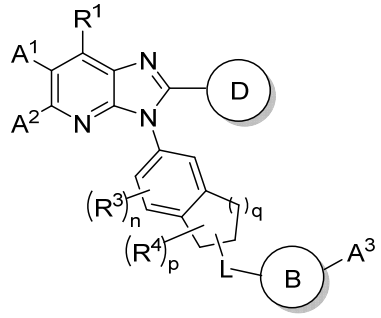
CLAIMS

WHAT IS CLAIMED IS:

1. A compound represented by the structure of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from:

hydrogen, halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle and 4- to 8-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, -CN, C_{1-6} alkyl, and C_{1-6} haloalkyl;

A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$,$-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, -

$OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, -CN;

C_{1-6} alkyl C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$,

-C(O)OR^{13}, -OC(O)R^{13}, -NO$_2$, and -CN; and

C$_{1-6}$ alkyl, C$_{2-6}$ alkenyl, and C$_{2-6}$ alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, -OR^{13}, -SR^{13}, -N(R^{13})$_2$, -C(O)R^{13}, -C(O)N(R^{13})$_2$, -N(R^{13})C(O)R^{13}, -C(O)OR^{13}, -OC(O)R^{13}, -NO$_2$, =O, =S, =N(R^{13}), and -CN;

R^4 is independently selected at each instance from:

halogen, -OR^{14}, -SR^{14}, -N(R^{14})$_2$, -C(O)R^{14}, -C(O)N(R^{14})$_2$, -N(R^{14})C(O)R^{14}, -C(O)OR^{14}, -OC(O)R^{14}, -NO$_2$, =O, =S, =N(R^{14}), and -CN; and

C$_{1-6}$ alkyl, C$_{2-6}$ alkenyl, and C$_{2-6}$ alkynyl, any one of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{14}, -SR^{14}, -N(R^{14})$_2$, -C(O)R^{14}, -C(O)N(R^{14})$_2$, -N(R^{14})C(O)R^{14}, -C(O)OR^{14}, -OC(O)R^{14}, -NO$_2$, =O, =S, =N(R^{14}), and -CN;

L is represented by -L^1-L^2-L^3-L^4-, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, -N(R^{15})-, -S-, -S(O)-, -S(O)$_2$-, -S(O)(NR^{15})-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S(O)$_2$-, -N(R^{15})S(O)$_2$N(R^{15})-, -S(O)(NR^{15})N(R^{15})-, -N(R^{15})N(R^{15})-, -(R^{15})NC(O)N(R^{15})-, and -(R^{15})NC(O)N(R^{15})N(R^{15})-; and

(b) C$_{1-6}$ alkylene, C$_{2-6}$ alkenylene, C$_{2-6}$ alkynylene, C$_{3-8}$ carbocyclene, and 3- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{15}, -SR^{15}, =O, =S, and -CN;

wherein L^1, L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent;

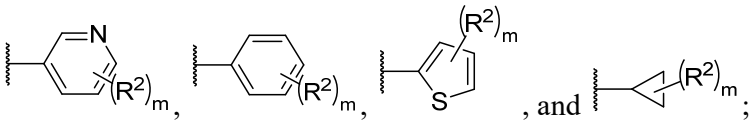
Ring B selected from 3- to 10-membered heterocyclene and C$_{3-10}$ carbocyclene, any of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{16}, -SR^{16}, -N(R^{16})$_2$, -C(O)N(R^{16})$_2$, -C(O)OR^{16}, -OC(O)R^{16}, -N(R^{16})C(O)R^{16}, -N(R^{16})S(O)$_2$R^{16}, -S(O)$_2$N(R^{16})$_2$, -N(R^{16})C(O)N(R^{16})$_2$, -N(R^{16})C(O)OR^{16}, -OC(O)N(R^{16})$_2$, -S(O)R^{16}, -S(O)$_2$R^{16}, -NO$_2$, =O, =S, =N(R^{16}), and -CN;

C$_{1-6}$ alkyl, C$_{2-6}$ alkenyl, and C$_{2-6}$ alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, -OR^{16}, -SR^{16}, -N(R^{16})$_2$, -C(O)N(R^{16})$_2$, -C(O)OR^{16}, -OC(O)R^{16}, -N(R^{16})C(O)R^{16}, -

$N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN; and

3- to 6-membered heterocycle and C_{3-6} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

Ring D is selected from: , and ;

R^2 is independently selected at each instance from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN;

A^3 is cysteine susceptible electrophile;

R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, and R^{16} are each independently selected at each occurrence from:

hydrogen,

C_{1-6} alkyl, optionally substituted with one or more substituents independently selected from halogen, -OH, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, C_{3-6} carbocycle, and 3- to 6- membered heterocycle; and

C_{3-6} carbocycle and 3- to 6-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OH, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, C_{1-6} alkyl, and C_{1-6} haloalkyl;

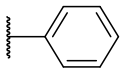
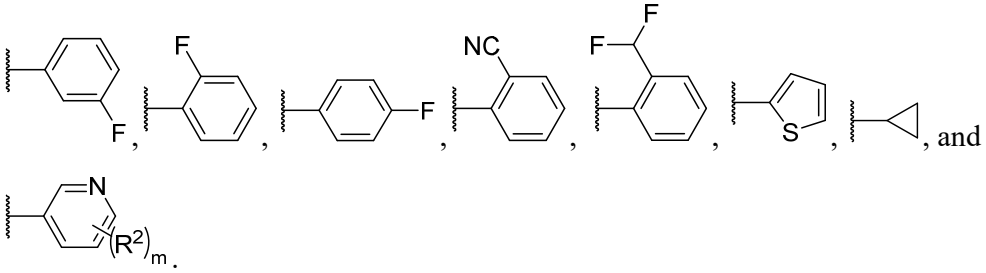
m is selected from 0, 1, 2, and 3;

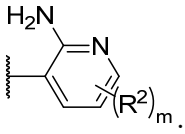
n is selected from 0, 1, 2, and 3;

q is selected from 1, 2, and 3; and

p is selected from 0, 1, 2, 3, 4, and 5.

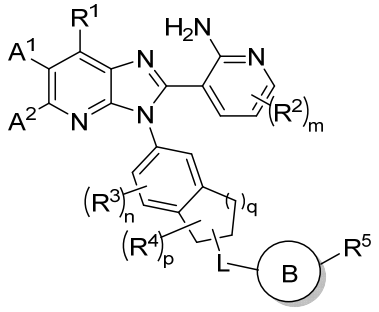
2. The compound or salt of claim 1, wherein the cysteine susceptible electrophile is selected from a haloacetamide, a haloalkyl ketone, a halo amidine, a halo benzylphosphonate, an acyloxyalkyl ketone, a sulfonyl oxirane, an epoxide, a diazoalkyl ketone, a halotriazine, an acrylamide, a cyano acrylamide, a vinyl sulfone, a vinyl sulfonamide, an acrylate, a fumarate, a carbonyl acrylate, a maleimide, a ketoamide, a nitrile, an alkene, an alkyne, a keto heterocycle, and an ynamide.

3. The compound or salt of claim 1, wherein Ring D is selected from , , and .

4. The compound or salt of claim 1, wherein Ring D is .

5. The compound or salt of claim 1, wherein the cysteine susceptible electrophile is an alpha-beta unsaturated carbonyl, an alpha-beta unsaturated sulfone, an alpha-beta unsaturated amide, and an alpha-beta unsaturated sulfonamide.

