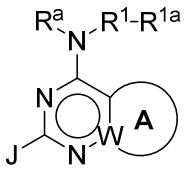
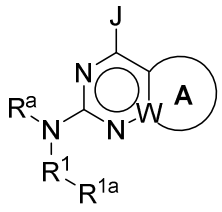
CLAIMS

1. A compound represented by formula (I) or formula (II):


(I)


(II);

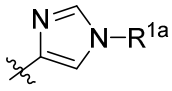
or a pharmaceutically acceptable salt thereof;

wherein:

A is a fused optionally substituted aromatic ring, heteroaromatic ring, partially unsaturated cycloalkyl ring, or partially unsaturated heterocycloalkyl ring;

W is C or N;

R^a represents H or alkyl;

$-R^1-R^{1a}$ represents , wherein R^{1a} represents optionally substituted phenyl;

J represents H, halo, $-OR^2$, $-NR^2R^3$, $-C(O)NR^2R^3$, -C(O)O(alkyl), -C(O)OH, aryl, or heteroaryl, wherein aryl or heteroaryl is optionally substituted by one or more occurrences of R^{2a};

R^2 represents optionally substituted alkyl, aralkyl, heteroaralkyl, cycloalkyl, heterocycloalkyl, (cycloalkyl)alkyl, (heterocycloalkyl)alkyl, or hydroxyalkyl;

R^3 represents H or alkyl; or

R^2 and R^3, taken together, form a heterocycloalkyl ring, optionally substituted by one or more occurrences of R^{2a};

R^{2a}, independently for each occurrence, represents halo, hydroxyl, -C(O)H, oxo, $-NH_2$, $-C(O)NH_2$, -C(O)OH, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NH(R^5)$, or optionally substituted alkyl,

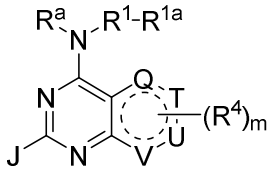
alkoxyl, hydroxyalkyl, heteroaryl, aryl, aryloxy, heteroaryloxy, arylalkyloxy, heteroarylalkyloxy, or -N(alkyl)$_2$;

or any two germinal or vicinal occurrences of R^{2a}, taken together, may form a spiro or fused cycloalkyl ring;

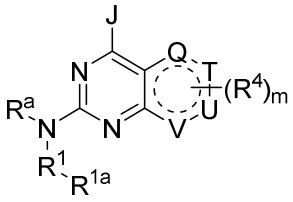
R^5, independently for each occurrence, represents optionally substituted alkyl, aralkyl, aryl, heteroaralkyl, heteroaryl, cycloalkyl, heterocycloalkyl, (cycloalkyl)alkyl, or (heterocycloalkyl)alkyl; and

R^x and R^y each independently represent H, alkyl, aralkyl, heteroaralkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, (cycloalkyl)alkyl, (heterocycloalkyl)alkyl, or hydroxyalkyl.

2. The compound of claim 1, wherein the compound is represented by formula (Ia) or formula (IIa):



(Ia)



(IIa);

wherein:

valence permitting, Q, T, U, and V each independently represent CH, CH_2, N, NH, O, or SO_2, wherein any hydrogen of a CH, CH_2, or NH group is optionally replaced by an occurrence of R^4;

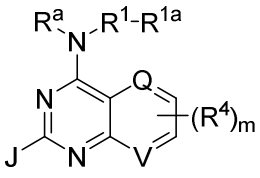
R^4, independently for each occurrence, represents halo, cyano, or optionally substituted alkyl, alkenyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkoxy, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkenyl, (heterocycloalkyl)alkyl, cycloalkyl, (cycloalkyl)alkyl, halocycloalkyl, hydroxycycloalkyl, aminocycloalkyl, aryloxy,

heteroaryloxy, arylalkyloxy, heteroarylalkyloxy, -$CH_2C(O)NH_2$, -$C(O)R^5$, -$C(O)OR^5$, or –$S(O)_2R^5$;

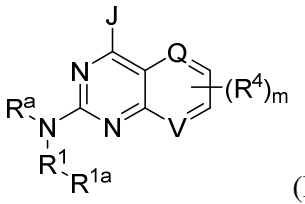
m is an integer from 0-4, as permitted by valence.

3. The compound of claim 2, wherein the compound is represented by:

a) formula (Ib) or (IIb):



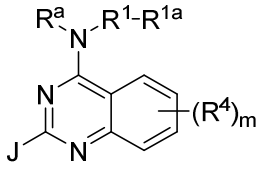
(Ib)



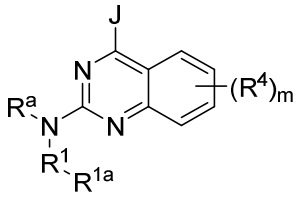
(IIb),

wherein Q represents CH or N, and V represents CH or N;

b) formula (Ic) or (IIc):

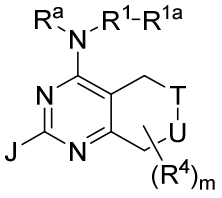


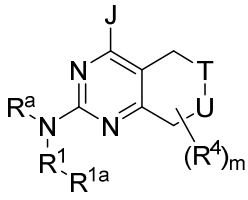
(Ic)



(IIc);

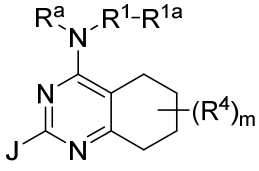
c) formula (Id) or (IId):

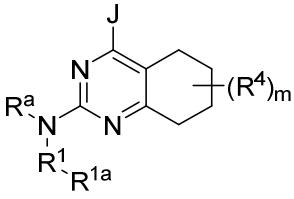

(Id)


(IId),

wherein T represents CH_2, NH, O, or SO_2, and U represents CH_2, NH, O, or SO_2; or

d) formula (Ie) or (IIe):

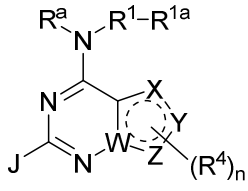

(Ie)

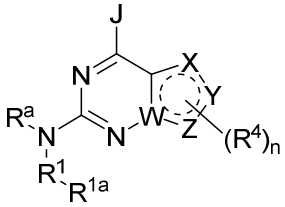

(IIe).

4. The compound of claim 3, wherein the compound is represented by formula (Ib) or (IIb), and wherein Q is N and V is CH, or wherein Q is CH and V is N.

5. The compound of claim 3, wherein the compound is represented by formula (Id) or (IId), and wherein T is NH and U is CH_2, or wherein T is CH_2 and U is NH.

6. The compound of claim 1, wherein the compound is represented by formula (Ij) or formula (IIj):


(Ij)


(IIj);

wherein:

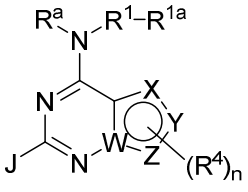
W is C or N;

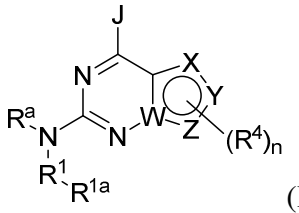
valence permitting, X, Y, and Z each independently represent CH, CH_2, CO, N, NH, O, S, or SO_2, wherein any hydrogen of a CH, CH_2, or NH group is optionally replaced by an occurrence of R^4;

R^4, independently for each occurrence, represents cyano, halo, or optionally substituted alkyl, alkenyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkoxy, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkenyl, (heterocycloalkyl)alkyl, cycloalkyl, (cycloalkyl)alkyl, halocycloalkyl, hydroxycycloalkyl, aminocycloalkyl, aryloxy, heteroaryloxy, arylalkyloxy, heteroarylalkyloxy, $-CH_2C(O)NH_2$, $-C(O)R^5$, $-C(O)OR^5$, or $–S(O)_2R^5$;

n is an integer from 0-4, as permitted by valence.

7. The compound of claim 6, wherein the compound is represented by formula (Ik) or (IIk):


(Ik)

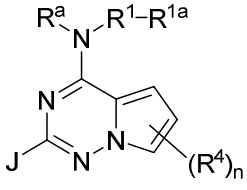


(IIk);

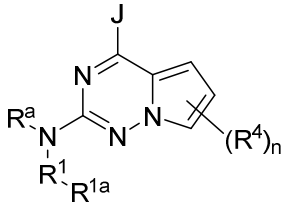
wherein X, Y, and Z each independently represent CH, N, NH, O, S, or SO_2.

8. The compound of claim 7, wherein the compound is represented by:

a) formula (Ik') or (IIk'):

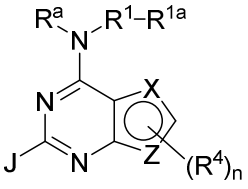


(Ik')

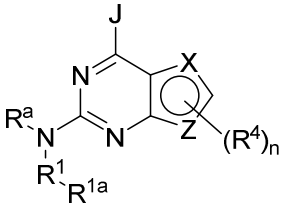


(IIk');

b) formula (Ik") or (IIk"):



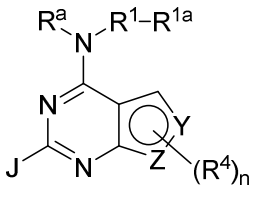
(Ik")

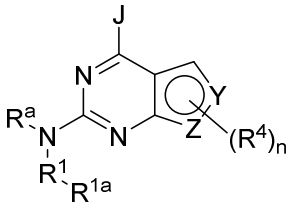


(IIk"),

wherein at least one of X and Z is selected from the group consisting of O, N, NH, and S; or

c) formula (In) or (IIn):


(In)


(IIn),

wherein each of Y and Z are selected from the group consisting of O, N, NH, and S.

9. The compound of claim 8, wherein the compound is represented by formula (Ik") or IIk"), and wherein:

a) one of X and Z is selected from the group consisting of O, NH, and S, and the other of X and Z is CH;

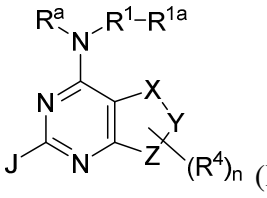
b) X is selected from the group consisting of O, NH, and S;

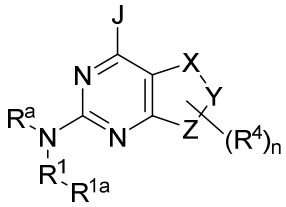
c) Z is selected from the group consisting of O, NH, and S;

d) each of X and Z are selected from the group consisting of O, N, NH, and S; or

e) one of X and Z is N and the other of X and Z is NH.

10. The compound of claim 6, wherein the compound is represented by formula (Im) or (IIm):


(Im)


(IIm);

wherein X, Y, and Z each independently represent CH_2, CO, NH, O, S, or SO_2.

11. The compound of claim 10, wherein:
    a) each of X, Y, and Z is CH_2; or
    b) one of X, Y, and Z is N or O.

12. The compound of any one of claims 1-11, wherein R^4, if present, is selected from the group consisting of optionally substituted alkyl, hydroxyalkyl, aminoalkyl, alkoxy, aryl, aralkyl, and (heterocycloalkyl)alkyl.

13. The compound of any one of claims 1-12, wherein R^a is H.

14. The compound of any one of claims 1-13, wherein R^{1a} is:
    a) phenyl, substituted by one or more occurrences of halo, hydroxyl, cyano, -C(O)NH_2, hydroxyalkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, -C(O)alkyl, -C(O)O-alkyl, heterocycloalkyl, -C(O)NH(alkyl), -C(O)N(alkyl)$_2$, -C(O)heterocycloalkyl, -C(O)(prolinol), -C(O)NH((cycloalkyl)alkyl), or -C(O)NH(cycloalkyl);
    b) phenyl, substituted by two or more occurrences of alkoxy;
    c) 3,4,5-trimethoxyphenyl; or
    d) substituted phenyl, wherein two adjacent substituents on the phenyl, taken together with the intervening atoms, form an optionally substituted cycloalkyl or heterocycloalkyl ring.

15. The compound of any one of claims 1-14, wherein:
    a) J is aryl, optionally substituted by one or more occurrences of R^{2a}; or
    b) J is $–NR^2R^3$.

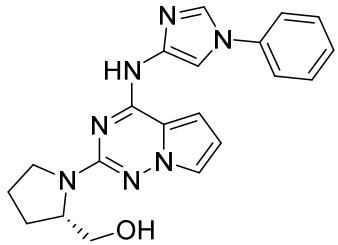
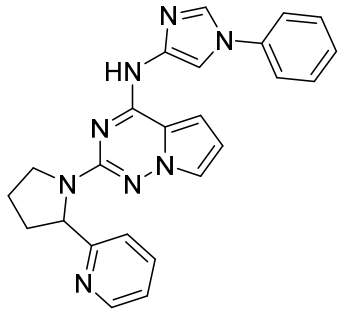
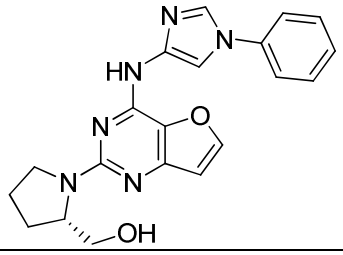
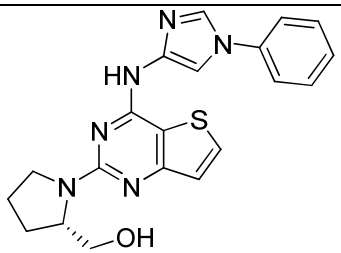
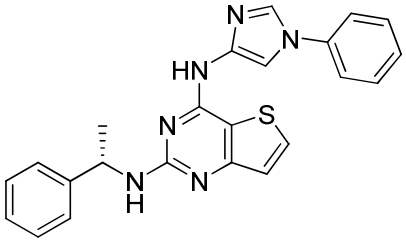
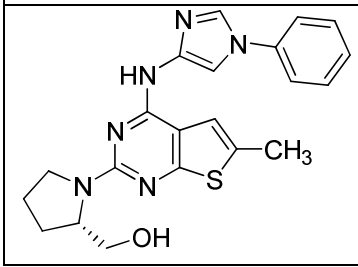
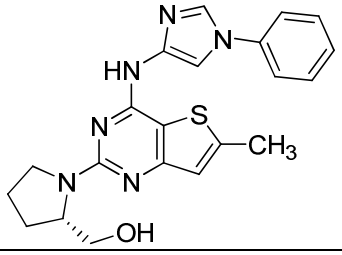
16. The compound of claim 15, wherein:

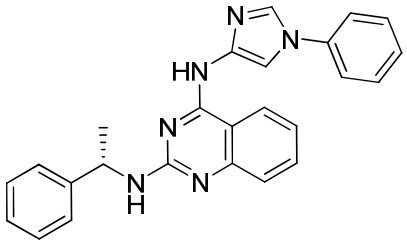
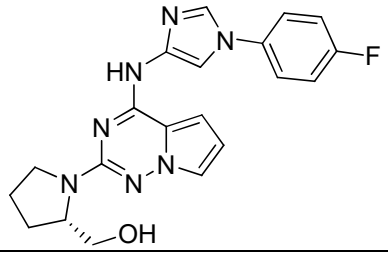
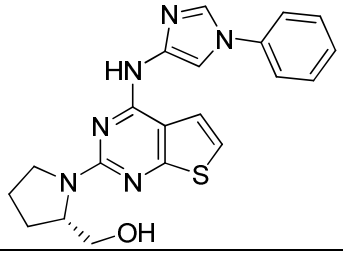
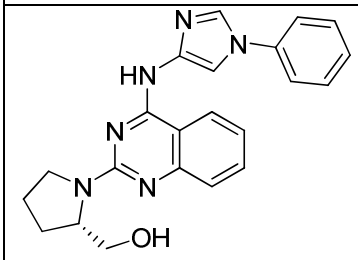
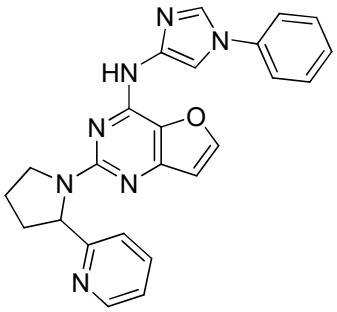
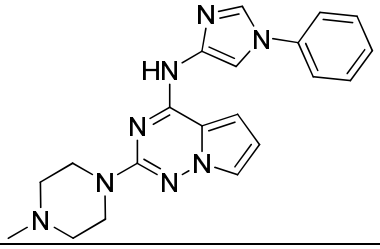
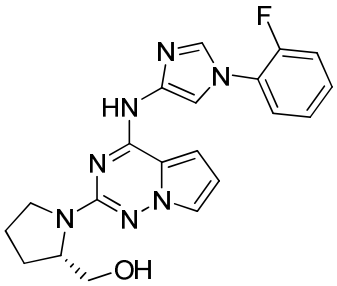
a) R^2 and R^3, taken together, form a heterocycloalkyl ring, optionally substituted by one or more occurrences of R^{2a}; or

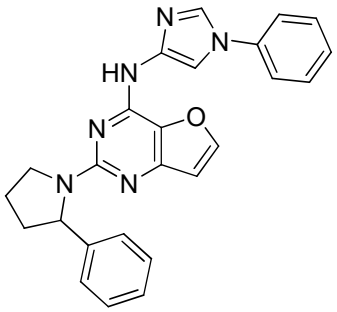
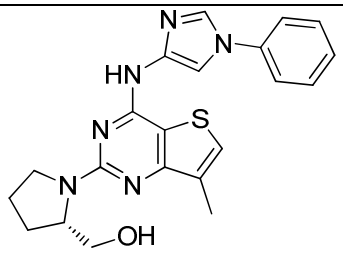
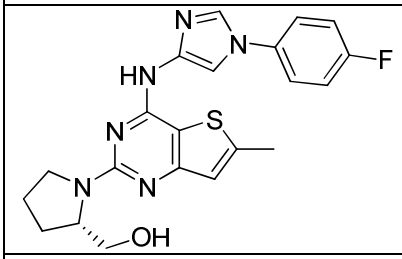
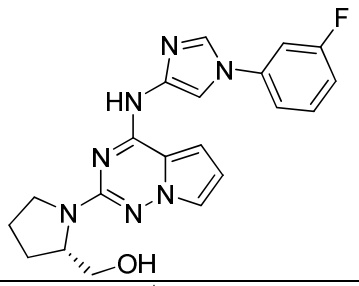
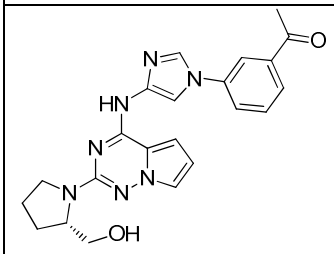
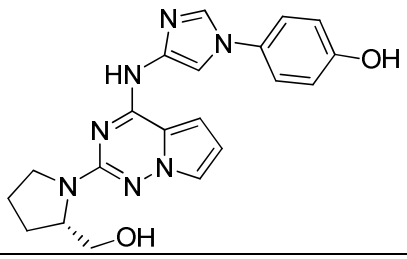
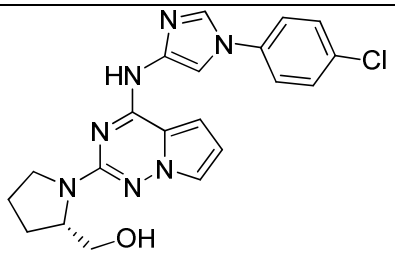
b) R^2 and R^3, taken together, form a pyrrolidine ring, optionally substituted by one or more occurrences of R^{2a}.

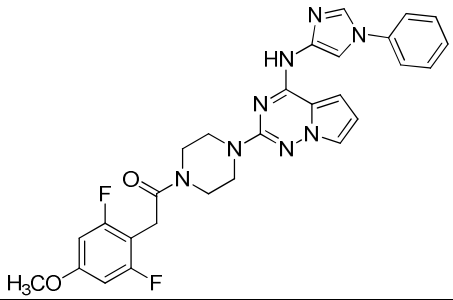
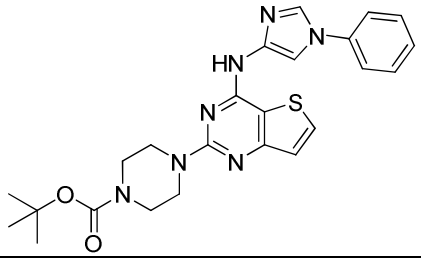
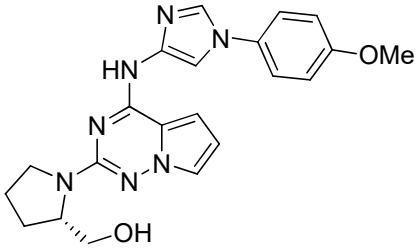
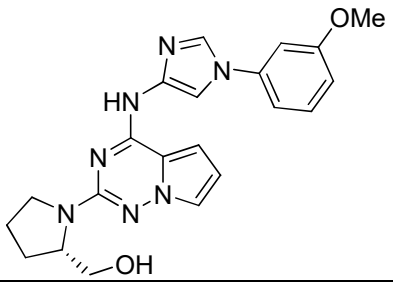
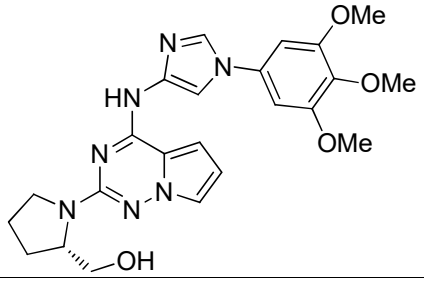
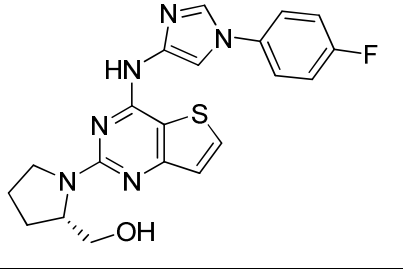
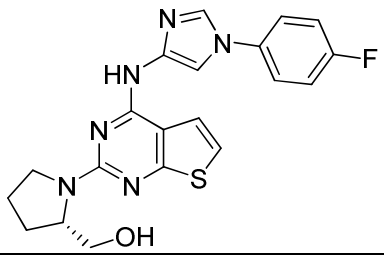
17. The compound of claim 15 or 16, wherein R^{2a}, independently for each occurrence, represents $-C(O)NH_2$, $-C(O)R^5$, hydroxyalkyl, heteroaryl, or aryl.

