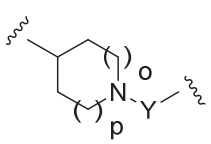
R^2 is selected from the group consisting of hydroxy, amino, cyano, and -CH_2R^4;R^3 is selected from the group consisting of hydrogen, -$OC(=O)NR^{11a}R^{11b}$, -$NHC(=O)R^5$, and -NHZ^1;

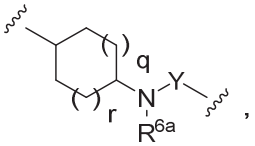
R^4 is selected from the group consisting of amino, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is selected from the group consisting of -$NR^{12a}R^{12b}$, C_{1-4} alkoxy, and C_{1-4} alkyl;

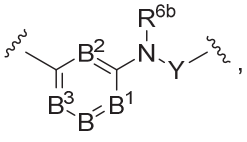
X is selected from the group consisting of:



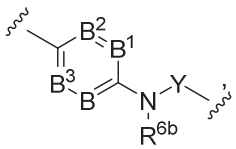
X-1 ,



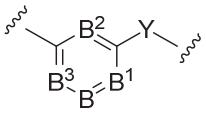
X-2 ,



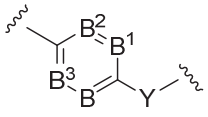
X-3 ,



X-4 ,



X-5 and



X-6 ;

wherein Y is attached to Z^2; or

X is absent;

Y is selected from the group consisting of -C(=O)- and -$S(=O)_2$-;

R^{6a} and R^{6b} are independently selected from the group consisting of hydrogen and C_{1-4} alkyl;

o, p, q, and r are each independently 0, 1, 2, or 3;

m and n are 0;

Z^1 is selected from the group consisting of -$C(=O)R^7$ and -$S(=O)_2R^7$;

Z^2 is selected from the group consisting of -$CH=CHR^{13}$, -$C\equiv CR^{13}$, -CH_2Cl, -CH_2Br, -CH_2I, alkyl, optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted cycloalkyl,

with proviso that Z^2 is -$CH=CHR^{13}$, -$C\equiv CR^{13}$, -CH_2Cl, -CH_2Br, or -CH_2I, when R^3 is hydrogen, -$OC(=O)NR^{11a}R^{11b}$, or -$NHC(=O)R^5$,

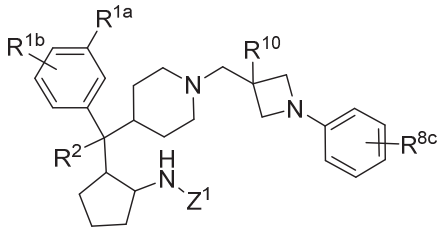
R^7 is selected from the group consisting of -$CH=CHR^{13}$, -$C\equiv CR^{13}$, -CH_2Cl, -CH_2Br, and -CH_2I;

R^{12a} and R^{12b} taken together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclo;

R^{13} is selected from the group consisting of hydrogen, C_{1-4} alkyl, and (amino)alkyl; and

s is 2, 3, 4, or 5.

In yet another aspect, the present disclosure refers to a compound having Formula **XX**:



XX,

or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen and halo;

R^2 is cyano;

Z^1 is selected from the group consisting of $-C(=O)R^7$ and $-S(=O)_2R^7$;

R^7 is selected from the group consisting of $-CH=CHR^{13}$, $-C\equiv CR^{13}$, $-CH_2Cl$, $-CH_2Br$, and $-CH_2I$;

R^{13} is selected from the group consisting of hydrogen and methyl;

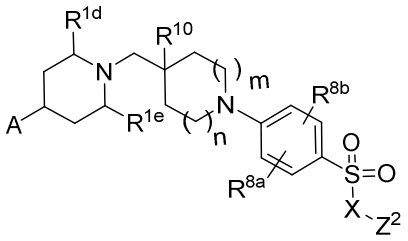
R^{10} is hydrogen; and

R^{8c} is selected from the group consisting of hydrogen, halo, cyano, hydroxy, amino, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{1-4} alkoxy.

In still another aspect, there is provided a pharmaceutical composition comprising the compound as disclosed herein, or the pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier. In another aspect, there is also provided the pharmaceutical composition as disclosed herein for use in therapy. In another aspect of the present disclosure, there is also provided the use of the compound of the present disclosure, or a pharmaceutically acceptable salt or solvate thereof, for

What is Claimed Is:

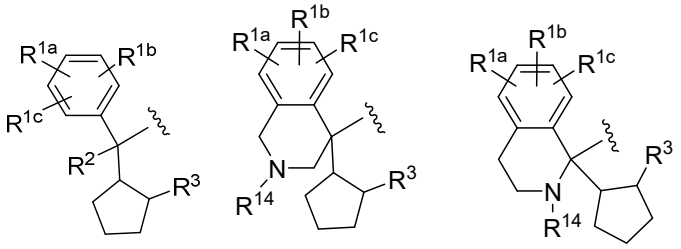
1. A compound having Formula **I**:



I,

or a pharmaceutically acceptable salt or solvate thereof, wherein:

A is selected from the group consisting of:



A-1 , A-2 and A-3 ;

R^{1a}, R^{1b}, and R^{1c} are each independently selected from the group consisting of hydrogen, halo, cyano, hydroxy, amino, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{1-4} alkoxy;

R^{1d} and R^{1e} are independently selected from the group consisting of hydrogen and C_{1-4} alkyl;

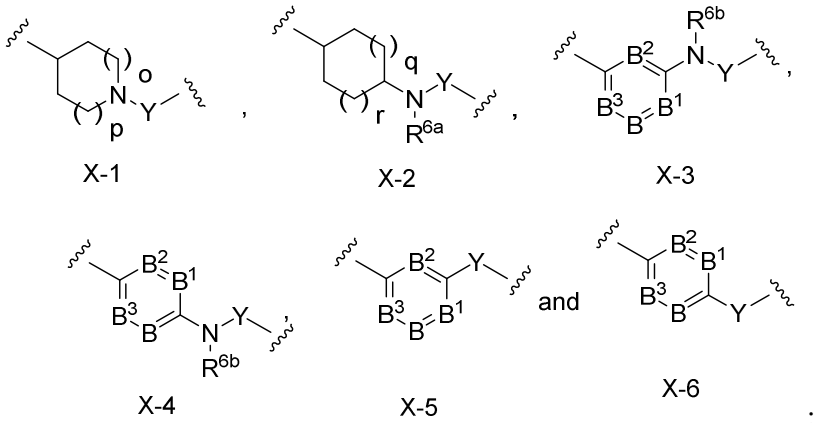
R^2 is selected from the group consisting of hydroxy, amino, cyano, and $-CH_2R^4$;

R^3 is selected from the group consisting of hydrogen, $-OC(=O)NR^{11a}R^{11b}$, $-NHC(=O)R^5$, and $-NHZ^1$;

R^4 is selected from the group consisting of amino, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is selected from the group consisting of $-NR^{12a}R^{12b}$, C_{1-4} alkoxy, and C_{1-4} alkyl;

