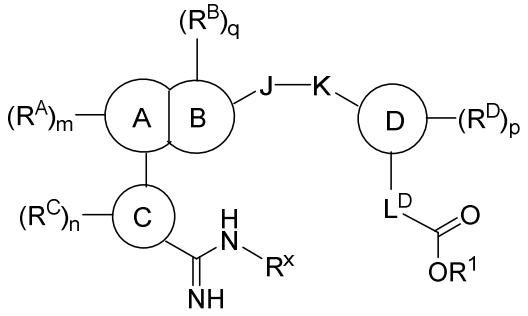
CLAIMS

1. A compound of formula (I), or a pharmaceutically acceptable salt thereof:



(I);

wherein:

ring A is arylene or heteroarylene;

ring B is arylene or heteroarylene;

ring A is fused to ring B at two and only two adjacent positions;

ring C is aryl or heteroaryl;

ring D is aryl or heteroaryl;

J represents $–CH_2–$, –NH–, $–CH_2CH_2–$, –C(O)–, –C≡C–, –O–, –S–, –S(O)–, $–SO_2–$, –N(alkyl)–, –CH(alkyl)–, –CH(aryl)–, $–C(alkyl)_2–$, –CH(cycloalkyl)–, or ;

K represents a bond, –O–, –NH–, –C(O)–, $–CH_2–$, –S–, –S(O)–, $–SO_2–$, –N(alkyl)–, –CH(alkyl)–, or –CH(cycloalkyl)–;

wherein at least one of J and K is a bond, –C(O)–, $–CH_2–$, $–CH_2CH_2–$, –CH(alkyl)–, or –CH(aryl)–;

L^D represents $–CH_2–$, $–CH_2CH_2–$, $–CF_2–$, –CH(F)–, $–CD_2–$, –CH(D)–, –CH(OH)–, –CH(alkyl)–, –CH(cycloalkyl)–, $–CHNH_2–$, –CH(NH(alkyl))–, –CH(NH(cycloalkyl))–, or a bond;

R^A, independently for each occurrence, represents H, halo, hydroxyl, cyano, amino, alkyl, optionally substituted alkoxy, hydroxyalkyl, optionally substituted aryloxy,

(aryloxy)alkyl, (cycloalkyl)alkoxy, (heterocycloalkyl)alkoxy, optionally substituted (heteroaryl)alkoxy, haloalkyl, haloalkoxy, (hydroxy)haloalkyl, alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl, optionally substituted (cycloalkyl)alkenyl, optionally substituted heterocycloalkyl, optionally substituted (heterocycloalkyl)alkyl, –C(O)OH, –C(O)NH_2–, –C(O)N(alkyl)$_2$–, –CH_2C(O)OH, –NO_2, –CH_2NH(optionally substituted alkyl), –CH_2NH(Boc), –CH_2N(Boc)(optionally substituted alkyl), –CH_2NH((cycloalkyl)alkyl), –CH_2N(alkyl)(cycloalkyl), –CH_2N(alkyl)((cycloalkyl)alkyl), –NH(optionally substituted alkyl), –NH(cycloalkyl), –NH((cycloalkyl)alkyl), –NH((heterocycloalkyl)alkyl), –N(alkyl)$_2$, –N(alkyl)((cycloalkyl)alkyl, –N(alkyl)((heterocycloalkyl)alkyl, –NH(heteroarylalkyl), –CH_2O(optionally substituted aryl), –C(O)O(alkyl), –C(O)NH(optionally substituted alkyl), –C(O)NH((cycloalkyl)alkyl), –NHC(O)O(alkyl), or –CH_2N(alkyl)$_2$;

R^B, independently for each occurrence, represents H, oxo, –C(O)O(alkyl), halogen, cyano, amino, –C(O)OH, –CH_2C(O)OH, –C(O)NH_2, –C(O)NH(cycloalkyl), –C(O)NH(alkyl), –C(O)NH(aryl), -C(O)NH(heteroaryl), –C(O)(alkyl), -S(O)$_2$alkyl, alkylaminoalkyl, alkylaminocycloalkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, (hydroxy)haloalkyl, or tosyl, or is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl, spirocycloalkyl, halocycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, spiroheterocycloalkyl, or (heterocycloalkyl)alkyl; or two geminal occurrences of R^B taken together with the atom to which they are attached form an optionally substituted spirocycloalkyl or a spiroheterocycloalkyl;

R^C, independently for each occurrence, represents H, halo, -OH, cyano, or amino, or is optionally substituted alkoxy, haloalkoxy, alkyl, cycloalkyl, heterocycloalkyl, or (heteroaryl)alkoxy;

R^x is H or OH;

R^D, independently for each occurrence, represents H, halo, hydroxyl, cyano, –NH_2, -NH(Ac), -NH(alkyl), -N(alkyl)$_2$, -NH(CO)(alkyl), –CH_2NH_2,

-$CH_2NHC(O)$(alkyl), –$C(O)NH_2$, –C(O)OH, or –NHC(O)O(alkyl), or is optionally substituted alkyl, alkoxy, cycloalkyl, (cycloalkyl)alkyl, hydroxyalkyl, aminoalkyl, haloalkoxy, or haloalkyl;

R^1 represents H or optionally substituted alkyl; and

m, n, p, and q are each independently 0, 1, or 2.

2. The compound of claim 1, wherein:

ring A is arylene or heteroarylene;

ring B is arylene or heteroarylene;

ring A is fused to ring B at two and only two adjacent positions;

ring C is aryl or heteroaryl;

ring D is aryl;

J represents $–CH_2–$ or –C(O)–;

K represents –O–, –NH–, or a bond;

L^D represents $–CH_2–$, –CH(OH)–, or a bond;

R^A, independently for each occurrence, represents H, optionally substituted alkoxy, or optionally substituted (heteroaryl)alkoxy;

R^B, independently for each occurrence, represents H, oxo, or is optionally substituted alkyl, aryl, cycloalkyl, (cycloalkyl)alkyl, or heterocycloalkyl;

R^C, independently for each occurrence, represents H, halo, -OH, or alkoxy;

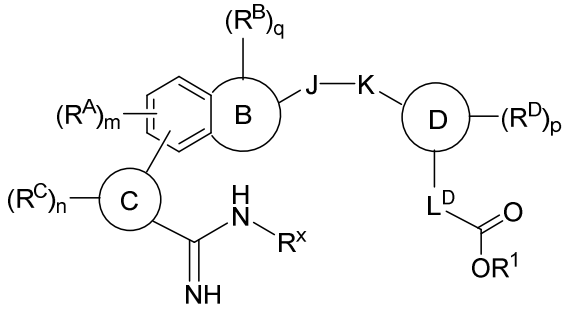
R^x is H or OH;

R^D, independently for each occurrence, represents H, or is optionally substituted alkyl or alkoxy;

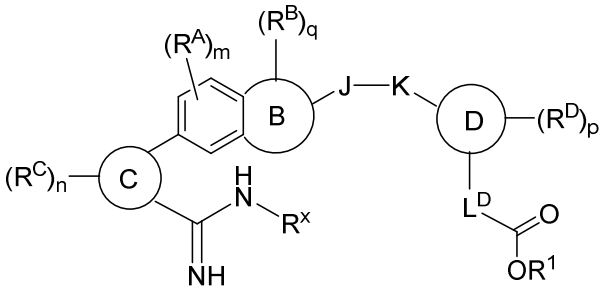
R^1 represents H; and

m, n, p, and q are each independently 0, 1, or 2.

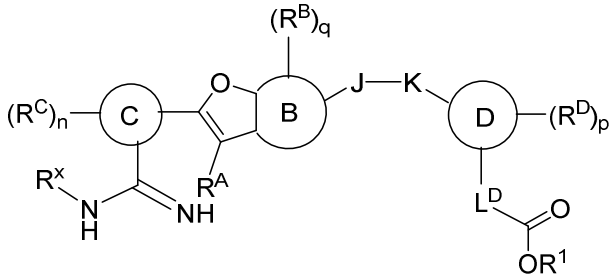
3. The compound of claim 1 or 2, having the structure of formula (Ia), (Ia-1), (Ib), (Ic), (Id), (Ie), (If), (Ig), (Ih), (Ij), or (Ik):



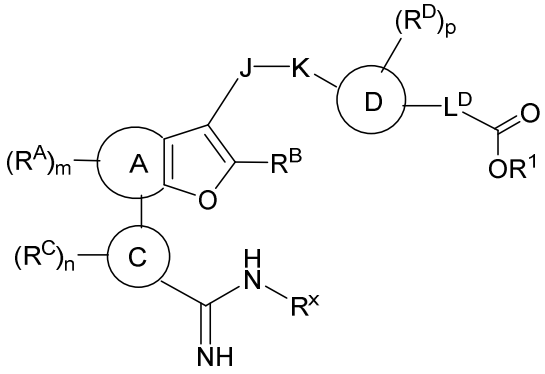
(Ia),



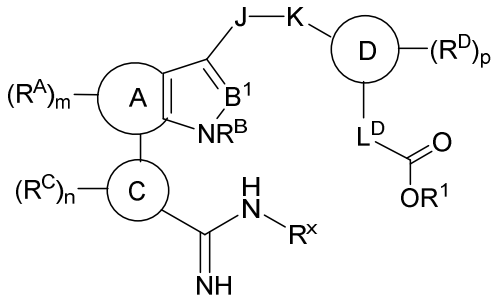
(Ia-1),



(Ib),

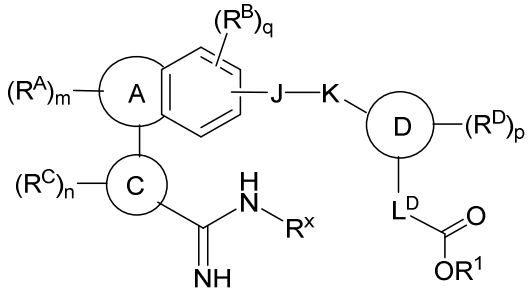


(Ic),

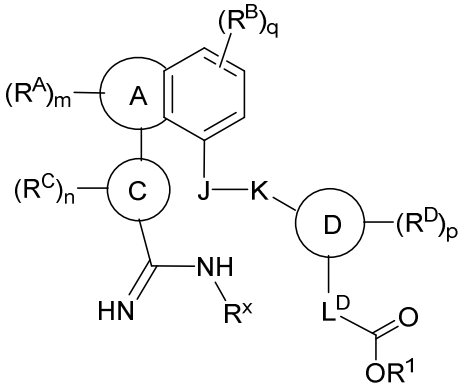


(Id);

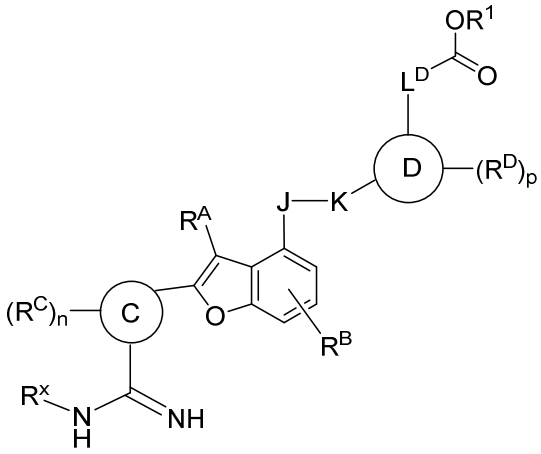
wherein B^1 represents N or CH;



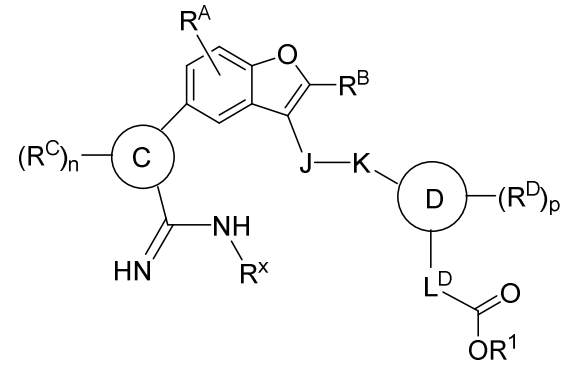
(Ie);



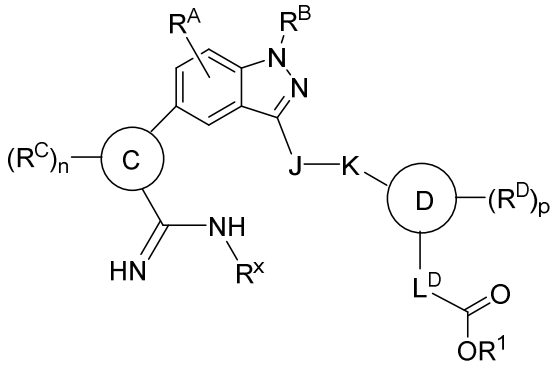
(If);



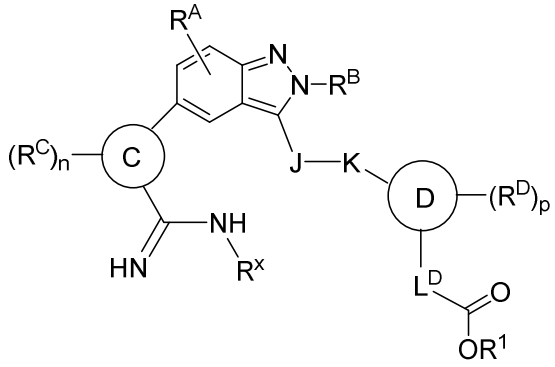
(Ig);



(Ih);

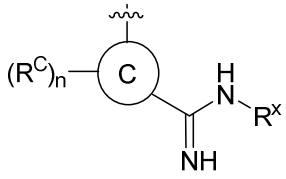


(Ij); or

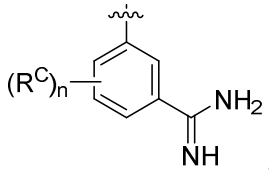


(Ik).

4. The compound of any one of claims 1-3, wherein



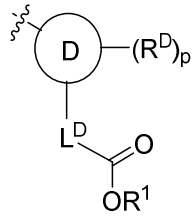
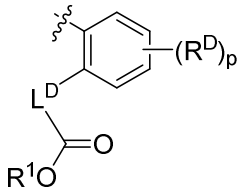
represents



.

5. The compound of any one of claims 1-4, wherein R^C represents H or alkoxy (e.g., methoxy).

6. The compound of any one of claims 1-5, wherein –J–K– represents –CH_2-O– or –C(O)-NH–.

7. The compound of any one of claims 1-6, wherein  represents .

8. The compound of any one of claims 1-7, wherein R^1 is H.

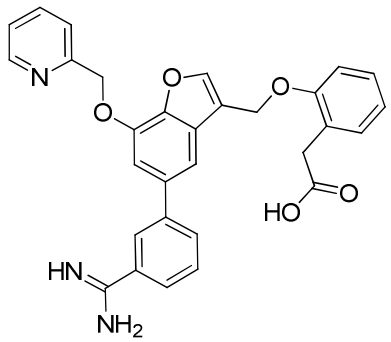
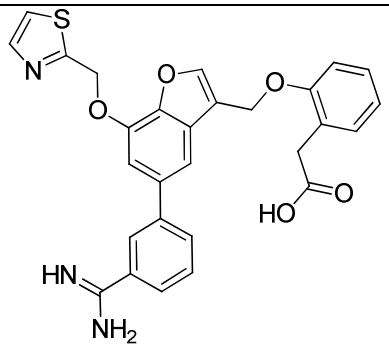
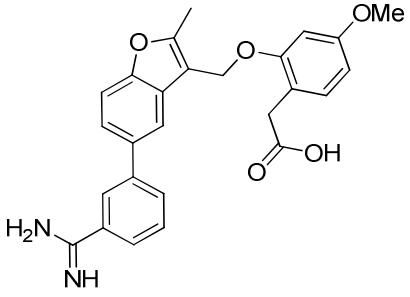
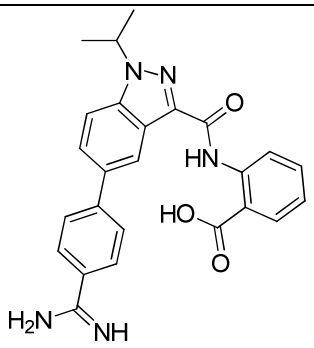
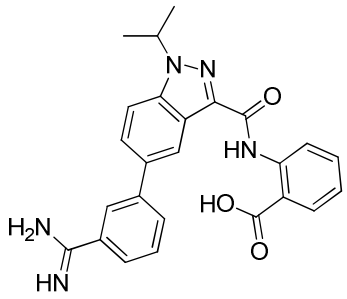
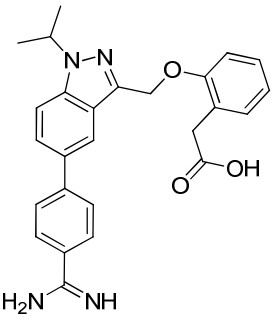
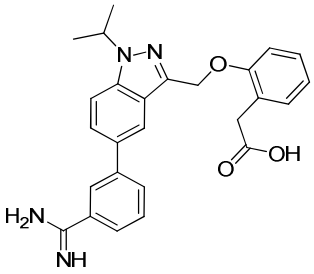
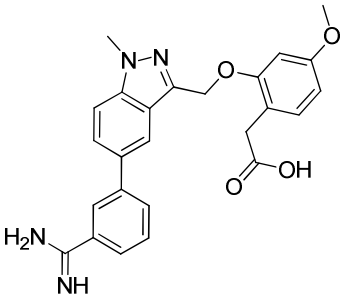
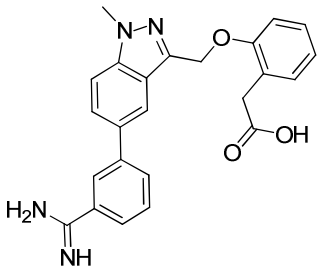
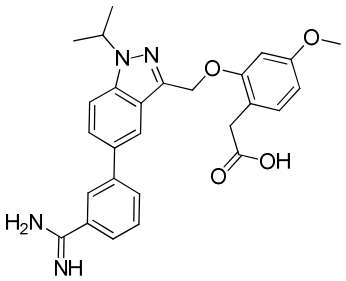
9. The compound of any one of claims 1-8, wherein L^D represents –CH_2– or a bond.

