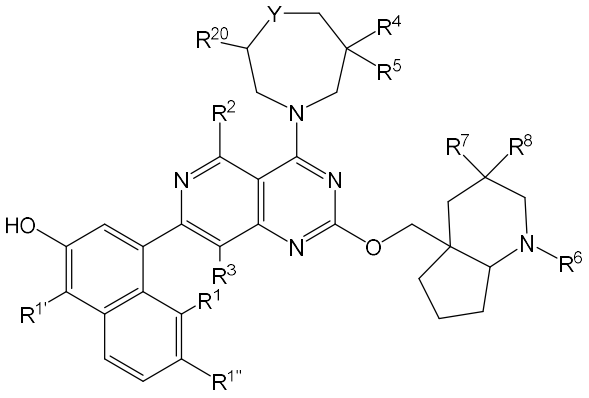
WHAT IS CLAIMED IS:

1. A compound of formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

Y is O or SO_2;

R^1 is hydrogen, halo, ethynyl or ethyl;

$R^{1'}$ is hydrogen, halo, or C_{1-3} alkyl;

$R^{1''}$ is selected from hydrogen, C_{2-3}alkenyl, C_{1-3} alkyl, C_{2-3} alkynyl, halo, and hydroxy;

R^2 is hydrogen;

R^3 is halo;

R^4 and R^5 are the same or different and each is hydrogen, C_{1-4} alkyl, hydroxy, C_{1-4} hydroxyalkyl, or C_{1-4} haloalkyl;

R^{20} is selected from hydrogen and hydroxyC_{1-4}alkyl;

R^6 is C_{1-6} alkyl optionally substituted with one or more deuterium atoms; C_{3-6} cycloalkyl optionally substituted with C_1-C_3alkoxy, C_1-C_3alkoxyC_{1-6} alkyl, amino, or cyanoethynyl; hydroxyC_{1-6} alkyl; haloC_{1-6} alkyl; hydroxy-haloC_{1-6} alkyl; methylsulfonylC_1-C_6alkyl; or $–(CH_2)_n$-A;

wherein A is a cyclic moiety selected from C_{3-6} cycloalkyl, C_{3-10} heterocycloalkyl, aryl, heteroaryl, spiro structures of any of these rings, and bicyclic structures of any of these rings, and n is 0, 1, 2, or 3;

wherein A is optionally substituted with one or more substituents selected from C_{1-4} alkyl, C_{1-4} alkylcarbonyl, C_{3-6} cycloalkylcarbonyl, hydroxy, halo, cyano, haloC_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4}alkyl, C_{1-4} alkoxycarbonyl, haloC_{1-4} alkoxycarbonyl, C_{1-4} alkylcarbamato, amido, C_{1-4} alkylamido, oxo, and methylsulfonyl; and

R^7 and R^8 are the same or different and each is hydrogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkylsulfonyl, or halo.

2. A compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein $R^{1''}$ is halo and wherein the halo is fluoro.

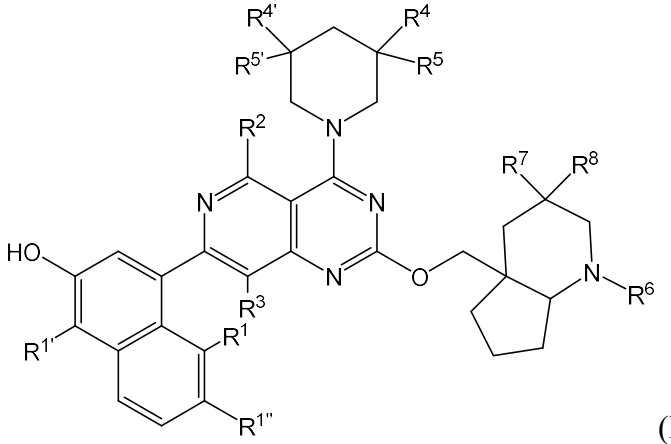
3. A compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–(CH_2)_n$-A.

4. A compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein n is 0.

5. A compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein n is 1.

6. A compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein A is a cyclic moiety selected from C_{4-6} cycloalkyl, C_{3-10} heterocycloalkyl, aryl, heteroaryl, spiro structures of any of these rings, and bicyclic structures of any of these rings.

7. A compound of formula (II):



(II),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is ethynyl or ethyl;

$R^{1'}$ is hydrogen or halo;

$R^{1''}$ is selected from hydrogen, C_{2-3}alkenyl, C_{1-3} alkyl, C_{2-3} alkynyl, halo, and hydroxy;

R^2 is hydrogen;

R^3 is halo;

R^4, R^5, $R^{4'}$, and $R^{5'}$ are the same or different and each is hydrogen, haloC_{1-4} alkyl , C_{1-4} alkyl, hydroxy, or hydroxyC_{1-4}alkyl, or, $R^{4'}$ and $R^{5'}$, together with the atom to which they are attached, form a five-membered heterocycloalkyl ring optionally substituted with oxo;

R^6 is C_{1-6} alkyl, hydroxyC_{1-6} alkyl, haloC_{1-6} alkyl, hydroxy-haloC_{1-6} alkyl, methylsulfonylC_1-C_6alkyl, or $–(CH_2)_n$-A;

wherein A is a cyclic moiety selected from C_{3-6} cycloalkyl, C_{3-7} heterocycloalkyl, spiro structures of either of these rings, and bicyclic structures of either of these rings, and n is 0, 1, or 2;

wherein A is optionally substituted with one or more substituents selected from C_{1-4} alkyl, C_{1-4} alkylcarbonyl, C_{3-6} cycloalkylcarbonyl, hydroxy, halo, haloC_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4}alkyl, C_{1-4} alkoxycarbonyl, haloC_{1-4} alkoxycarbonyl, C_{1-4} alkylcarbamato, amido, C_{1-4} alkylamido, oxo, and methylsulfonyl; and

R^7 and R^8 are the same or different and each is hydrogen, C_{1-6} alkyl, C_{1-6} alkylsulfonyl, or halo.

8. A compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein $R^{1''}$ is halo and wherein the halo is fluoro.

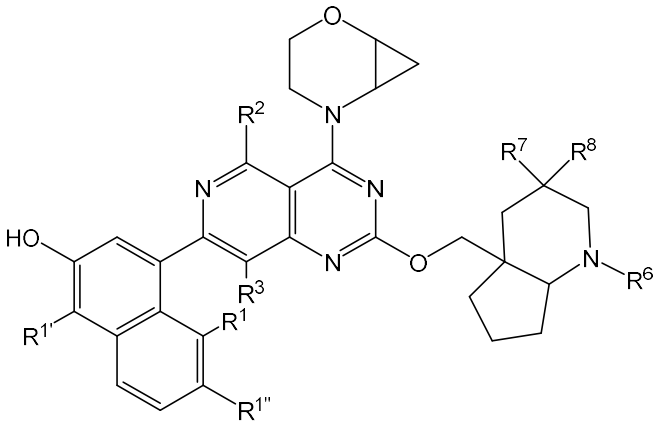
9. A compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–(CH_2)_n$-A.

10. A compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein n is 0.

11. A compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein n is 1.

12. A compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein A is a cyclic moiety selected from C_{4-6} cycloalkyl, C_{3-10} heterocycloalkyl, aryl, heteroaryl, spiro structures of any of these rings, and bicyclic structures of any of these rings.

13. A compound of formula (III):



(III),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is ethynyl or ethyl;

$R^{1'}$ is hydrogen or halo;

$R^{1''}$ is selected from hydrogen, C_{2-3}alkenyl, C_{1-3} alkyl, C_{2-3} alkynyl, halo, and hydroxy;

R^2 is hydrogen;

R^3 is halo;

R^6 is C_{1-6} alkyl, hydroxyC_{1-6} alkyl, haloC_{1-6} alkyl, hydroxy-haloC_{1-6} alkyl, methylsulfonylC_1-C_6alkyl, or $–(CH_2)_n$-A;

wherein A is a cyclic moiety selected from C_{3-6} cycloalkyl, C_{3-7} heterocycloalkyl, spiro structures of either of these rings, and bicyclic structures of either of these rings, and n is 0, 1, or 2;

wherein A is optionally substituted with one or more substituents selected from C_{1-4} alkyl, C_{1-4} alkylcarbonyl, C_{3-6} cycloalkylcarbonyl, hydroxy, halo, hydroxyC_{1-6} alkyl, haloC_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4}alkyl, C_{1-4} alkoxycarbonyl, haloC_{1-4} alkoxycarbonyl, C_{1-4} alkylcarbamato, amido, C_{1-4} alkylamido, oxo, and methylsulfonyl; and

R^7 and R^8 are the same or different and each is hydrogen, C_{1-6} alkyl, C_{1-6} alkylsulfonyl, or halo.

14. A compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein $R^{1''}$ is halo and wherein the halo is fluoro.

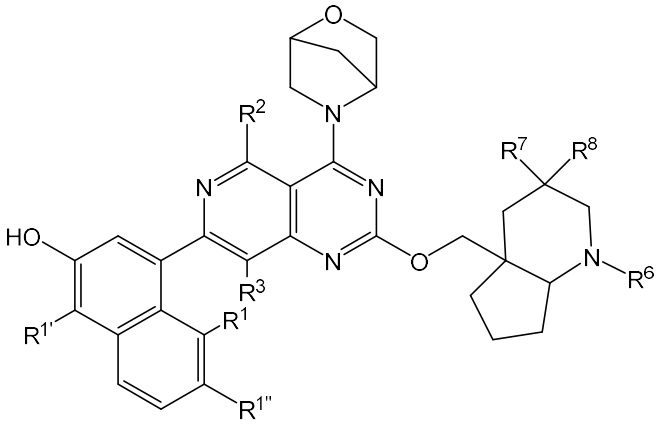
15. A compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–(CH_2)_n$-A.

16. A compound of claim 15, or a pharmaceutically acceptable salt thereof, wherein n is 0.

17. A compound of claim 15, or a pharmaceutically acceptable salt thereof, wherein n is 1.

18. A compound of claim 15, or a pharmaceutically acceptable salt thereof, wherein A is a cyclic moiety selected from C_{4-6} cycloalkyl, C_{3-10} heterocycloalkyl, aryl, heteroaryl, spiro structures of any of these rings, and bicyclic structures of any of these rings.

19. A compound of formula (IV):



(IV),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is ethynyl or ethyl;

$R^{1'}$ is hydrogen or halo;

$R^{1''}$ is selected from hydrogen, C_{2-3}alkenyl, C_{1-3} alkyl, C_{2-3} alkynyl, halo, and hydroxy;

R^2 is hydrogen;

R^3 is halo;

R^6 is C_{1-6} alkyl, hydroxyC_{1-6} alkyl, haloC_{1-6} alkyl, hydroxy-haloC_{1-6} alkyl, methylsulfonylC_1-C_6alkyl, or $–(CH_2)_n$-A;

wherein A is a cyclic moiety selected from C_{3-6} cycloalkyl, C_{3-7} heterocycloalkyl, spiro structures of either of these rings, and bicyclic structures of either of these rings, and n is 0, 1, or 2;

wherein A is optionally substituted with one or more substituents selected from C_{1-4} alkyl, C_{1-4} alkylcarbonyl, C_{3-6} cycloalkylcarbonyl, hydroxy, halo, haloC_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4}alkyl, C_{1-4} alkoxycarbonyl, haloC_{1-4} alkoxycarbonyl, C_{1-4} alkylcarbamato, amido, C_{1-4} alkylamido, oxo, and methylsulfonyl; and

R^7 and R^8 are the same or different and each is hydrogen, C_{1-6} alkyl, C_{1-6} alkylsulfonyl, or halo.

20. A compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein $R^{1''}$ is halo and wherein the halo is fluoro.

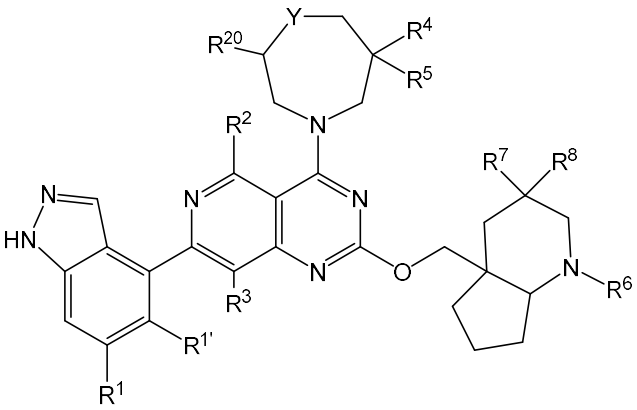
21. A compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–(CH_2)_n$-A.

22. A compound of claim 21, or a pharmaceutically acceptable salt thereof, wherein n is 0.

23. A compound of claim 21, or a pharmaceutically acceptable salt thereof, wherein n is 1.

24. A compound of claim 21, or a pharmaceutically acceptable salt thereof, wherein A is a cyclic moiety selected from C_{4-6} cycloalkyl, C_{3-10} heterocycloalkyl, aryl, heteroaryl, spiro structures of any of these rings, and bicyclic structures of any of these rings.

25. A compound of formula (V):



(V),

or a pharmaceutically acceptable salt thereof, wherein:

Y is O or SO_2;

R^1 and $R^{1'}$ are the same or different and each is hydrogen, halo, C_{1-4} alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

R^2 is hydrogen;

R^3 is halo;

R^4 and R^5 are the same or different and each is hydrogen, C_{1-4} alkyl, or hydroxy;

R^{20} is selected from hydrogen and hydroxyC_{1-4}alkyl;

R^6 is C_{1-6} alkyl, hydroxyC_{1-6} alkyl, haloC_{1-6} alkyl, hydroxy-haloC_{1-6} alkyl, methylsulfonylC_1-C_6alkyl, or $–(CH_2)_n$-A;

wherein A is a cyclic moiety selected from C_{3-6} cycloalkyl, C_{3-7} heterocycloalkyl, spiro structures of either of these rings, and bicyclic structures of either of these rings, and n is 0, 1, or 2;

wherein A is optionally substituted with one or more substituents selected from C_{1-4} alkyl, C_{1-4} alkylcarbonyl, cyano, C_{3-6} cycloalkylcarbonyl, hydroxy, halo, haloC_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4}alkyl, C_{1-4} alkoxycarbonyl, haloC_{1-4} alkoxycarbonyl, C_{1-4} alkylcarbamato, amido, C_{1-4} alkylamido, oxo, hydroxy C_{1-4}alkyl, and methylsulfonyl; and

R^7 and R^8 are the same or different and each is hydrogen, C_{1-6} alkyl, C_{1-6} alkylsulfonyl, or halo.

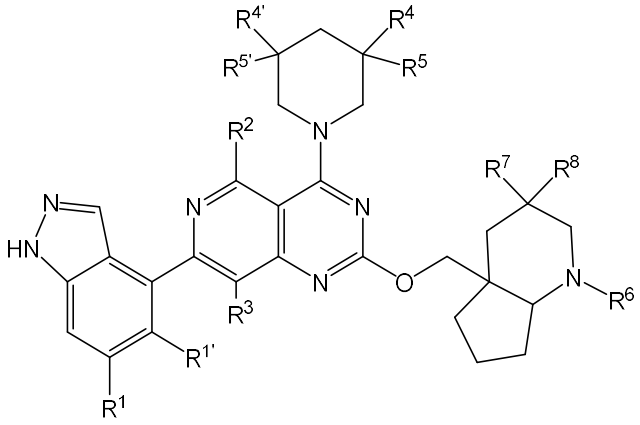
26. A compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–(CH_2)_n$-A.

27. A compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein n is 0.

28. A compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein n is 1.

29. A compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein A is a cyclic moiety selected from C_{4-6} cycloalkyl, C_{3-10} heterocycloalkyl, aryl, heteroaryl, spiro structures of any of these rings, and bicyclic structures of any of these rings.

30. A compound of formula (VI):



(VI),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 and $R^{1'}$ are the same or different and each is hydrogen, halo, C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

R^2 is hydrogen;

R^3 is halo;

R^4, R^5, $R^{4'}$, and $R^{5'}$ are the same or different and each is hydrogen, haloC_{1-4} alkyl , C_{1-4} alkyl, hydroxy, or hydroxyC_{1-4}alkyl, or, $R^{4'}$ and $R^{5'}$, together with the atom to which they are attached, form a five-membered heterocycloalkyl ring optionally substituted with oxo;

R^6 is C_{1-6} alkyl, hydroxyC_{1-6} alkyl, haloC_{1-6} alkyl, hydroxy-haloC_{1-6} alkyl, methylsulfonylC_1-C_6alkyl, or $–(CH_2)_n$-A;

wherein A is a cyclic moiety selected from C_{3-6} cycloalkyl, C_{3-7} heterocycloalkyl, spiro structures of either of these rings, and bicyclic structures of either of these rings, and n is 0, 1, or 2;

wherein A is optionally substituted with one or more substituents selected from C_{1-4} alkyl, C_{1-4} alkylcarbonyl, C_{3-6} cycloalkylcarbonyl, hydroxy, halo, haloC_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4}alkyl, C_{1-4} alkoxycarbonyl, haloC_{1-4} alkoxycarbonyl, C_{1-4} alkylcarbamato, amido, C_{1-4} alkylamido, oxo, and methylsulfonyl; and

R^7 and R^8 are the same or different and each is hydrogen, C_{1-6} alkyl, C_{1-6} alkylsulfonyl, or halo.

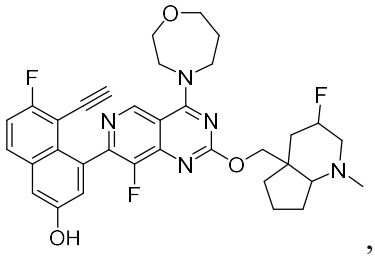
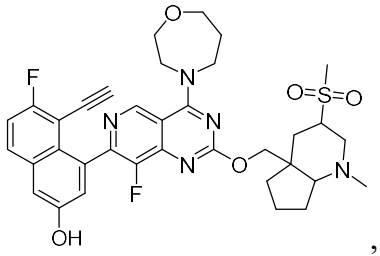
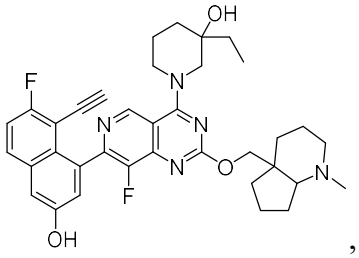
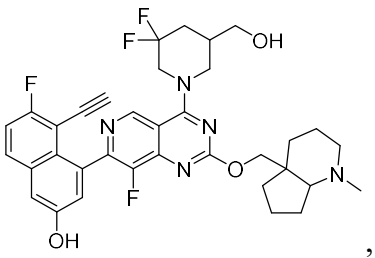
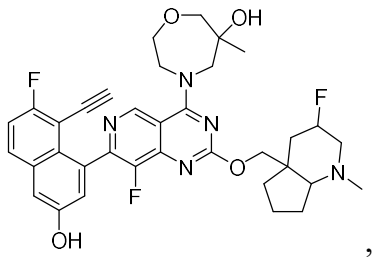
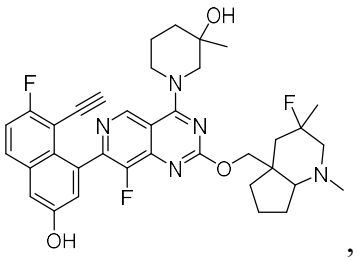
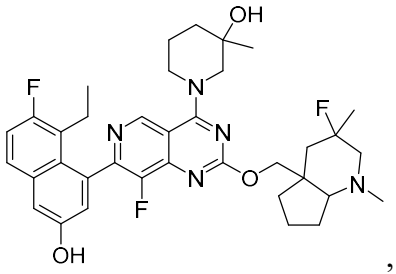
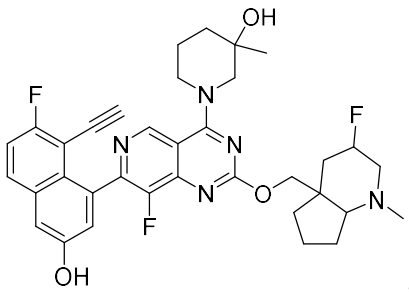
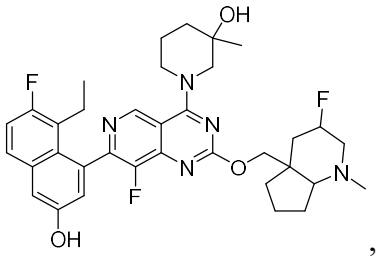
31. A compound of claim 30, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–(CH_2)_n$-A.

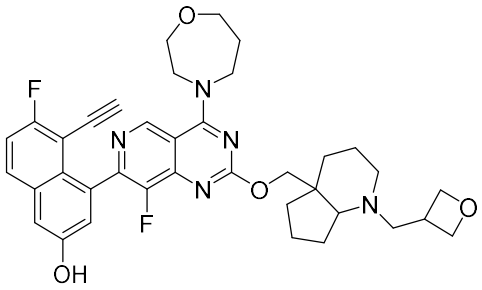
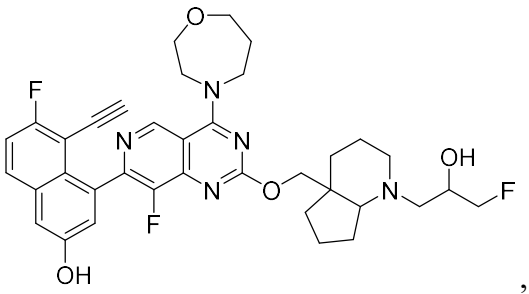
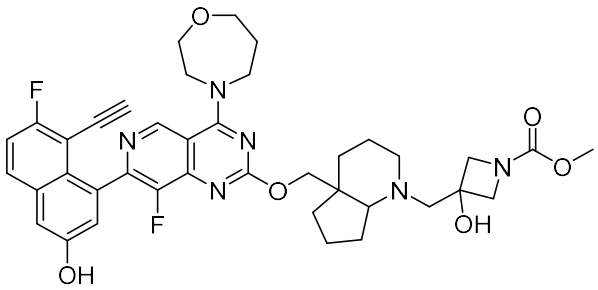
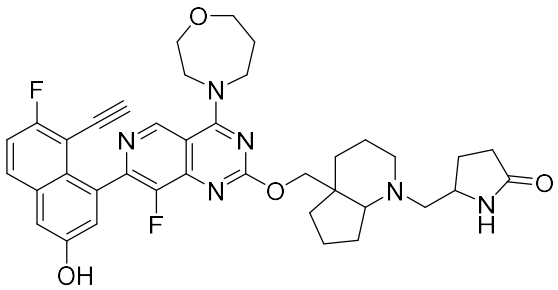
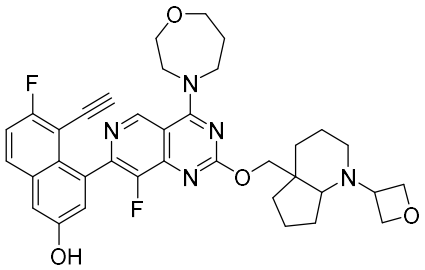
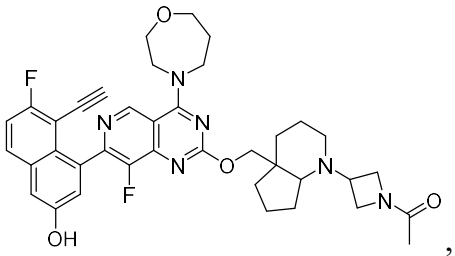
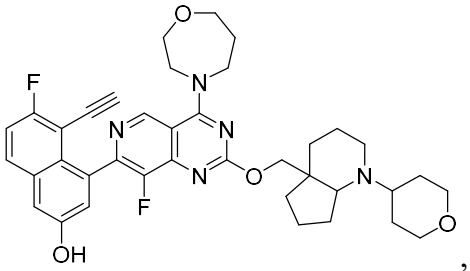
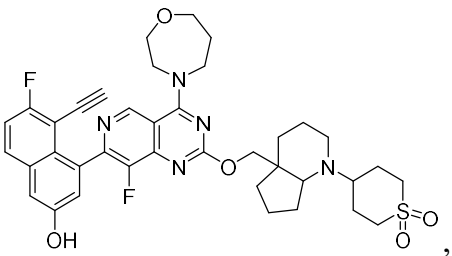
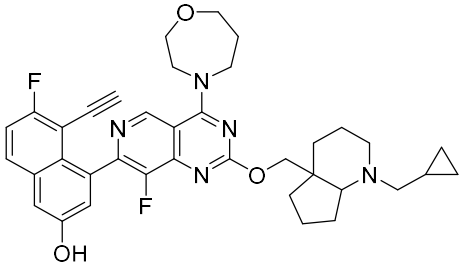
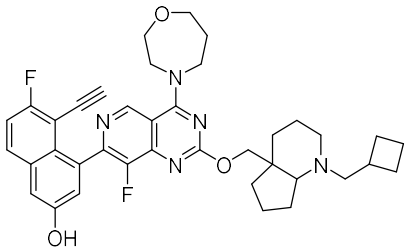
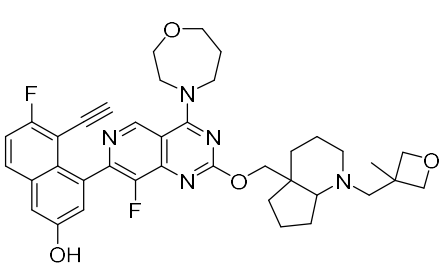
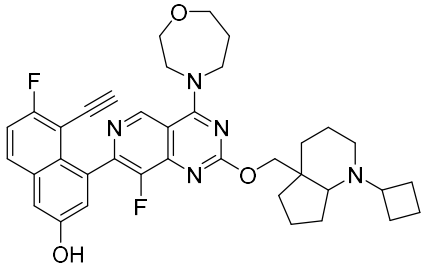
32. A compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein n is 0.

