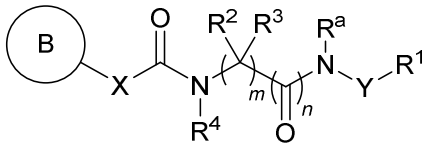
CLAIMS

1. A compound represented by Formula (I), or a pharmaceutically acceptable salt thereof:



(I);

wherein, independently for each occurrence:

R^1 represents substituted aryl, heteroaryl, cycloalkyl, or heterocycloalkyl;

wherein when R^1 represents aryl or heteroaryl, the aryl or heteroaryl is substituted by one or more substituents independently selected from the group consisting of halogen, –CN, alkoxy, haloalkoxy, alkyl, haloalkyl, alkenyl, dialkylamino, heterocycloalkyl, aryl, and heteroaryl; and

when R^1 represents cycloalkyl or heterocycloalkyl, the cycloalkyl or heterocycloalkyl is substituted by one or more substituents selected from the group consisting of halogen, azide, $(C_1\text{-}C_{10})$alkyl, unsubstituted or substituted aryl$(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, $(C_3\text{-}C_7)$cycloalkyl, hydroxyl, $(C_1\text{-}C_{10})$alkoxy, $(C_1\text{-}C_{10})$haloalkoxy, $(C_1\text{-}C_{10})$haloalkyl, $(C_1\text{-}C_{10})$alkoxy$(C_1\text{-}C_{10})$alkyl, amino, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl, ether, $(C_1\text{-}C_{10})$alkylthio, sulfonyl, sulfonamido, ketone, aldehyde, ester, –C(O)($(C_1\text{-}C_{10})$alkyl), unsubstituted or substituted heterocycloalkyl, $(C_6\text{-}C_{10})$aryl, heteroaryl, fluoro$(C_1\text{-}C_{10})$alkyl, and cyano;

R^2 and R^3 each independently represent H, F, or alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, hydroxyalkyl, (alkylthio)alkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl;

or R^2 and R^3, taken together with the carbon atom to which they are bonded, form an optionally substituted cycloalkyl or heterocycloalkyl ring;

R^4 represents H or optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, (heterocycloalkyl)alkyl, aralkyl, heteroaralkyl, hydroxyalkyl, or haloalkyl;

X represents NH, CH_2, CHF, CF_2, $CH(C_1\text{-}C_6)$alkyl, or $C((C_1\text{-}C_6)alkyl)_2$;

Y is absent or represents CH_2, C(O), $CR^{15}R^{16}$, $S(O)_2$, or optionally substituted (C_3-C_7)cycloalkylene, arylene, or heteroarylene;

R^a represents H or optionally substituted (C_1-C_6)alkyl, (heterocycloalkyl)alkyl, or (C_3-C_7)cycloalkyl;

m is an integer from 1-6;

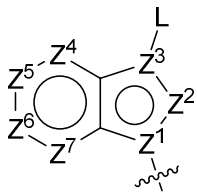
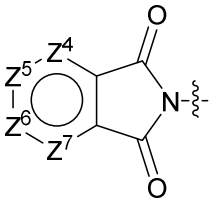
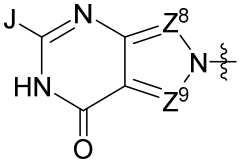
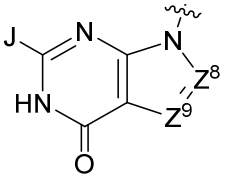
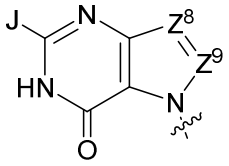
n is 0 or 1;

R^{15} and R^{16} are each independently selected from the group consisting of H, hydroxy, halogen, $-C(O)OR^{17}$, $-OR^{17}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, alkyl, hydroxyalkyl, haloalkyl, alkoxyalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, and (heterocycloalkyl)alkyl, wherein alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, and (heterocycloalkyl)alkyl are optionally substituted with one or more substituents selected from the group consisting of -CN, $-OR^{17}$, $-NR^{17}R^{18}$, halo, and alkyl;

or R^{15} and R^{16} may be taken together with the intervening atom to form an optionally substituted carbocyclic or heterocyclic ring;

R^{17} and R^{18} are each independently selected from the group consisting of H, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, and (heterocycloalkyl)alkyl;

or R^{17} and R^{18}, when attached to the same atom, may be taken together with the intervening atom to form an optionally substituted heterocyclic ring;

B represents , , , , or ;

Z^1 and Z^3 each independently represent C or N;

Z^2 represents N, CH, or CF;

Z^4 represents N or CR^8;

Z^5 represents N or CR^5;

Z^6 represents N or CR^6;

Z^7 represents N or CR^9;

Z^8 and Z^9 each independently represent N or CR^{19};

R^5 and R^6 each independently represent H, halogen, $-CN$, $-NO_2$, $-OR^{13}$, $-NR^{13}R^{14}$, $-C(O)R^{13}$, $-C(O)OR^{13}$, $-C(O)NR^{13}R^{14}$, $-OC(O)R^{13}$, $-NR^{13}C(O)R^{14}$, $-OC(O)NR^{13}R^{14}$, $-OC(O)OR^{13}$, $-NR^{13}C(O)OR^{14}$, $-NR^{13}C(O)NR^{13}R^{14}$, $-OS(O)_p(R^{13})$, $-NR^{13}S(O)_p(R^{14})$, or optionally substituted alkyl, alkenyl, alkynyl, haloalkyl, aralkyl, heteroaralkyl, heteroaryl, aryl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl;

L represents $-H$, $-CN$, $-C(O)R^7$, $-CH(OH)R^7$, or $-S(O)_p$(alkyl);

R^7, independently for each occurrence, represents H, NH_2, CH_3, OH, CF_3, CH_2OH, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, $NH(C_1$-C_6)alkyl, $N((C_1$-C_6)alkyl)$_2$;

R^8 and R^9 each independently represent H, halogen, $-OR^{13}$, $-NR^{13}R^{14}$, $-C(O)R^{13}$, $-C(O)OR^{13}$, $-C(O)NR^{13}R^{14}$, $-OC(O)R^{13}$, $-NR^{13}C(O)R^{14}$, $-OC(O)NR^{13}R^{14}$,

$-OC(O)OR^{13}$, $-NR^{13}C(O)OR^{14}$, $-NR^{13}C(O)NR^{13}R^{14}$, $-OS(O)_p(R^{13})$, $-NR^{13}S(O)_p(R^{14})$, or optionally substituted alkyl, alkenyl, alkynyl, haloalkyl, aralkyl, heteroaralkyl, heteroaryl, or aryl;

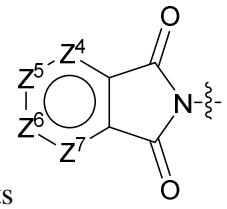
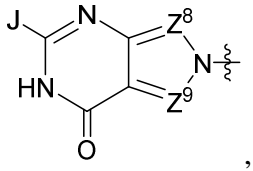
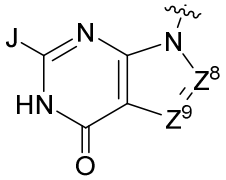
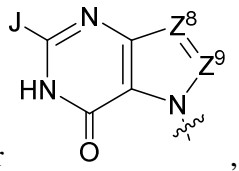
or R^5 and R^8, or R^5 and R^6, or R^6 and R^9 may be taken together with the intervening atoms to form an optionally substituted heterocyclic or carbocyclic ring;

R^{13} and R^{14}, independently for each occurrence, represent H or optionally substituted alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl; or, when R^{13} and R^{14} are attached to the same atom, R^{13} and R^{14} taken together with the atom may form an optionally substituted heterocyclic ring;

R^{19}, independently for each occurrence, represents H, F, CN, $-C(O)R^7$, $-CH(OH)R^7$, or $-S(O)_p$(alkyl);

J represents H or NH_2; and

p is 0, 1, or 2;

wherein, if Z^1 is N, or if  represents , , , or , then X represents CH_2;

further wherein when a group is optionally substituted, the optionally substituents are selected from the group consisting of halogen, azide, $(C_1$-$C_{10})$alkyl, unsubstituted or substituted aryl$(C_1$-$C_{10})$alkyl, $(C_2$-$C_{10})$alkenyl, $(C_2$-$C_{10})$alkynyl, $(C_3$-$C_7)$cycloalkyl, hydroxyl, $(C_1$-$C_{10})$alkoxy, $(C_1$-$C_{10})$haloalkoxy, $(C_1$-$C_{10})$haloalkyl, $(C_1$-$C_{10})$alkoxy$(C_1$-$C_{10})$alkyl, amino, nitro, sulfhydryl, imino, amido, phosphonate, phosphinate, carbonyl, carboxyl, silyl,

ether, (C_1-C_{10})alkylthio, sulfonyl, sulfonamido, ketone, aldehyde, ester, −C(O)((C_1-C_{10})alkyl), unsubstituted or substituted heterocycloalkyl, (C_6-C_{10})aryl, heteroaryl, fluoro(C_1-C_{10})alkyl, and cyano.

2. The compound of claim 1, wherein *n* is 1.

3. The compound of claim 1 or 2, wherein R^1 represents aryl or heteroaryl, substituted by one or more substituents independently selected from the group consisting of halogen, −CN, alkoxy, haloalkoxy, alkyl, haloalkyl, alkenyl, dialkylamino, heterocycloalkyl, aryl, and heteroaryl.

4. The compound of any one of claims 1-3, wherein R^1 represents aryl or heteroaryl, substituted by one or more substituents, at least one of which is halogen.

5. The compound of any one of claims 1-4, wherein Y is absent.

6. The compound of any one of claims 1-4, wherein Y is CH_2.

7. The compound of any one of claims 1-4, wherein Y is $CR^{15}R^{16}$.

8. The compound of claim 7, wherein R^{15} and R^{16} are selected from the group consisting of H, alkyl, hydroxyalkyl, haloalkyl, alkoxyalkyl, aralkyl, heteroaralkyl, (cycloalkyl)alkyl, and (heterocycloalkyl)alkyl;

wherein alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, and (heterocycloalkyl)alkyl are optionally substituted with one or more substituents selected from the group consisting of -CN, -OR^{17}, -$NR^{17}R^{18}$, halo, and alkyl; and

further wherein R^{17} and R^{18} are each independently selected from the group consisting of H and alkyl.

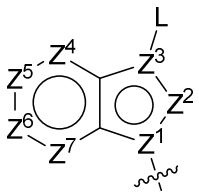
9. The compound of any one of claims 1-8, wherein R^2 is H; and R^3 represents H or optionally substituted alkyl, alkoxyalkyl, hydroxyalkyl, (alkylthio)alkyl, cycloalkyl, or (cycloalkyl)alkyl.

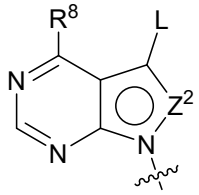
10. The compound of any one of claims 1-9, wherein R^4 represents H or optionally substituted alkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, aralkyl, hydroxyalkyl, or haloalkyl.

11. The compound of any one of claims 1-10, wherein R^4 represents H or optionally substituted alkyl or cycloalkyl.

12. The compound of any one of claims 1-11, wherein R^a is H.

13. The compound of any one of claims 1-12, wherein *m* is 1.

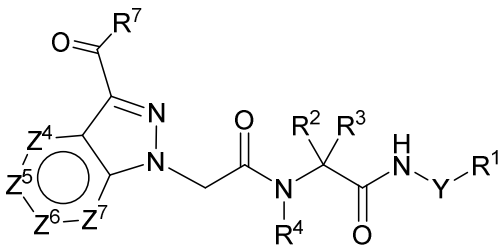
14. The compound of any one of claims 1-13, wherein  represents .

15. The compound of any one of claims 1-14, wherein  represents .

16. The compound of any one of claims 1-15, wherein L represents $-C(O)R^7$.

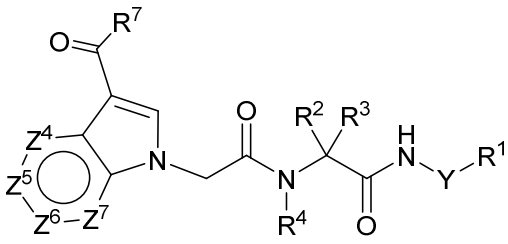
17. The compound of any one of claims 1-16, wherein X represents NH or CH_2.

18. The compound of any one of claims 1-17, having the structure of Formula (Ia):



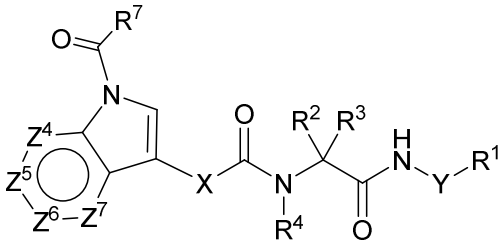
(Ia).

19. The compound of any one of claims 1-17, having the structure of Formula (Ib):



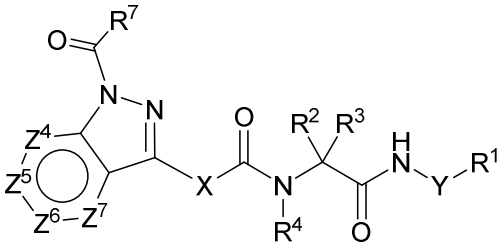
(Ib).

20. The compound of any one of claims 1-17, having the structure of Formula (Ic):



(Ic).

21. The compound of any one of claims 1-17, having the structure of Formula (Id):



(Id).

22. The compound of claim 20 or 21, wherein X is NH.

23. The compound of any one of claims 18-22, wherein:
Z^4 represents CR^8;
Z^5 represents CR^5;
Z^6 represents CR^6; and
Z^7 represents CR^9.

24. The compound of any one of claims 18-23, wherein Z^4 and Z^7 each represent CH.

25. The compound of any one of claims 18-24, wherein Z^5 represents CR^5; and Z^6 represents CR^6; and

R^5 and R^6 each independently represent H, halogen, $-NR^{13}R^{14}$, $-C(O)R^{13}$, $-C(O)OR^{13}$, $-C(O)NHR^{14}$, $-NHC(O)NR^{13}R^{14}$, $-NHS(O)_2(R^{14})$, or optionally substituted alkyl, alkenyl, alkynyl, heteroaryl, or aryl.

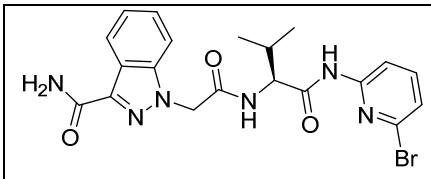
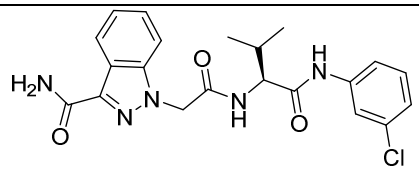
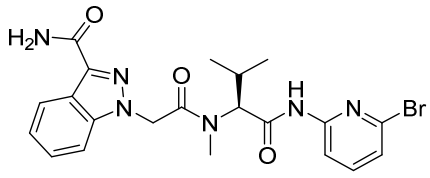
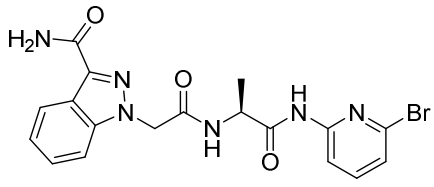
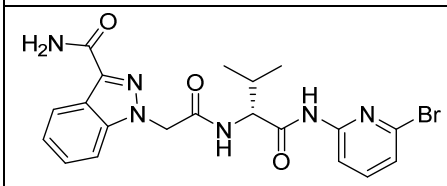
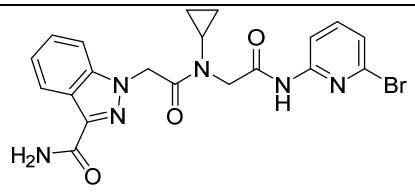
26. The compound of claim 25, wherein R^5 and R^6 each independently represent H or alkyl, alkenyl, alkynyl, heteroaryl, or aryl, optionally substituted with one or more substituents selected from the group consisting of aryl, heteroaryl, silyl, alkyl, amino, alkylamino, dialkylamino, $-C(O)$(alkyl), and halogen.

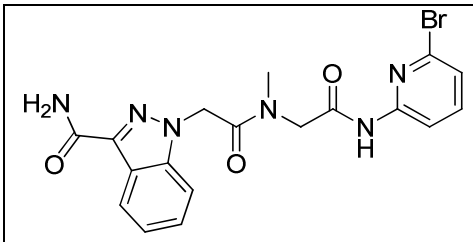
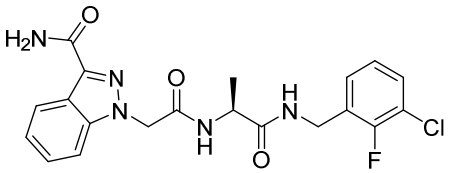
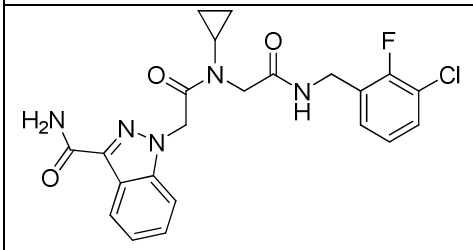
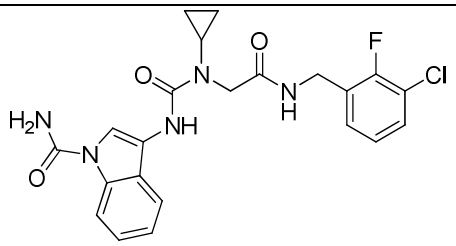
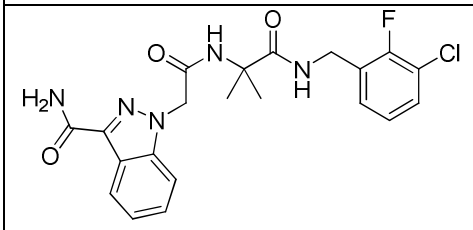
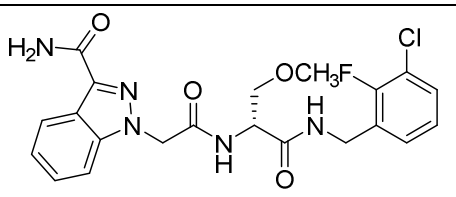
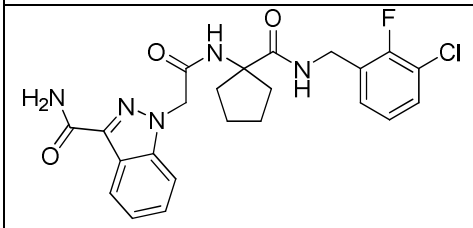
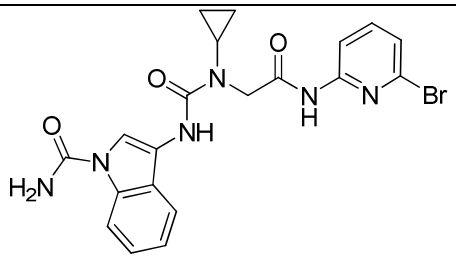
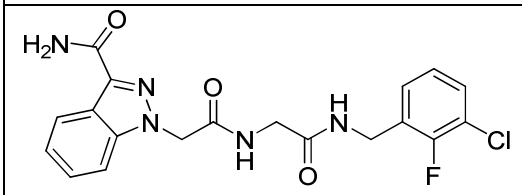
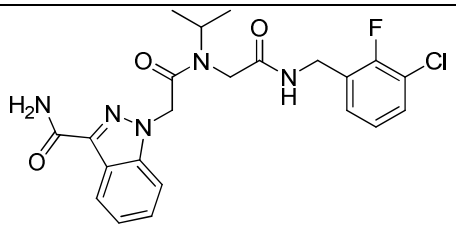
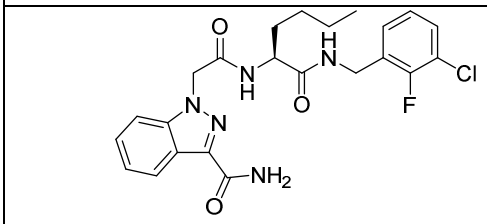
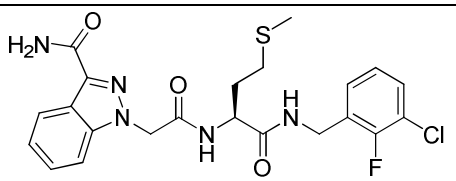
27. The compound of claim 25, wherein R^{13} and R^{14}, independently for each occurrence, represent H or optionally substituted aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, or (cycloalkyl)alkyl.