X is selected from the group consisting of:



;

wherein Y is attached to Z^2; or

X is absent;

Y is selected from the group consisting of -C(=O)- and -$S(=O)_2$-;

R^{6a} and R^{6b} are independently selected from the group consisting of hydrogen and C_{1-4} alkyl;

o, p, q, and r are each independently 0, 1, 2, or 3;

m and n are 0;

Z^1 is selected from the group consisting of -C(=O)R^7 and -$S(=O)_2R^7$;

Z^2 is selected from the group consisting of -CH=CHR^{13}, -C≡CR^{13}, -CH_2Cl, -CH_2Br, -CH_2I, alkyl, optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted cycloalkyl,

with proviso that Z^2 is -CH=CHR^{13}, -C≡CR^{13}, -CH_2Cl, -CH_2Br, or -CH_2I, when R^3 is hydrogen, -OC(=O)$NR^{11a}R^{11b}$, or -NHC(=O)R^5,

R^7 is selected from the group consisting of -CH=CHR^{13}, -C≡CR^{13}, -CH_2Cl, -CH_2Br, and -CH_2I;

R^{8a} and R^{8b} are independently selected from the group consisting of hydrogen, hydrogen, halo, cyano, hydroxy, amino, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{1-4} alkoxy;

R^{9a} is selected from the group consisting of hydrogen, hydrogen, halo, cyano, hydroxy, amino, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{1-4} alkoxy;

R^{10} is selected from the group consisting of hydrogen, halo, C_{1-4} alkyl, and hydroxy;

R^{11a} and R^{11b} are independently selected from the group consisting of hydrogen and C_{1-4} alkyl; or

R^{11a} and R^{11b} taken together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclo; and

R^{12a} and R^{12b} are independently selected from the group consisting of hydrogen and C_{1-4} alkyl; or

R^{12a} and R^{12b} taken together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclo;

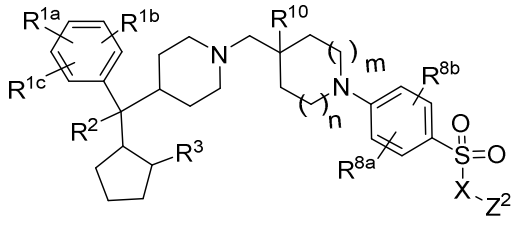
R^{13} is selected from the group consisting of hydrogen, C_{1-4} alkyl, and (amino)alkyl;

R^{14} is selected from the group consisting of hydrogen and C_{1-4} alkyl; and

B, B^1, B^2, and B^3 are each independently selected from the group consisting of $=CR^{9a}$- and =N-,

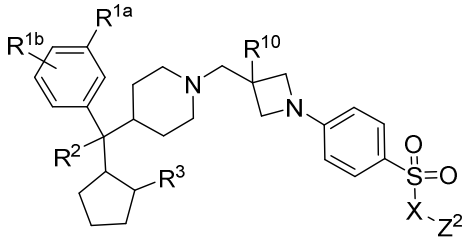
with proviso that at least one of B, B^1, B^2, and B^3 is $=CR^{9a}$-.

2. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, having Formula **I-A-I**:



I-A-I.

3. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, having Formula **X**:



X,

wherein:

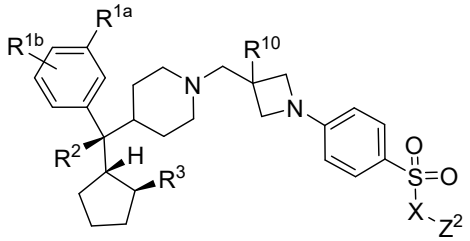
X is selected from the group consisting of X-1, X-2, X-3, X-4, X-5, and X-6; or

X is absent;

Z^2 is selected from the group consisting of -CH=CHR^{13} and -C≡CR^{13}; and

R^3 is selected from the group consisting of -OC(=O)N$R^{11a}R^{11b}$ and -NHC(=O)R^5.

4. The compound of claim 1 or 3, or a pharmaceutically acceptable salt or solvate thereof, having Formula **XI**:



XI.

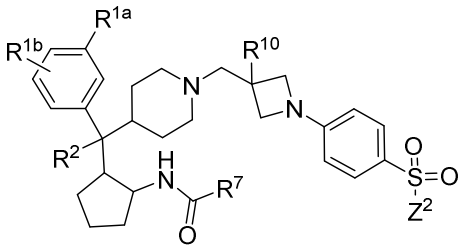
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein X is X-1.

6. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein X is X-2.

7. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein X is X-3 and B, B^1, B^2, and B^3 are =CR^{9a}-.

8. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein X is X-4 and B, B^1, B^2, and B^3 are =CR^{9a}-.

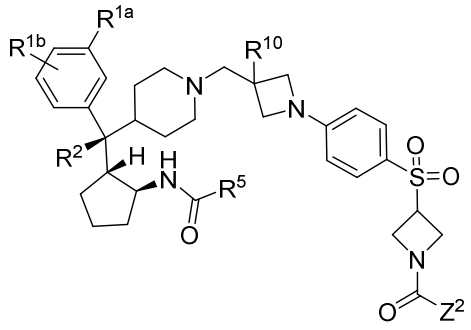
9. The compound of claim 2, or a pharmaceutically acceptable salt or solvate thereof, having Formula **XII**:



XII

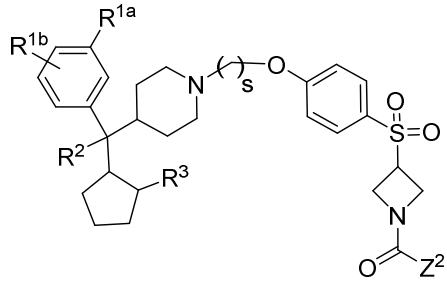
wherein Z^2 is selected from the group consisting of alkyl, optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted cycloalkyl.

10. The compound of claim 2, or a pharmaceutically acceptable salt or solvate thereof, having Formula **XIV**:

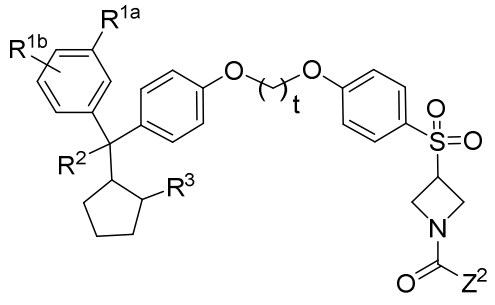


XIV.