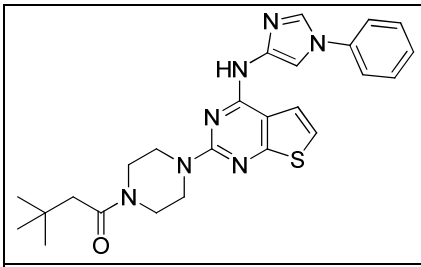
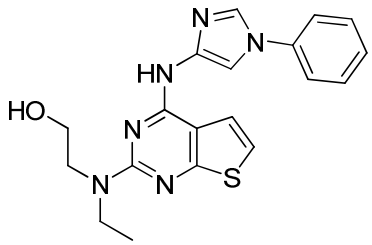
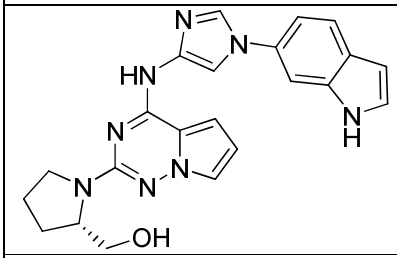
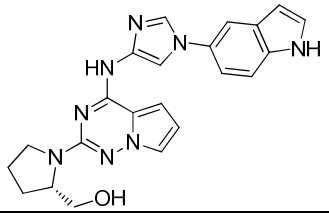
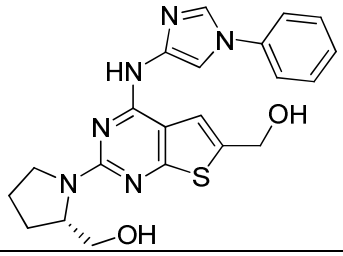
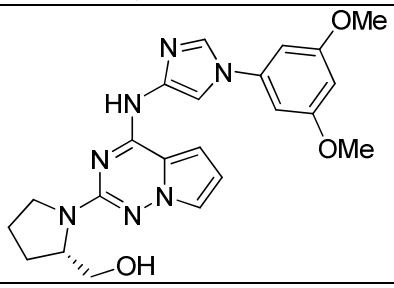
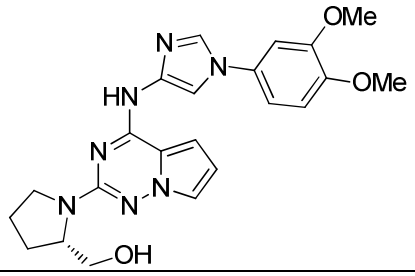
18. The compound of claim 1, selected from the following table:

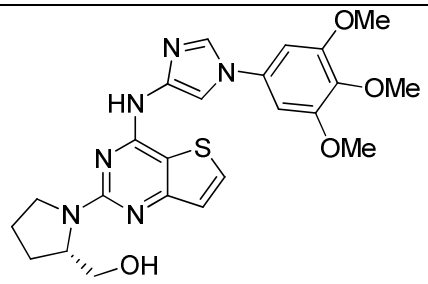
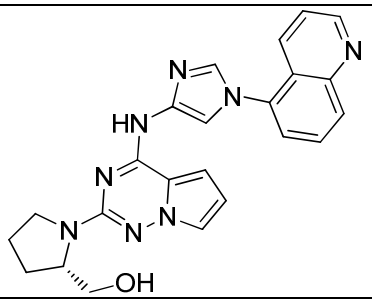
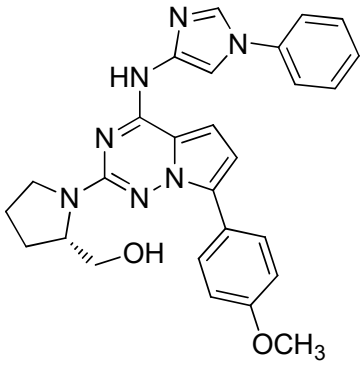
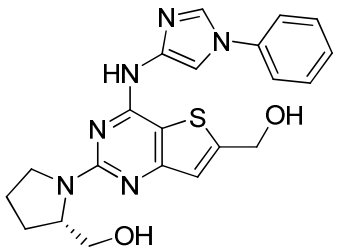
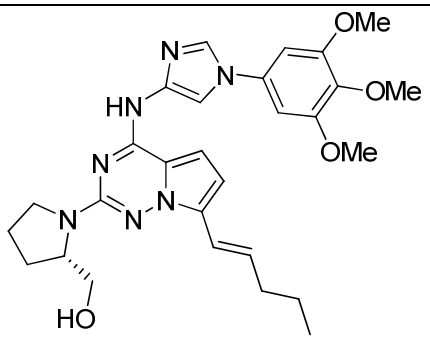
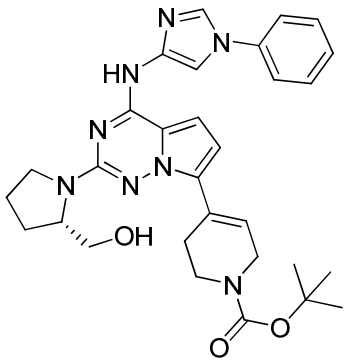
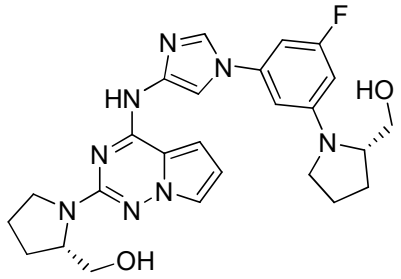
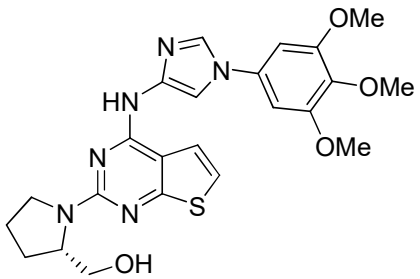
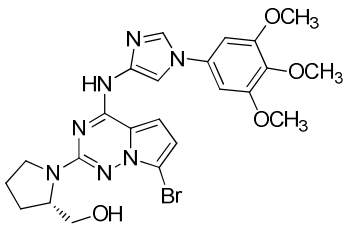
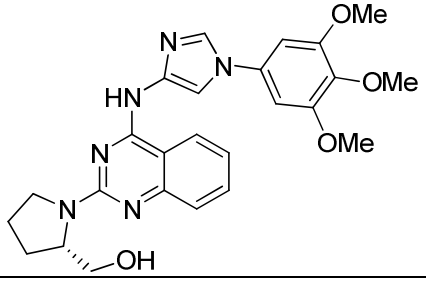
	
	
	
	

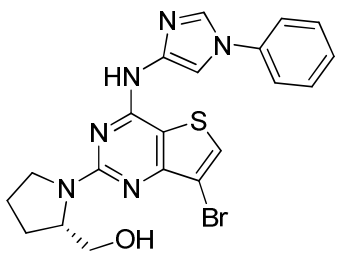
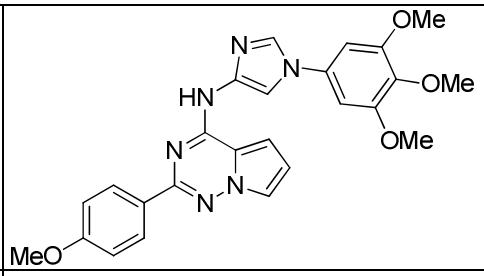
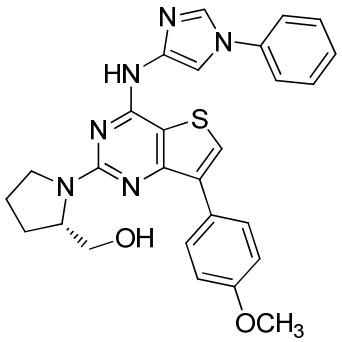
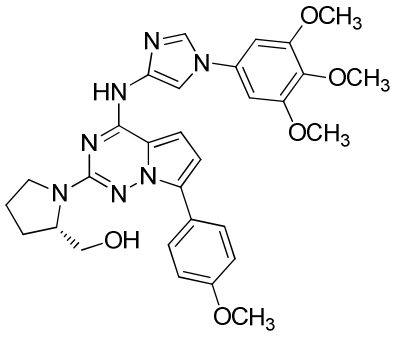
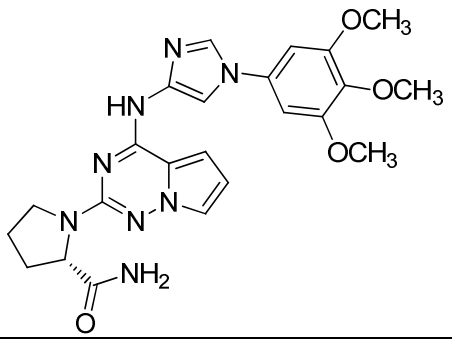
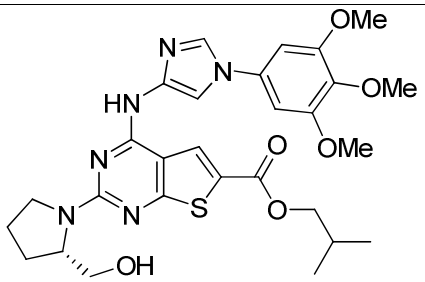
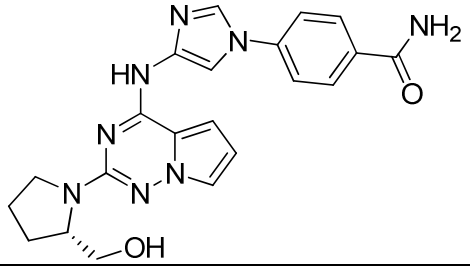
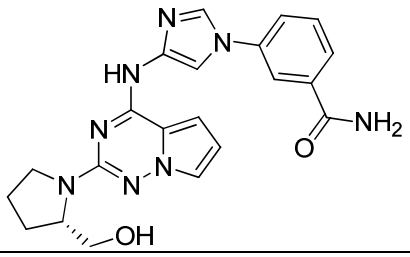
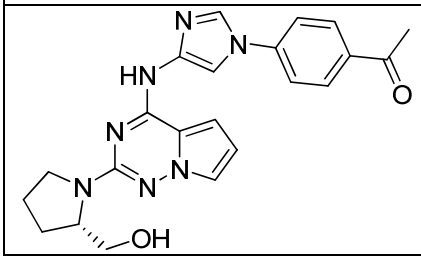
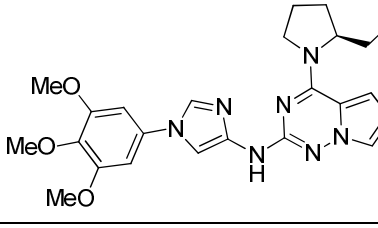
	
	
	
	
	

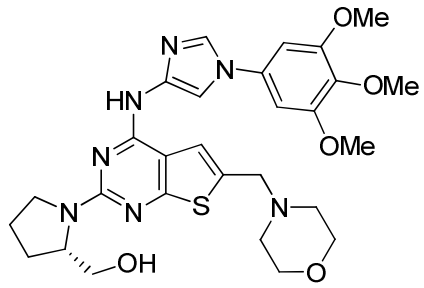
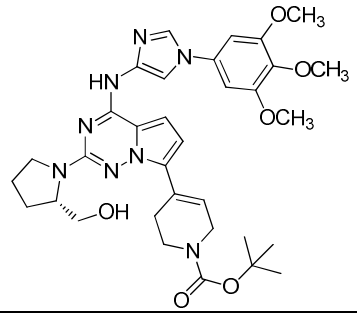
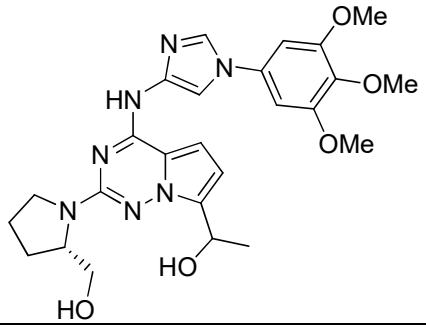
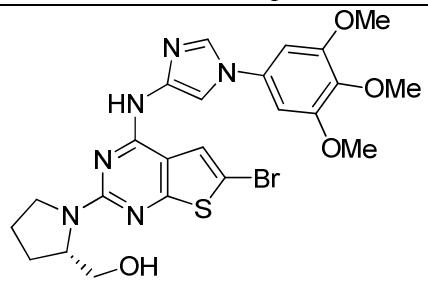
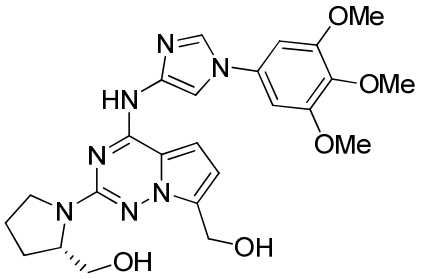
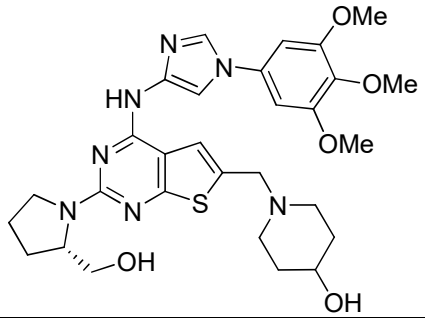
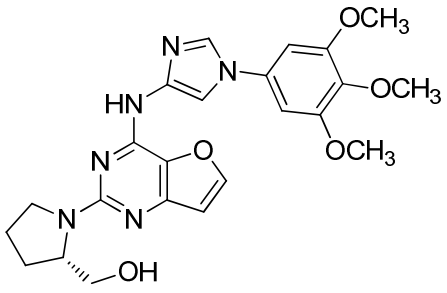
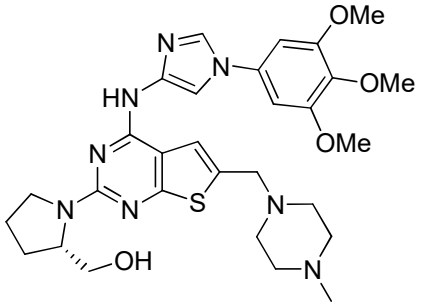
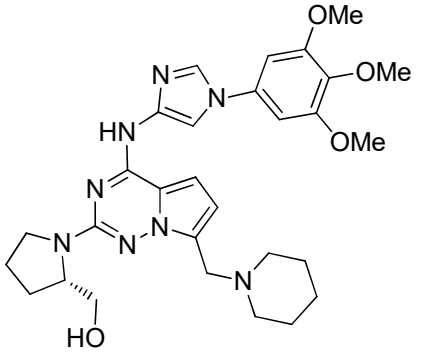
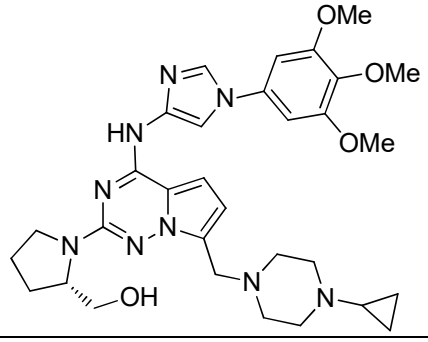
	
	
	
	
	

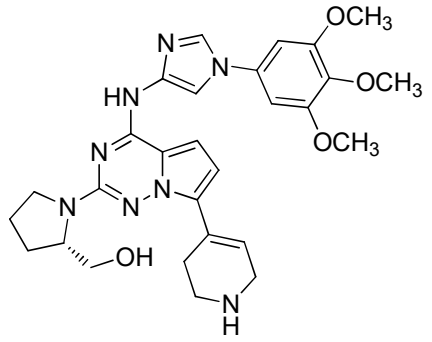
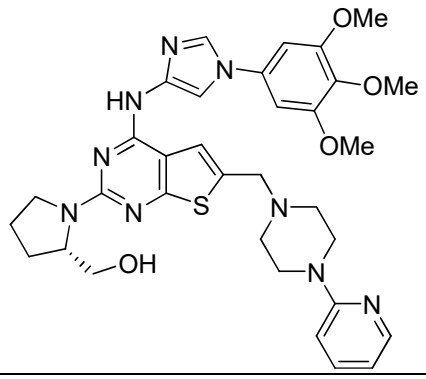
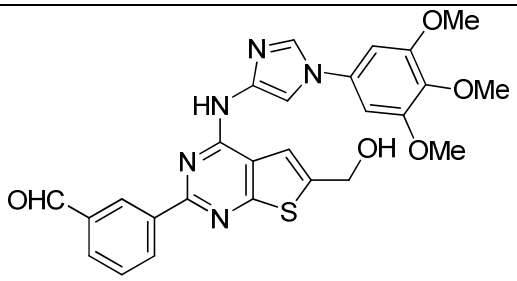
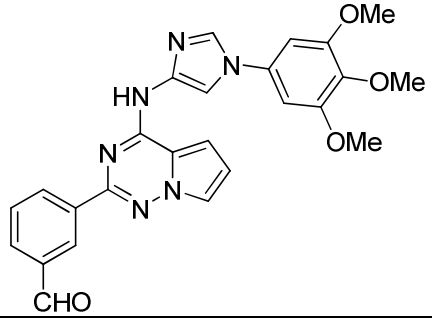
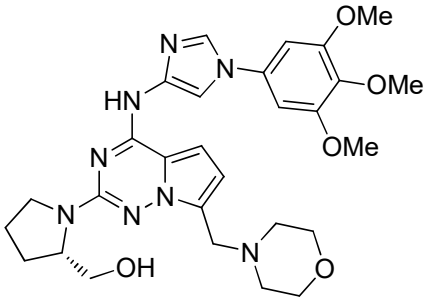
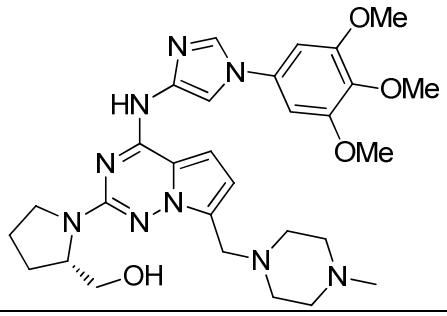
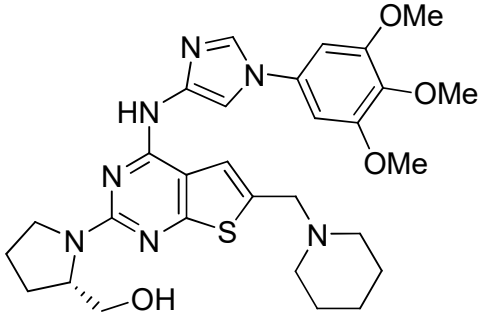
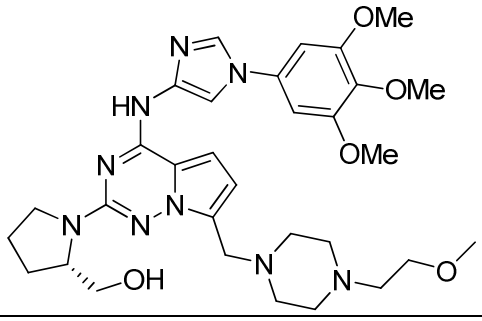
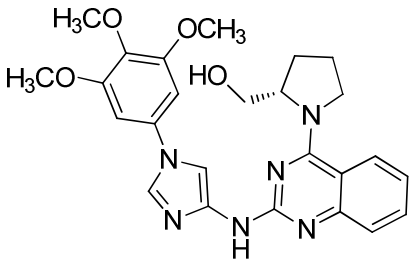
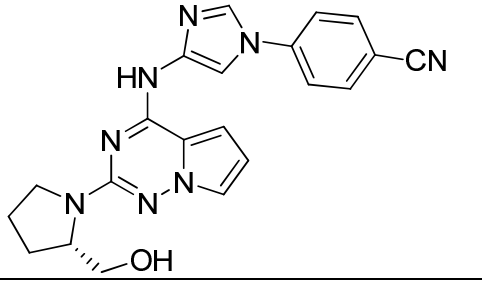
	
	
	
	
	

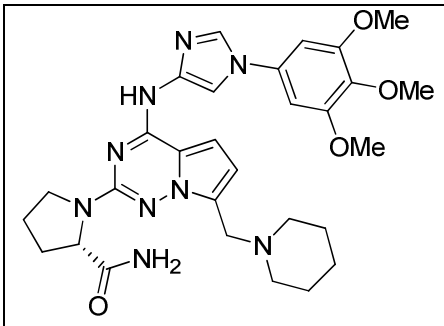
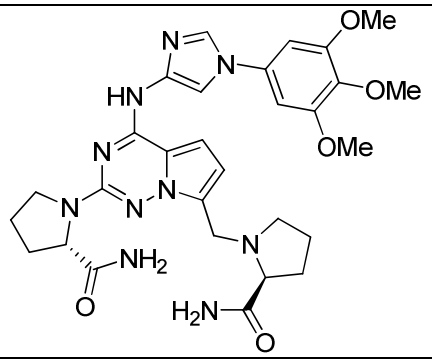
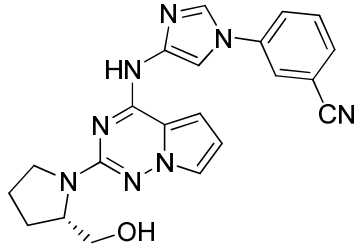
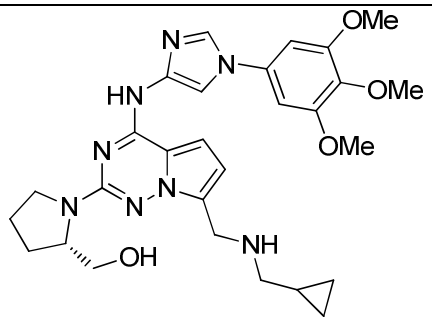
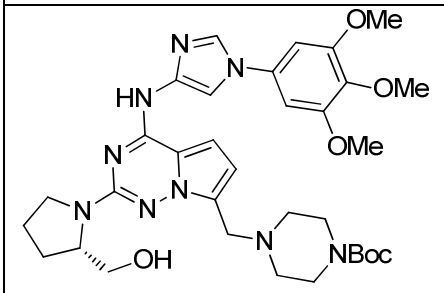
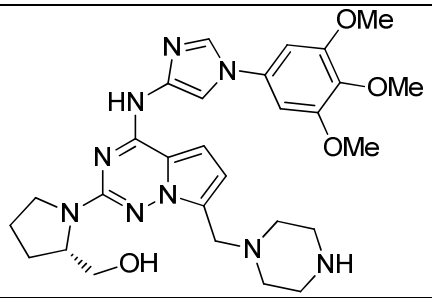
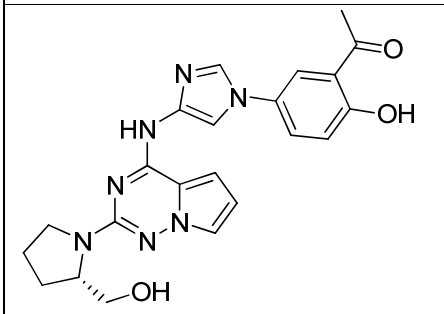
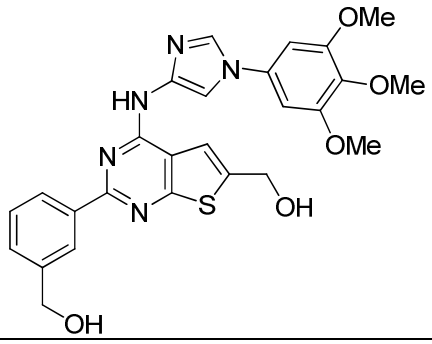
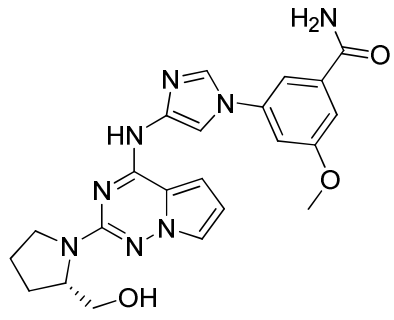
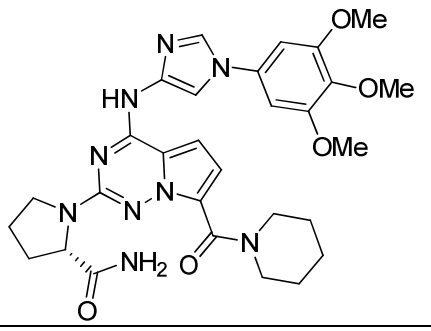
	
	
	
	
	
	

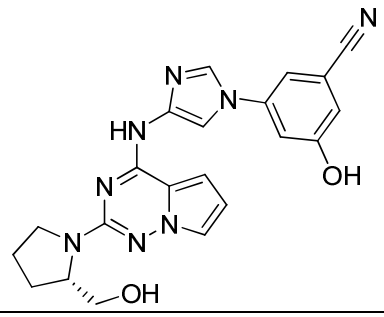
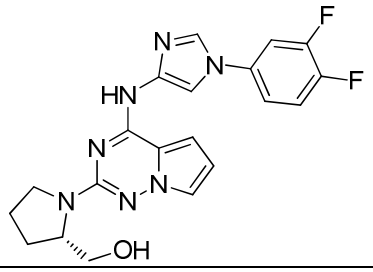
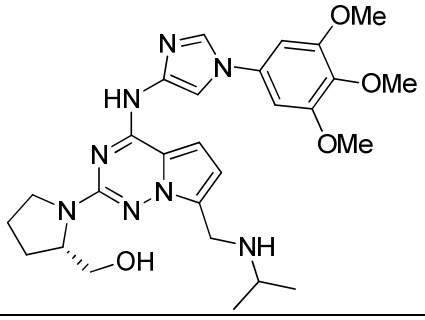
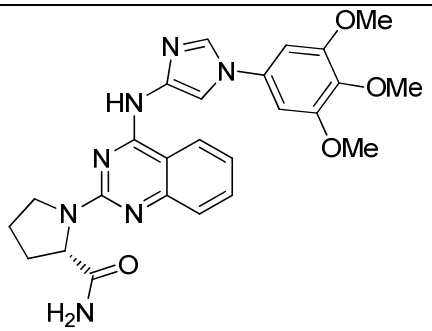
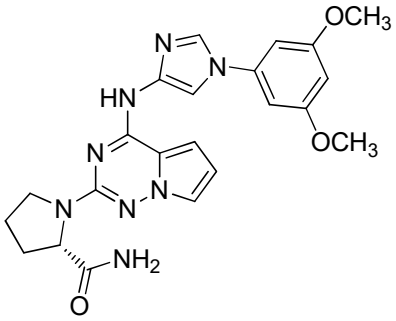
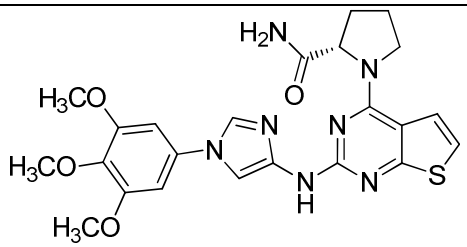
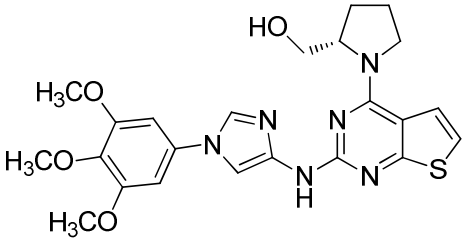
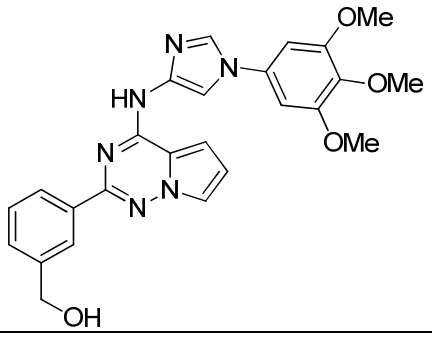
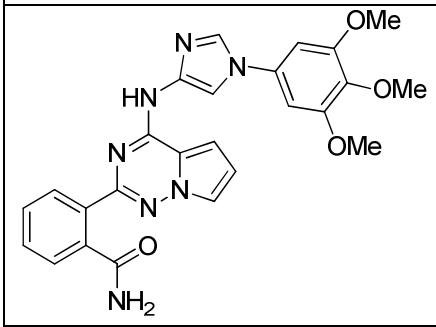
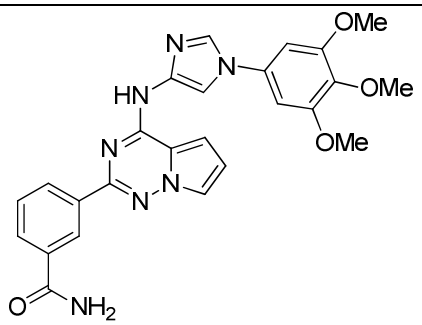
	
	
	
	
	