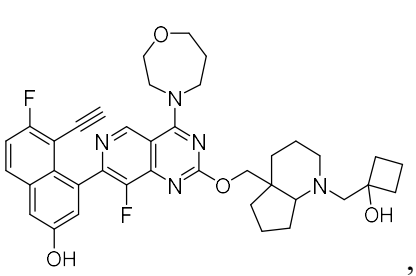
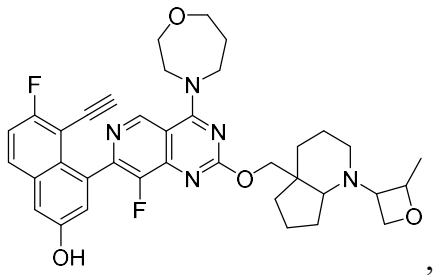
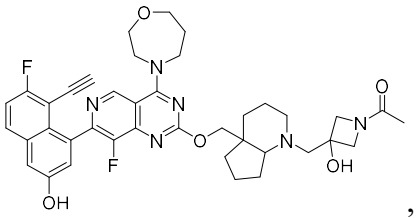
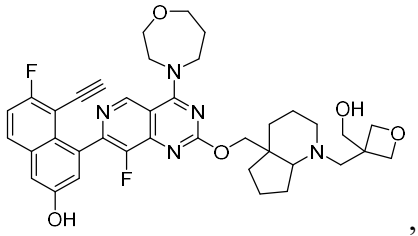
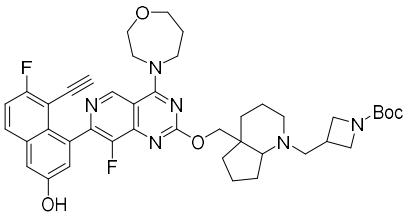
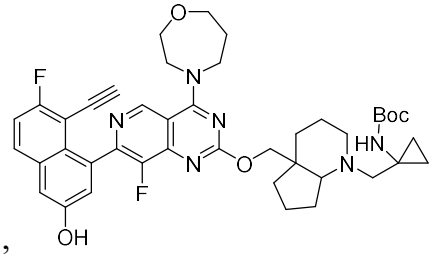
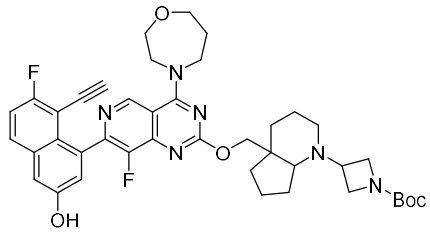
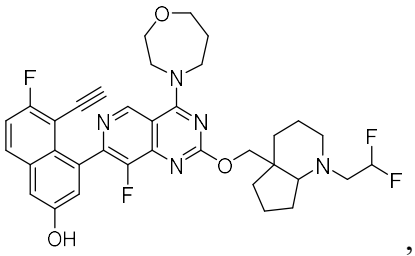
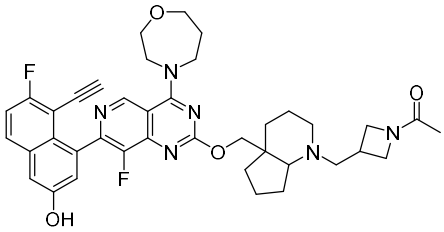
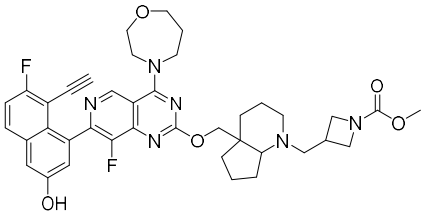
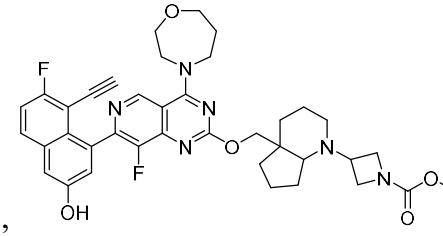
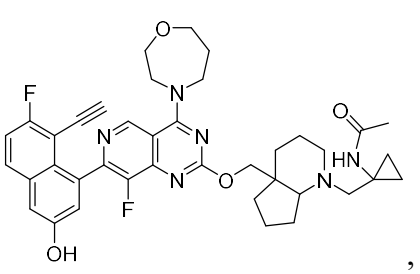
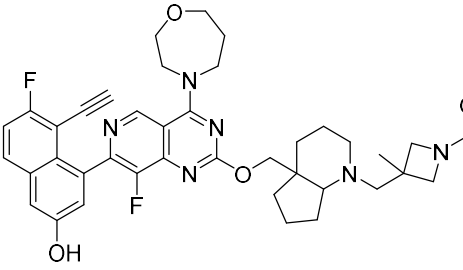
33. A compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein n is 1.

34. A compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein A is a cyclic moiety selected from C_{4-6} cycloalkyl, C_{3-10} heterocycloalkyl, aryl, heteroaryl, spiro structures of any of these rings, and bicyclic structures of any of these rings.

35. A compound selected from the group consisting of

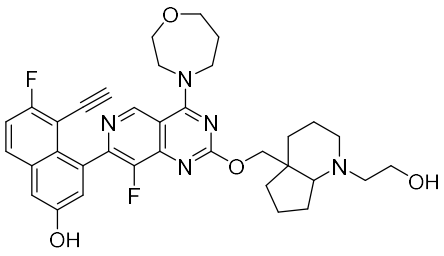
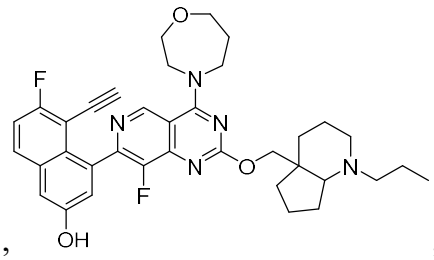
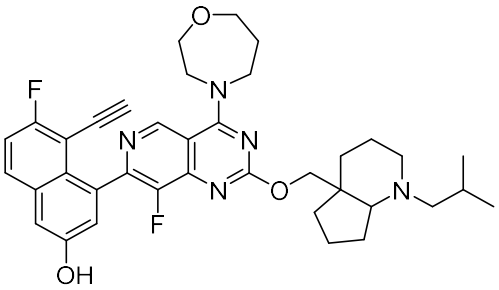
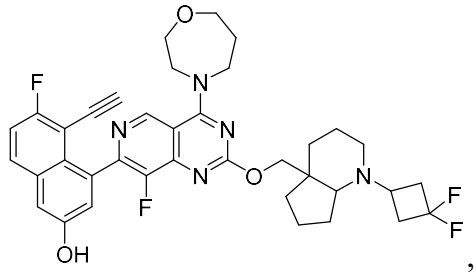
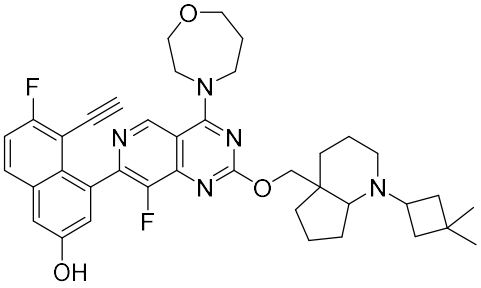
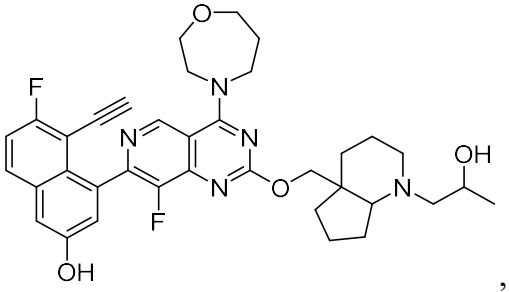
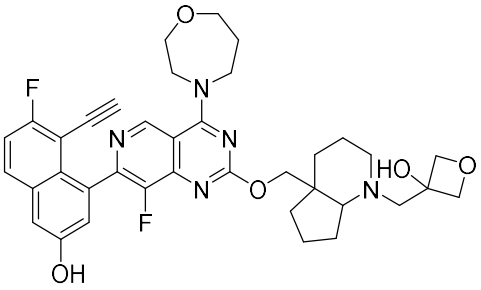
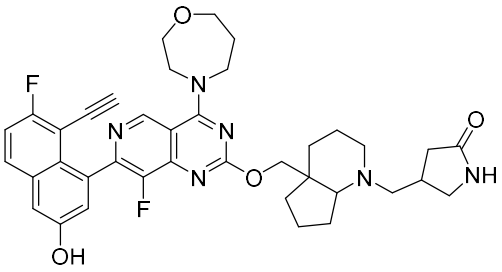
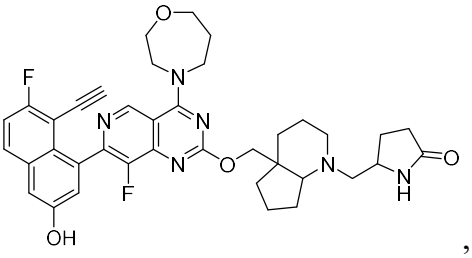
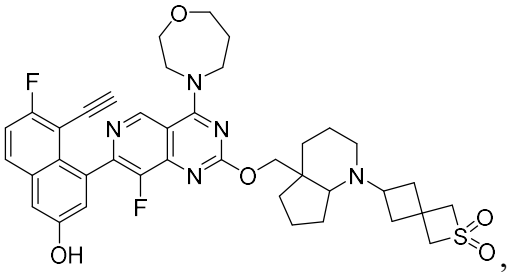
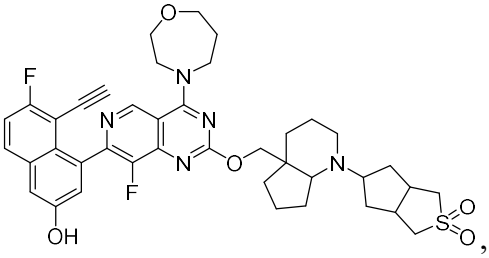
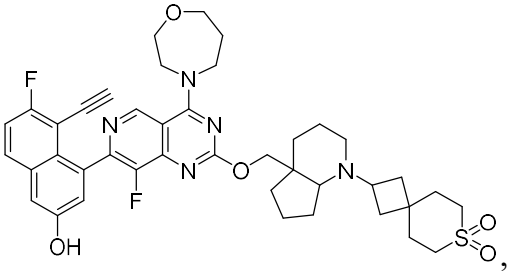

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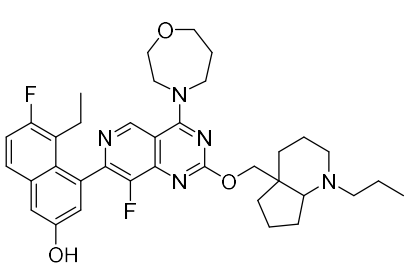
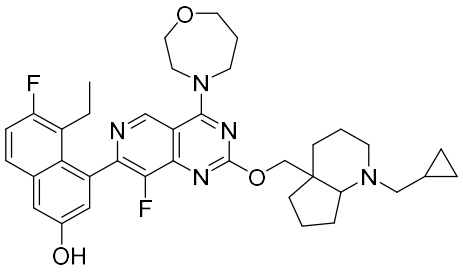
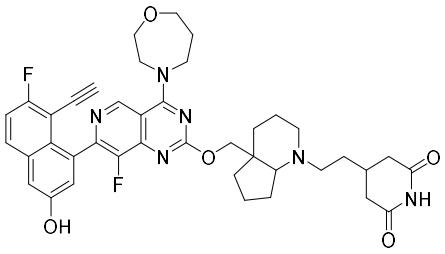
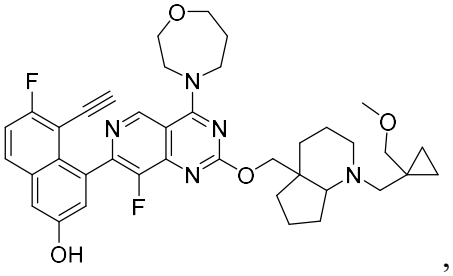
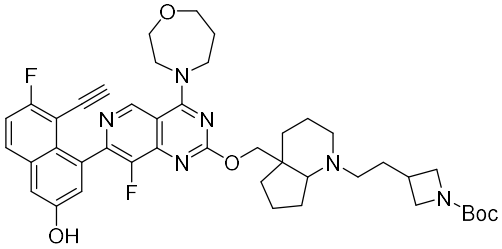
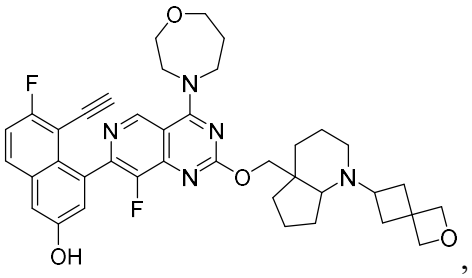
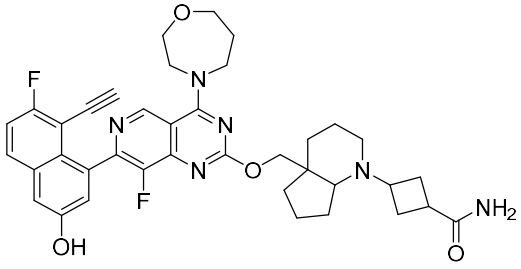
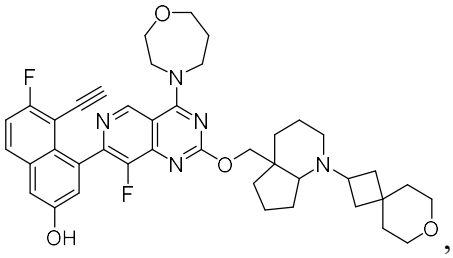
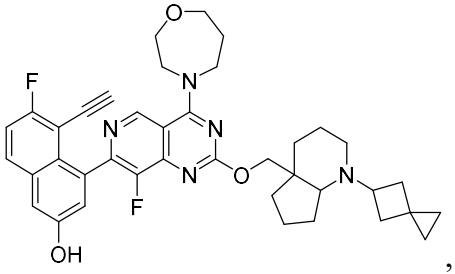
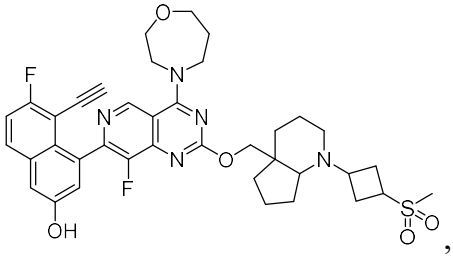
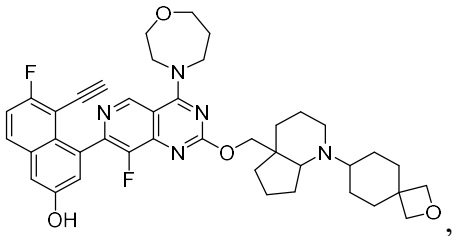
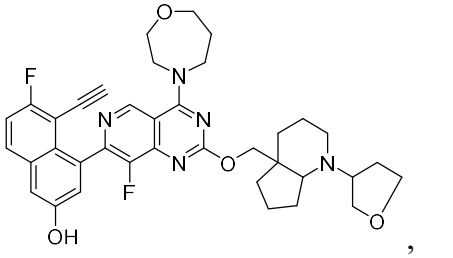

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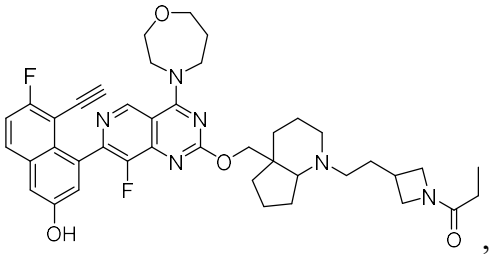
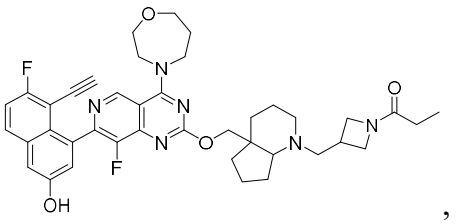
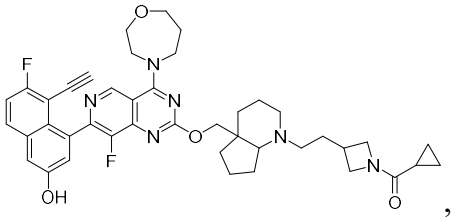
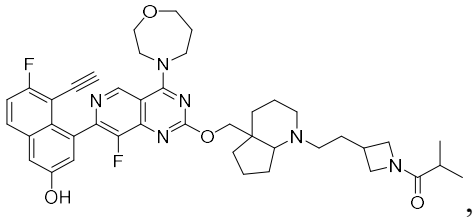
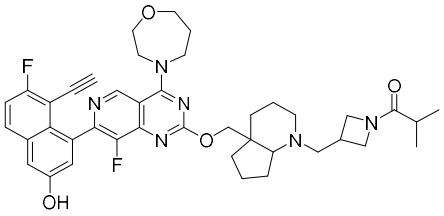
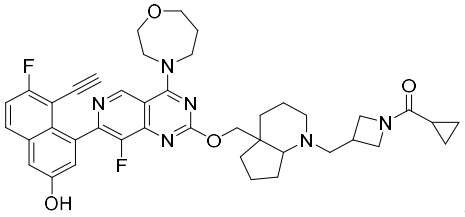
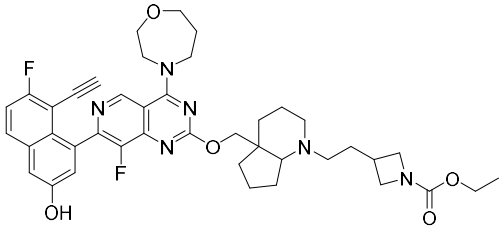
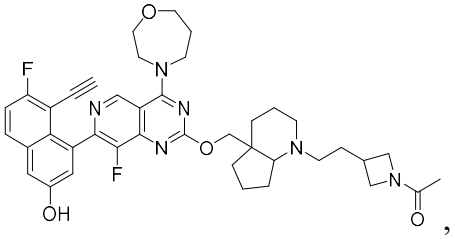
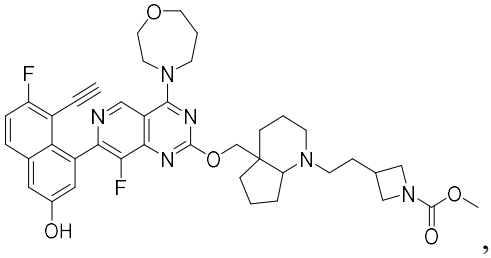
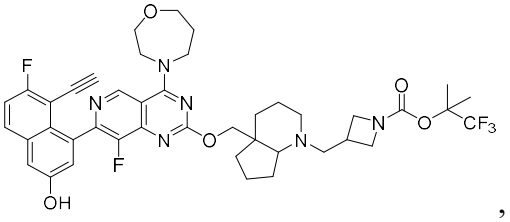
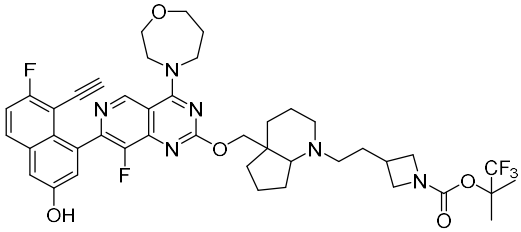

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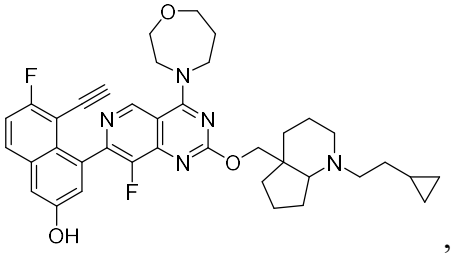
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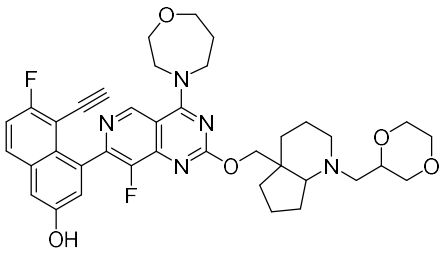
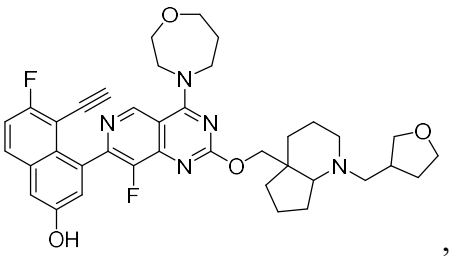
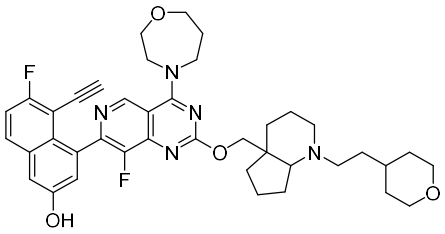
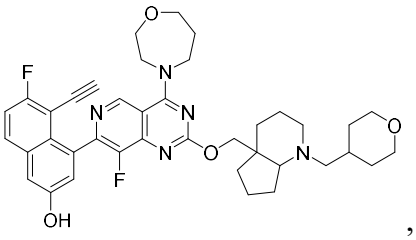
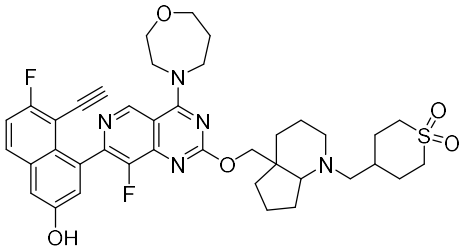
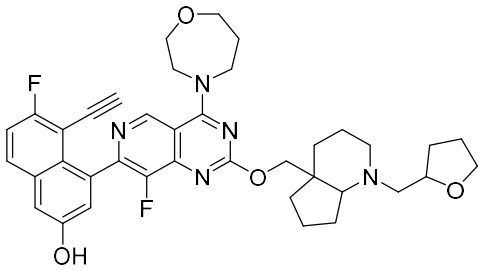
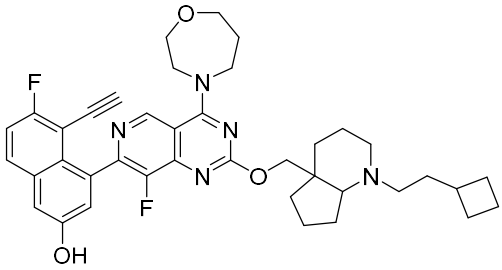
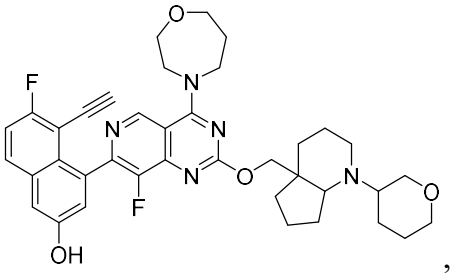
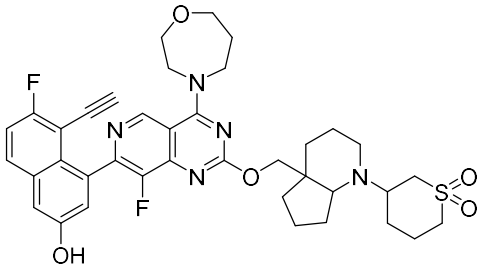
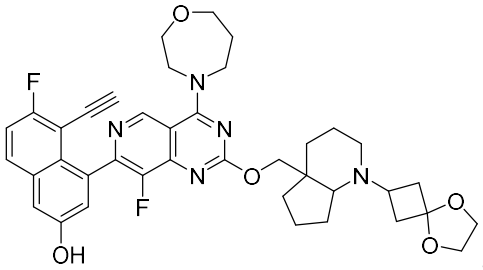
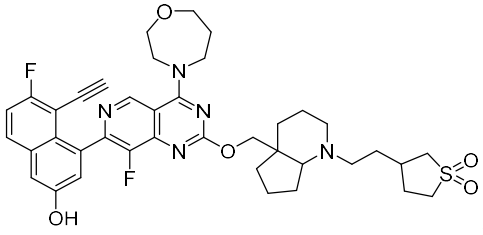
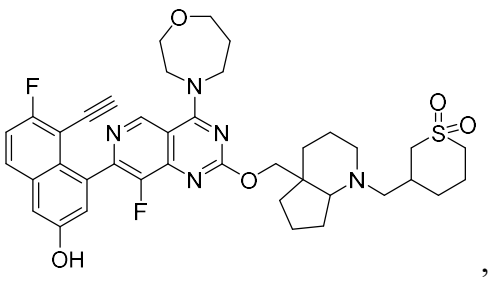

