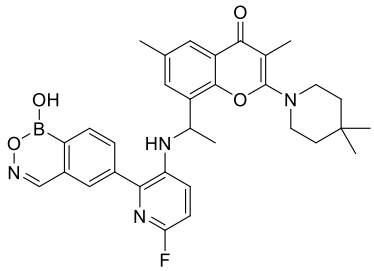
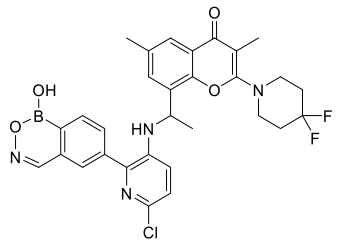
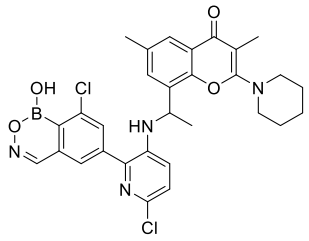
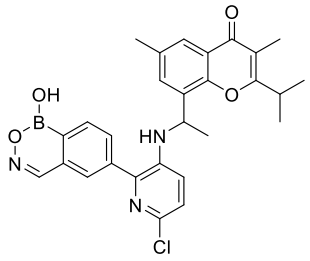
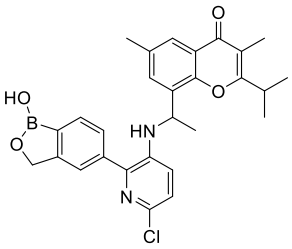
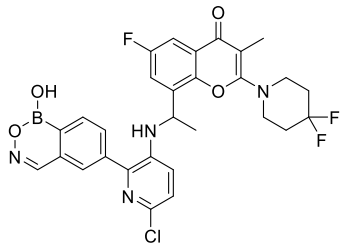
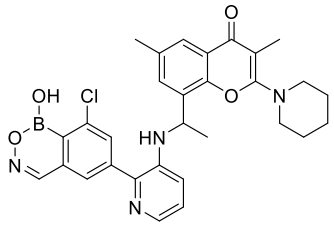
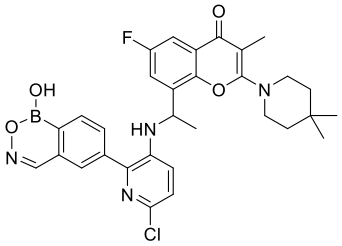
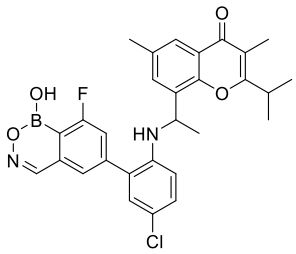
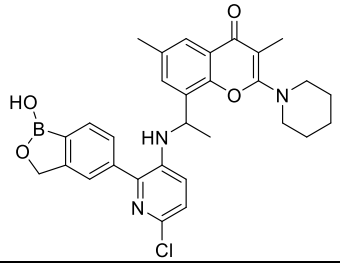
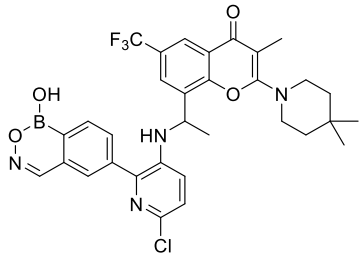
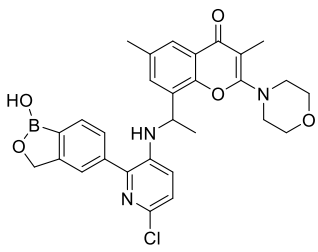
		
		
		
		
		