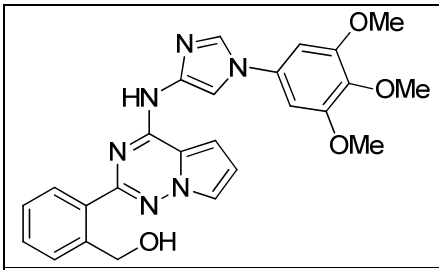
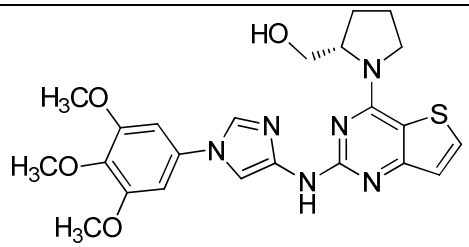
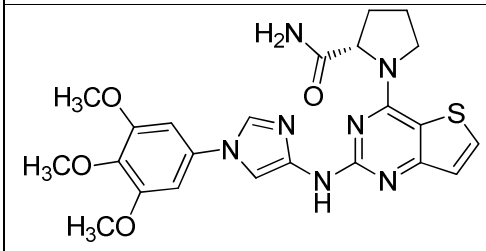
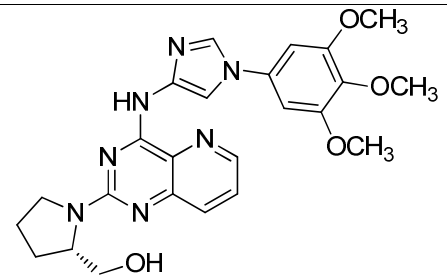
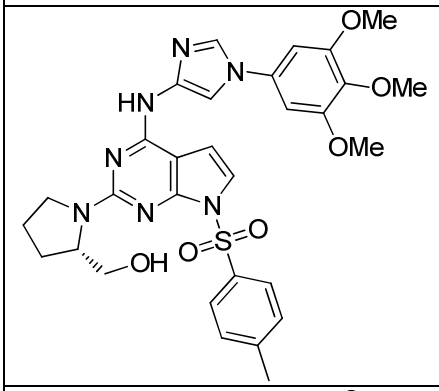
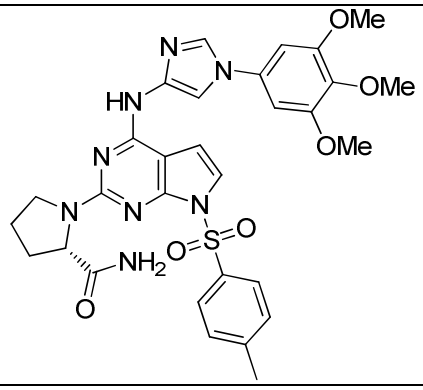
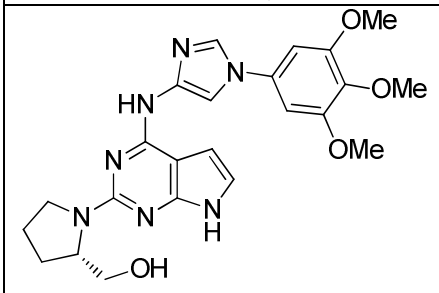
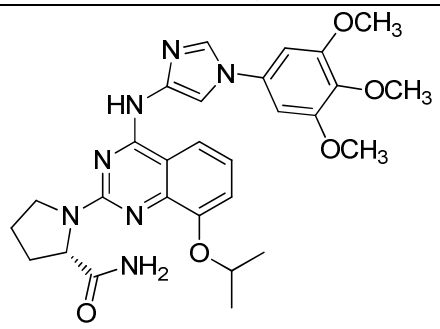
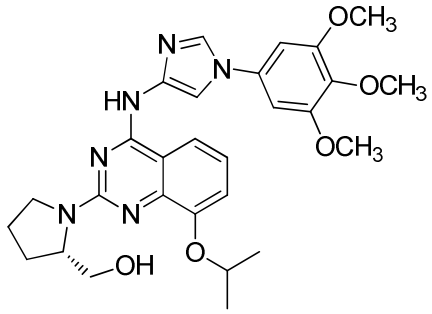
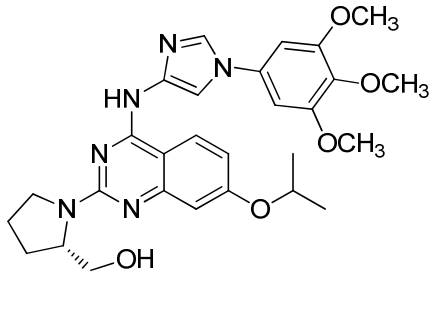
	
	
	
	
	

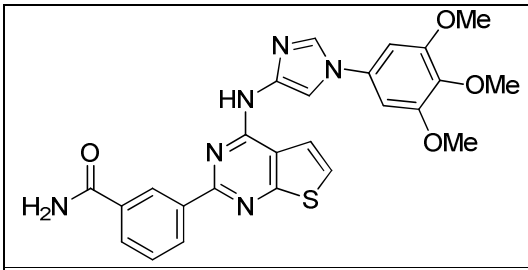
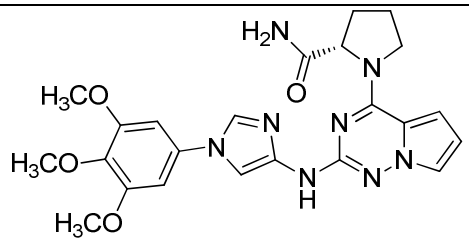
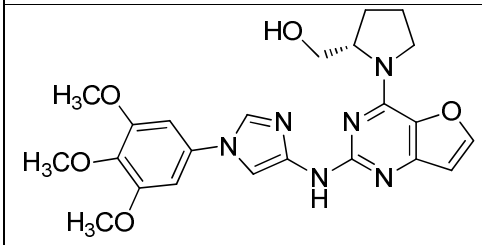
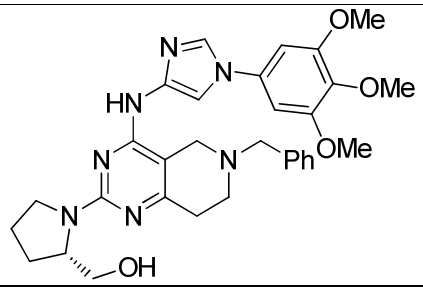
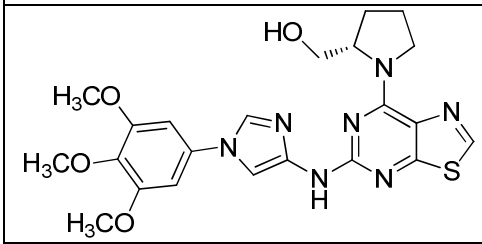
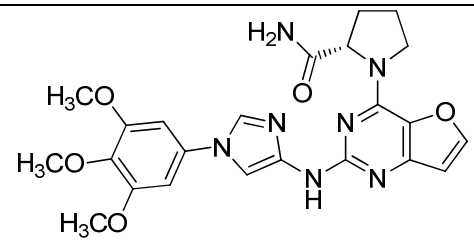
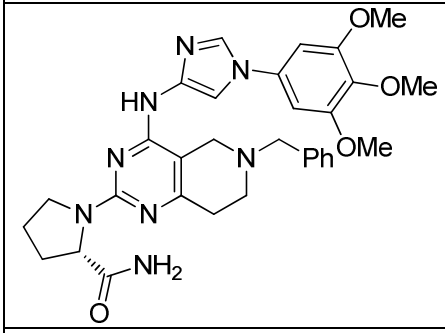
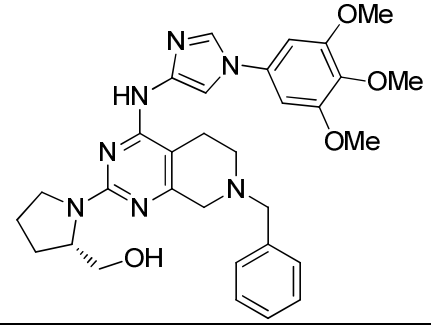
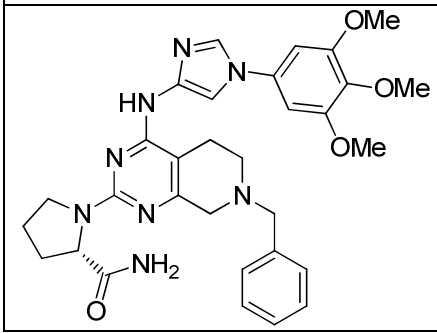
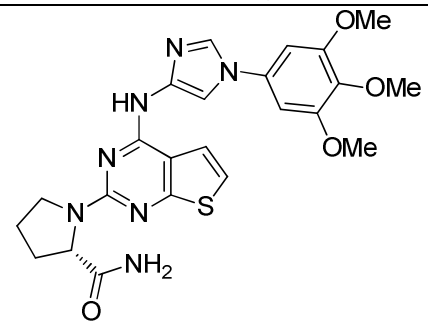
	
	
	
	
	

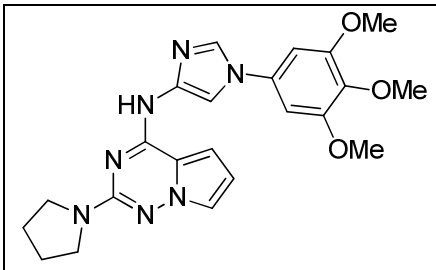
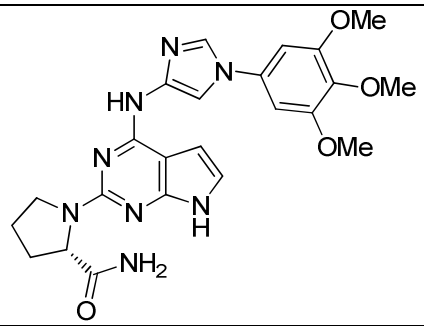
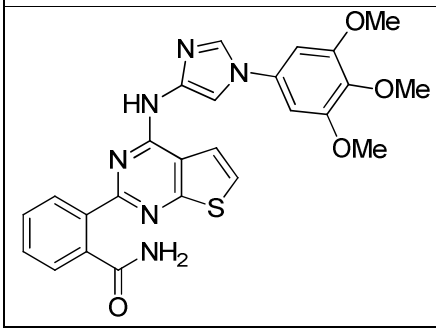
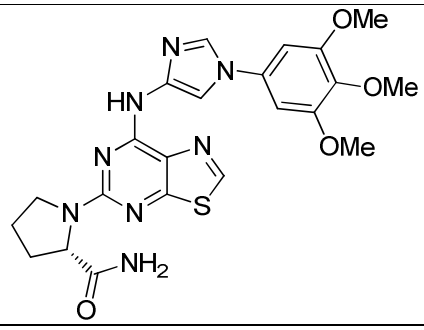
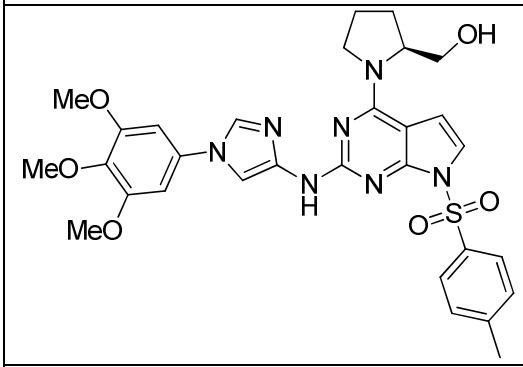
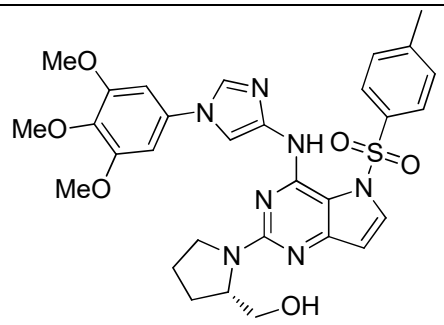
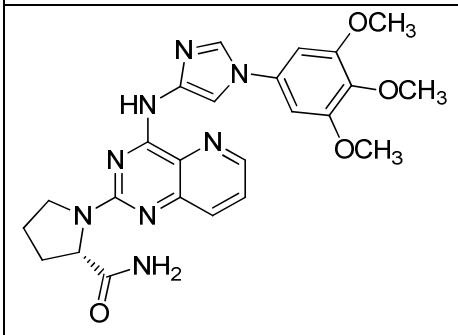
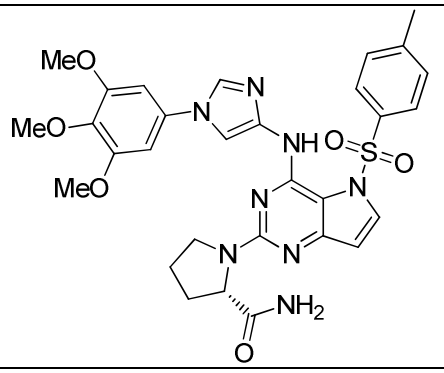
	
	
	
	
	

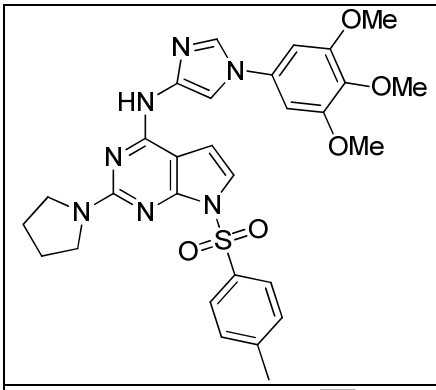
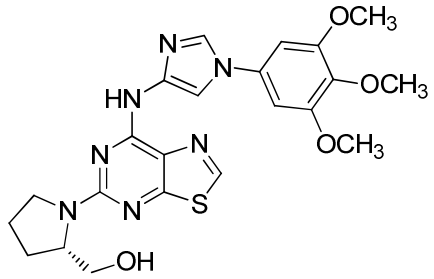
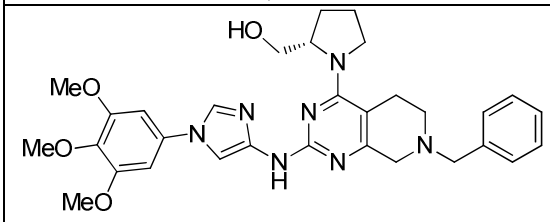
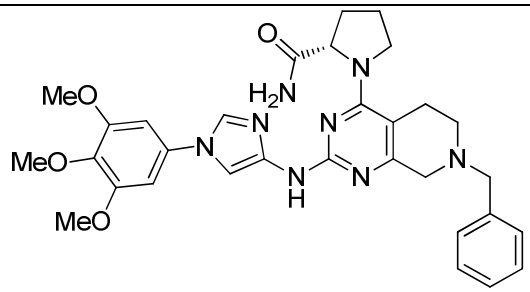
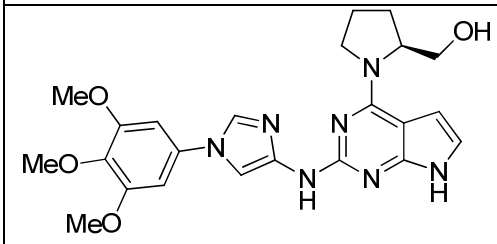
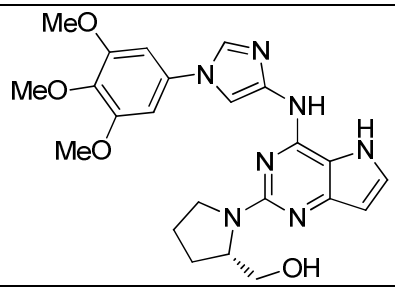
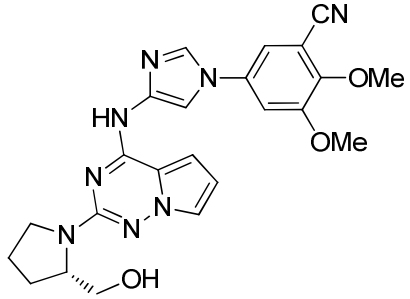
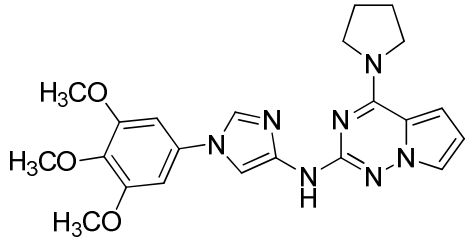
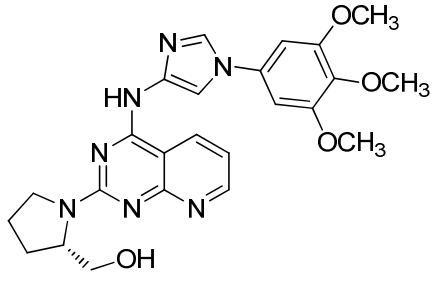
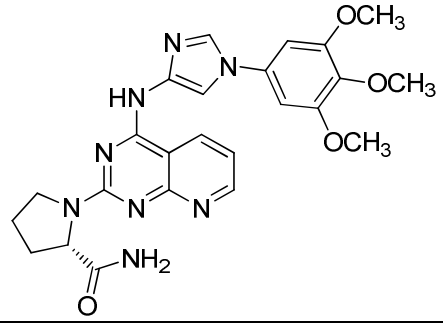
	
	
	
	
	

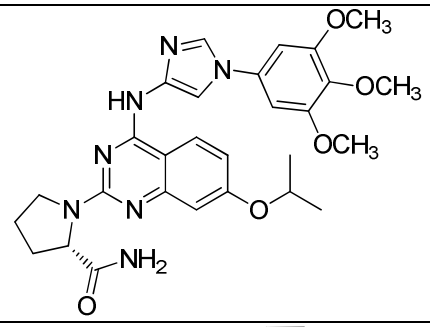
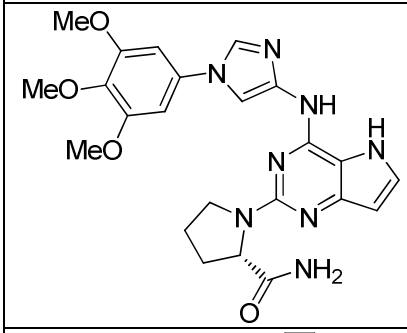
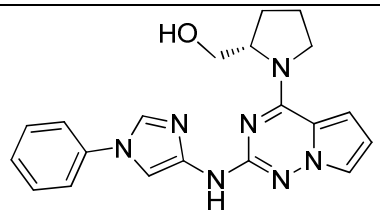
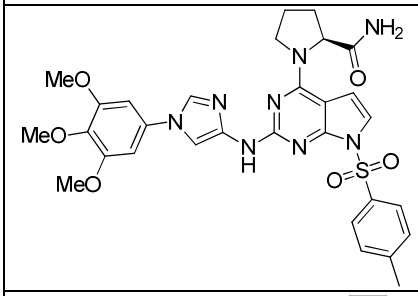
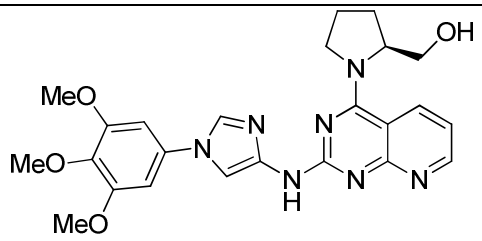
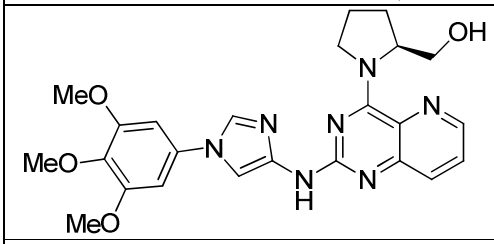
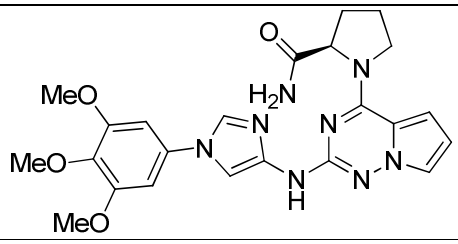
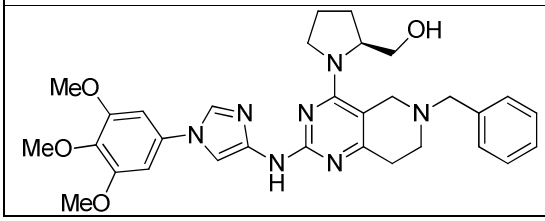
	
	
	
	
	

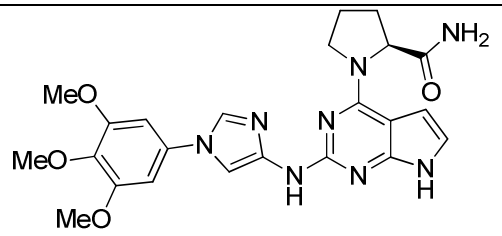
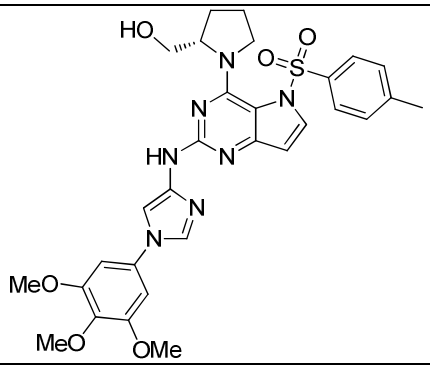
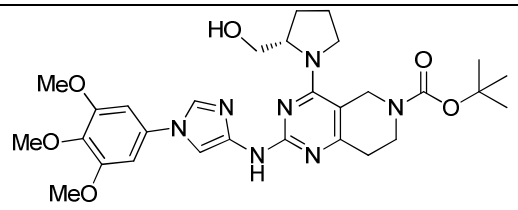
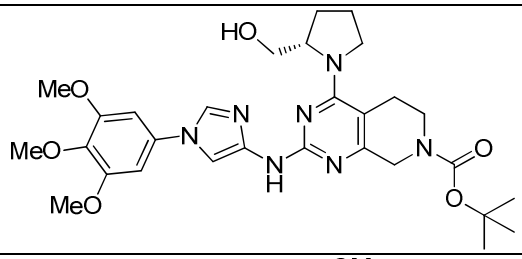
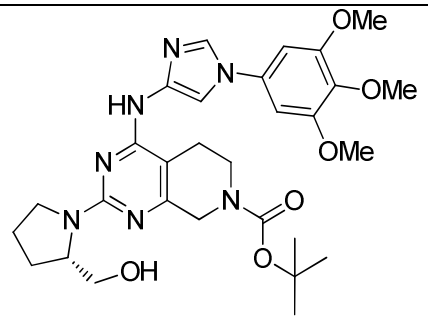
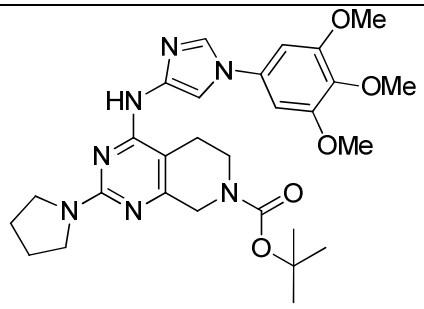
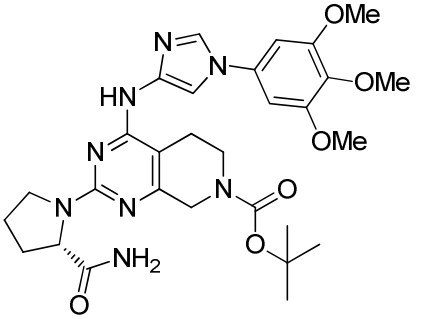
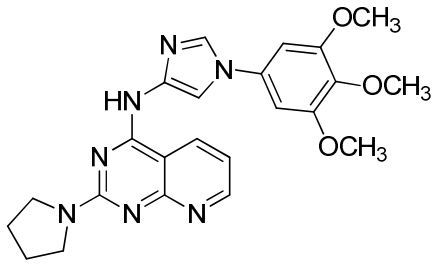
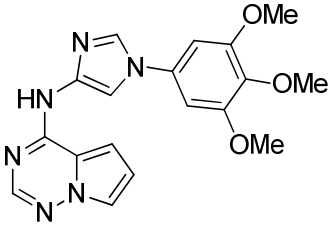
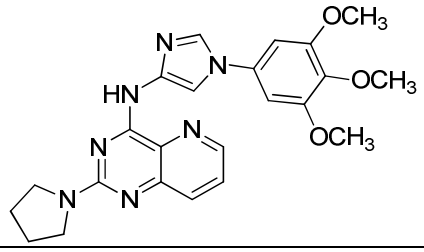
	
	
	
	

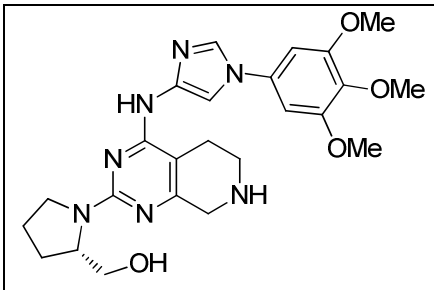
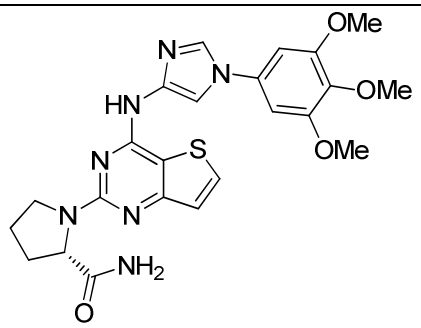
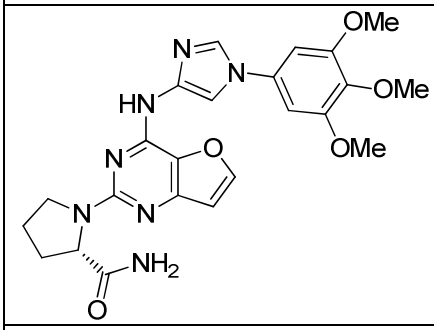
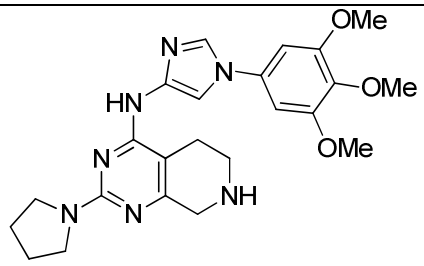
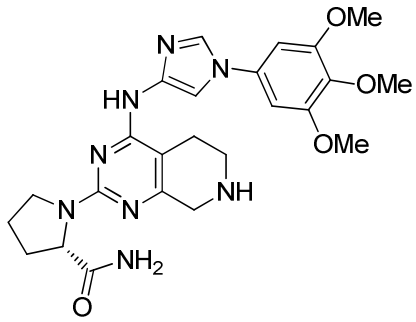
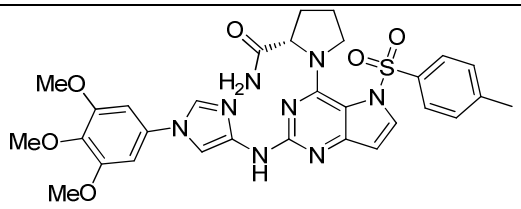
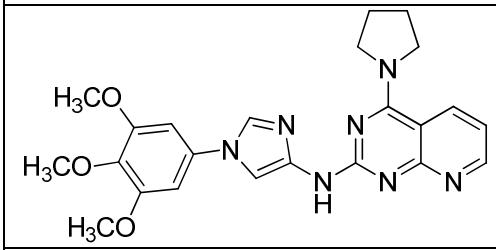
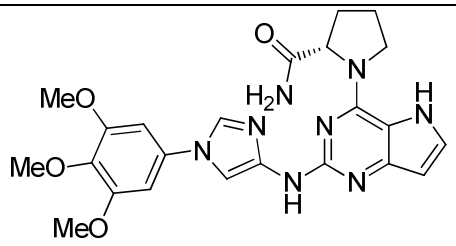
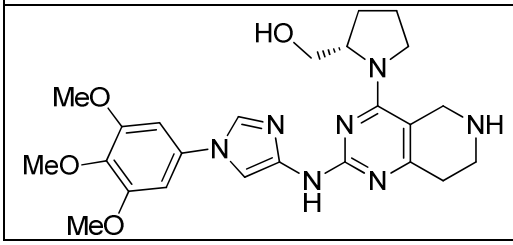
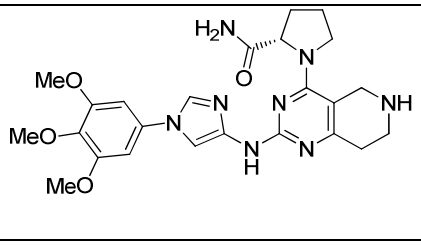
	