11. A compound having Formula **XV** or Formula **XVI**:



XV,



XVI,

or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, halo, cyano, hydroxy, amino, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{1-4} alkoxy;

R^2 is selected from the group consisting of hydroxy, amino, cyano, and $-CH_2R^4$;

R^3 is selected from the group consisting of hydrogen, -OC(=O)$NR^{11a}R^{11b}$, -NHC(=O)R^5, and -NHZ^1;

R^4 is selected from the group consisting of amino, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is selected from the group consisting of -$NR^{12a}R^{12b}$, C_{1-4} alkoxy, and C_{1-4} alkyl;

Z^1 is selected from the group consisting of -C(=O)R^7 and -S(=O)$_2R^7$;

Z^2 is selected from the group consisting of -CH=CHR^{13}, -C≡CR^{13}, -CH_2Cl, -CH_2Br, -CH_2I, alkyl, optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted cycloalkyl,

with proviso that Z^2 is -CH=CHR^{13}, -C≡CR^{13}, -CH_2Cl, -CH_2Br, or -CH_2I, when R^3 is hydrogen, -OC(=O)$NR^{11a}R^{11b}$, or -NHC(=O)R^5,

R^7 is selected from the group consisting of -CH=CHR^{13}, -C≡CR^{13}, -CH_2Cl, -CH_2Br, and -CH_2I;

R^{11a} and R^{11b} are independently selected from the group consisting of hydrogen and C_{1-4} alkyl; or

R^{11a} and R^{11b} taken together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclo; and

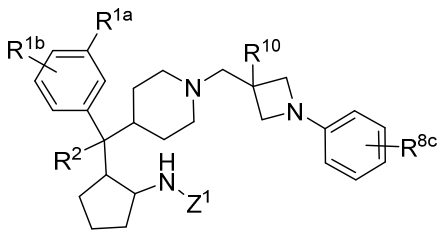
R^{12a} and R^{12b} are independently selected from the group consisting of hydrogen and C_{1-4} alkyl; or

R^{12a} and R^{12b} taken together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclo;

R^{13} is selected from the group consisting of hydrogen, C_{1-4} alkyl, and (amino)alkyl; and

s is 2, 3, 4, or 5.

12. A compound having Formula **XX**:



XX,

or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen and halo;

R^2 is cyano;

Z^1 is selected from the group consisting of $-C(=O)R^7$ and $-S(=O)_2R^7$;

R^7 is selected from the group consisting of $-CH=CHR^{13}$, $-C\equiv CR^{13}$, $-CH_2Cl$, $-CH_2Br$, and $-CH_2I$;

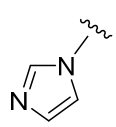
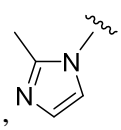
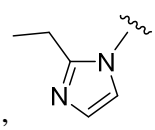
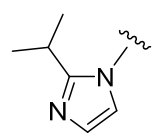
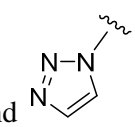
R^{13} is selected from the group consisting of hydrogen and methyl;

R^{10} is hydrogen; and

R^{8c} is selected from the group consisting of hydrogen, halo, cyano, hydroxy, amino, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{1-4} alkoxy.

13. The compound of claim 12, wherein R^{13} is hydrogen.

14. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt or solvate thereof, wherein R^2 is CH_2R^4 and R^4 is:

 ,  ,  ,  and  .

15. The compound of any one of claims 1-14, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{10} is hydrogen.

16. The compound of any one of claims 1-15, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1a} and R^{1b} are independently selected from the group consisting of hydrogen and halogen.

17. The compound of any one of claims 1-16, or a pharmaceutically acceptable salt or solvate thereof, wherein:

Z^2 is $-CH=CHR^{13}$;

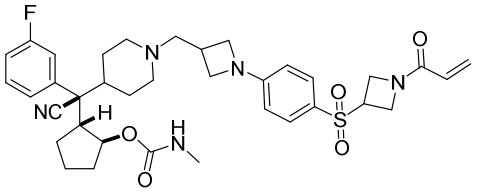
R^{13} is $-CH_2-NR^{22c}R^{22d}$; and

R^{22c} and R^{22d} are each independently selected from the group consisting of hydrogen and C_{1-4} alkyl, or

R^{22c} and R^{22d} are taken together to form a 4- to 8-membered optionally substituted heterocyclo.

18. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein the compound is any one or more of :

1



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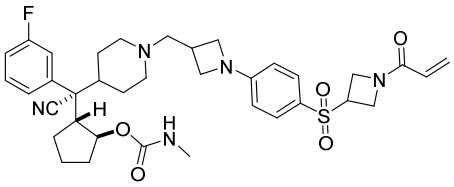

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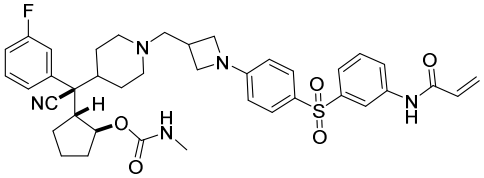

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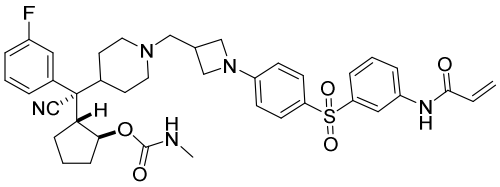

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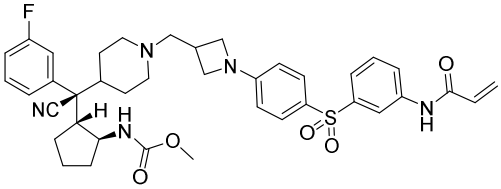

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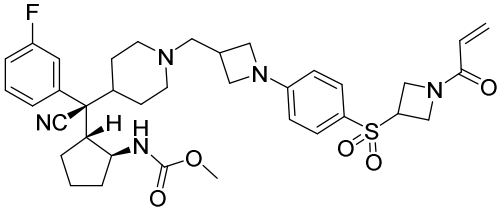

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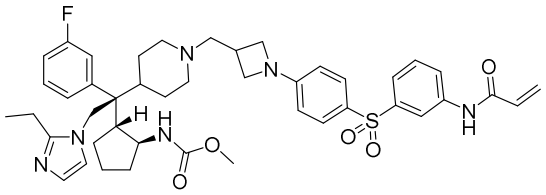

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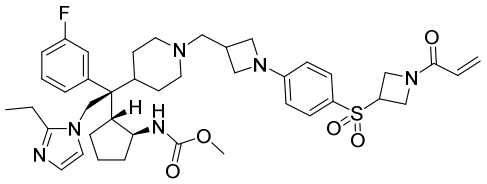

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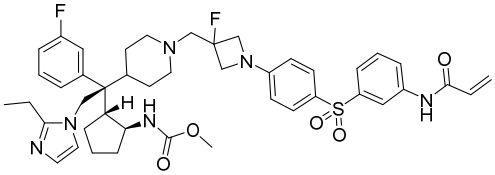

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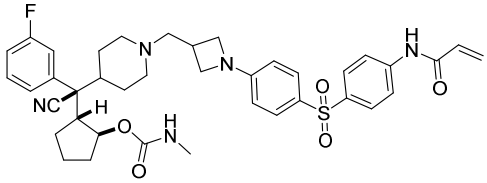