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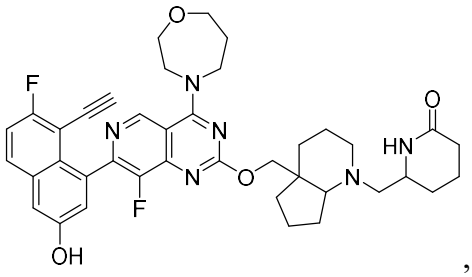
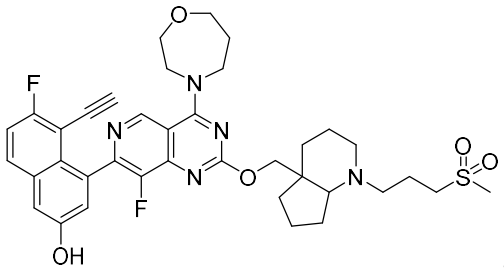
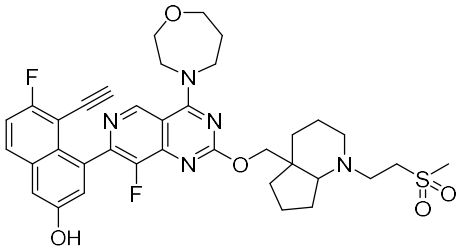
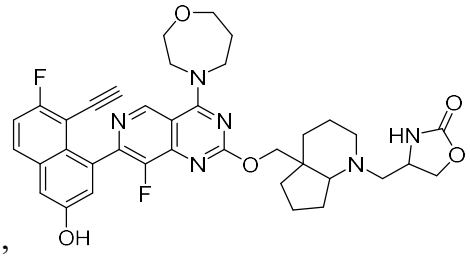
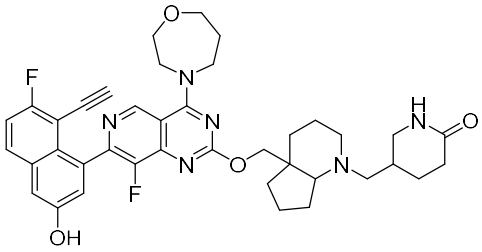
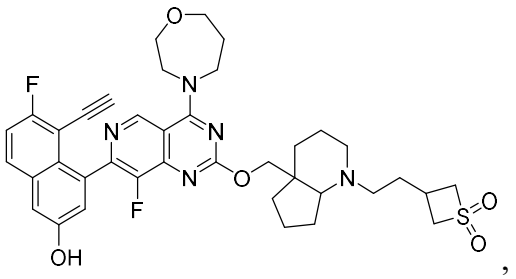
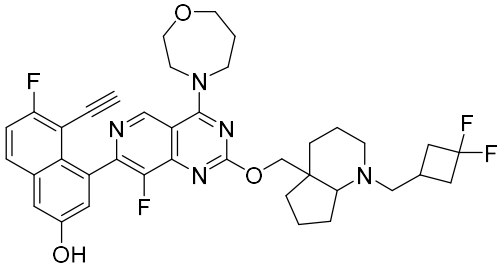
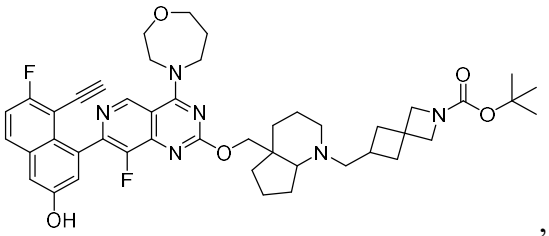
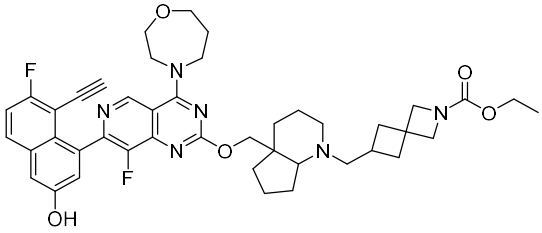
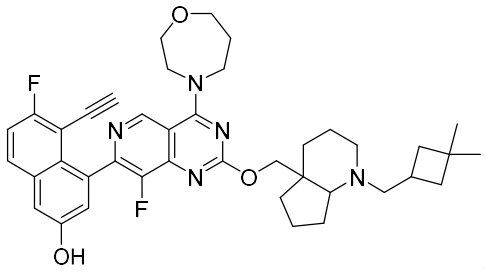
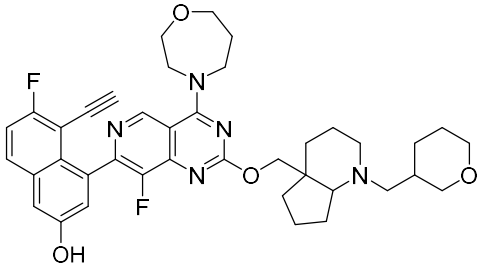
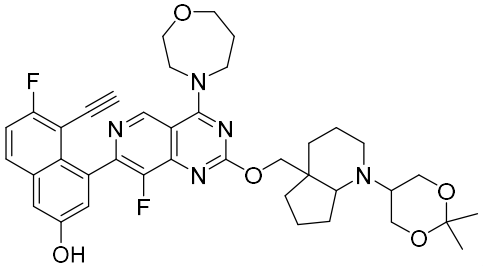

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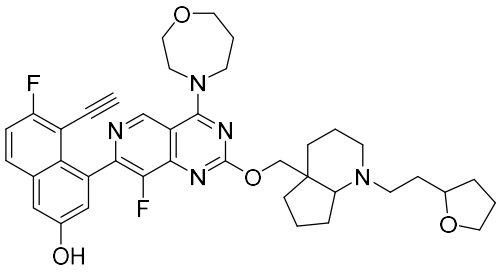
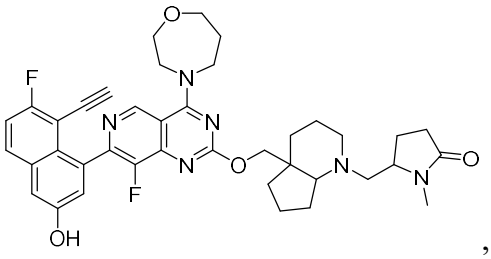
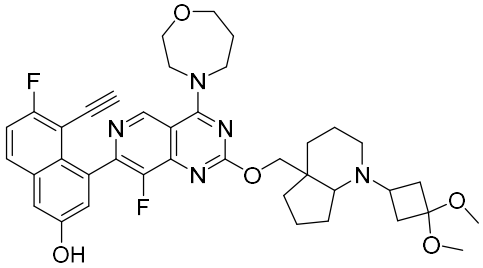
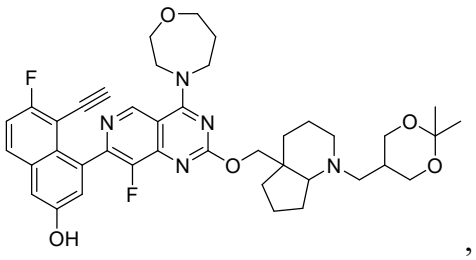
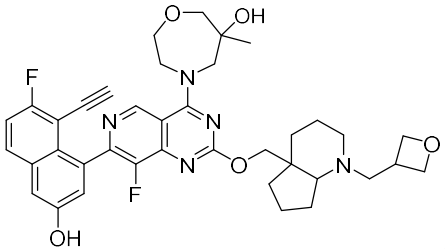
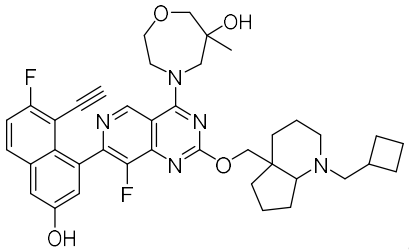
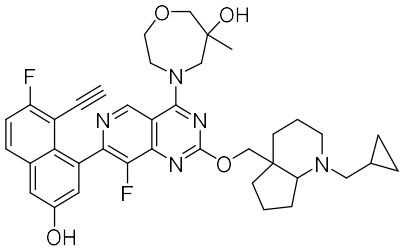
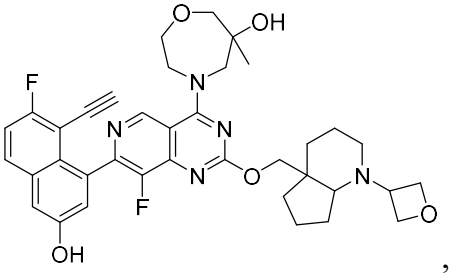
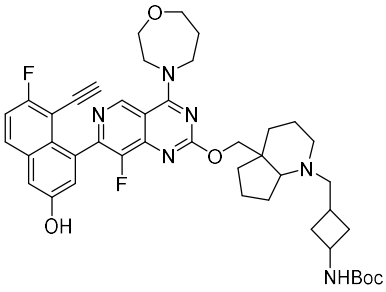
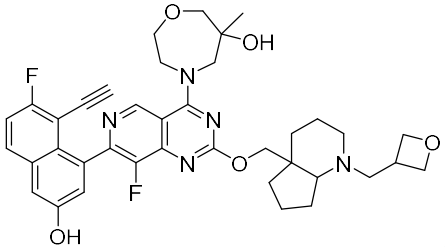

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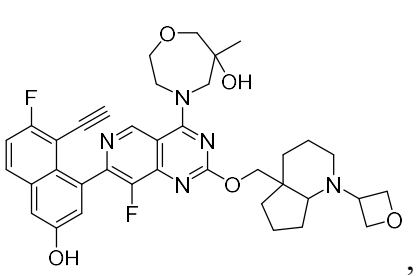
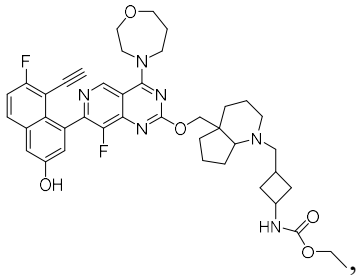
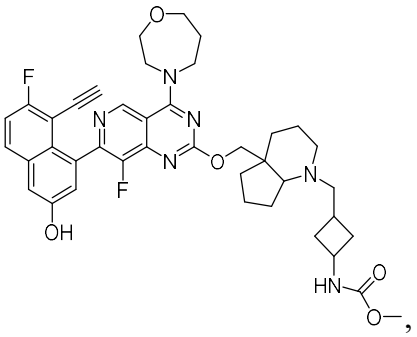
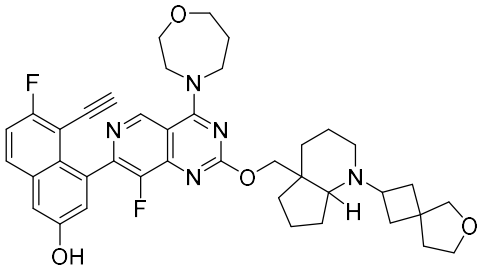
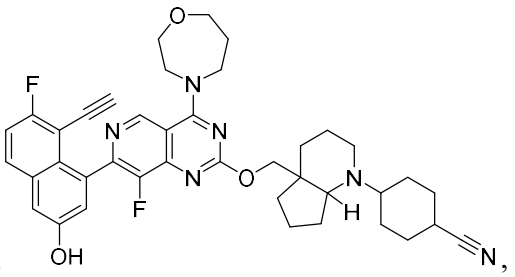
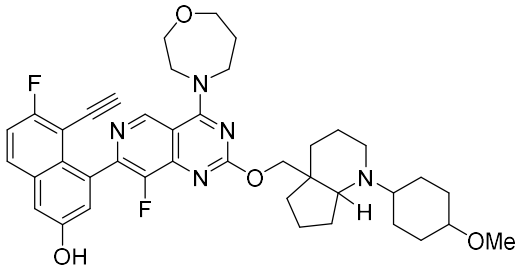
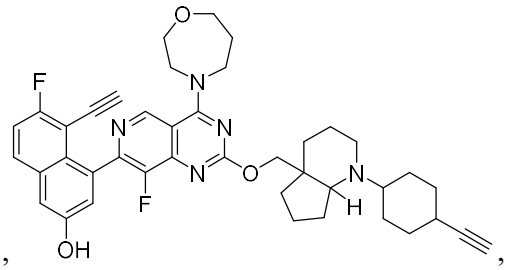
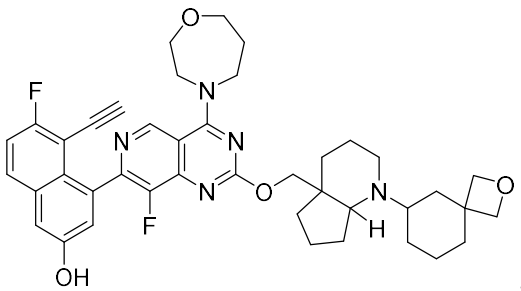
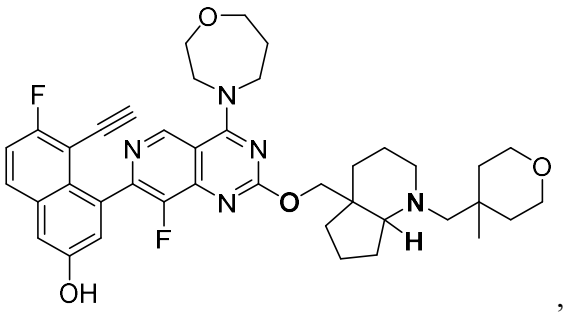
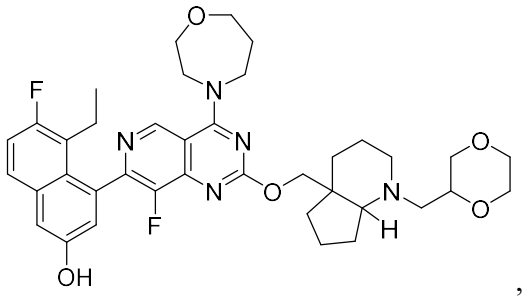
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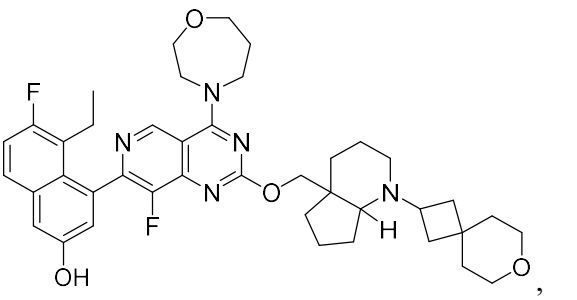

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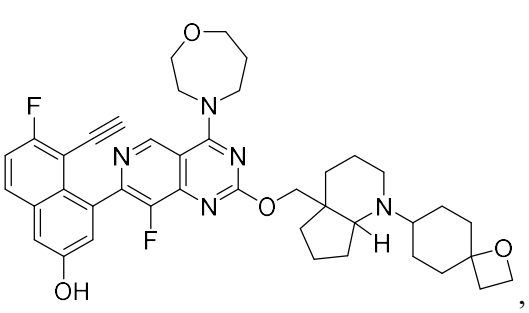
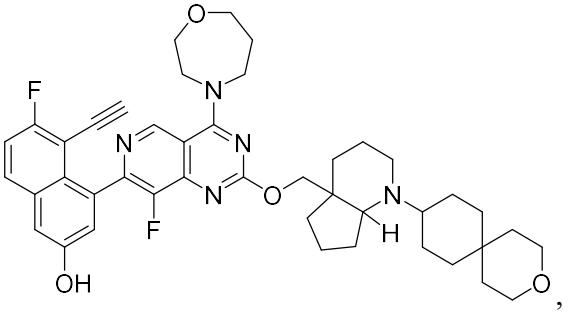
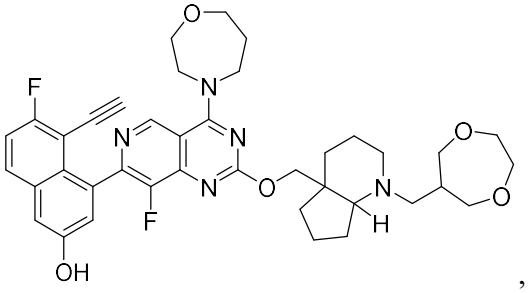
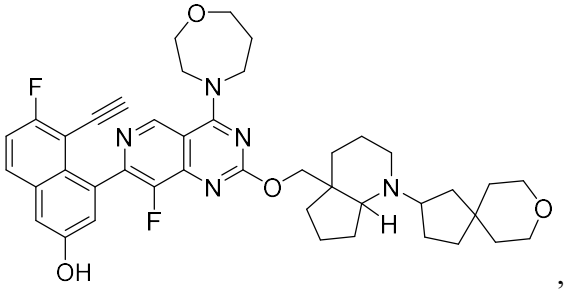
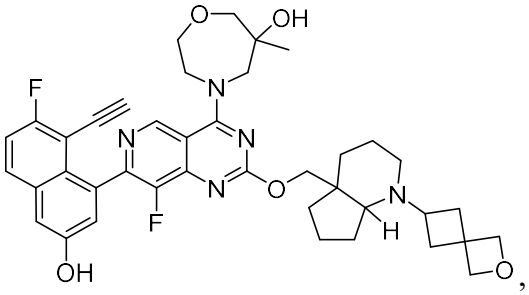
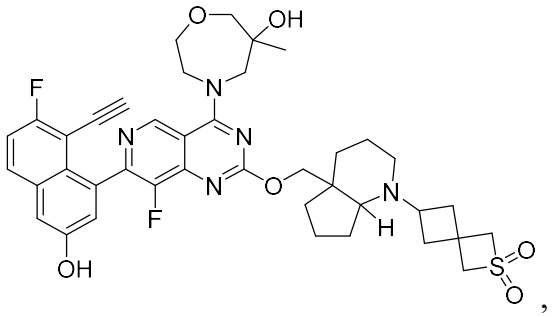
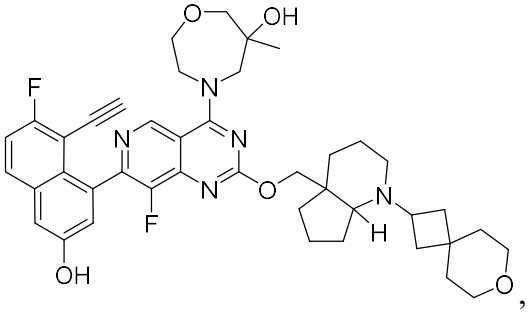
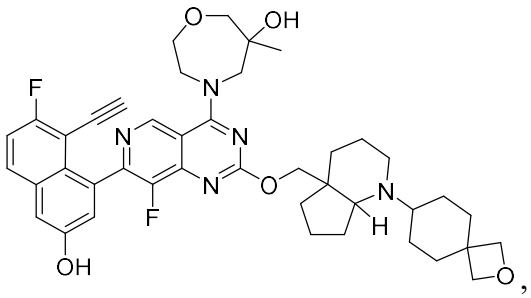
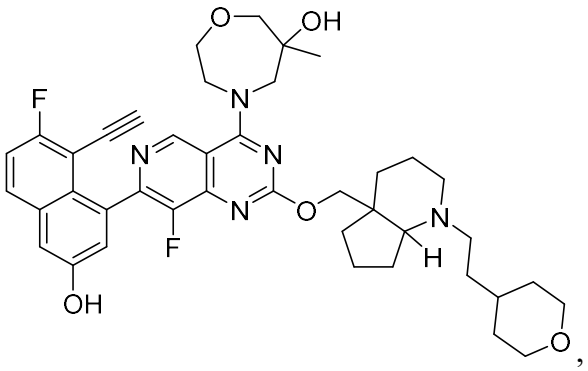
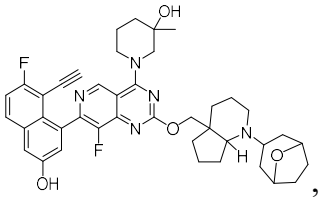
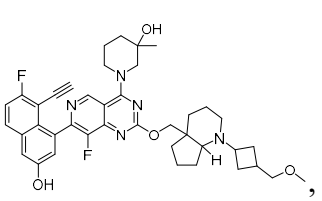
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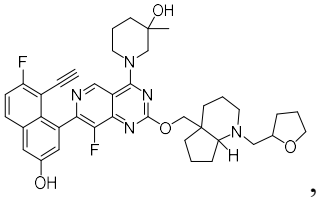
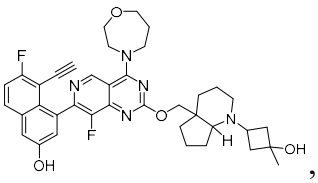
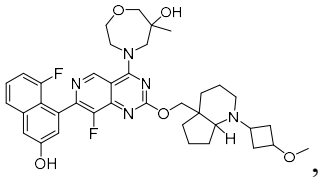
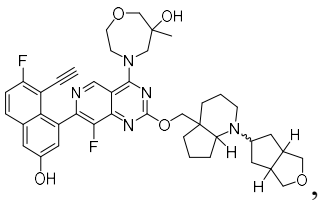
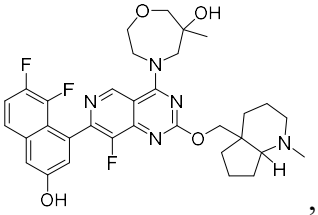
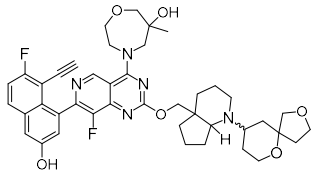
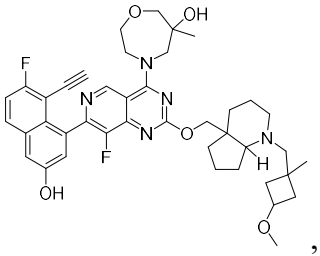
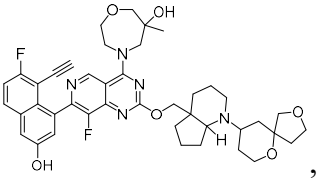
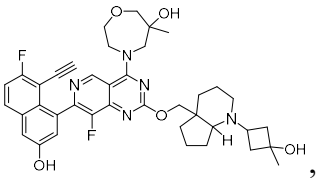
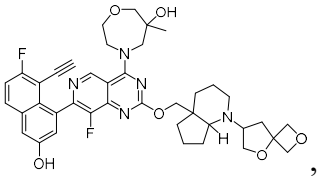
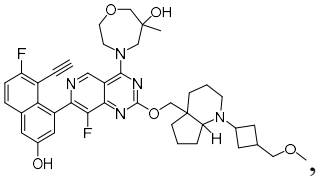
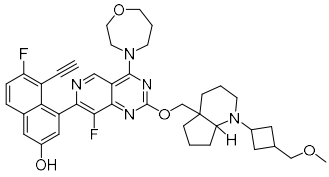
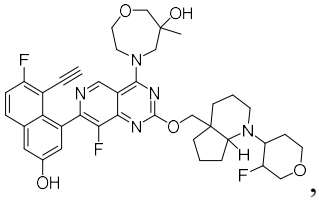
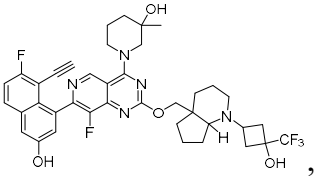
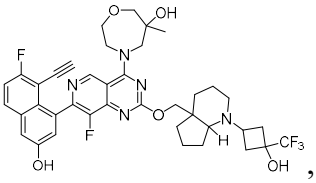
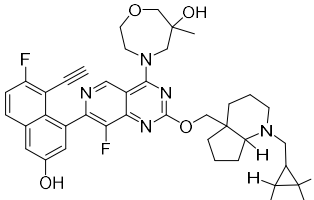
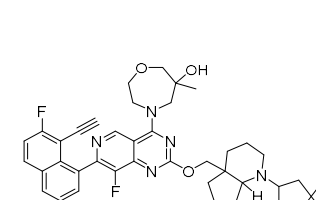
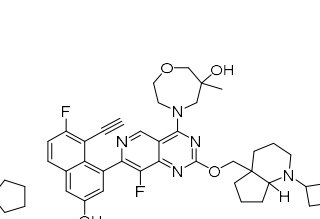
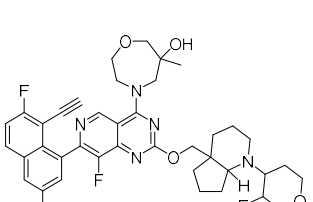
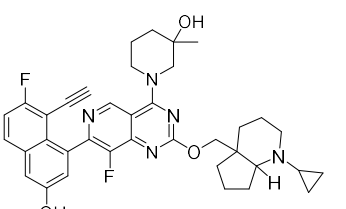
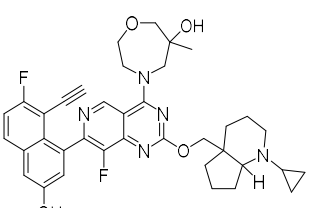
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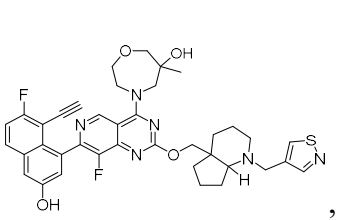
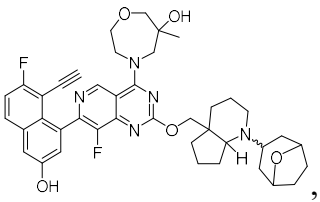
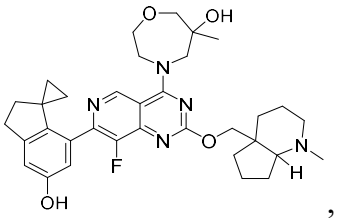
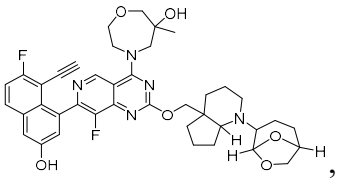
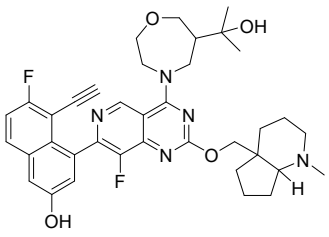
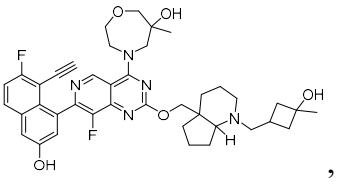
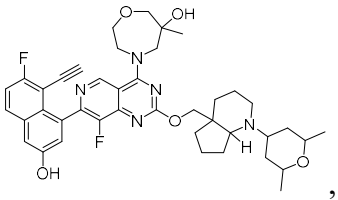
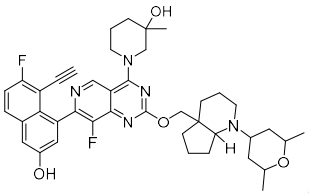
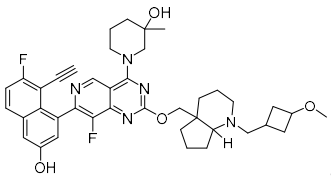
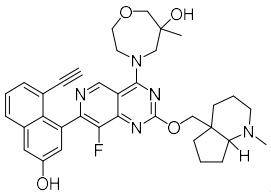
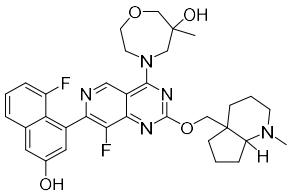
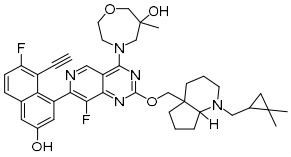
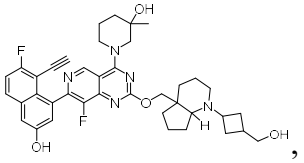
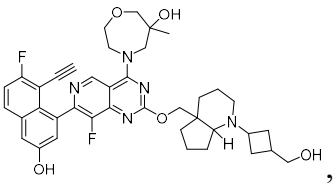
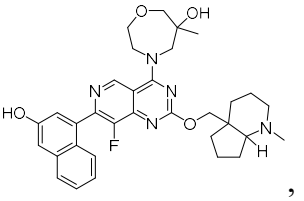
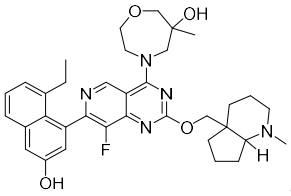
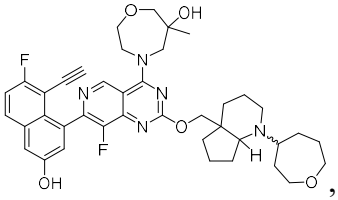
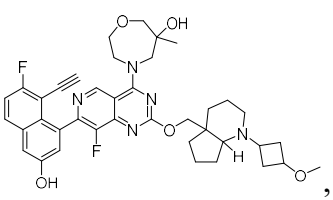
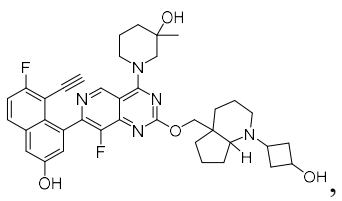
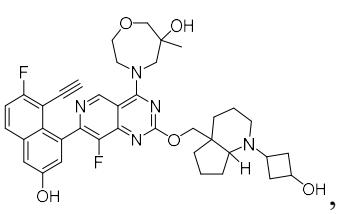
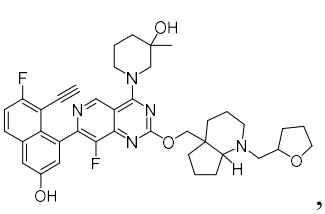
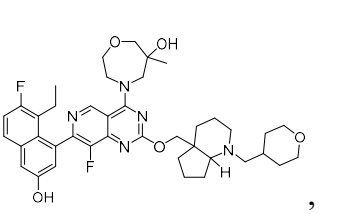
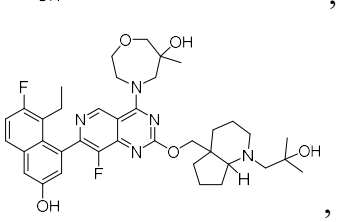
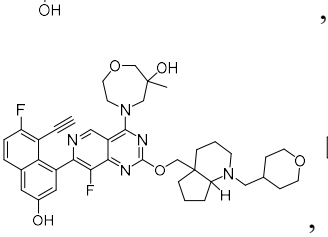
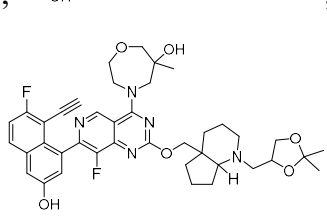
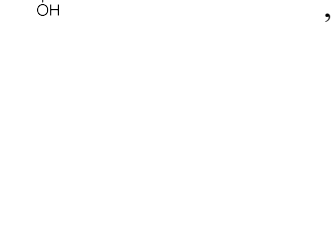
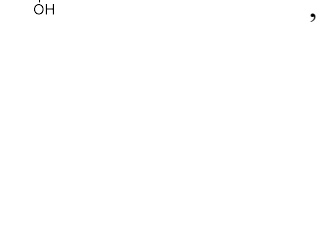
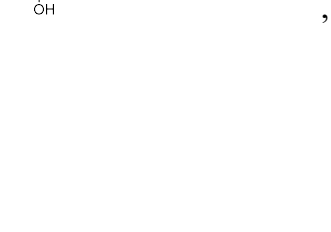