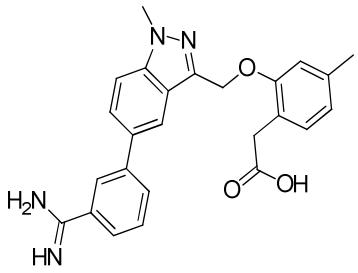
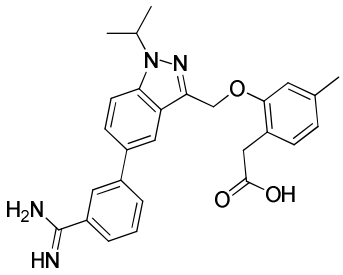
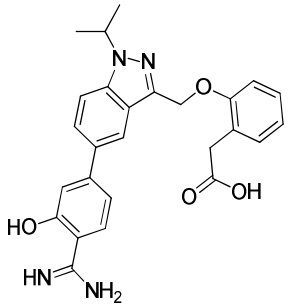
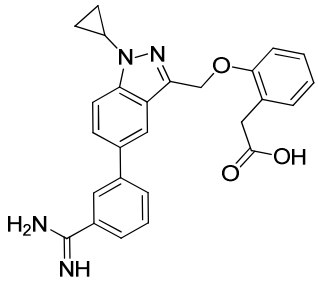
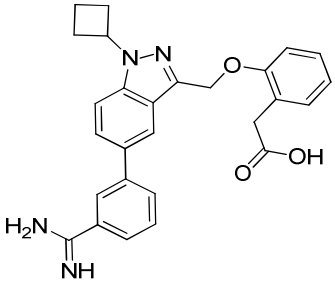
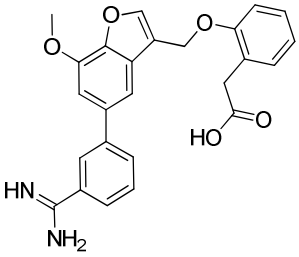
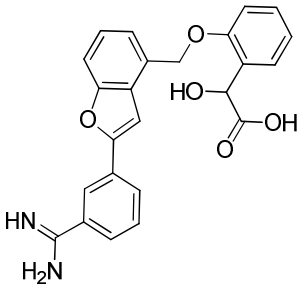
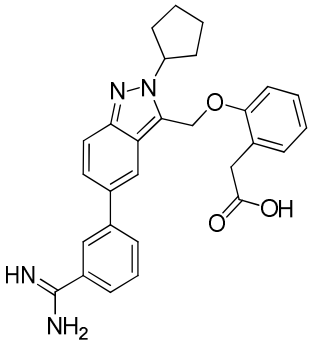
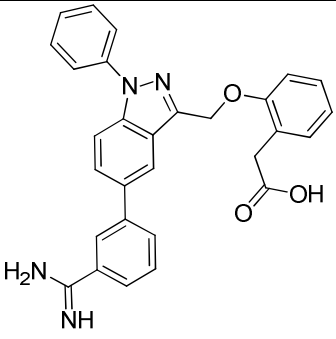
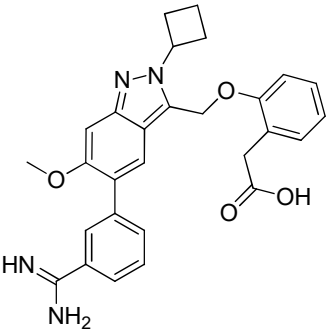
10. The compound of any one of claims 1-9, wherein R^D, independently for each occurrence, represents H, alkyl, or alkoxy.

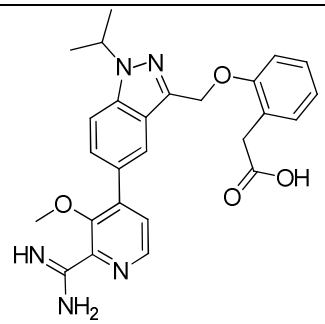
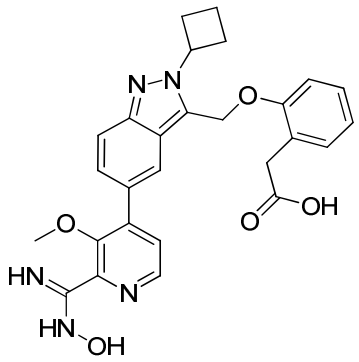
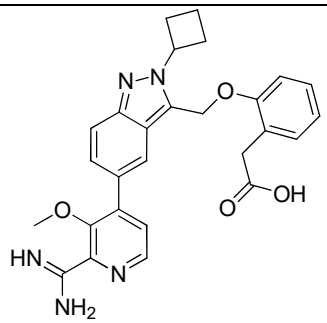
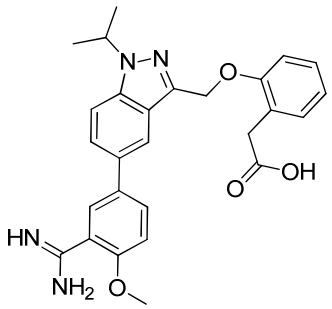
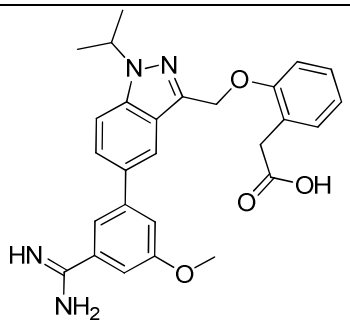
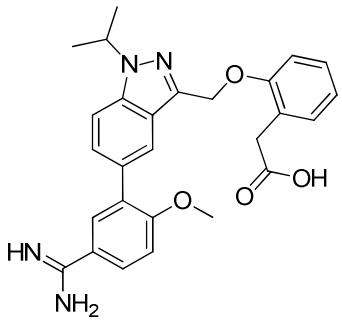
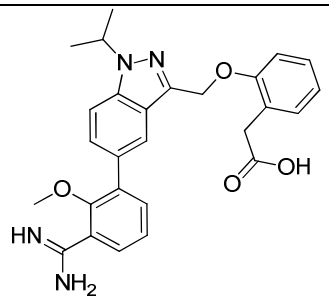
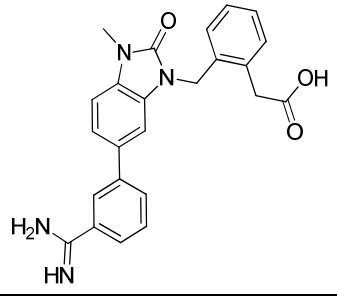
11. The compound of any one of claims 1-10, wherein R^B, independently for each occurrence, represents H, alkyl, cycloalkyl, (cycloalkyl)alkyl, or heterocycloalkyl.

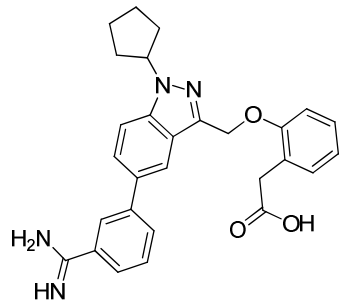
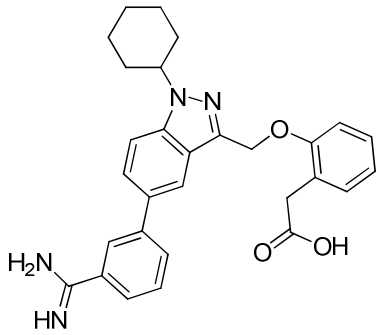
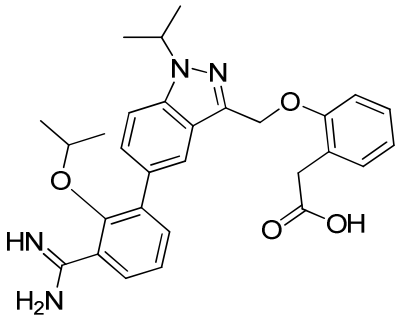
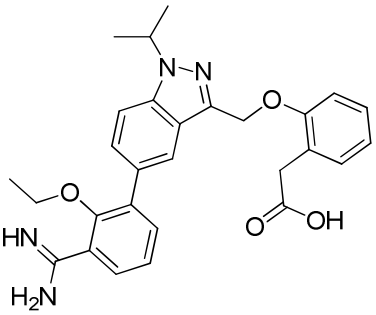
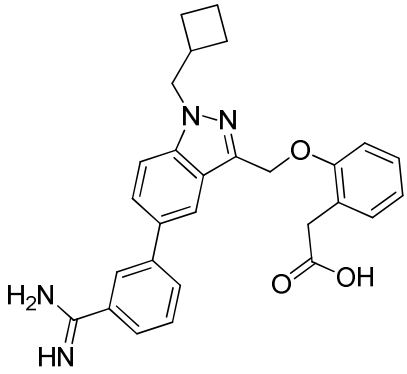
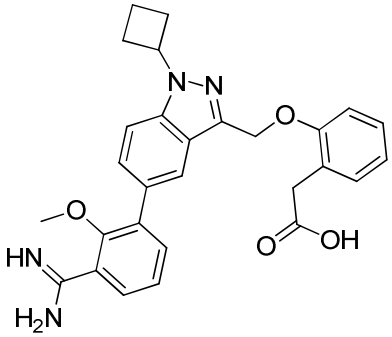
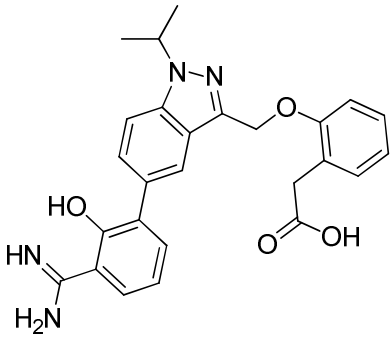
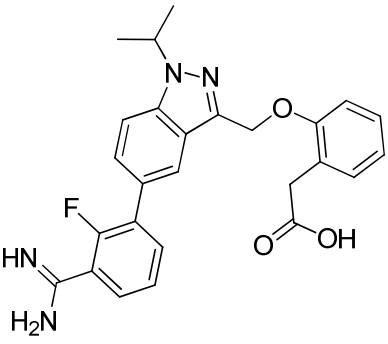
12. The compound of any one of claims 1-11, wherein R^A, independently for each occurrence, represents H, optionally substituted alkoxy, or optionally substituted (heteroaryl)alkoxy.

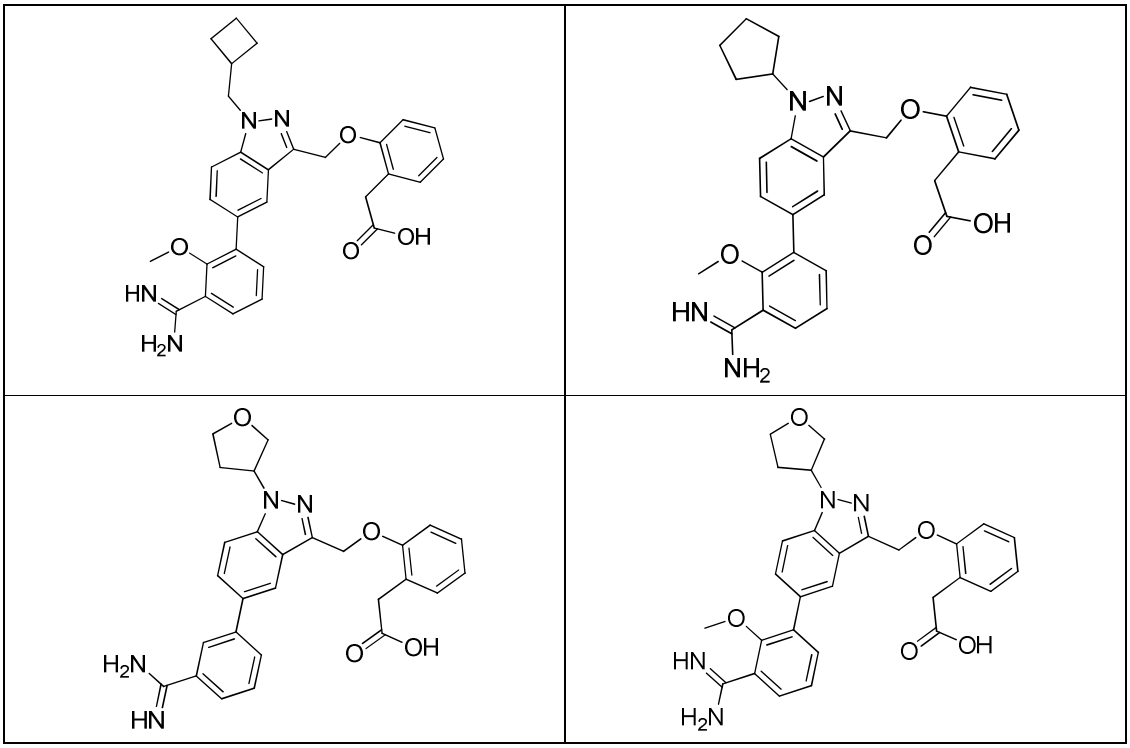
13. The compound of claim 1, selected from the following table:

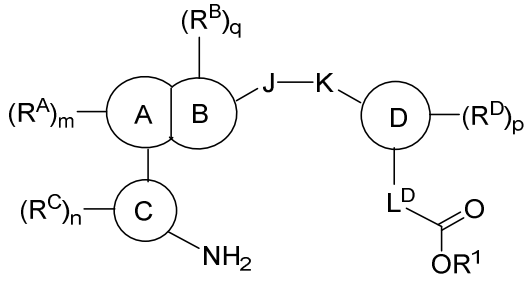
	
	
	
	



.

14. A compound of formula (II), or a pharmaceutically acceptable salt thereof:



(II);

wherein:

ring A is arylene or heteroarylene;

ring B is arylene or heteroarylene;

ring A is fused to ring B at two and only two adjacent positions;

ring C is a bicyclic ring system, where the ring attached to ring A is aryl or heteroaryl;

ring D is aryl or heteroaryl;

J represents $–CH_2–$, –NH–, $–CH_2CH_2–$, –C(O)–, –C≡C–, –O–, –S–, –S(O)–, $–SO_2–$, –N(alkyl)–, –CH(alkyl)–, –CH(aryl)–, $–C(alkyl)_2–$, –CH(cycloalkyl)–, or ;

K represents a bond, –O–, –NH–, –C(O)–, $–CH_2–$, –S–, –S(O)–, $–SO_2–$, –N(alkyl)–, –CH(alkyl)–, or –CH(cycloalkyl)–;

wherein at least one of J and K is a bond, –C(O)–, $–CH_2–$, $–CH_2CH_2–$, –CH(alkyl)–, or –CH(aryl)–;

L^D represents $–CH_2–$, $–CH_2CH_2–$, $–CF_2–$, –CH(F)–, $–CD_2–$, –CH(D)–, –CH(OH)–, –CH(alkyl)–, –CH(cycloalkyl)–, $–CHNH_2–$, –CH(NH(alkyl))–, –CH(NH(cycloalkyl))–, or a bond;

R^A, independently for each occurrence, represents H, halo, hydroxyl, cyano, amino, alkyl, optionally substituted alkoxy, hydroxyalkyl, optionally substituted aryloxy, (aryloxy)alkyl, (cycloalkyl)alkoxy, (heterocycloalkyl)alkoxy, optionally substituted (heteroaryl)alkoxy, haloalkyl, haloalkoxy, (hydroxy)haloalkyl, alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl, optionally substituted (cycloalkyl)alkenyl, optionally substituted heterocycloalkyl, optionally substituted (heterocycloalkyl)alkyl, –C(O)OH, $–C(O)NH_2$, $–C(O)N(alkyl)_2–$, $–CH_2C(O)OH$, $–NO_2$, $–CH_2NH$(optionally substituted alkyl), $–CH_2NH$(Boc), $–CH_2N$(Boc)(optionally substituted alkyl), $–CH_2NH$((cycloalkyl)alkyl), $–CH_2N$(alkyl)(cycloalkyl), $–CH_2N$(alkyl)((cycloalkyl)alkyl), –NH(optionally substituted alkyl), –NH(cycloalkyl), –NH((cycloalkyl)alkyl), –NH((heterocycloalkyl)alkyl), $–N(alkyl)_2$, –N(alkyl)((cycloalkyl)alkyl, –N(alkyl)((heterocycloalkyl)alkyl, –NH(heteroarylalkyl), $–CH_2O$(optionally

substituted aryl), –C(O)O(alkyl), –C(O)NH(optionally substituted alkyl), –C(O)NH((cycloalkyl)alkyl), –NHC(O)O(alkyl), or $–CH_2N(alkyl)_2$;

R^B, independently for each occurrence, represents H, oxo, –C(O)O(alkyl), halogen, cyano, amino, –C(O)OH, $–CH_2C(O)OH$, $–C(O)NH_2$, –C(O)NH(cycloalkyl), –C(O)NH(alkyl), –C(O)NH(aryl), -C(O)NH(heteroaryl), –C(O)(alkyl), $-S(O)_2$alkyl, alkylaminoalkyl, alkylaminocycloalkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, (hydroxy)haloalkyl, or tosyl, or is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl, spirocycloalkyl, halocycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, spiroheterocycloalkyl, or (heterocycloalkyl)alkyl; or two geminal occurrences of R^B taken together with the atom to which they are attached form an optionally substituted spirocycloalkyl or a spiroheterocycloalkyl;

R^C, independently for each occurrence, represents H, halo, -OH, cyano, or amino, or is optionally substituted alkoxy, haloalkoxy, alkyl, cycloalkyl, heterocycloalkyl, or (heteroaryl)alkoxy;

R^D, independently for each occurrence, represents H, halo, hydroxyl, cyano, $–NH_2$, -NH(Ac), -NH(alkyl), $-N(alkyl)_2$, -NH(CO)(alkyl), $–CH_2NH_2$, $-CH_2NHC(O)$(alkyl), $–C(O)NH_2$, –C(O)OH, or –NHC(O)O(alkyl), or is optionally substituted alkyl, alkoxy, cycloalkyl, (cycloalkyl)alkyl, hydroxyalkyl, aminoalkyl, haloalkoxy, or haloalkyl;

R^1 represents H or optionally substituted alkyl; and

m, n, p, and q are each independently 0, 1, or 2.

15. The compound of claim 14, wherein:

ring (A) is arylene or heteroarylene;

ring (B) is arylene or heteroarylene;

ring (A) is fused to ring (B) at two and only two adjacent positions;

ring (C) is a bicyclic ring system, where the ring attached to ring (A) is aryl or heteroaryl;

ring  is aryl;

J represents –CH_2– or –C(O)–;

K represents –O– or –NH–;

L^D represents –CH_2– or –CH(alkyl)–;

R^A, independently for each occurrence, represents H, cyano, alkyl, optionally substituted alkoxy, optionally substituted heteroaryl, optionally substituted aminoalkyl, -C(O)NH_2, or –NH((cycloalkyl)alkyl);

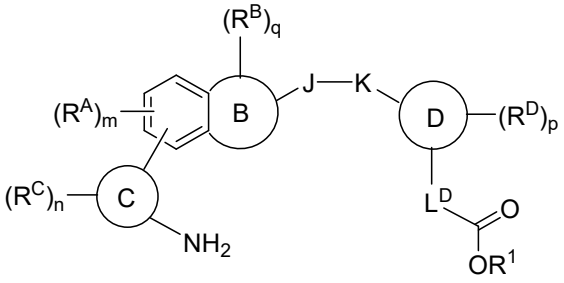
R^B, independently for each occurrence, represents H, oxo, alkoxyalkyl, or haloalkyl, or is optionally substituted alkyl, aryl, cycloalkyl, (cycloalkyl)alkyl, spirocycloalkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl;

R^C, independently for each occurrence, represents H or halo, or is optionally substituted alkoxy or alkyl;

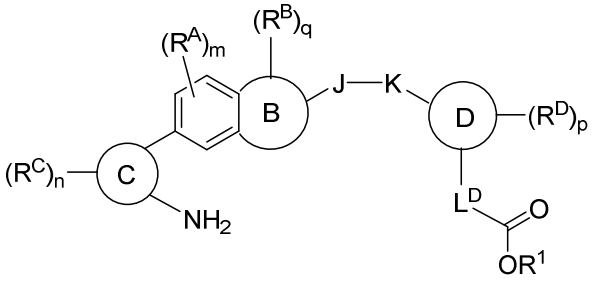
R^D, independently for each occurrence, represents H, halo, cyano, or –C(O)OH, or is optionally substituted alkyl, cycloalkyl, alkoxy, haloalkoxy, or haloalkyl;

R^1 represents H or optionally substituted alkyl.