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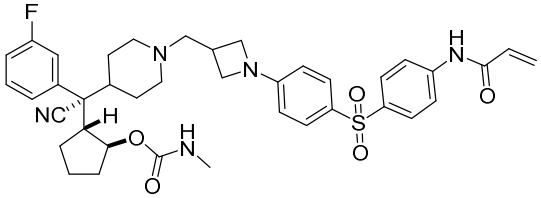

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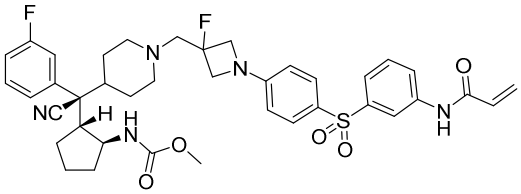

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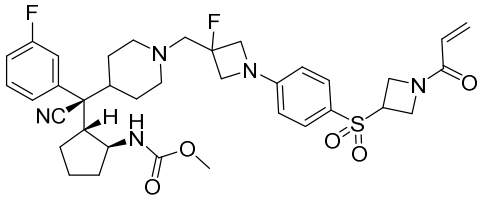

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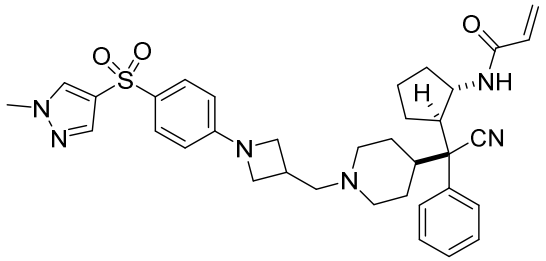

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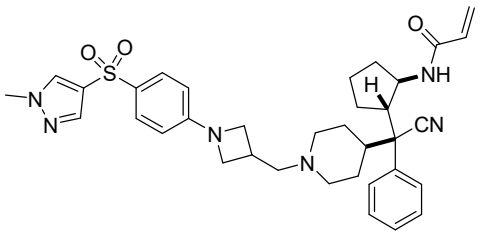

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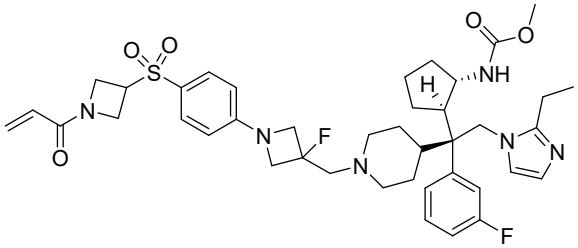

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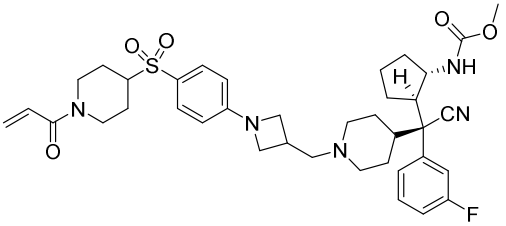

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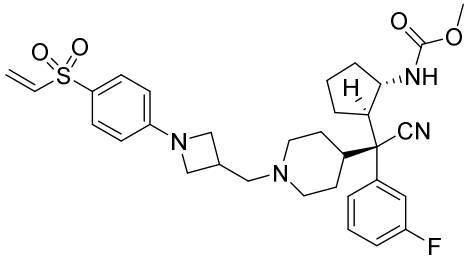

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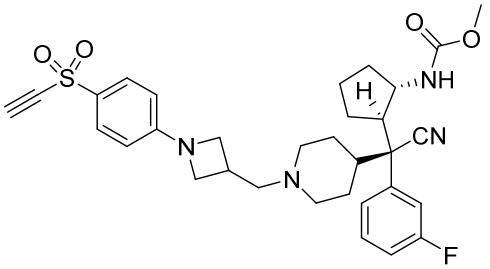

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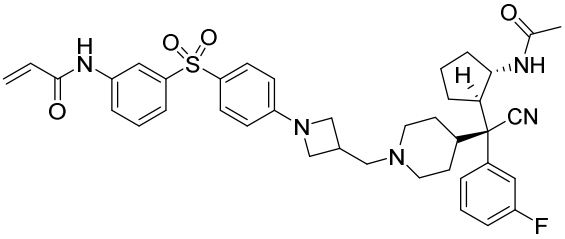

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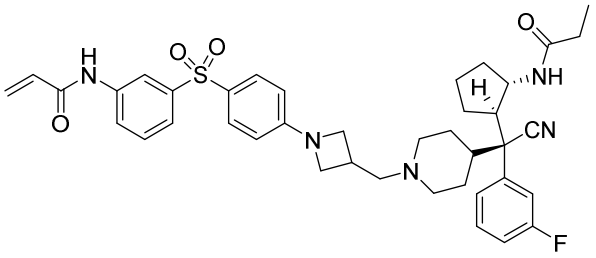

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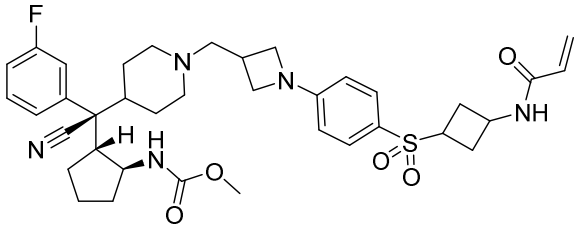

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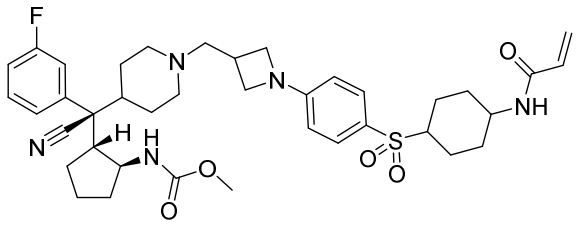

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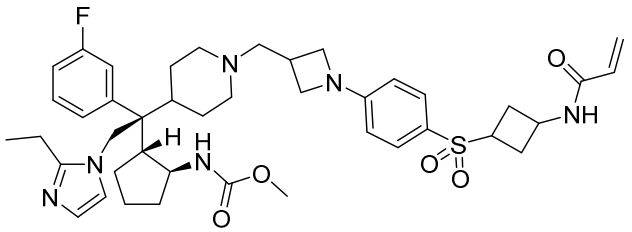

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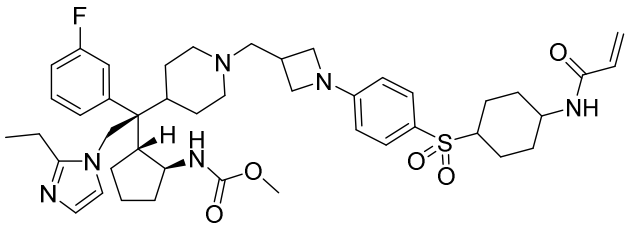

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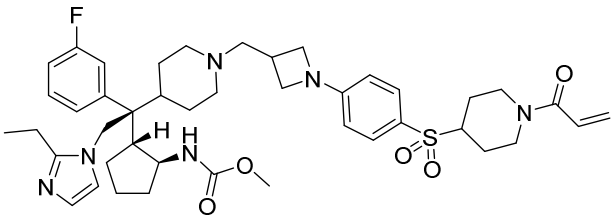