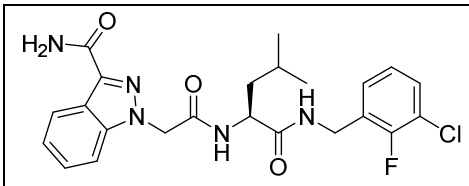
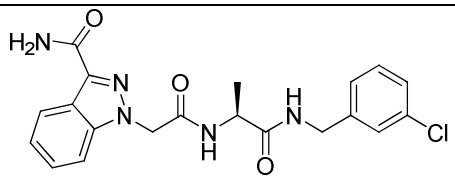
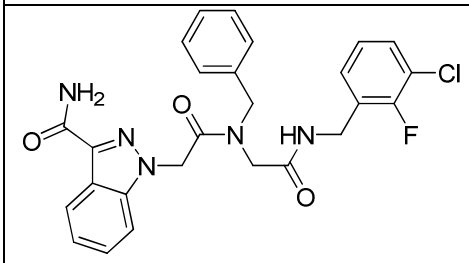
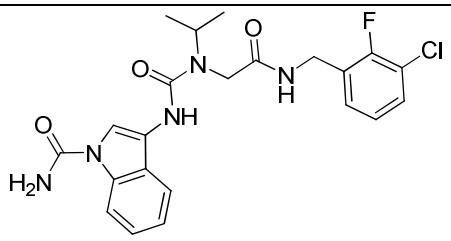
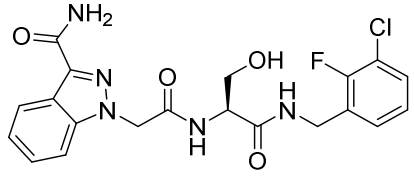
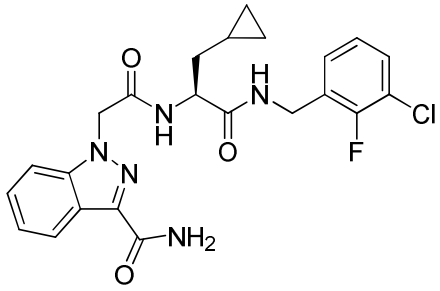
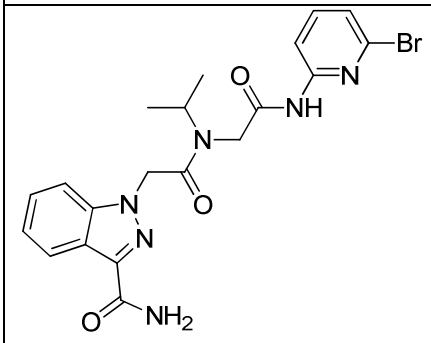
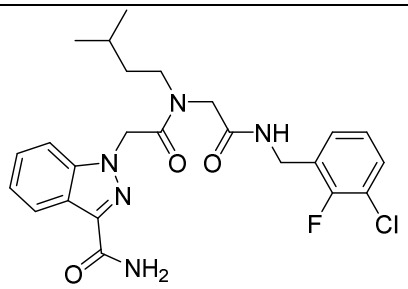
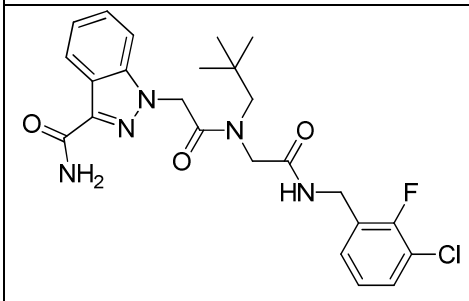
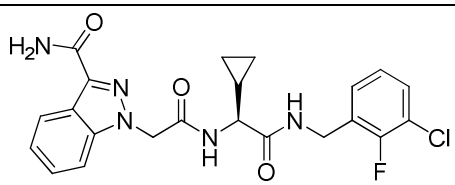
28. The compound of any one of claims 16-27, wherein R^7 represents NH_2, CH_3, or CF_3.

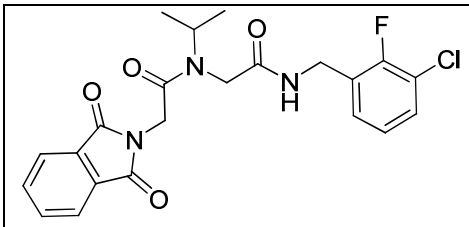
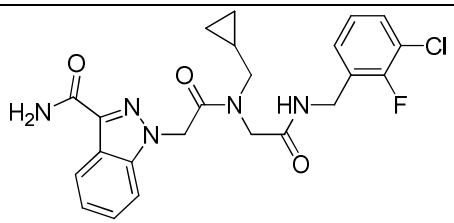
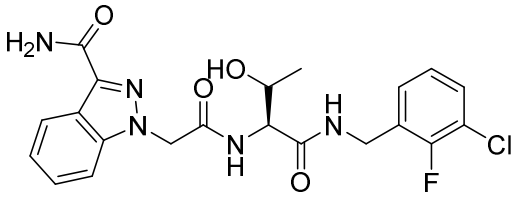
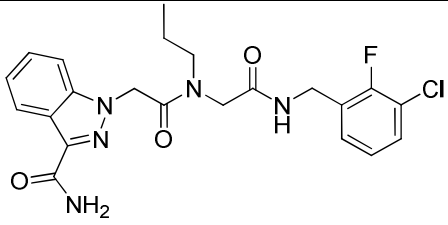
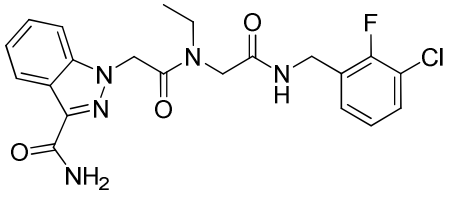
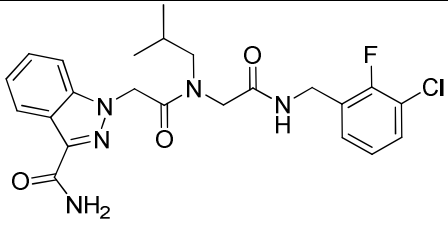
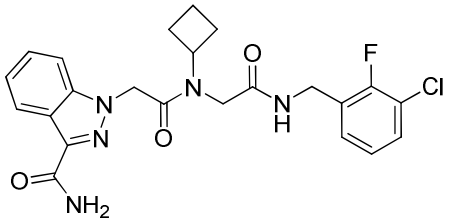
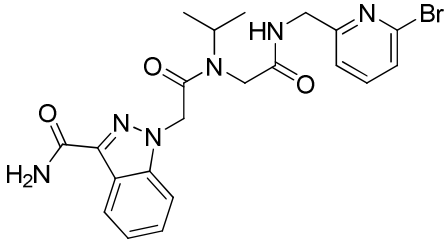
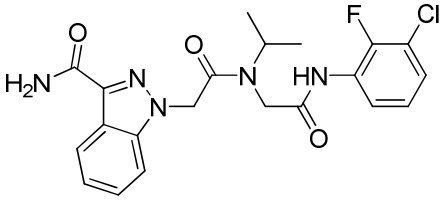
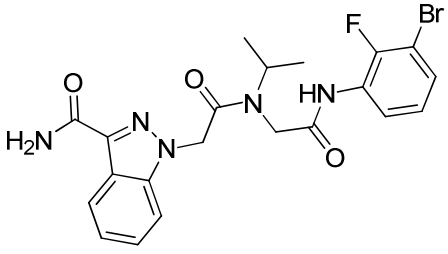
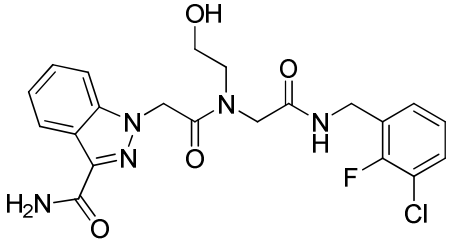
29. The compound of any one of claims 16-28, wherein R^7 represents NH_2.

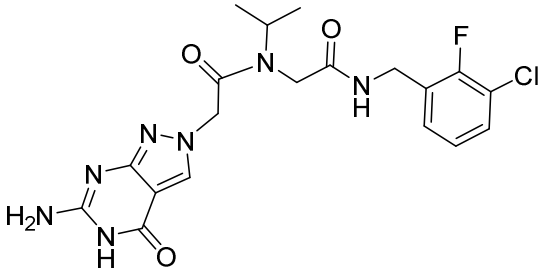
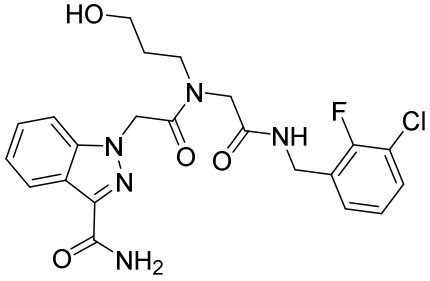
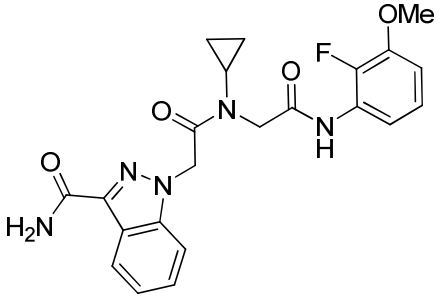
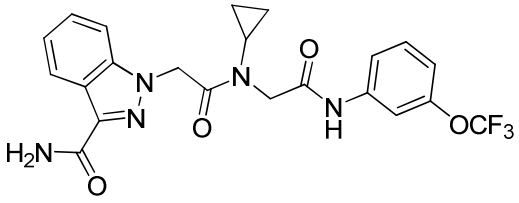
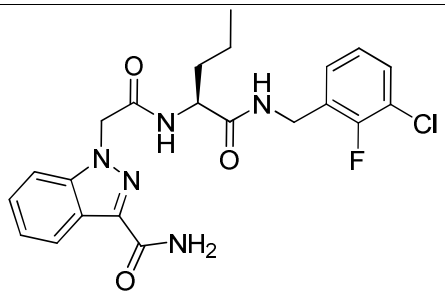
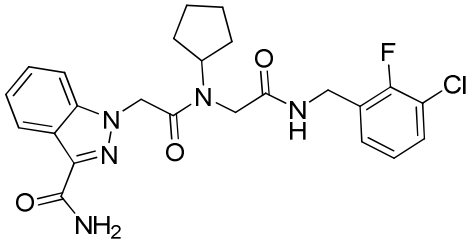
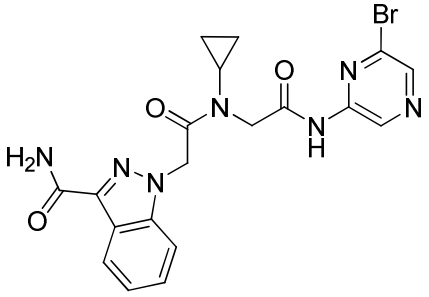
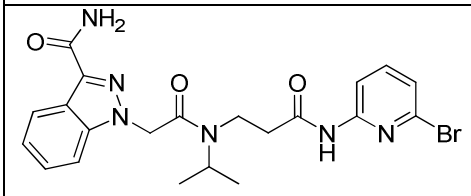
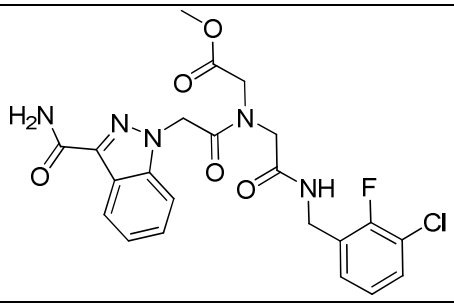
30. The compound of claim 1, or a pharmaceutically acceptable salt thereof, selected from the following table:

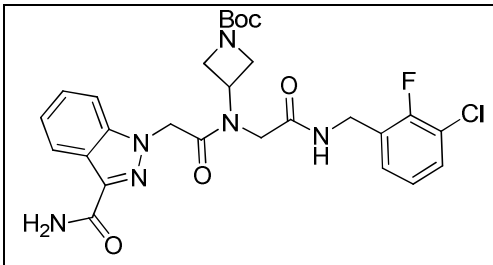
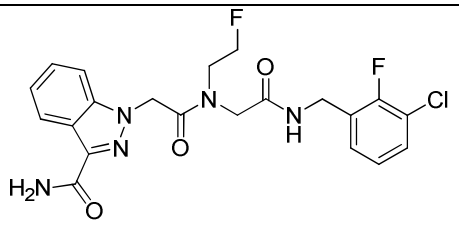
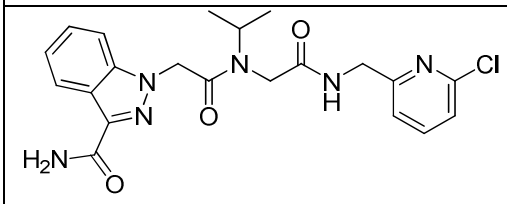
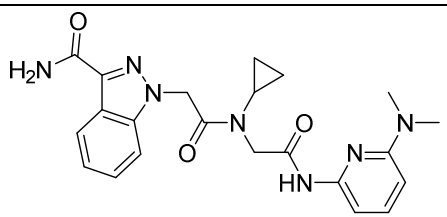
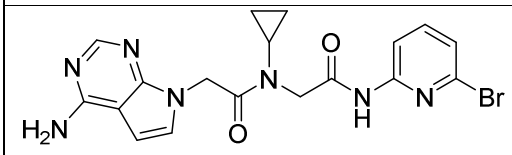
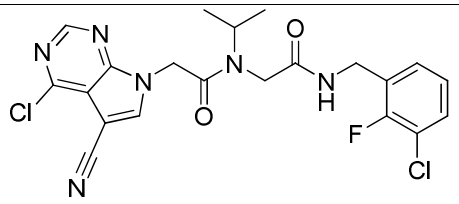
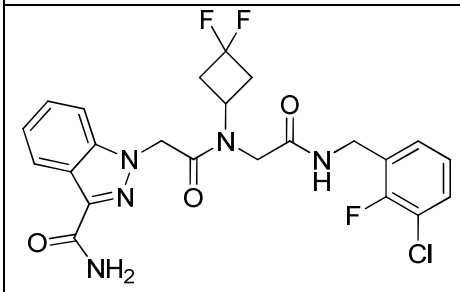
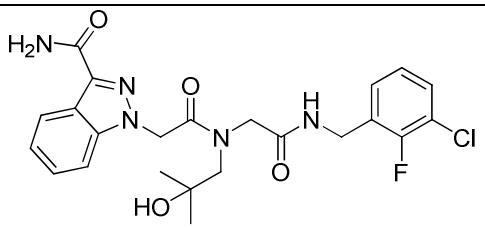
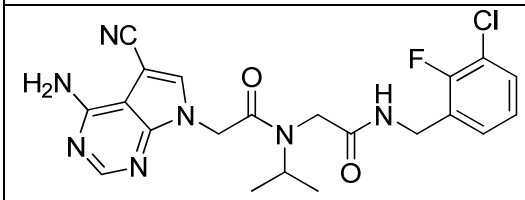
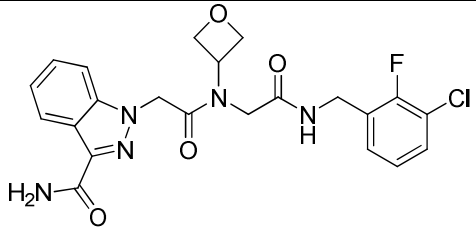
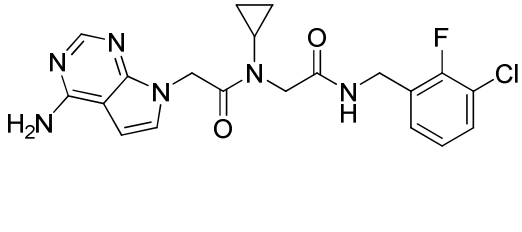
	
	
	

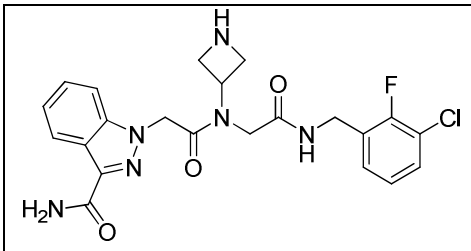
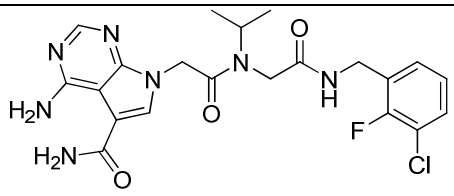
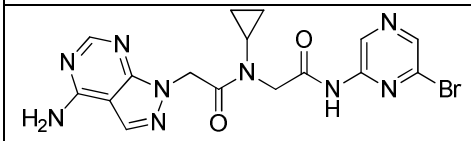
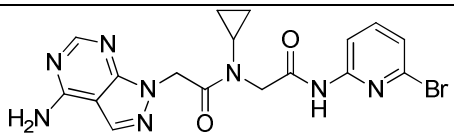
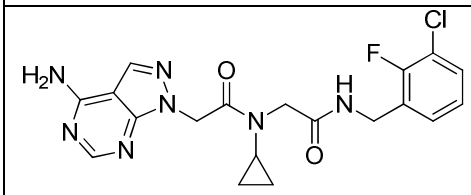
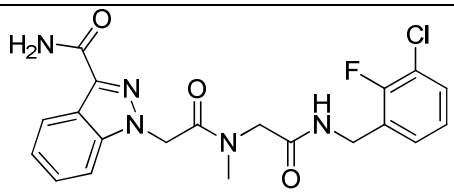
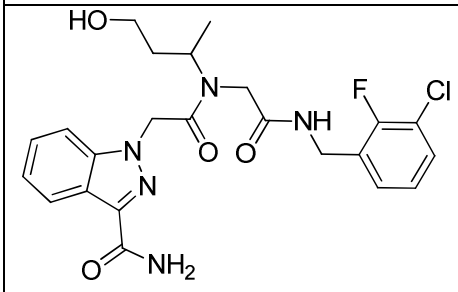
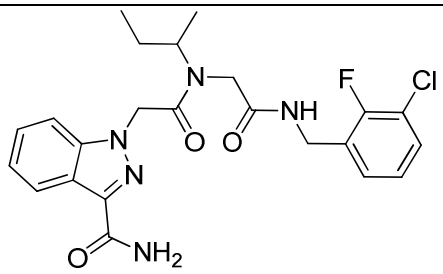
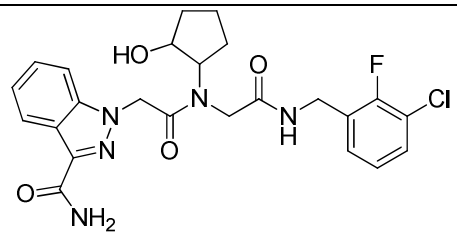
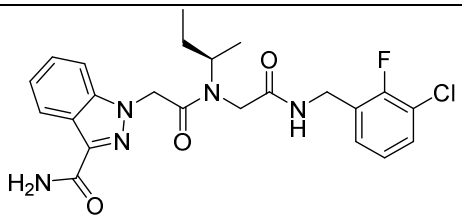
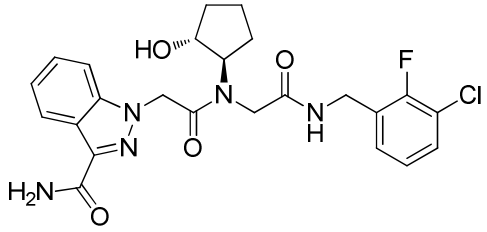
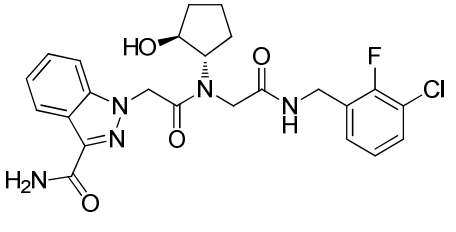
	
	
	
	
	
	

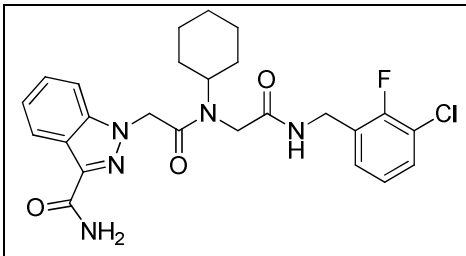
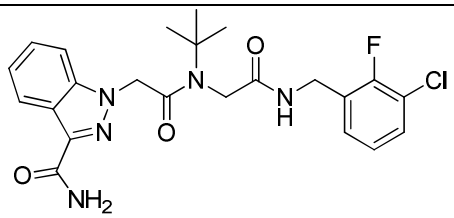
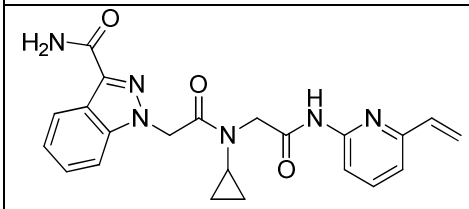
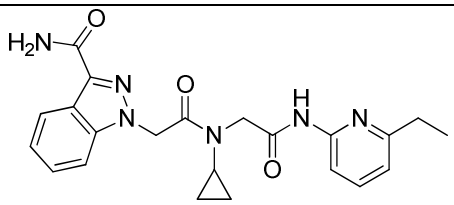
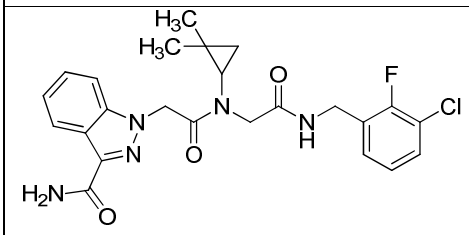
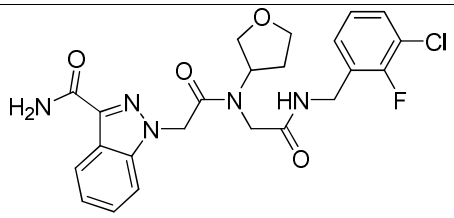
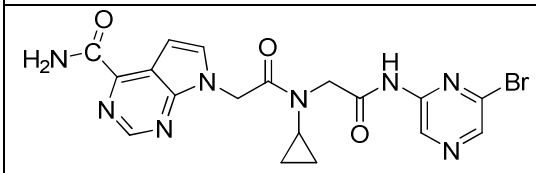
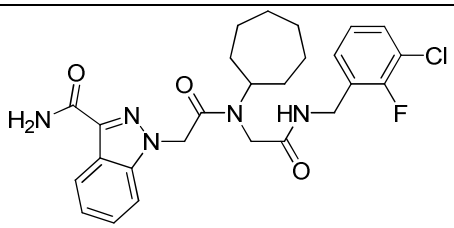
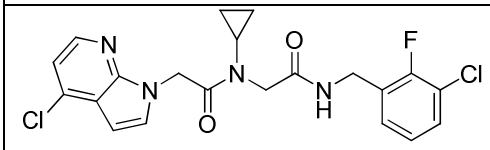
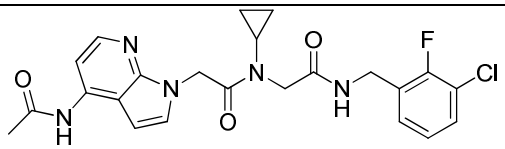
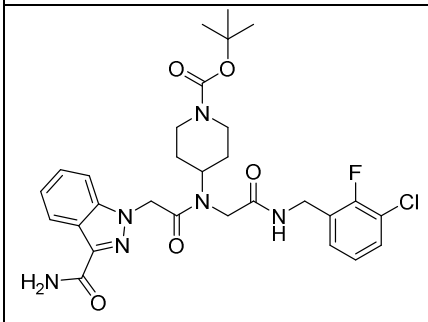
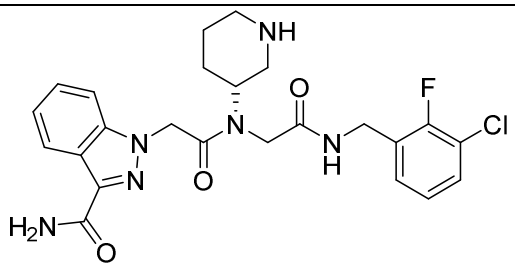
	