6. The compound or salt of claim 1, wherein the structure of Formula (I) is represented by the structure of Formula (II-A):

 (II-A),

or a pharmaceutically acceptable salt thereof, wherein:

the cysteine susceptible electrophile is R^5;

R^5 is selected from:

$-C(O)R^{17}$, $-S(O)_2R^{17}$, $-N(R^{19})C(O)(R^{17})$, $-C(O)N(R^{17})(R^{19})$, $-N(R^{19})S(O)_2R^{17}$, $-S(O)_2N(R^{17})(R^{19})$, and -CN;

C_{1-6} alkyl substituted with one or more substituents independently selected from $-C(O)R^{17}$, $-S(O)_2R^{17}$, $-N(R^{19})C(O)(R^{17})$, $-C(O)N(R^{17})(R^{19})$, $-N(R^{19})S(O)_2R^{17}$, $-S(O)_2N(R^{17})(R^{19})$, and -CN;

C_{2-6} alkenyl and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from $-C(O)R^{19}$, $-S(O)_2R^{19}$, -

$N(R^{19})C(O)(R^{19})$,-$C(O)N(R^{19})_2$, -$N(R^{19})S(O)_2R^{19}$, -$S(O)_2N(R^{19})(R^{19})$, and -CN; and

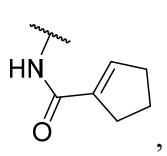
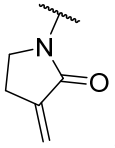
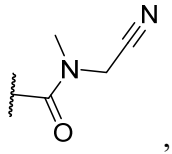
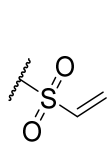
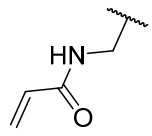
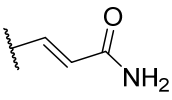
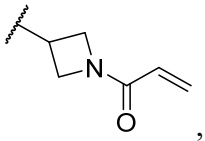
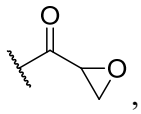
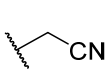
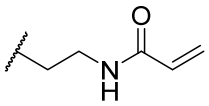
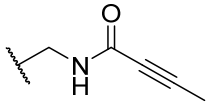
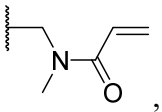
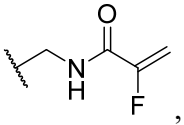
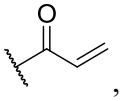
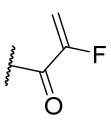
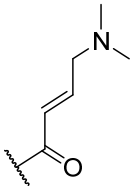
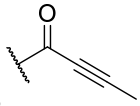
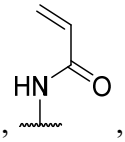
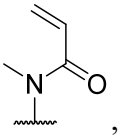
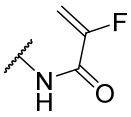
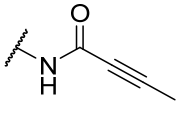
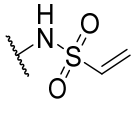
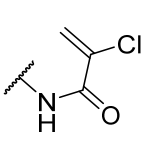
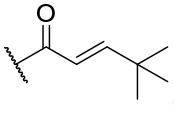
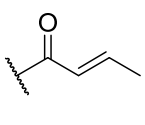
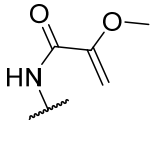
C_{3-6} carbocycle and 3- to 6-membered heterocycle, each of which is substituted with one or more substituents independently selected from =O, C_{2-6} alkenyl, C_{2-6} alkynyl, -$C(O)R^{17}$, -$S(O)_2R^{17}$, -$N(R^{19})C(O)(R^{17})$, -$C(O)N(R^{17})(R^{19})$, -$N(R^{19})S(O)_2R^{17}$, -$S(O)_2N(R^{17})(R^{19})$, and -CN;

R^{17} is independently selected at each occurrence from:

C_{2-6} alkenyl and C_{2-6} alkynyl each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{18}, -SR^{18}, -$N(R^{18})_2$, -$C(O)N(R^{18})_2$, -$C(O)OR^{18}$, -$OC(O)R^{18}$, -$N(R^{18})C(O)R^{18}$, -$N(R^{18})S(O)_2R^{18}$, -$S(O)_2N(R^{18})_2$, -$N(R^{18})C(O)N(R^{18})_2$, -$N(R^{18})C(O)OR^{18}$, -$OC(O)N(R^{18})_2$, -$S(O)R^{18}$, -$S(O)_2R^{18}$, -NO_2, and -CN; and

R^{18} and R^{19} are each independently selected at each occurrence from: hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle.

7. The compound or salt of claim 1, wherein the cysteine susceptible electrophile is selected from:

-CN, , , , , , , , , , , , , , , , , , , , , , , , , , and .

8. The compound or salt of claim 1, wherein A^1 and A^2 are each independently selected from (i) and (ii):

(i) hydrogen, halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)O(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN; and

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)C(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

3- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN.

9. The compound or salt of claim 1, wherein A^1 and A^2 are each independently selected from (i) and (iii):

(i) hydrogen, halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN; and

(iii) 3- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

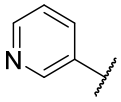
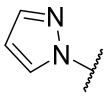
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

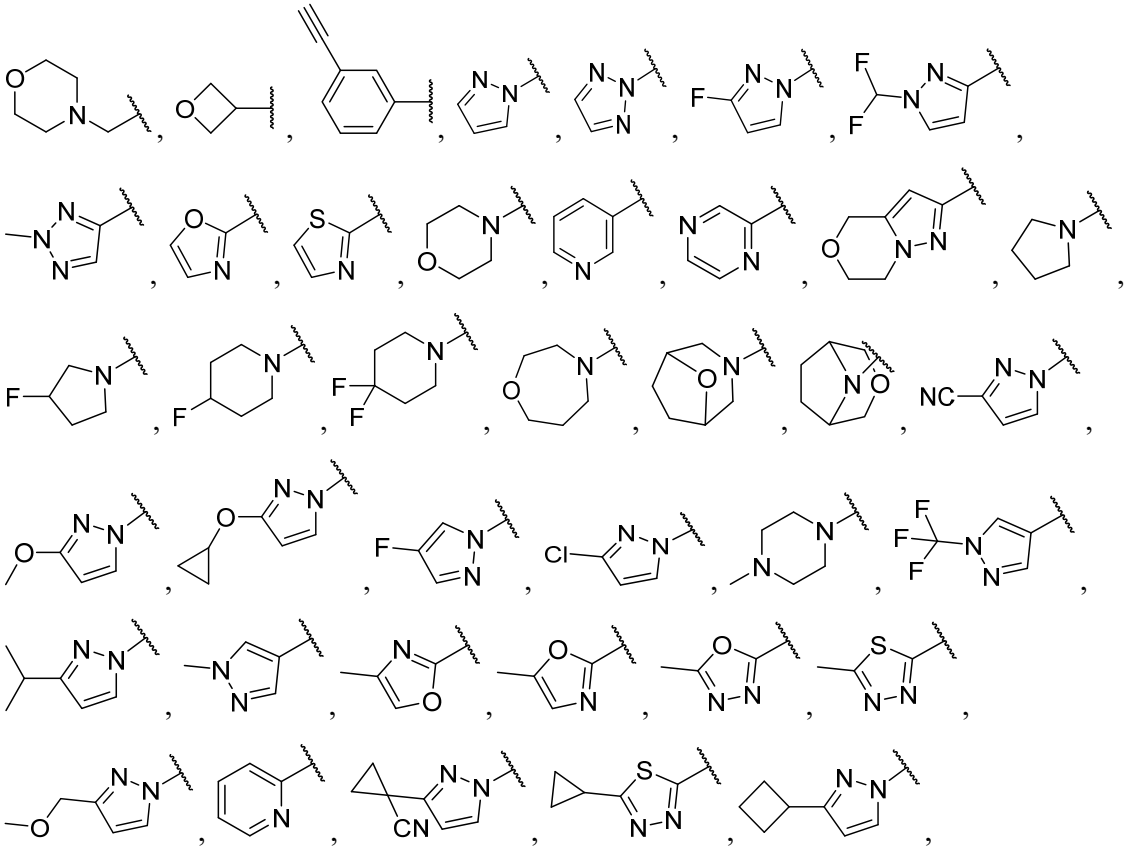
C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

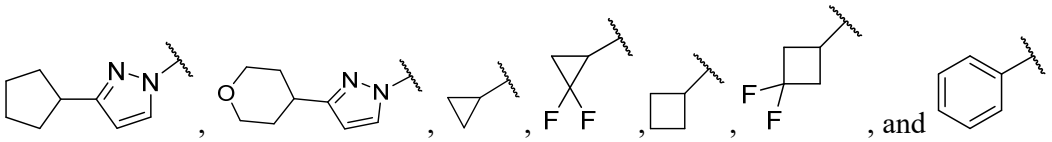
halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $N(R^{11})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN.