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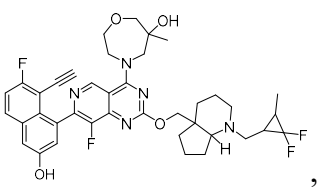
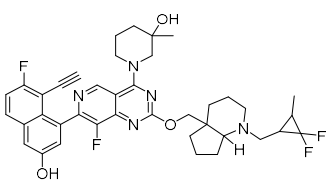
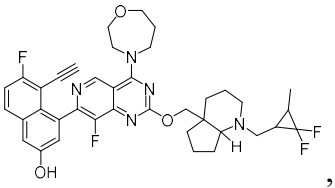
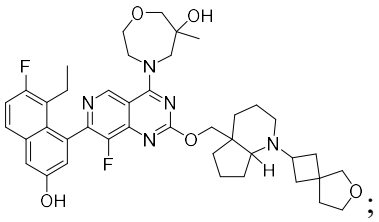
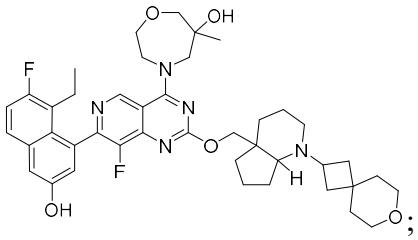
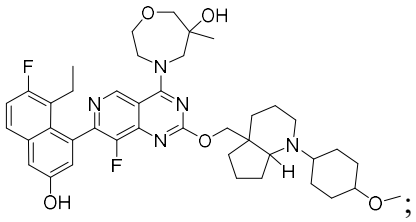
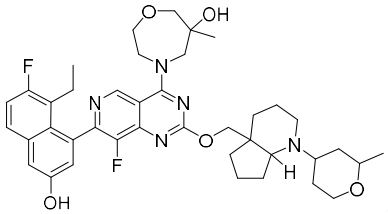
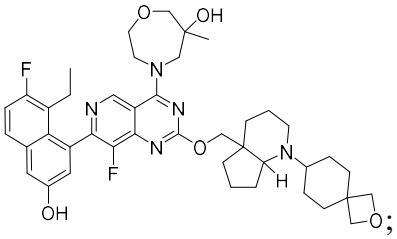
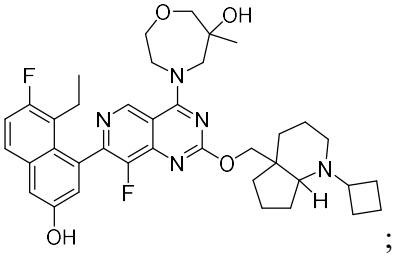
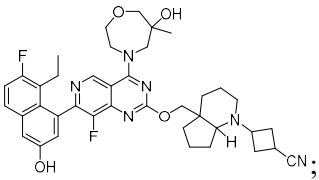
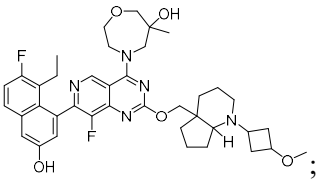
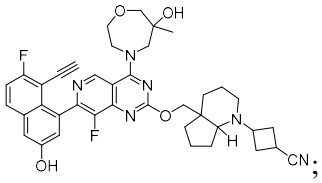
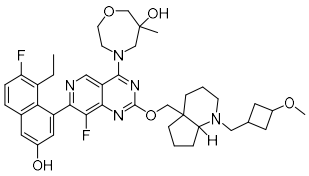
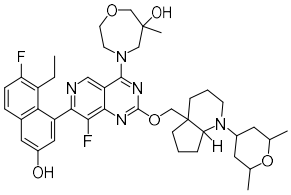
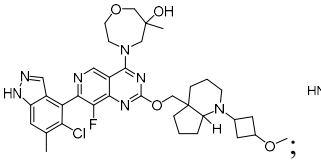
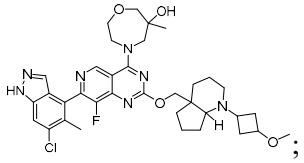
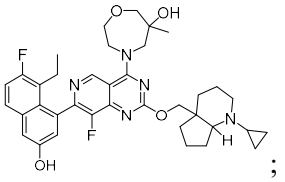
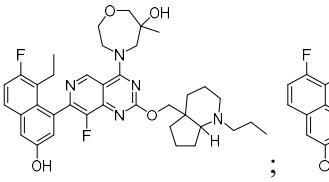
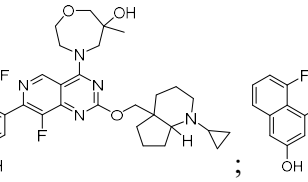
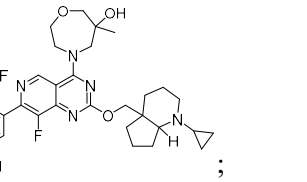

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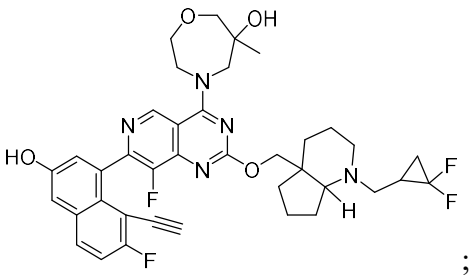
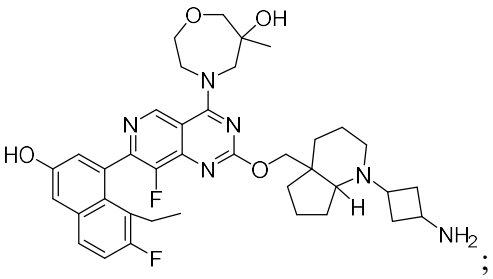
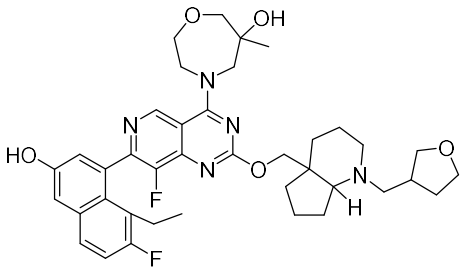
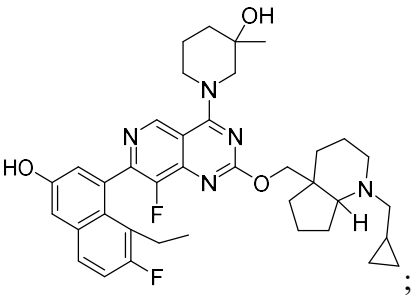
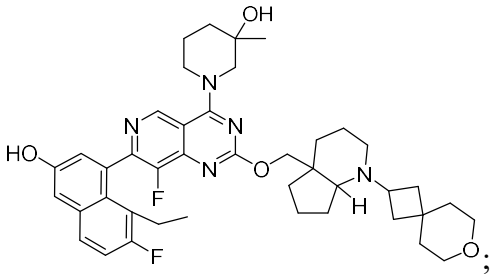
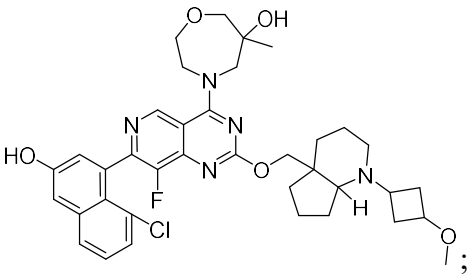
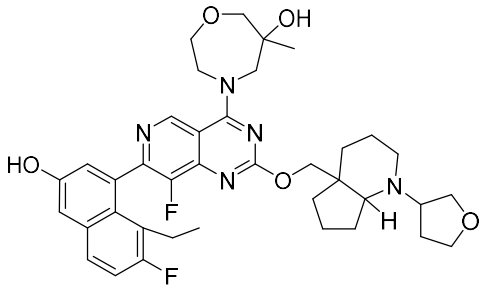
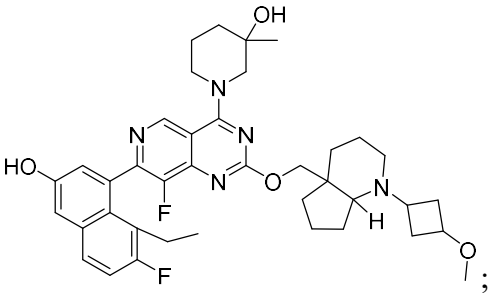
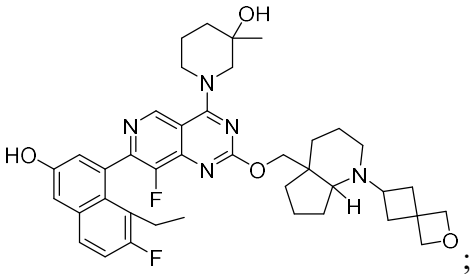
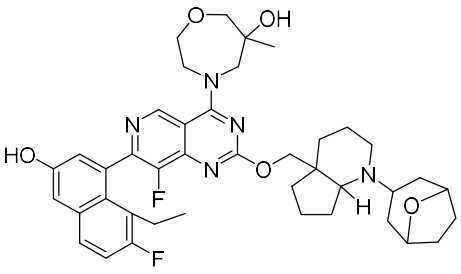
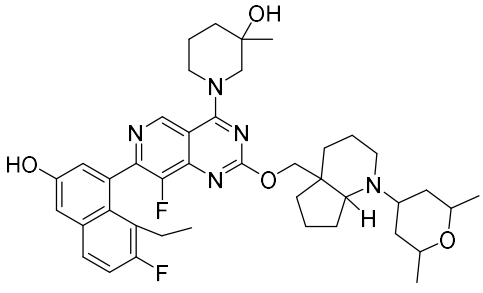
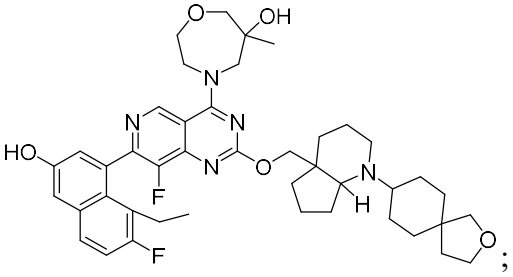

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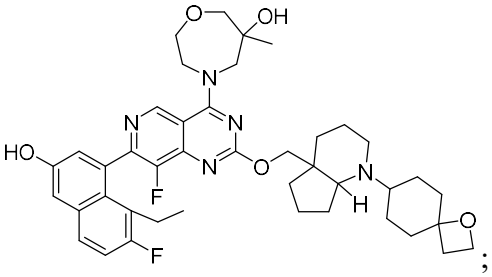
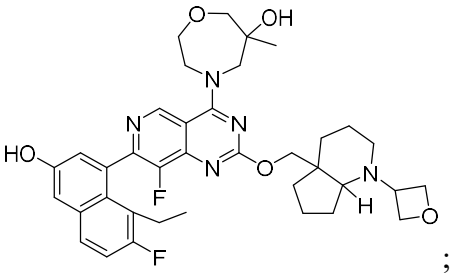
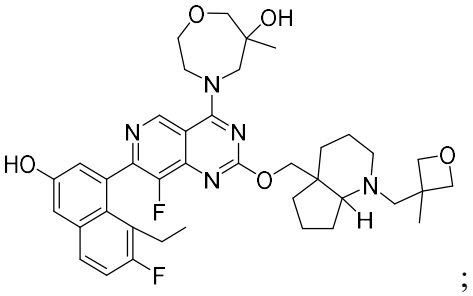
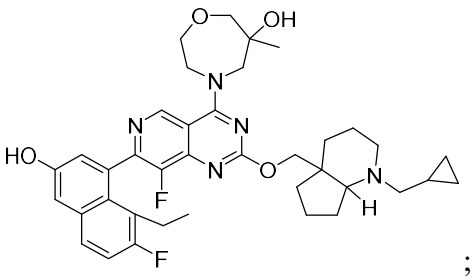
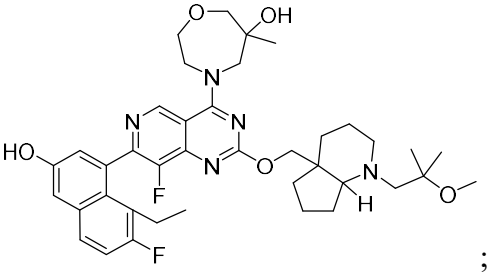
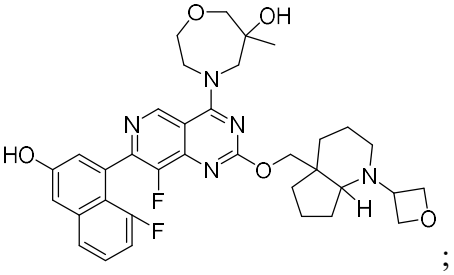
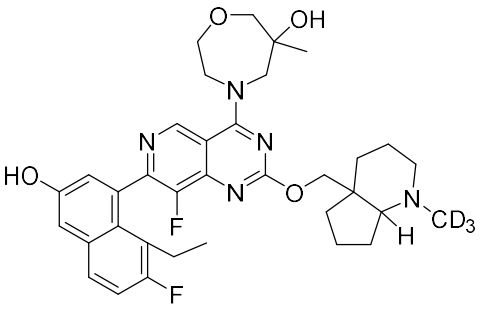
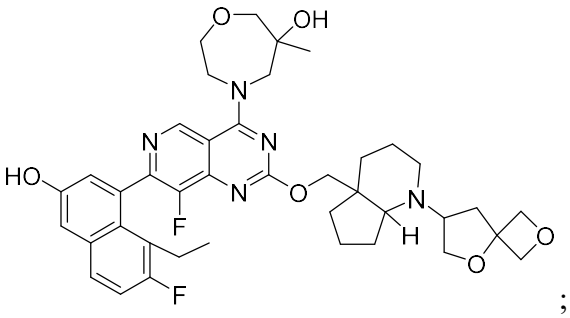
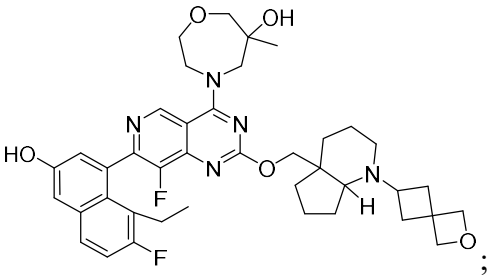
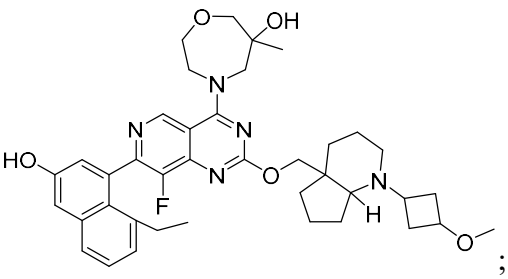
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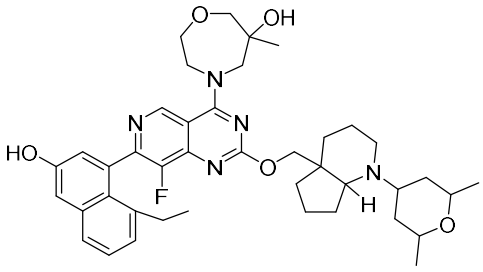
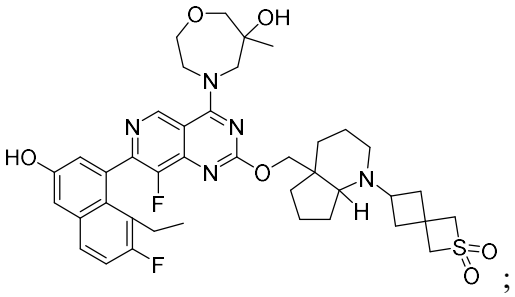
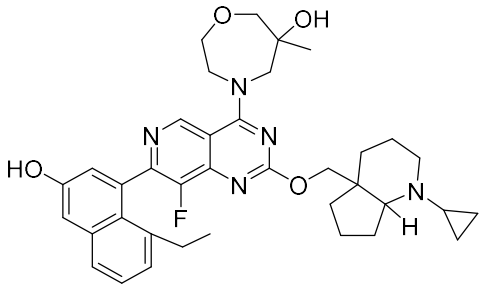
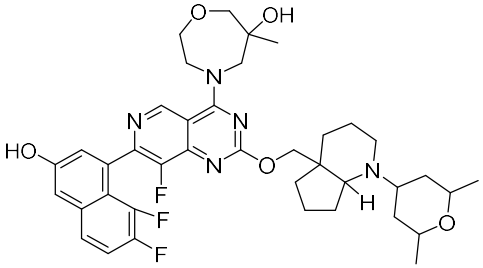
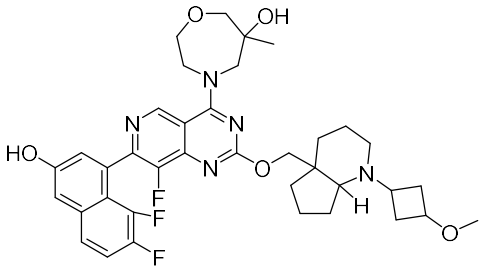
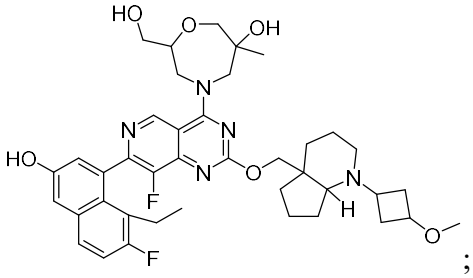
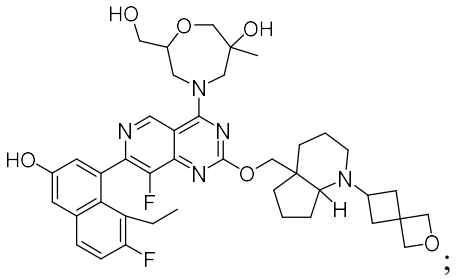
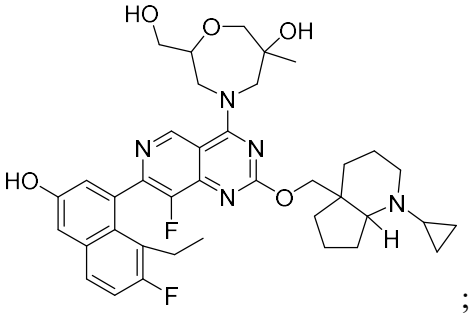
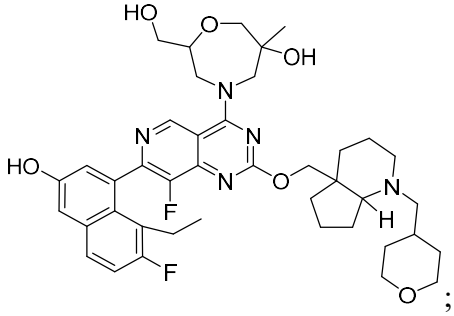
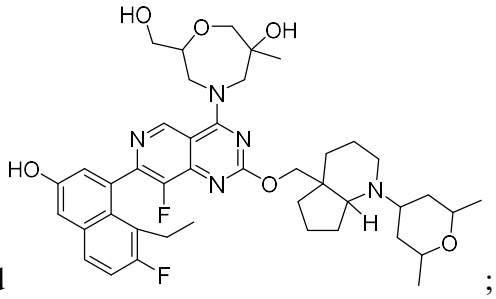
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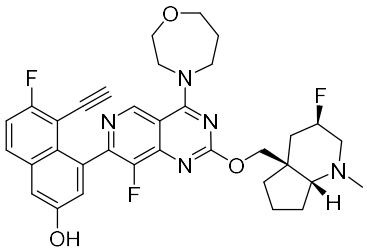
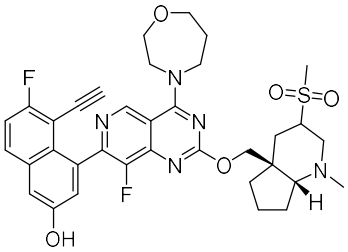
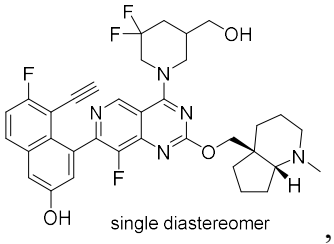
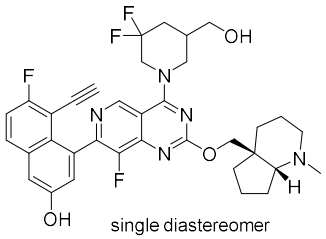
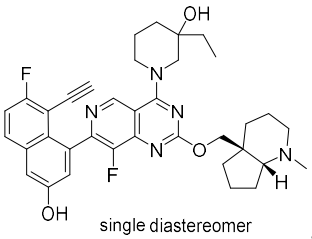
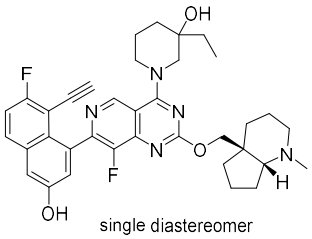
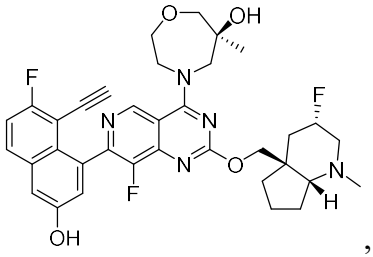
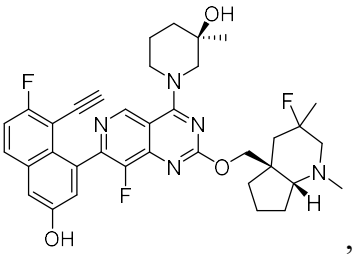
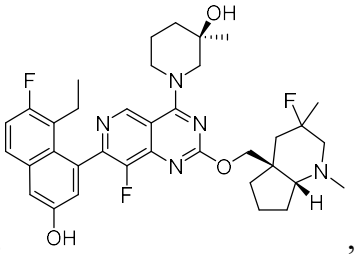
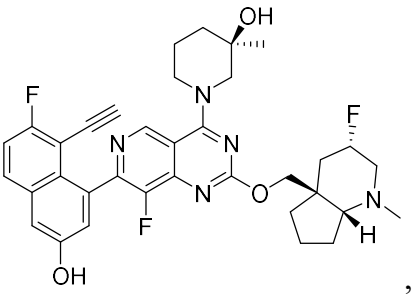
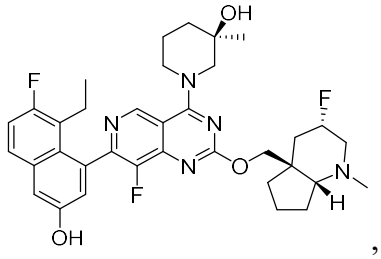
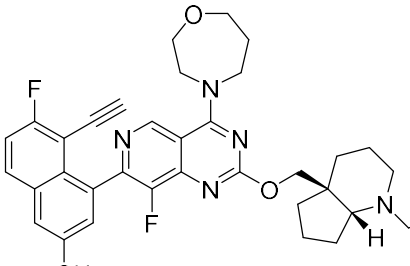