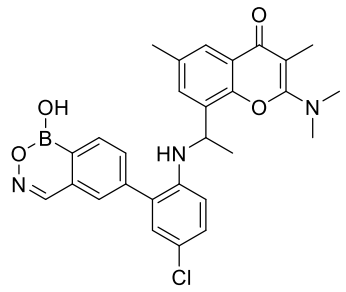
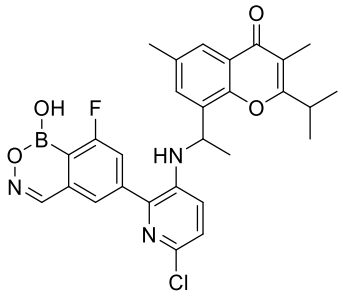
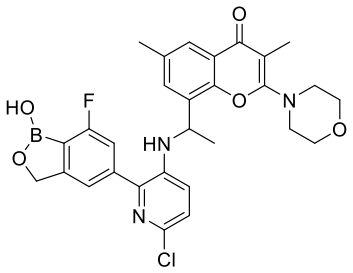
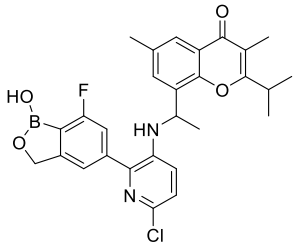
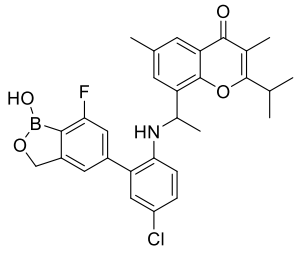
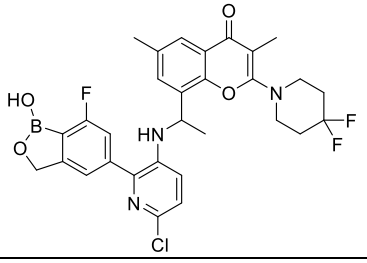
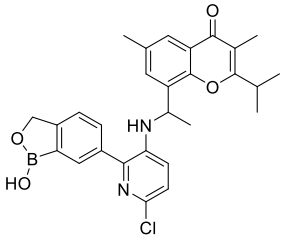
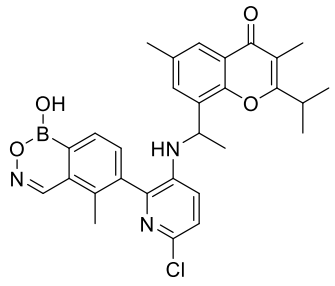
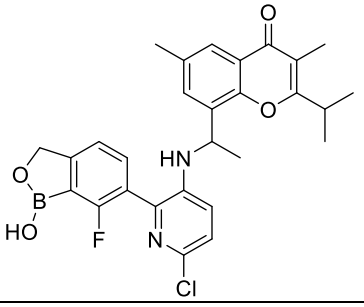
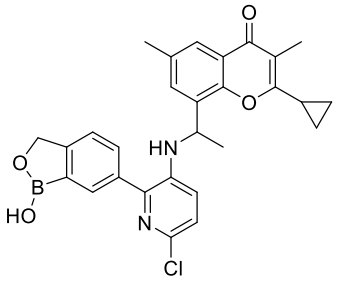
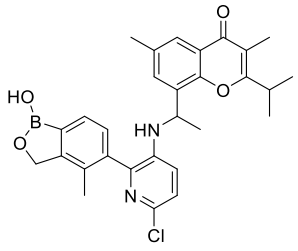
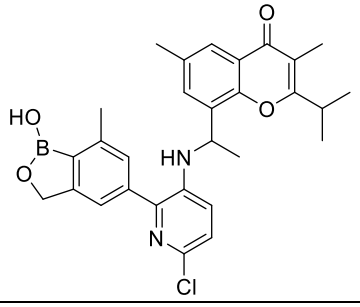
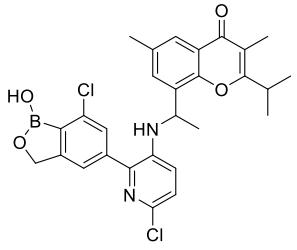
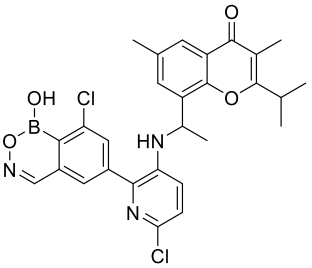
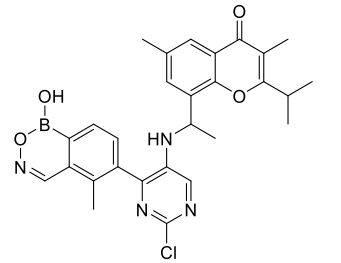
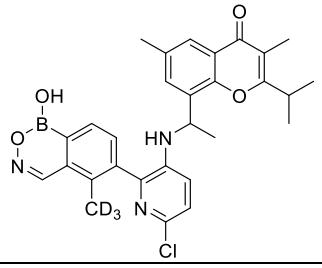
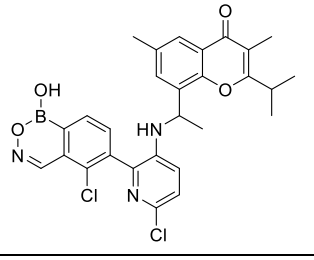
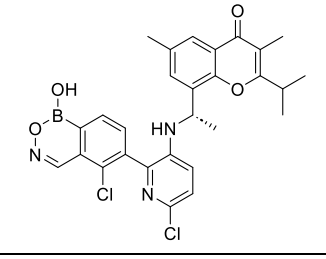
		