	
	
	
	

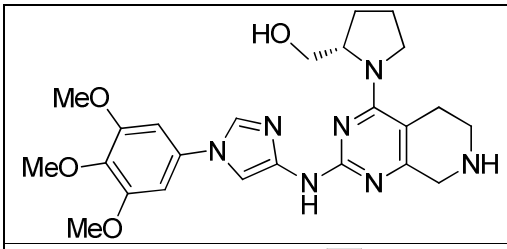
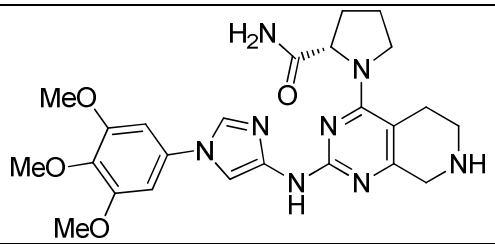
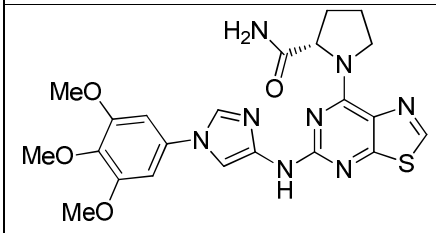
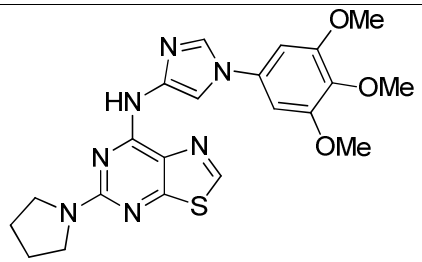
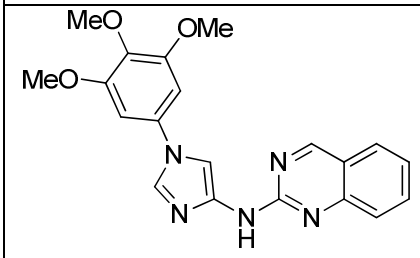
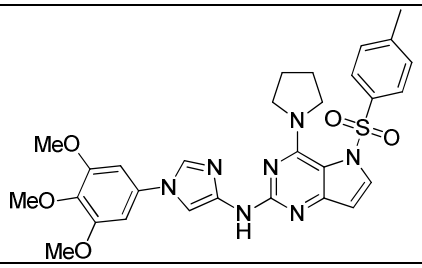
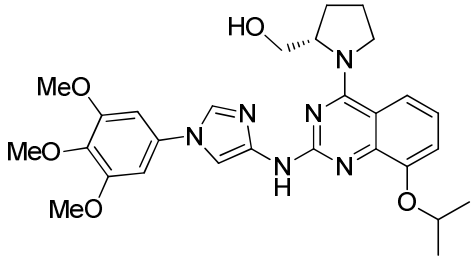
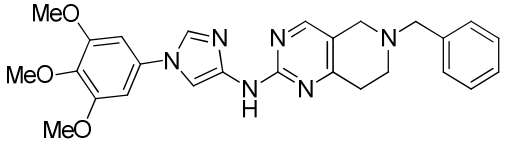
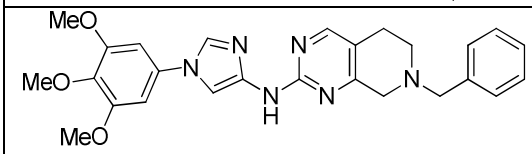
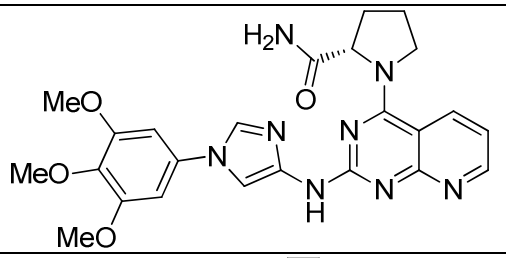
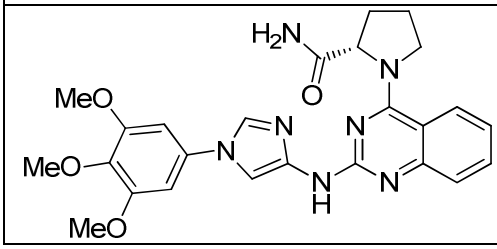
	
	
	
	
	

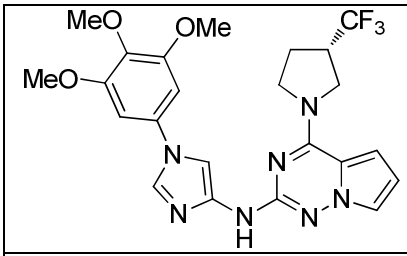
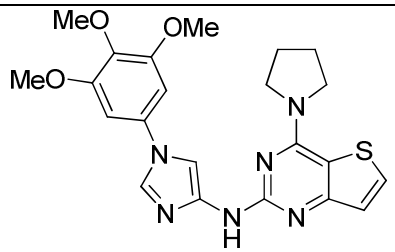
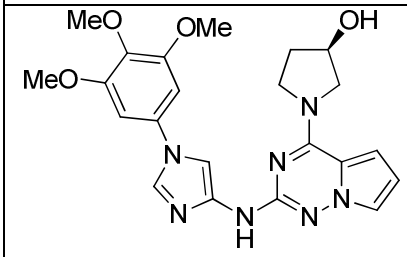
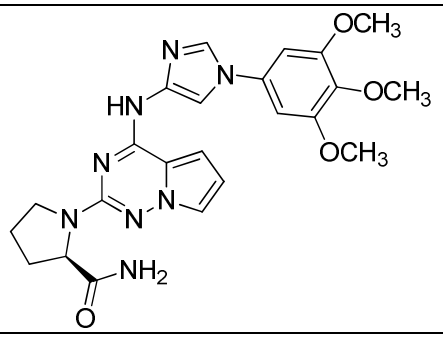
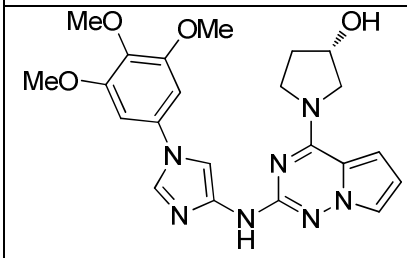
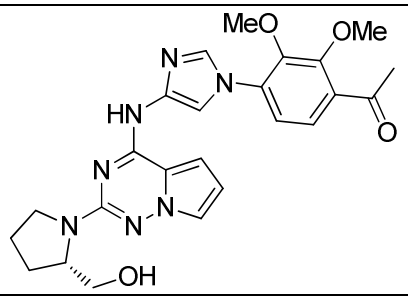
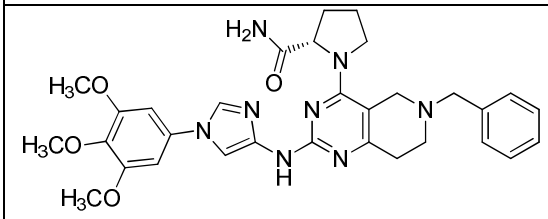
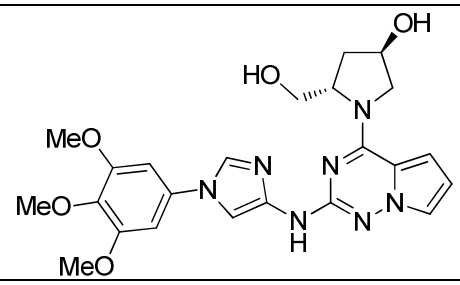
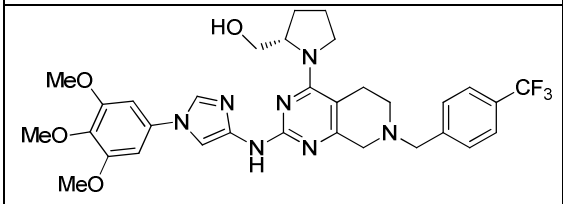
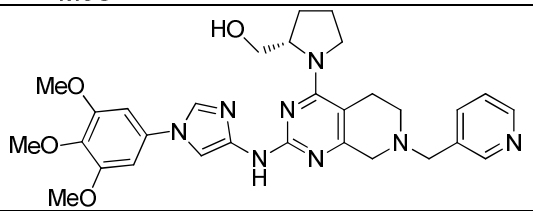
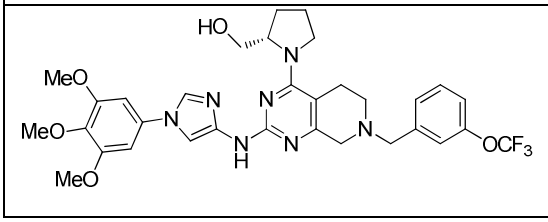
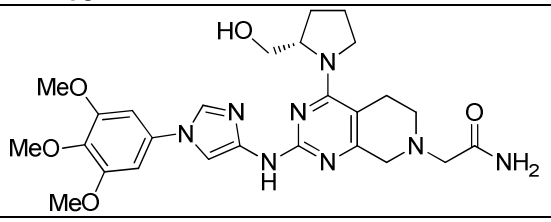
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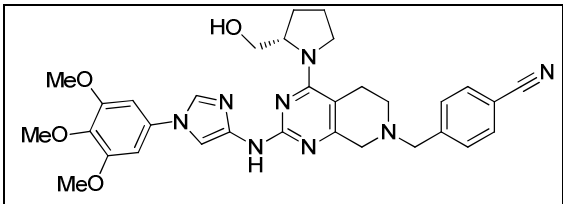
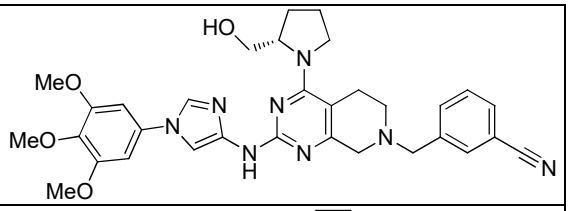
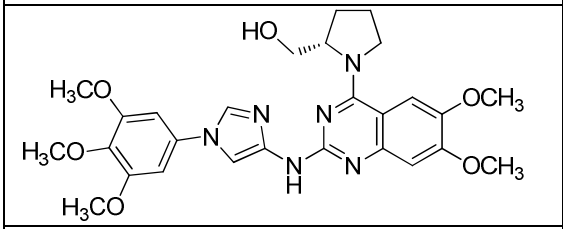
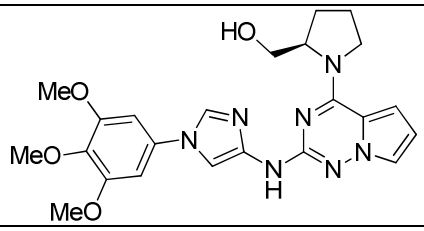
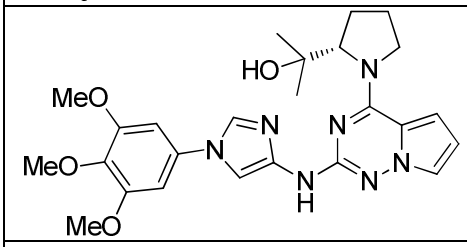
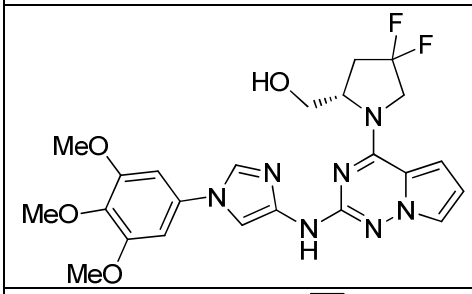
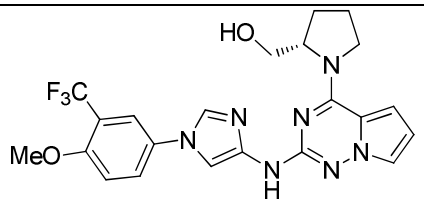
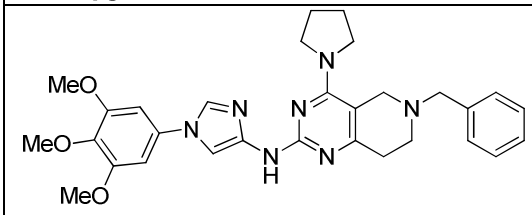
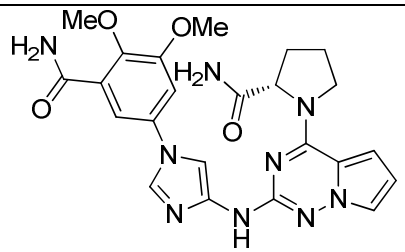
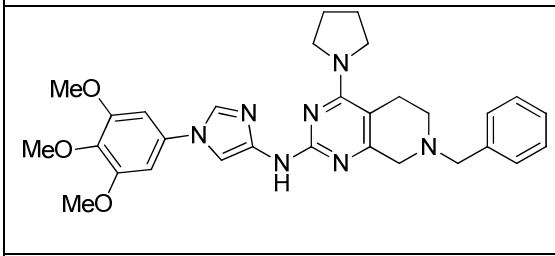
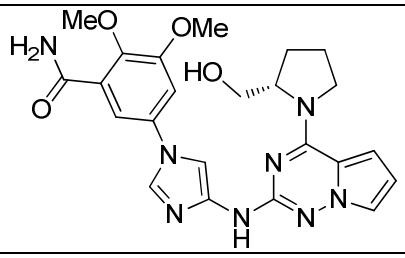
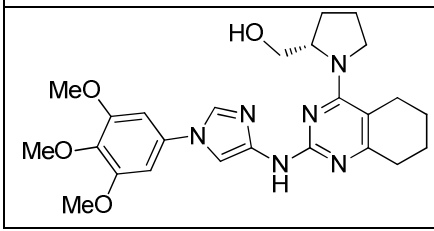
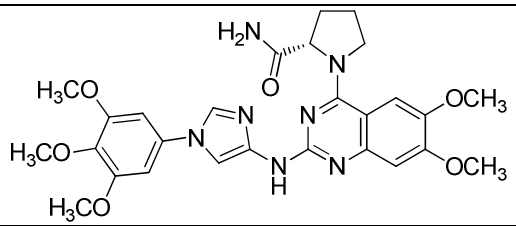
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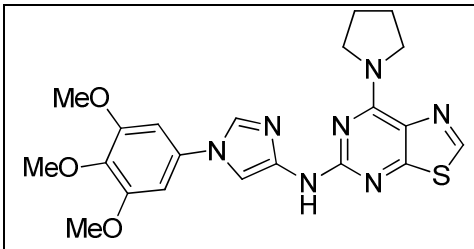
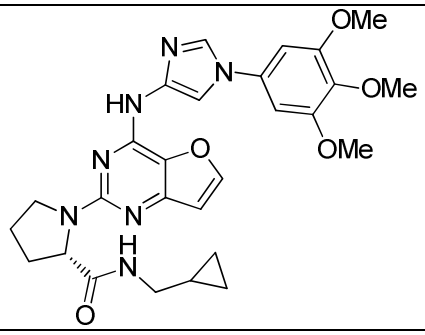
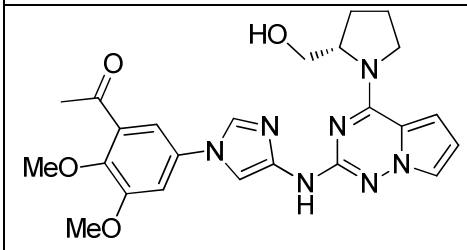
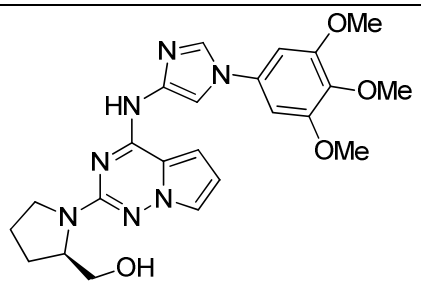
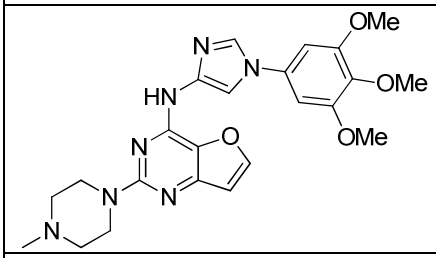
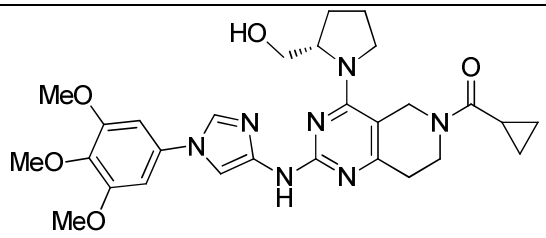
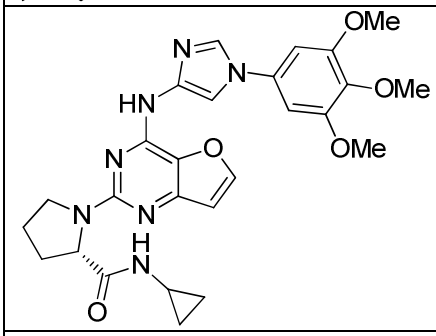
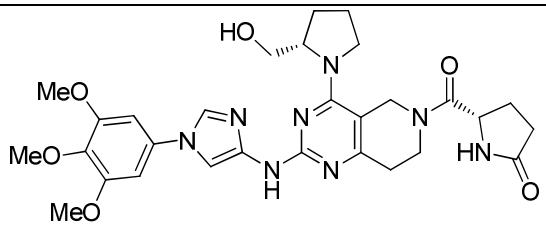
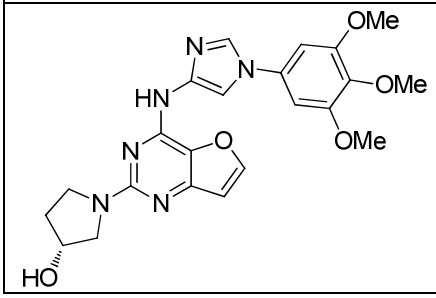
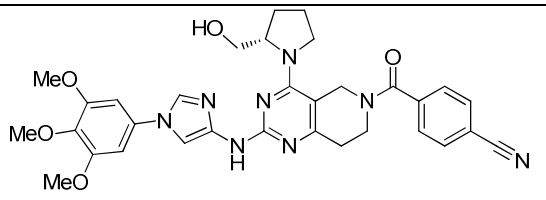
	
	
	
	
	

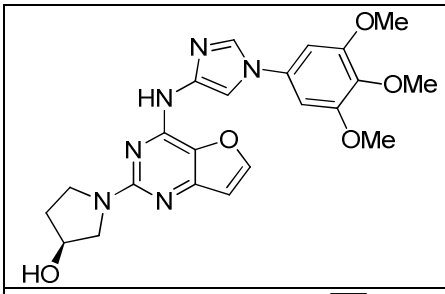
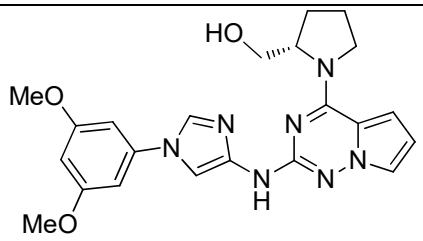
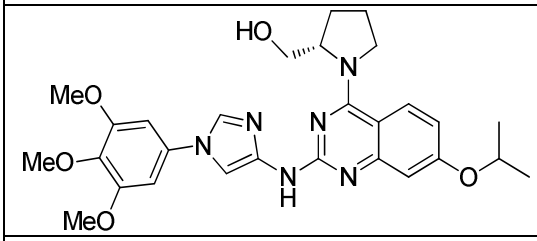
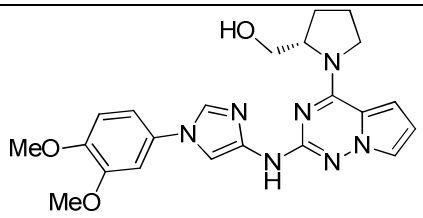
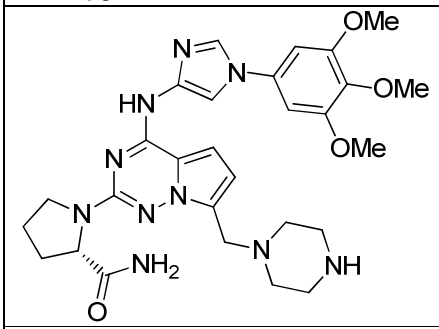
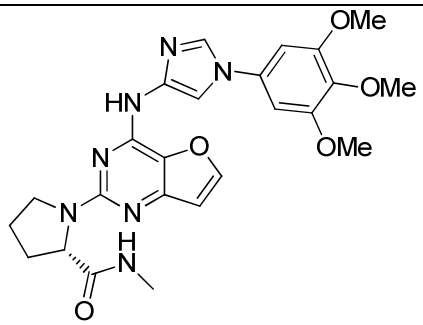
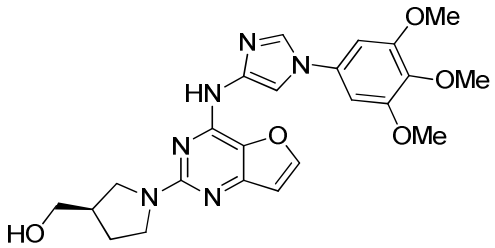
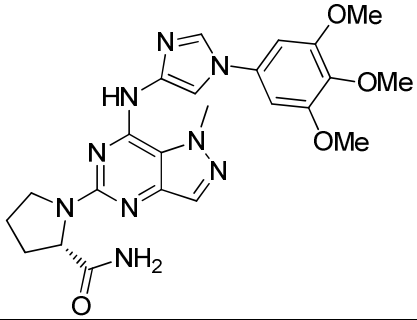
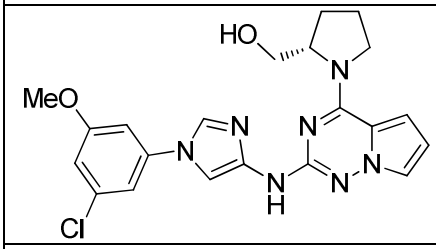
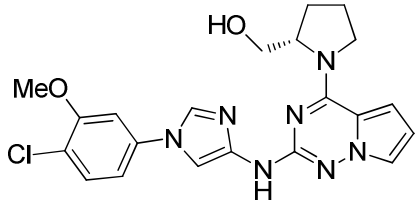
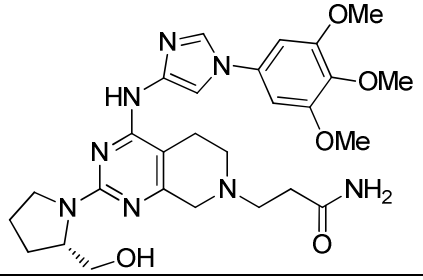
	
	
	
	
	