10. The compound or salt of claim 1, wherein A^1 is selected from hydrogen, fluoro, methyl, , , and .

11. The compound or salt of claim 1, wherein A^2 is selected from methyl,





12. The compound or salt of claim 1, wherein Ring B is selected from 3- to 10-membered heterocyclene and C_{3-10} carbocyclene, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

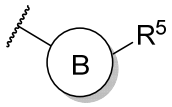
4- to 6-membered heterocycle and C_{3-6} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

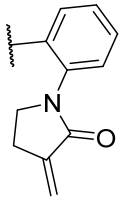
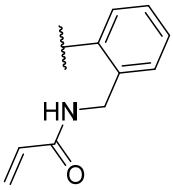
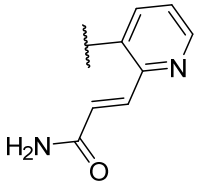
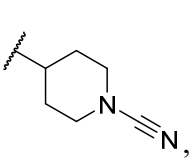
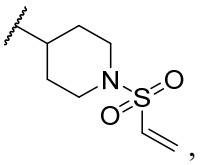
13. The compound or salt of claim 1, wherein Ring B is selected from azetidinylene, pyrrolidinylene, piperidinylene, phenylene, pyridinylene, indolinylene, 3-azabicyclo[3.2.1]octanylene, cyclobutylene, cyclohexylene, pyrazolylene, 1,2,3,4-tetrahydroquinolinylene, azaspiro[3.5]nonanylene, azaspiro[3.3]heptanylene, azaspiro[3.4]octanylene, 1,4-oxazepanylene, 3-azabicyclo[3.1.1]heptanylene, 3-oxa-6-azabicyclo[3.2.2]nonanylene, piperazinylene, azepanylene, 2-azabicyclo[2.2.2]octanylene, 2-abicyclo[2.2.1]heptanylene each of which is optionally substituted with one or more substituents independently selected from:

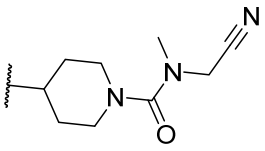
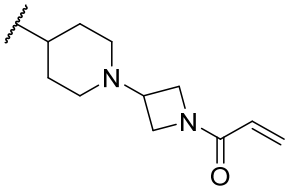
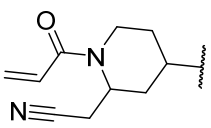
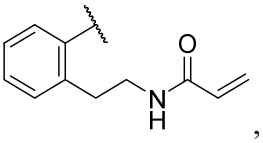
halogen, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

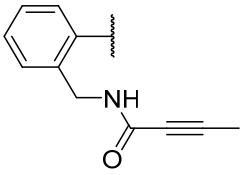
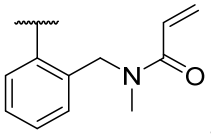
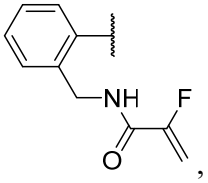
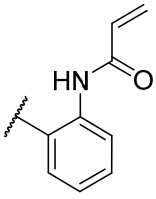
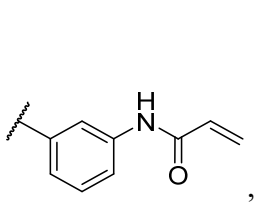
C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

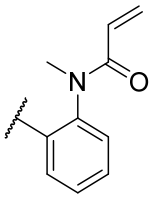
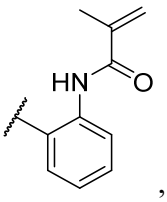
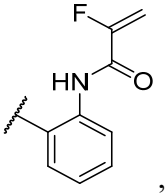
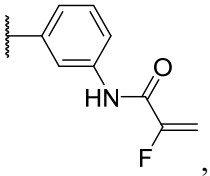
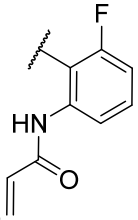
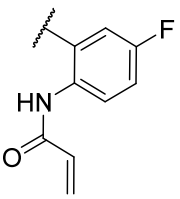
C_{3-6} carbocycle optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

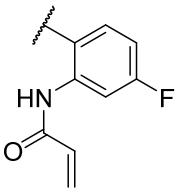
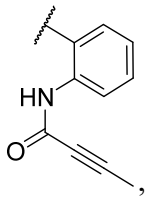
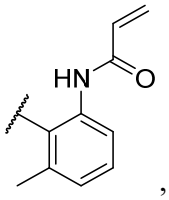
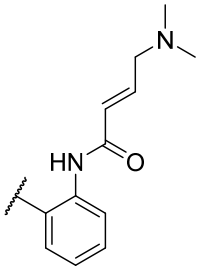
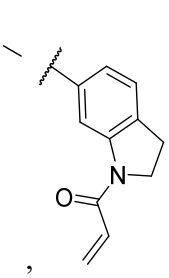
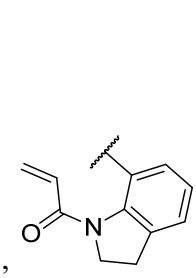
14. The compound or salt of claim 6, wherein  is selected from:

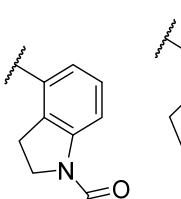
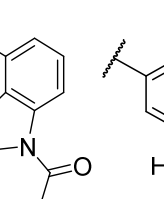
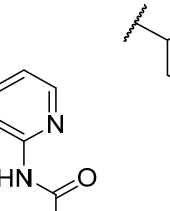
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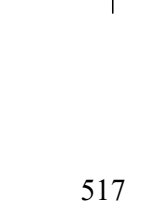
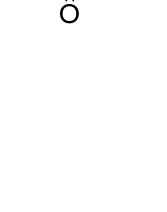
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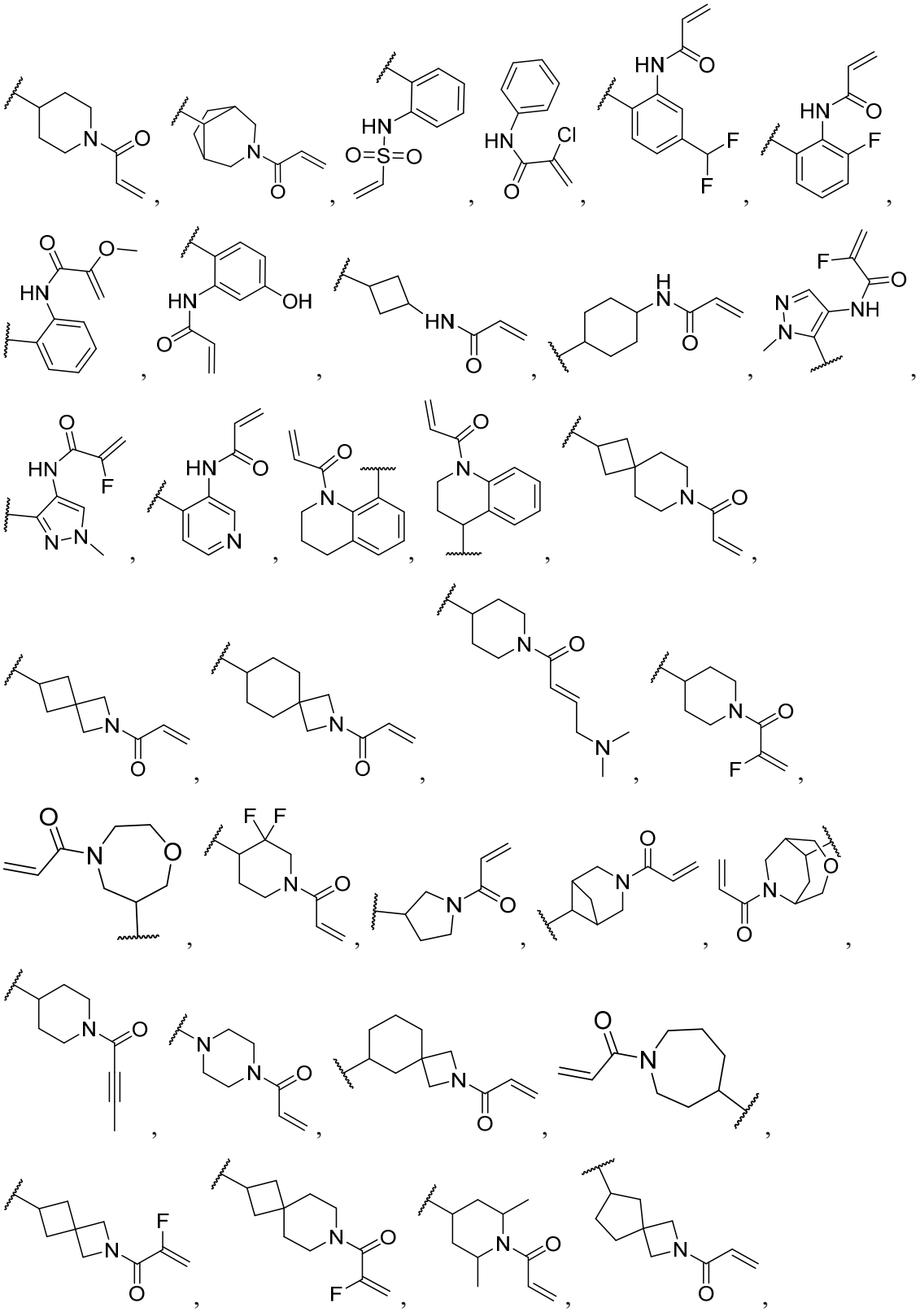
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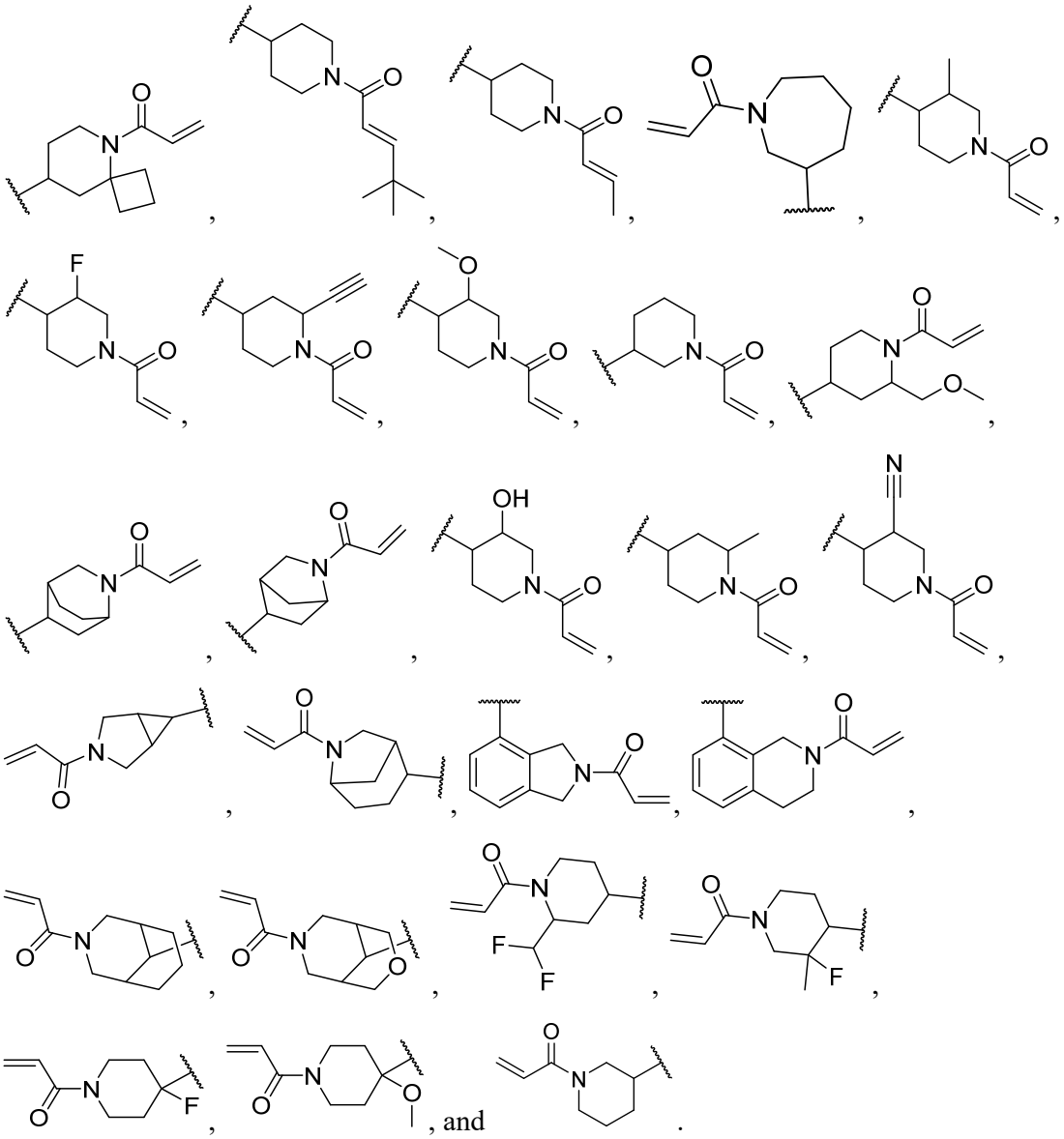
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15. The compound or salt of claim 1, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, -N(R^{15})-, -S-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S(O)$_2$, -N(R^{15})N(R^{15})-, and -(R^{15})NC(O)N(R^{15})-; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-6} carbocyclene, and 3- to 6-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{15}, and -CN;

wherein L^2, L^3, and L^4 are each optionally absent; and

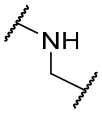
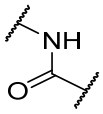
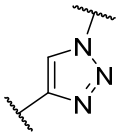
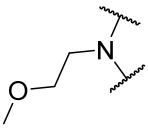
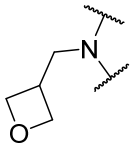
wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent.

16. The compound or salt of claim 1, wherein L^4 is absent.

17. The compound or salt of claim 1, wherein L^3 is absent.

18. The compound or salt of claim 1, wherein L^2 is absent or methylene.

19. The compound or salt of claim 1, wherein L^1 is selected from -O-, -N(R^{15})-, -N(R^{15})C(O)-, C_{1-6} alkylene, and 3- to 6-membered heterocyclene.