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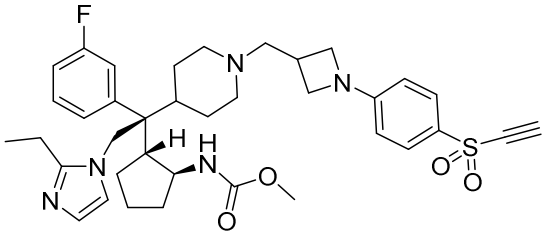

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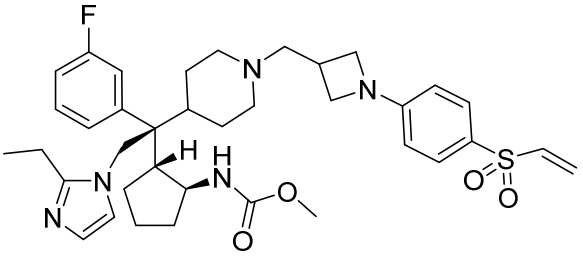

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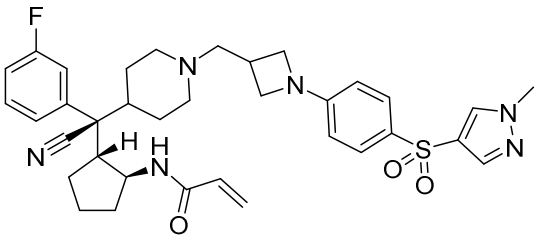

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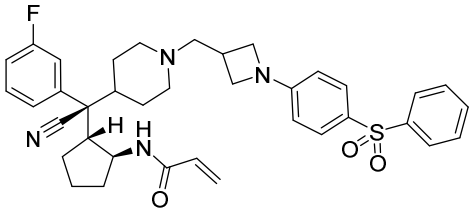

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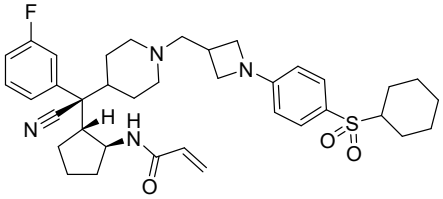

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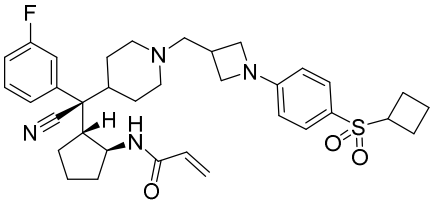

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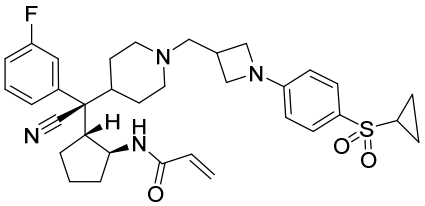

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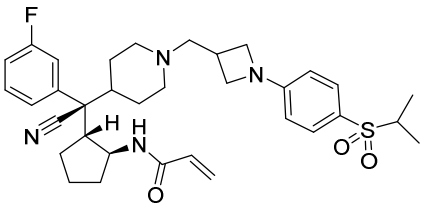

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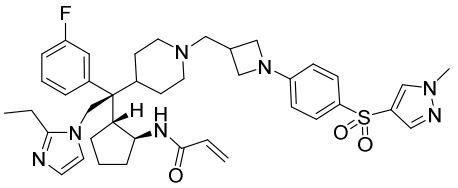

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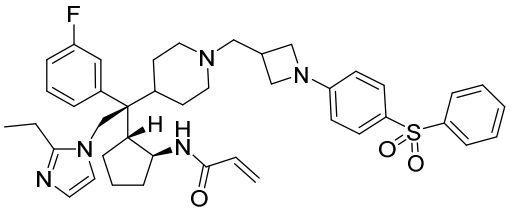

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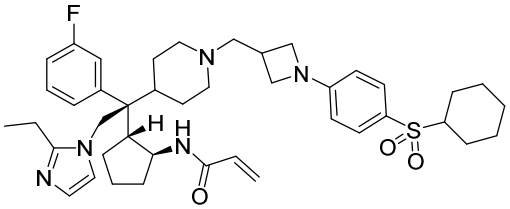

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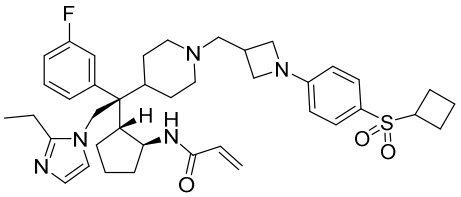

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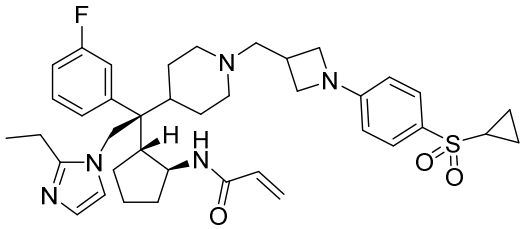

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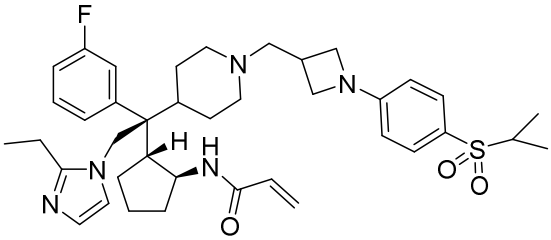

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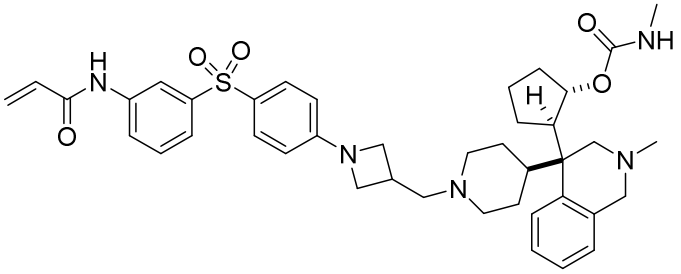

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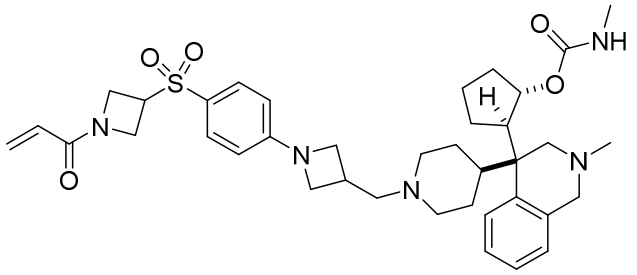

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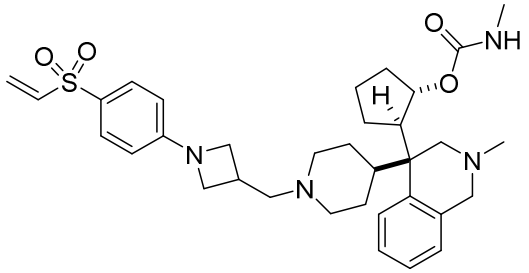