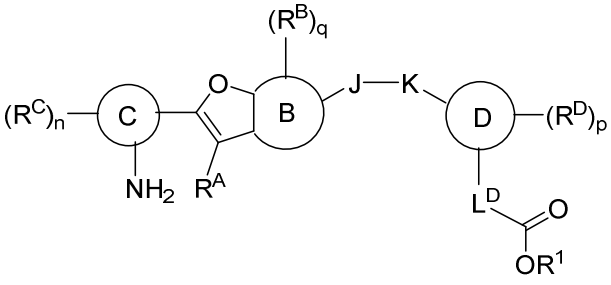
16. The compound of claim 14 or 15, having the structure of formula (IIa), (IIa-1), (IIb), (IIc), (IId), (IIe), (IIf), (IIf-1), (IIg), (IIh), (IIj), (IIk), (IIm), (IIn), or (IIo):



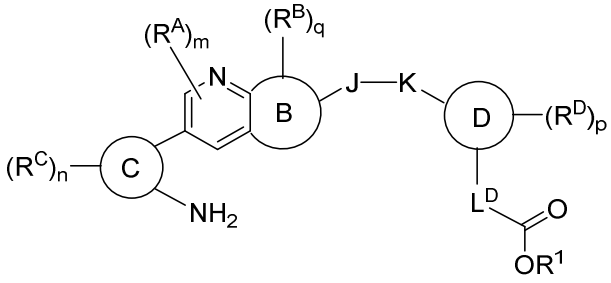
(IIa);



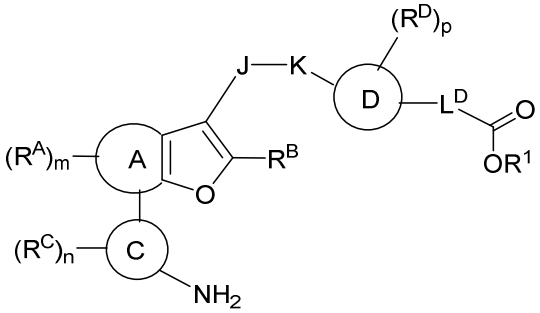
(IIa-1);



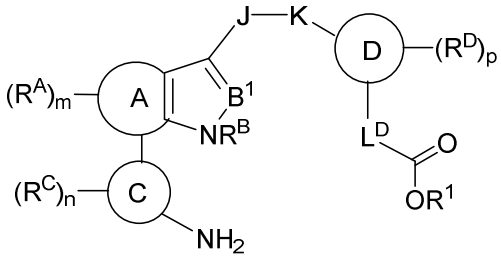
(IIb);



(IIc);

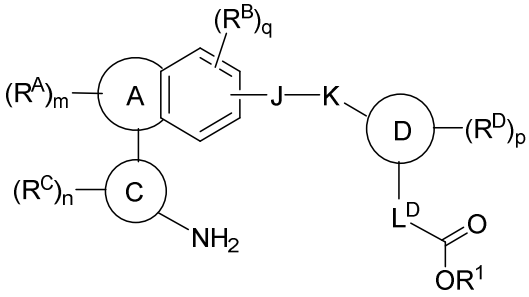


(IId);

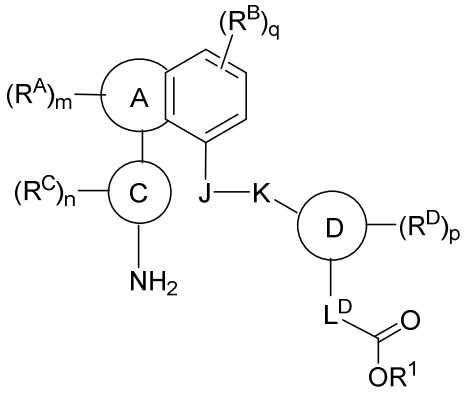


(IIe);

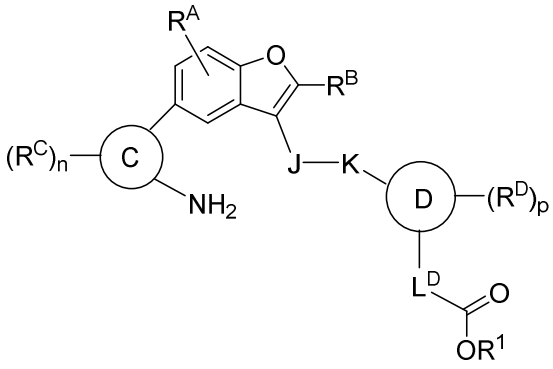
wherein B^1 represents N or CH;



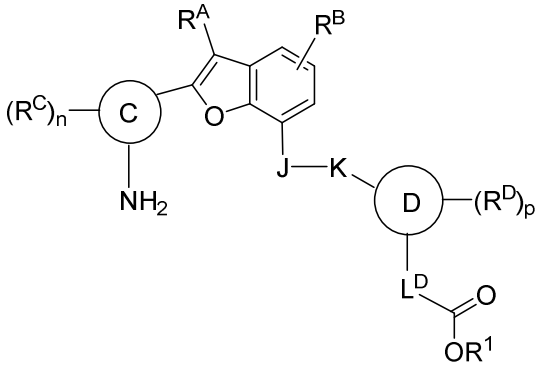
(IIf);



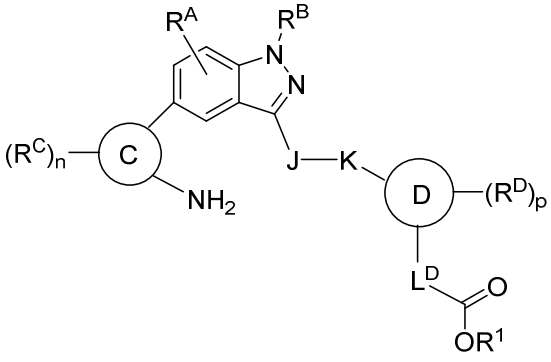
(IIf-1);



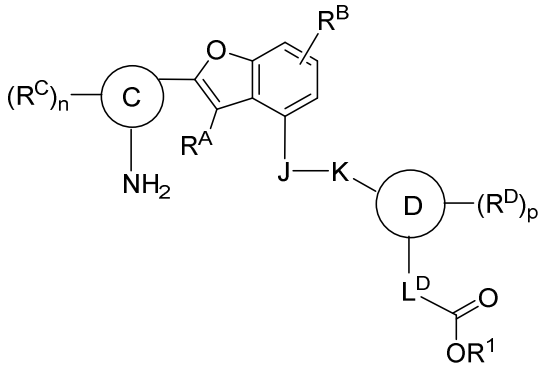
(IIg);



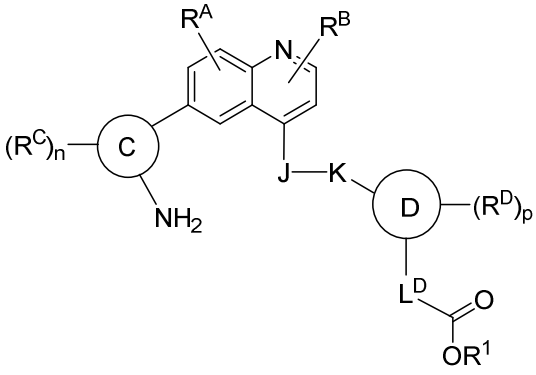
(IIh);



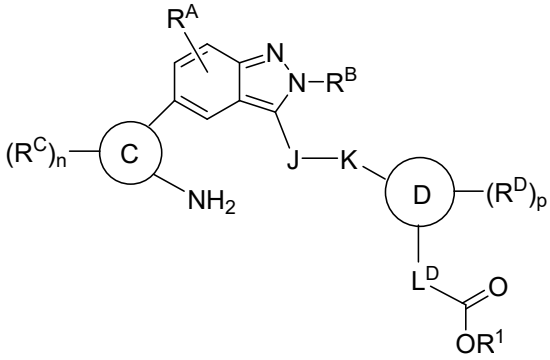
(IIj);



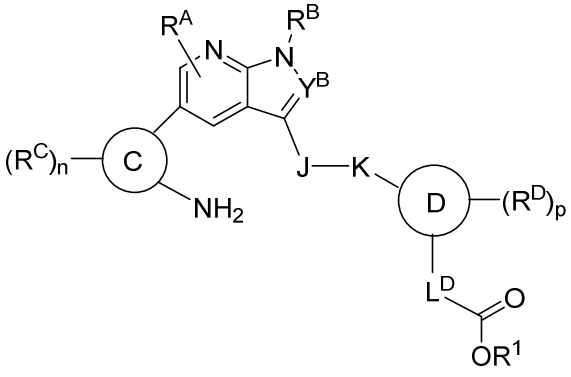
(IIk);



(IIm);

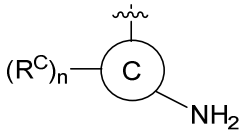
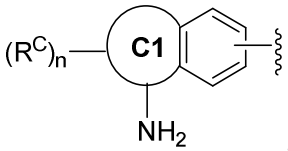


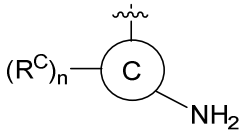
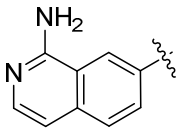
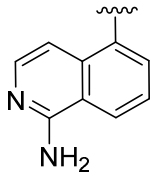
(IIn); or



(IIo);

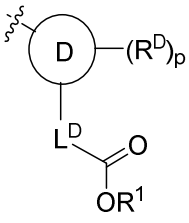
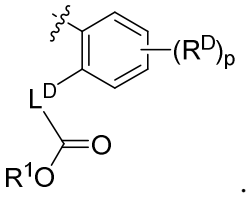
wherein Y^B is H or CH.

17. The compound of any one of claims 14-16, wherein  represents , wherein ring  represents a 5- or 6-membered heteroaryl containing at least one nitrogen atom.

18. The compound of any one of claims 14-16, wherein  represents  or .

19. The compound of any one of claims 14-16, wherein R^C, independently for each occurrence, represents H, alkoxy, or alkyl.

20. The compound of any one of claims 14-19, wherein –J–K– represents $–CH_2-O–$ or –C(O)-NH–.

21. The compound of any one of claims 14-20, wherein  represents .

22. The compound of any one of claims 14-21, wherein R^1 is H.

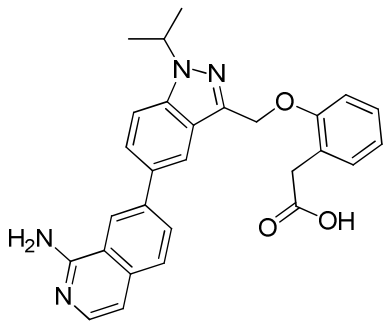
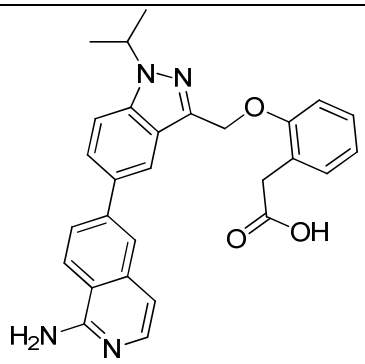
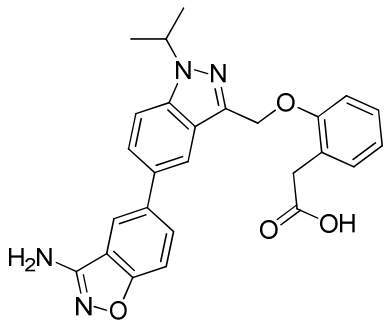
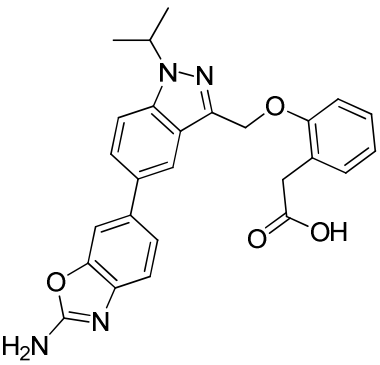
23. The compound of any one of claims 14-22, wherein L^D represents $–CH_2–$ or –CH(alkyl)–.

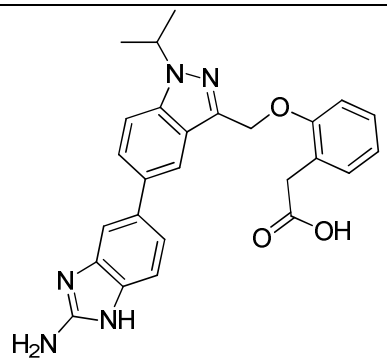
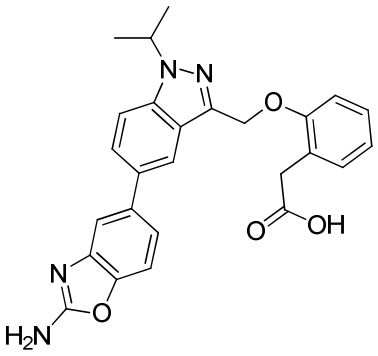
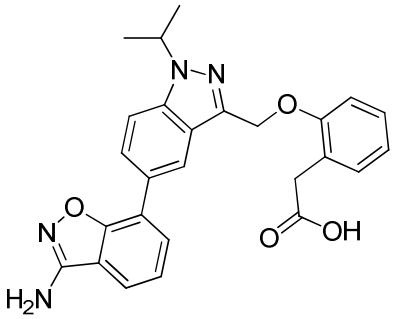
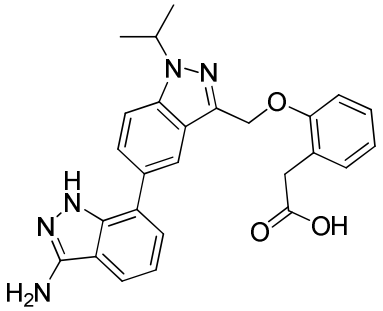
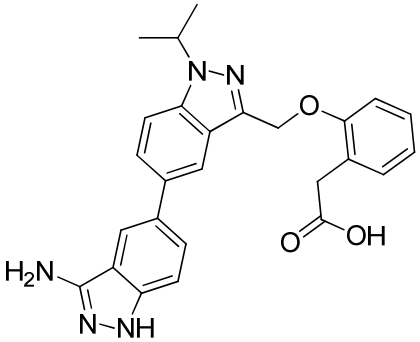
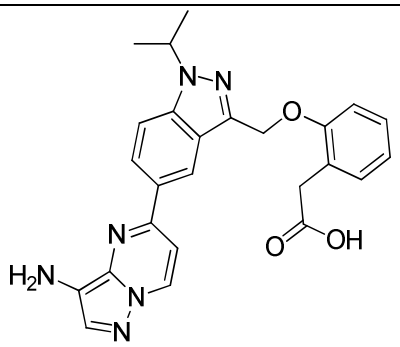
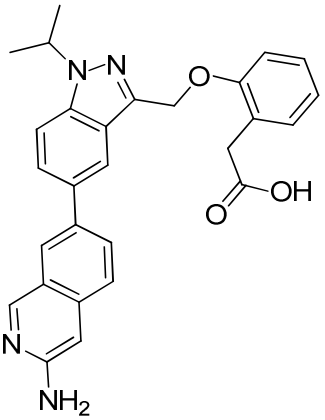
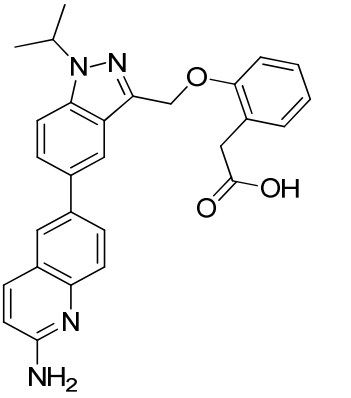
24. The compound of any one of claims 14-23, wherein R^D, independently for each occurrence, represents H, alkyl, or alkoxy.

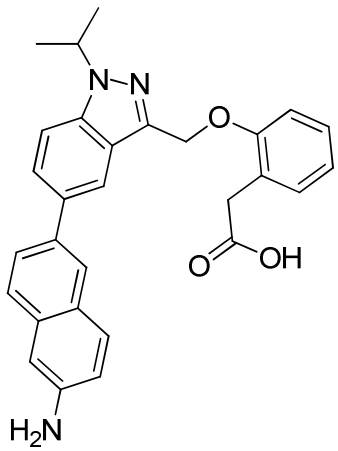
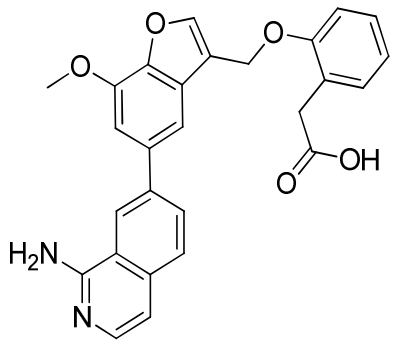
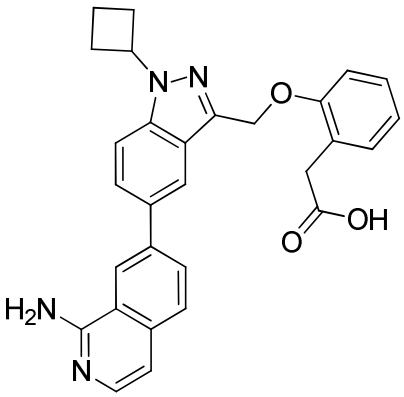
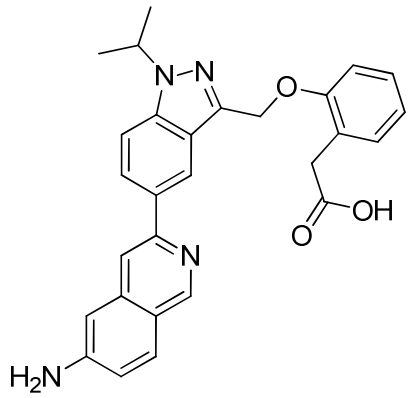
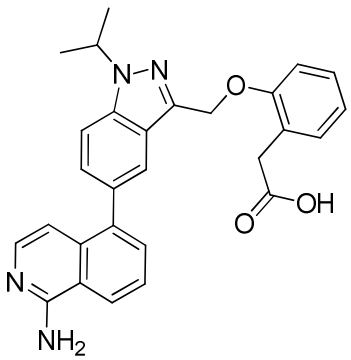
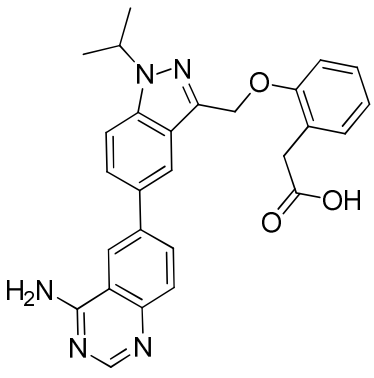
25. The compound of any one of claims 14-24, wherein R^B, independently for each occurrence, represents H, alkoxyalkyl, or haloalkyl, or is optionally substituted alkyl, aryl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl.