20. The compound or salt of claim 1, wherein L is selected from: -O-, -NH-, -CH_2-, -N(CH_3)-, , , , , and .

21. The compound or salt of claim 1, wherein R^1 is selected from hydrogen, methoxy, -CN, methyl, ethyl, and (methoxy)methyl.

22. The compound or salt of claim 1, wherein q is 1.

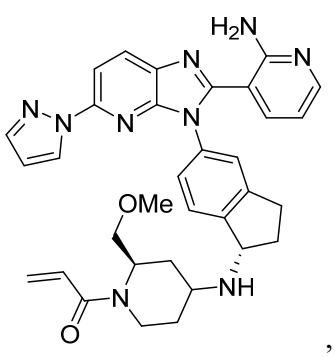
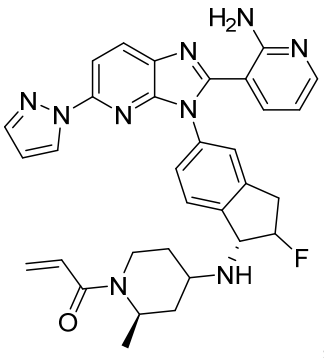
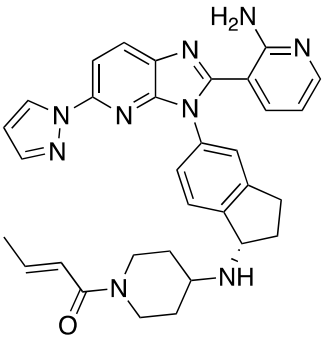
23. The compound or salt of claim 1, wherein m is 0.

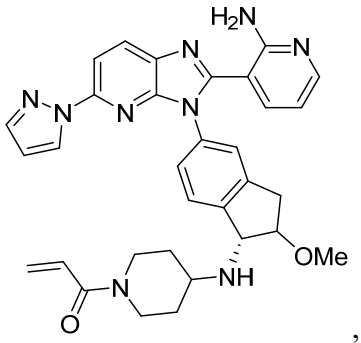
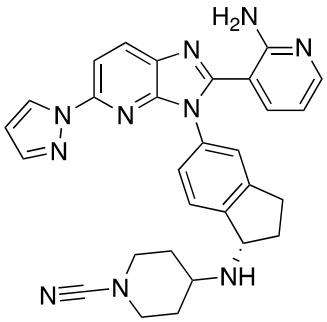
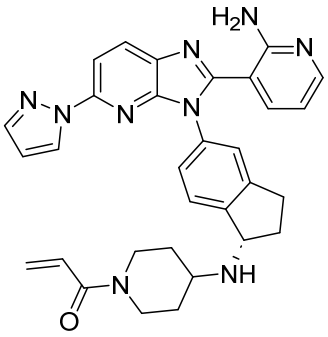
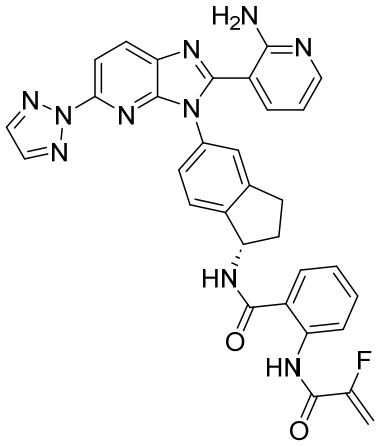
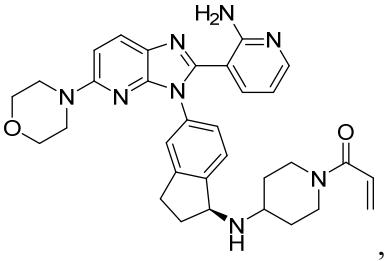
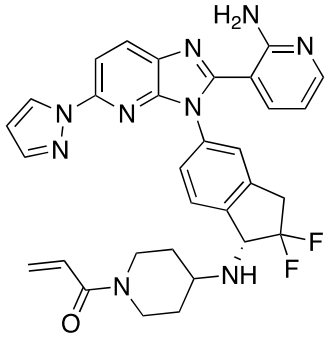
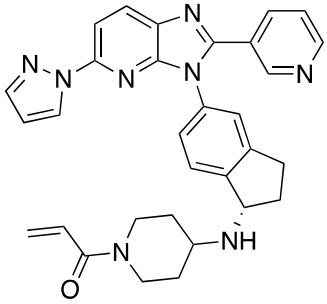
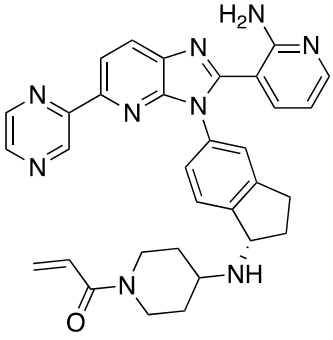
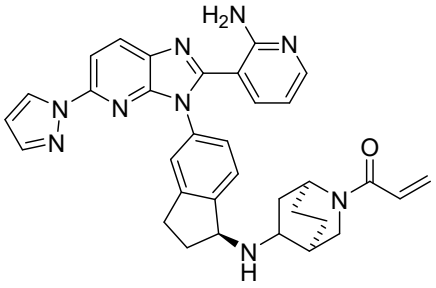
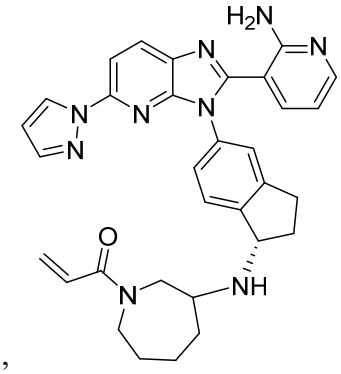
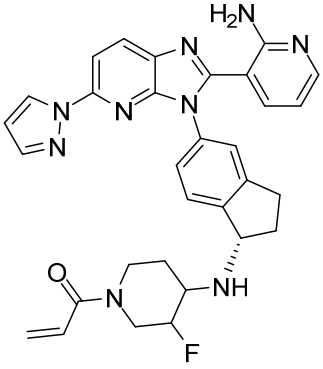
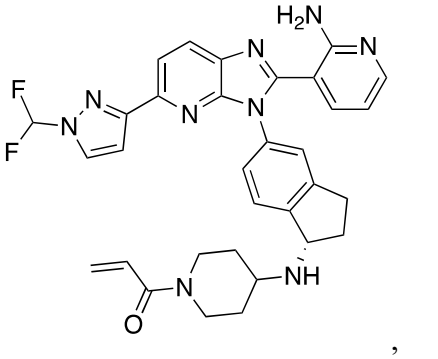
24. The compound or salt of claim 1, wherein n is 0.