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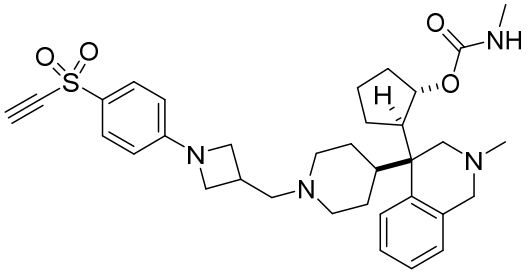

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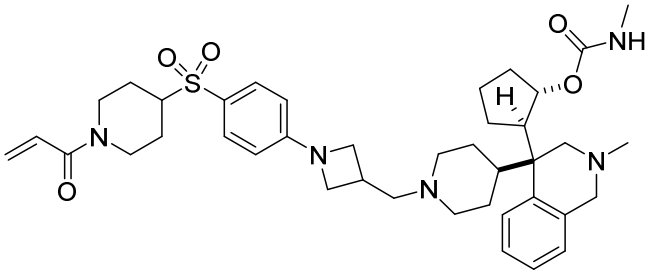

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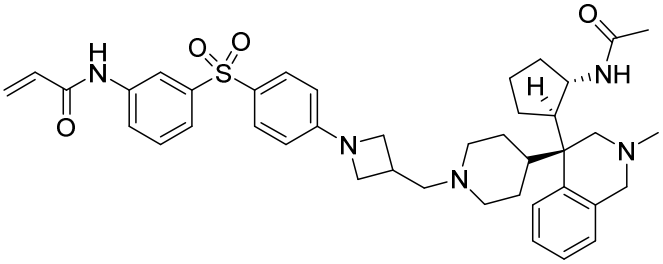

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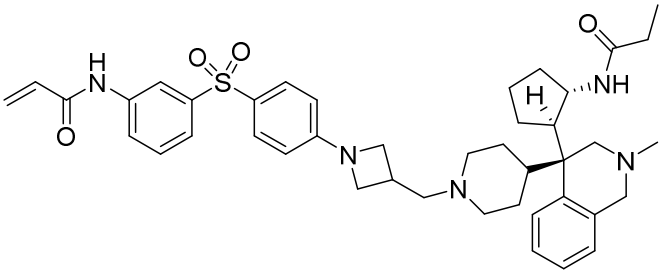

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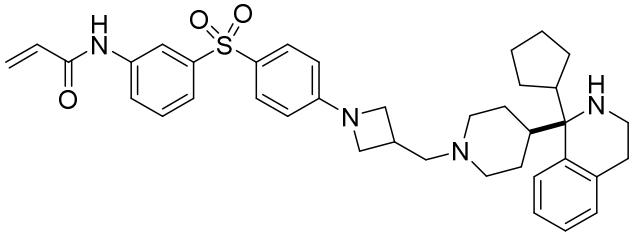

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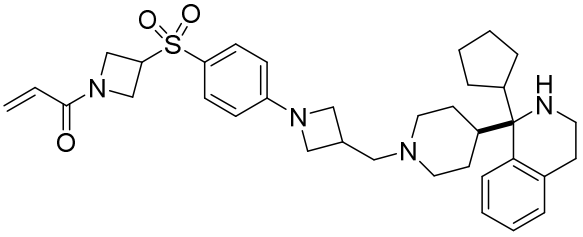

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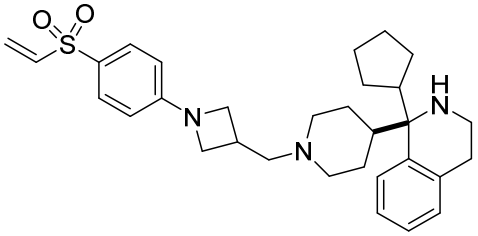

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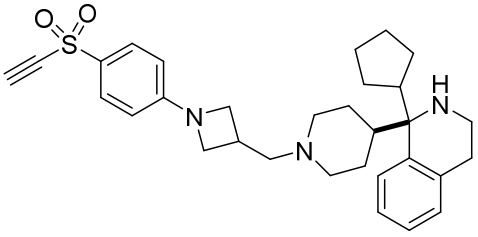

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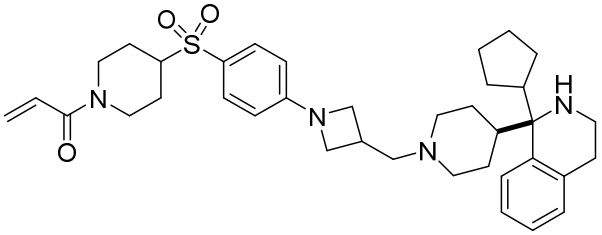

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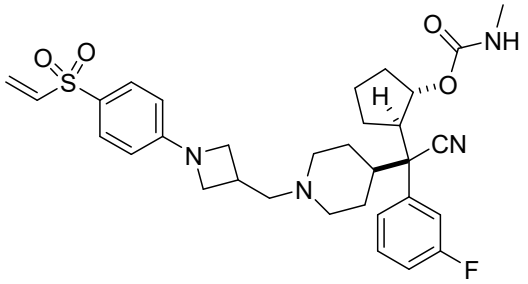

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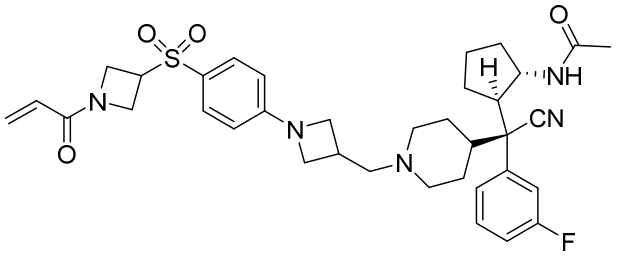

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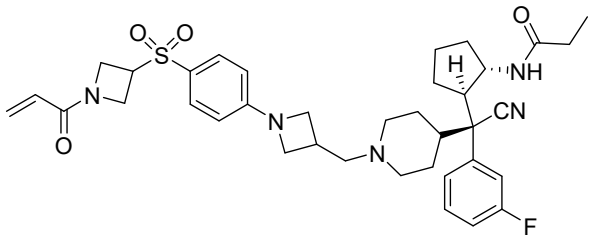

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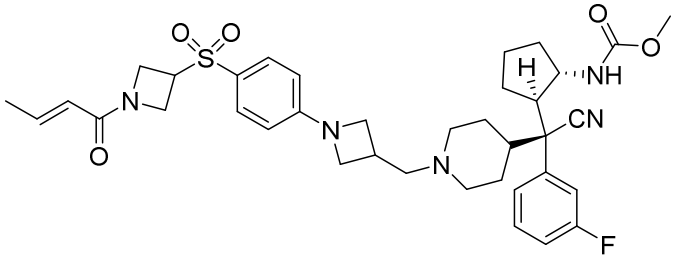