	
	
	
	

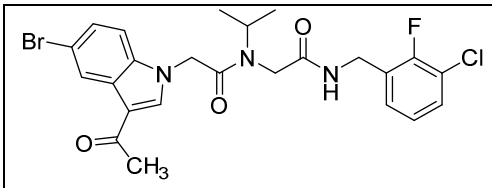
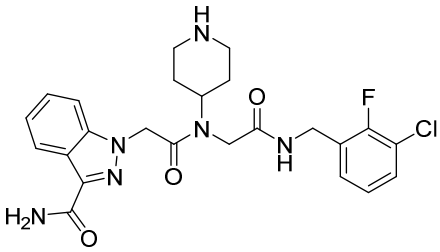
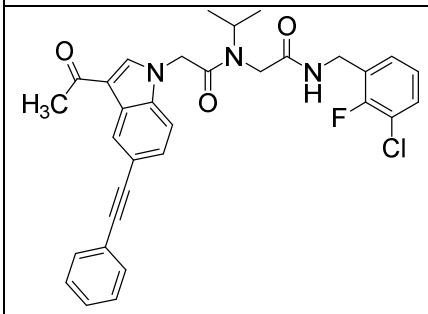
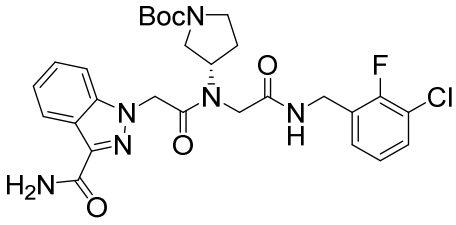
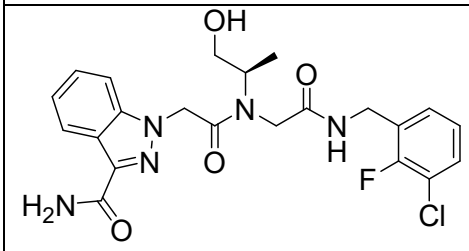
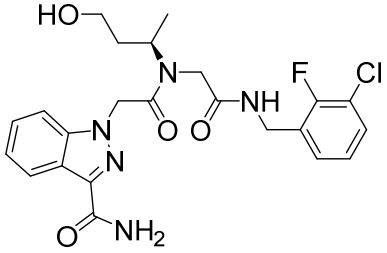
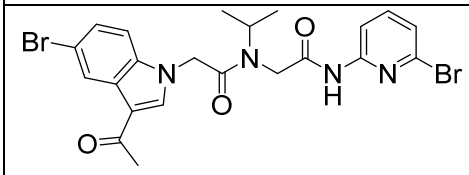
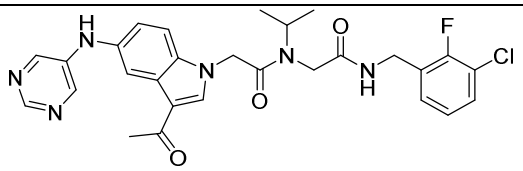
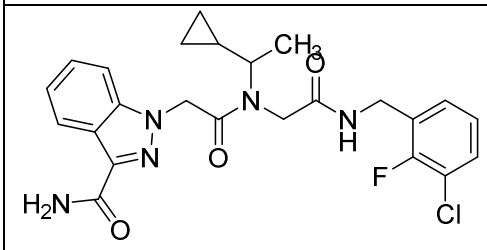
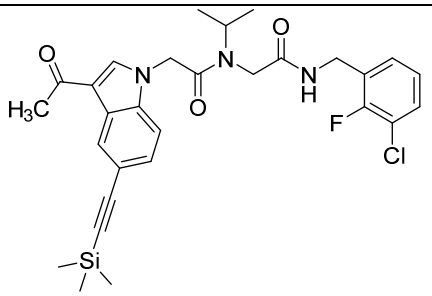
	
	
	
	
	
	

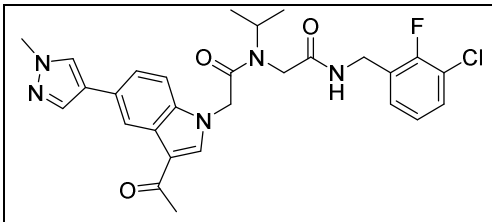
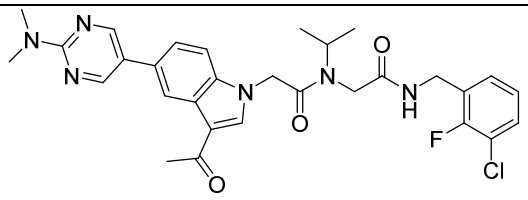
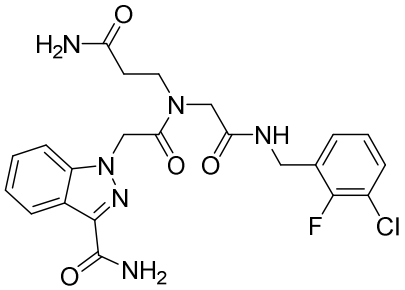
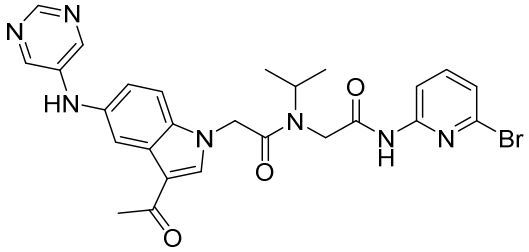
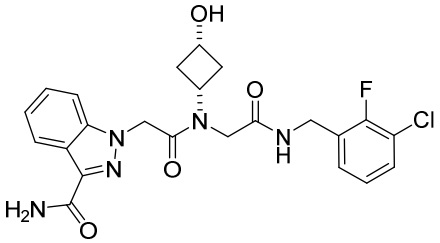
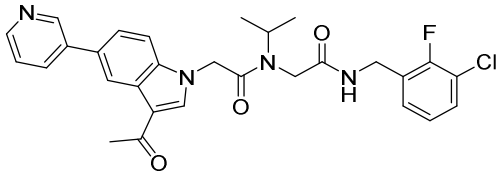
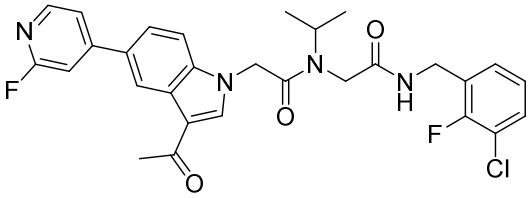
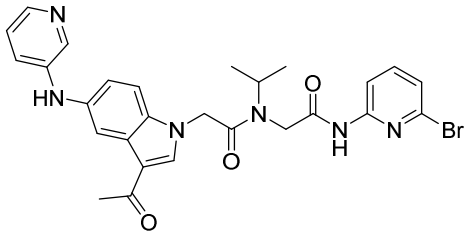
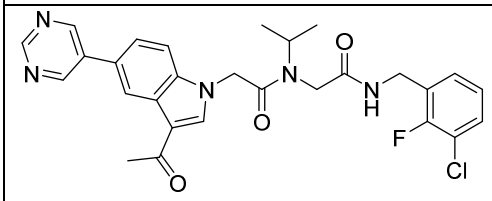
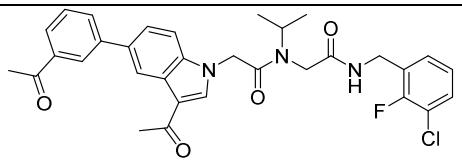
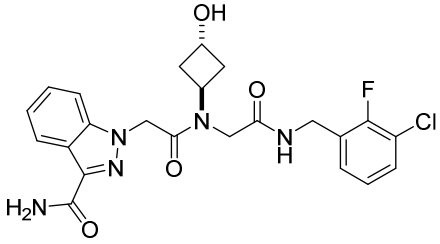
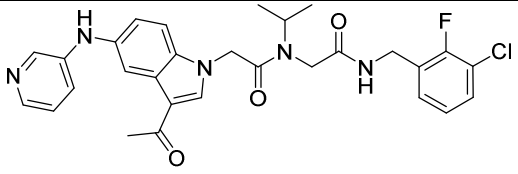
	
	
	
	
	

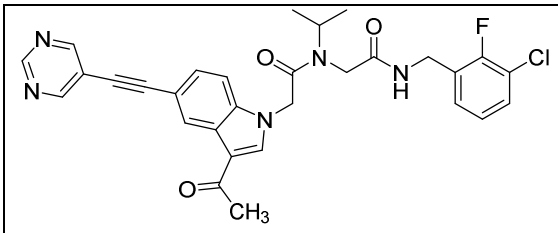
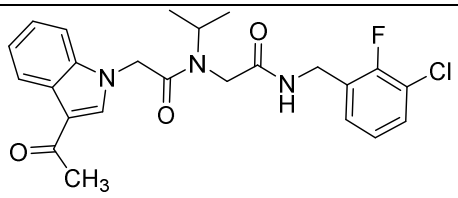
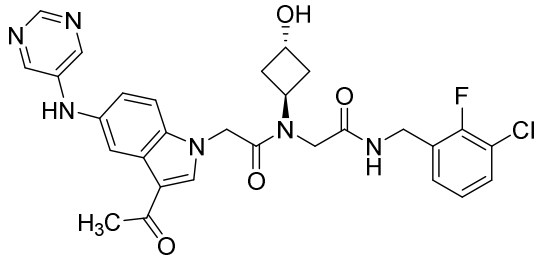
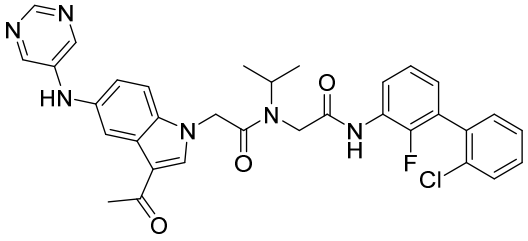
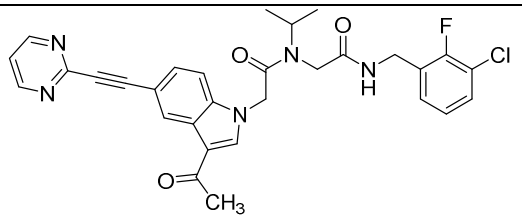
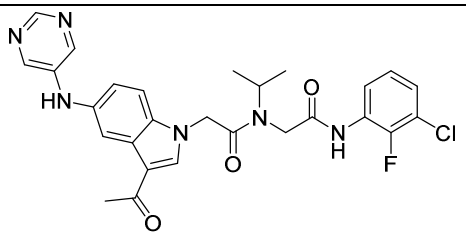
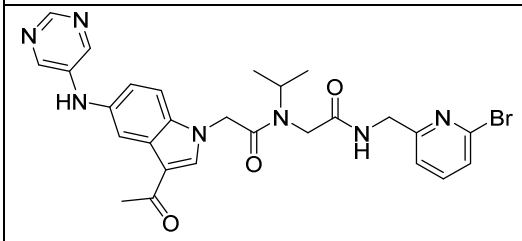
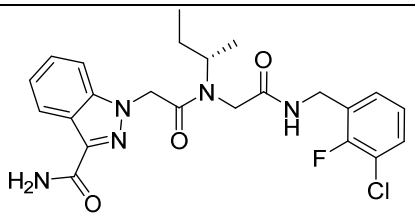
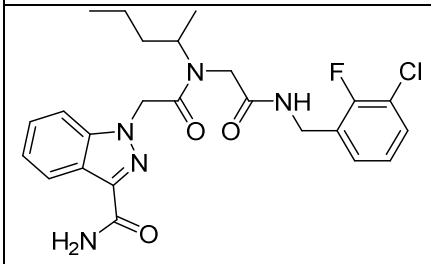
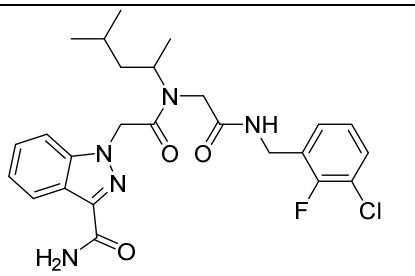
	
	
	
	
	
	

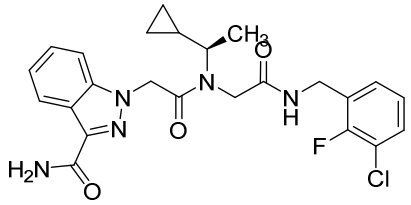
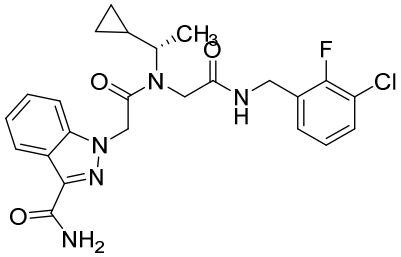
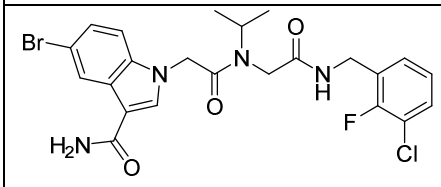
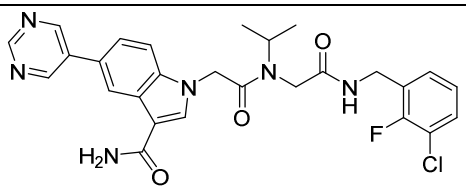
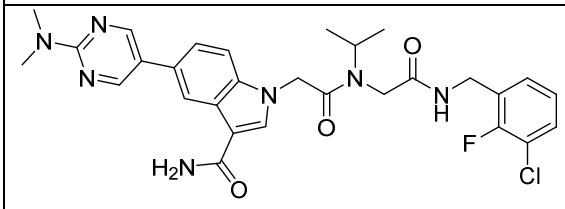
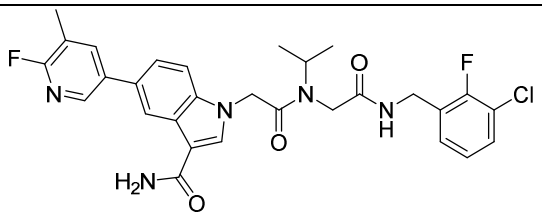
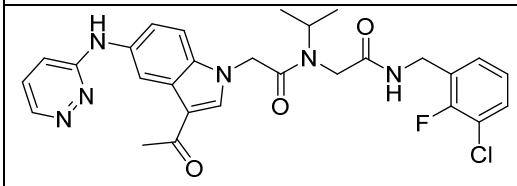
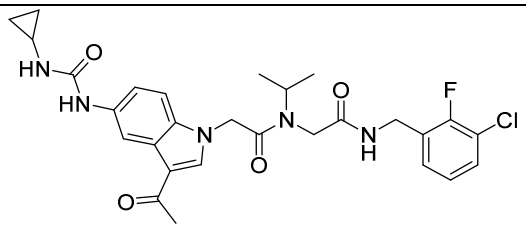
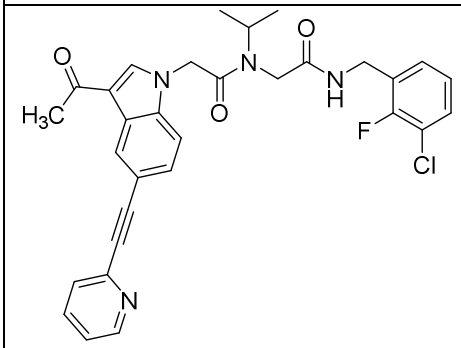
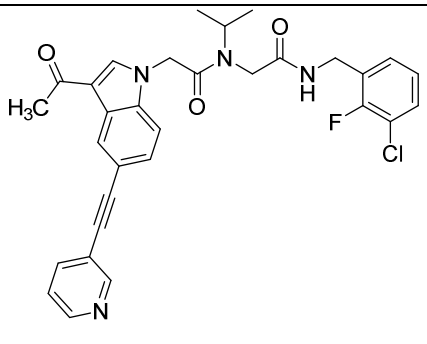
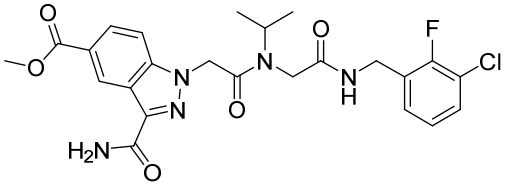
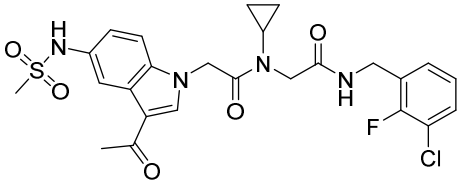
	
	
	
	
	
	

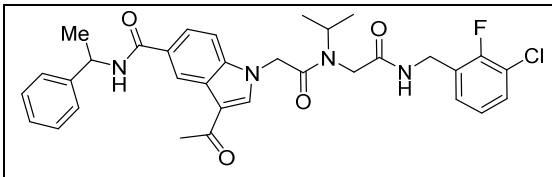
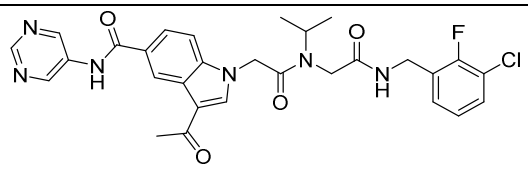
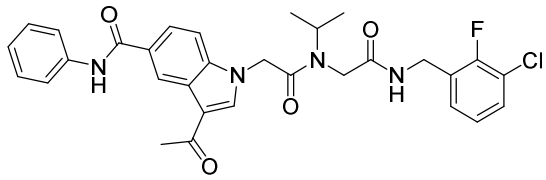
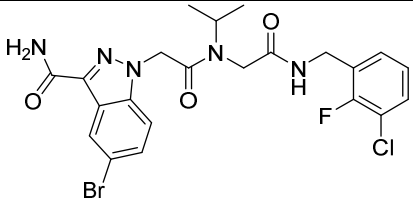
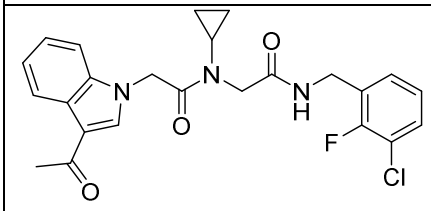
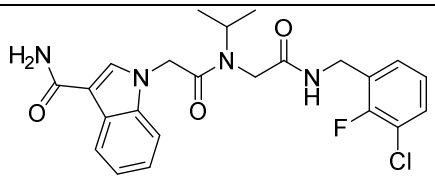
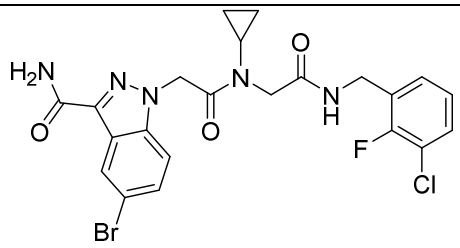
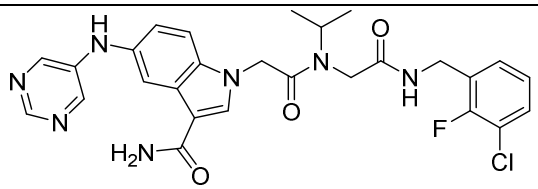
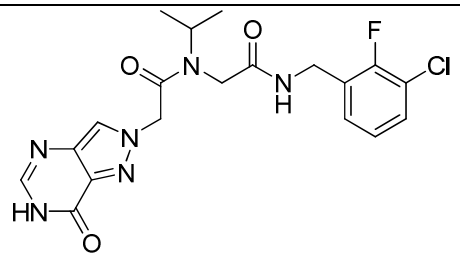
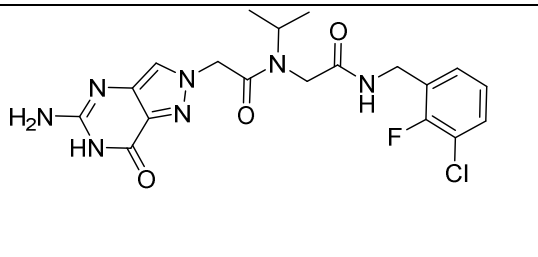
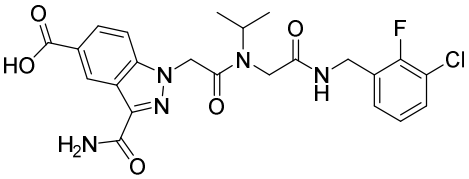
	