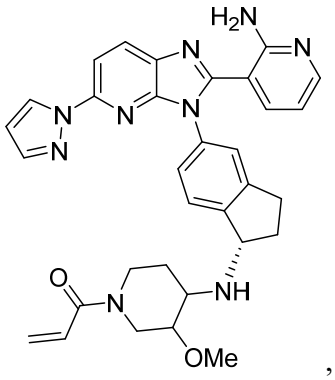
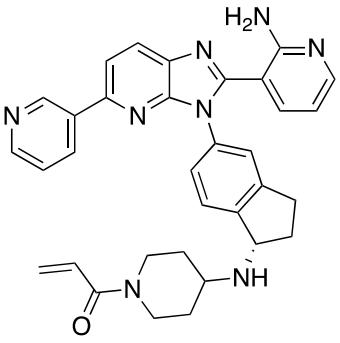
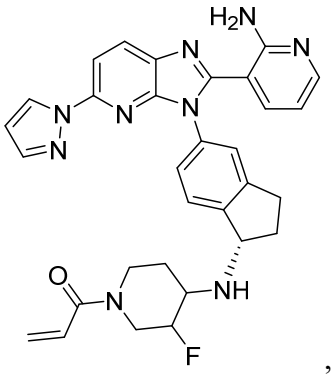
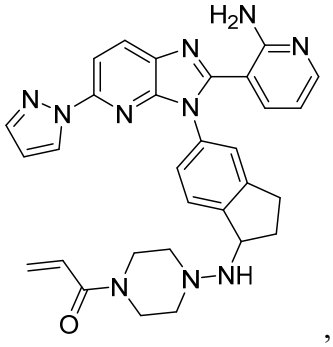
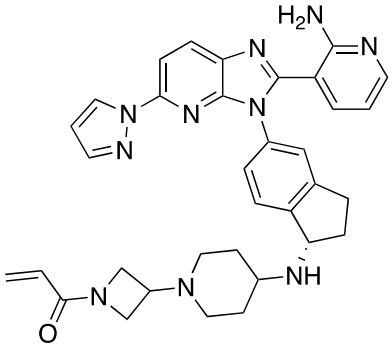
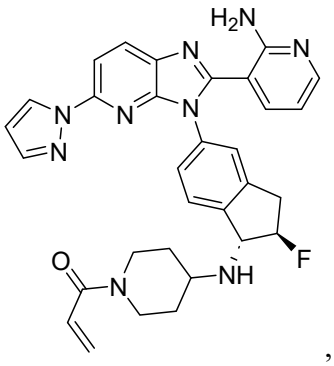
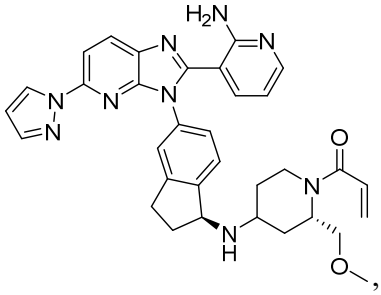
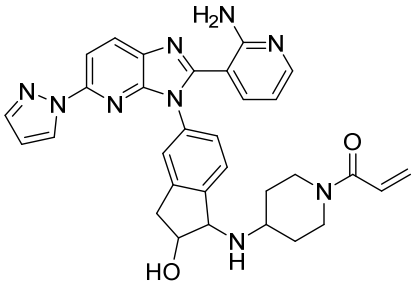
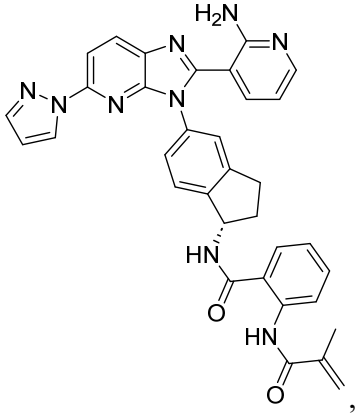
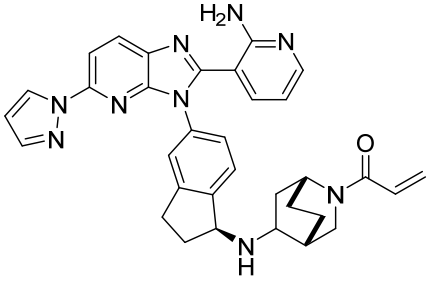
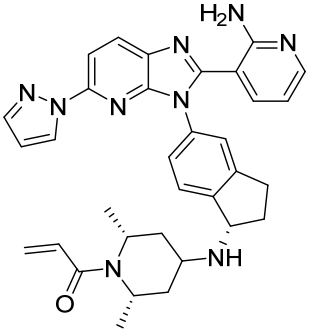
25. The compound or salt of claim 1, wherein p is selected from 0, 1, and 2.

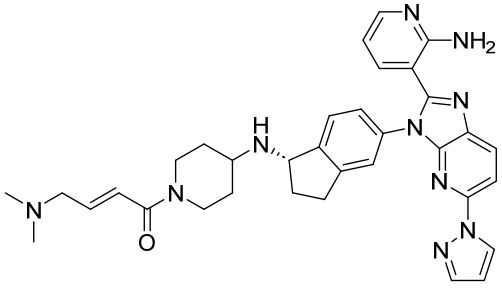
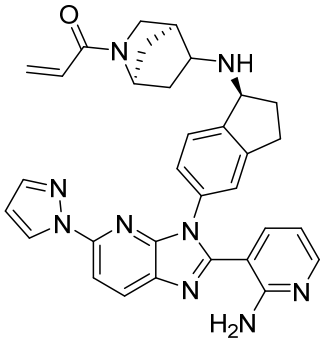
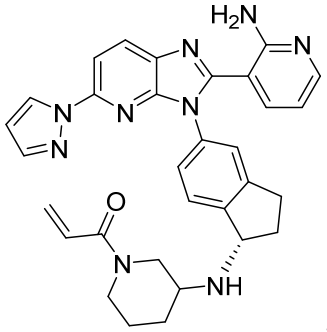
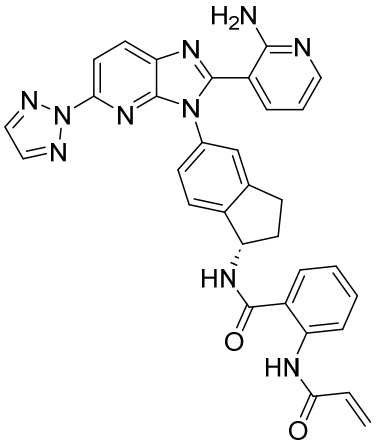
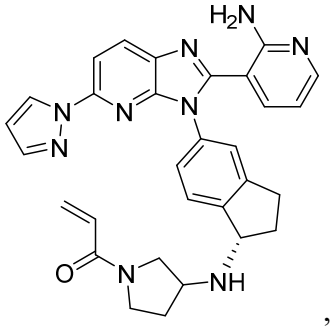
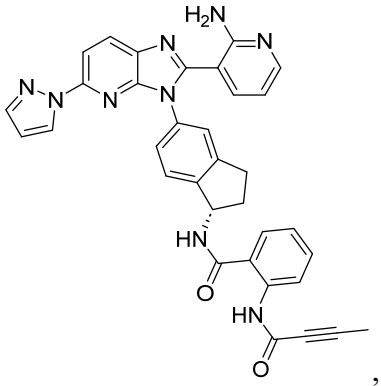
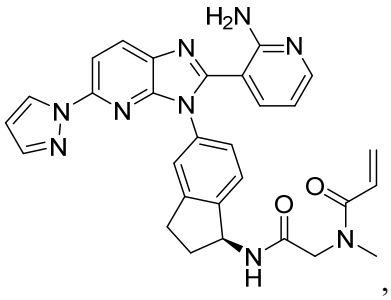
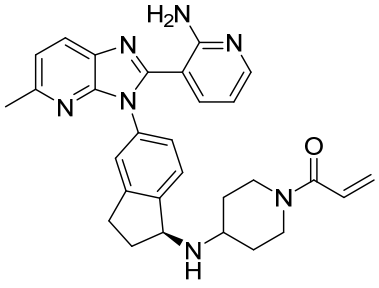
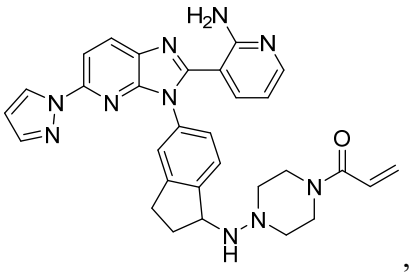
26. The compound or salt of claim 1, wherein R^4 is selected from fluoro, -OH, and -OCH_3.