		
		
		
		

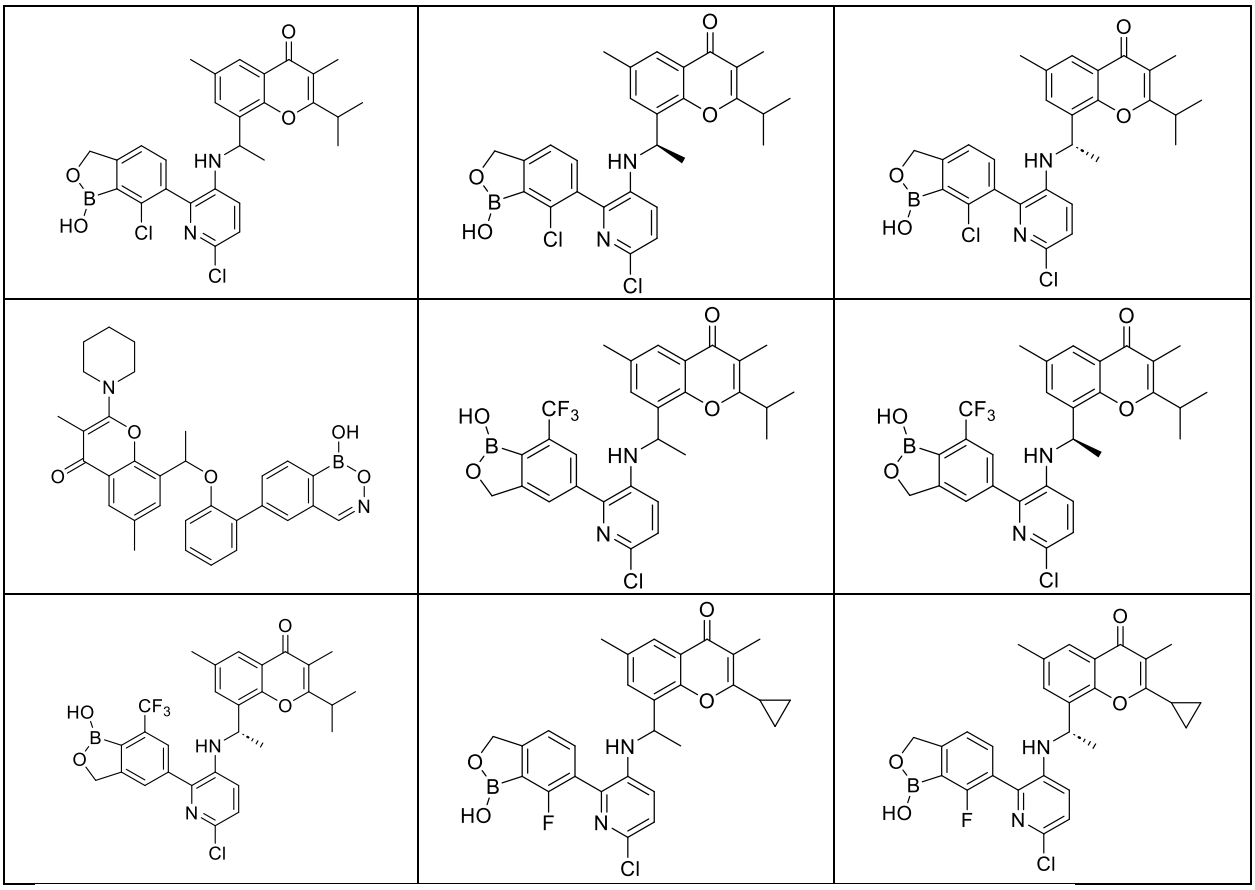
		
		
		
		
		
		



or a tautomer, enantiomer, diastereomer, mixture, salt, hydrate, solvate, or deuterated form thereof.

43. The compound of any one of claims 1 to 42, wherein the compound is:

    (i) a racemate; or is.

    (ii) a single stereoisomer substantially free of any alternative forms,

    optionally, wherein the stereoisomeric form is R; or is

    a tautomeric form of a preferred equilibria.

44. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 43 and a pharmaceutically acceptable excipient.

45. A method of inhibiting cell proliferation comprising contacting a cell with an effective amount of a compound of any one of claims 1 to 43.

46. Use of the compound of any one of claims 1 to 43 in the manufacture of a medicament for the treatment of cancer or a PI3K-mediated disease or disorder in a patient in need thereof.

47. Use of the compound of any one of claims 1 to 43 in the manufacture of a medicament for the treatment of a disease or disorder mediated by one or more PIK3CA genes, wherein the treatment comprises modulating one or more of wild type or one or more mutations of the one or more PIK3CA genes,

    optionally, comprising modulating one mutation; or

optionally, comprising modulating two or more mutations; or

optionally, comprising modulating wild type,

optionally, wherein the modulation is inhibition, or

optionally, wherein the modulation is selective inhibition for one or more mutations over wild-type.

48. The use of claim 47, wherein the PIK3CA is:

a PIK3CA mutant; or