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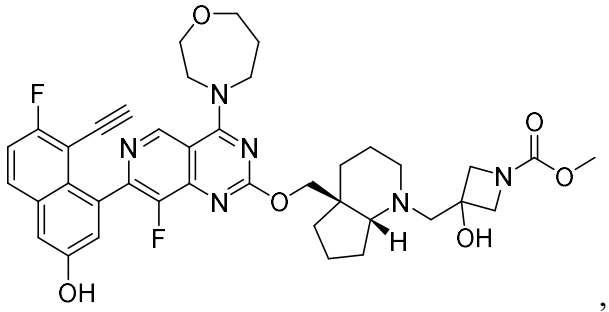
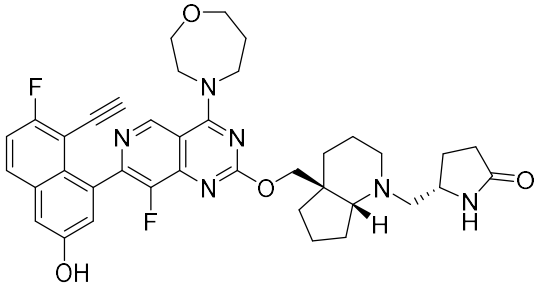
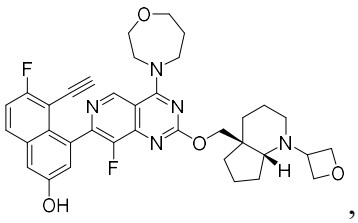
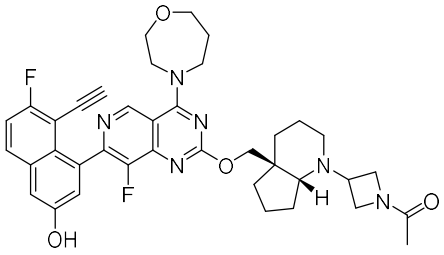
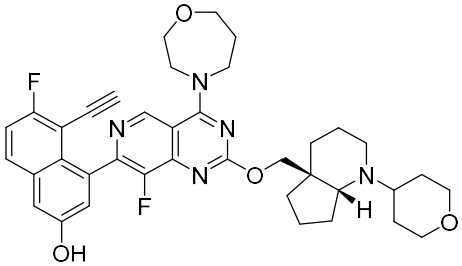
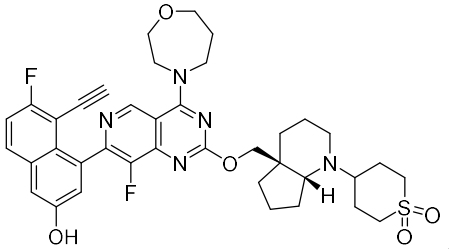
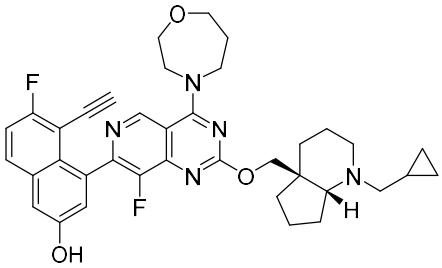
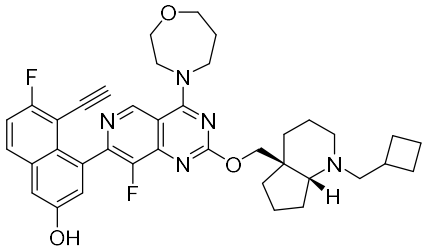
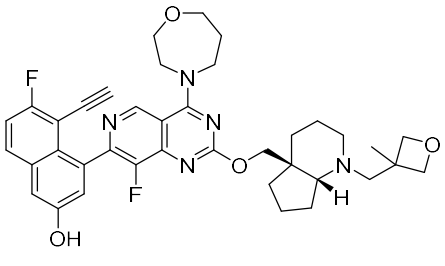
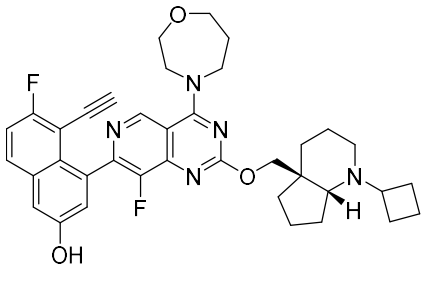
or a pharmaceutically acceptable salt thereof.

36. A compound selected from the group consisting of

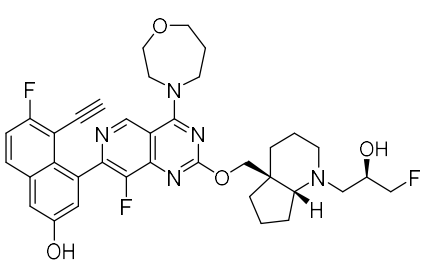
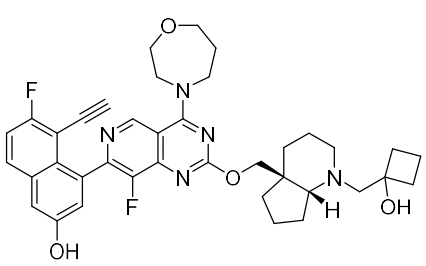

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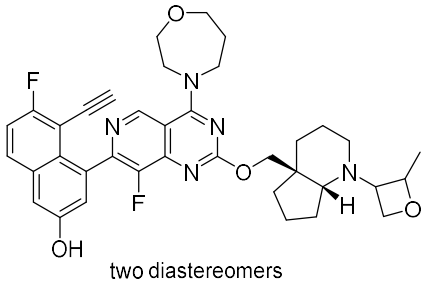
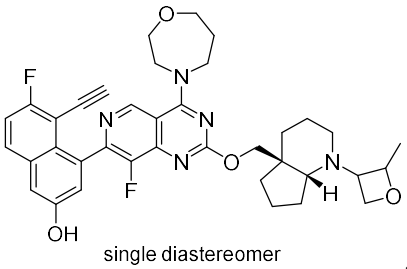
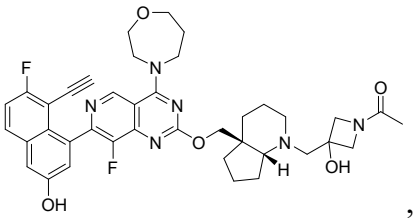
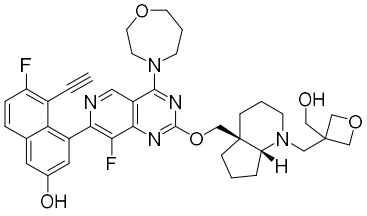
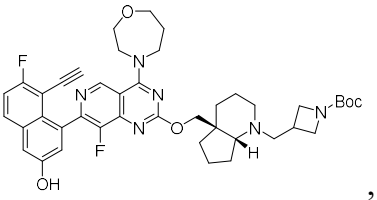
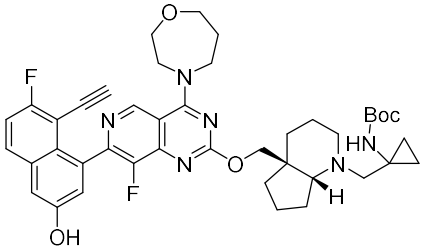
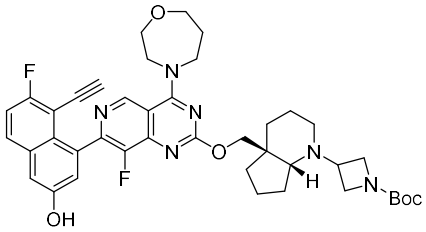
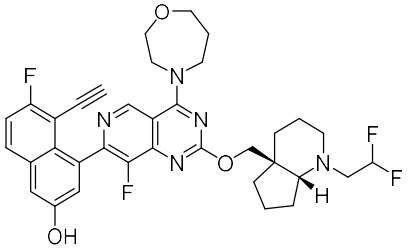
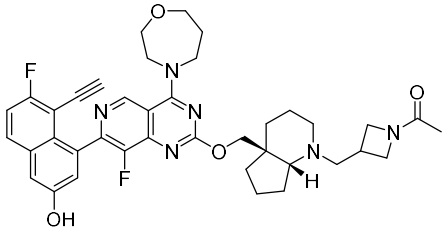
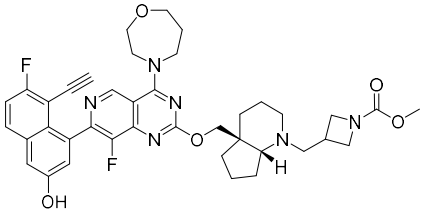
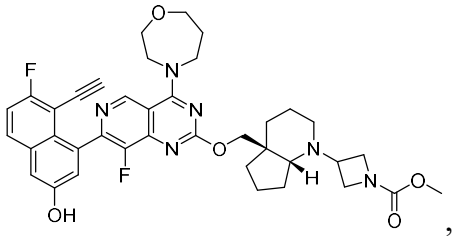
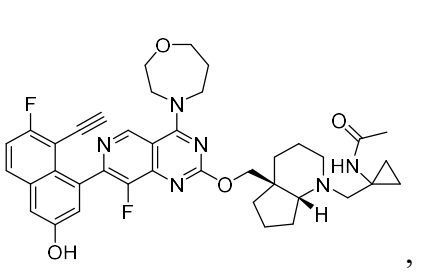
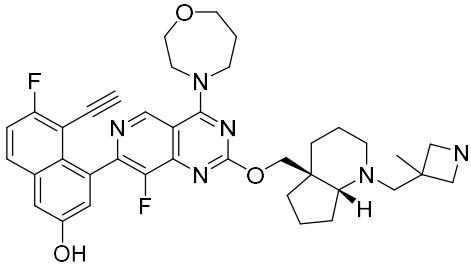
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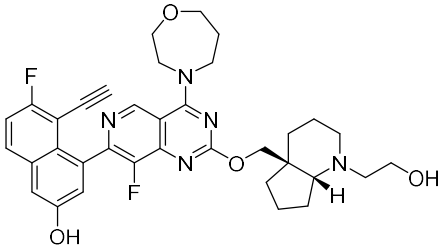
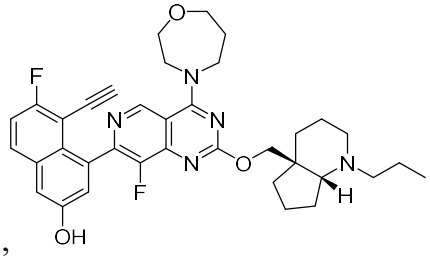
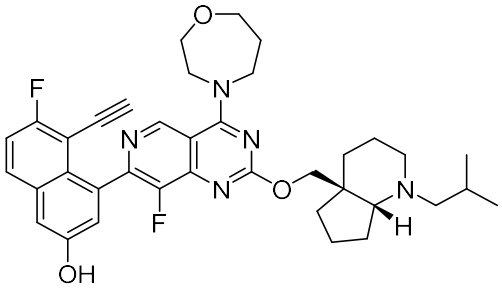
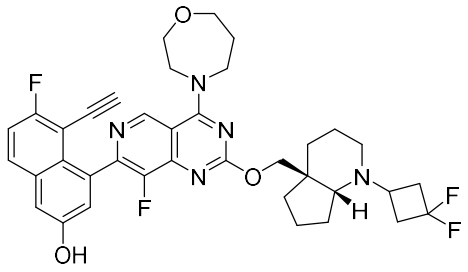
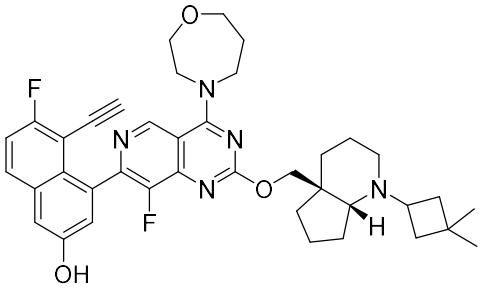
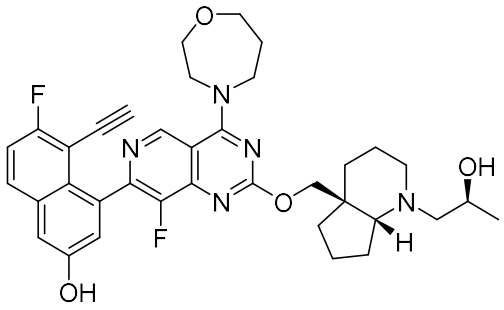
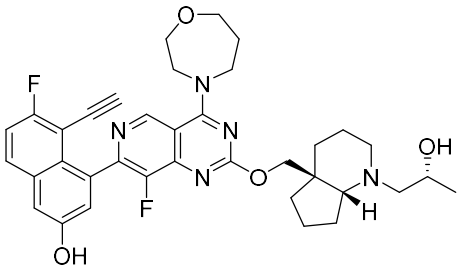
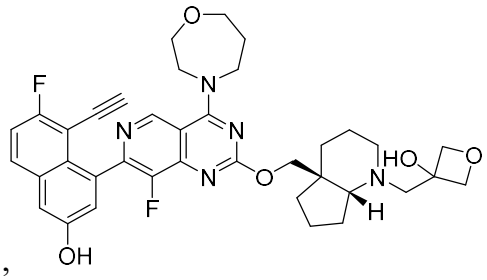
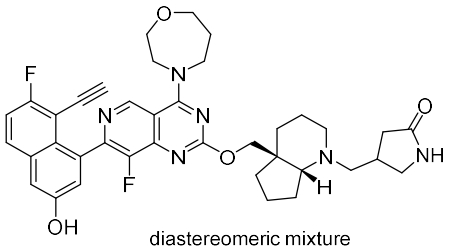
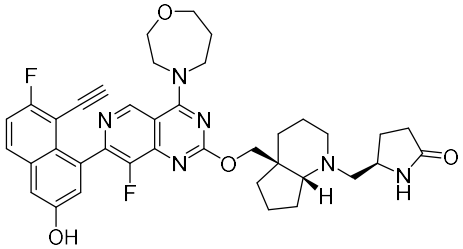
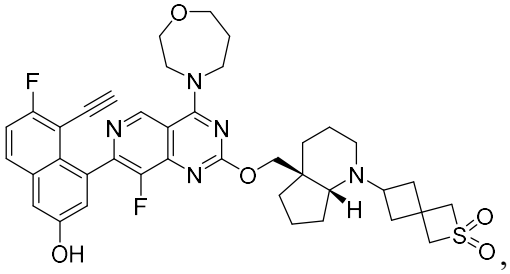
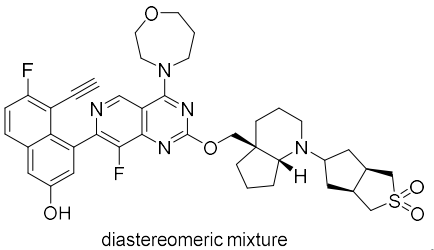
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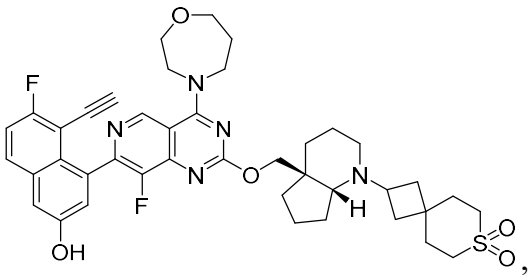
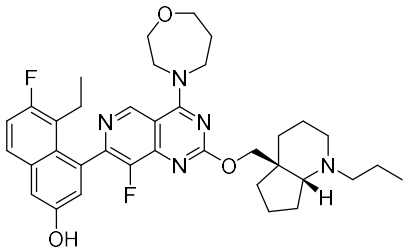
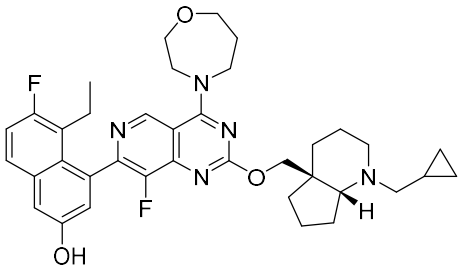
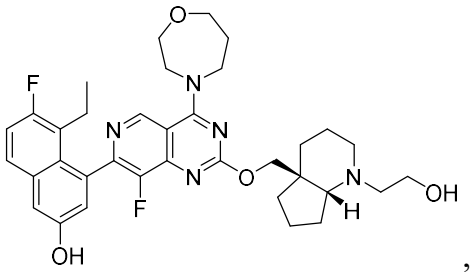
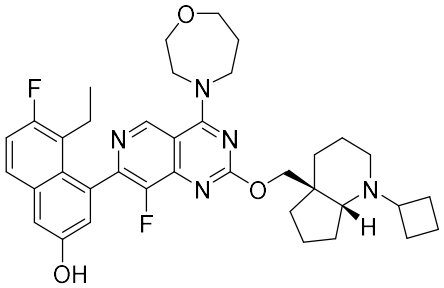
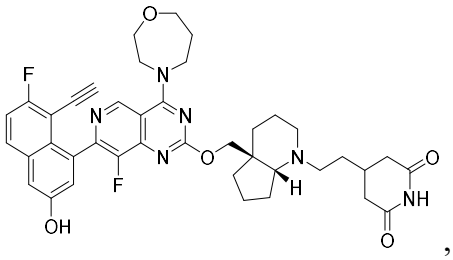
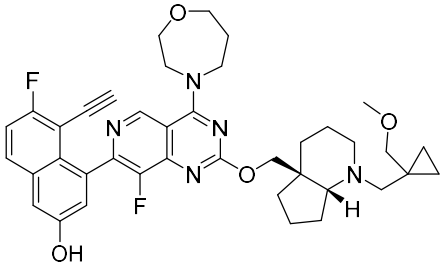
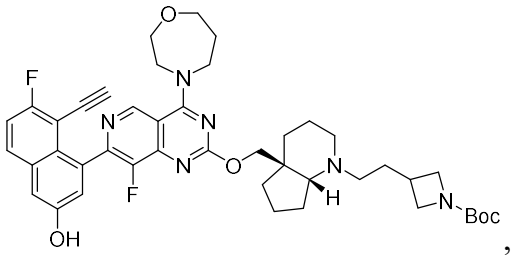
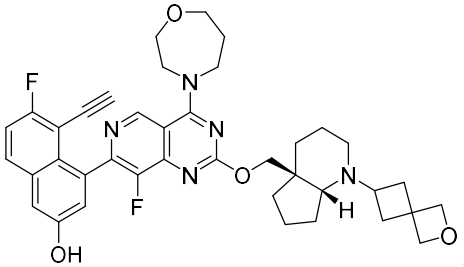
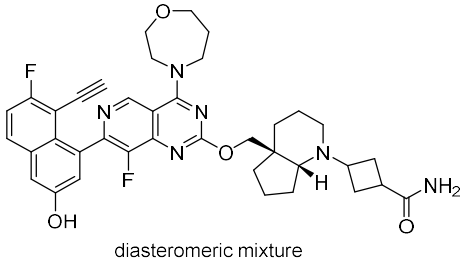
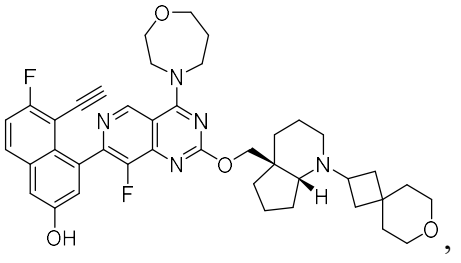
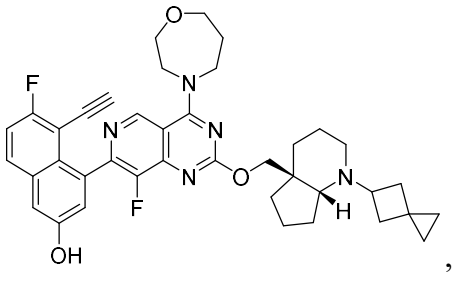
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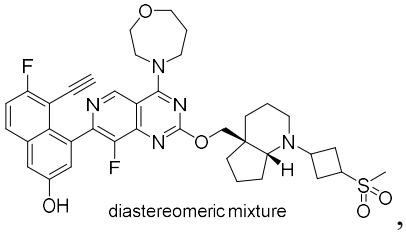

two diastereomers ,

single diastereomer ,

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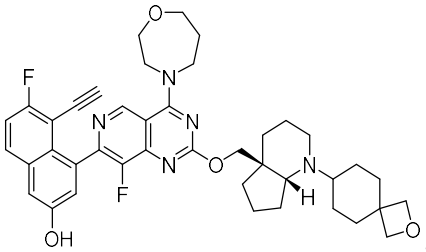
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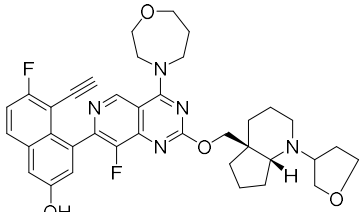
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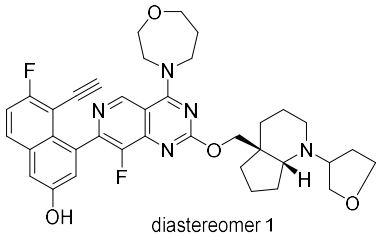

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diastereomeric mixture
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diastereomeric mixture
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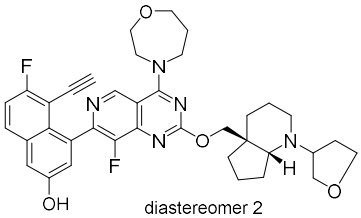

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diasteromeric mixture
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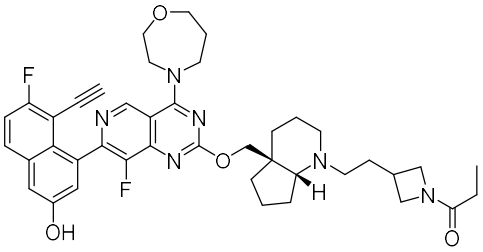

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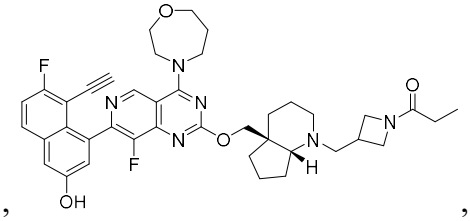