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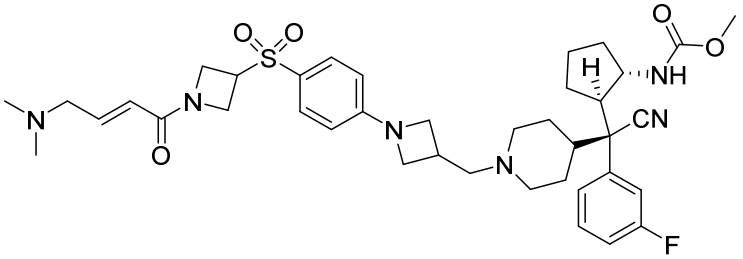

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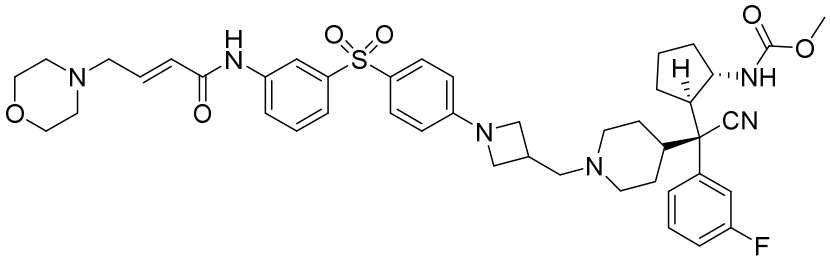

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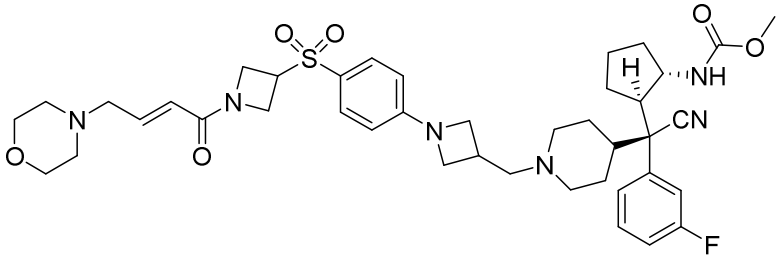

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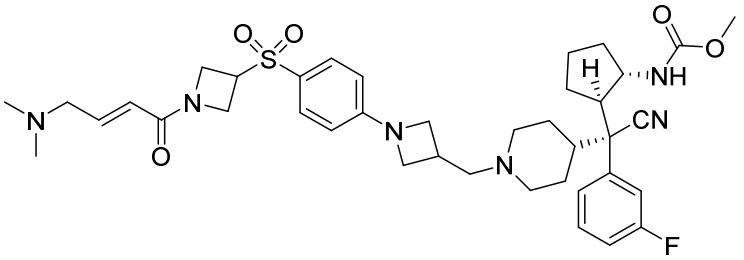

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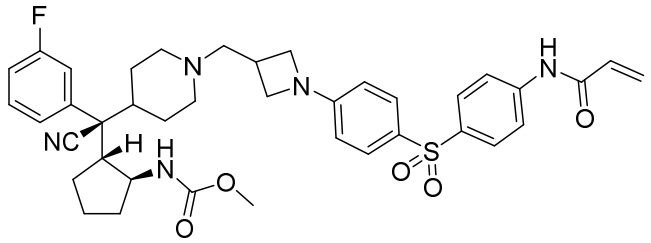

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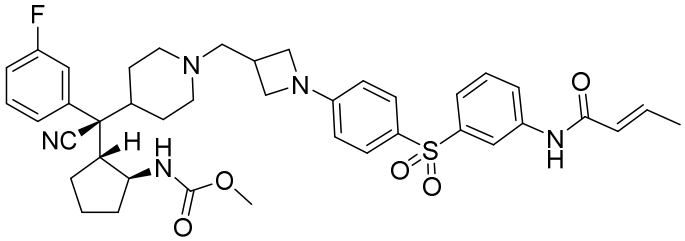

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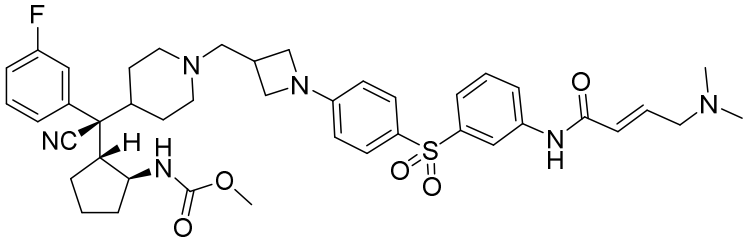

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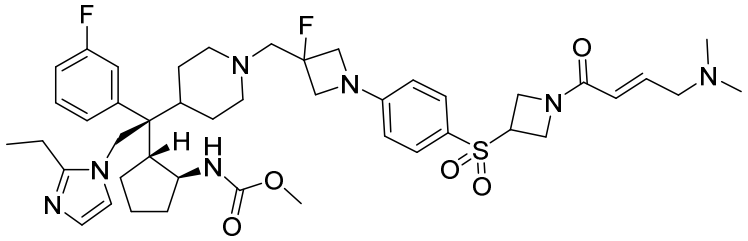

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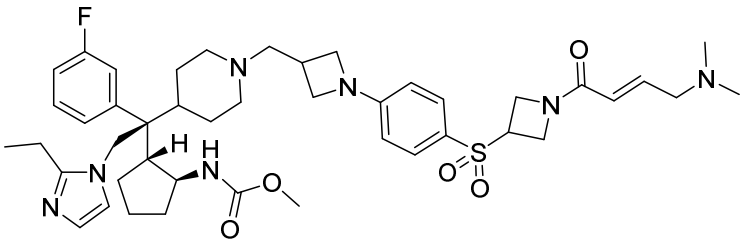

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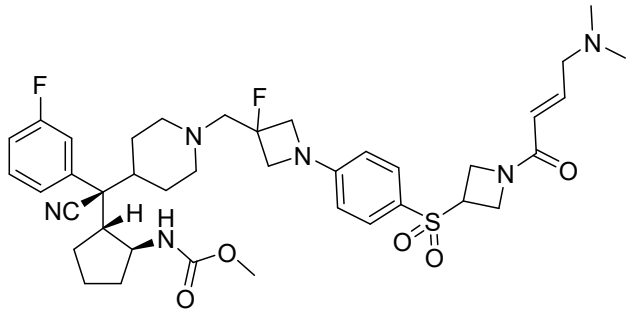

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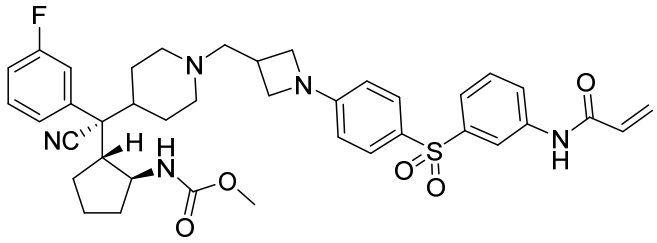