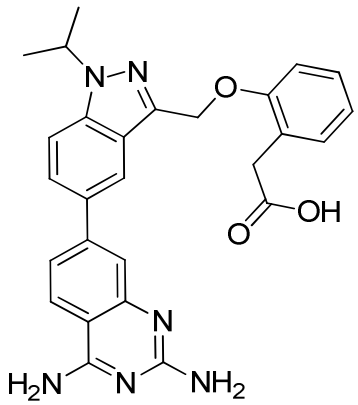
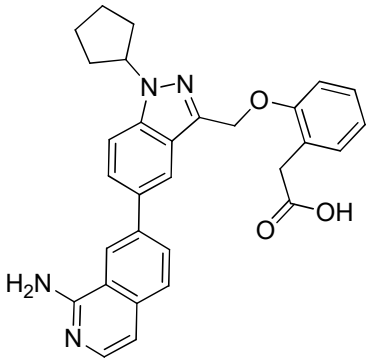
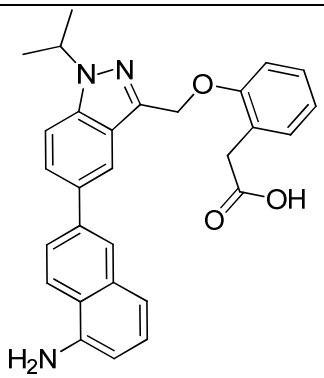
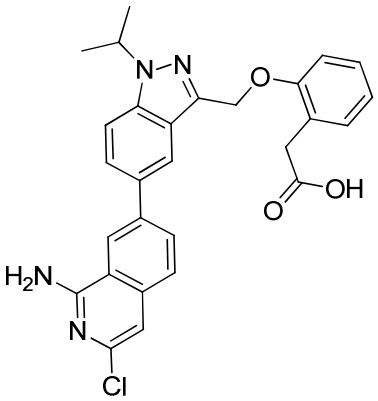
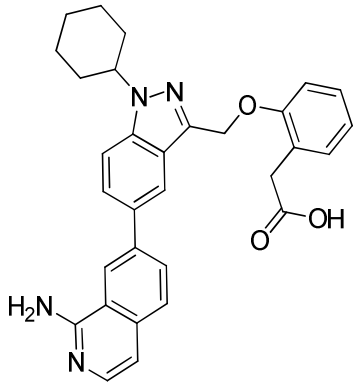
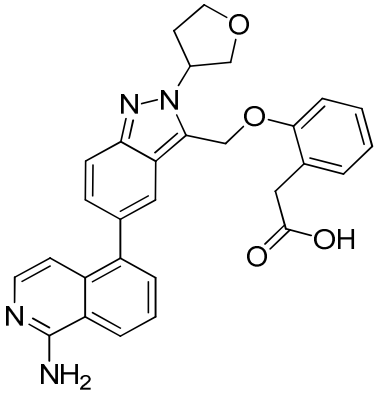
26. The compound of any one of claims 14-25, wherein R^A, independently for each occurrence, represents H, cyano, alkyl, optionally substituted alkoxy, optionally substituted heteroaryl, or –NH((cycloalkyl)alkyl).

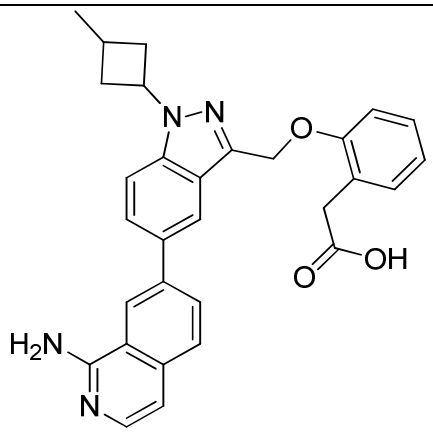
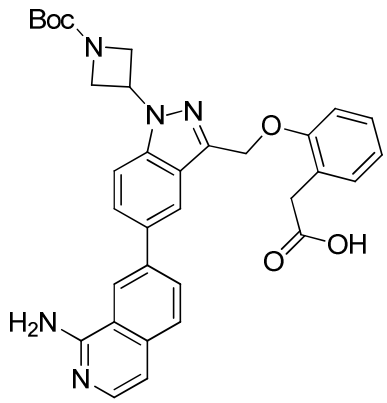
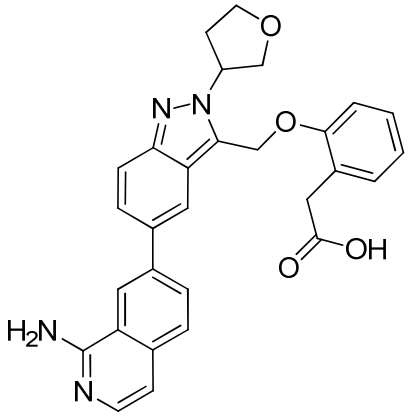
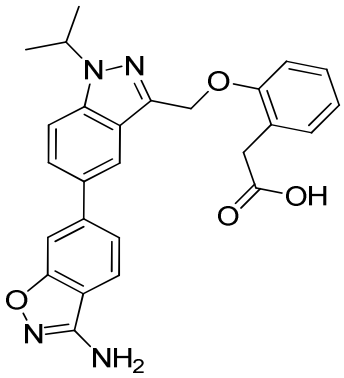
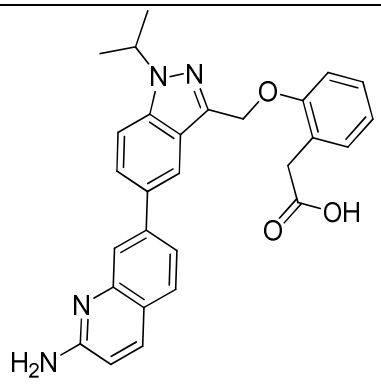
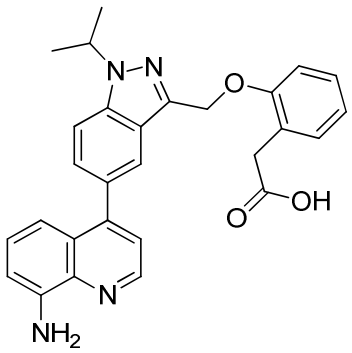
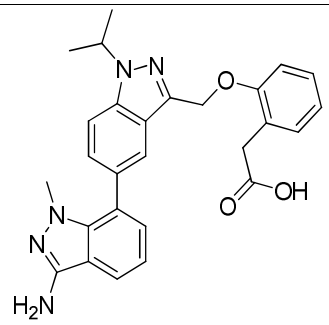
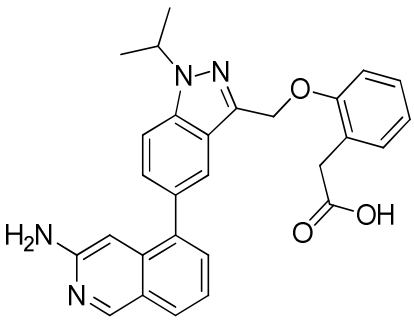
27. The compound of claim 14, selected from the following table:

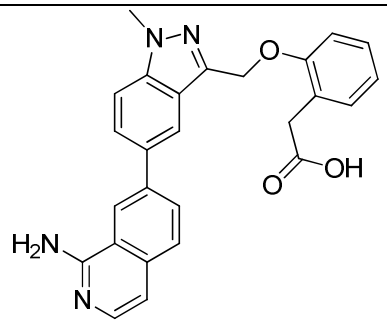
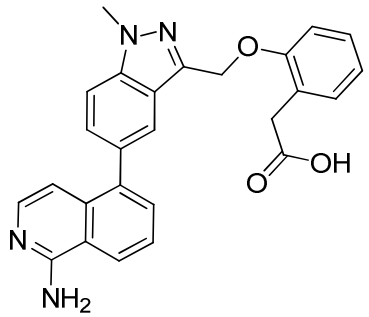
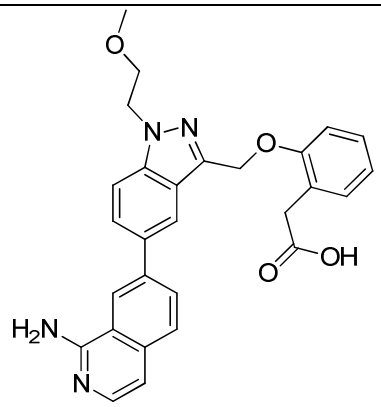
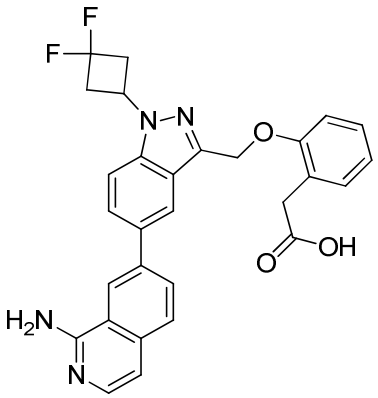
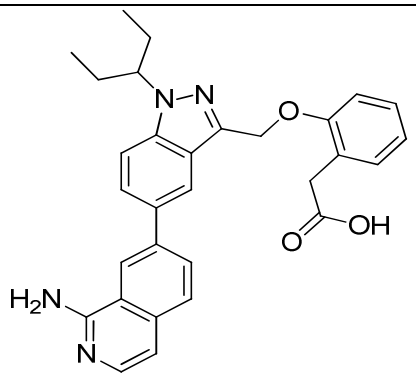
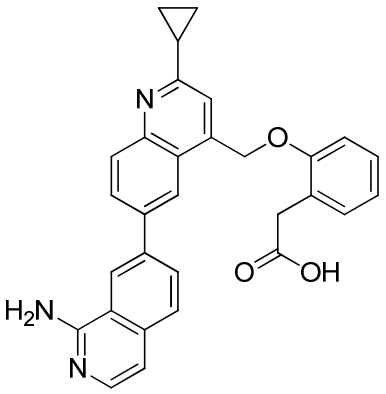
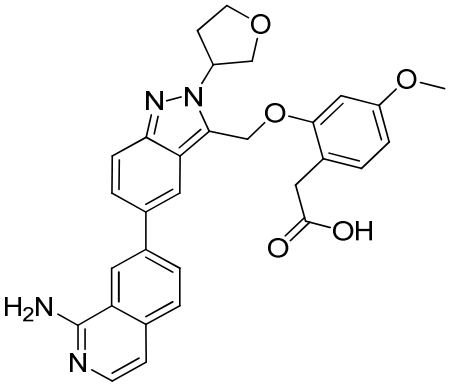
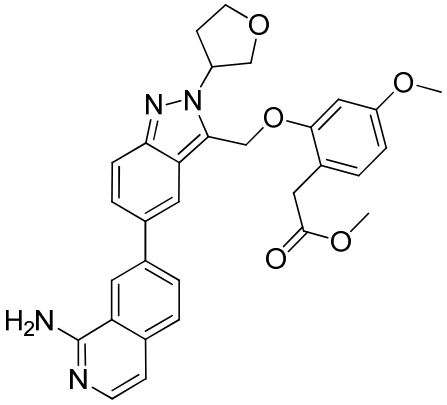
	
	

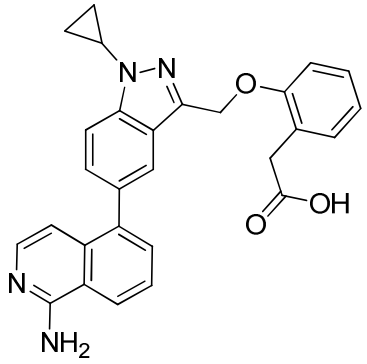
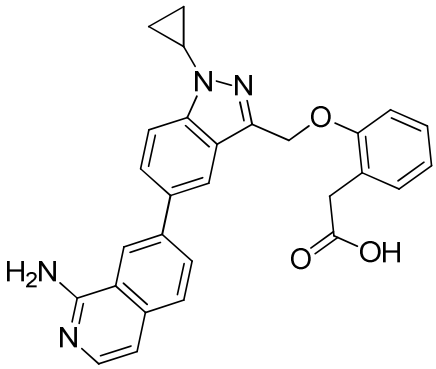
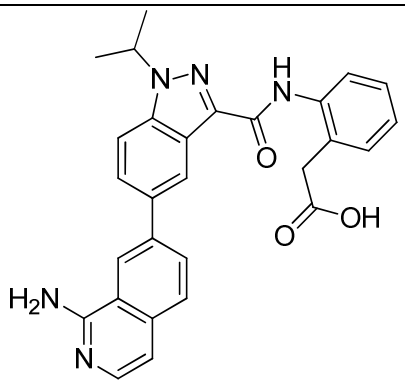
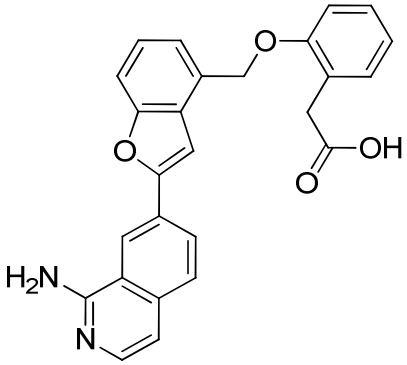
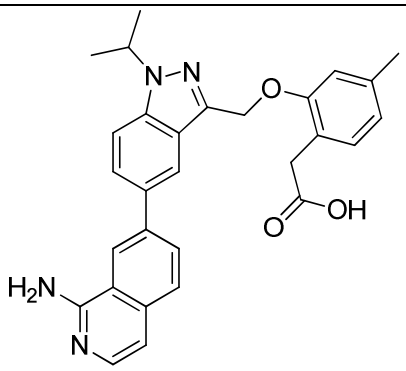
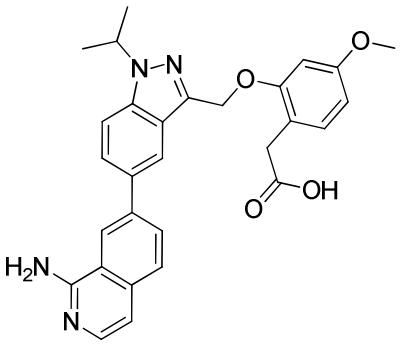
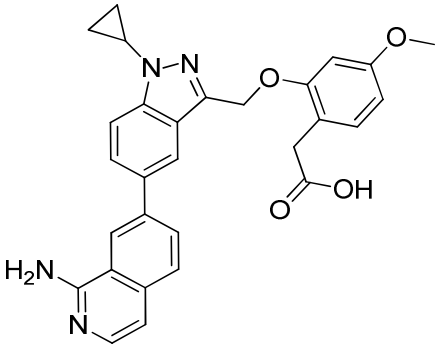
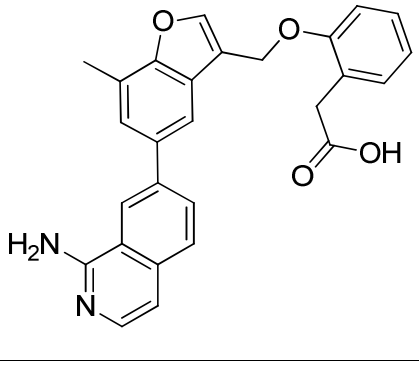
	
	
	
	

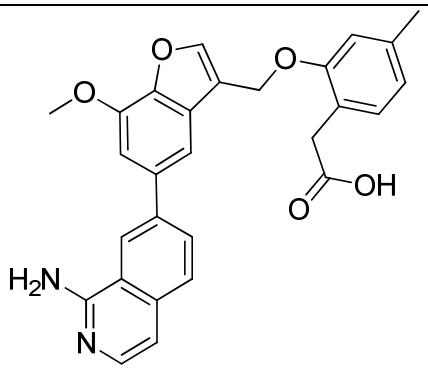
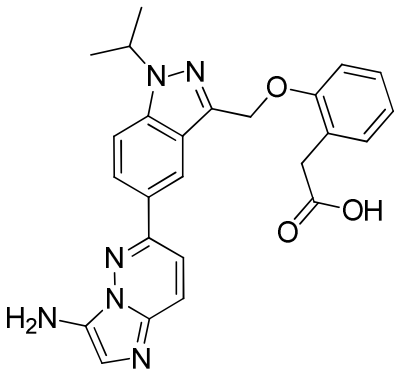
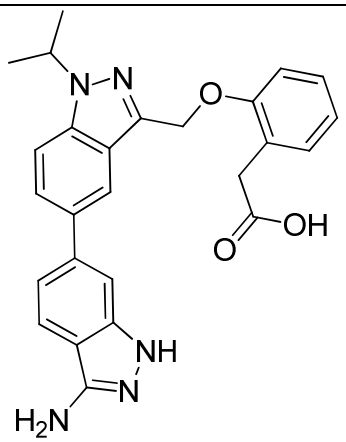
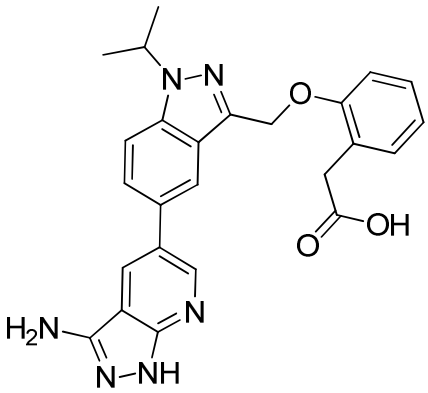
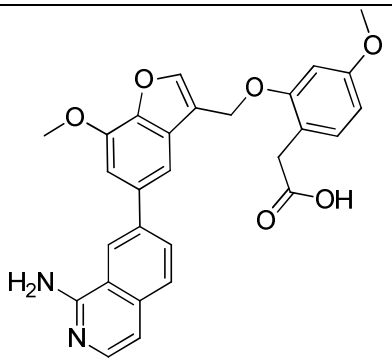
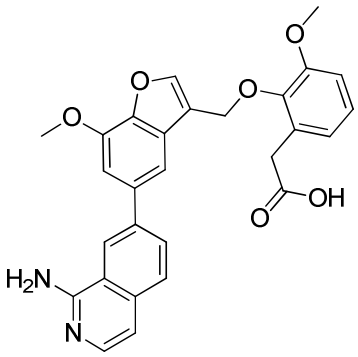
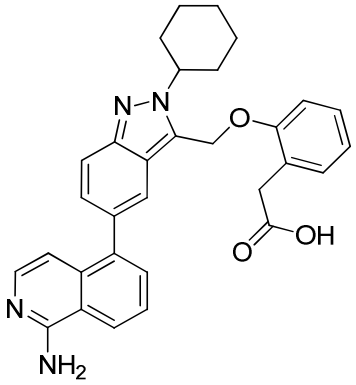
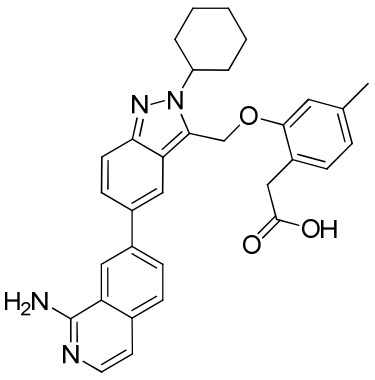
	