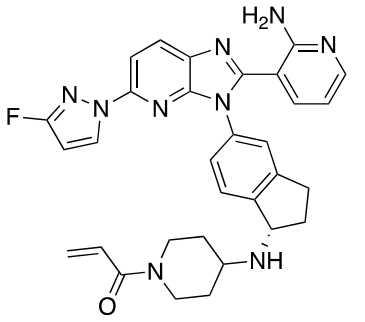
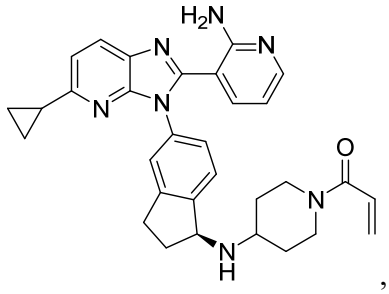
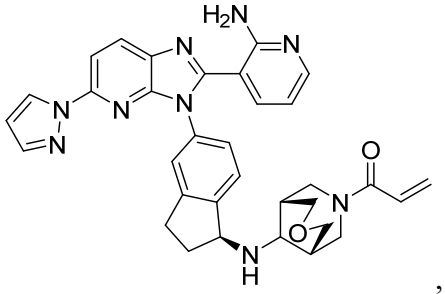
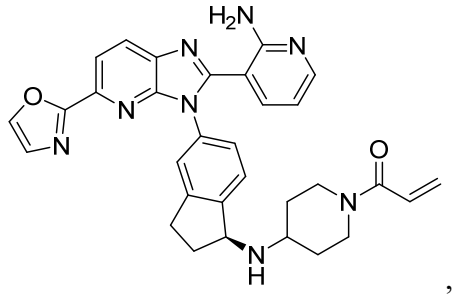
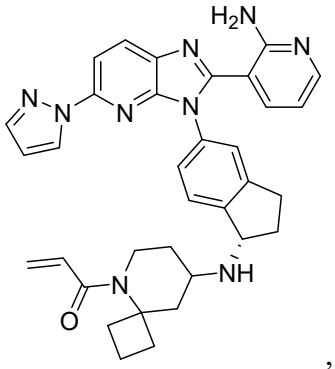
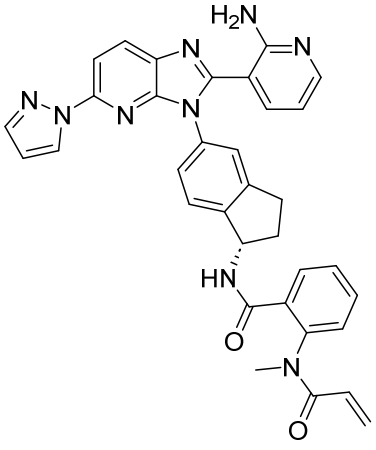
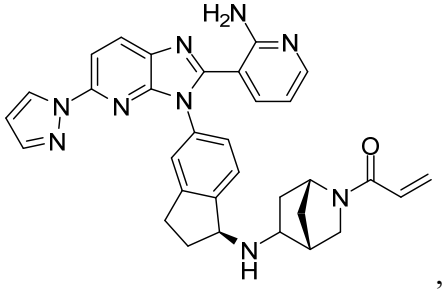
27. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is selected from:

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, or a pharmaceutically acceptable salt of any one thereof.

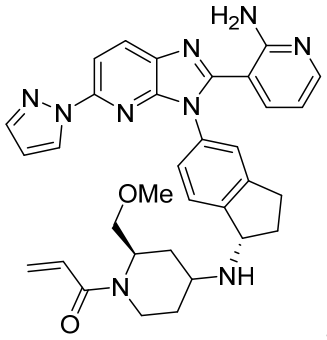
28. A pharmaceutical composition comprising a compound or salt of claim 1 and a pharmaceutically acceptable excipient.

29. Use of a compound or salt of claim 1, or a pharmaceutical composition comprising a compound or salt of claim 1 and a pharmaceutically acceptable excipient; in the

manufacture of a medicament for treating cancer, wherein the compound or pharmaceutical composition is to be administered to a subject, wherein the administration modulates the activity of wild-type AKT1 or the activity of a mutant AKT1; and wherein the cancer is selected from prostate cancer, breast cancer, colorectal cancer, and meningioma.

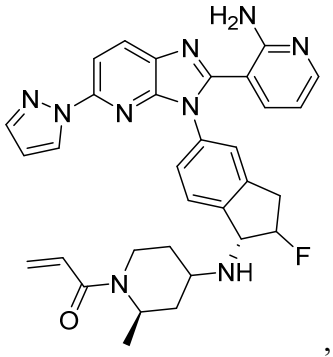
30. An AKT1 protein covalently bound to a compound, wherein the compound is covalently bound to a cysteine residue of the AKT1 protein, and wherein the compound is a compound or salt of claim 1.

31. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



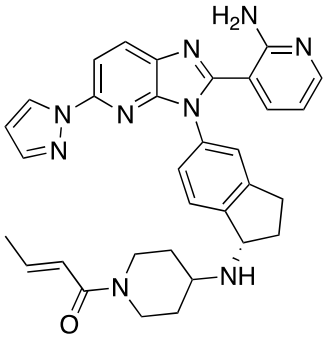
, or a pharmaceutically acceptable salt thereof.

32. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



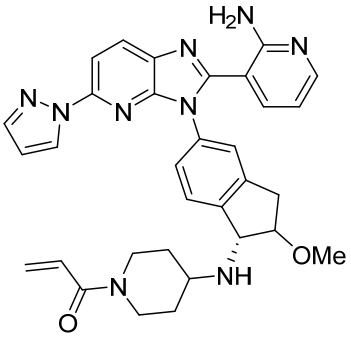
, or a pharmaceutically acceptable salt thereof.

33. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



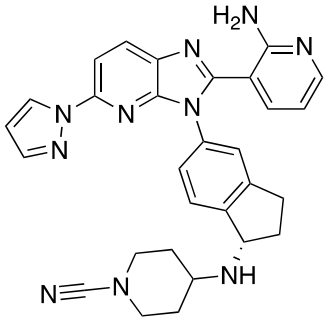
, or a pharmaceutically acceptable salt thereof.

34. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



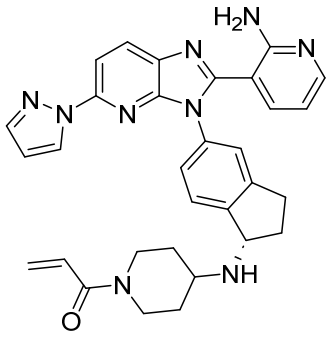
, or a pharmaceutically acceptable salt thereof.

35. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



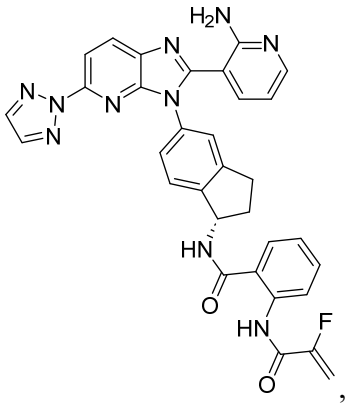
, or a pharmaceutically acceptable salt thereof.

36. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



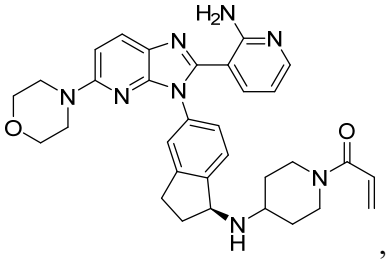
, or a pharmaceutically acceptable salt thereof.

37. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



, or a pharmaceutically acceptable salt thereof.

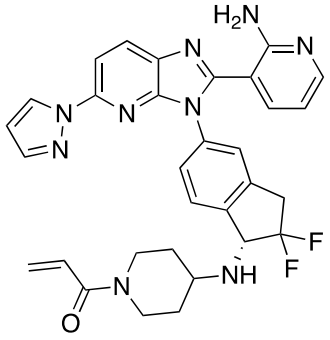
38. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



, or a pharmaceutically acceptable salt thereof.