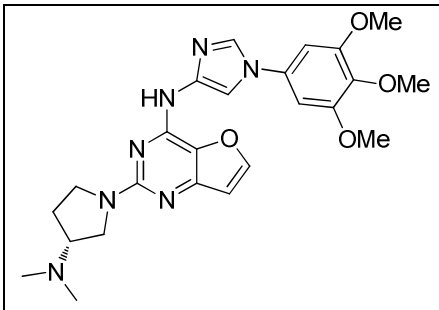
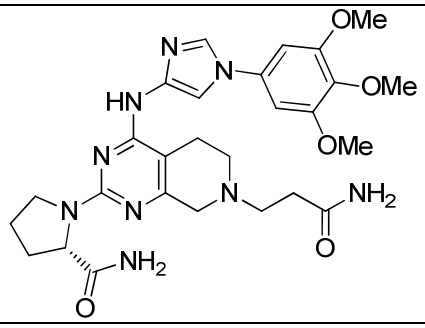
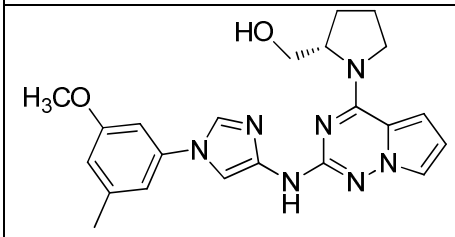
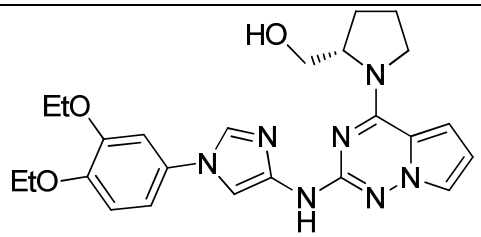
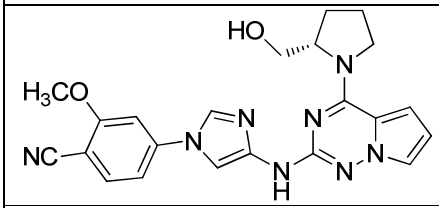
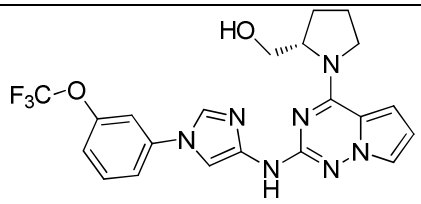
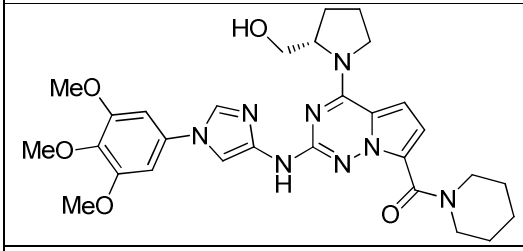
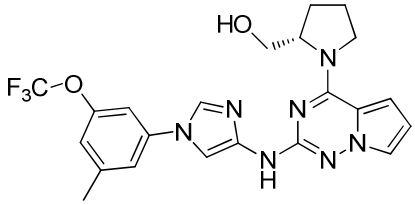
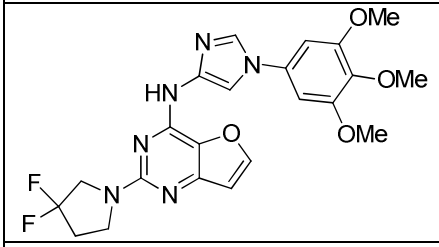
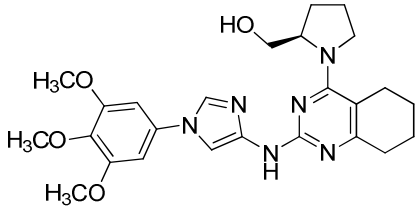
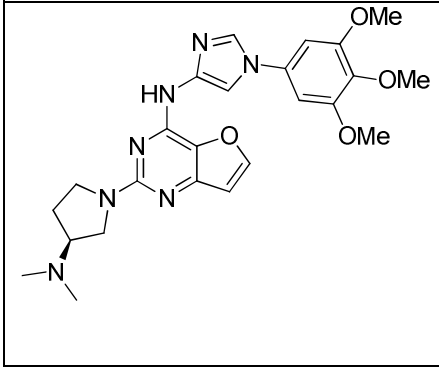
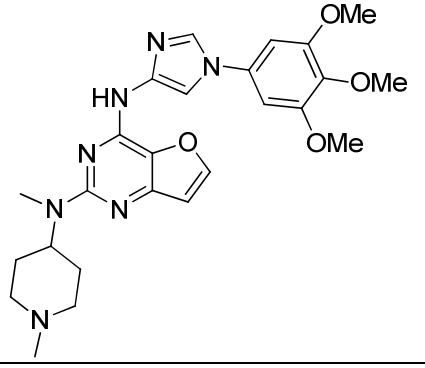
	
	
	
	
	
	

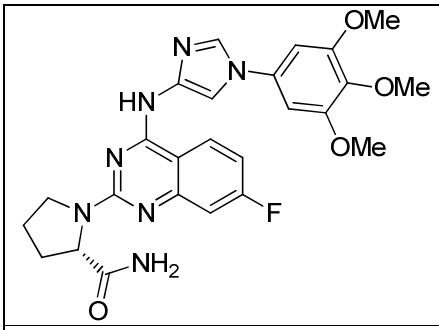
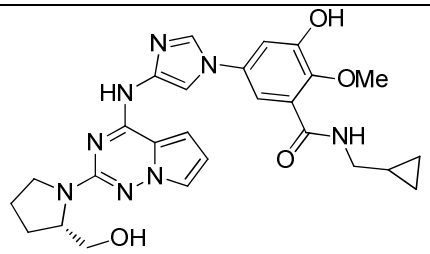
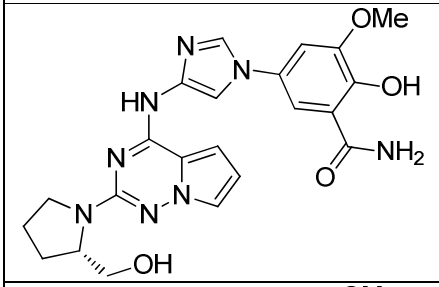
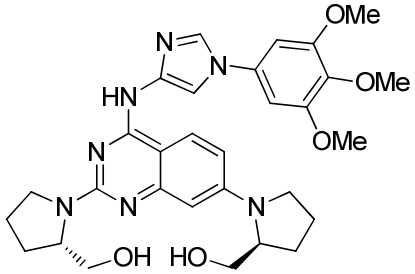
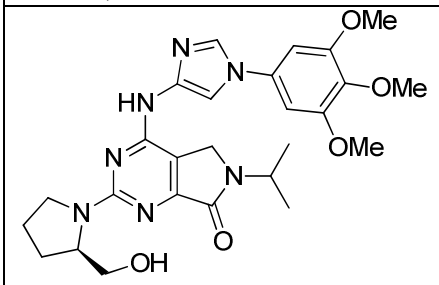
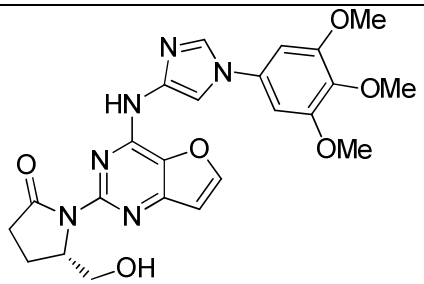
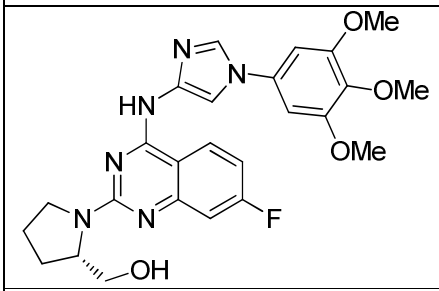
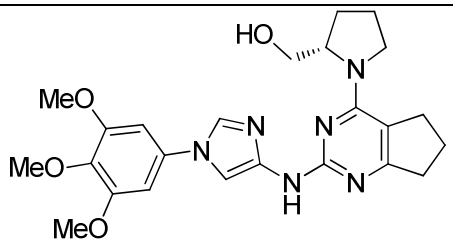
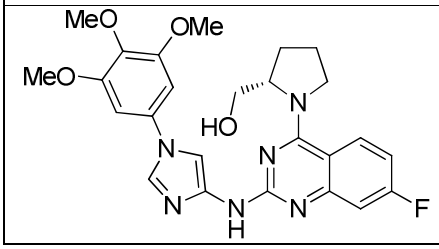
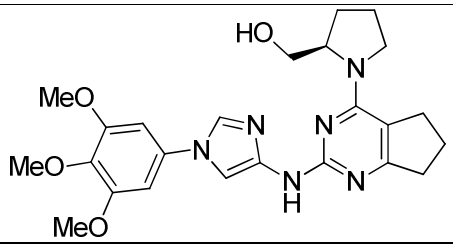
	
	
	
	
	
	

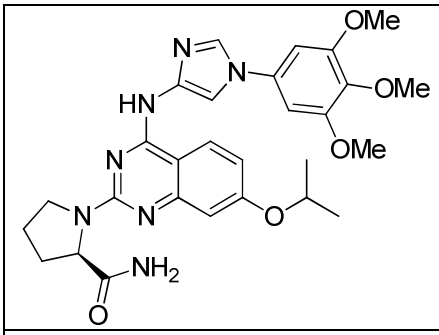
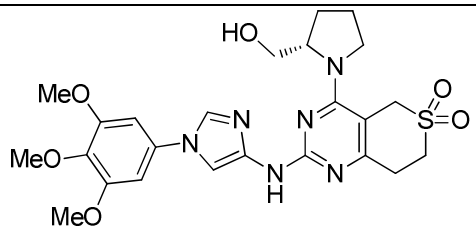
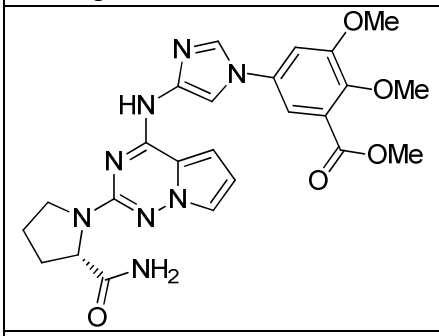
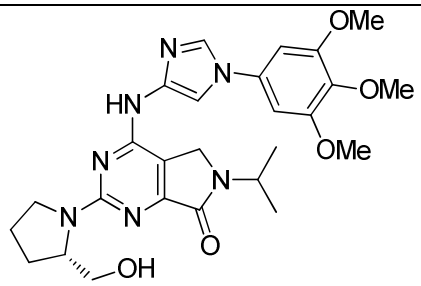
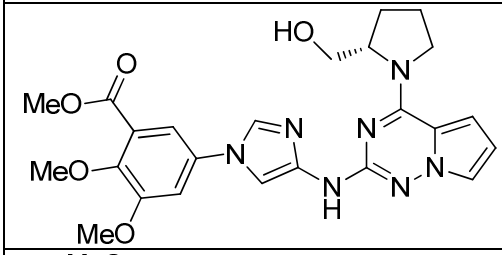
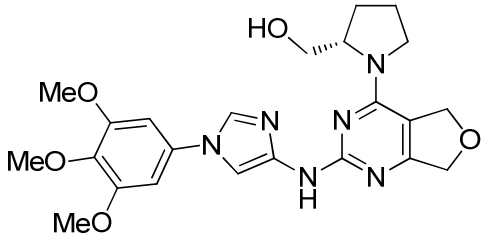
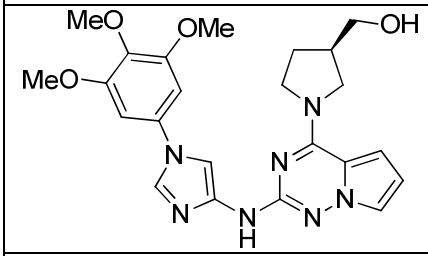
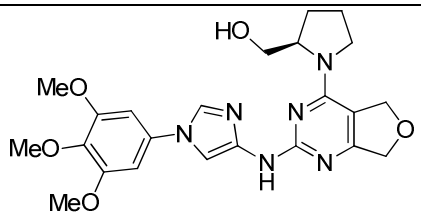
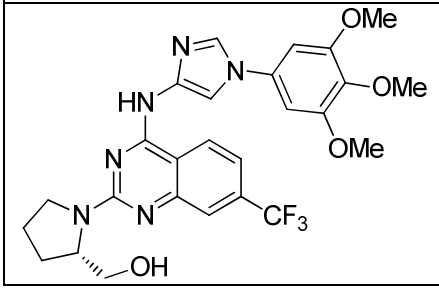
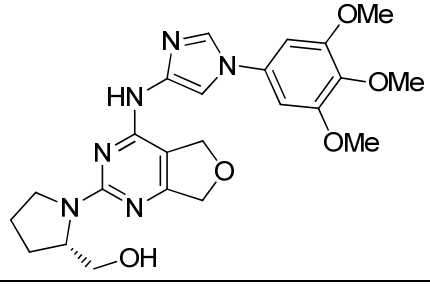
	
	
	
	
	
	
	

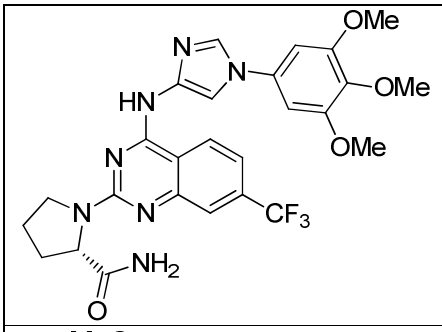
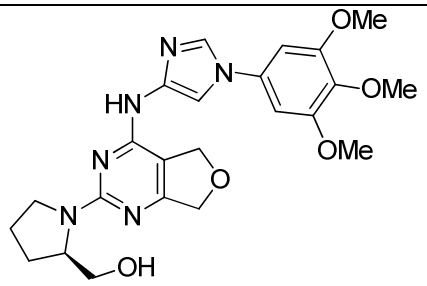
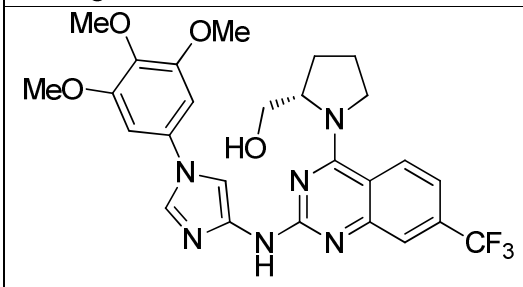
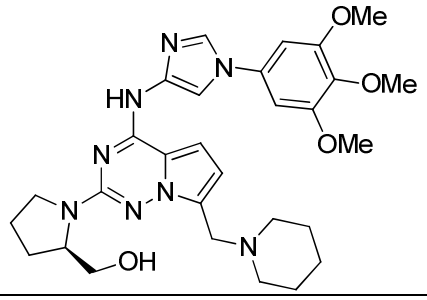
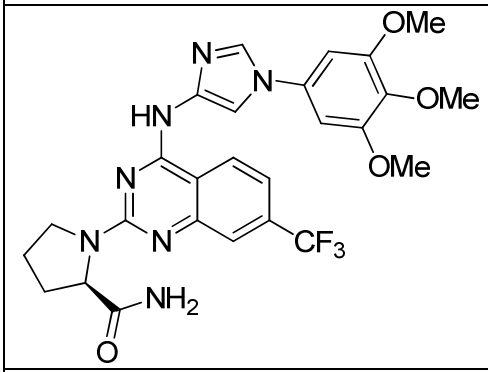
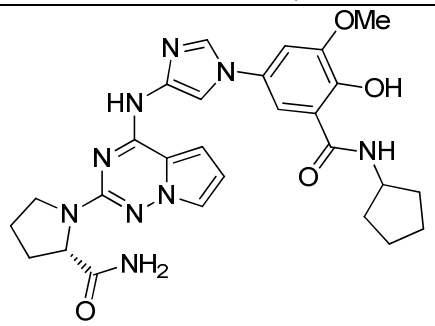
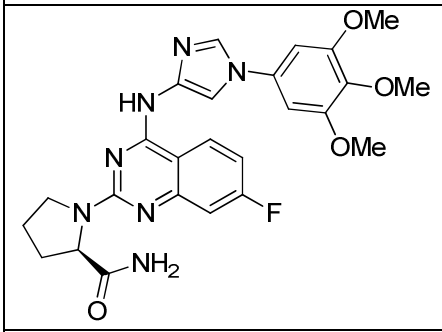
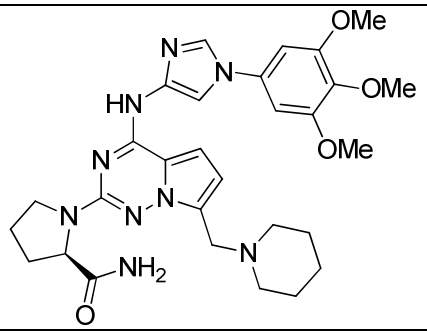
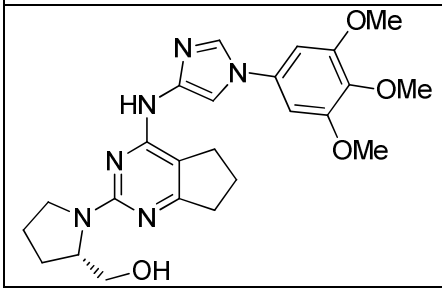
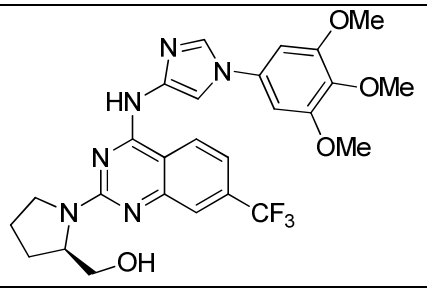
	
	
	
	
	

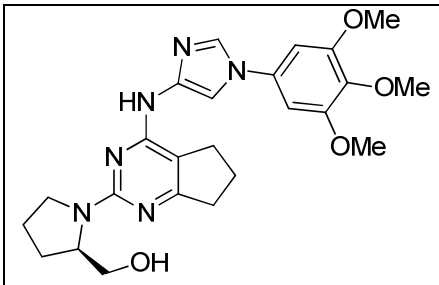
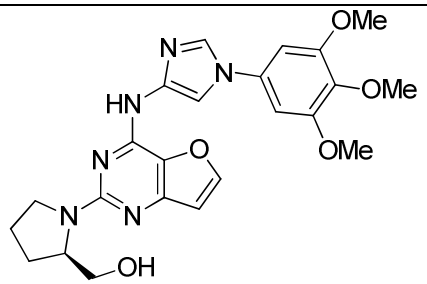
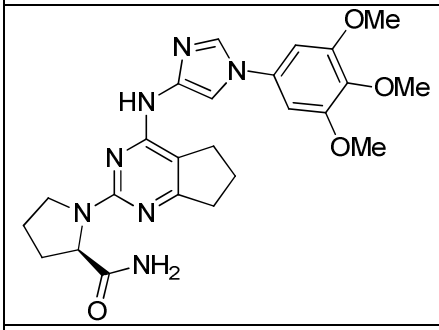
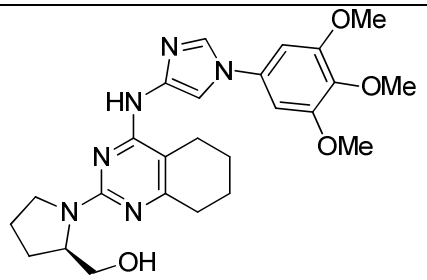
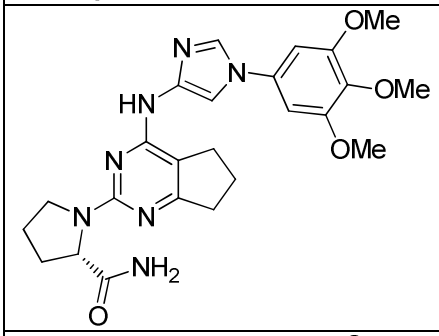
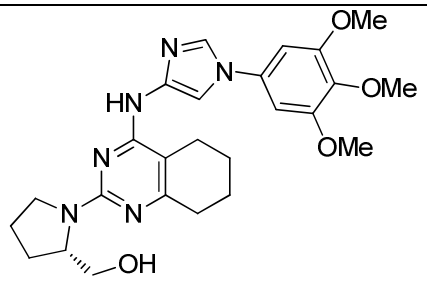
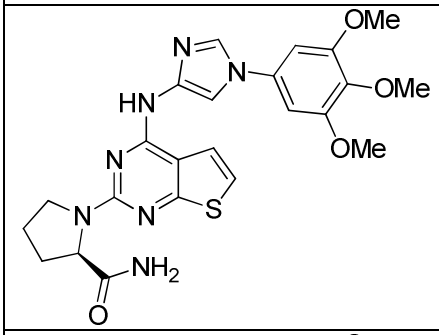
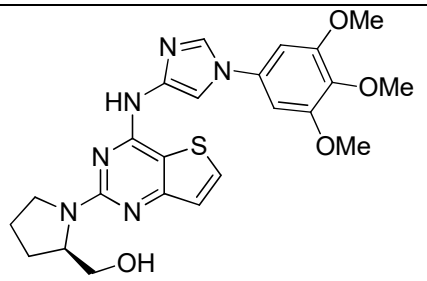
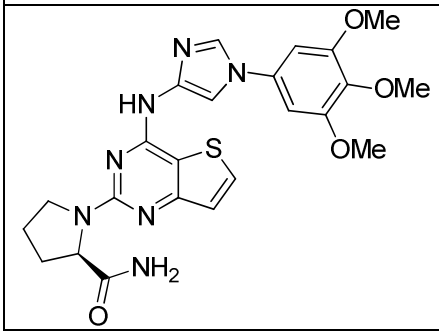
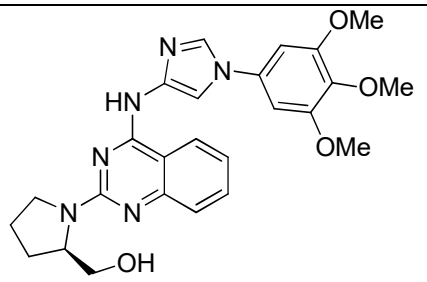
	
	
	
	
	
	

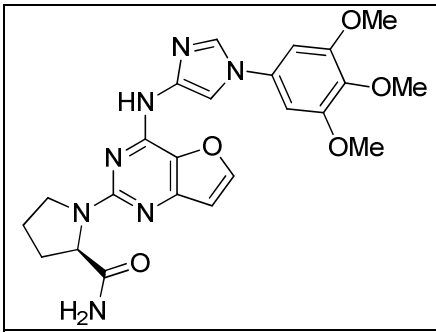
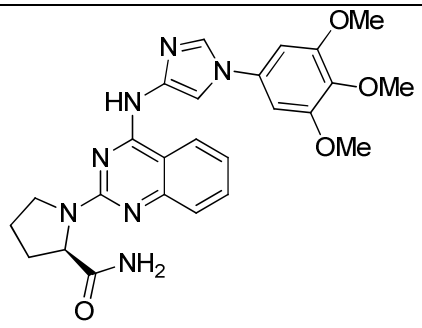
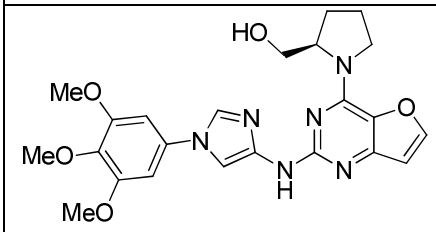
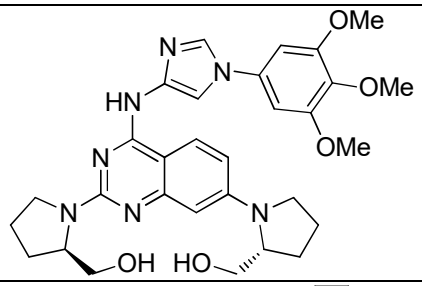
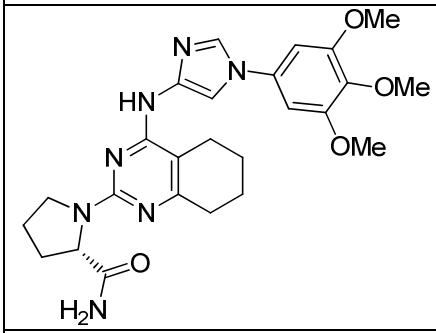
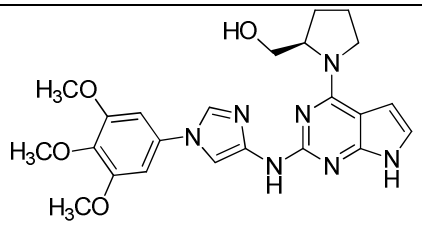
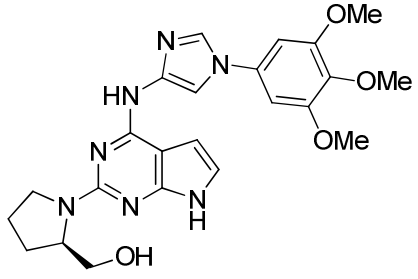
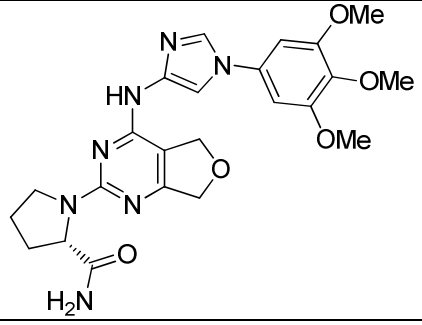
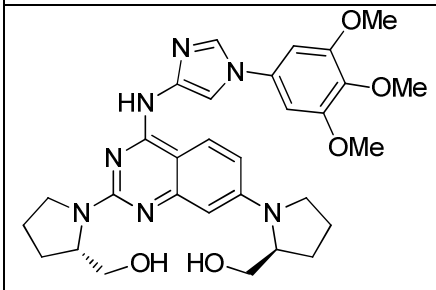
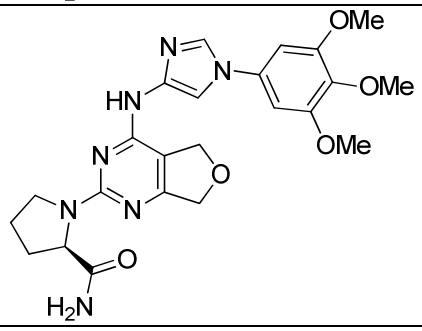
	
	
	
	
	
	