	
	

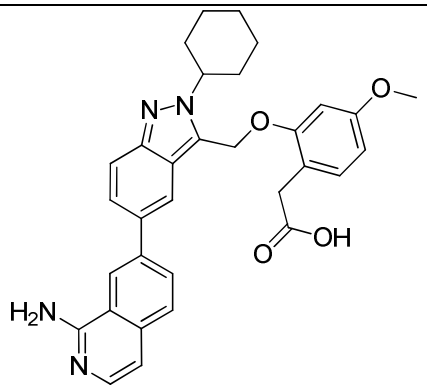
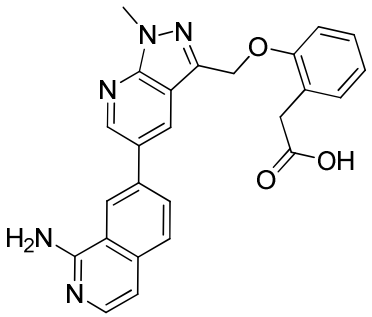
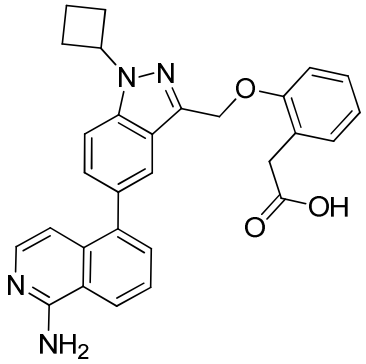
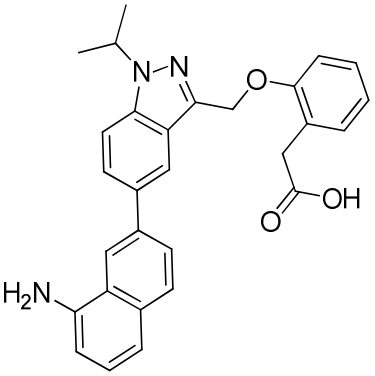
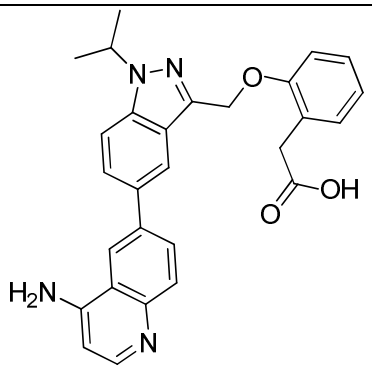
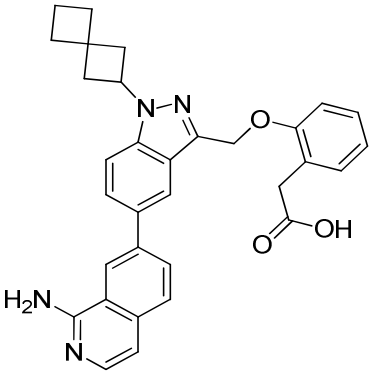
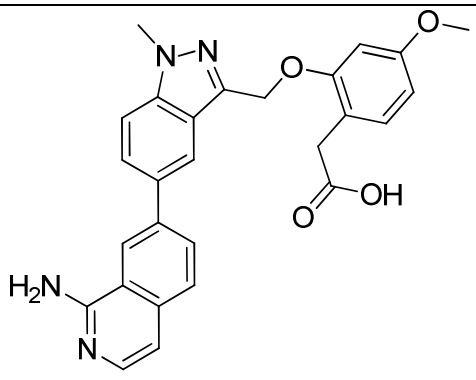
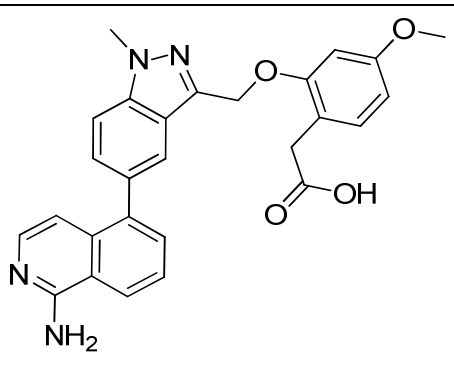
	
	
	

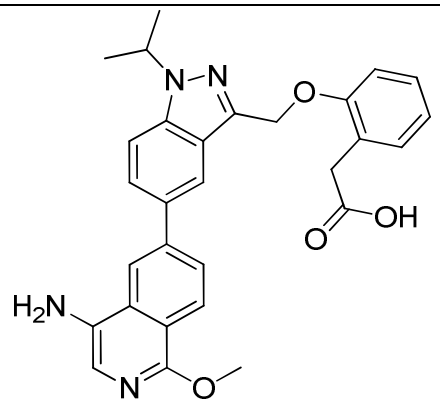
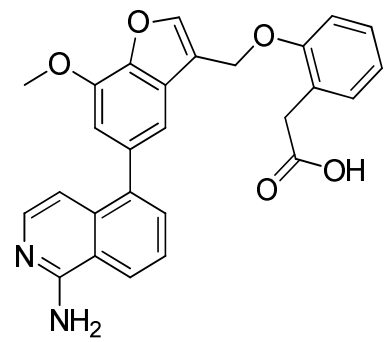
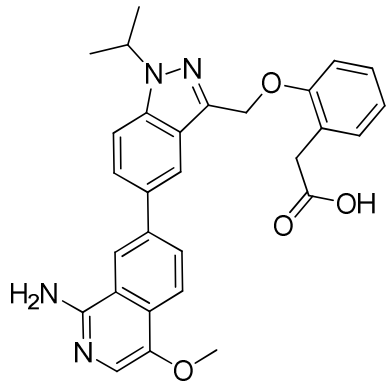
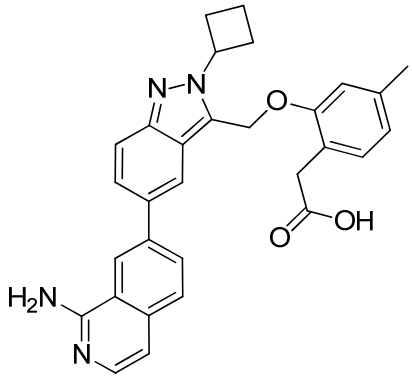
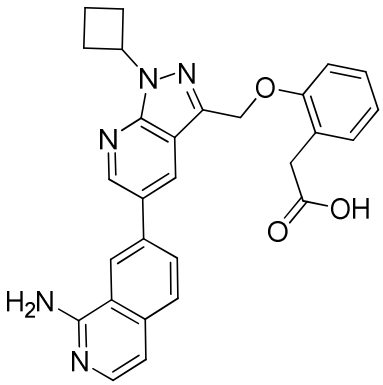
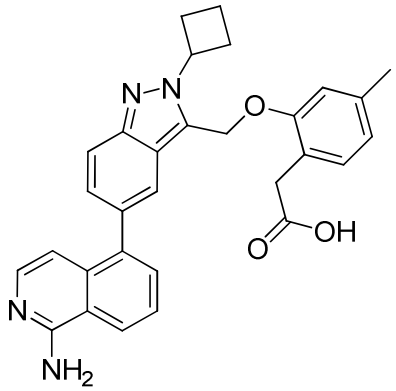
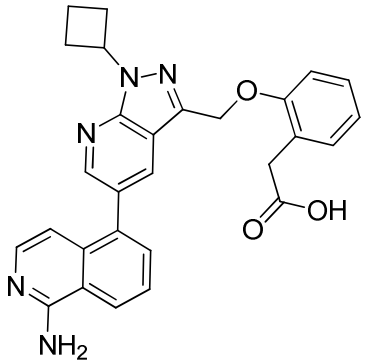
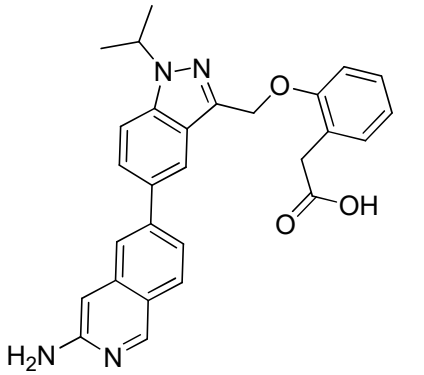
	
	
	
	

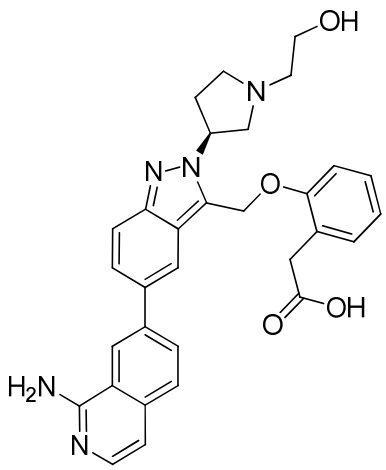
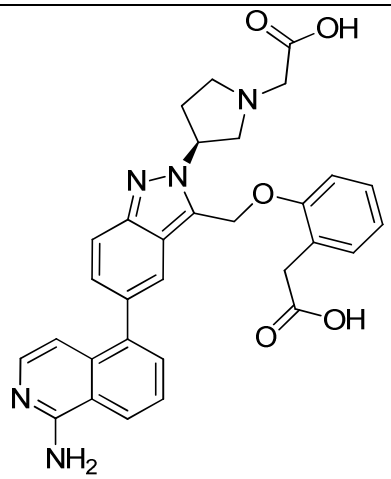
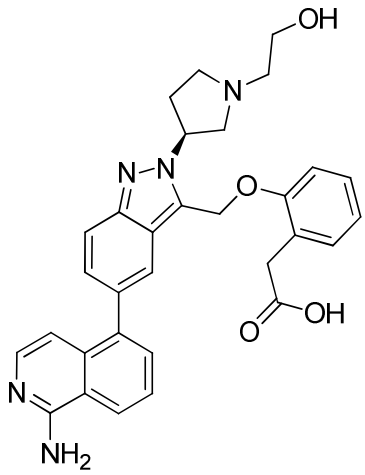
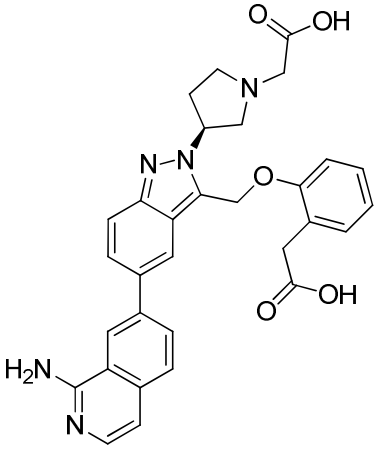
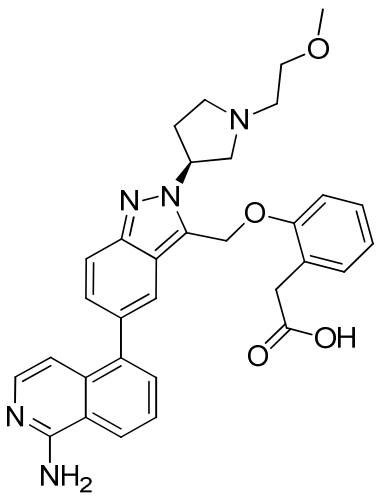
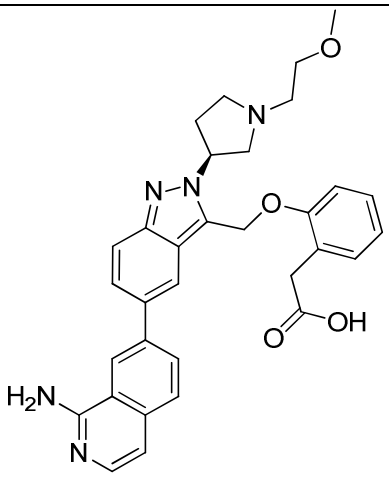
	
	
	
	

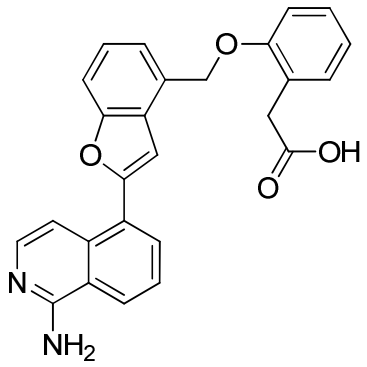
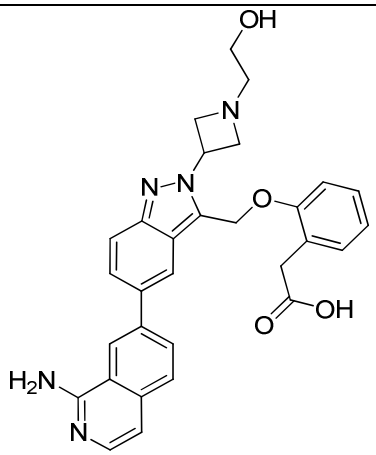
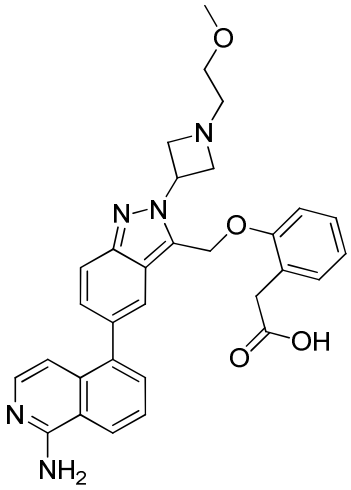
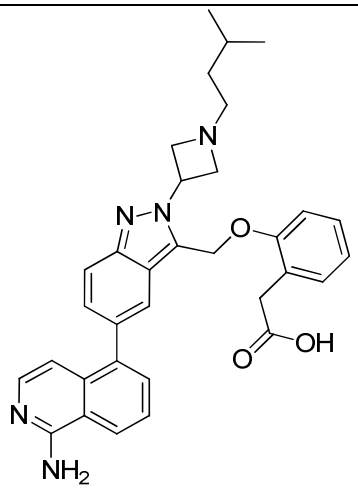
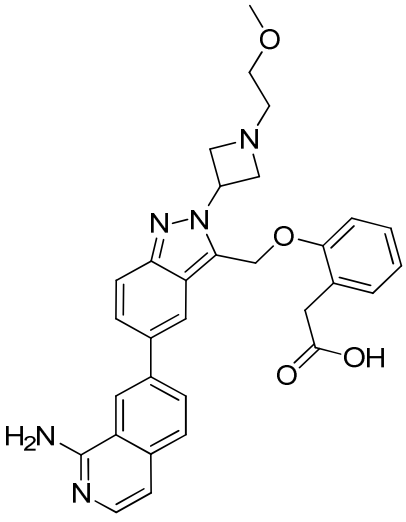
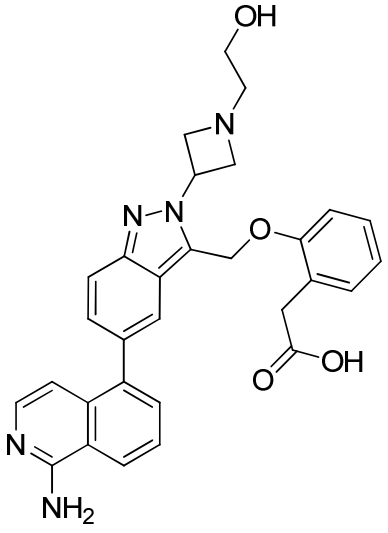
	
	
	
	

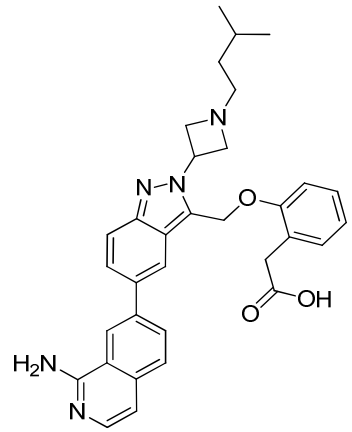
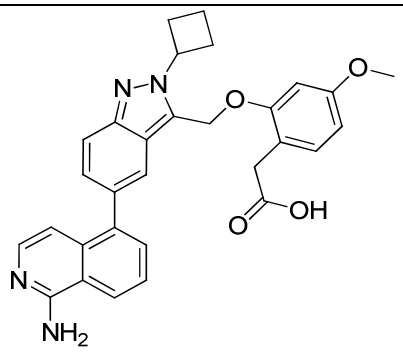
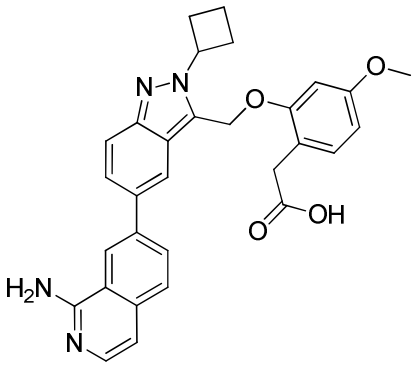
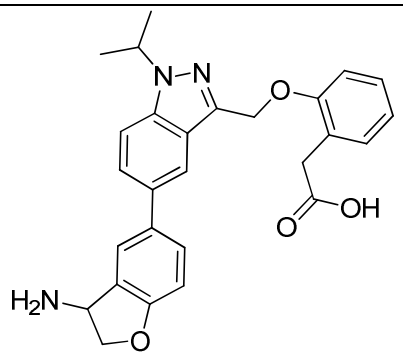
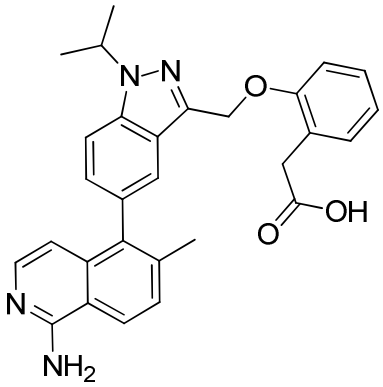
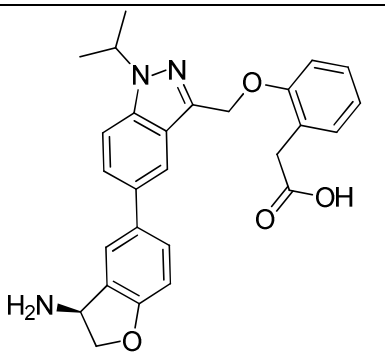
	