	
	
	
	
	

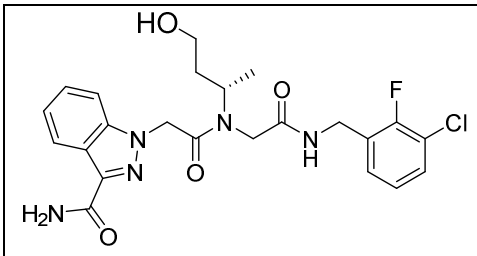
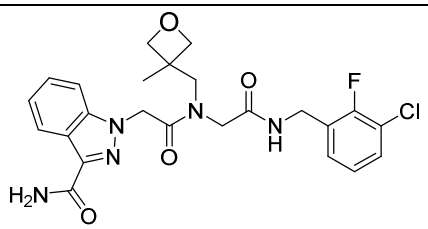
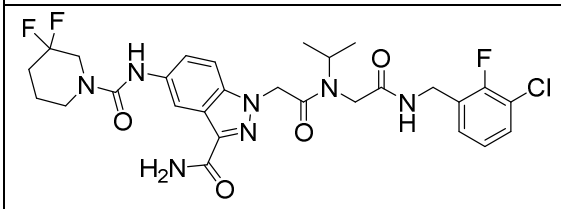
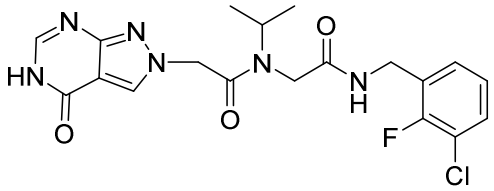
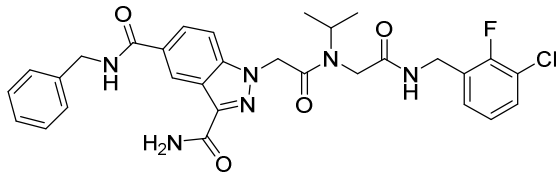
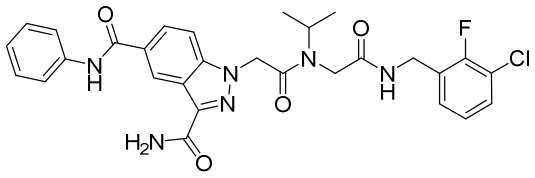
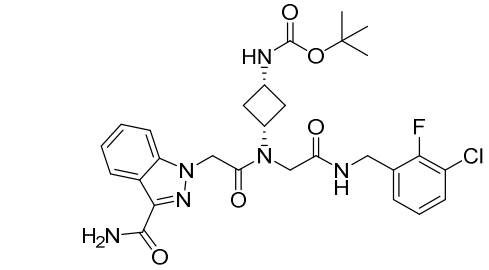
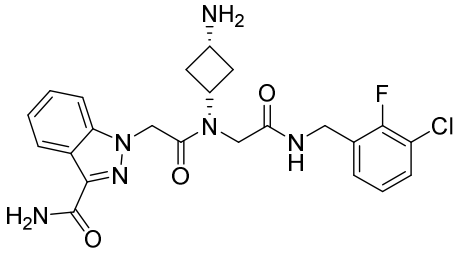
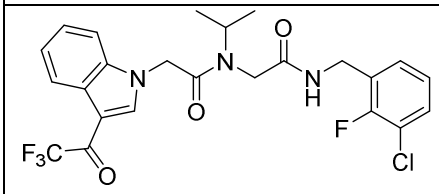
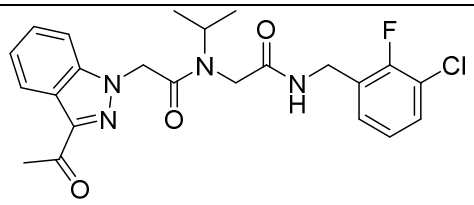
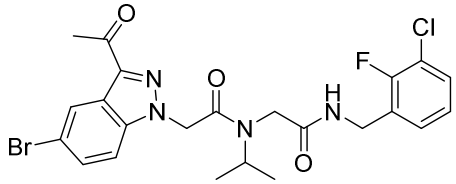
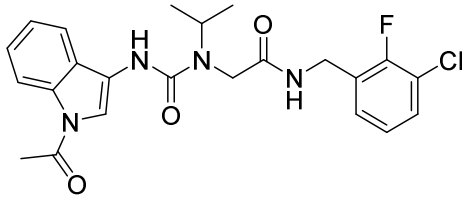
	
	
	
	
	

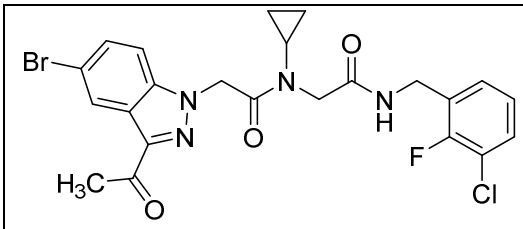
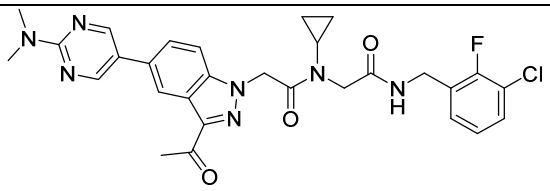
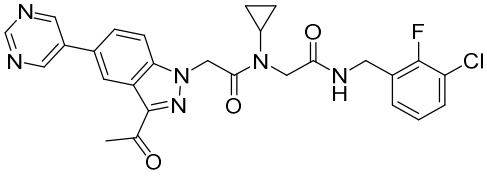
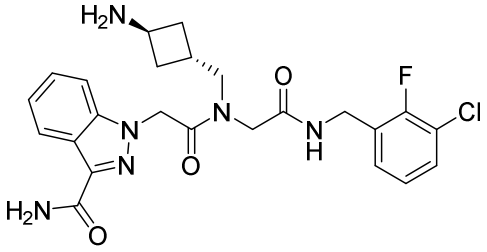
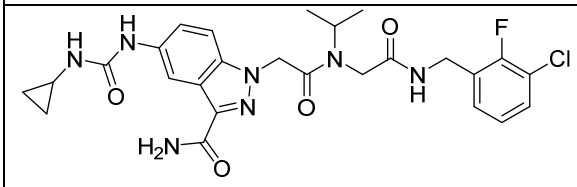
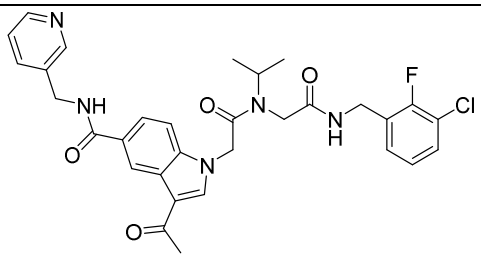
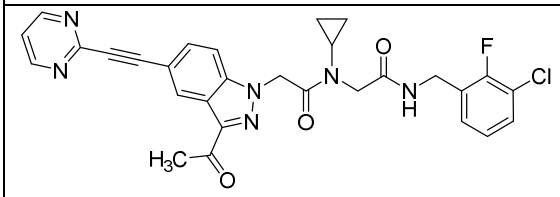
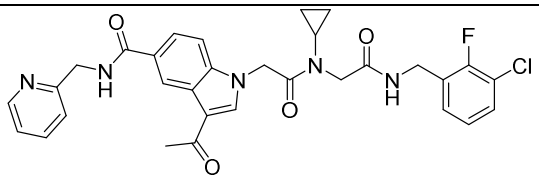
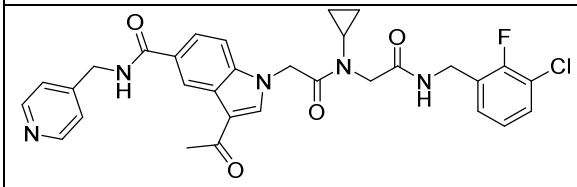
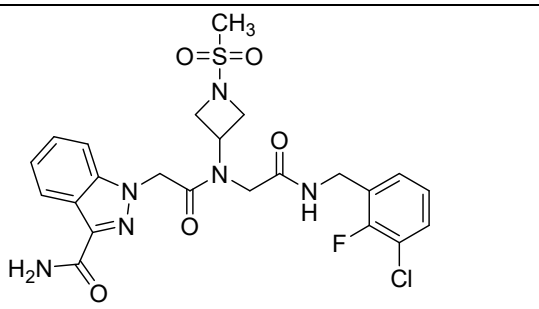
	
	
	
	
	
	

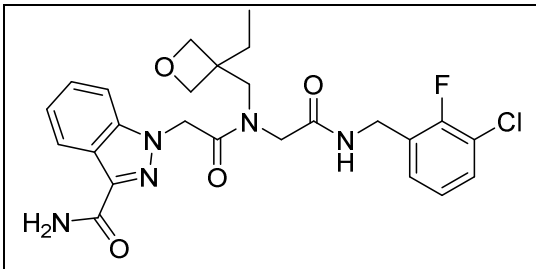
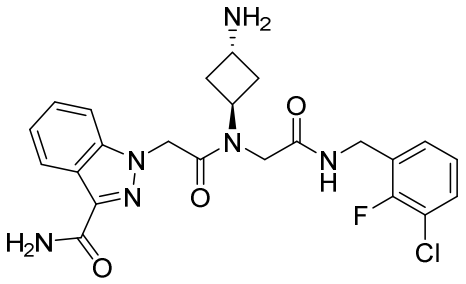
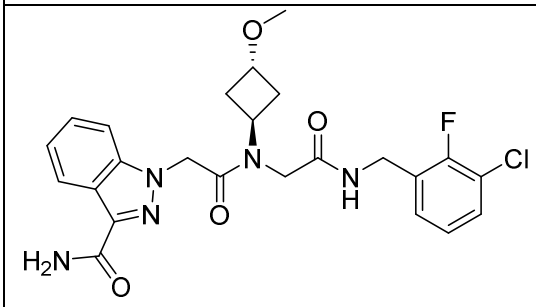
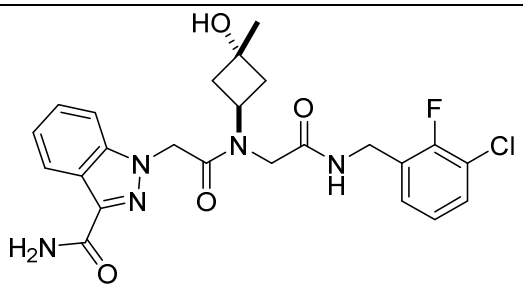
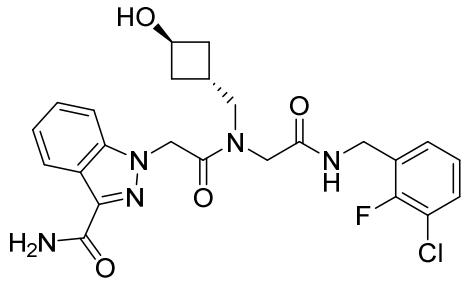
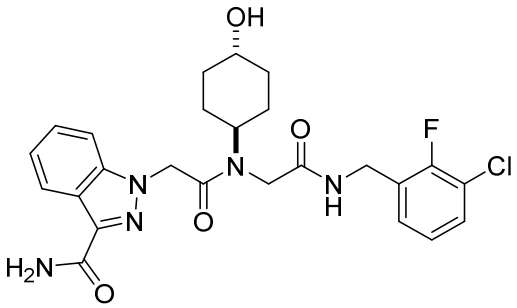
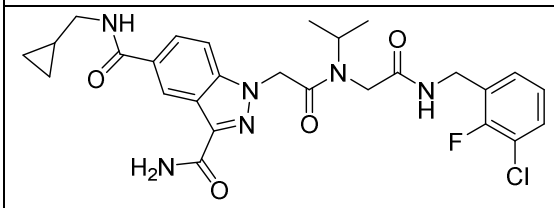
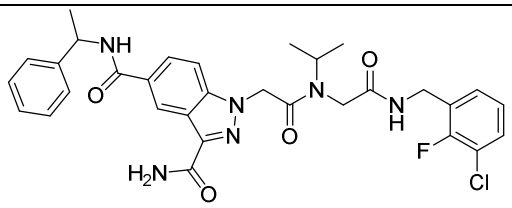
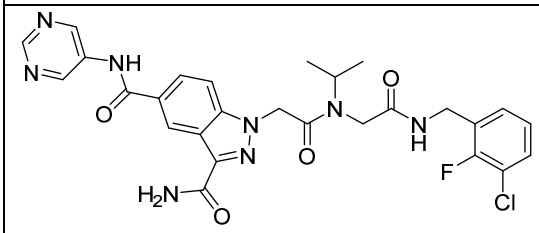
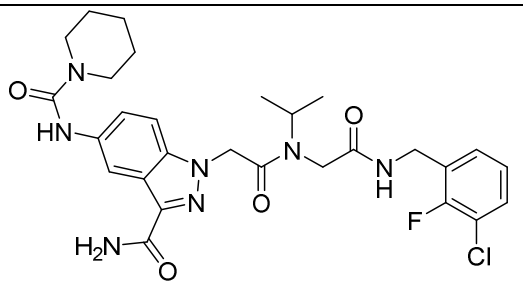
	
	
	
	
	

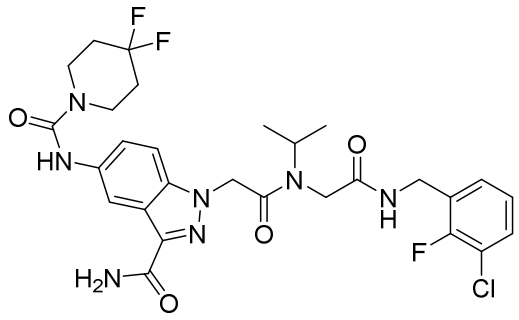
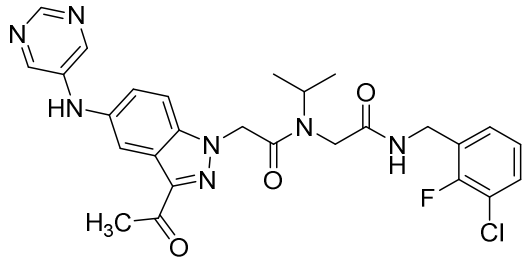
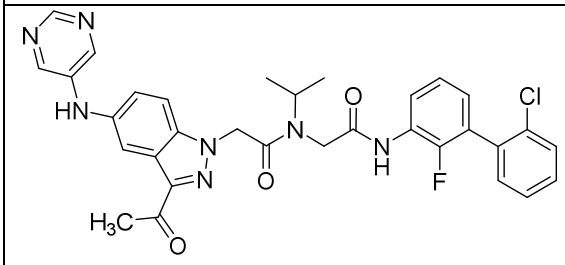
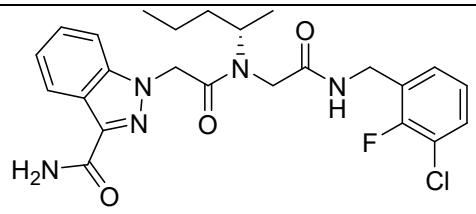
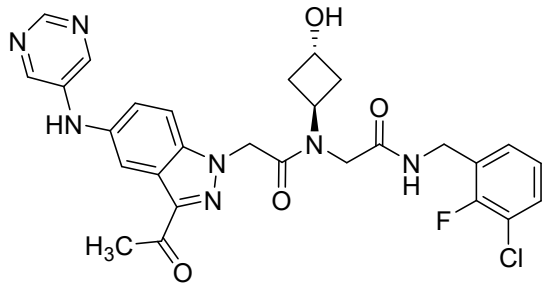
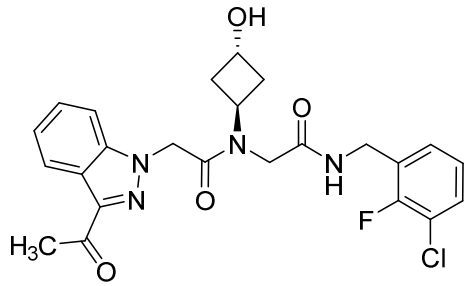
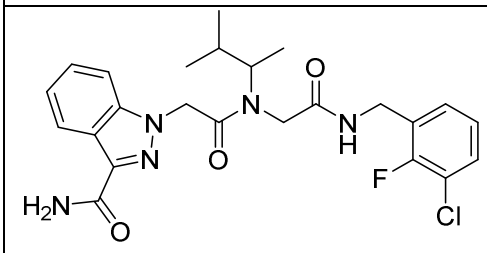
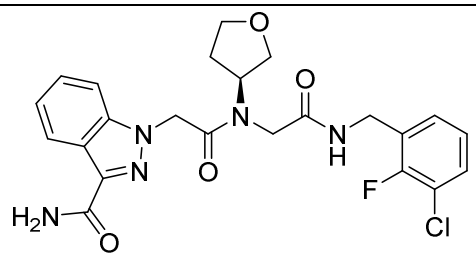
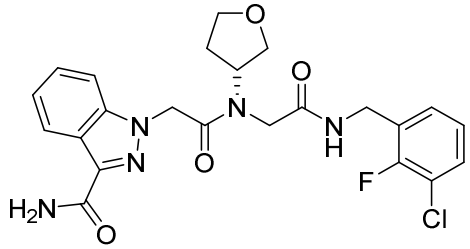
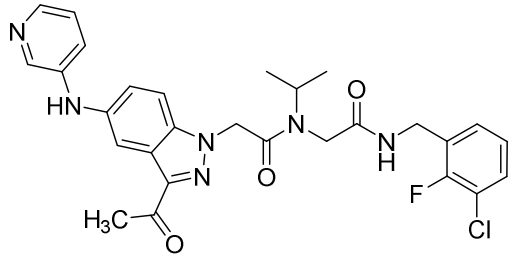
	
	
	
	
	
	

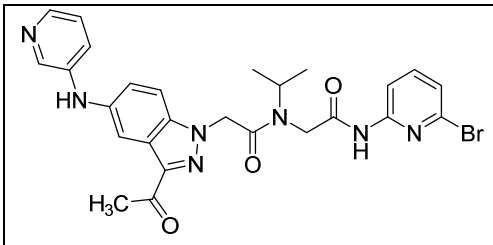
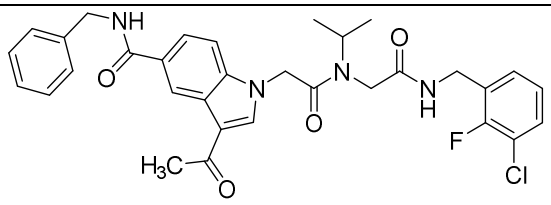
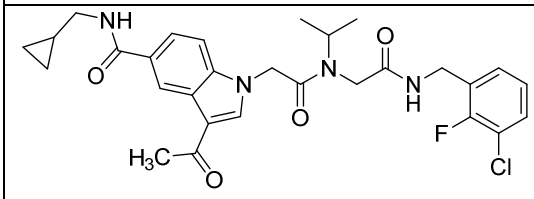
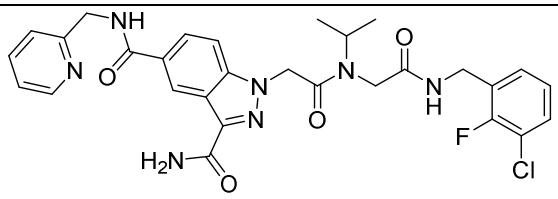
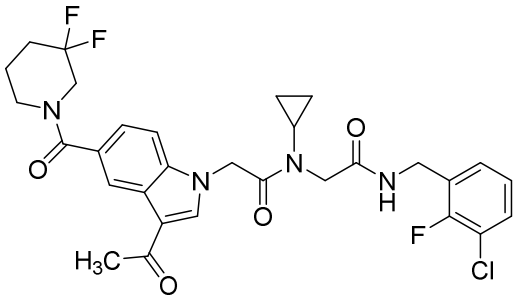
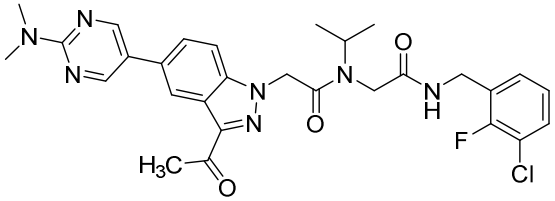
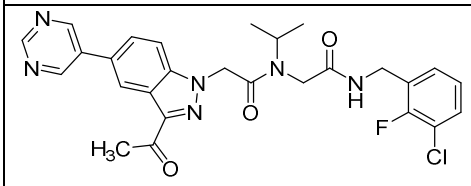
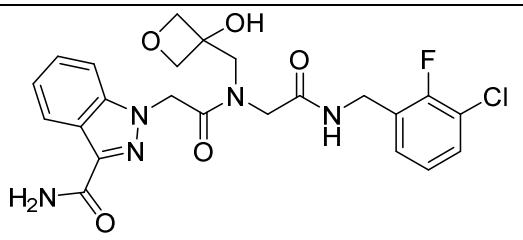
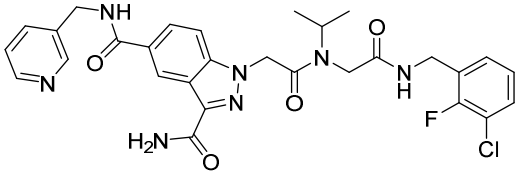
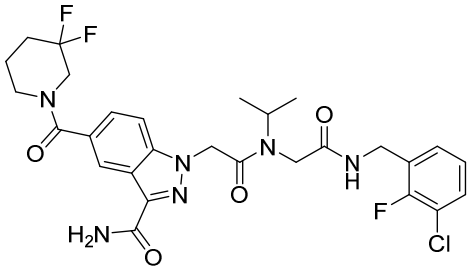
	