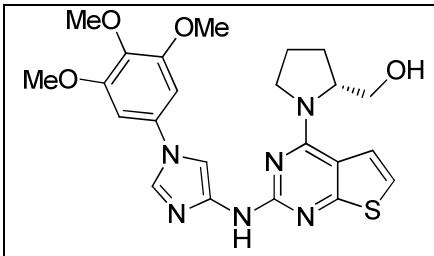
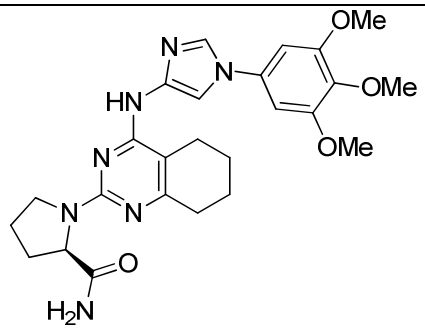
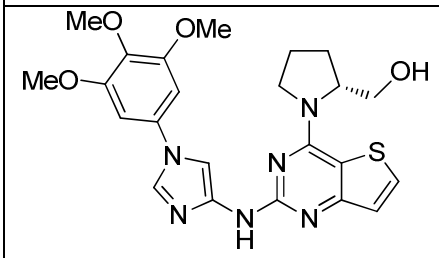
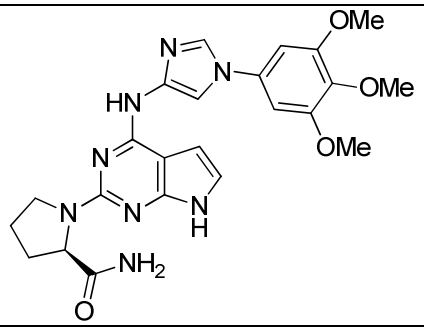
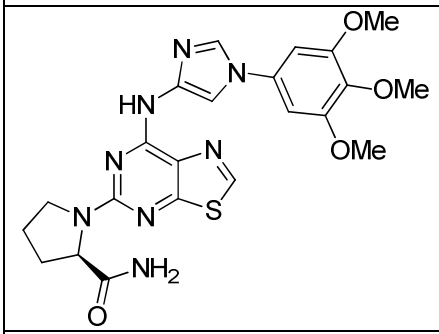
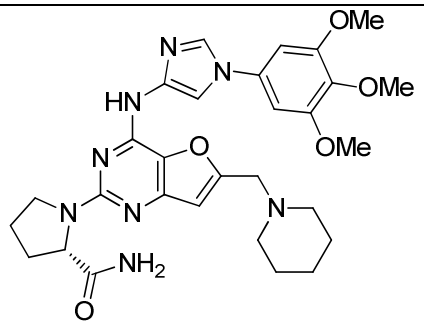
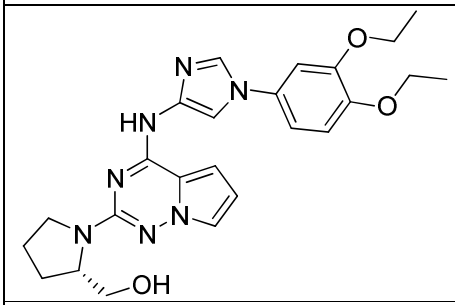
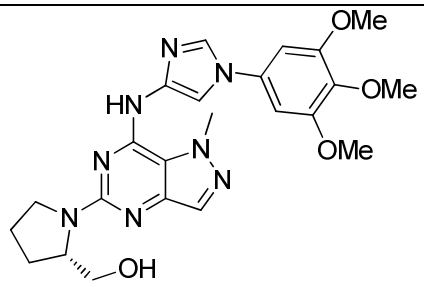
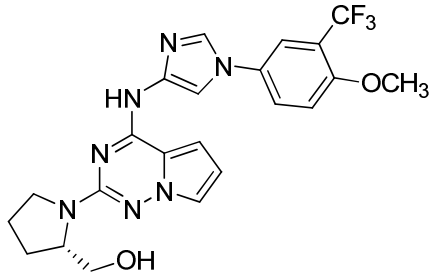
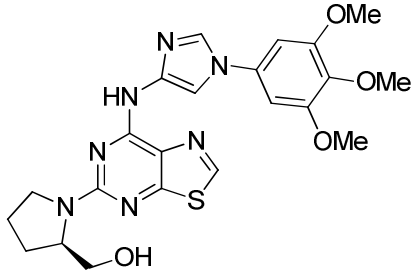
	
	
	
	
	

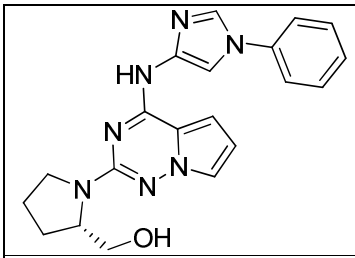
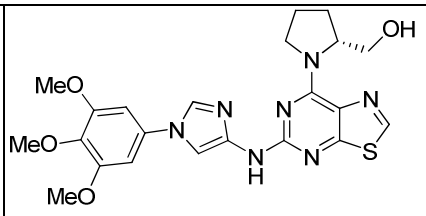
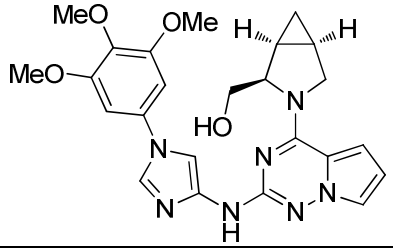
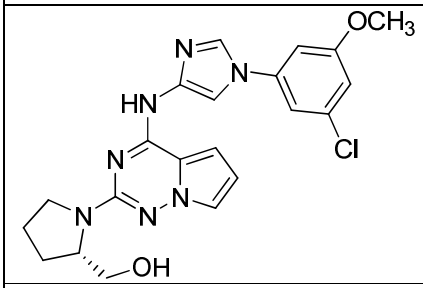
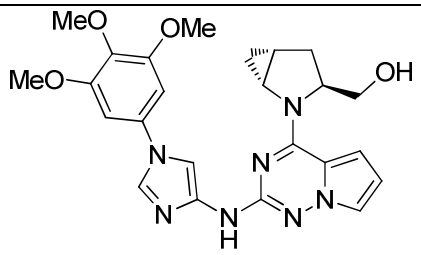
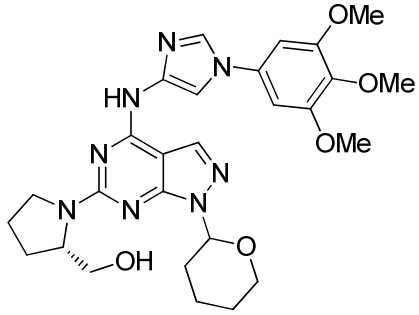
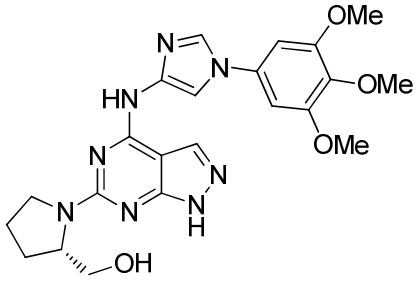
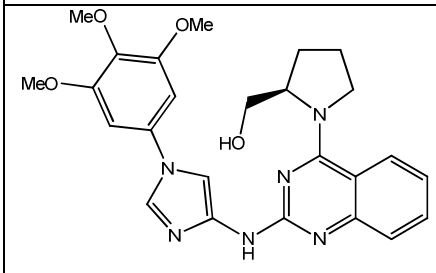
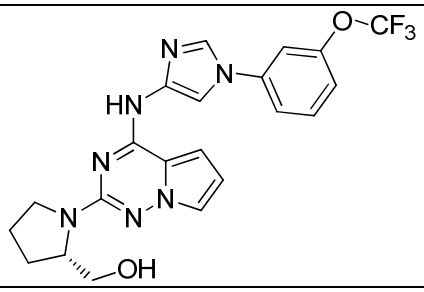
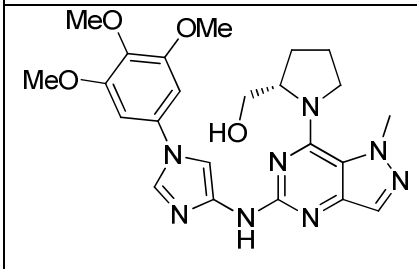
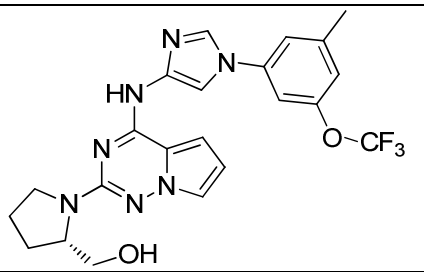
	
	
	
	
	

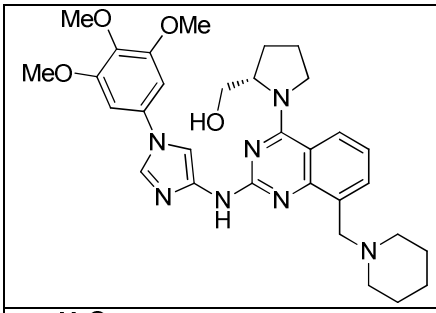
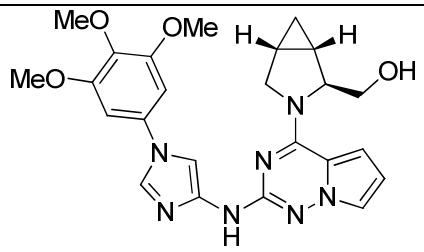
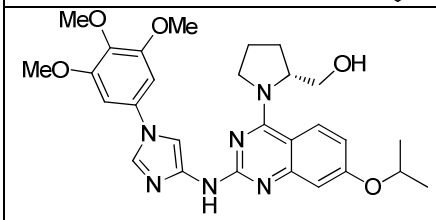
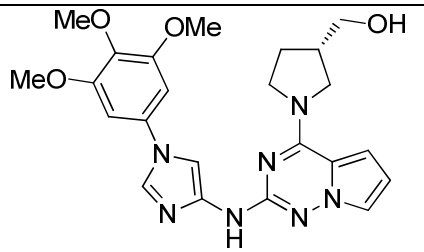
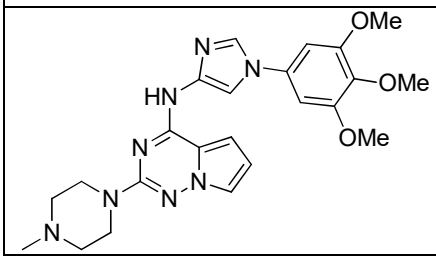
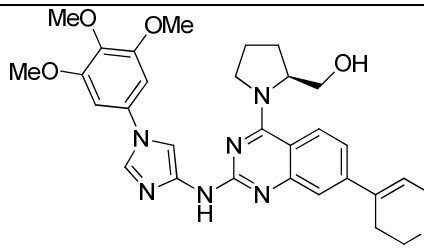
	
	
	
	
	

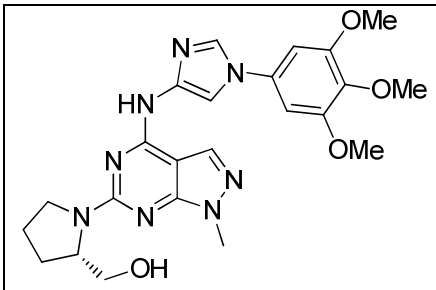
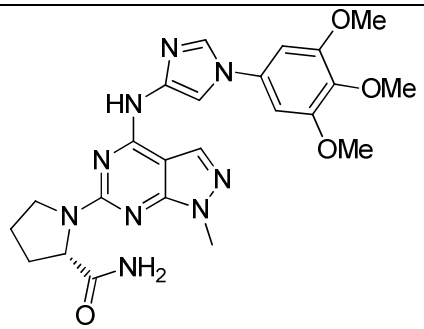
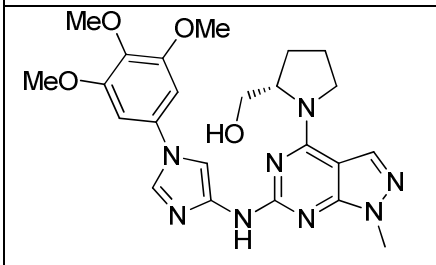
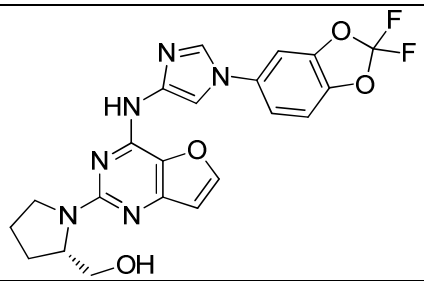
	
	
	
	
	

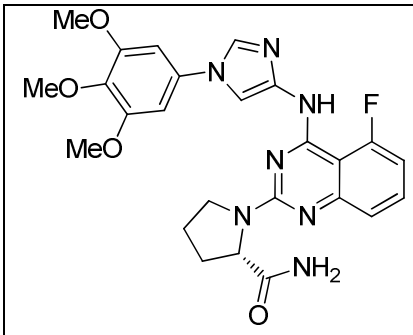
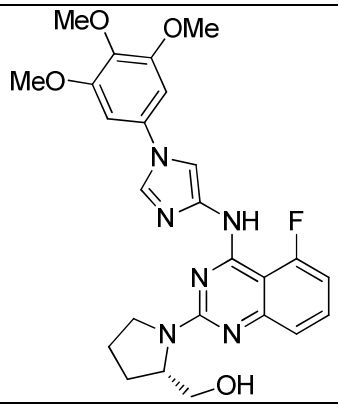
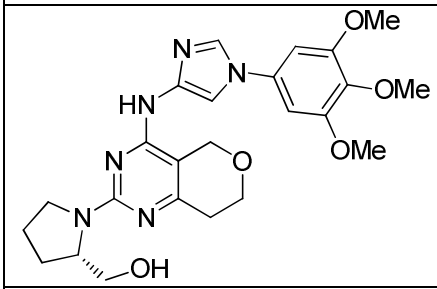
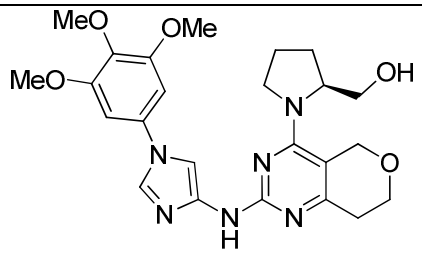
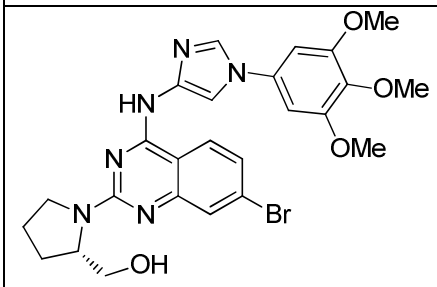
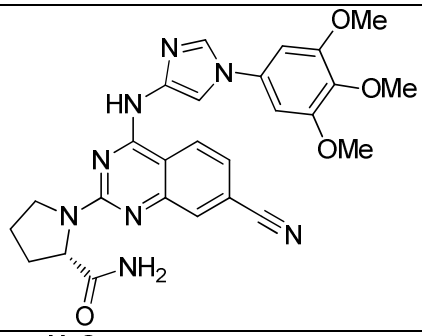
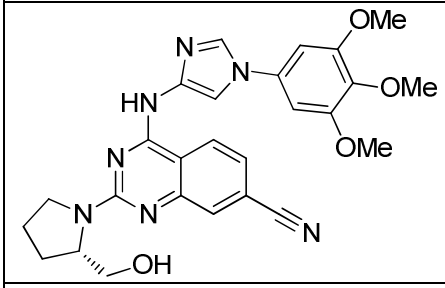
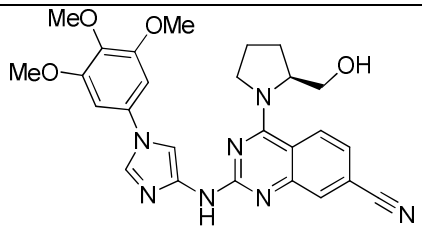
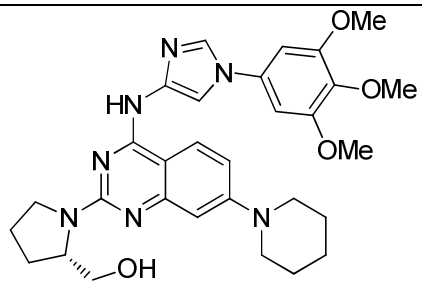
	
	
	
	
	
	

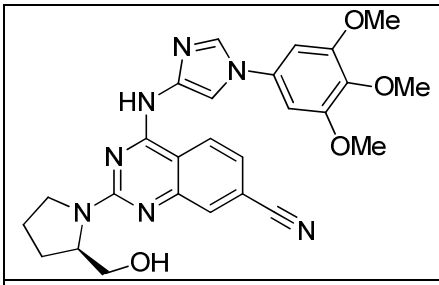
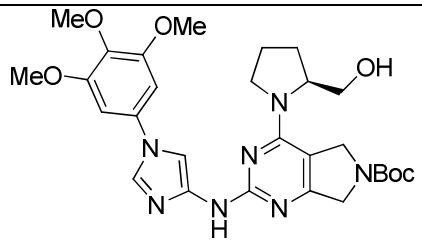
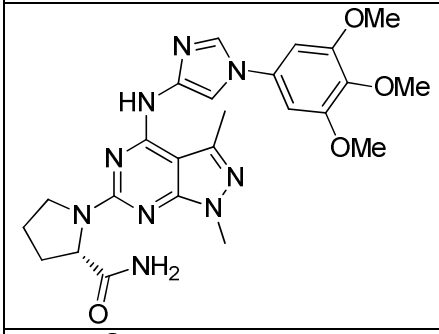
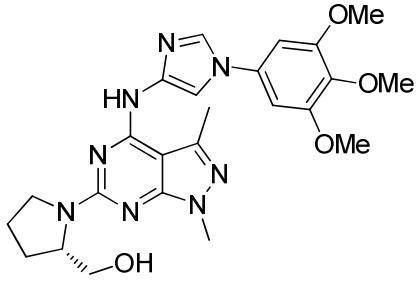
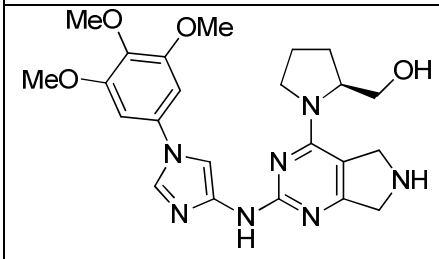
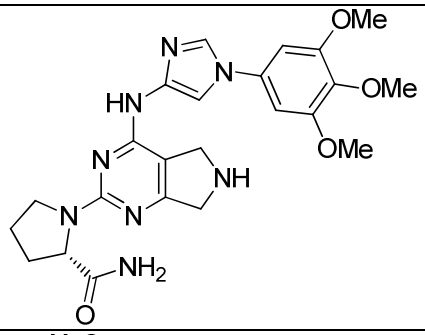
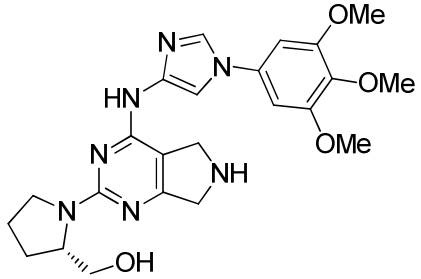
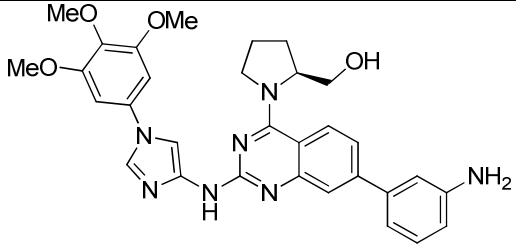
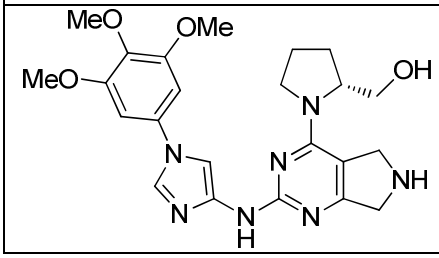
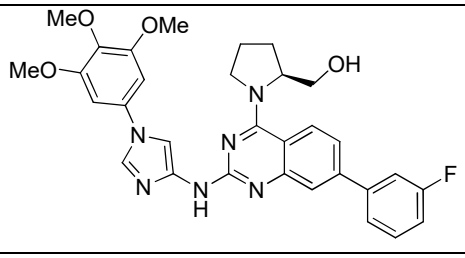
	
	
	

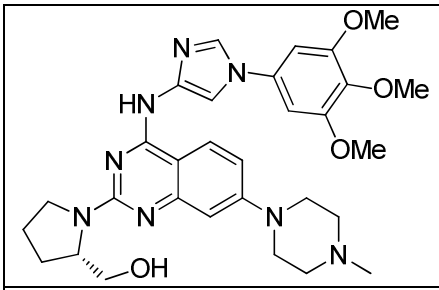
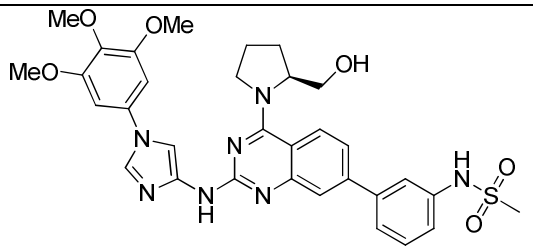
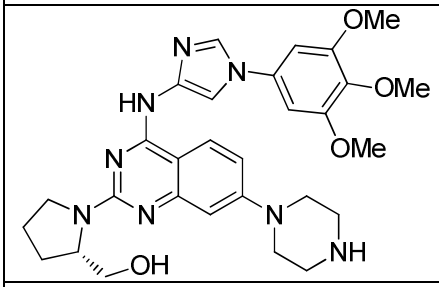
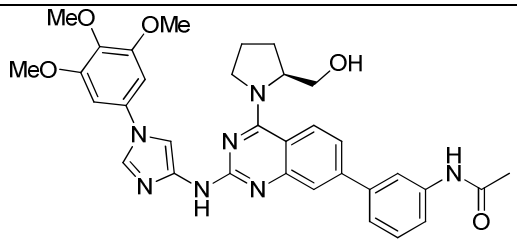
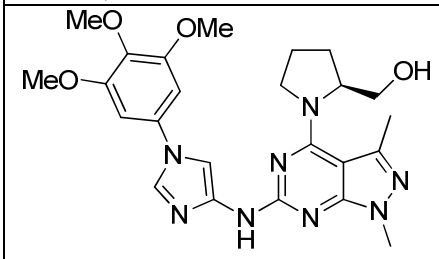
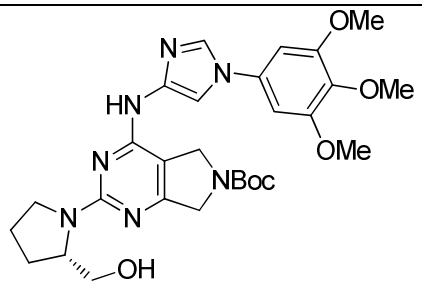
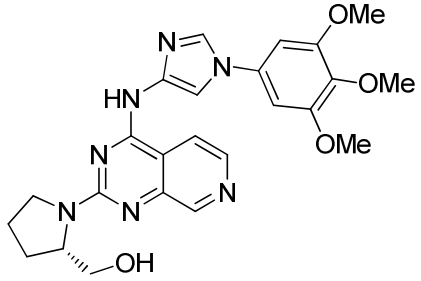
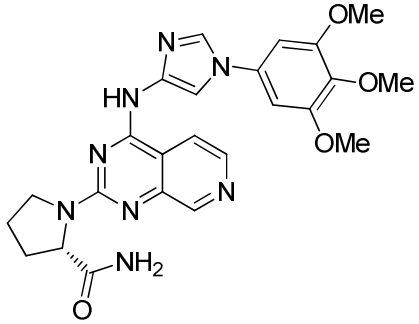
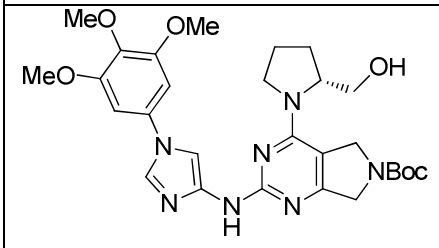
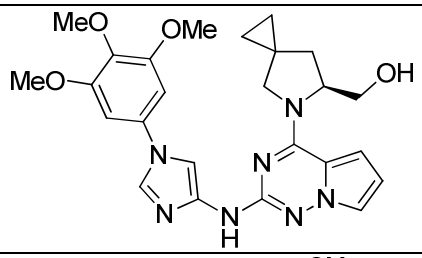
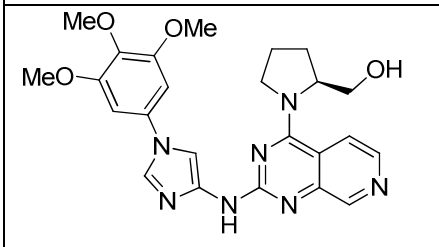
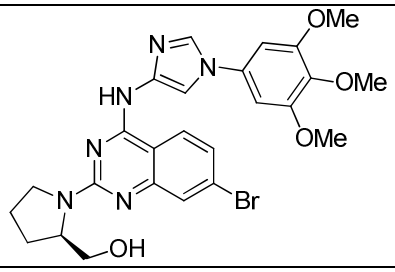
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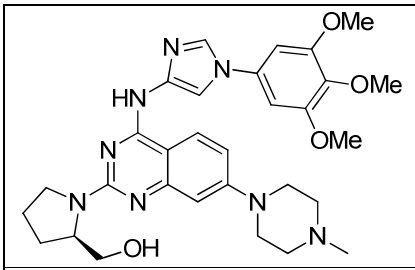
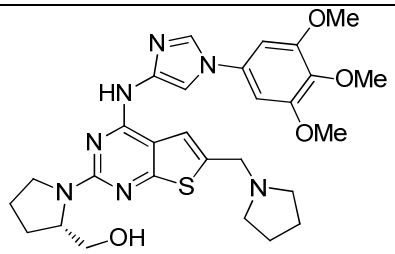
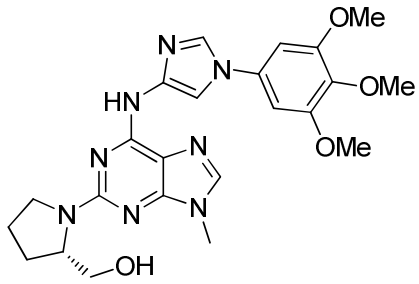
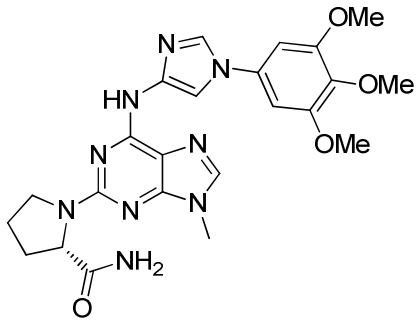
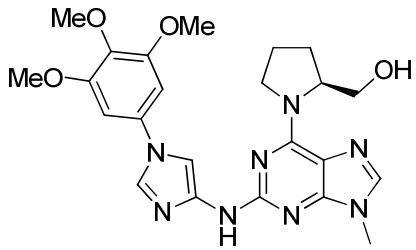
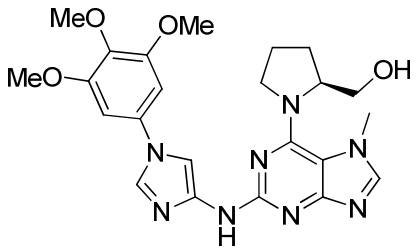
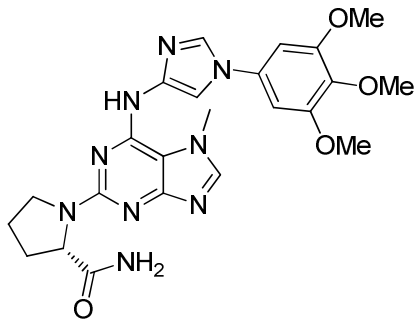
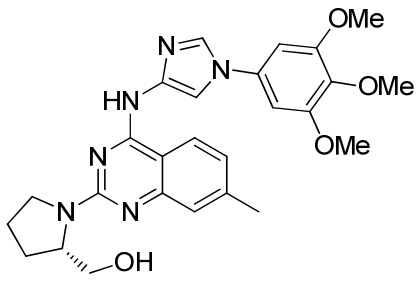
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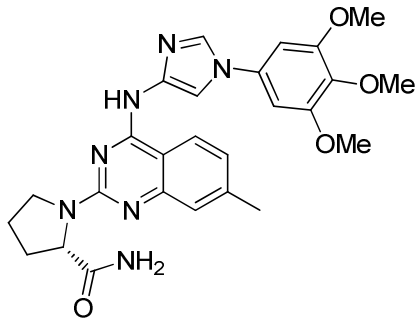
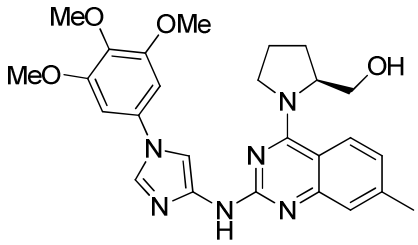
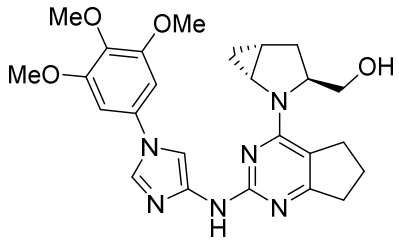
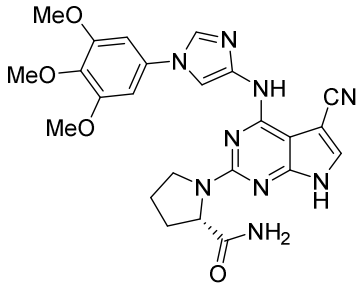
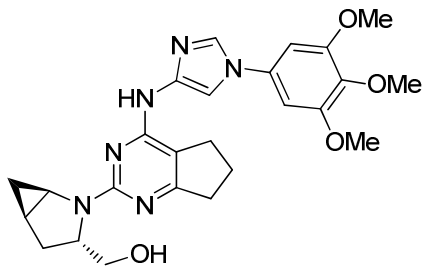
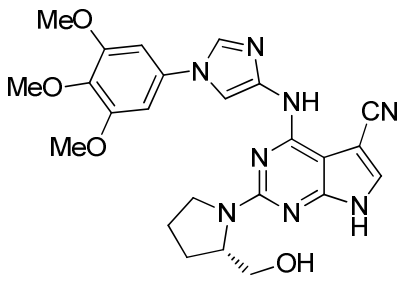
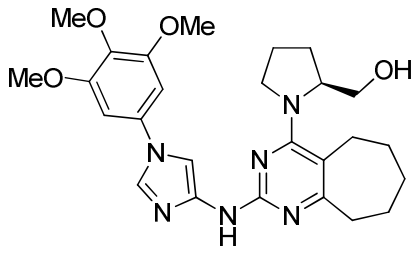
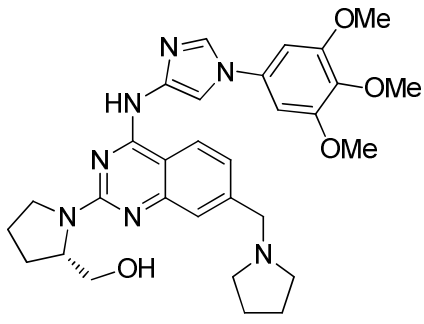
	