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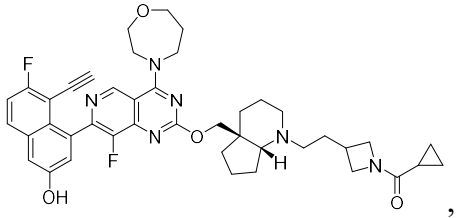

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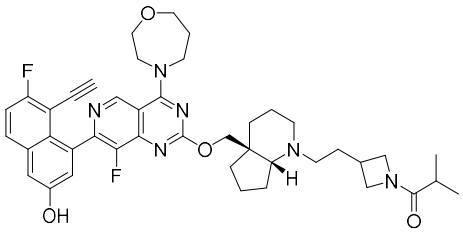

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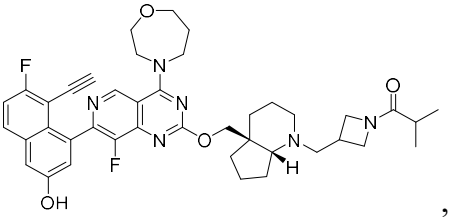

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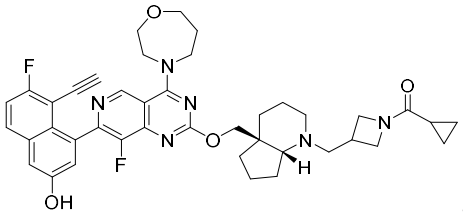

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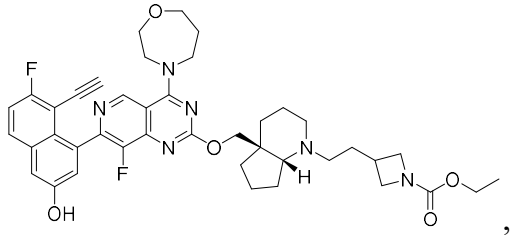

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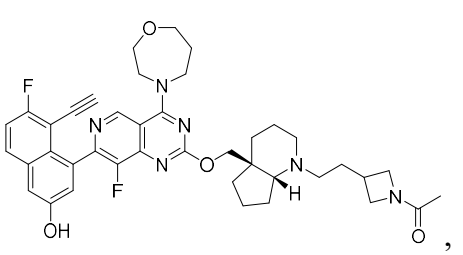

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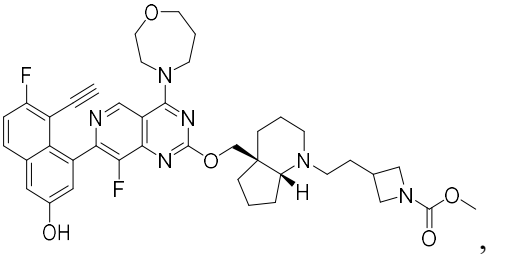

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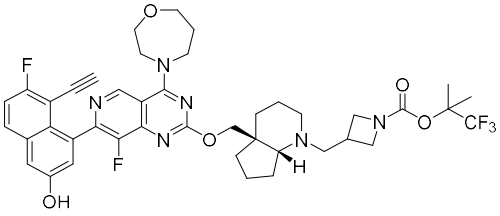
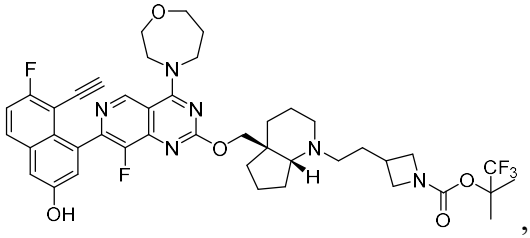
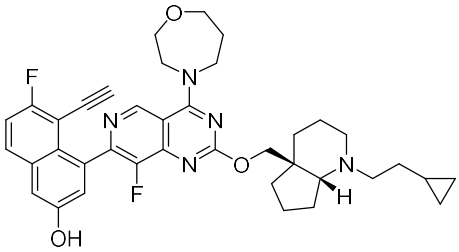
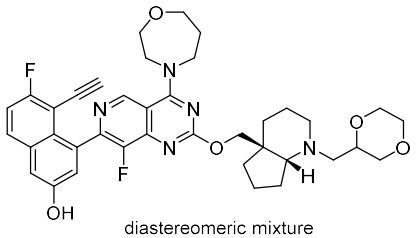
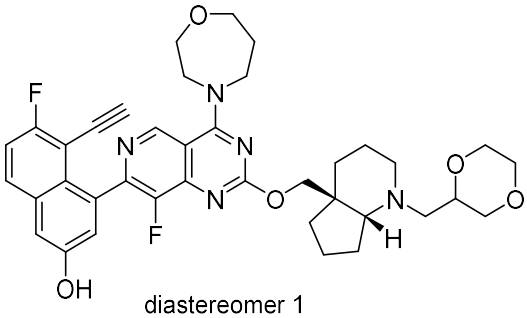
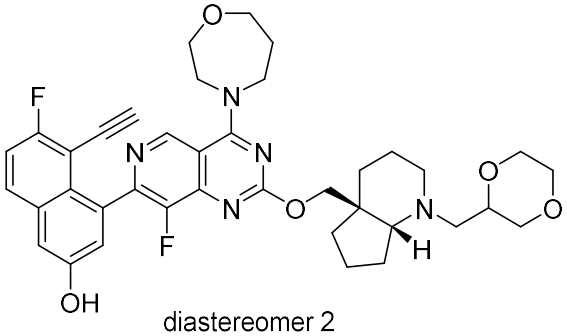
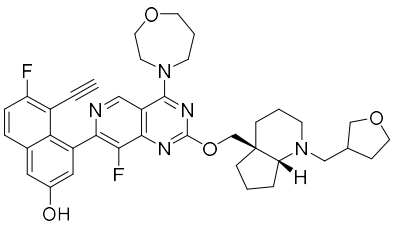
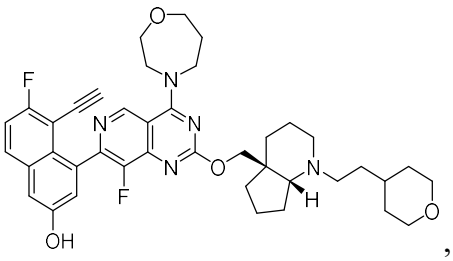
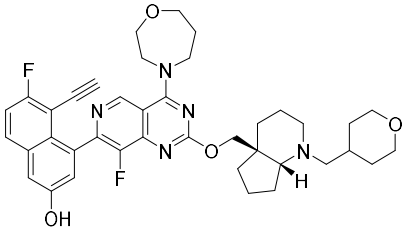
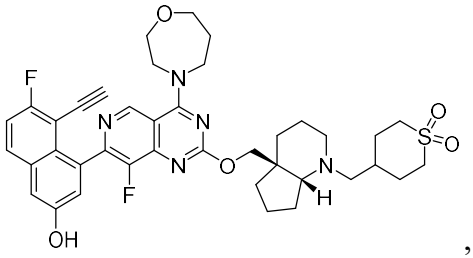
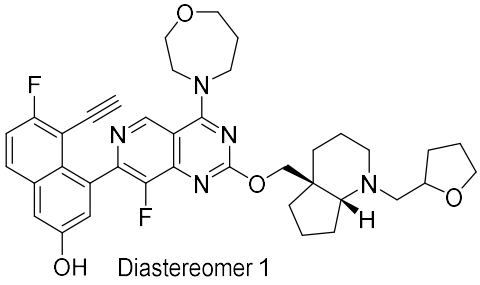
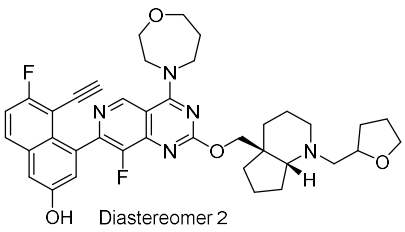

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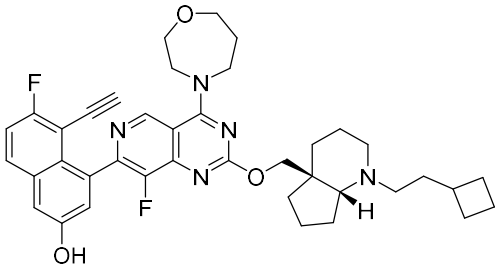
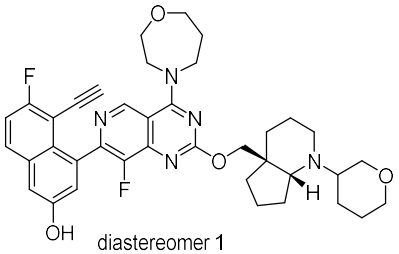
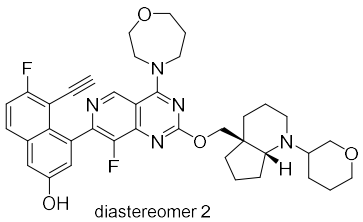
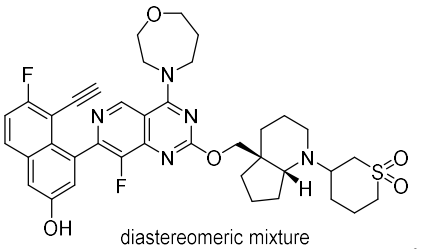
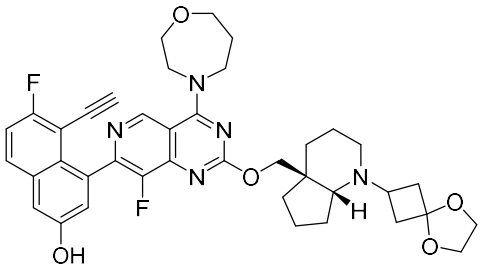
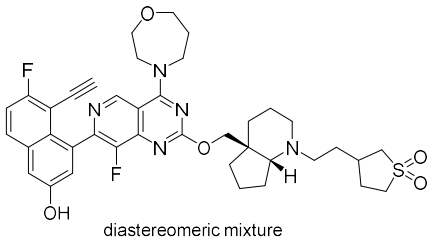
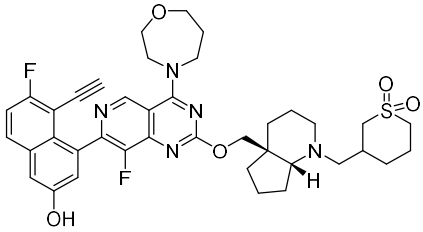
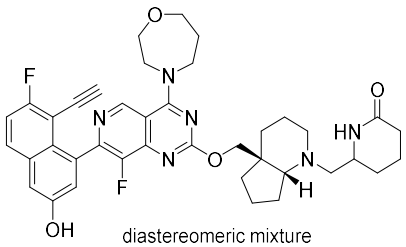
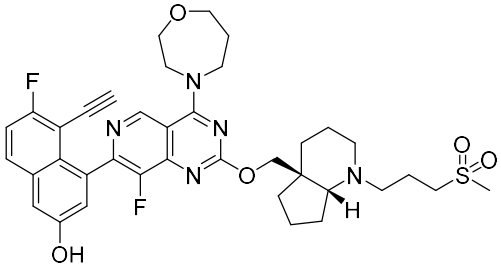
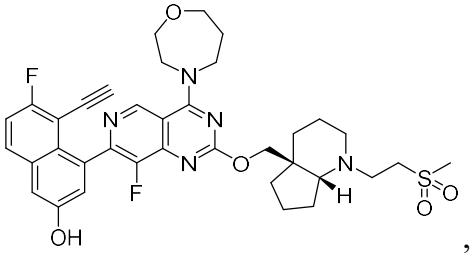
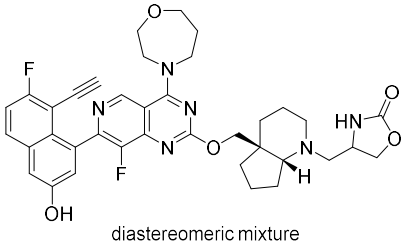
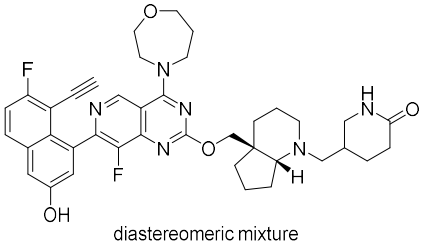

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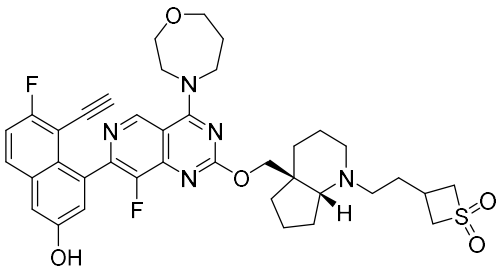
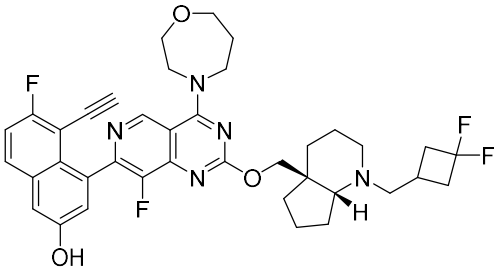
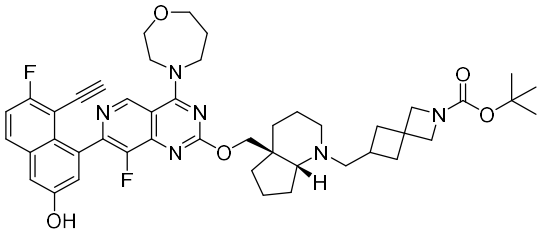
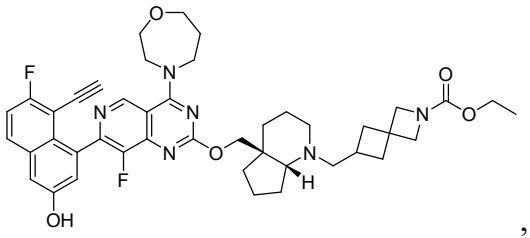
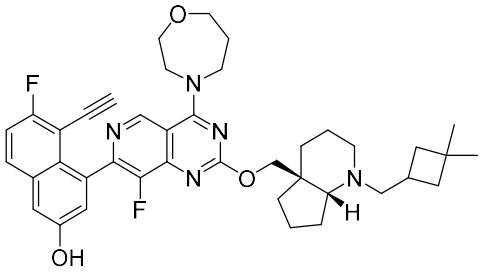
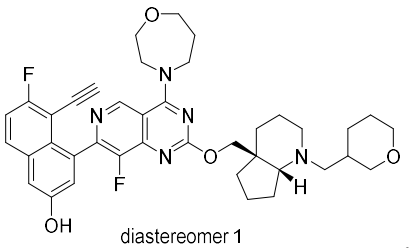
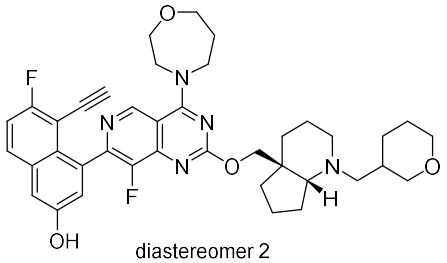
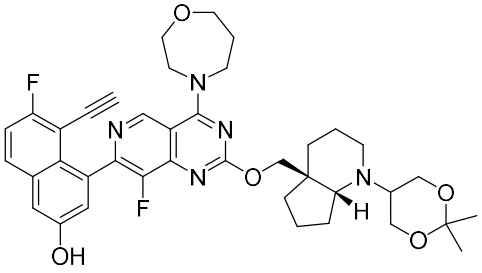
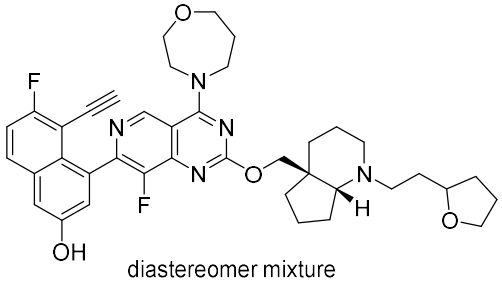
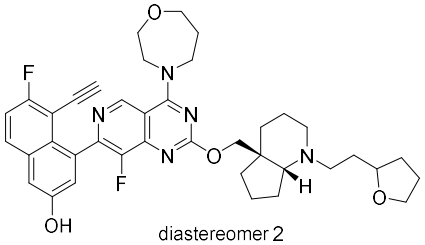
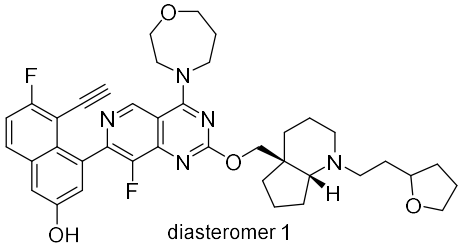
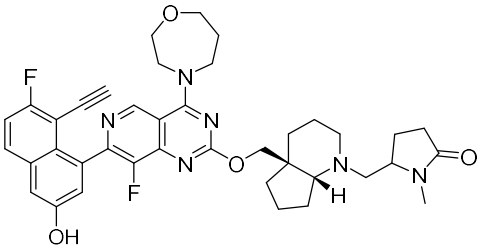

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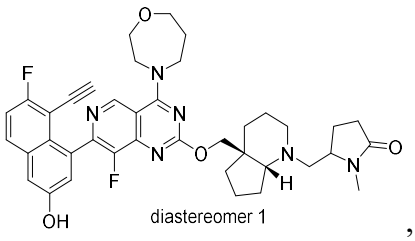
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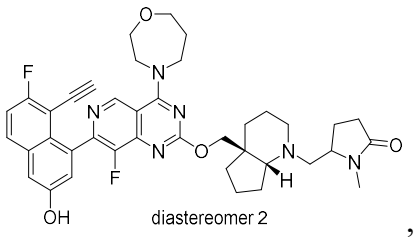
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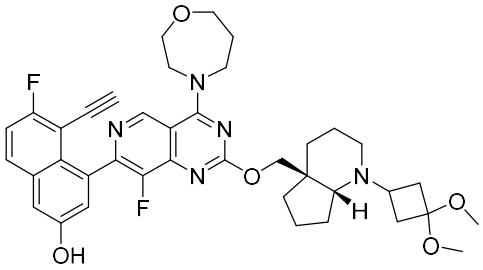

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diastereomeric mixture
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diastereomer 1
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diastereomer 2
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diastereomeric mixture
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Diastereomer 1
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Diastereomer 2
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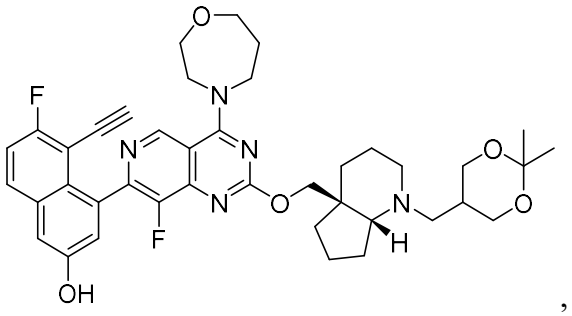

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diastereomer 1
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diastereomer 2
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diastereomeric mixture
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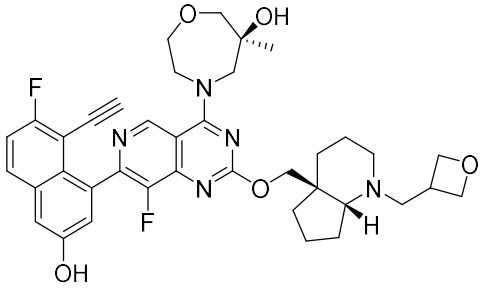

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diastereomer 1
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diastereomer 2
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diastereomer mixture
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diastereomer 2
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diasteromer 1
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diastereomer mixture
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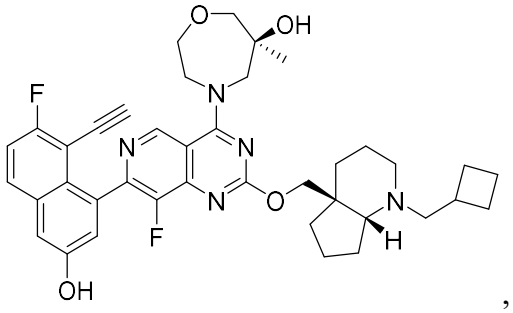

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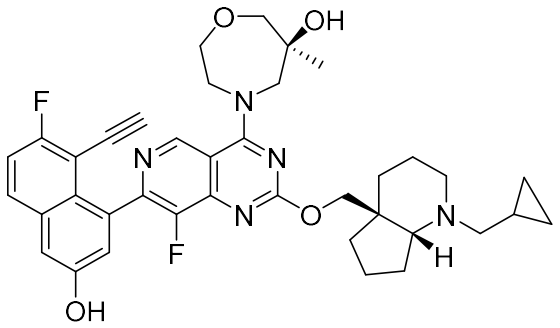

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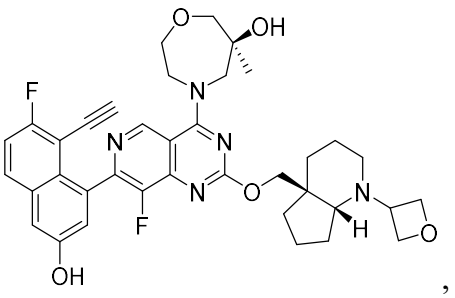

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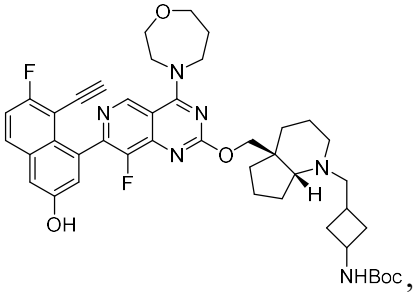

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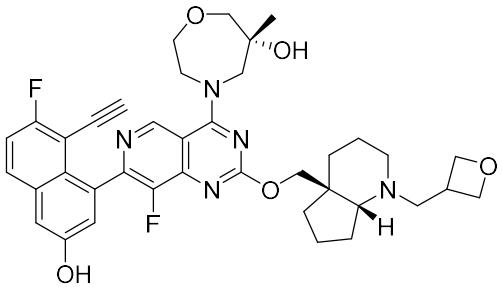

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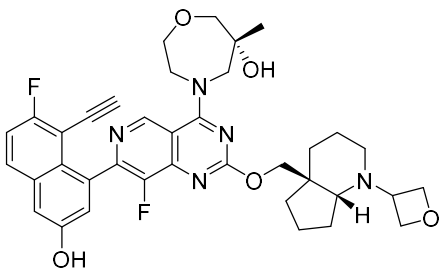
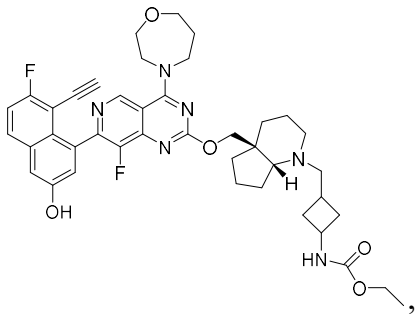
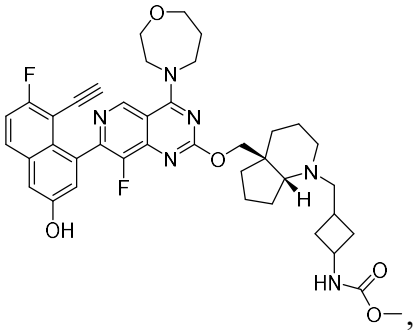
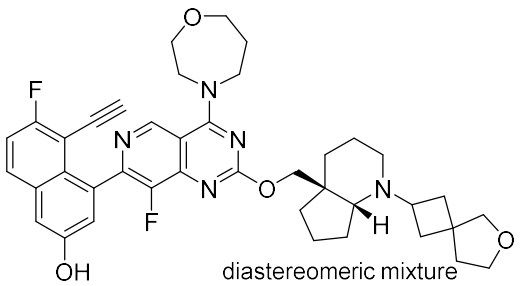
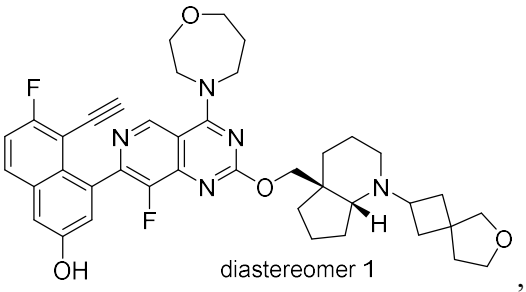
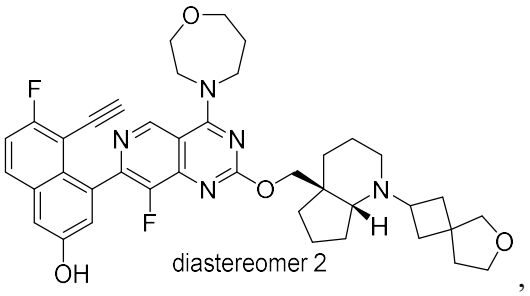
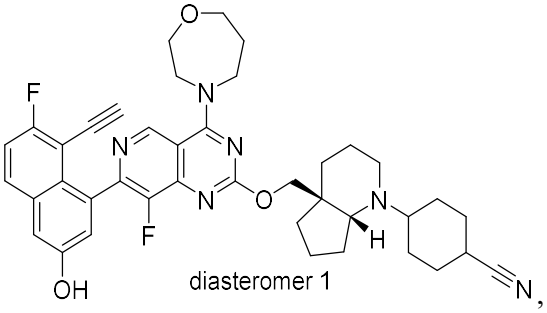
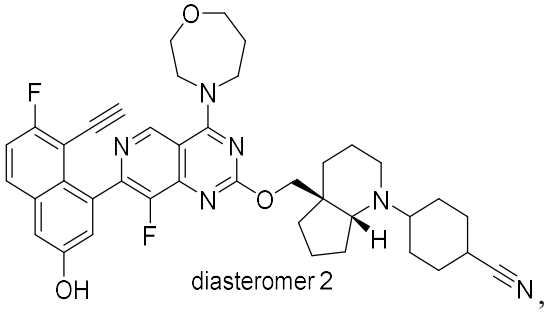
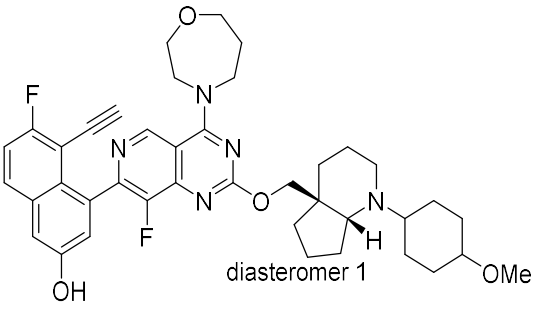
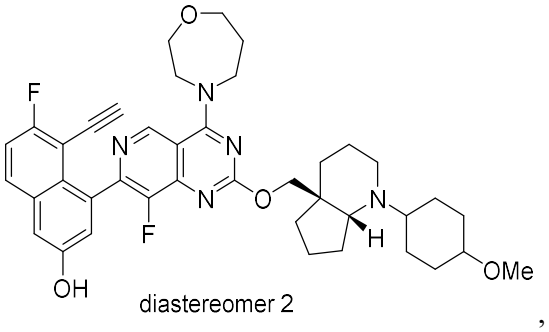