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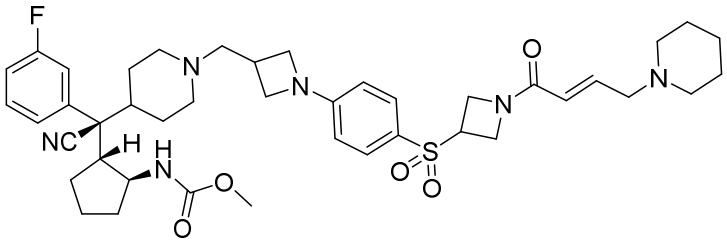

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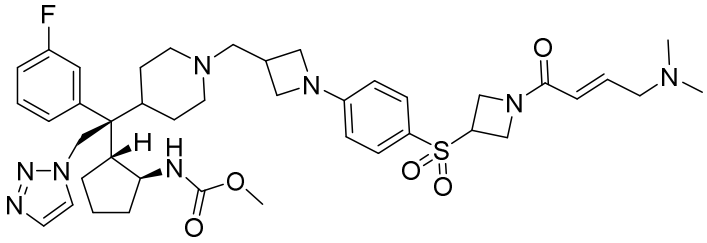

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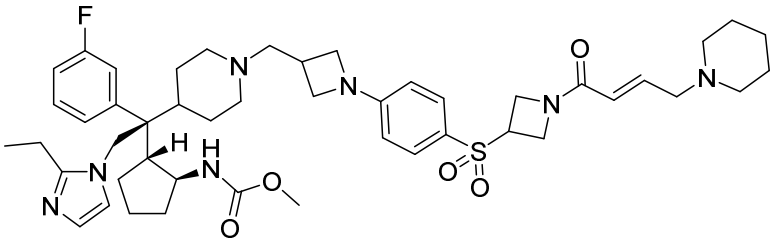
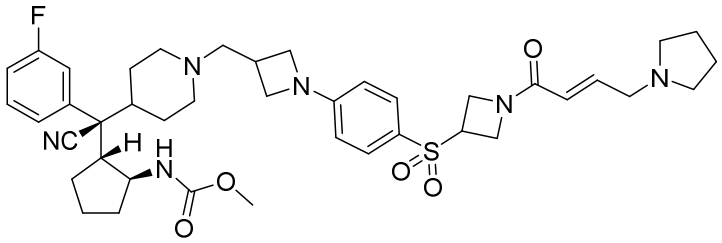
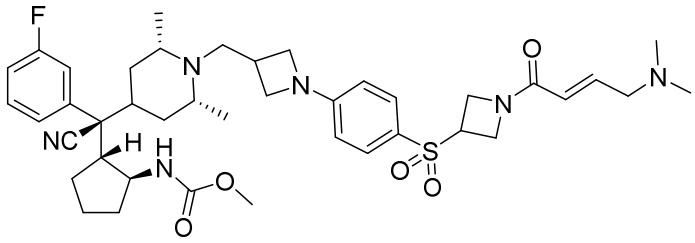
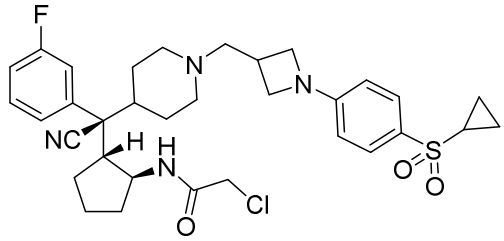
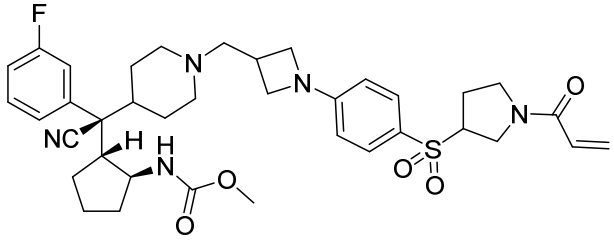
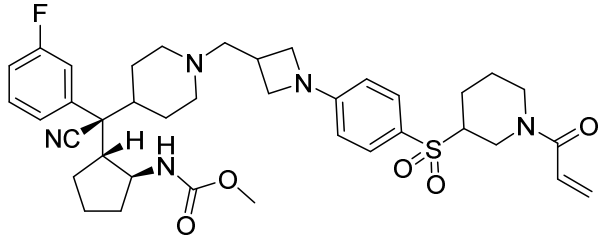


74 

75 

76 

77 

78 

19. The compound of claim 11, wherein the compound is selected from the group consisting of:

methyl ((1S,2R)-2-((S)-cyano(1-(3-(4-((1-((E)-4-(dimethylamino)but-2-enoyl)azetidin-3-yl)sulfonyl) phenoxy)propyl)piperidin-4-yl)(3-fluorophenyl)methyl)cyclopentyl) carbamate;

methyl ((1S,2R)-2-((R)-(4-(2-(4-((1-acryloylazetidin-3-yl)sulfonyl)phenoxy)ethoxy)phenyl)(cyano)(3-fluorophenyl)methyl)cyclopentyl) carbamate; and

methyl ((1S,2R)-2-((S)-(4-(2-(4-((1-acryloylazetidin-3-yl)sulfonyl)phenoxy)ethoxy)phenyl)(cyano)(3-fluorophenyl)methyl)cyclopentyl) carbamate, or a pharmaceutically acceptable salt or solvate thereof.

20. The compound of claim 12, wherein the compound is selected from the group consisting of:

N-((1S,2R)-2-((S)-cyano(1-((1-(4-cyanophenyl)azetidin-3-yl)methyl)piperidin-4-yl)(3-fluorophenyl)methyl)cyclopentyl)ethenesulfonamide;

N-((1S,2R)-2-((S)-cyano(1-((1-(4-cyanophenyl)azetidin-3-yl)methyl)piperidin-4-yl)(3-fluorophenyl)methyl)cyclopentyl)acrylamide;

2-chloro-N-((1S,2R)-2-((S)-cyano(1-((1-(4-cyanophenyl)azetidin-3-yl)methyl)piperidin-4-yl)(3-fluorophenyl)methyl)cyclopentyl)acetamide; and

N-((1S,2R)-2-((S)-cyano(1-((1-(4-cyanophenyl)azetidin-3-yl)methyl)piperidin-4-yl)(3-fluorophenyl)methyl)cyclopentyl)propiolamide, or a pharmaceutically acceptable salt or solvate thereof.

21. A pharmaceutical composition comprising the compound of any one of claims 1-20, or the pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier.

22. The pharmaceutical composition of claim 21 for use in therapy.

23. Use of the compound of any one of claims 1-20, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for treatment of cancer, a chronic autoimmune disorder, an inflammatory condition, a proliferative disorder, sepsis, or a viral infection.

24. The use of claim 23 for treatment of cancer.

25. The use of claim 24, wherein the cancer is selected from the group consisting of acute monocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, and mixed lineage leukemia.