	
	
	
	
	

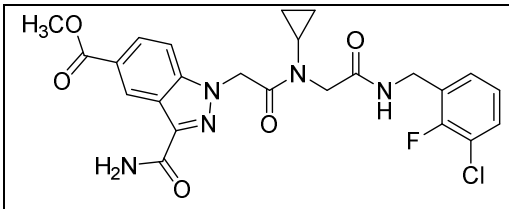
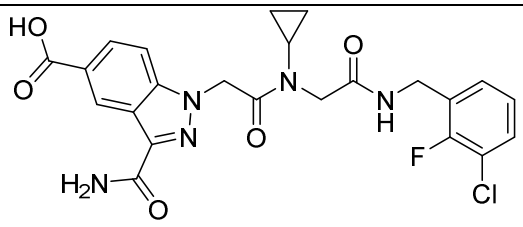
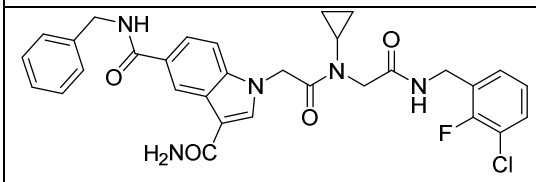
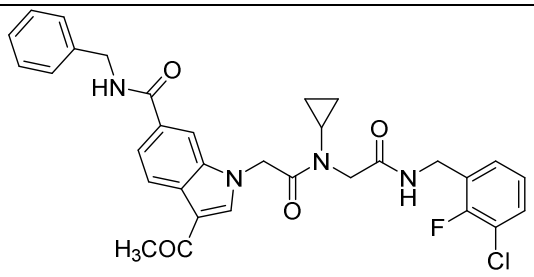
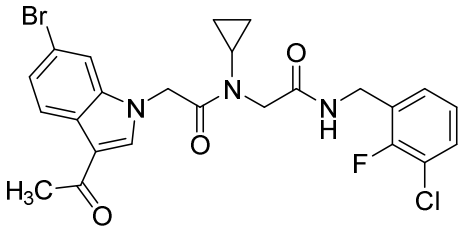
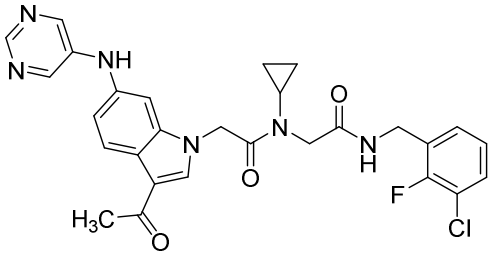
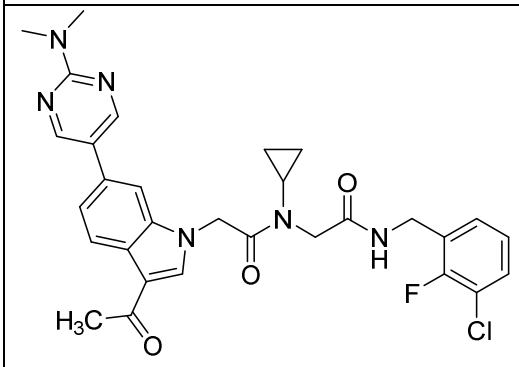
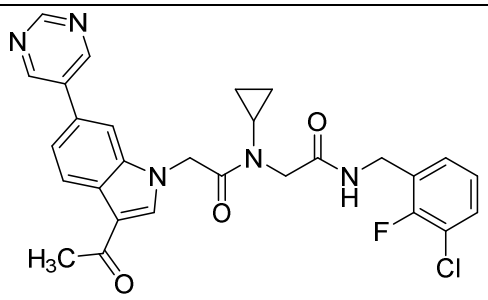
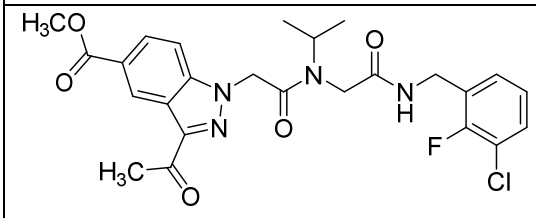
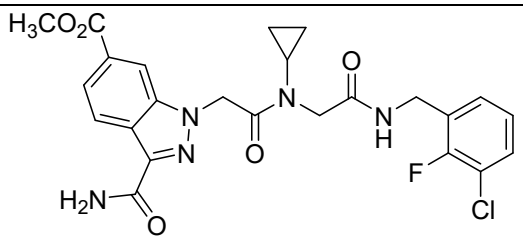
	
	
	
	
	
	

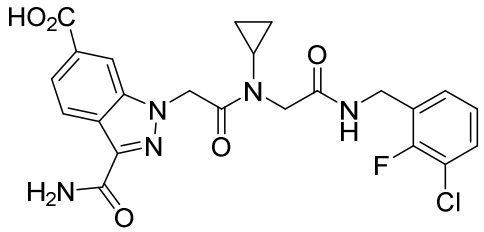
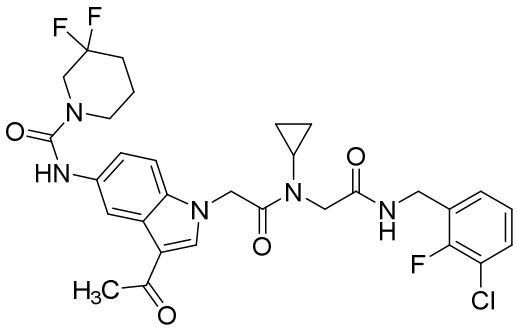
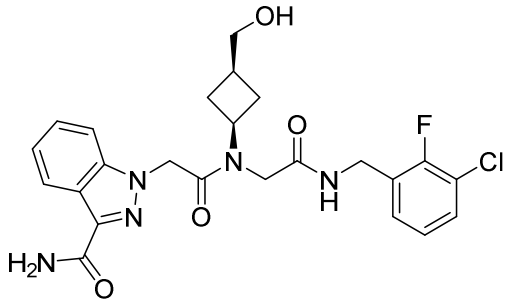
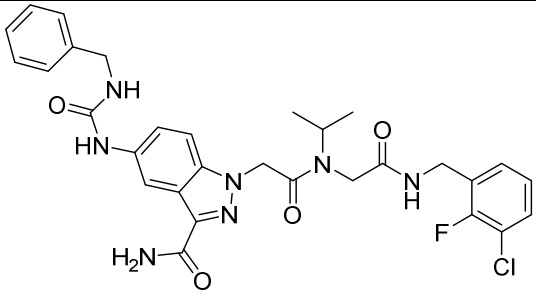
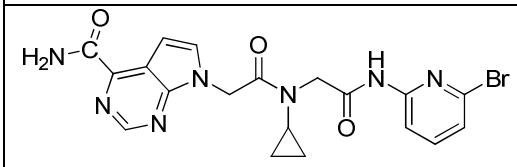
	
	
	
	
	

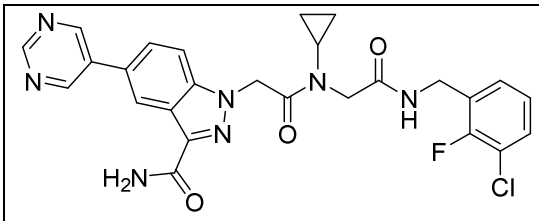
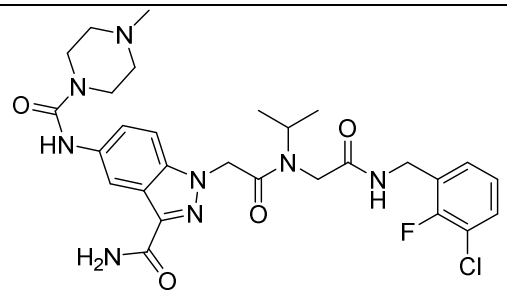
	
	
	
	
	

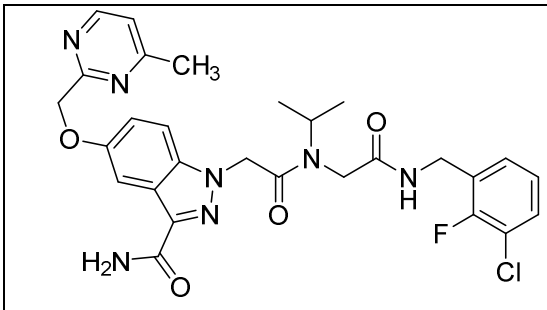
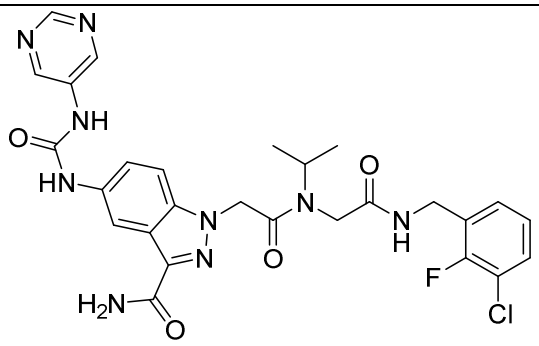
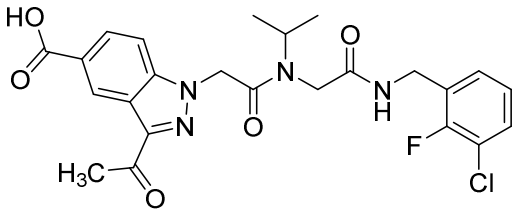
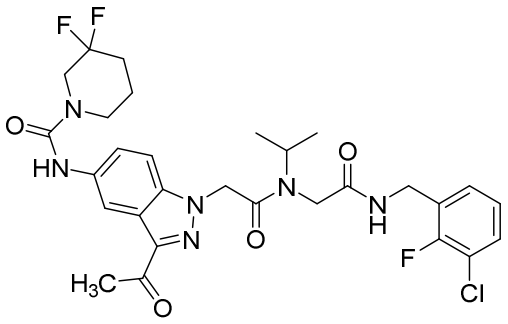
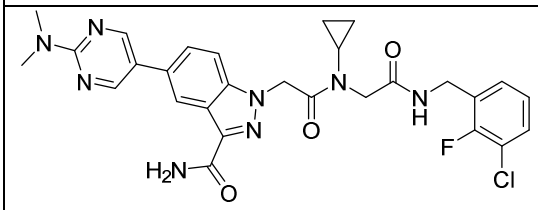
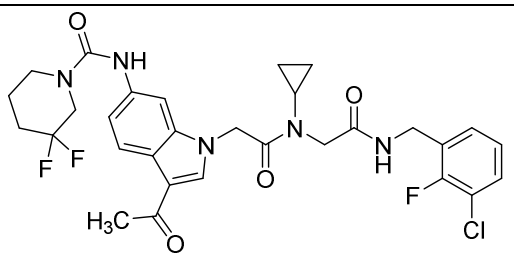
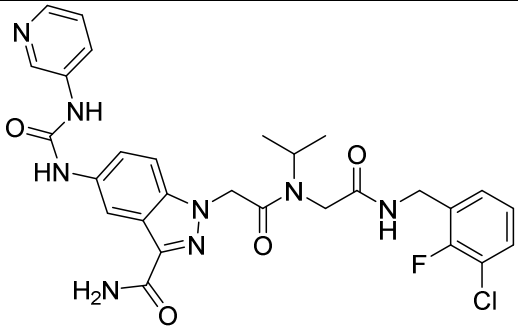
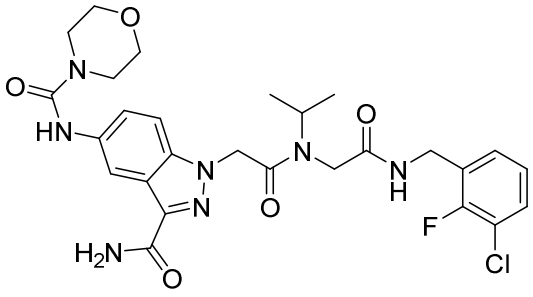
	
	
	
	
	

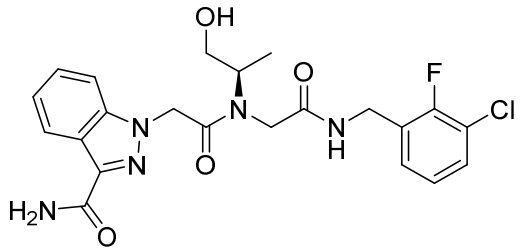
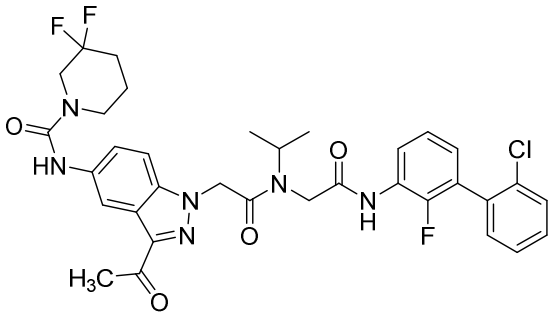
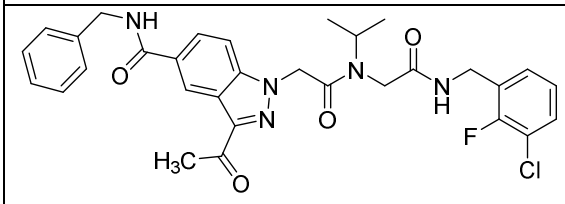
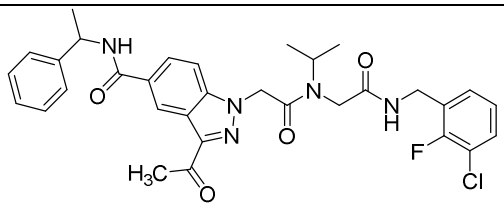
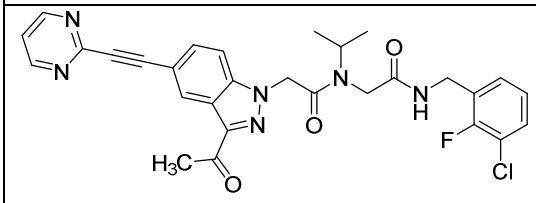
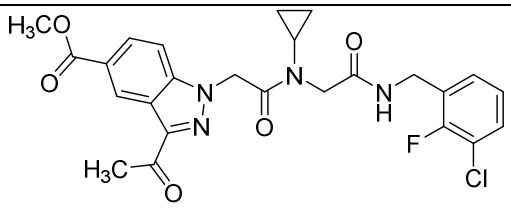
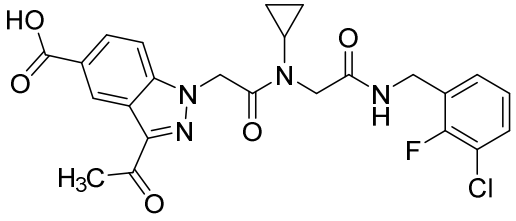
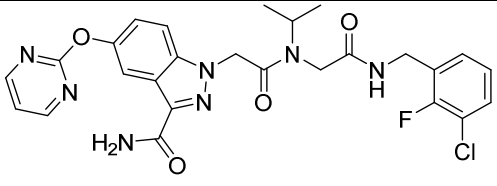
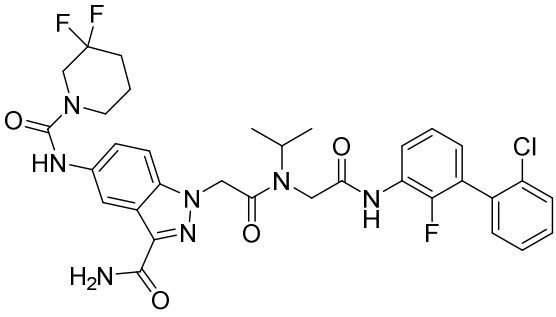
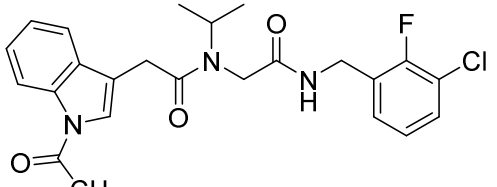
	
	
	
	
	

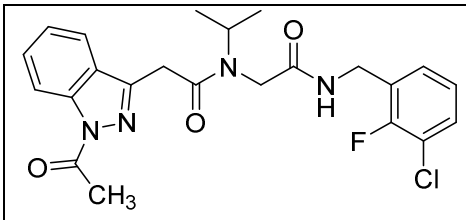
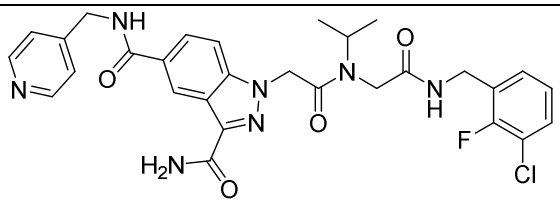
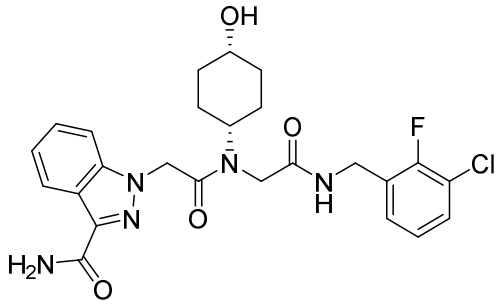
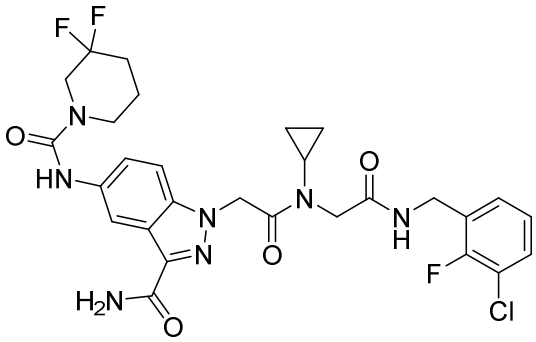
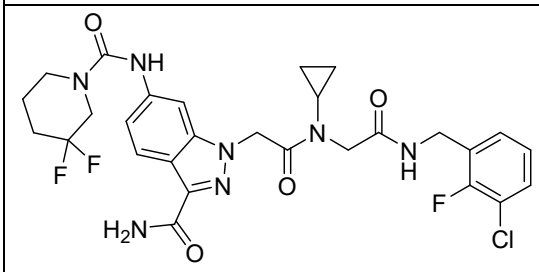
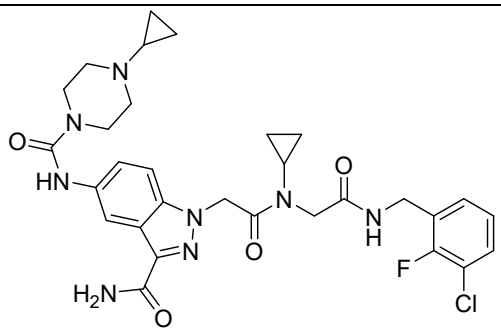
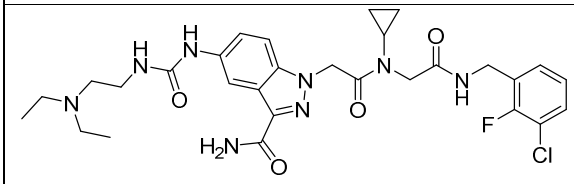
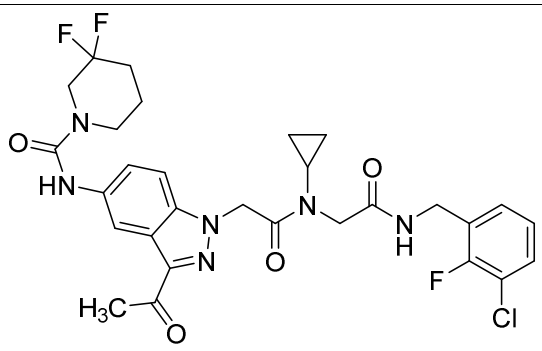
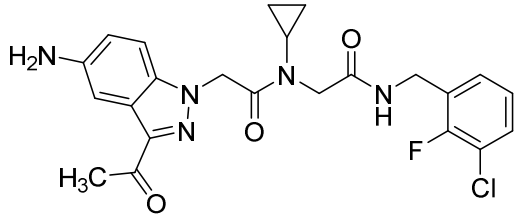
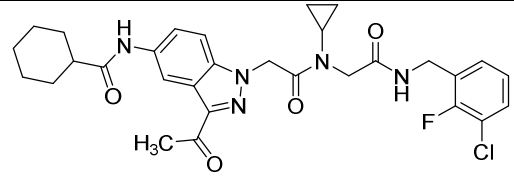
	