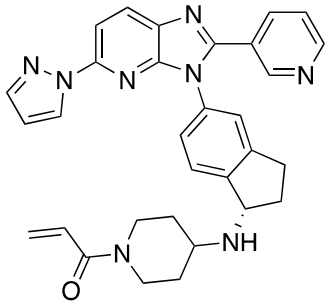
39. The compound or salt of claim 1, wherein the compound or salt of Formula (I)

is



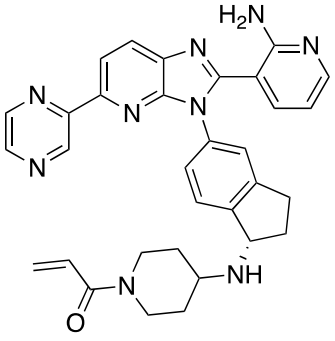
, or a pharmaceutically acceptable salt thereof.

40. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



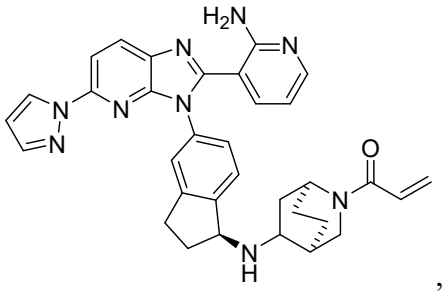
, or a pharmaceutically acceptable salt thereof.

41. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



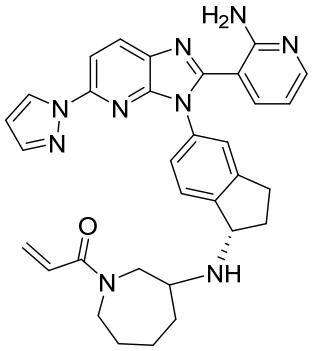
, or a pharmaceutically acceptable salt thereof.

42. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



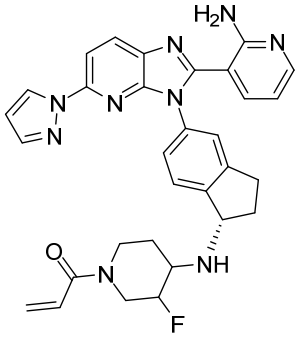
, or a pharmaceutically acceptable salt thereof.

43. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



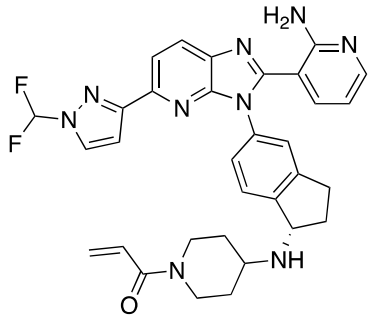
, or a pharmaceutically acceptable salt thereof.

44. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



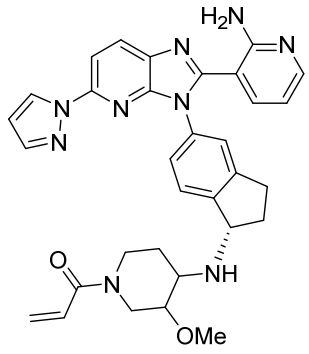
, or a pharmaceutically acceptable salt thereof.

45. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



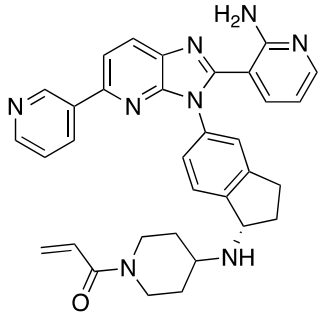
, or a pharmaceutically acceptable salt thereof.

46. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



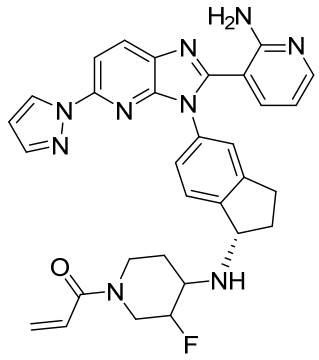
, or a pharmaceutically acceptable salt thereof.

47. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



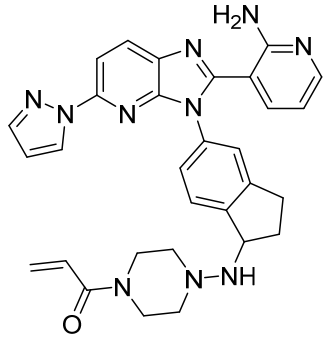
, or a pharmaceutically acceptable salt thereof.

48. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



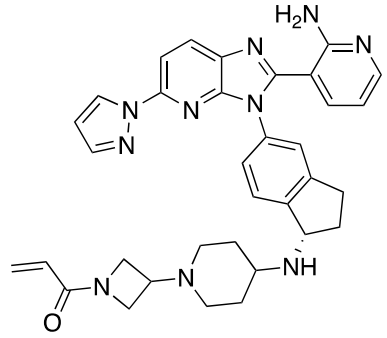
, or a pharmaceutically acceptable salt thereof.

49. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



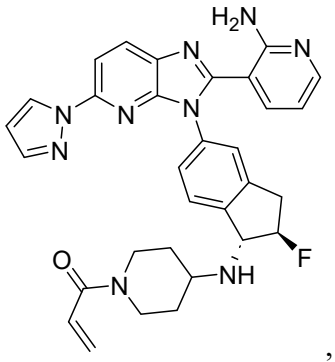
, or a pharmaceutically acceptable salt thereof.

50. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



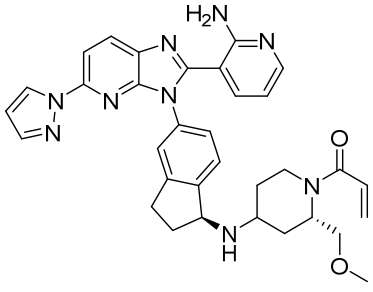
, or a pharmaceutically acceptable salt thereof.

51. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



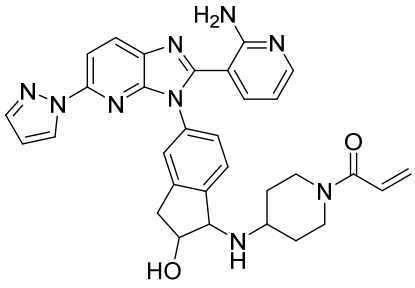
, or a pharmaceutically acceptable salt thereof.

52. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



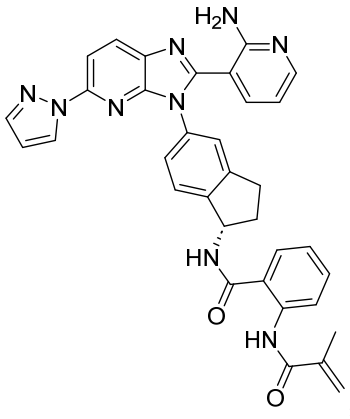
, or a pharmaceutically acceptable salt thereof.

53. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



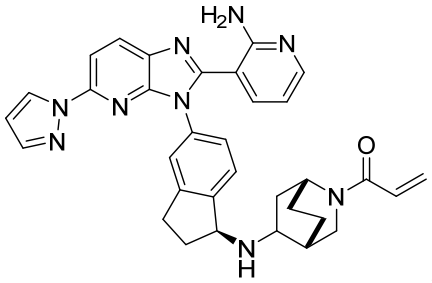
, or a pharmaceutically acceptable salt thereof.

54. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



, or a pharmaceutically acceptable salt thereof.

55. The compound or salt of claim 1, wherein the compound or salt of Formula (I) is



, or a pharmaceutically acceptable salt thereof.