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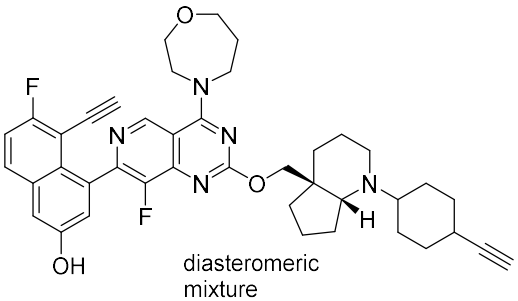

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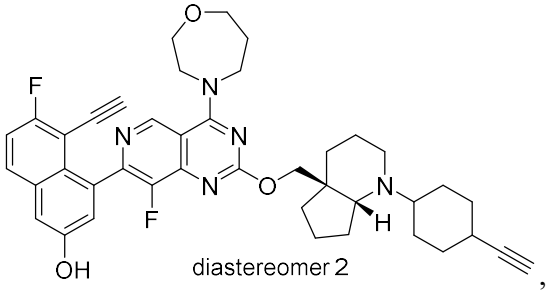

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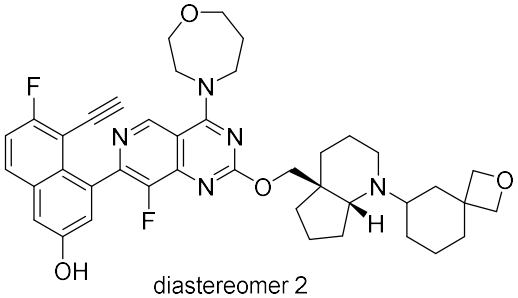

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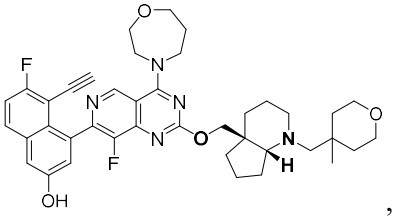

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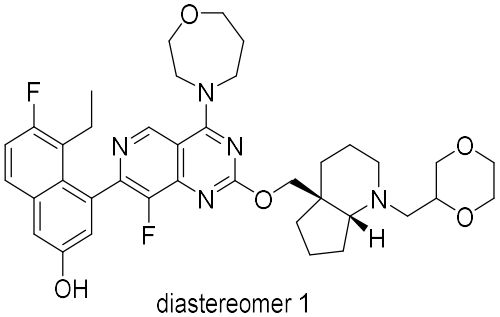

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diastereomeric mixture
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diastereomer 1
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diastereomer 2
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diasteromer 1
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diasteromer 2
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diasteromer 1
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diastereomer 2
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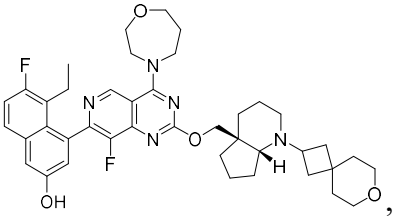

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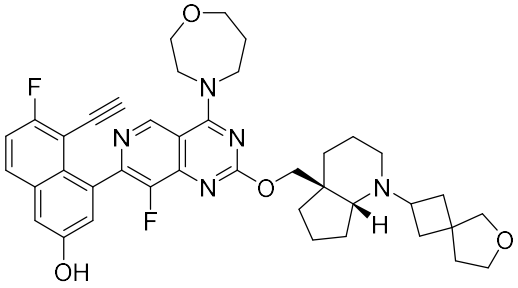

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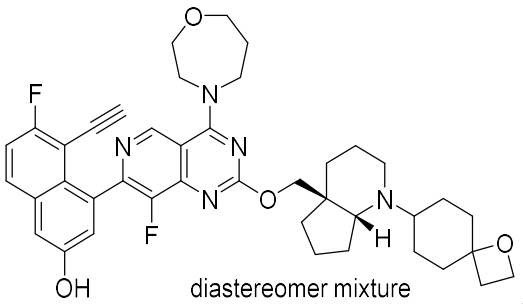

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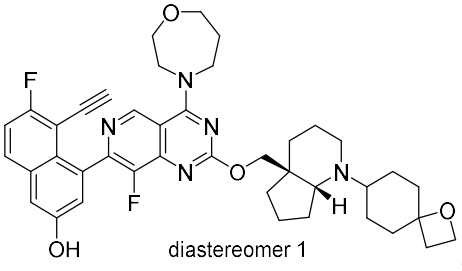

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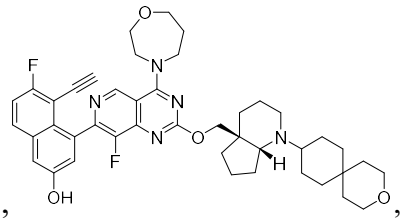

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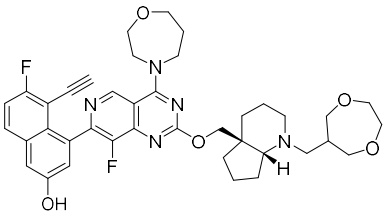

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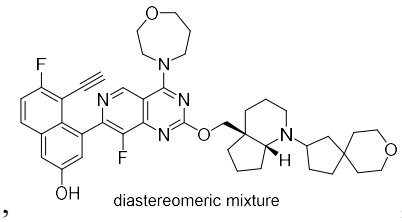

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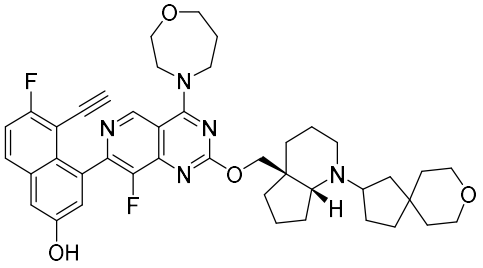

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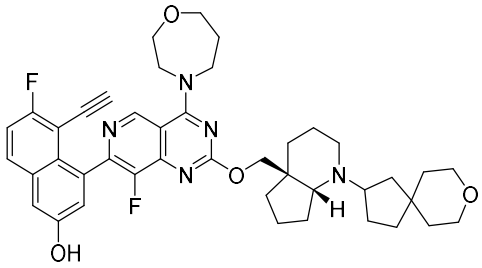

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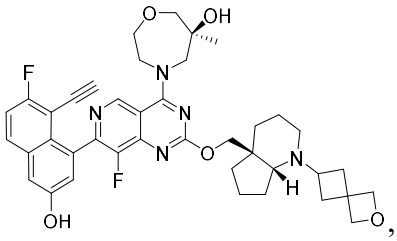

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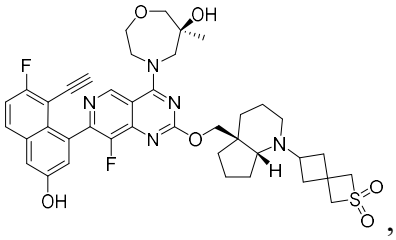


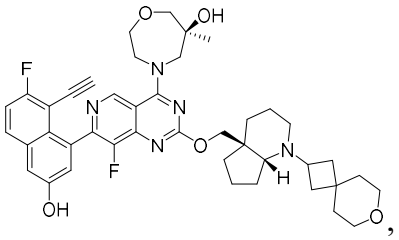

diastereomeric mixture

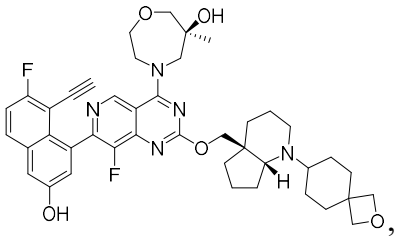

diastereomer 1

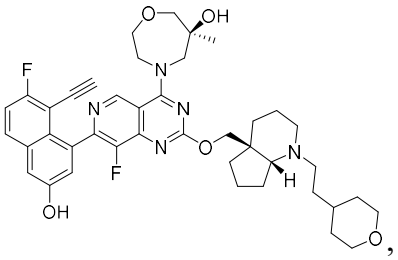

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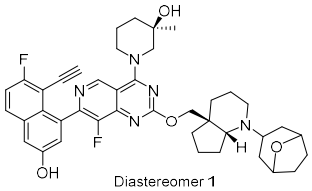


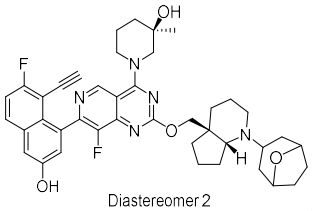


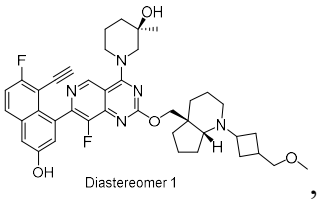


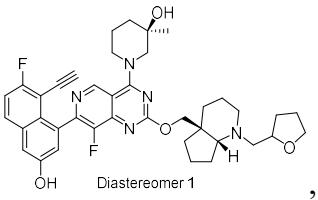


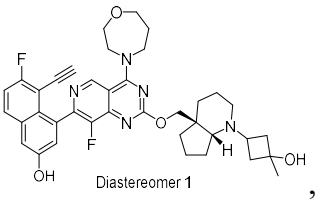


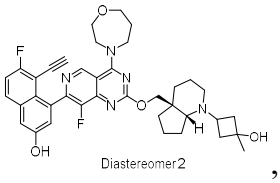

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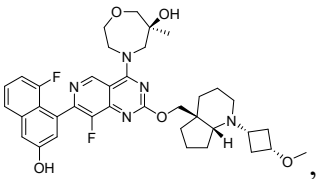

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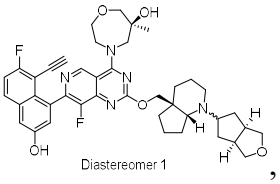

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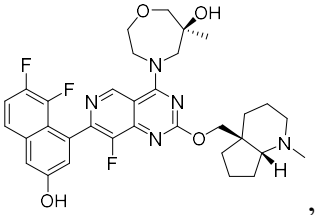

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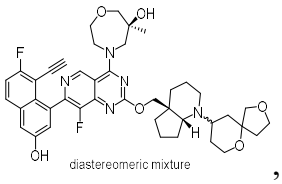

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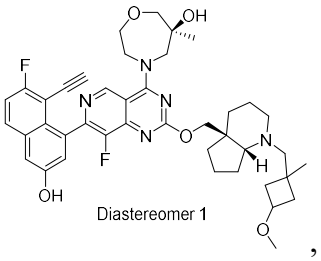
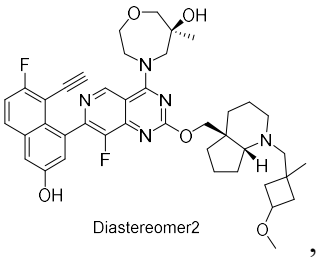
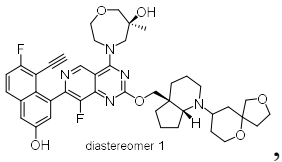
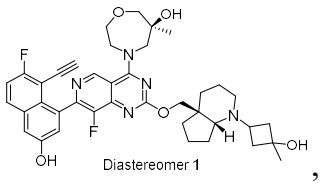
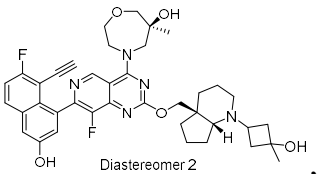
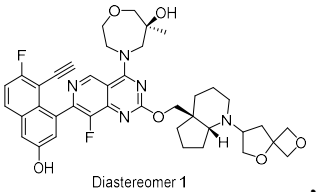
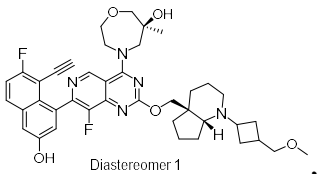
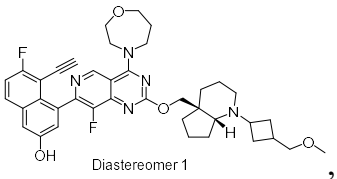
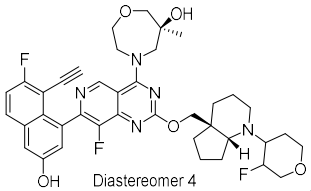
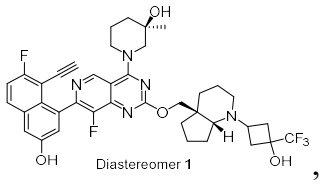
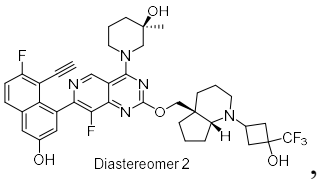
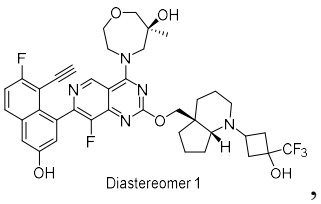
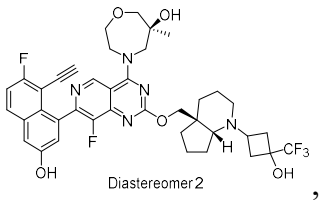
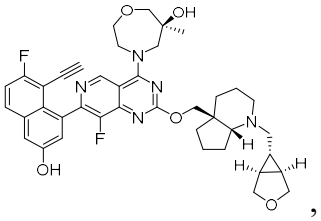
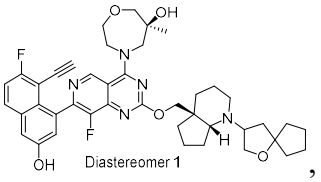
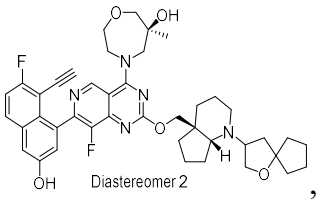
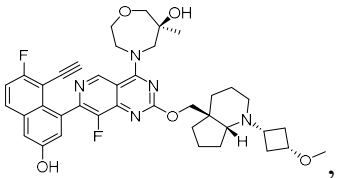
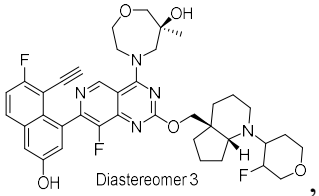
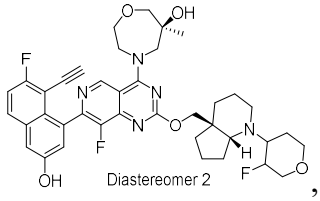
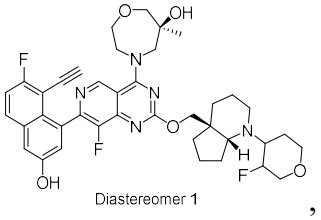
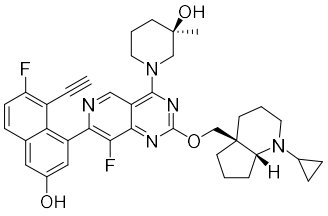
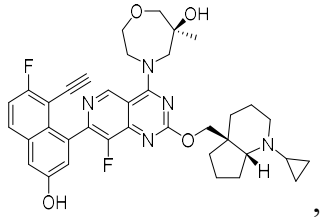

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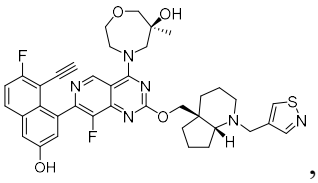
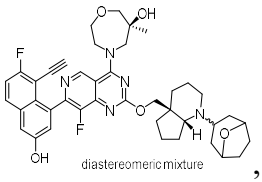
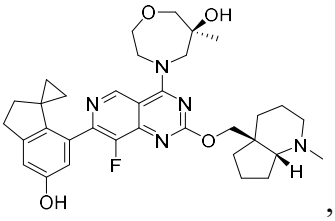
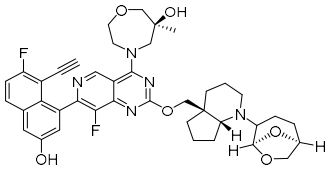
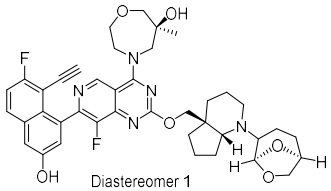
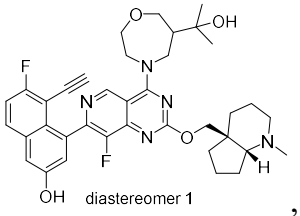
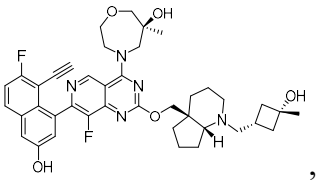
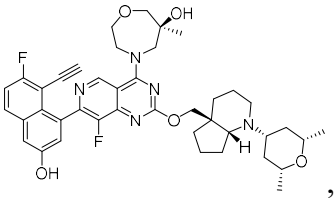
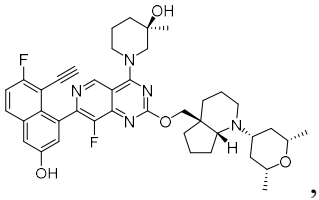
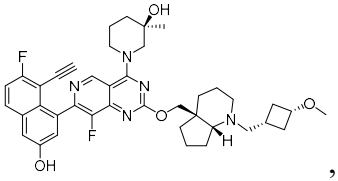
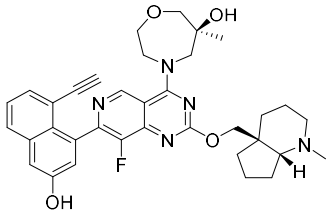
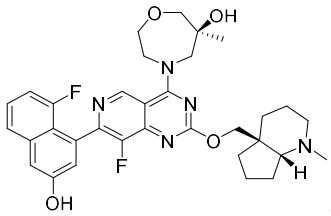
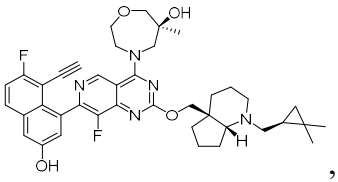
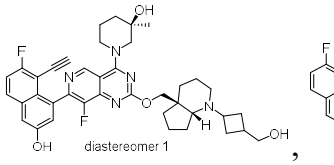
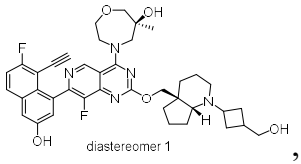
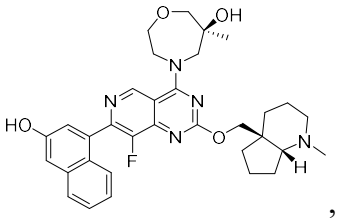
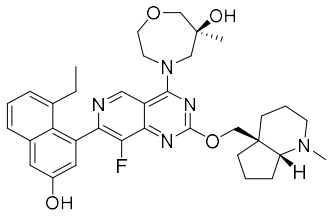
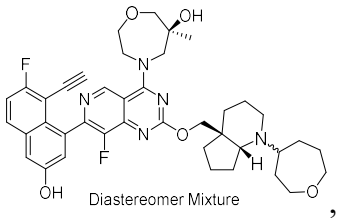
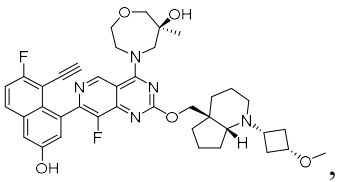
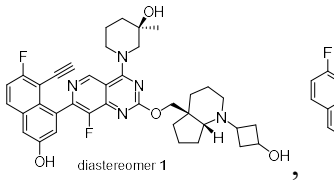
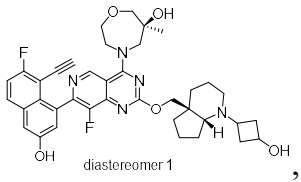
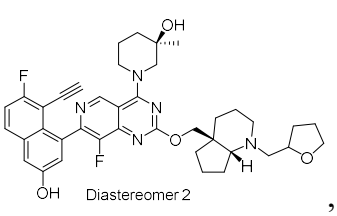
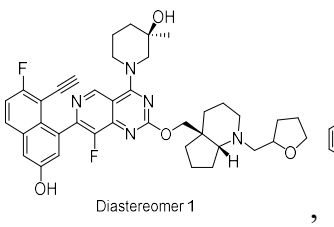
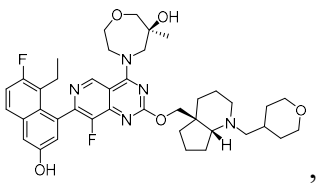


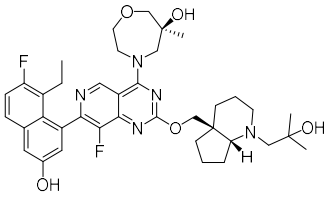
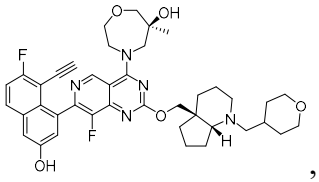
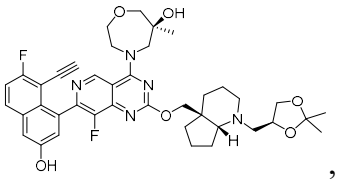

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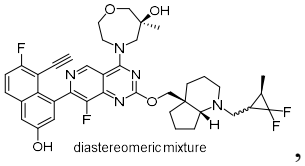
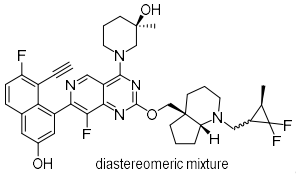
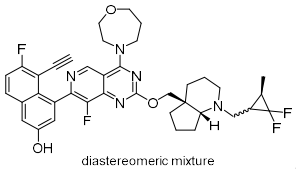
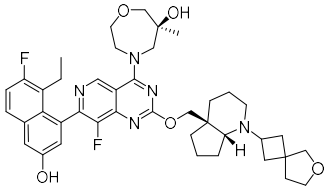


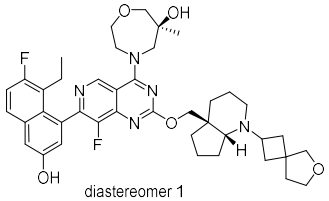
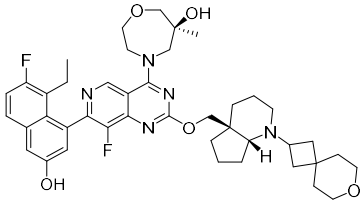
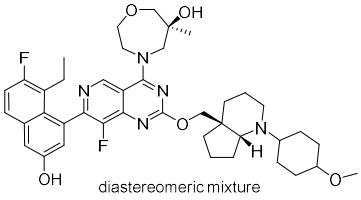

diastereomeric mixture

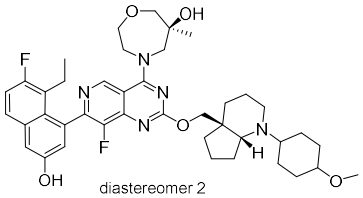
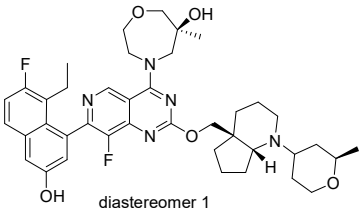
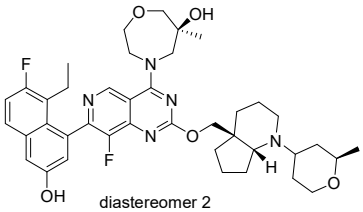