	
	

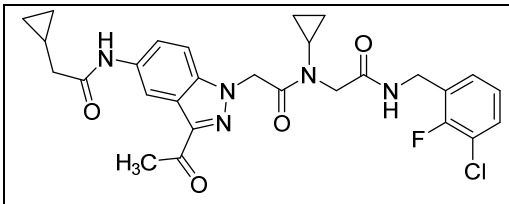
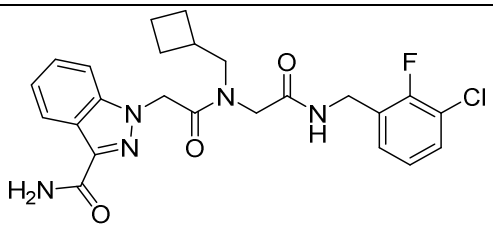
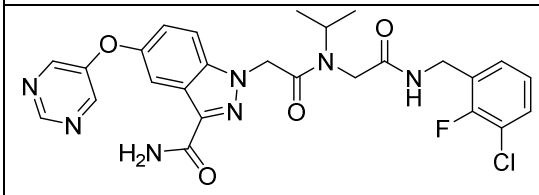
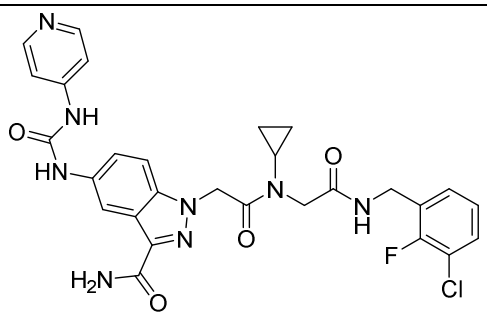
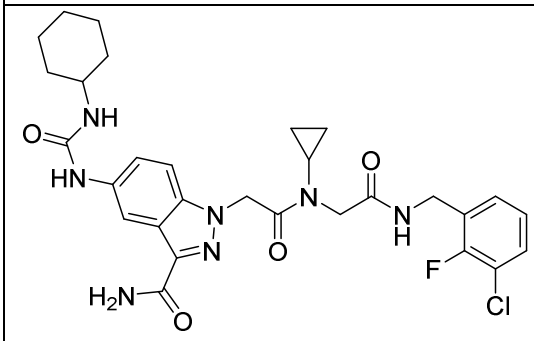
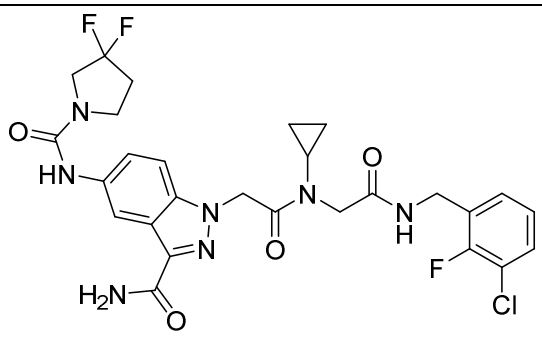
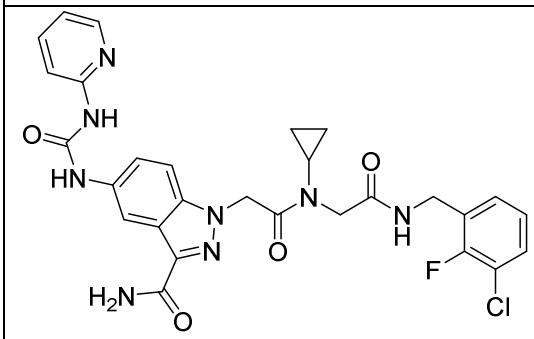
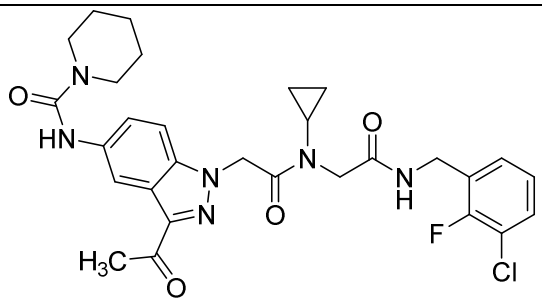
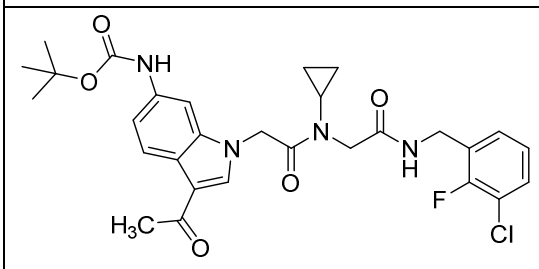
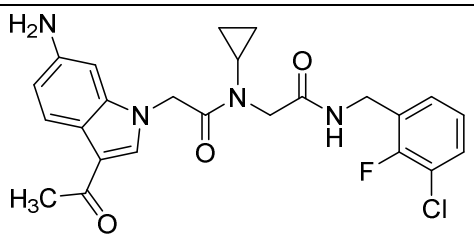
31. The compound of claim 1, or a pharmaceutically acceptable salt thereof, selected from the following table:

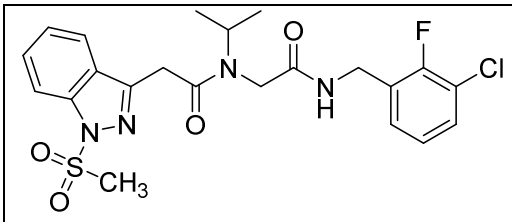
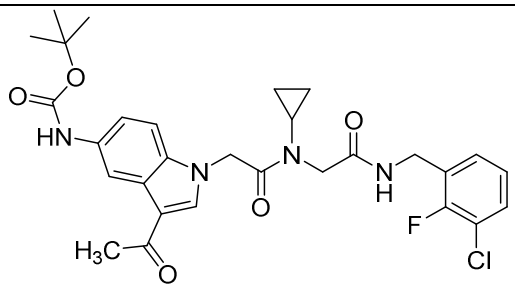
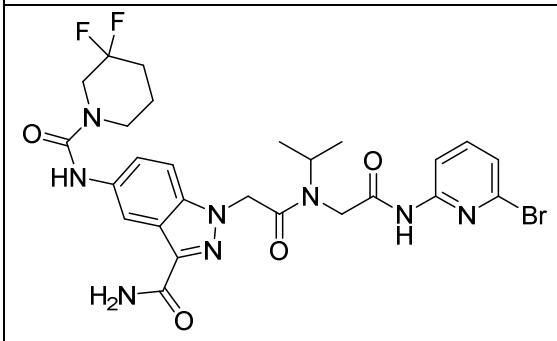
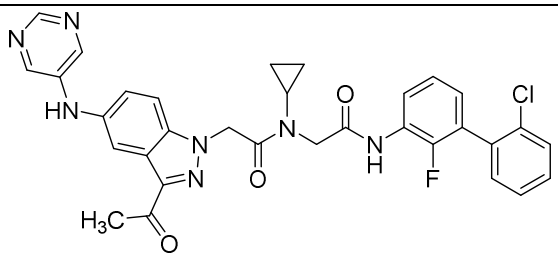
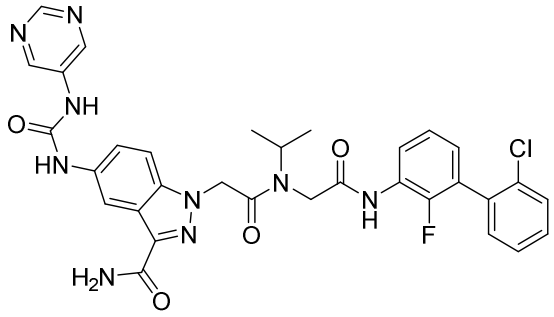
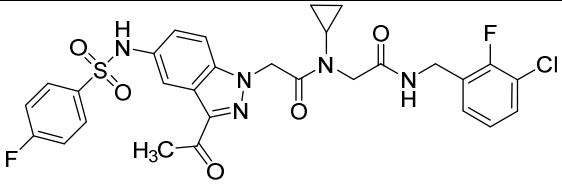
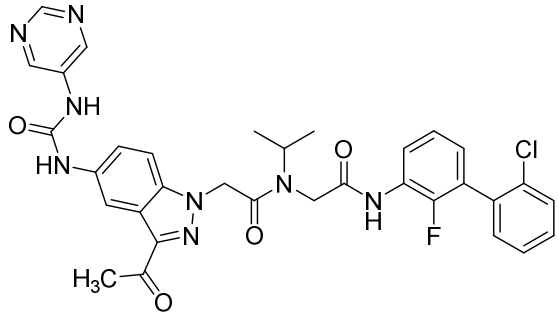
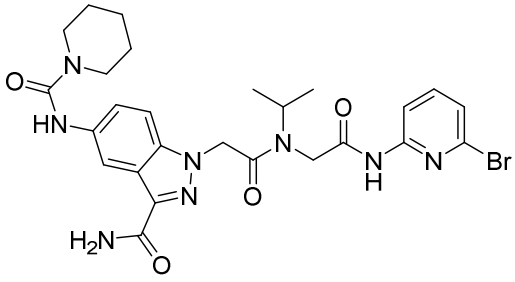
	

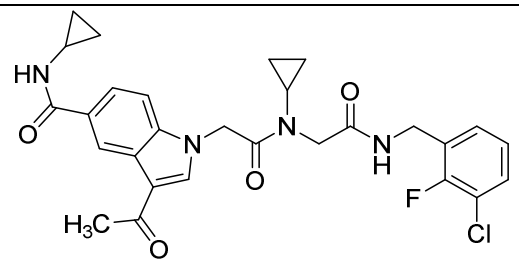
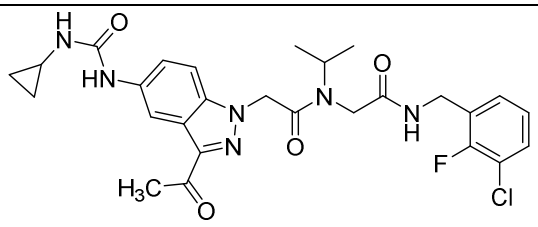
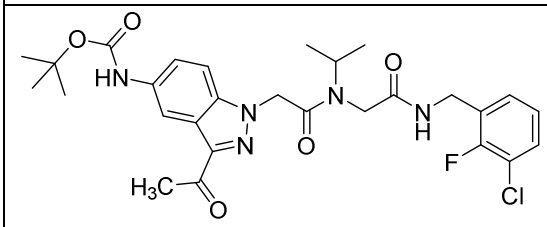
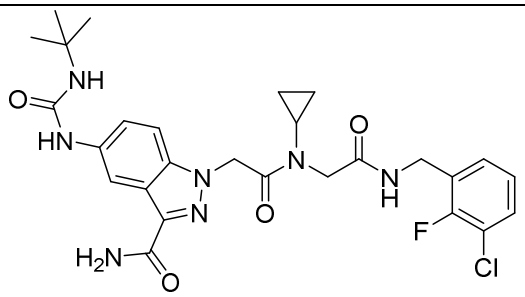
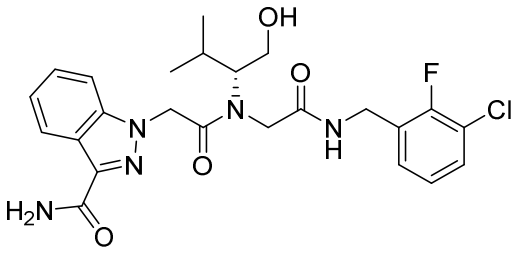
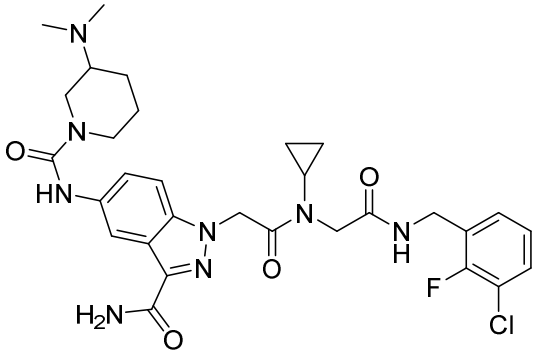
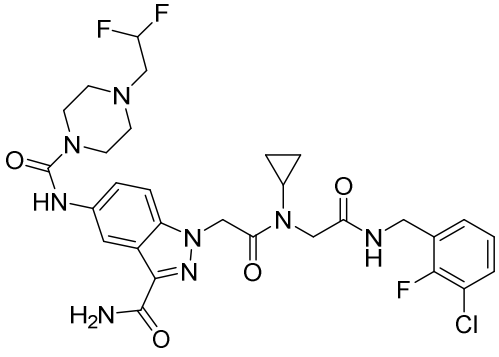
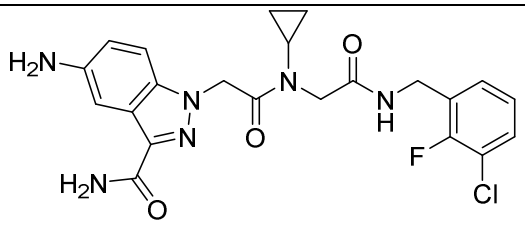
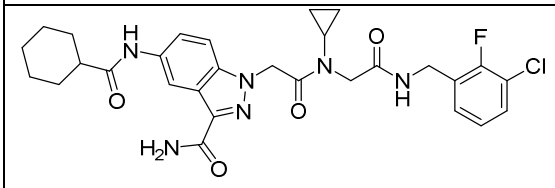
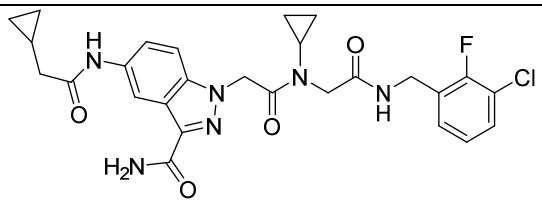
	
	
	
	

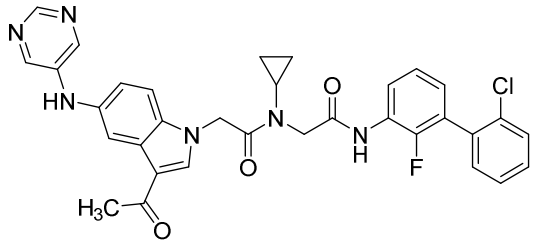
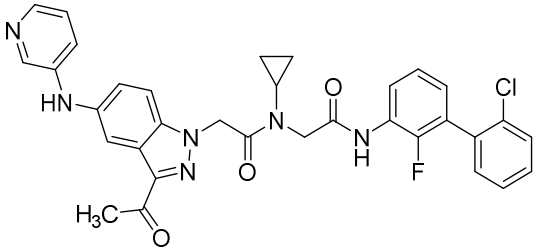
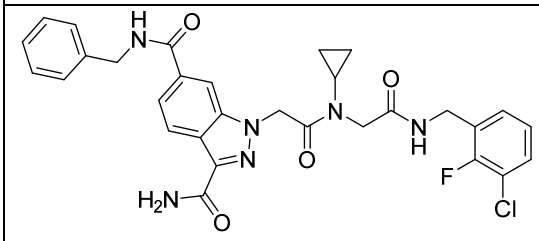
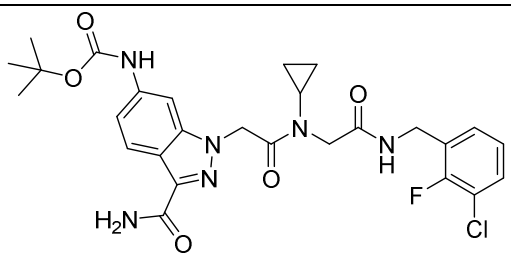
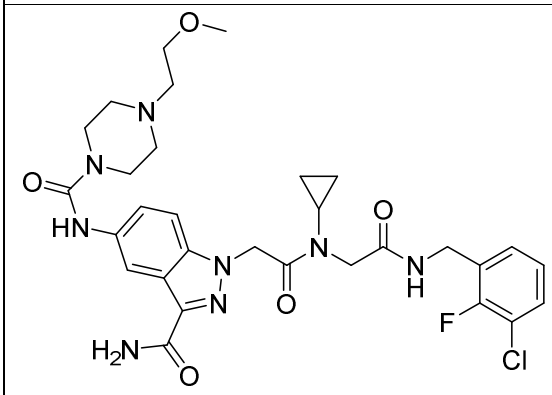
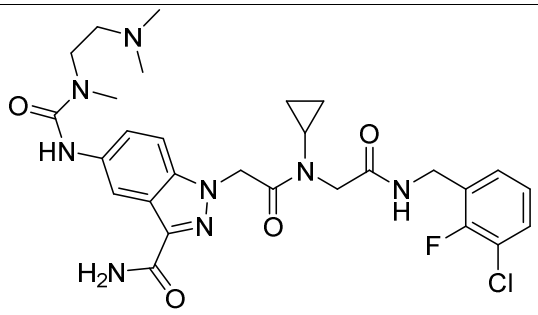
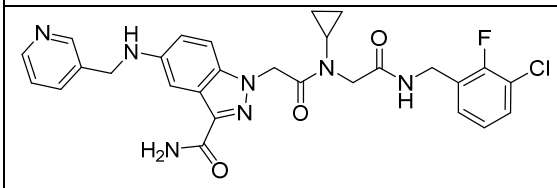
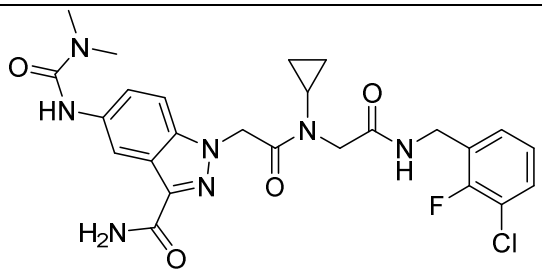
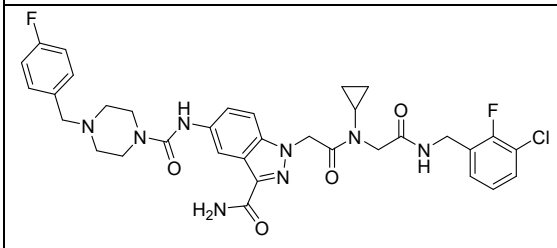
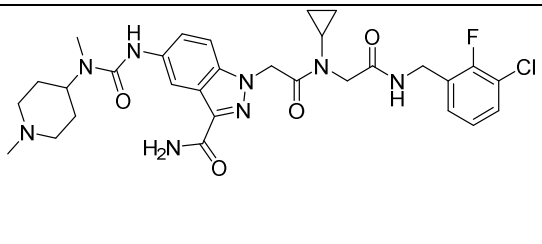
	
	
	
	
	