the PIK3CA mediates a cancer; or

the PIK3CA regulates cancer initiation, progression, or metasasis.

49. The use of claim 47 or 48, wherein:

(i) the one or more mutations are any p110 mutation; or

the one or more mutations are selected from one or more mutations of H1047, E545, E542, N345, E726, C420, Q546, G118, E453, Q546, G1049, M1043, K111, E81, N1044, and E110; or

(iii) the one or more mutations are selected from one or more mutations of H1047, E545, and E542; or

(iv) wherein the mutations are selected from H1047X, E545X, and E542X,

optionally, wherein the mutation is H1047X.

optionally, wherein the mutation is H1047L,

,optionally, wherein the mutation is H1047R,

optionally wherein a mutation is E545X,

optionally, wherein the mutation is E545K,

optionally, wherein a mutation is E542X.

optionally, wherein the mutation is E542K.

50. The use of any one of claims 47 to 49, further comprising the compound chemically capturing a solvent accessible surface area of a protein,

optionally, wherein the solvent accessible surface area comprises one or more amino acid residue,

optionally, wherein the amino acid residue is selected from one or more of arginine, histidine, lysine, glutamic acid, serine, threonine, or glutamine,

optionally, wherein the amino acid residue is histidine,

optionally, wherein the histidine is HIS1048.

51. The use of claim 50, wherein chemical capture is interacting,

optionally, wherein interacting is binding,

optionally, wherein binding is covalent binding,

optionally, wherein binding is hydrogen bonding.