Diastereomer 1
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Diastereomer2
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diastereomer 1
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Diastereomer 1
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Diastereomer 2
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Diastereomer 1
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Diastereomer 1
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Diastereomer 1
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Diastereomer 4
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Diastereomer 1
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Diastereomer 2
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Diastereomer 1
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Diastereomer 2
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Diastereomer 1
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Diastereomer 2
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Diastereomer 3
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Diastereomer 2
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Diastereomer 1
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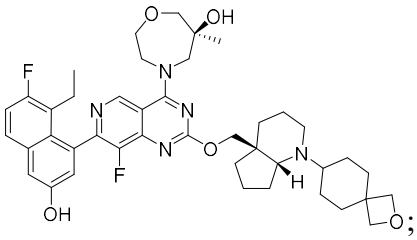
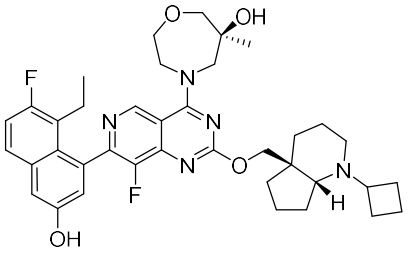
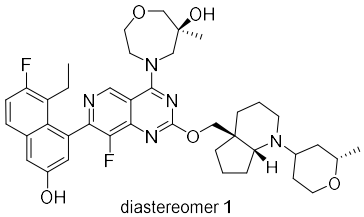

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diastereomeric mixture
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Diastereomer 2
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Diastereomer 1
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diastereomer 1
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diastereomer 1
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diastereomer 1
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Diastereomer Mixture
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diastereomer 1
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diastereomer 1
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Diastereomer 2
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Diastereomer 1
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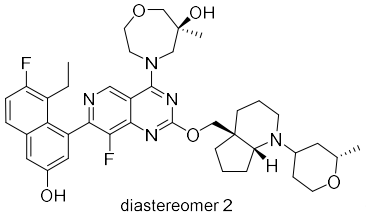
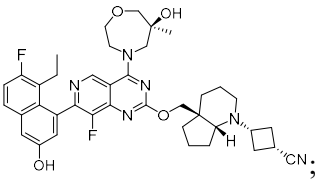
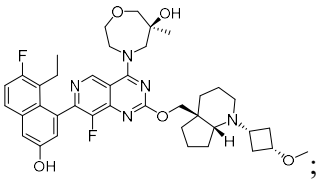

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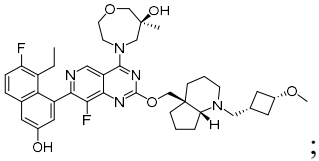
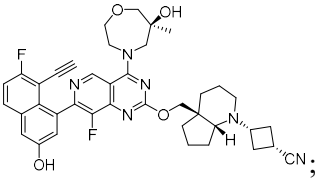
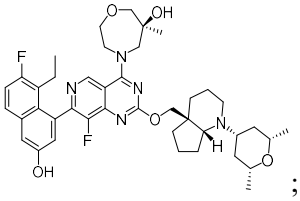
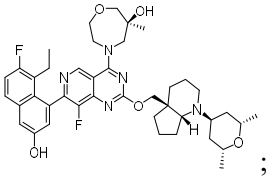

diastereomeric mixture
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diastereomeric mixture
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diastereomeric mixture
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diastereomeric mixture

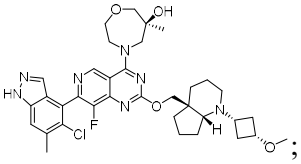
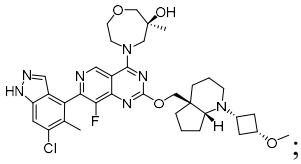
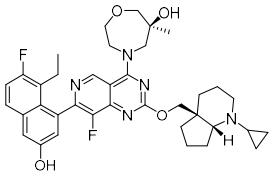
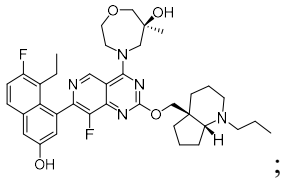
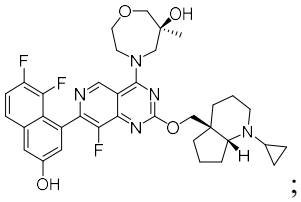
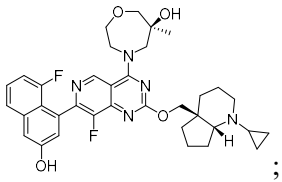
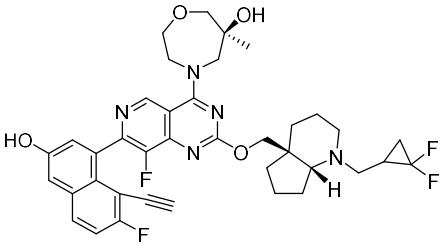
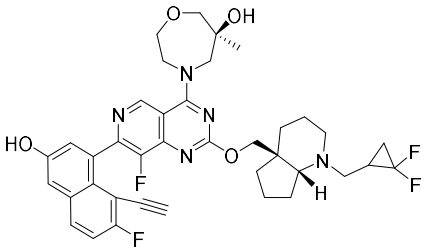
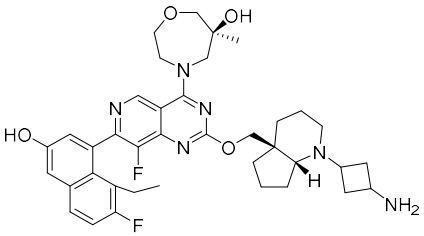
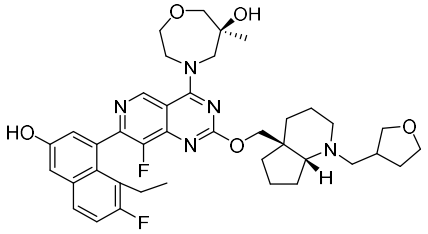
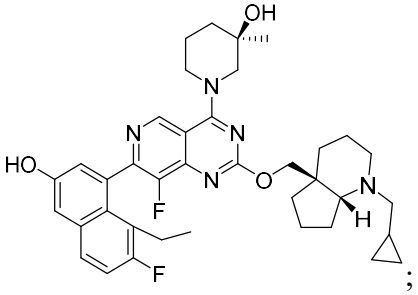
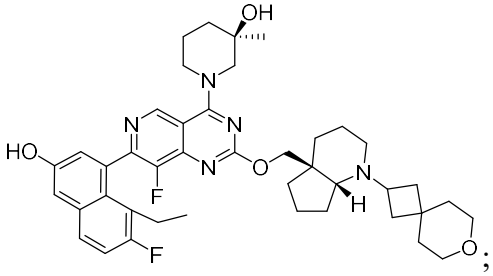
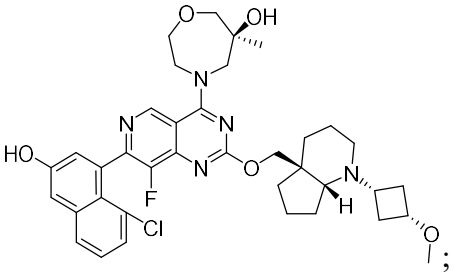
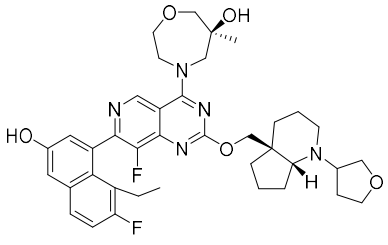
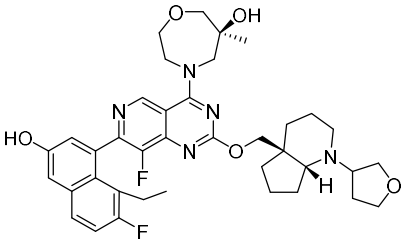
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diastereomer 1

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diastereomeric mixture
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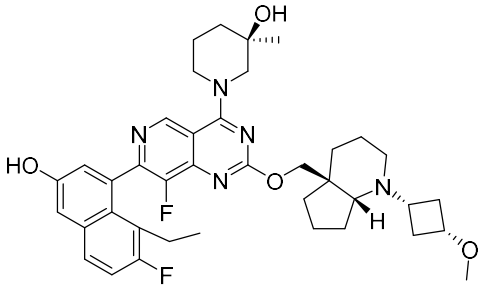

diastereomer 2
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diastereomer 1
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diastereomer 2

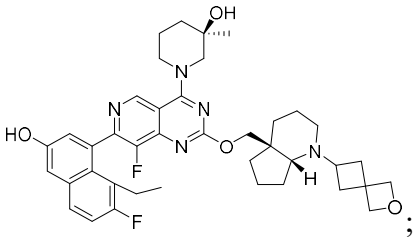

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diastereomer 1

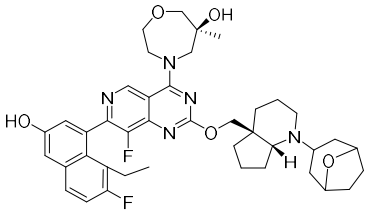

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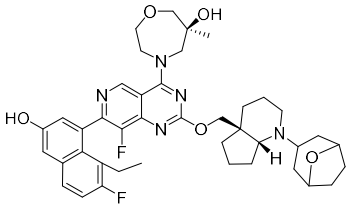

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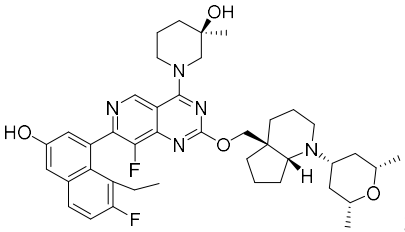

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diastereomer 1 ;

diastereomer 2 ;

Homochiral isomer ;

Homochiral isomer ;

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Diastereomer 1 ;

Diastereomer 2 ;

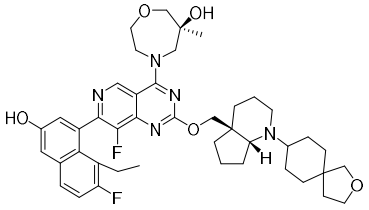

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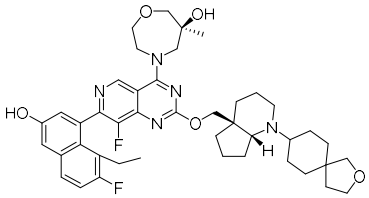

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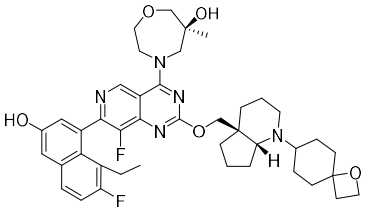

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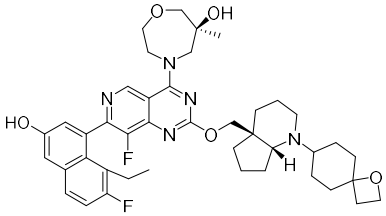

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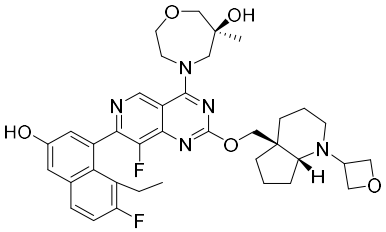

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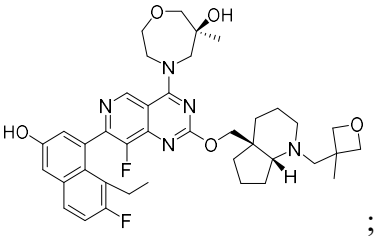

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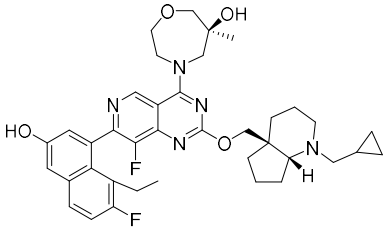

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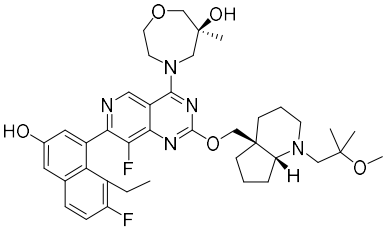

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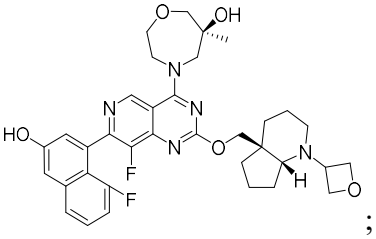

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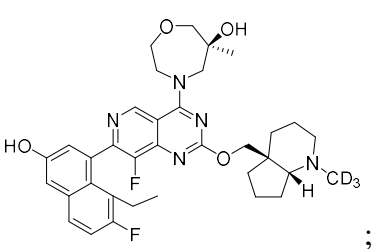

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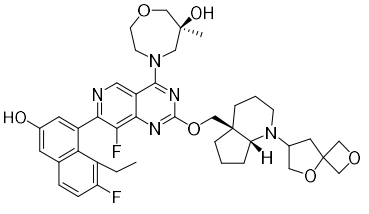

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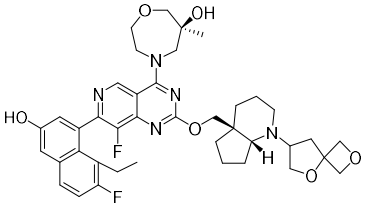

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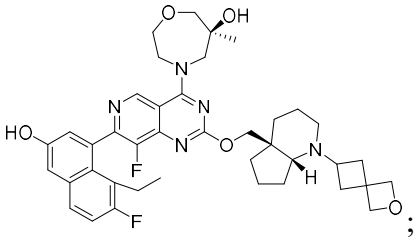
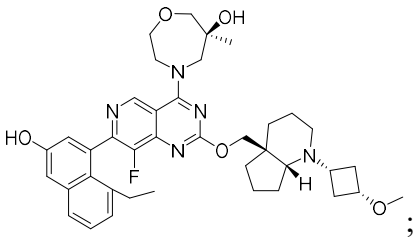
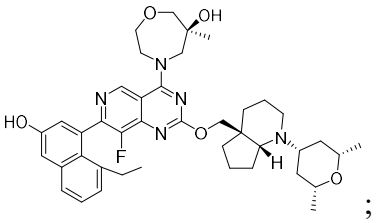
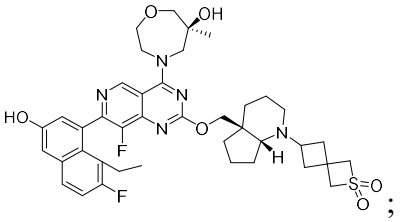
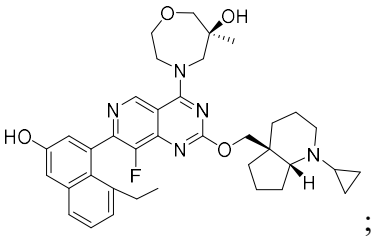
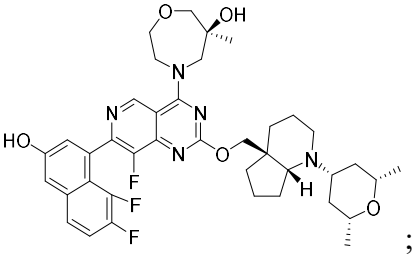
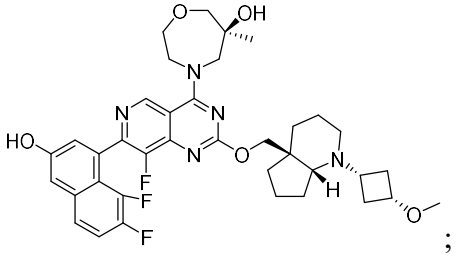
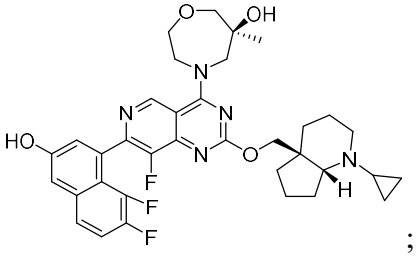
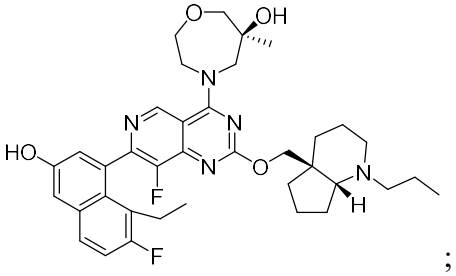
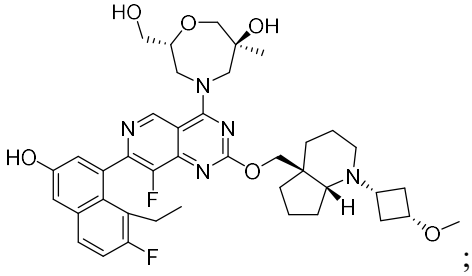
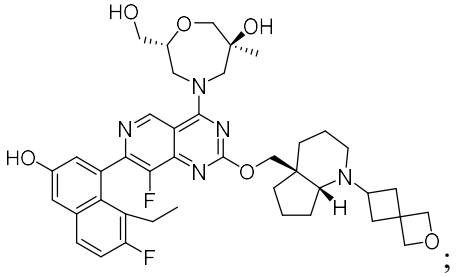

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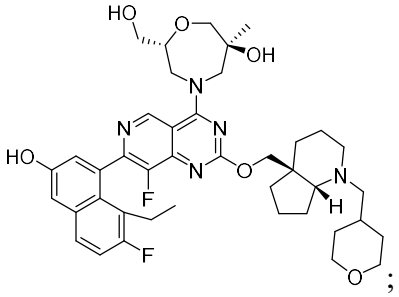
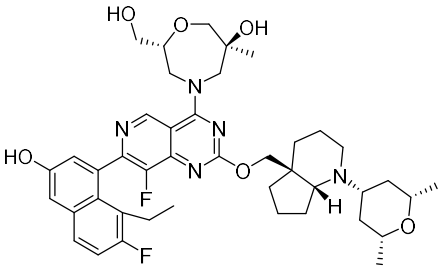
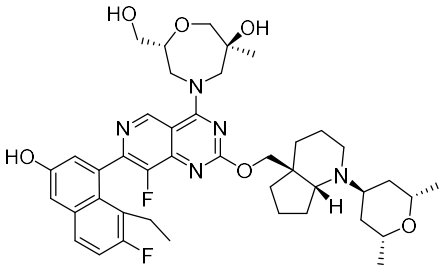

Diastereomer 1 ;


Diastereomer 2 ;


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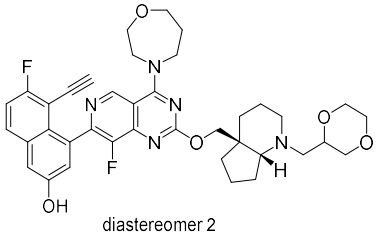
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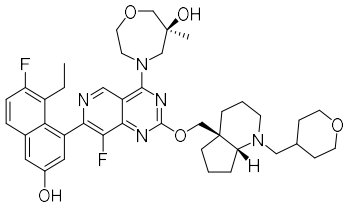
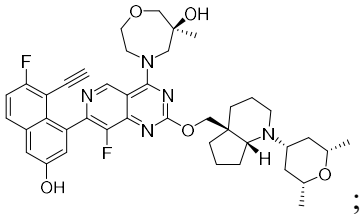
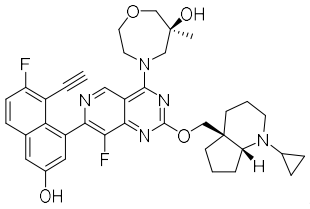
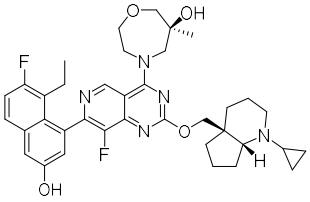
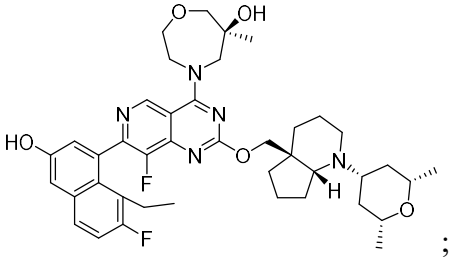
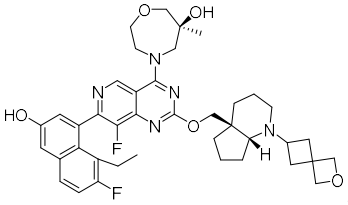
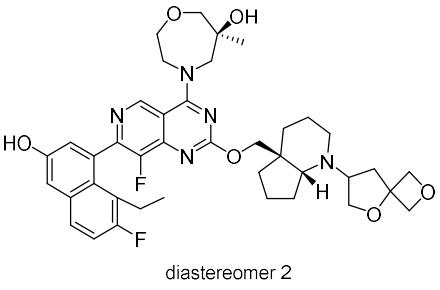
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or a pharmaceutically acceptable salt thereof.

37. A compound selected from the group consisting of:

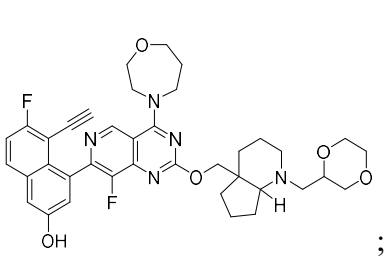
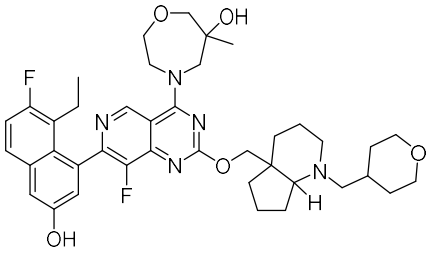
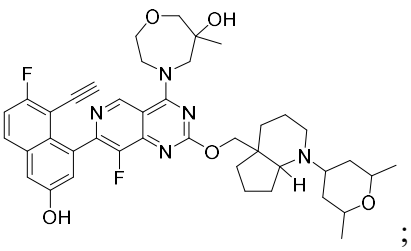
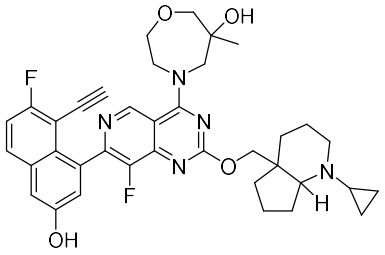
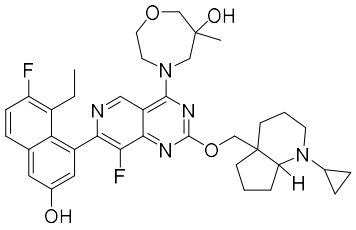
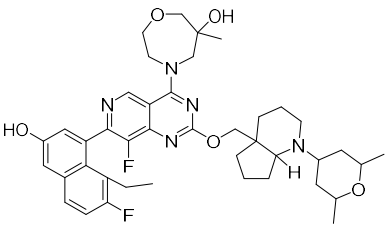
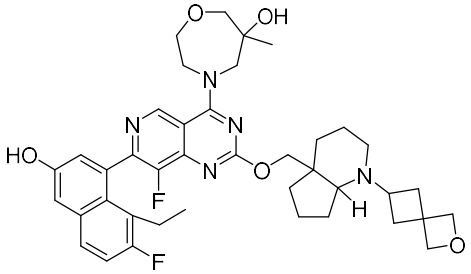
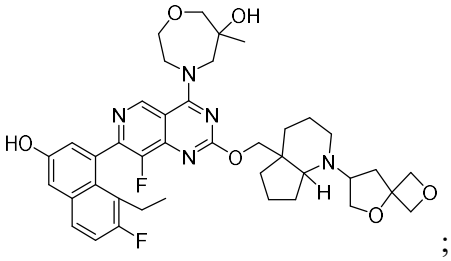


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or a pharmaceutically acceptable salt thereof.

38. A compound selected from the group consisting of:


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or a pharmaceutically acceptable salt thereof.

39. A pharmaceutical composition comprising a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

40. An oral dosage form comprising a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

41. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for inhibiting KRAS G12A, KRAS G12C, KRAS G12D, KRAS G12R, KRAS G12S, KRAS G12V, KRAS G13D and/or KRAS Q61H in a subject in need thereof, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to the subject.

42. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a cancer susceptible to KRAS G12A, KRAS G12C, KRAS G12D, KRAS G12R, KRAS G12S, KRAS G12V, KRAS G13D and/or KRAS Q61H inhibition in a subject in need thereof, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to the subject.

43. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a cancer expressing a KRAS mutation and/or a KRAS copy number amplification in a subject in need thereof, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to the subject.

44. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a cancer expressing a KRAS G13R, Q61R, A146T, A146V, A59G, G12A, G12C, G12D, G12R, G12S, G12V, G13C, G13D, Q61H, Q61K, and/or a KRAS Q61L mutation, and/or a KRAS copy number amplification, in a subject in need thereof, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to the subject.

45. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a cancer expressing KRAS G12A, KRAS G12C, KRAS G12D, KRAS G12R, KRAS G12S, KRAS G12V, KRAS G13D, and/or KRAS Q61H mutation in a subject in need thereof, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to the subject.

46. Use of a compound of any one of claims 1 to 38, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a cancer in a subject in need thereof, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to the subject.

47. The use of claim 46, wherein the cancer is pancreatic cancer, colorectal cancer, lung cancer, gastric cancer, breast cancer, bladder cancer, cervical cancer, ovarian cancer, cancer of the uterus, or a combination thereof.

48. The use of claim 47, wherein the cancer is pancreatic cancer, colorectal cancer, or non-small cell lung cancer.