	
	
	

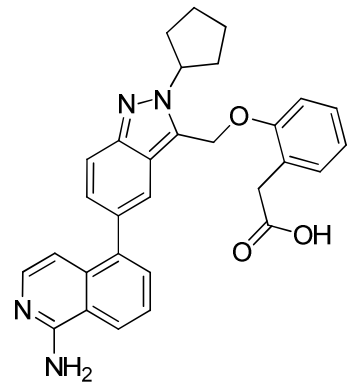
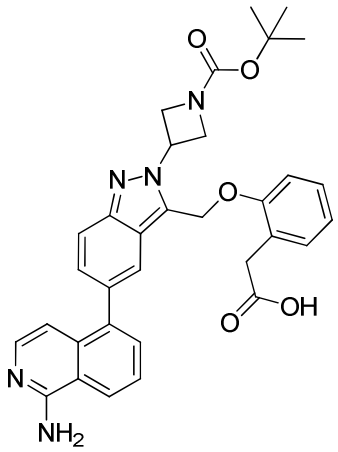
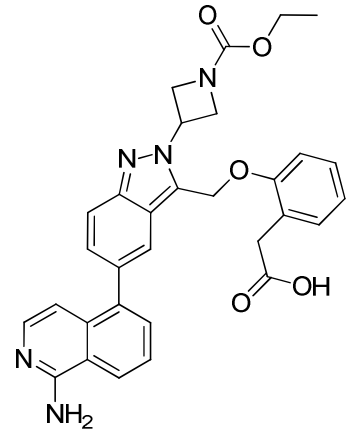
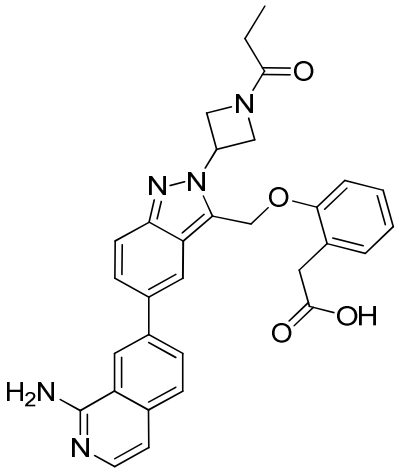
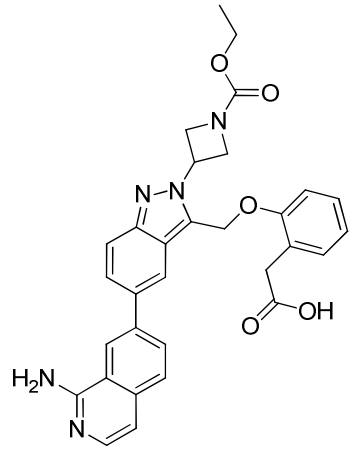
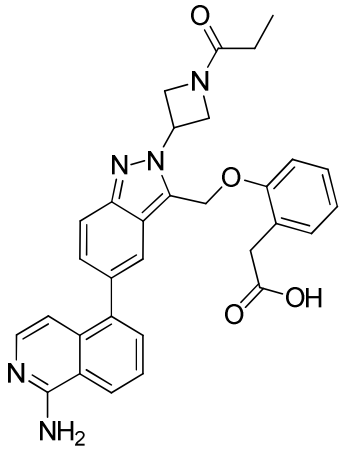
	
	
	
	

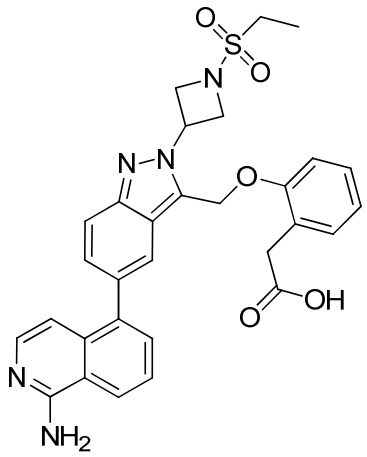
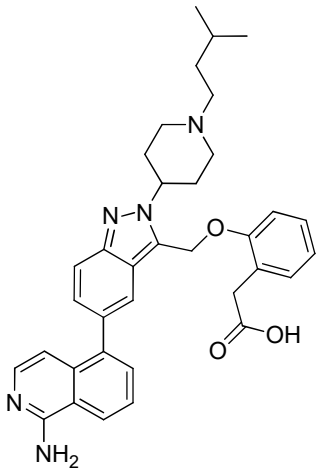
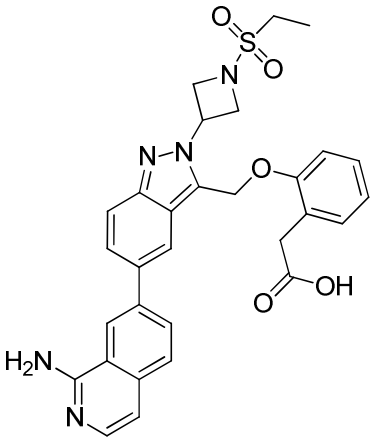
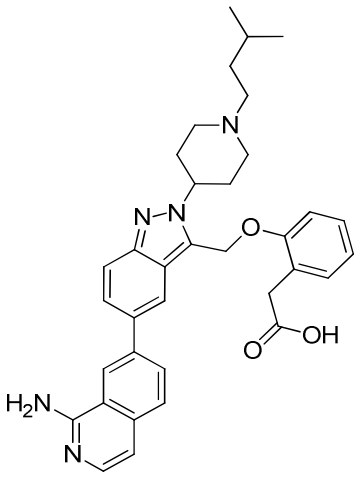
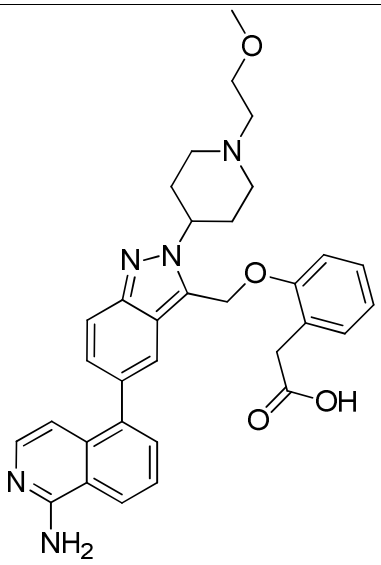
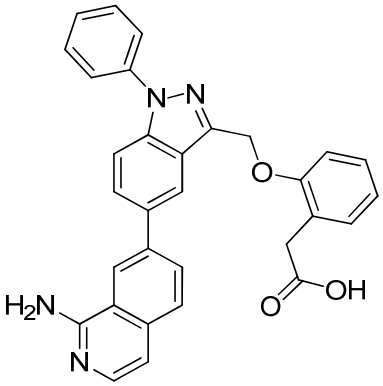
	
	
	
	

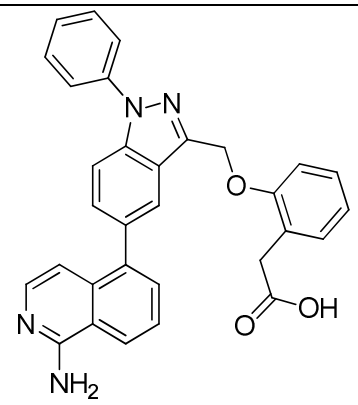
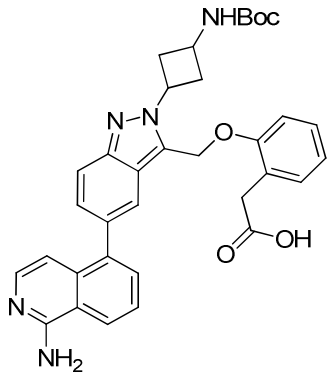
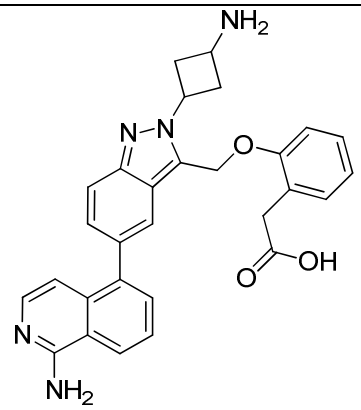
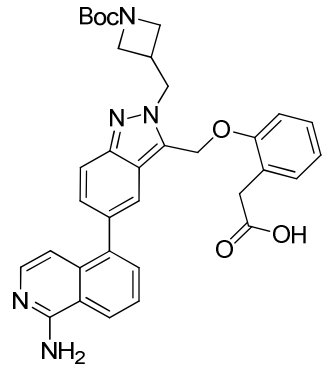
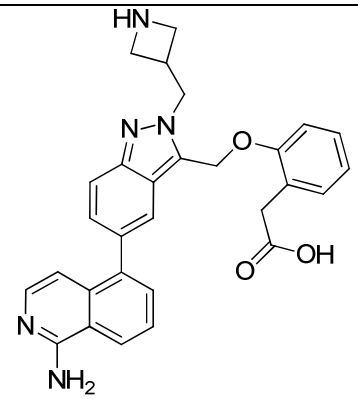
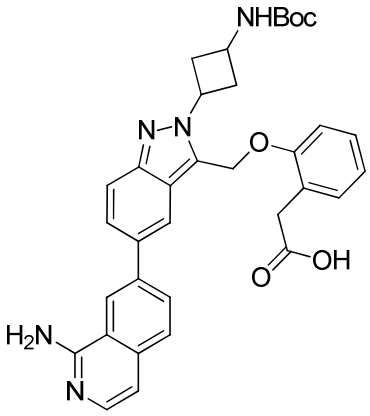
	
	
	

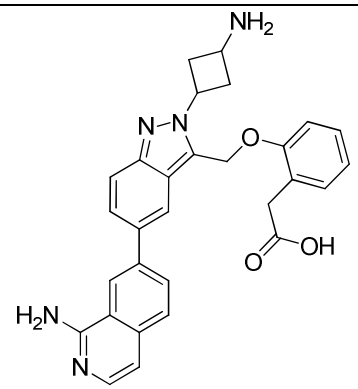
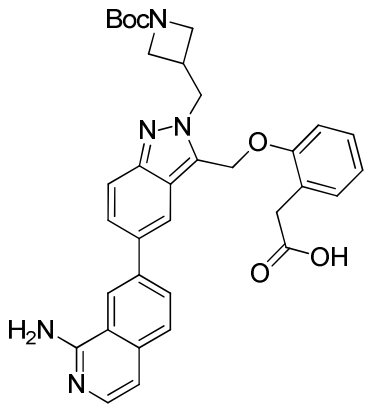
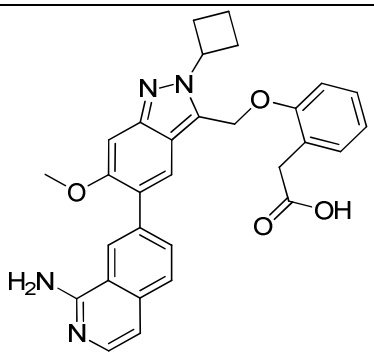
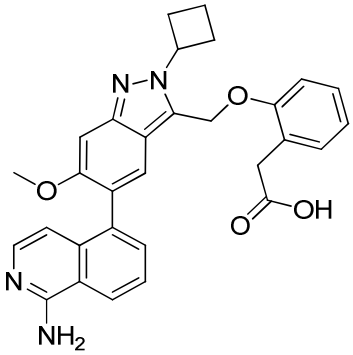
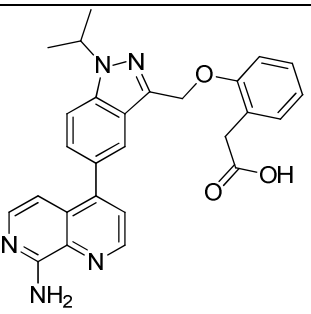
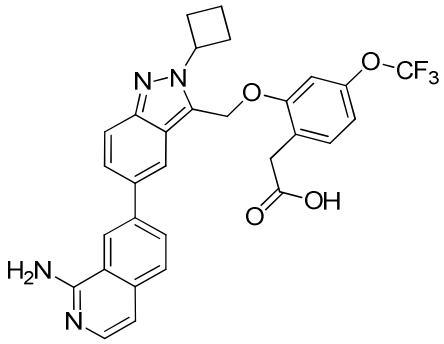
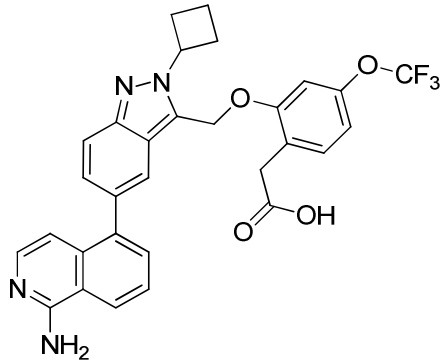
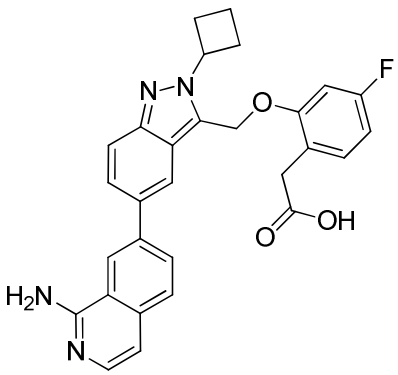
	
	
	

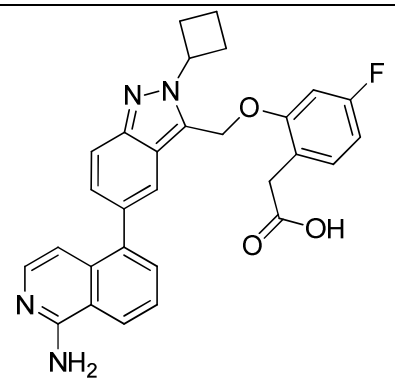
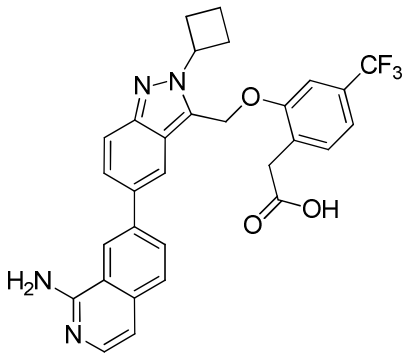
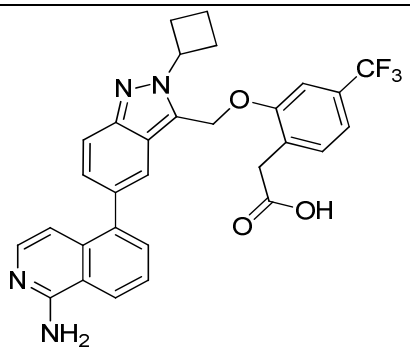
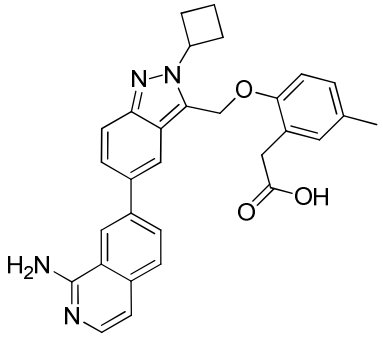
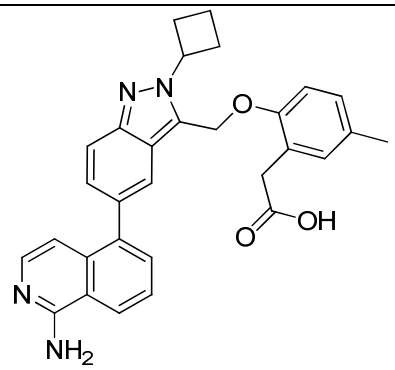
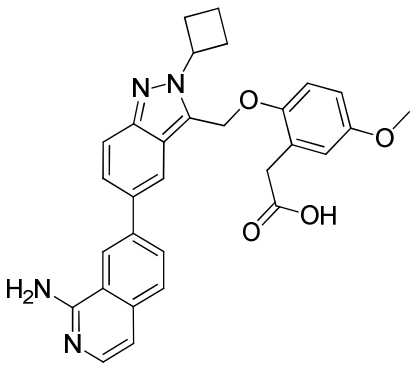
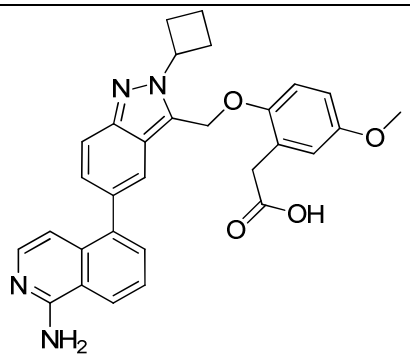
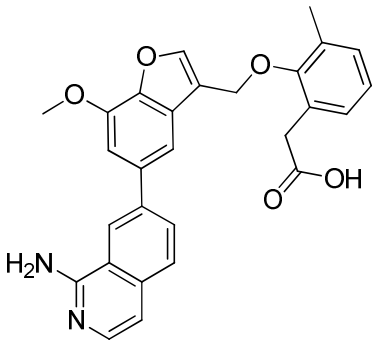
	
	
	

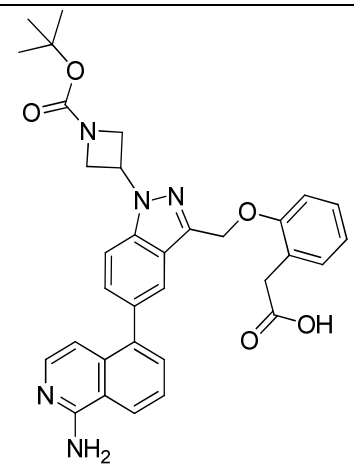
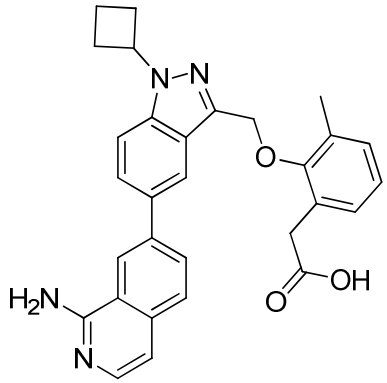
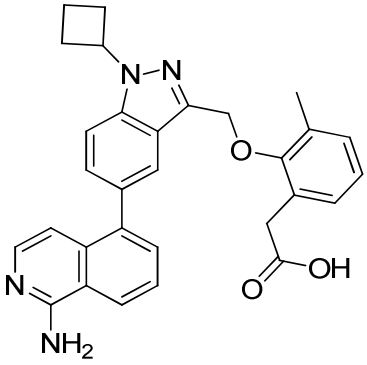
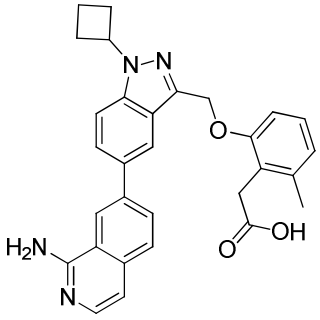
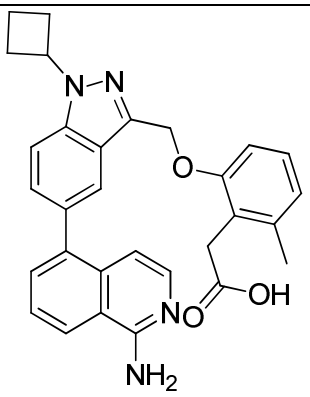
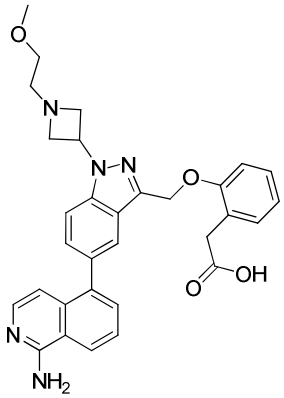
	