52. Use of the compound of any one of claims 1 to 43 in the manufacture of a medicament for inhibiting PI3K activity in a cell, wherein a solvent accessible surface area of a protein is to be modulated with the medicament,
optionally, wherein the modulating is in vitro, or
optionally, wherein the modulating is in vivo,
optionally, wherein the PI3K targeted gene is PIK3CA,
optionally, wherein the PI3K is PI3Kα,
optionally, wherein the PI3Kα is a PI3Kα mutant,
optionally, wherein the PI3Kα is a PI3Kα wild type,
optionally, wherein the PI3K mediates a cancer,
optionally, wherein the PI3K regulates cancer initiation, progression, or metastasis,optionally, wherein modulation is inhibition, or optionally, wherein modulation is selective inhibition over wild-type, providing preferential inhibition at a multiple level of: greater than 1, between about 1.5 to about 20 or greater, between about 1.5 and 100 or greater.
53. The use of claim 52, wherein one or more mutations are selected from one or more mutations of H1047, E545, E542, N345, E726, C420, Q546, G118, E453, Q546, G1049, M1043, K111, E81, N1044, and E110,
optionally, wherein one or more mutations are selected from one or more mutations of H1047, E545, and E542,
optionally, wherein the mutations are selected from H1047X, E545X, and E542X,
optionally, wherein a mutation is H1047X, or
optionally, wherein the mutation is H1047L, or
optionally, wherein the mutation is H1047R, or
optionally, wherein the mutation is GLU545X, or
optionally, wherein the mutation is E545K, or
optionally, wherein the mutation is GLU542X, or
optionally, wherein the mutation is E542K.
54. The use of claim 52 or 53, further comprising the compound chemically capturing a solvent accessible surface area of the protein,
optionally, wherein the solvent accessible surface area comprises one or more amino acid residue,
optionally, wherein the amino acid residue is selected from one or more of arginine, histidine, lysine, glutamic acid, serine, threonine, or glutamine,
optionally, wherein the amino acid residue is histidine,
optionally, wherein the histidine is H1048.

55. Use of the compound of any one of claims 1 to 41 in the manufacture of a medicament for the inhibition of PI3K wherein the inhibition comprises chemically capturing a solvent accessible surface area and modulating a p110 mutated protein subunit,
optionally, wherein the solvent accessible surface area comprises one or more amino acid residue,
optionally, wherein the amino acid residue is selected from one or more of arginine, histidine, lysine, glutamic acid, serine, threonine, or glutamine,
optionally, wherein the amino acid residue is histidine,
optionally, wherein the histidine is H1048.
56. The use of claim 55, wherein the p110 mutated protein subunit comprises at least one amino acid mutation compared to the wild type p110 protein subunit,
optionally, wherein the at least one amino acid mutations are selected from one or more mutations of H1047, E545, E542, N345, E726, C420, Q546, G118, E453, Q546, G1049, M1043, K111, E81, N1044, and E110,
optionally, wherein the one or more mutations are selected from one or more of H1047, E545, and E542.
57. Use of a compound of any one of claims 1 to 43 in the manufacture of a medicament for the treatment of a disease or disorder mediated by PI3Kα, wherein the treatment comprises chemically capturing a solvent accessible amino acid residue and modulating one or more of H1047X, E545X, and E542X,
optionally, wherein the amino acid residue is selected from one or more of arginine, histidine, lysine, glutamic acid, serine, threonine, or glutamine,
optionally, wherein the amino acid residue is histidine,
optionally, wherein the histidine is HIS1048.
58. The use of claim 57, wherein chemical capture is interacting,
optionally, wherein interacting is binding,
optionally, wherein binding is covalent binding,
optionally, wherein binding is hydrogen bonding.
59. The use of claim 57 or 58, comprising modulating one or more of H1047L and H1047R,
optionally, comprising modulating GLU545K,
optionally, comprising modulating GLU542K.
60. Use of the compound of any one of claims 1 to 43 in the manufacture of a medicament for the inhibition of a PIK3CA gene target protein (PI3K) or treatment of a disease or disorder mediated by PIK3CA, wherein the inhibition or treatment comprises modulating two or more mutant

variants selected from mutations of H1047, E545, E542, N345, E726, C420, Q546, G118, E453, Q546, G1049, M1043, K111, E81, N1044, and E110,

optionally, wherein the two or more mutant variants are selected from mutations of H1047, E545, and E542.