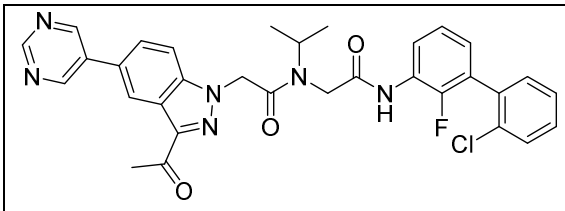
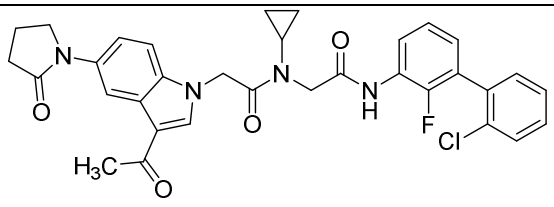
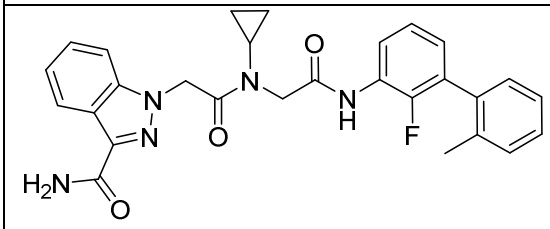
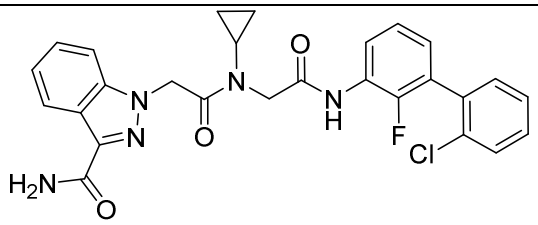
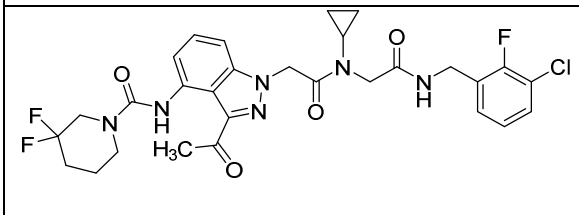
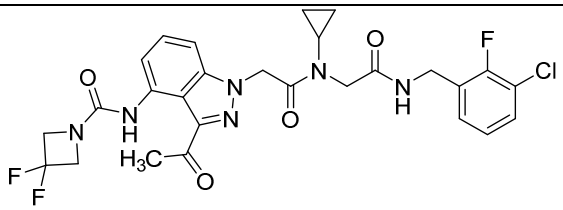
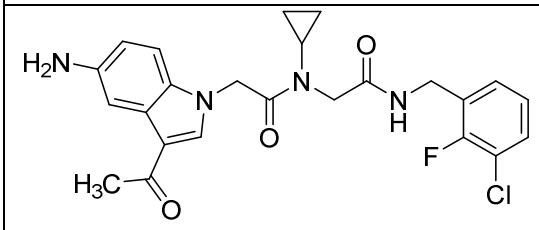
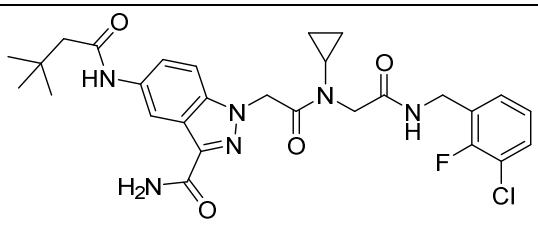
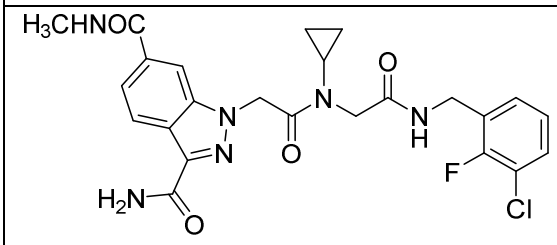
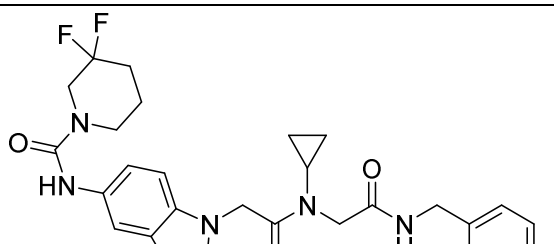
	
	
	
	
	

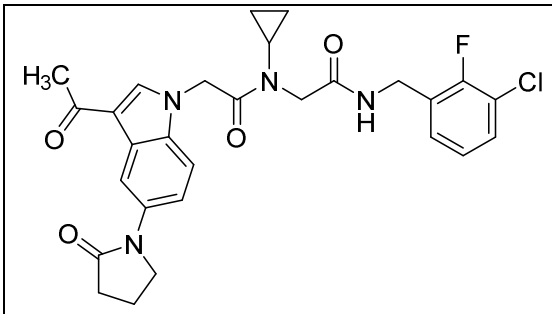
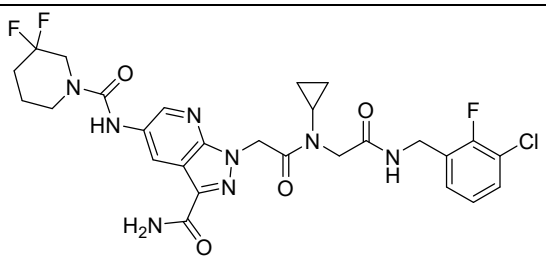
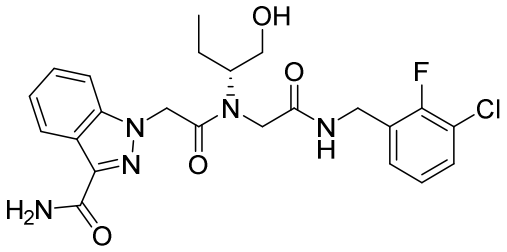
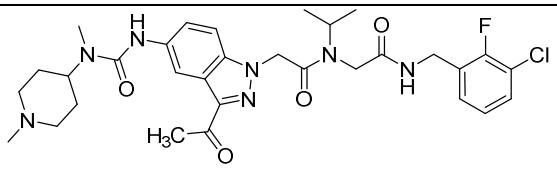
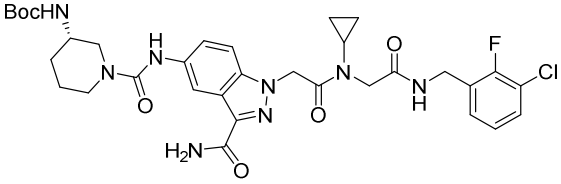
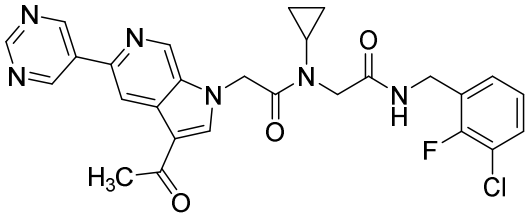
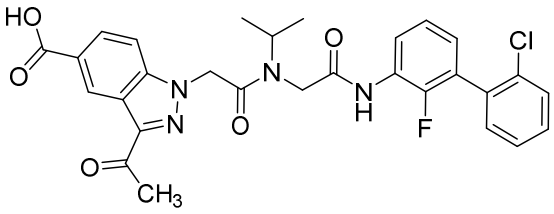
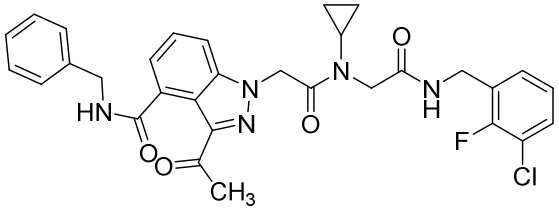
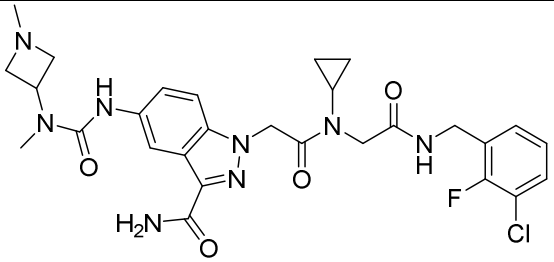
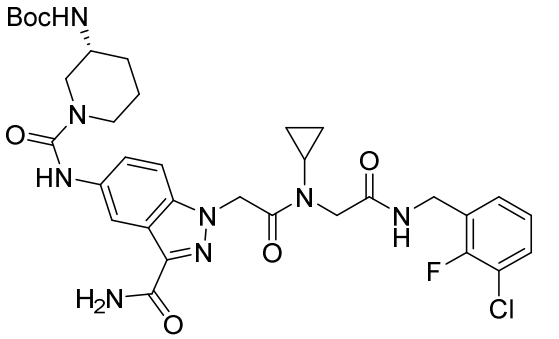
	
	
	
	
	

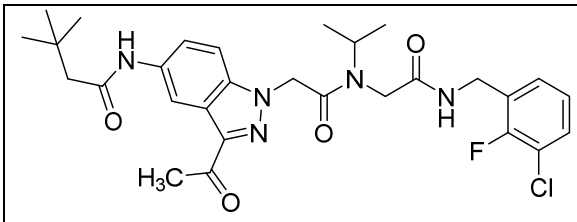
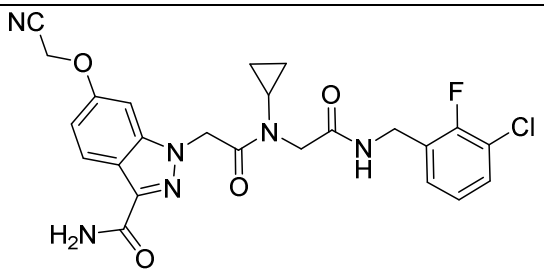
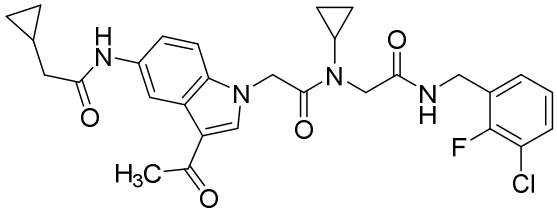
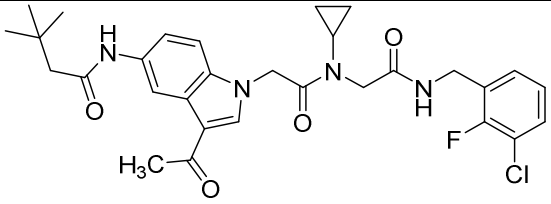
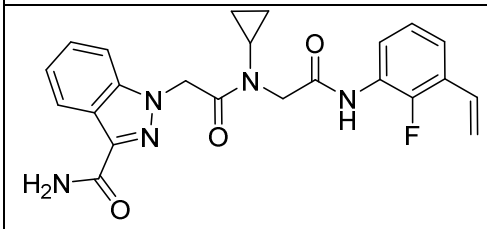
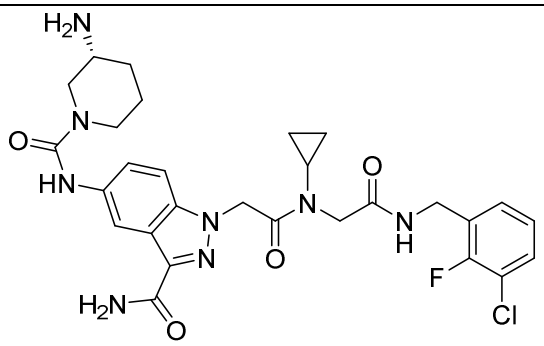
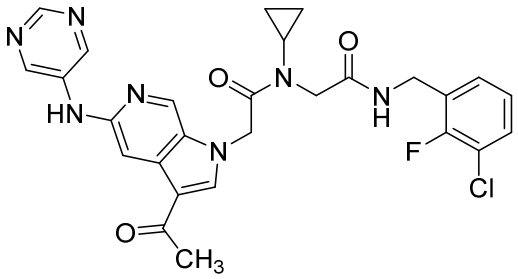
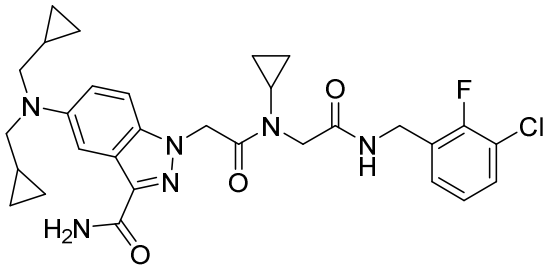
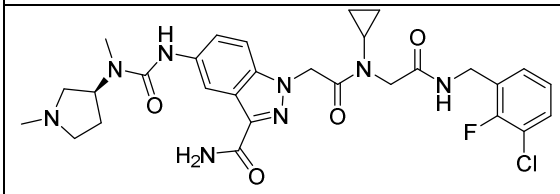
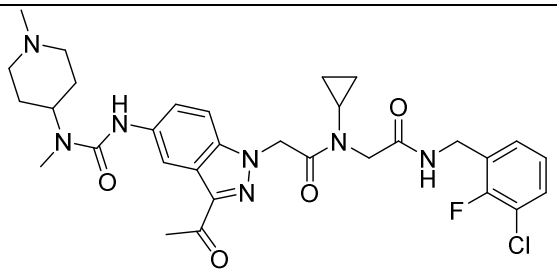
	
	
	
	

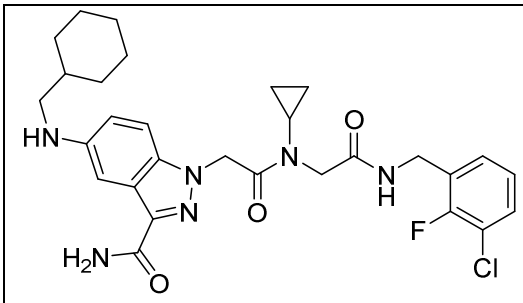
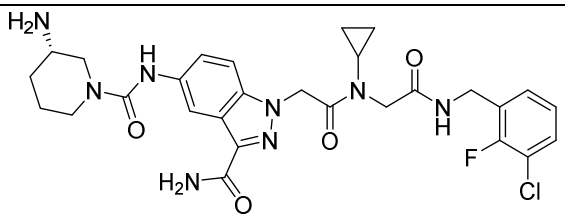
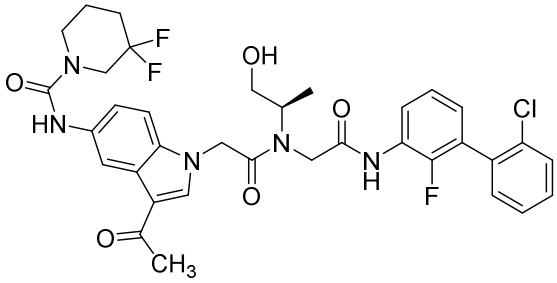
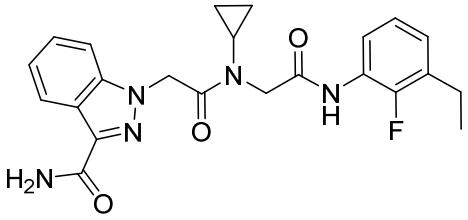
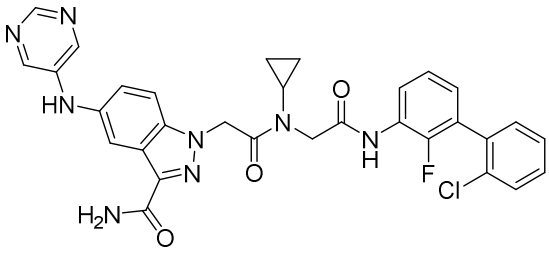
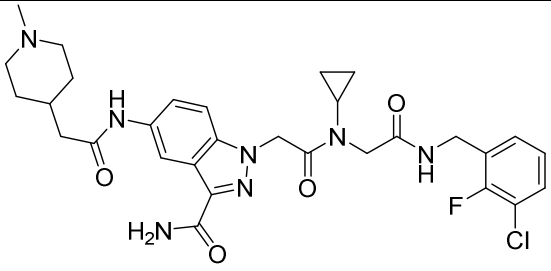
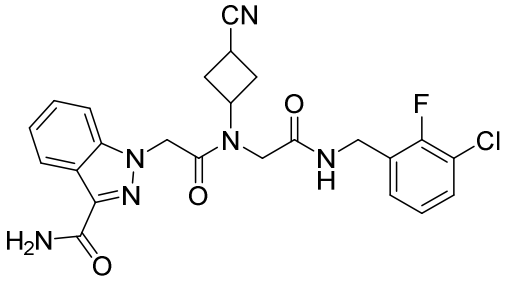
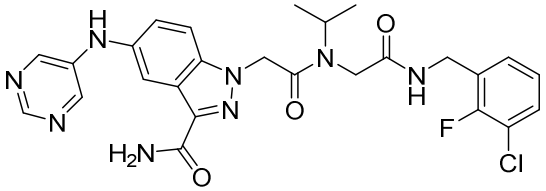
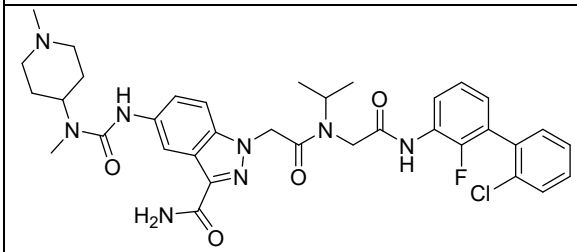
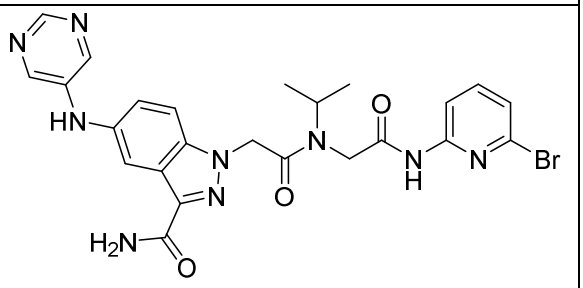
	
	
	
	
	

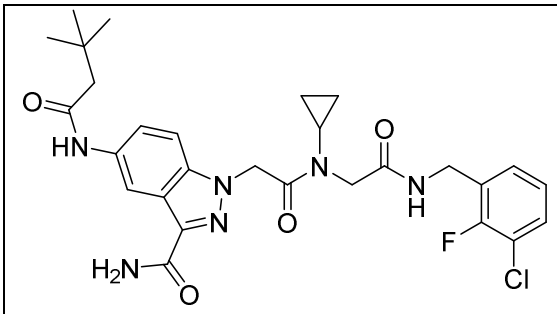
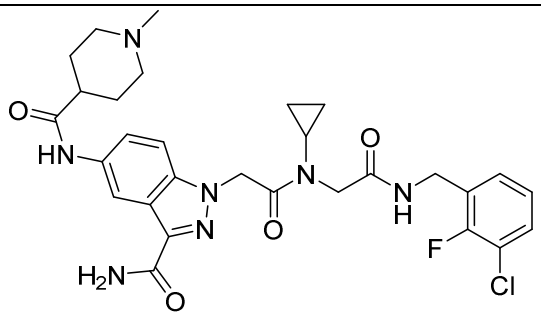
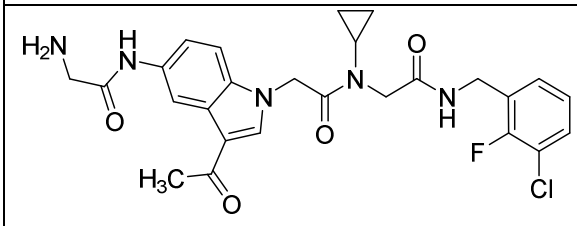
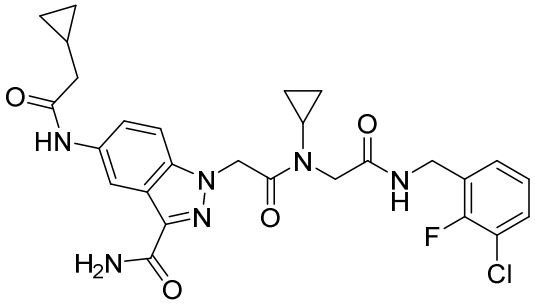
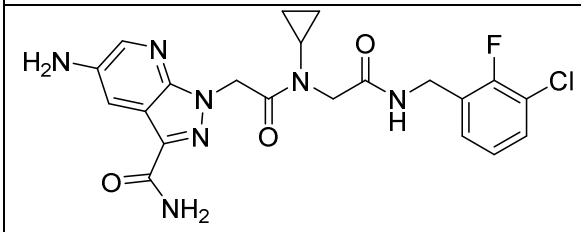
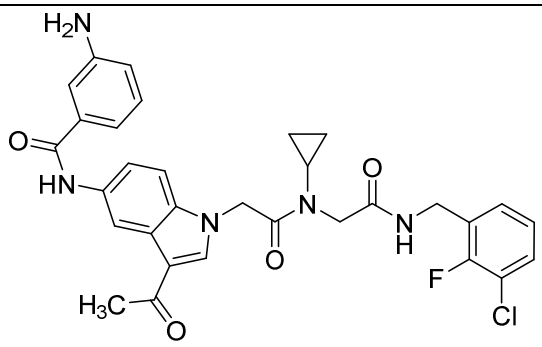
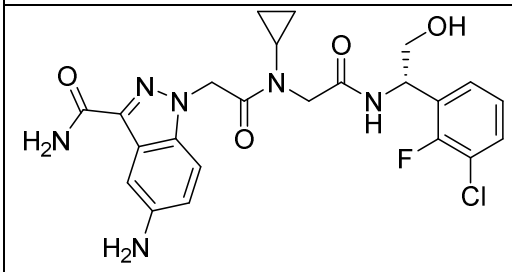
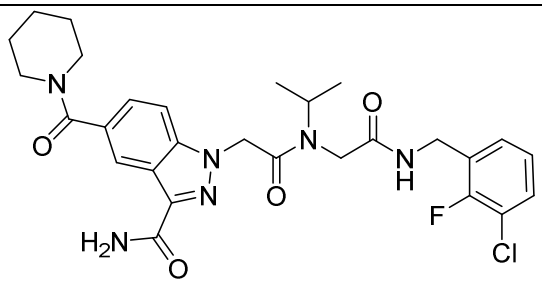
	
	
	
	
	