	

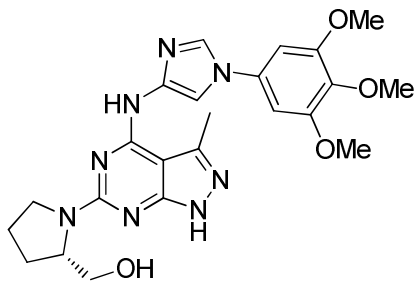
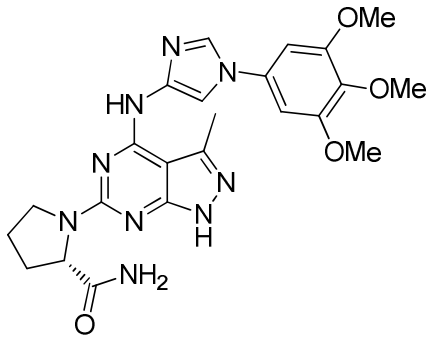
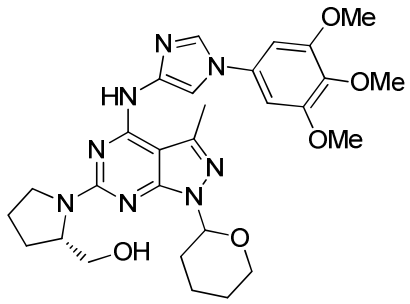
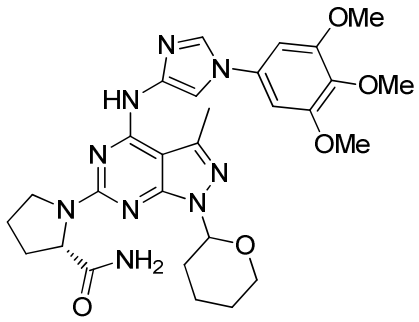
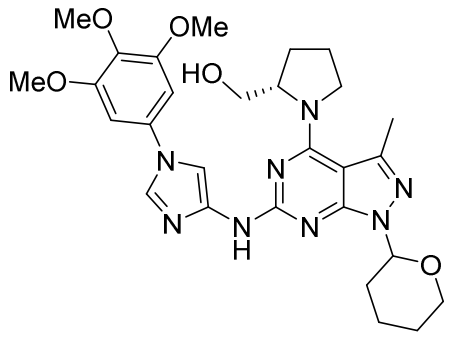
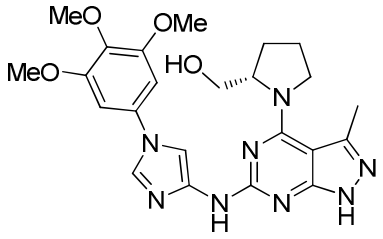
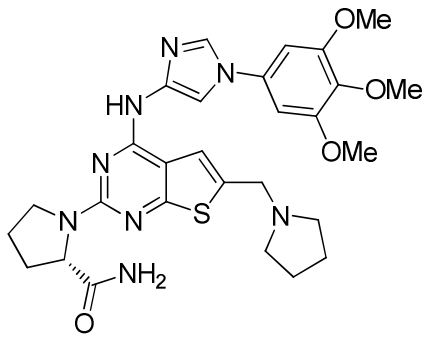
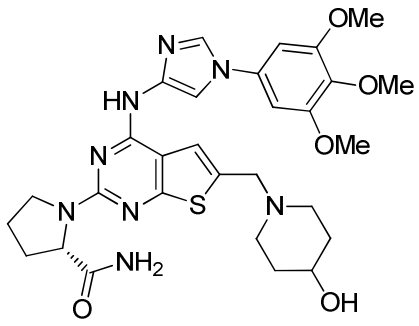
	
	
	
	
	

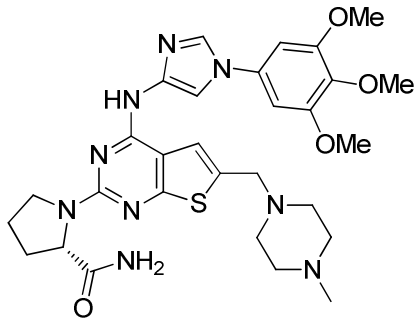
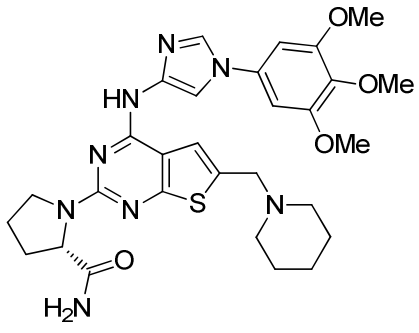
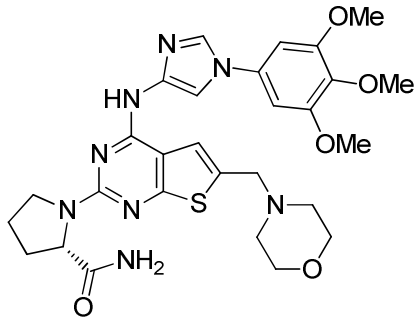
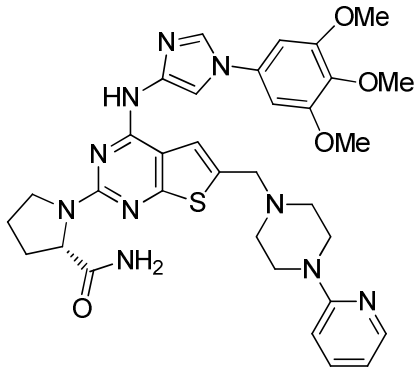
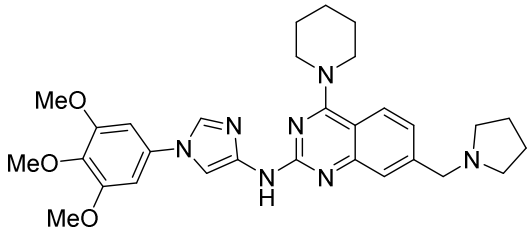
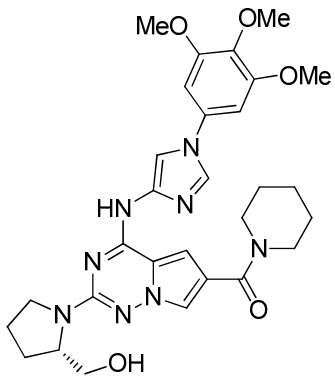
	
	
	
	
	

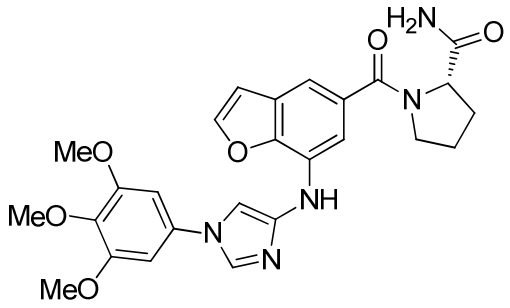
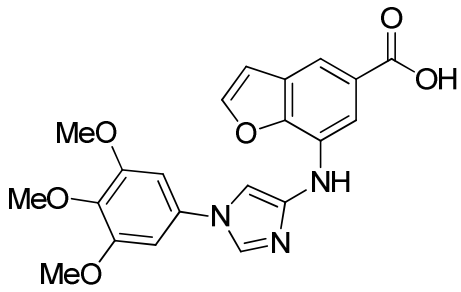
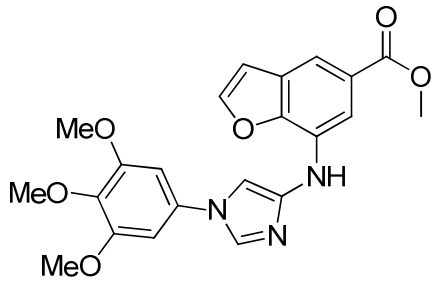
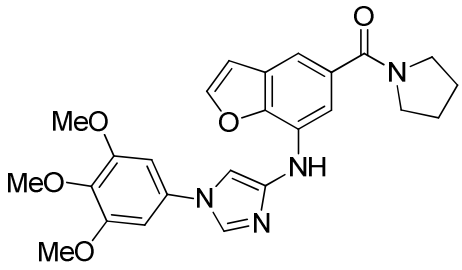
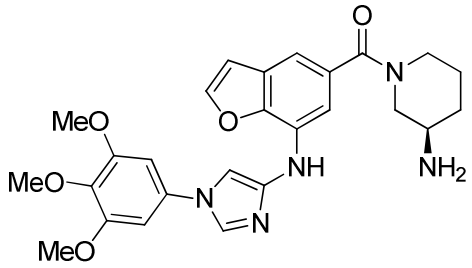
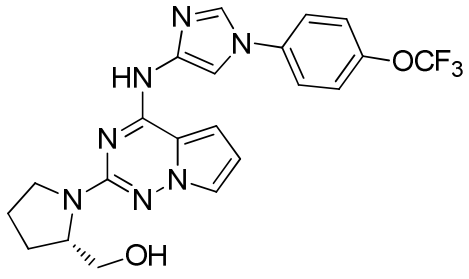
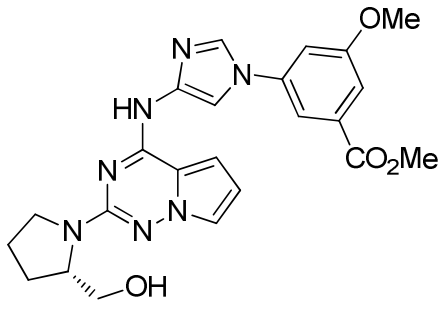
	
	
	
	
	
	

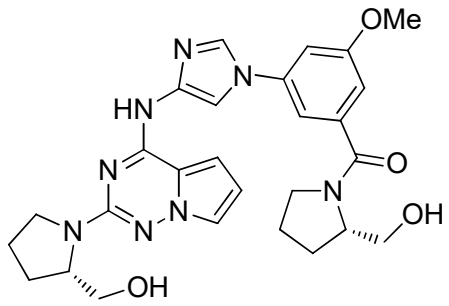
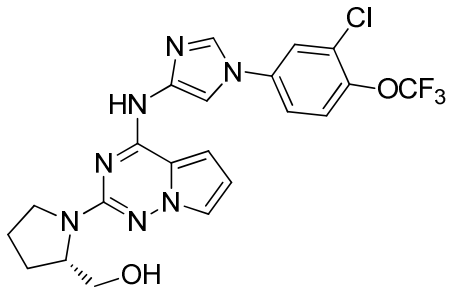
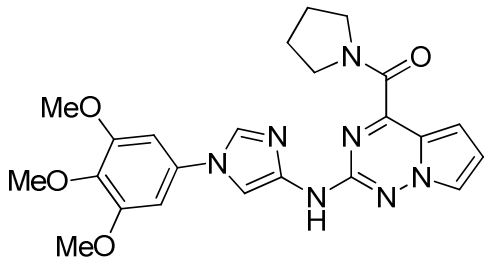
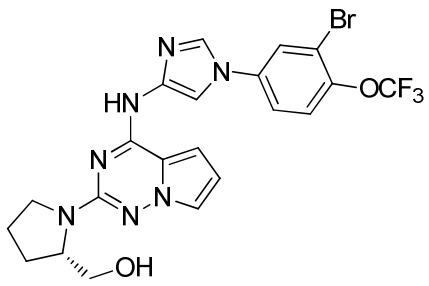
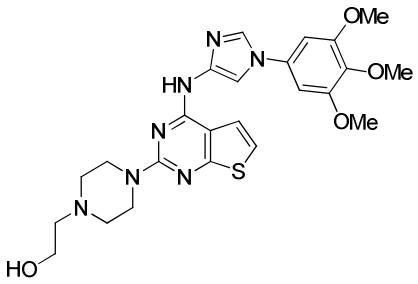
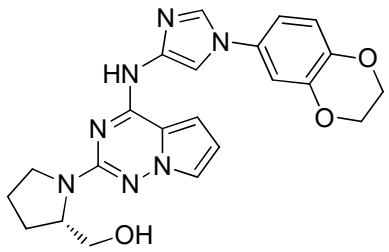
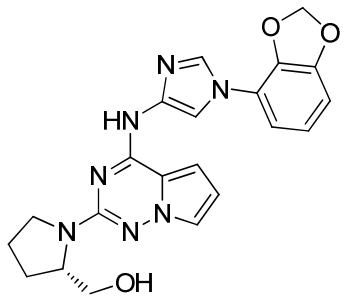
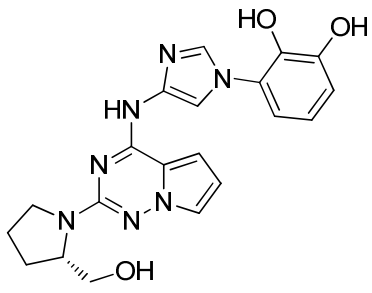
	
	
	
	

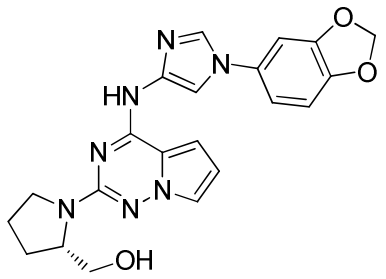
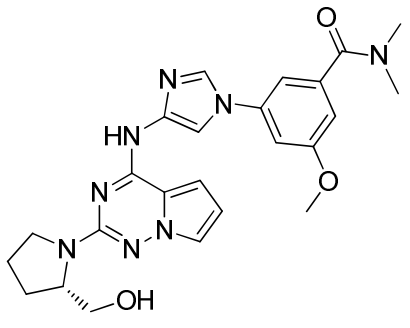
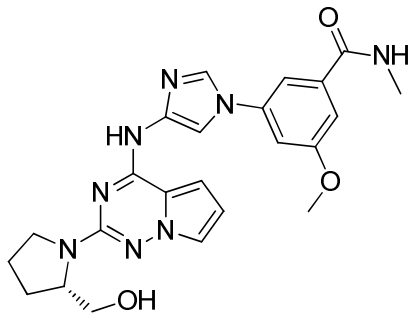
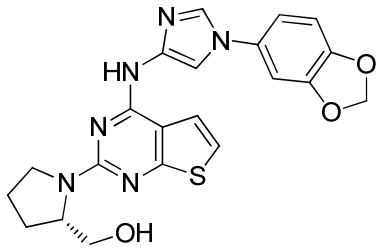
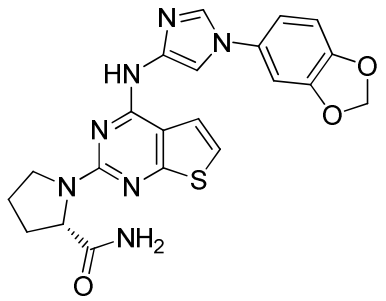
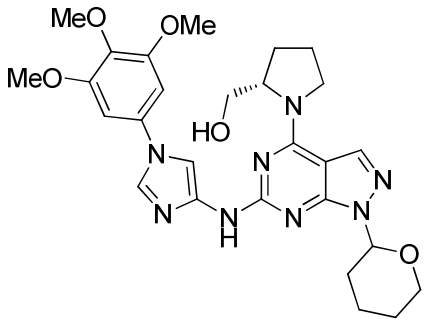
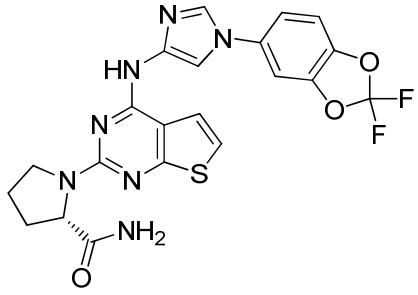
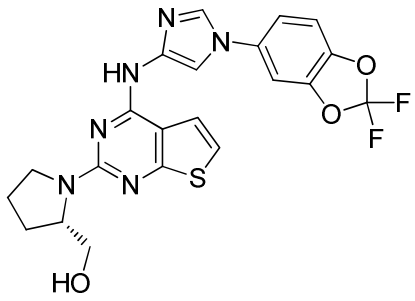
	
	
	
	

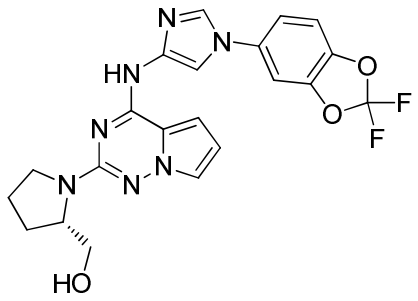
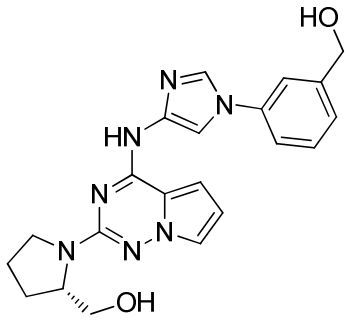
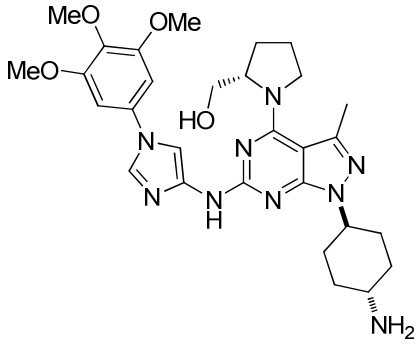
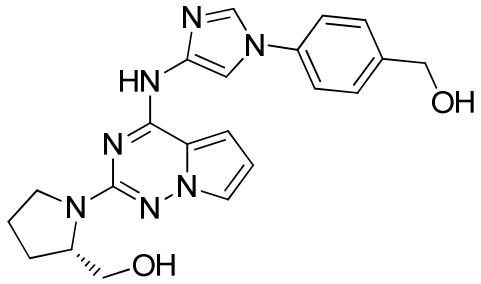
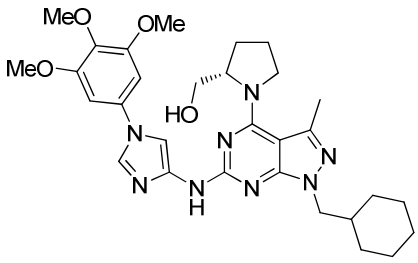
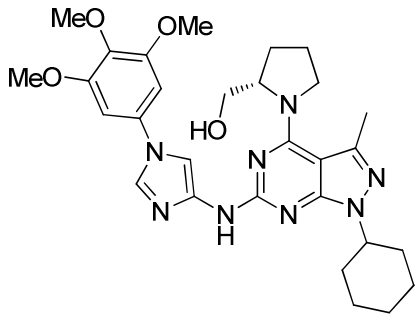
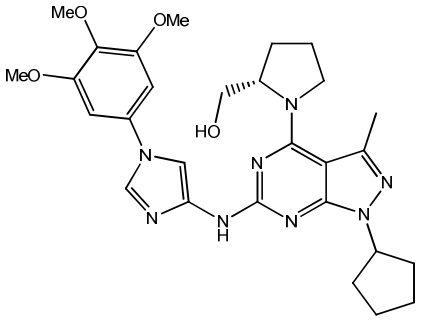
	
	
	
	

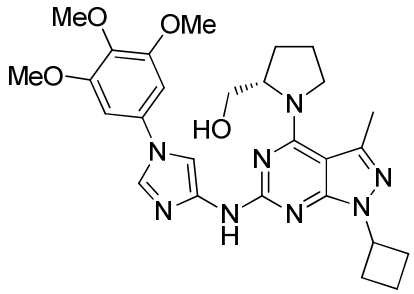
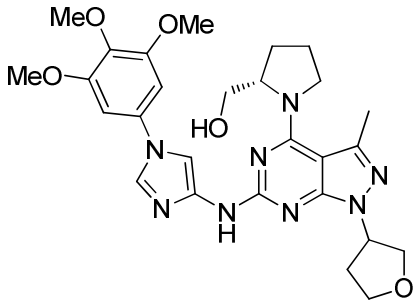
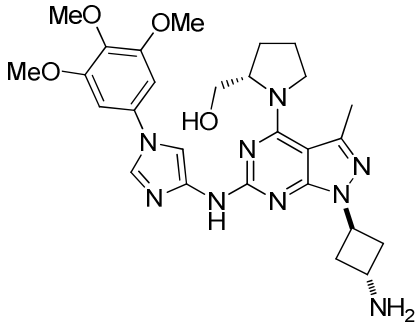
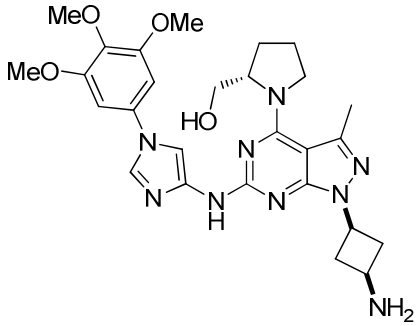
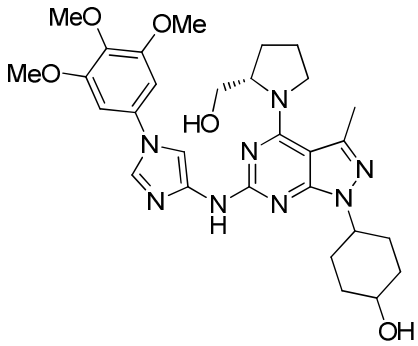
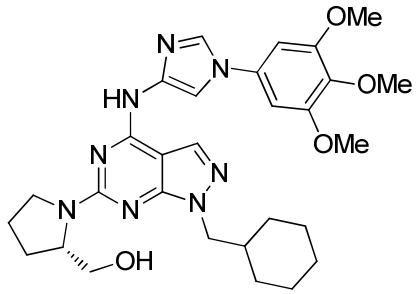
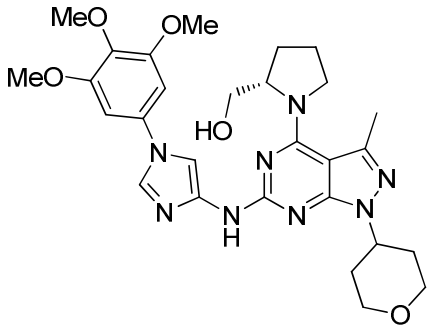
	