61. Use of the compound of any one of claims 1 to 43 in the manufacture of a medicament for modulating a PI3K to treat a disease or disorder by interacting the compound with at least two mutant variants,

optionally, wherein the PI3K gene target is PIK3CA,

optionally, wherein the PI3K mediates a cancer, or

optionally, wherein the PI3K regulates cancer initiation, progression, or metastasis,

optionally, wherein modulation is inhibition, or

optionally, wherein modulation is selective inhibition over wild-type.

62. The use of claim 61, wherein the mutant variants are selected from mutations of H1047, E545, E542, N345, E726, C420, Q546, G118, E453, Q546, G1049, M1043, K111, E81, N1044, and E110,

optionally wherein the mutant variants are selected from mutations of one or more of H1047, E545, and E542,

optionally, wherein the mutation is H1047X,

optionally, wherein the mutation is H1047L,

optionally, wherein the mutation is H1047R,

optionally, wherein the mutation is E545X,

optionally, wherein the mutation is E545K,

optionally, wherein the mutation is GLU542,

optionally, wherein the mutation is E542K.

63. The use of any one of claims 61 to 62, further comprising the compound of any one of claims 1 to 43 chemically capturing a solvent accessible surface area of a protein,

optionally, wherein the solvent accessible surface area comprises one or more amino acid residue,

optionally, wherein the amino acid residue is selected from one or more of arginine, histidine, lysine, glutamic acid, serine, threonine, or glutamine,

optionally, wherein the amino acid residue is histidine,

optionally, wherein the histidine is HIS1048.

64. The use of claim 63, wherein chemical capture is interacting,

optionally, wherein interacting is binding,

optionally, wherein binding is covalent binding,

optionally, wherein binding is hydrogen bonding.

65. The use of any one of claims 46 to 64, wherein:
    (i) the disease or disorder is cancer; or
    (ii) the disease or disorder is PROS: PIK3CA-Related Overgrowth Spectrum; or
    (iii) the disease or disorder is breast cancer, colorectal cancer, uterine cancer, bladder cancer, lung cancer, giloma, head and neck cancer, or other solid tumors,
    optionally wherein the disease or disorder is breast cancer.
66. The use of any one of claims 46 to 65 further comprising:
    (i) administration of one or more additional therapeutic agent, or
    (ii) administration of two or more additional therapeutic agents,
    optionally, wherein the additional therapeutic agents are selected from selective estrogen receptor degraders, Protac-mediated estrogen receptor inhibitors, complete estrogen receptor antagonists, sarcoplasmic reticulum calcium ATPase inhibitors, CDK2/4/6 inhibitors, CDK4/6 inhibitors, and aromatase inhibitors,
    optionally, wherein the additional therapeutic agents are selected from fulvestrant, vepdegestrant, palazestrant, imlunestrant, elacestrant, giredestrant, camizestrant, palbociclib, ribociclib, abemaciclib, anastronzole, exemestane, and letrozole.
67. The use of claim 66, wherein:
    each agent is provided in a separate dosage form, or
    one or more agent is provided in a combined dosage form.
68. Use of the compound of any one of claims 1 to 43 in the manufacture of a medicament for the modulation of one or more PI3K enzymes to regulate one or more of disease initiation and progression, wherein the modulation comprises interaction with at least one histidine and modulation of at least one surface accessible amino acid or residue,
    optionally, wherein one or more PI3K is inhibited,
    optionally, wherein the PI3K is PI3Kα,
    optionally, wherein the PI3Kα is a mutated variant thereof.
69. Use of the compound of any one of claims 1 to 43 in the manufacture of a medicament for the treatment of cancer in a patient in need thereof, wherein the treatment comprises determining that the cancer is associated with a PI3K wild-type or one or more PI3K mutations, optionally, wherein the PI3K is a mutated variant thereof.
70. A compound of any one of claims 1 to 43, for use in therapy.
71. Use of a compound of any one of claims 1 to 43, in the manufacture of a medicament for: (i) the treatment of cancer,

(ii) the inhibition of activity of PI3K.

(iii) the treatment of a PI3K-mediated disease or disorder,

optionally, wherein the PI3K is PI3Kα,

optionally, wherein the PI3Kα is wild type,

optionally, wherein the PI3Kα is a mutated variant thereof.

72. A process for preparing a compound of any one of claims 1 to 43.