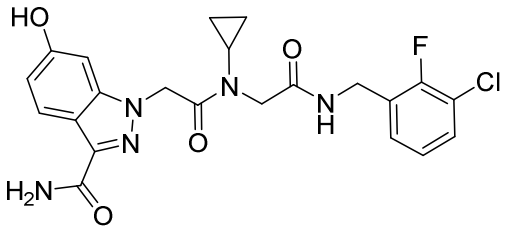
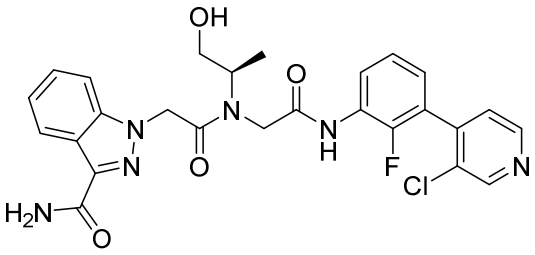
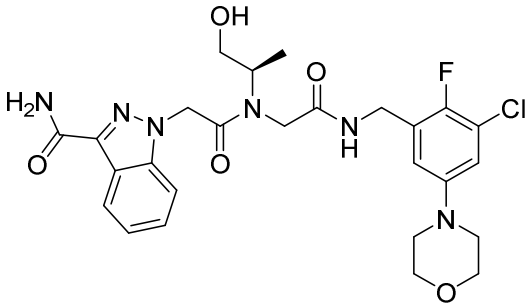
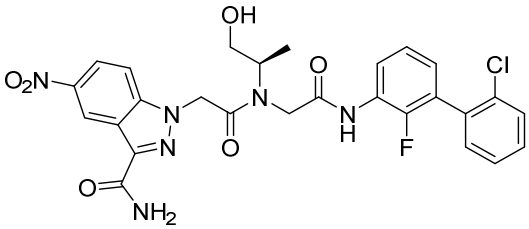
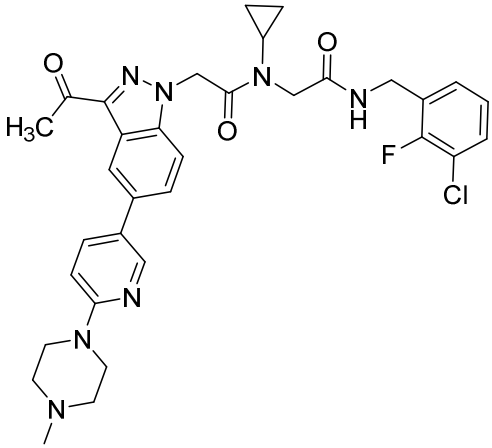
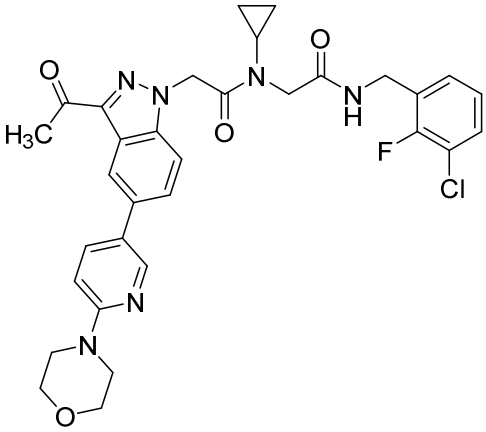
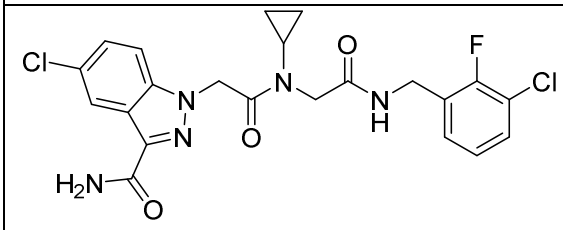
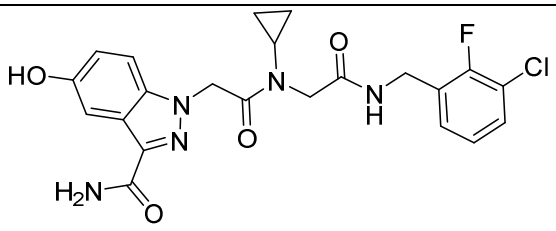
	
	
	
	
	

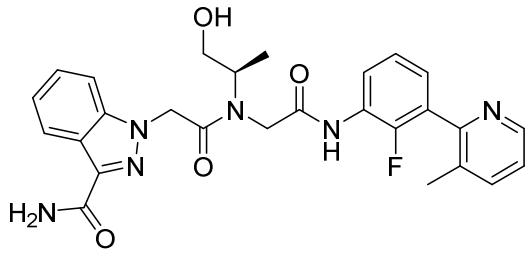
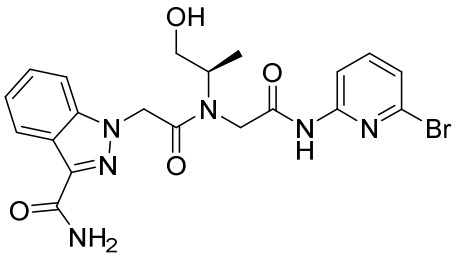
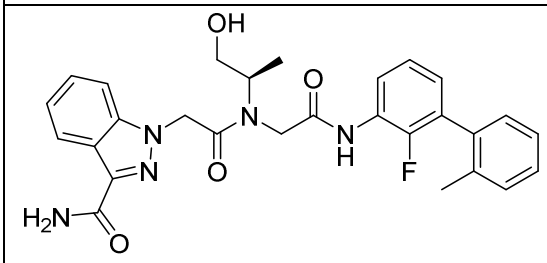
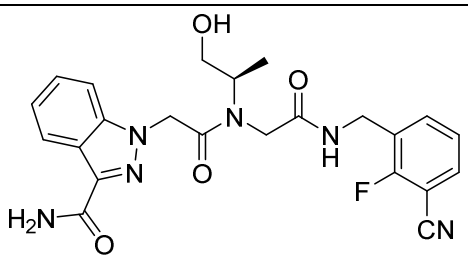
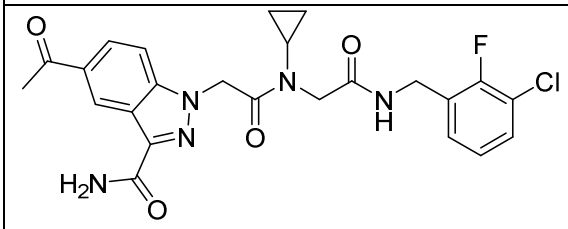
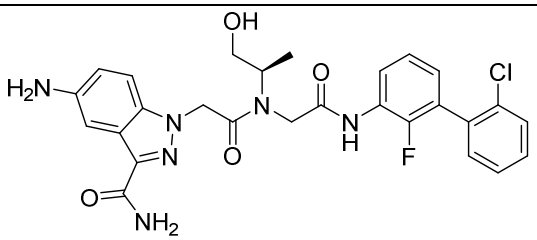
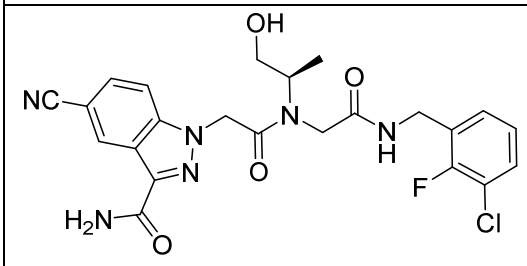
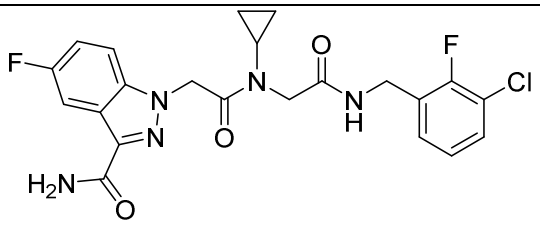
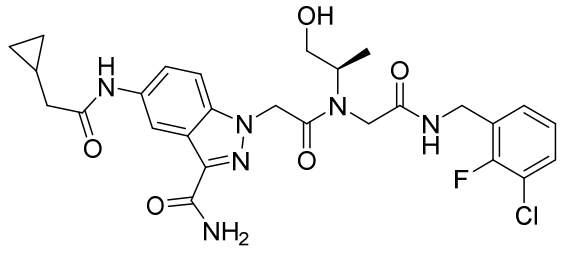
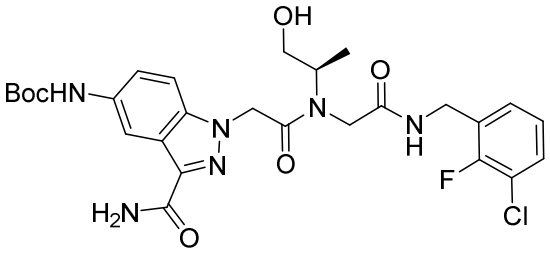
	
	
	
	
	

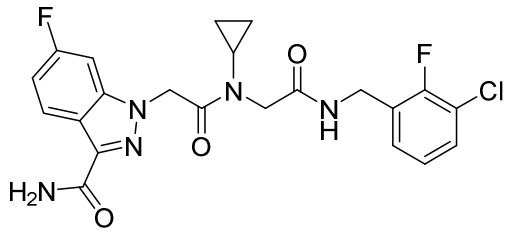
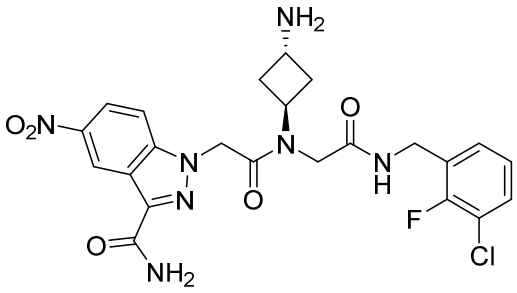
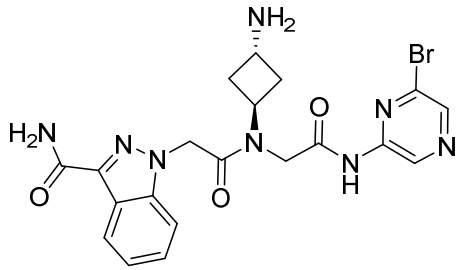
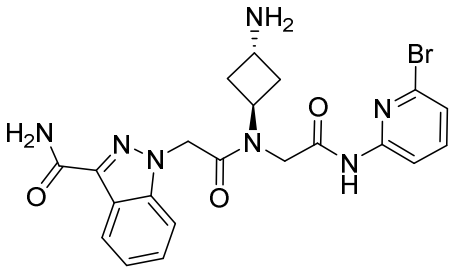
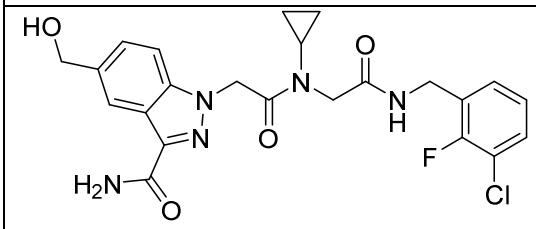
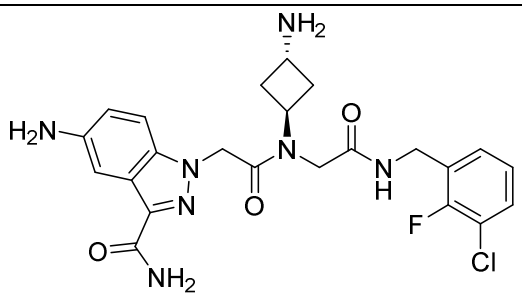
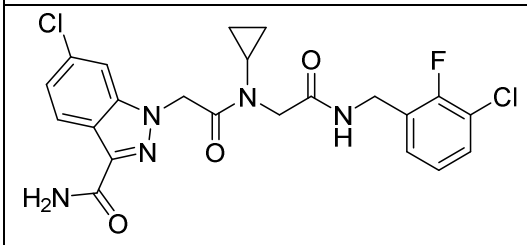
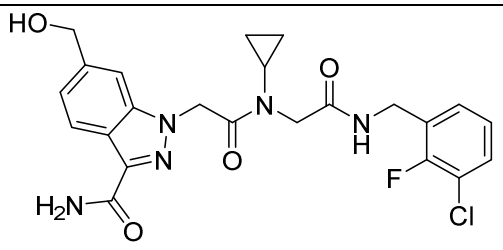
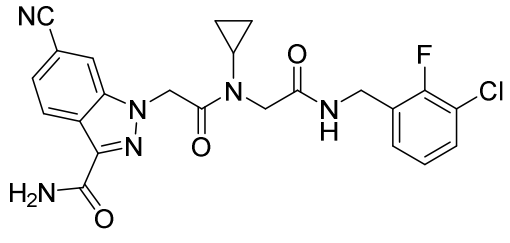
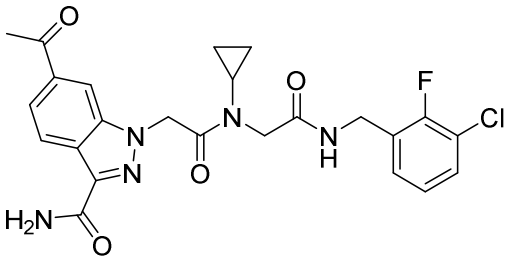
	
	
	
	
	

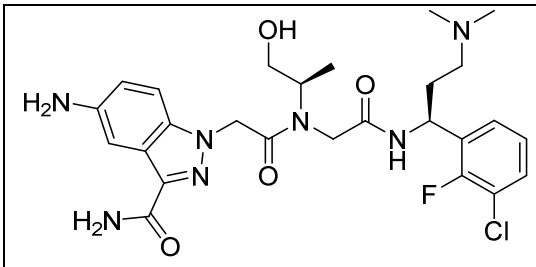
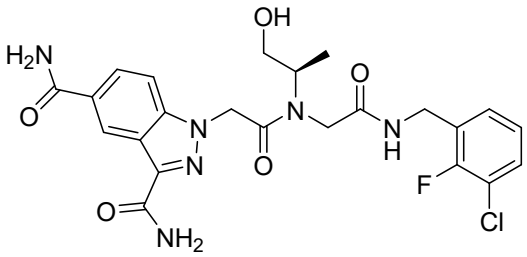
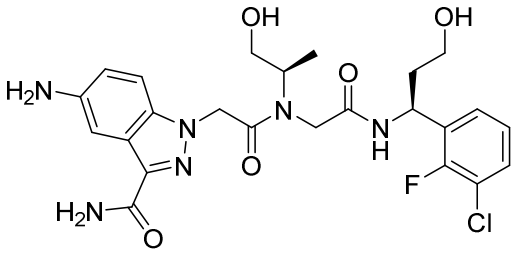
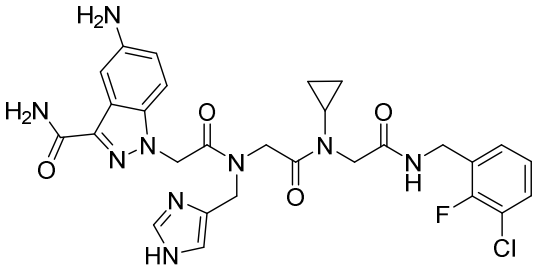
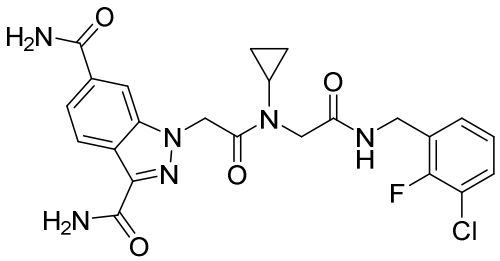
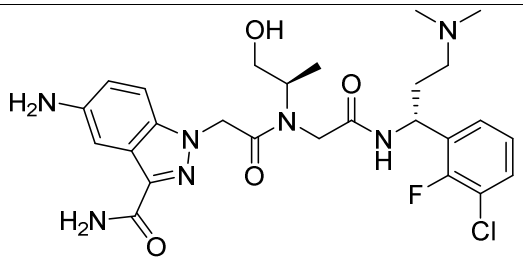
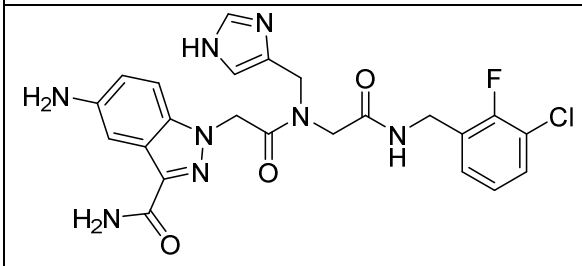
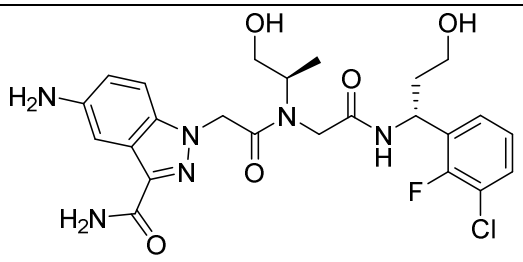
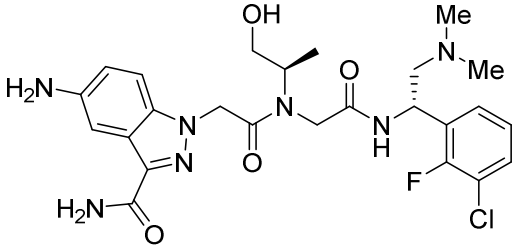
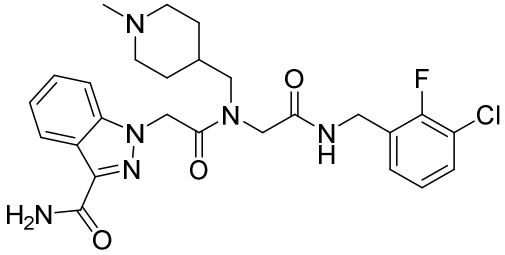
	
	
	
	
	

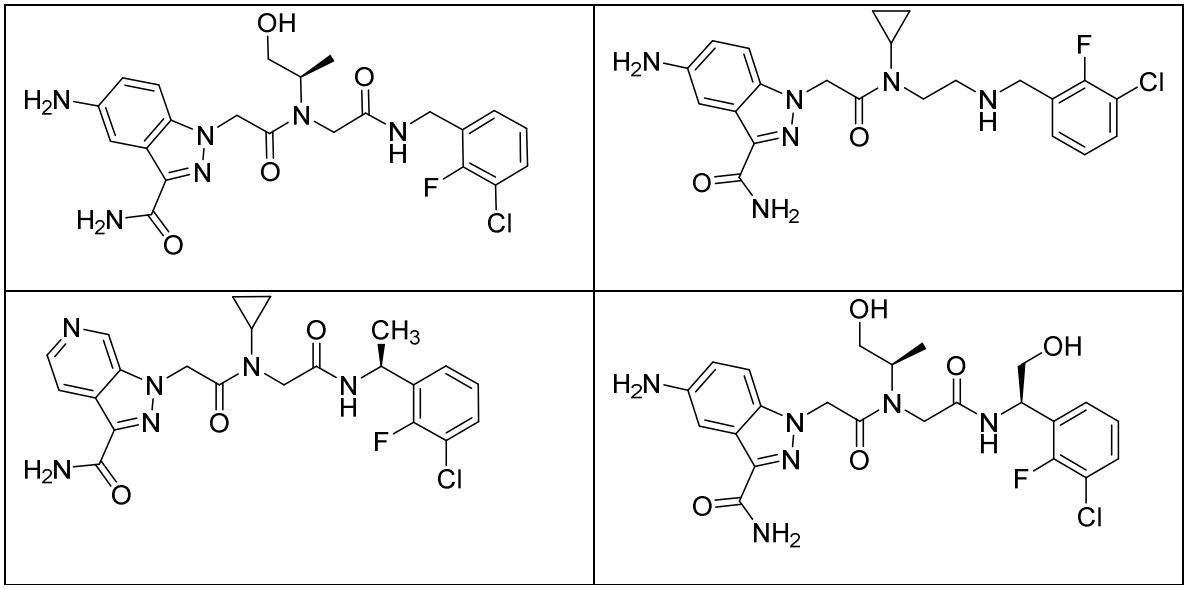
	
	
	
	



32. A pharmaceutical composition, comprising a compound of any one of claims 1-31; and a pharmaceutically acceptable carrier.

33. Use of the compound of any one of claims 1-31 in the manufacture of a medicament for the treatment or prevention of a disease or condition characterized by aberrant complement system activity; wherein the disease or condition characterized by aberrant complement system activity is selected from the group consisting of immunological disorder, a disease of central nervous system, renal disease, cardiovascular disease, paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, neurodegenerative disease, neurological disease, organ transplant rejection, myasthenia gravis, neuromyelitis optica, membranoproliferative glomerulonephritis, dense-deposit disease, cold agglutinin disease, and catastrophic antiphospholipid syndrome.

34. The use of claim 33, wherein the disease or condition characterized by aberrant complement system activity is an immunological disorder.

35. The use of claim 33, wherein the disease or condition characterized by aberrant complement system activity is a disease of the central nervous system.

36. The use of claim 33, wherein the disease or condition characterized by aberrant complement system activity is a neurodegenerative disease or neurological disease.

37. The use of claim 33, wherein the disease or condition characterized by aberrant complement system activity is a renal disease.

38. The use of claim 33, wherein the disease or condition characterized by aberrant complement system activity is a cardiovascular disease.

39. The use of claim 33, wherein the disease or condition characterized by aberrant complement system activity is selected from the group consisting of paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, organ transplant rejection, myasthenia gravis, neuromyelitis optica, membranoproliferative glomerulonephritis, dense-deposit disease, cold agglutinin disease, and catastrophic antiphospholipid syndrome.

40. A compound of any one of claims 1-31 for use in treating or preventing a disease or condition characterized by aberrant complement system activity; wherein the disease or condition characterized by aberrant complement system activity is selected from the group consisting of immunological disorder, a disease of central nervous system, renal disease, cardiovascular disease, paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, neurodegenerative disease, neurological disease, organ transplant rejection, myasthenia gravis, neuromyelitis optica, membranoproliferative glomerulonephritis, dense-deposit disease, cold agglutinin disease, and catastrophic antiphospholipid syndrome.