	
	

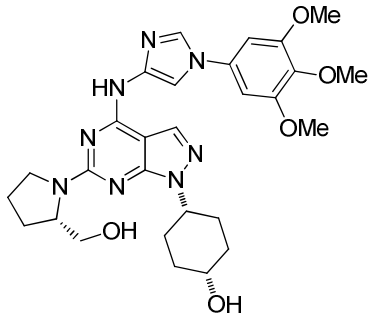
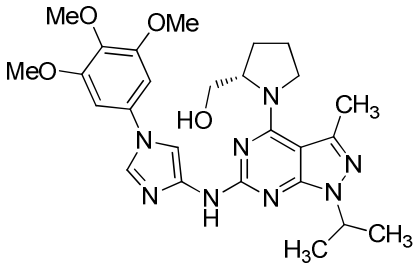
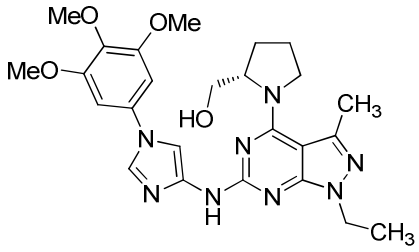
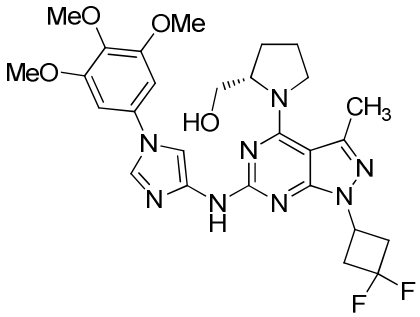
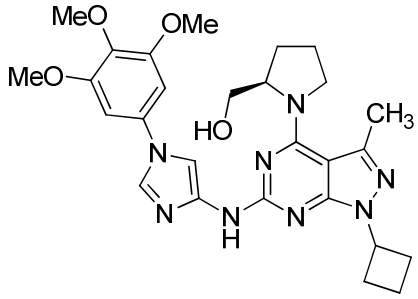
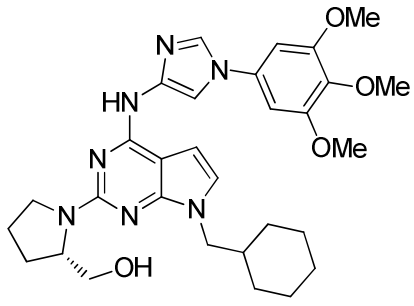
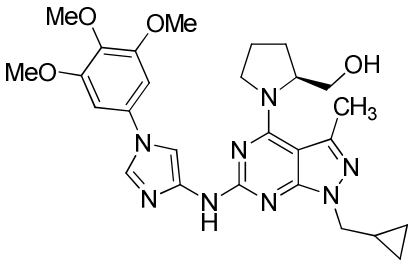
	
	
	
	

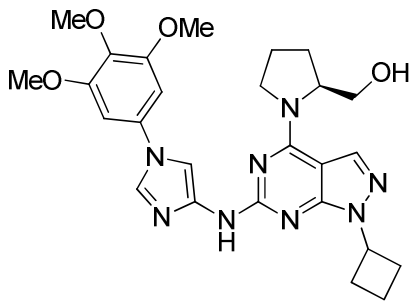
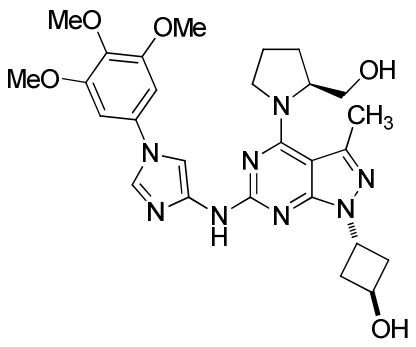
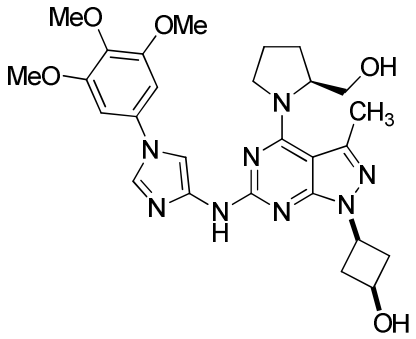
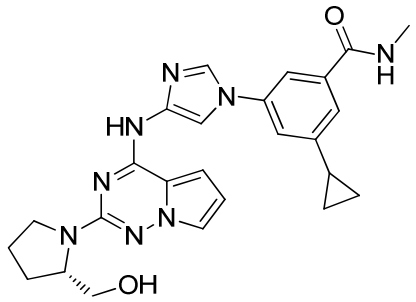
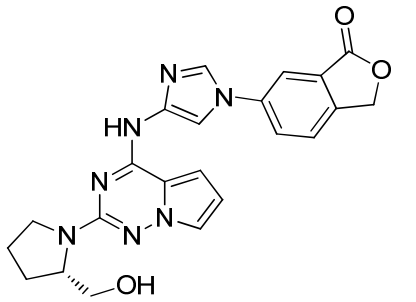
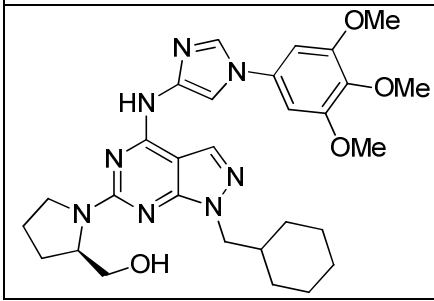
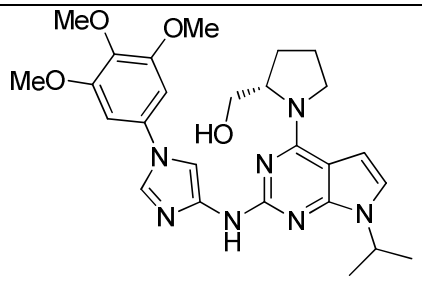
	
	
	
	

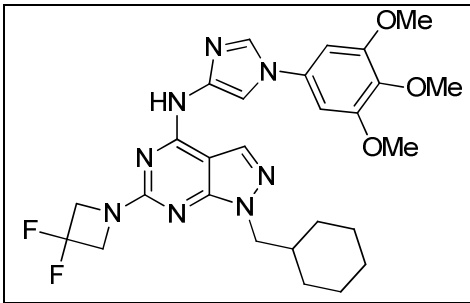
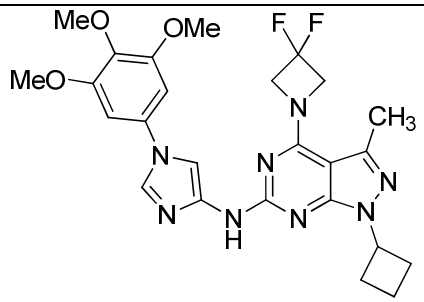
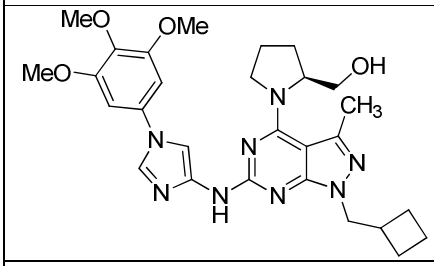
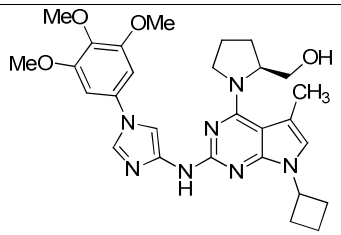
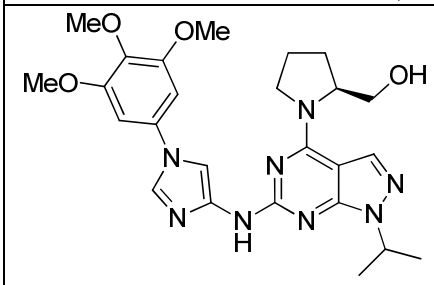
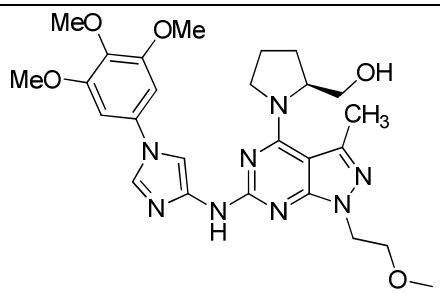
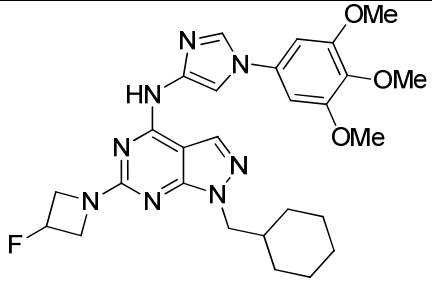
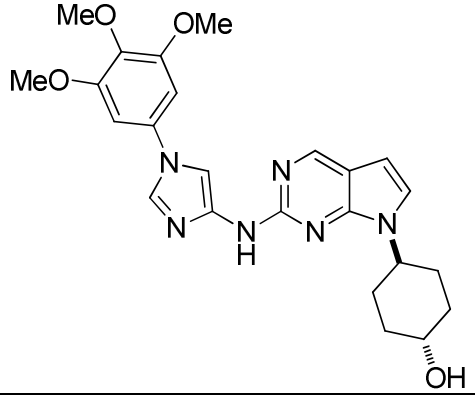
	
	
	
	

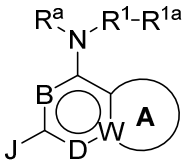
	
	
	
	

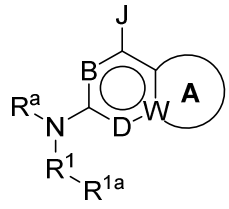
	
	
	
	

21. A compound represented by formula (III) or formula (IV):



(III)



(IV)

or a pharmaceutically acceptable salt thereof;

wherein:

A is a fused optionally substituted aromatic ring, heteroaromatic ring, partially unsaturated cycloalkyl ring, or partially unsaturated heterocycloalkyl ring;

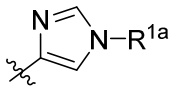
W is C or N;

B is CH or N;

D is CH or N;

provided that when B is CH, then D is N; or when D is CH, then B is N;

R^a represents H or alkyl;

$-R^1-R^{1a}$ represents 

, wherein R^{1a} represents optionally substituted phenyl;

J represents H, halo, $-OR^2$, $-NR^2R^3$, $-C(O)NR^2R^3$, -C(O)O(alkyl), -C(O)OH, aryl, or heteroaryl, wherein aryl or heteroaryl is optionally substituted by one or more occurrences of R^{2a};

R^2 represents optionally substituted alkyl, aralkyl, heteroaralkyl, cycloalkyl, heterocycloalkyl, (cycloalkyl)alkyl, (heterocycloalkyl)alkyl, or hydroxyalkyl;

R^3 represents H or alkyl; or

R^2 and R^3, taken together, form a heterocycloalkyl ring, optionally substituted by one or more occurrences of R^{2a};

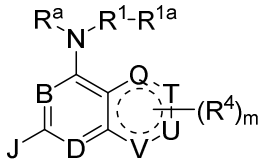
R^{2a}, independently for each occurrence, represents halo, hydroxyl, -C(O)H, oxo, $-NH_2$, $-C(O)NH_2$, -C(O)OH, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NH(R^5)$, or optionally substituted alkyl, alkoxyl, hydroxyalkyl, heteroaryl, aryl, aryloxy, heteroaryloxy, arylalkyloxy, heteroarylalkyloxy, or $-N(alkyl)_2$;

or any two germinal or vicinal occurrences of R^{2a}, taken together, may form a spiro or fused cycloalkyl ring;

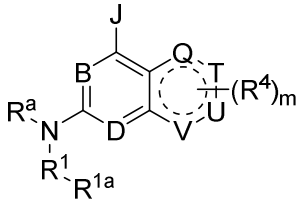
R^5, independently for each occurrence, represents optionally substituted alkyl, aralkyl, aryl, heteroaralkyl, heteroaryl, cycloalkyl, heterocycloalkyl, (cycloalkyl)alkyl, or (heterocycloalkyl)alkyl; and

R^x and R^y each independently represent H, alkyl, aralkyl, heteroaralkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, (cycloalkyl)alkyl, (heterocycloalkyl)alkyl, or hydroxyalkyl.

22. The compound of claim 21, wherein the compound is represented by formula (IIIa) or formula (IVa):



(IIIa)



(IVa);

wherein:

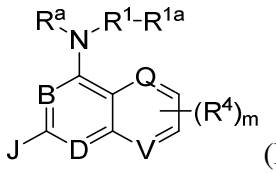
valence permitting, Q, T, U, and V each independently represent CH, CH_2, N, NH, O, or SO_2, wherein any hydrogen of a CH, CH_2, or NH group is optionally replaced by an occurrence of R^4;

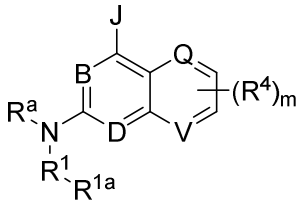
R^4, independently for each occurrence, represents halo, cyano, or optionally substituted alkyl, alkenyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkoxy, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkenyl, (heterocycloalkyl)alkyl, cycloalkyl, (cycloalkyl)alkyl, halocycloalkyl, hydroxycycloalkyl, aminocycloalkyl, aryloxy, heteroaryloxy, arylalkyloxy, heteroarylalkyloxy, $-CH_2C(O)NH_2$, $-C(O)R^5$, $-C(O)OR^5$, or $–S(O)_2R^5$;

m is an integer from 0-4, as permitted by valence.

23. The compound of claim 22, wherein the compound is represented by:

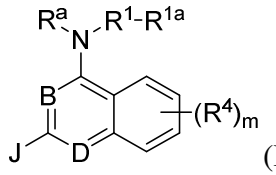
a) formula (IIIb) or (IVb):

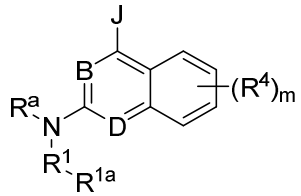

(IIIb)


(IVb),

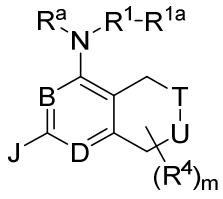
wherein Q represents CH or N, and V represents CH or N;

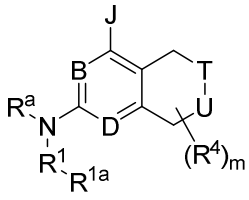
b) formula (IIIc) or (IVc):


(IIIc)


(IVc);

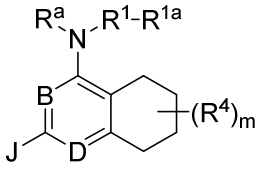
c) formula (IIId) or (IVd):

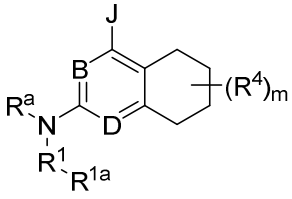

(IIId)


(IVd),

wherein T represents CH_2, NH, O, or SO_2, and U represents CH_2, NH, O, or SO_2; or

d) formula (IIIe) or (IVe):

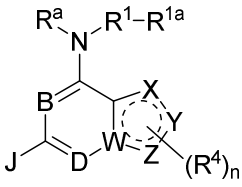

(IIIe)

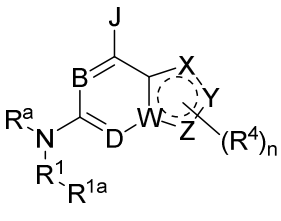

(IVe).

24. The compound of claim 23, wherein the compound is represented by formula (IIIb) or (IVb), and wherein Q is N and V is CH, or wherein Q is CH and V is N.

25. The compound of claim 23, wherein the compound is represented by formula (IIId) or (IVd), and wherein T is NH and U is CH_2, or wherein T is CH_2 and U is NH.

26. The compound of claim 21, wherein the compound is represented by formula (IIIj) or formula (IVj):


(IIIj)


(IVj);

wherein:

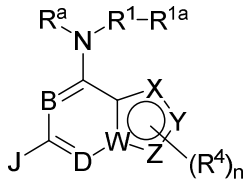
W is C or N;

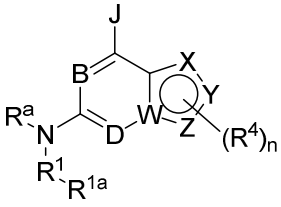
valence permitting, X, Y, and Z each independently represent CH, CH_2, CO, N, NH, O, S, or SO_2, wherein any hydrogen of a CH, CH_2, or NH group is optionally replaced by an occurrence of R^4;

R^4, independently for each occurrence, represents halo, cyano, or optionally substituted alkyl, alkenyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkoxy, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkenyl, (heterocycloalkyl)alkyl, cycloalkyl, (cycloalkyl)alkyl, halocycloalkyl, hydroxycycloalkyl, aminocycloalkyl, aryloxy, heteroaryloxy, arylalkyloxy, heteroarylalkyloxy, $-CH_2C(O)NH_2$, $-C(O)R^5$, $-C(O)OR^5$, or $–S(O)_2R^5$;

n is an integer from 0-4, as permitted by valence.

27. The compound of claim 26, wherein the compound is represented by formula (IIIk) or (IVk):

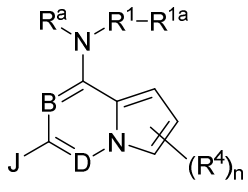

(IIIk)

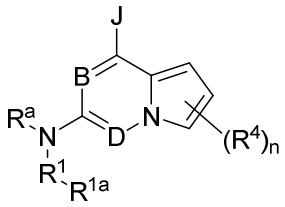

(IVk);

wherein X, Y, and Z each independently represent CH, N, NH, O, S, or SO_2.

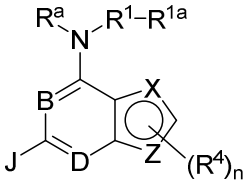
28. The compound of claim 27, wherein the compound is represented by:

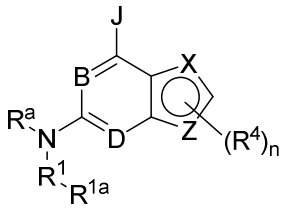
a) formula (IIIk') or (IVk'):


(IIIk')


(IVk');

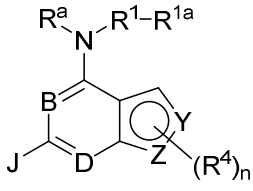
b) formula (IIIk") or (IVk"):

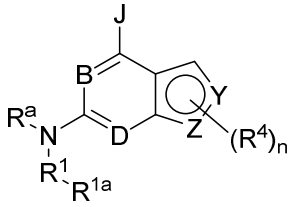

(IIIk")


(IVk"),

wherein at least one of X and Z is selected from the group consisting of O, N, NH, and S; or

c) formula (IIIn) or (IVn):


(IIIn)


(IVn),

wherein each of Y and Z are selected from the group consisting of O, N, NH, and S.

29. The compound of claim 28 wherein the compound is represented by formula (IIIk") or (IVk"), and wherein:

a) one of X and Z is selected from the group consisting of O, NH, and S, and the other of X and Z is CH;

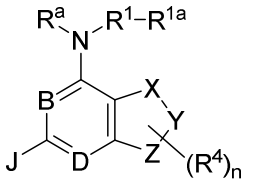
b) X is selected from the group consisting of O, NH, and S;

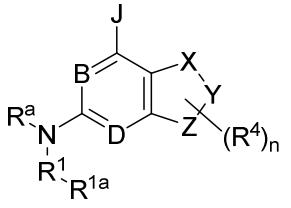
c) Z is selected from the group consisting of O, NH, and S;

d) each of X and Z are selected from the group consisting of O, N, NH, and S; or

e) one of X and Z is N and the other of X and Z is NH.

30. The compound of claim 26, wherein the compound is represented by formula (IIIm) or (IVm):


(IIIm)


(IVm);

wherein X, Y, and Z each independently represent CH_2, CO, NH, O, S, or SO_2.

31. The compound of claim 30, wherein:
    a) each of X, Y, and Z is CH_2; or
    b) one of X, Y, and Z is N or O.

32. The compound of any one of claims 21-31, wherein R^4, if present, is selected from the group consisting of optionally substituted alkyl, hydroxyalkyl, aminoalkyl, alkoxy, aryl, aralkyl, and (heterocycloalkyl)alkyl.

33. The compound of any one of claims 21-32, wherein R^a is H.

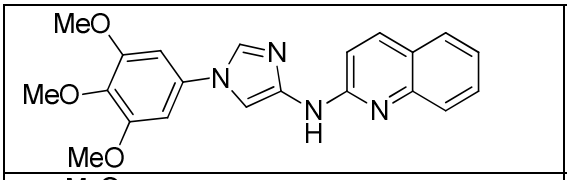
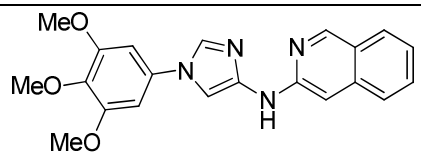
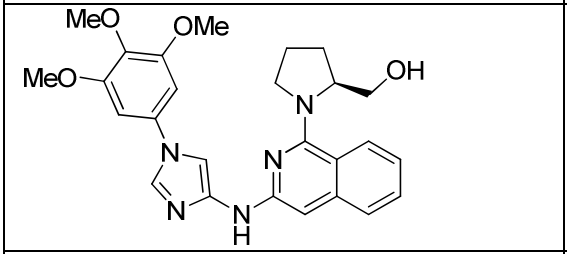
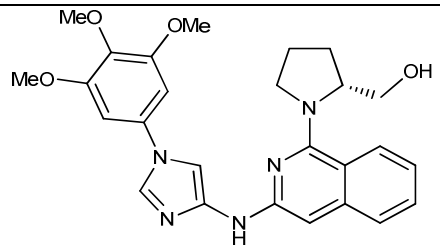
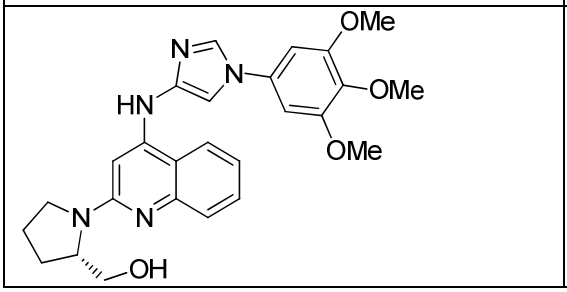
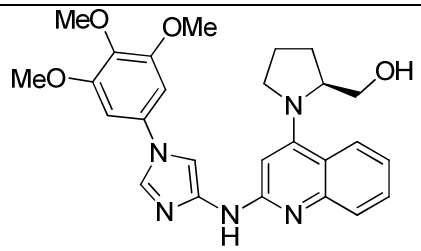
34. The compound of any one of claims 21-33, wherein R^{1a} is:
    a) phenyl, substituted by one or more occurrences of halo, hydroxyl, cyano, -C(O)NH_2, hydroxylalkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, -C(O)alkyl, -C(O)O-alkyl, heterocycloalkyl, -C(O)NH(alkyl), -C(O)N(alkyl)$_2$, -C(O)heterocycloalkyl, -C(O)(prolinol), -C(O)NH((cycloalkyl)alkyl), or -C(O)NH(cycloalkyl);
    b) phenyl, substituted by two or more occurrences of alkoxy;
    c) 3,4,5-trimethoxyphenyl; or
    d) substituted phenyl, wherein two adjacent substituents on the phenyl, taken together with the intervening atoms, form an optionally substituted cycloalkyl or heterocycloalkyl ring.

35. The compound of any one of claims 21-34, wherein:
    a) J is aryl, optionally substituted by one or more occurrences of R^{2a}; or
    b) J is $–NR^2R^3$.

36. The compound of claim 35, wherein:
    a) R^2 and R^3, taken together, form a heterocycloalkyl ring, optionally substituted by one or more occurrences of R^{2a}; or
    b) R^2 and R^3, taken together, form a pyrrolidine ring, optionally substituted by one or more occurrences of R^{2a}.

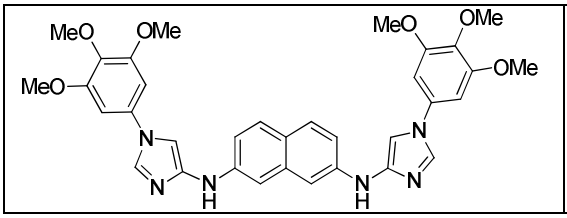
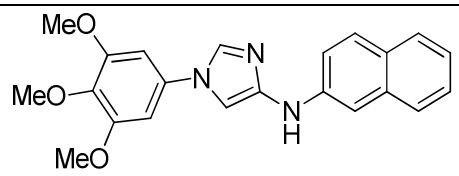
37. The compound of claim 35 or 36, wherein R^{2a}, independently for each occurrence, represents -C(O)NH_2, -C(O)R^5, hydroxyalkyl, heteroaryl, or aryl.

38. The compound of claim 21, selected from the following table:

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39. A compound, or a pharmaceutically acceptable salt thereof, selected from the following table:

40. A pharmaceutical composition, comprising a compound of any one of claims 1-39, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable excipient.

41. Use of the compound of any one of claims 1-39, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of fibrodysplasia ossificans progressiva.

42. Use of the compound of any one of claims 1-39, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of cancer.

43. The use of claim 42, wherein the cancer is a glioma.

44. The use of claim 43, wherein the glioma is diffuse intrinsic pontine glioma.