	
	

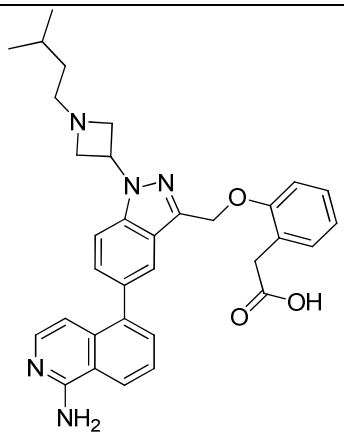
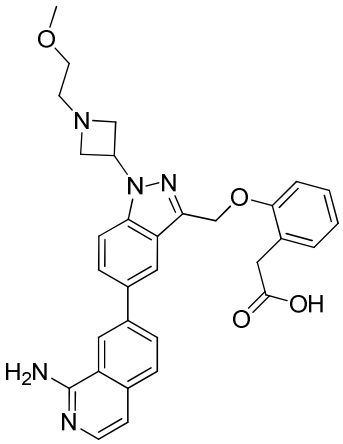
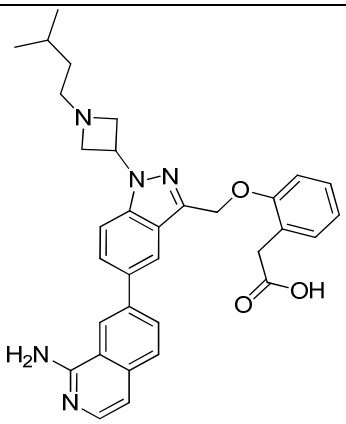
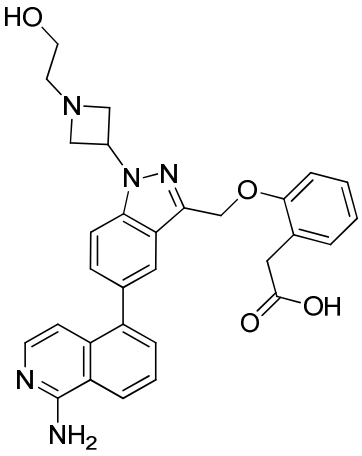
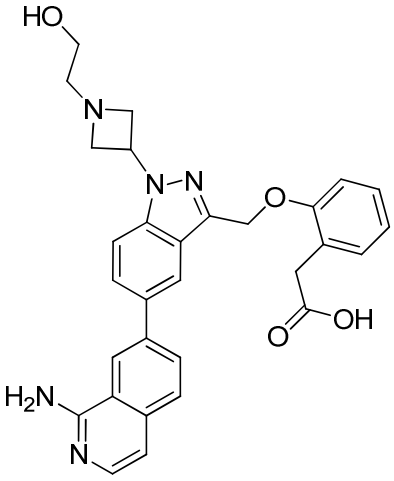
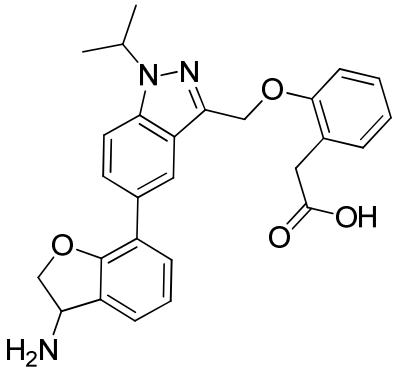
	
	
	

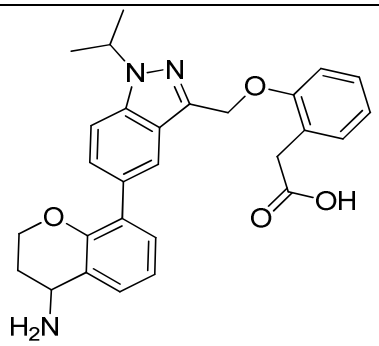
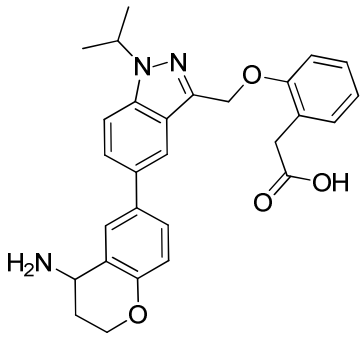
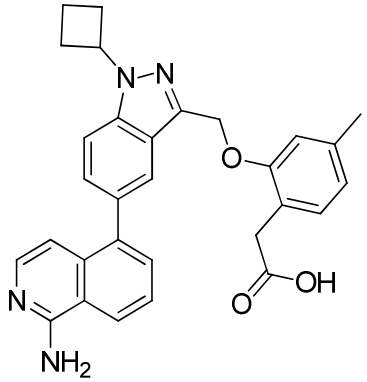
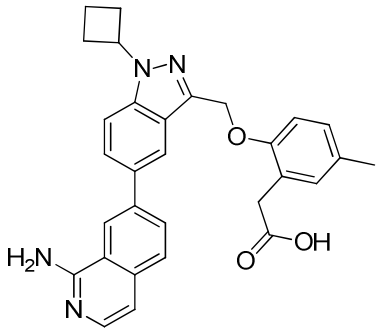
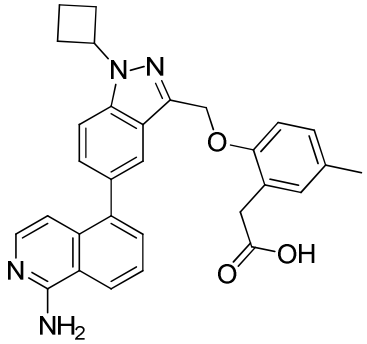
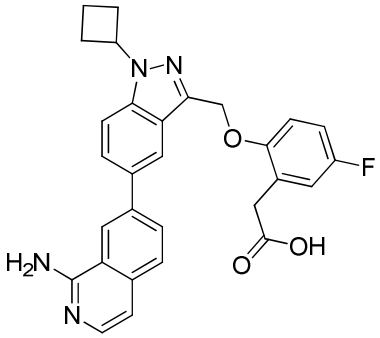
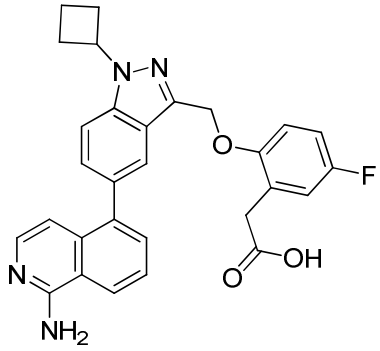
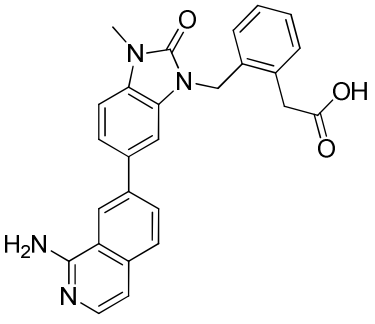
	
	
	

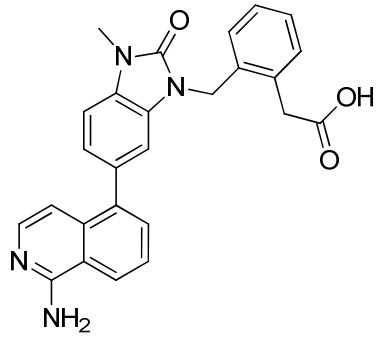
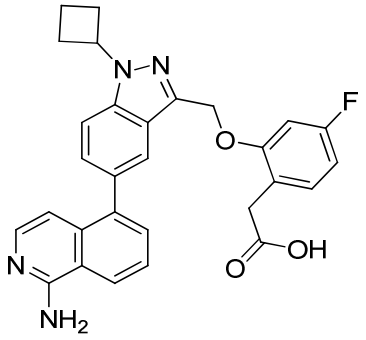
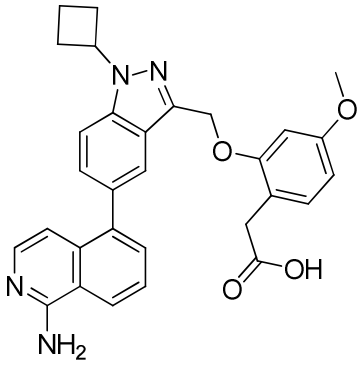
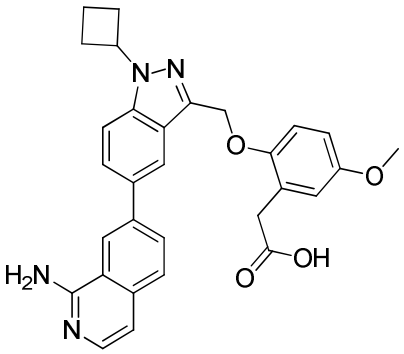
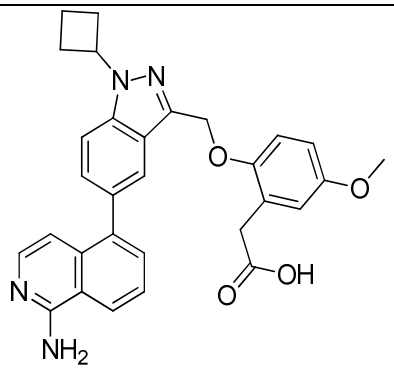
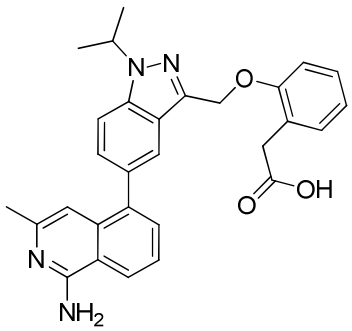
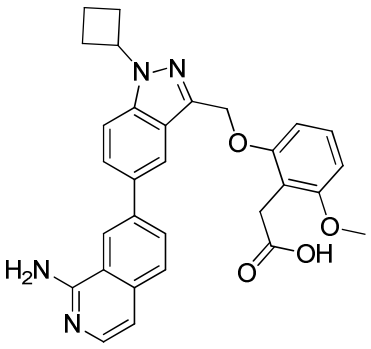
	
	
	
	

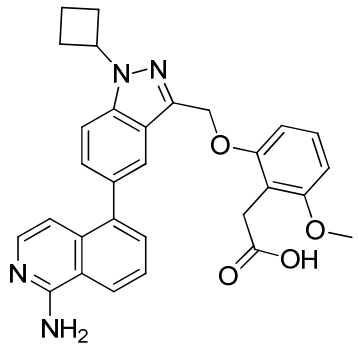
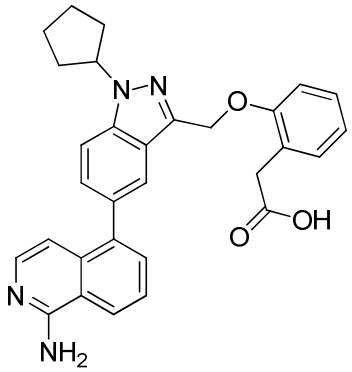
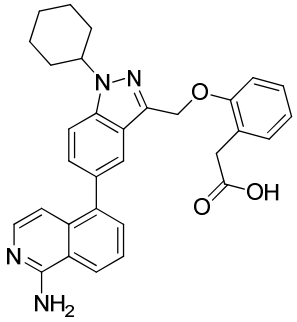
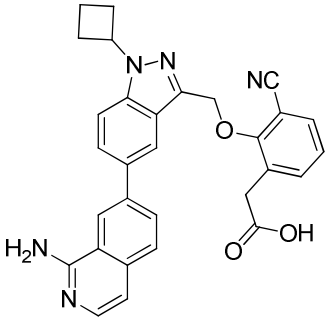
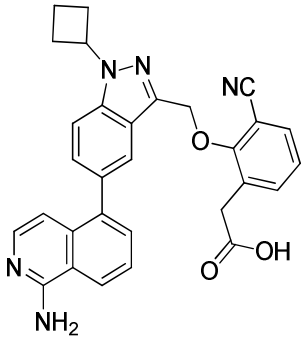
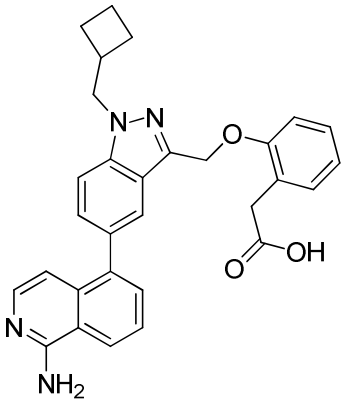
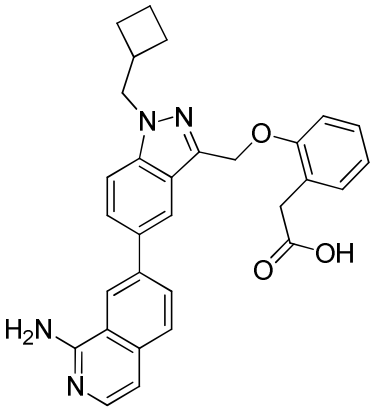
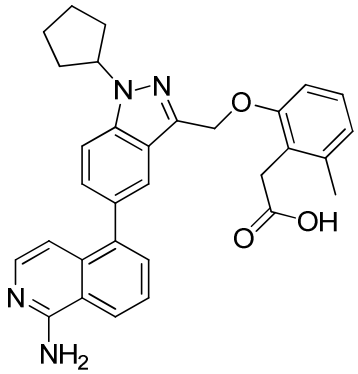
	
	
	
	

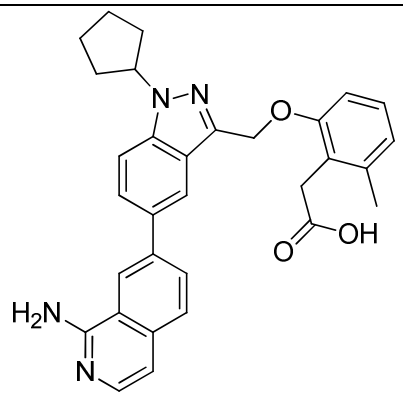
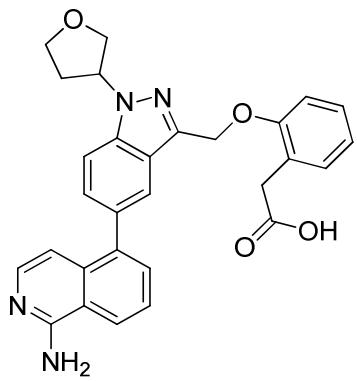
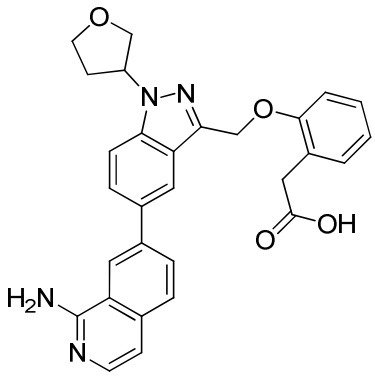
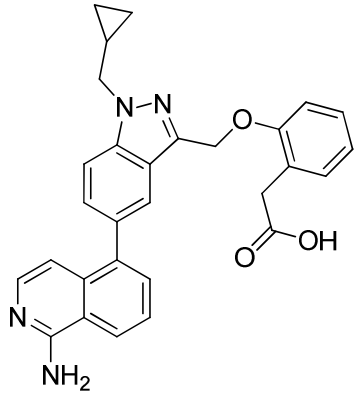
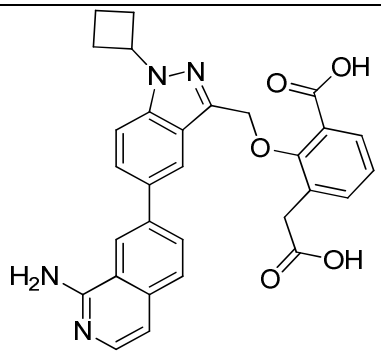
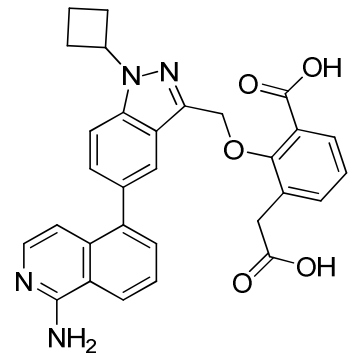
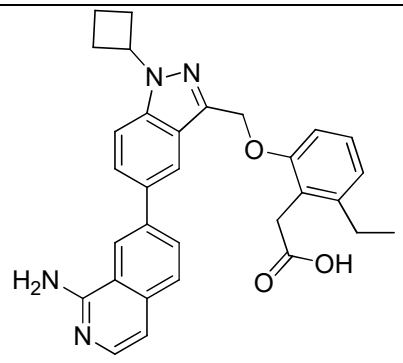
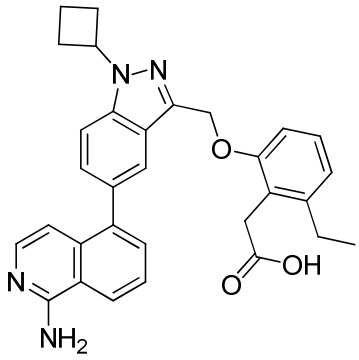
	
	
	

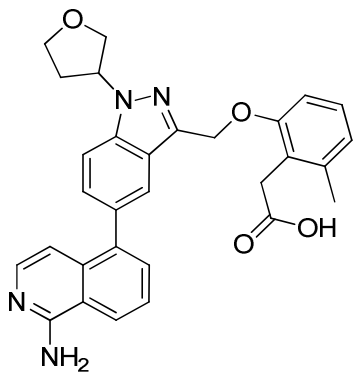
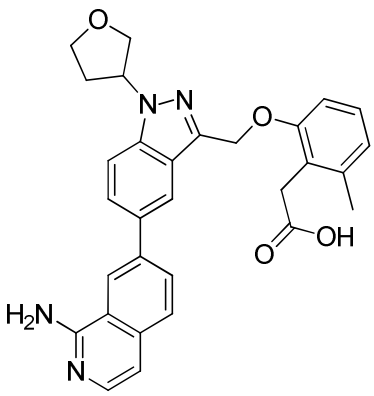
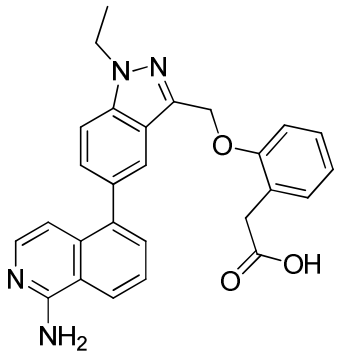
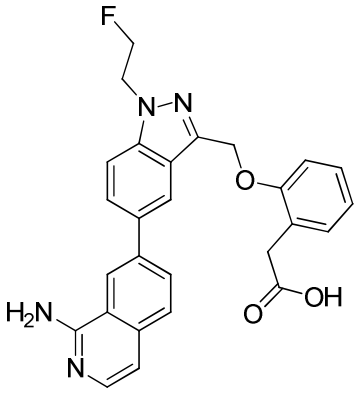
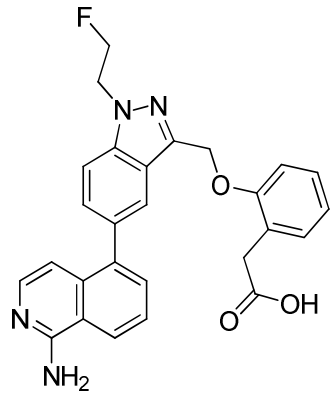
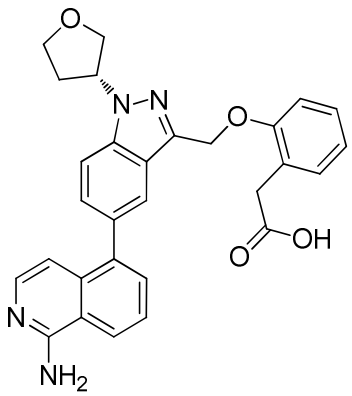
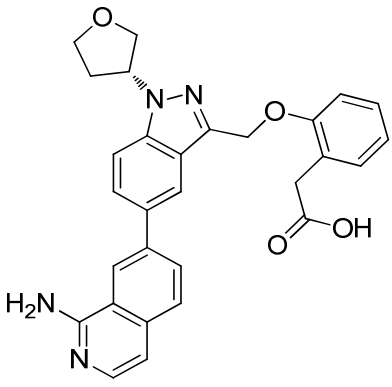
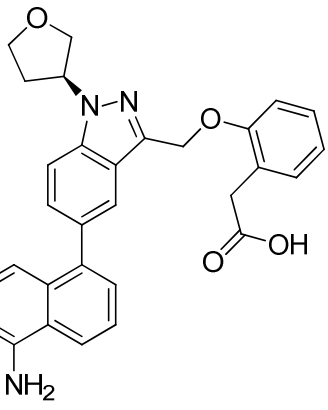
	
	
	

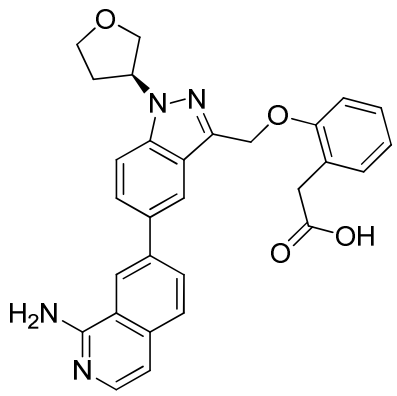
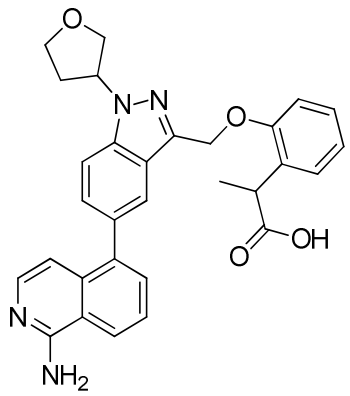
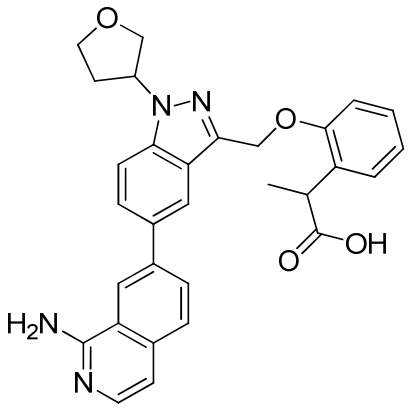
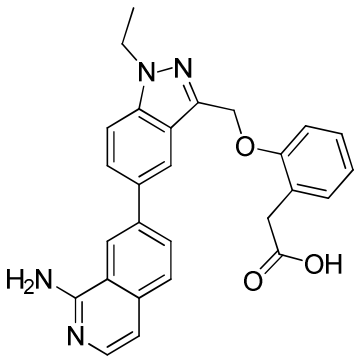
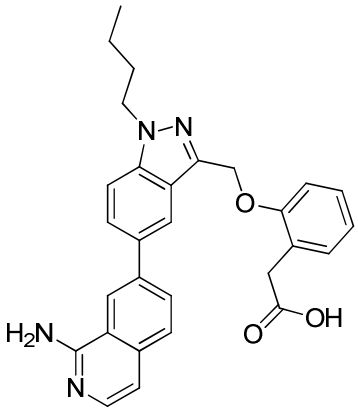
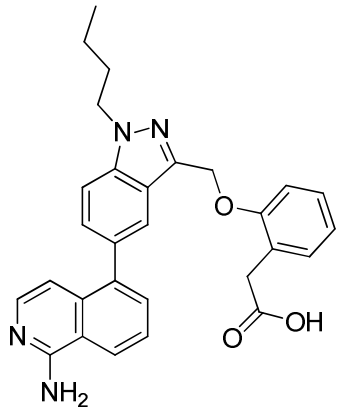
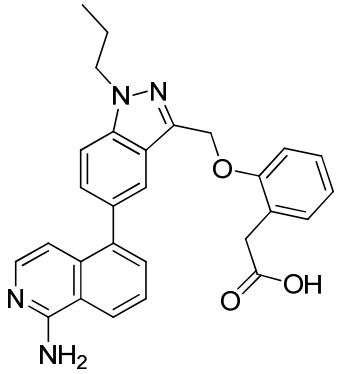
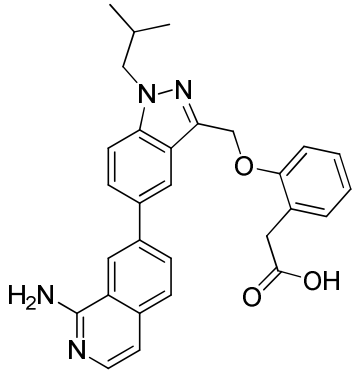
	
	
	
	

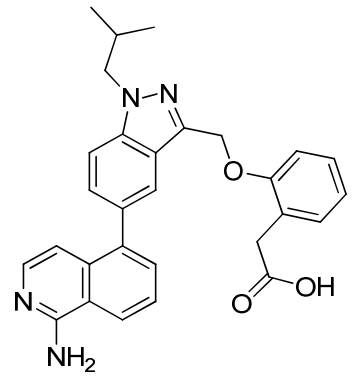
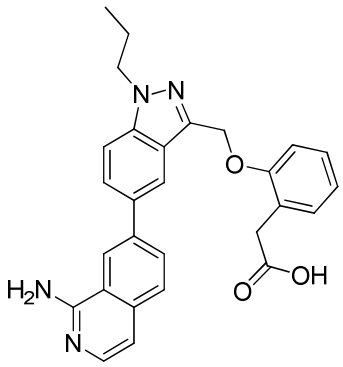
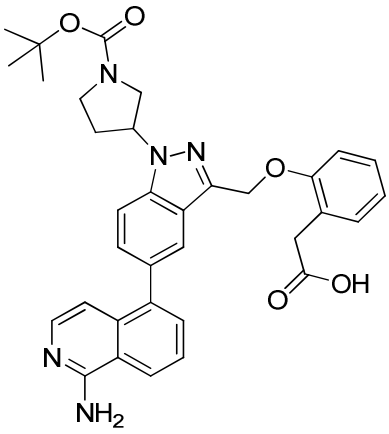
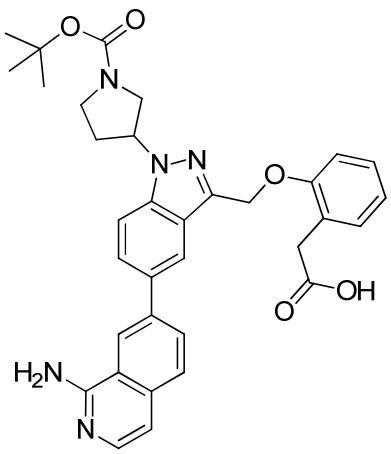
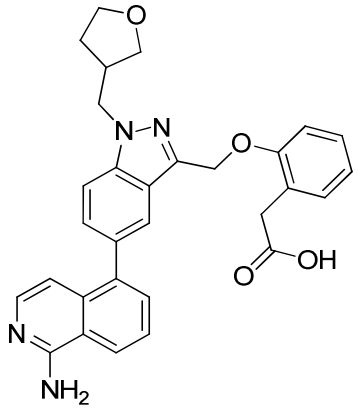
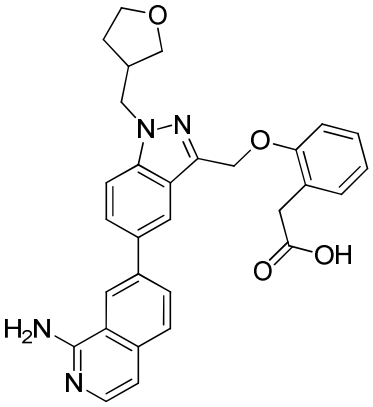
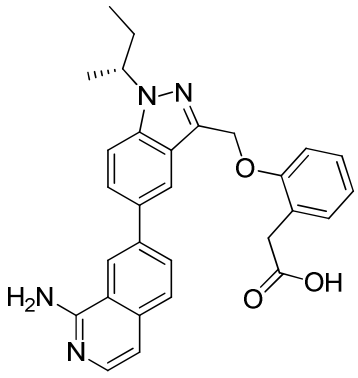
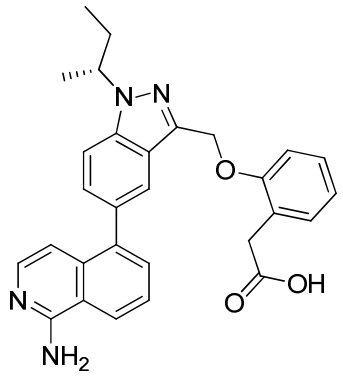
	
	
	
	

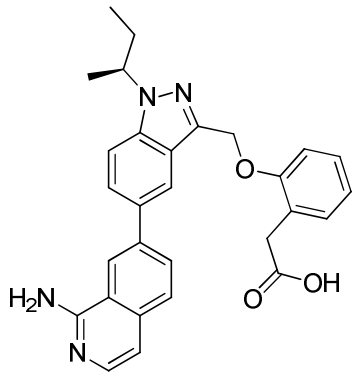
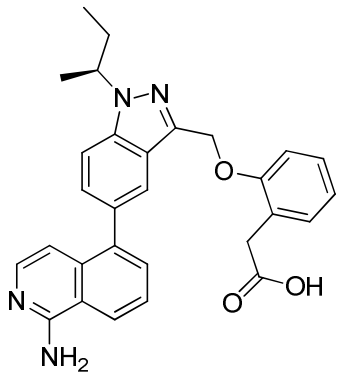
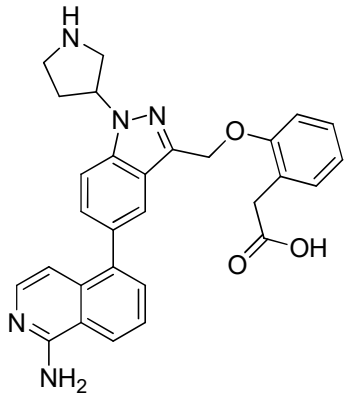
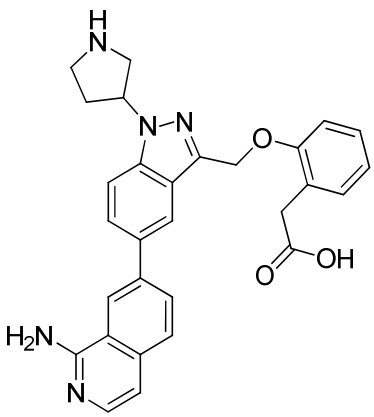
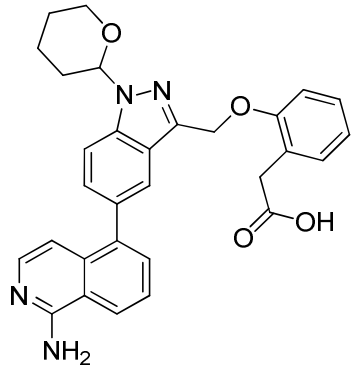
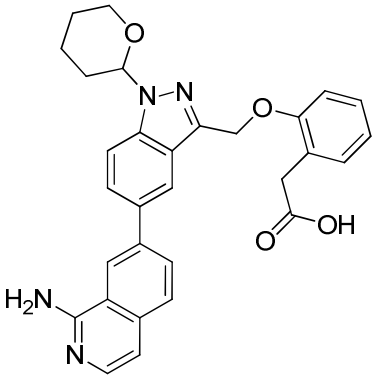
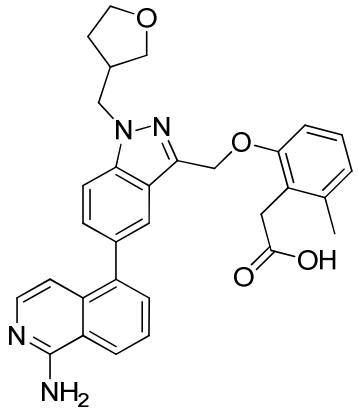
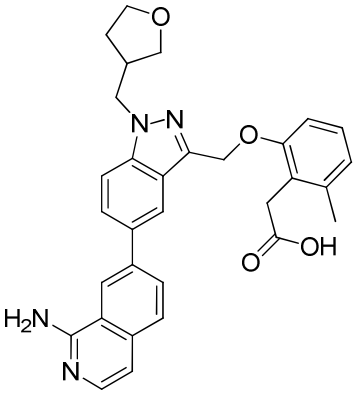
	
	
	
	

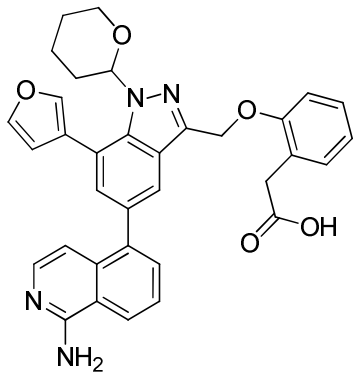
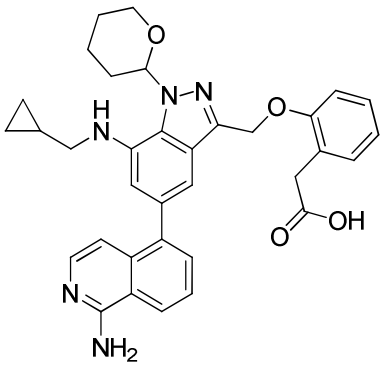
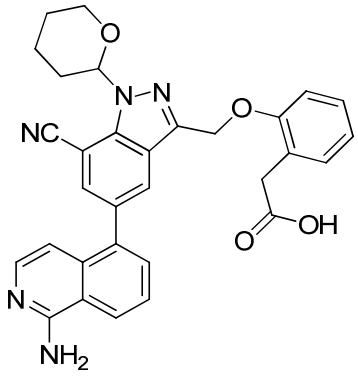
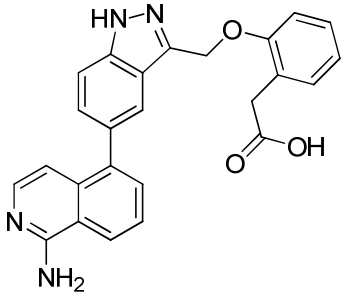
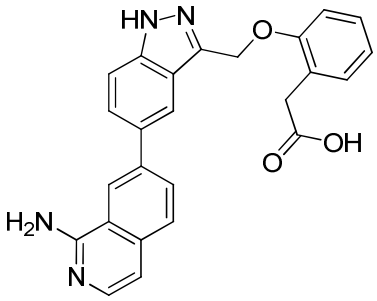
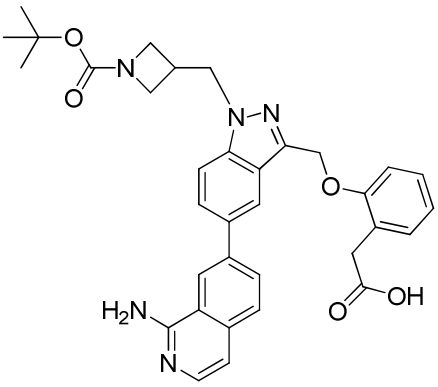
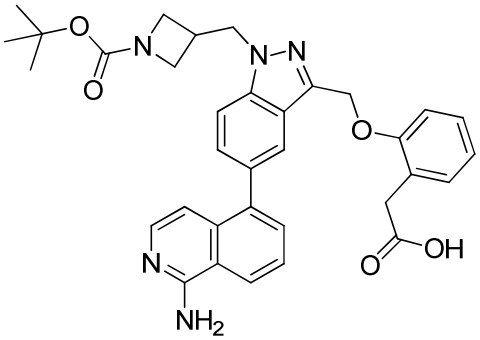
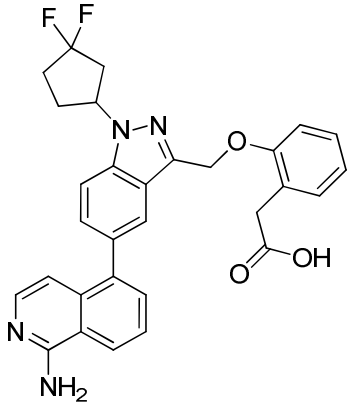
	
	
	
	

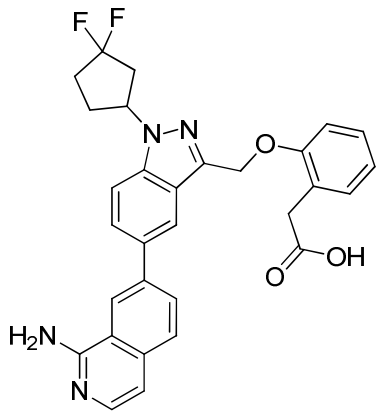
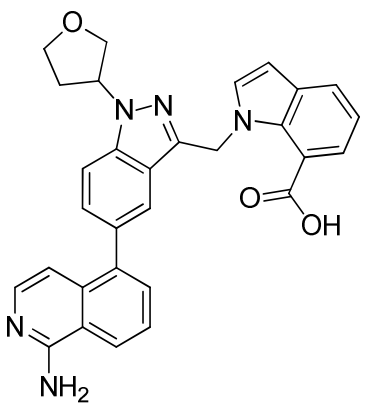
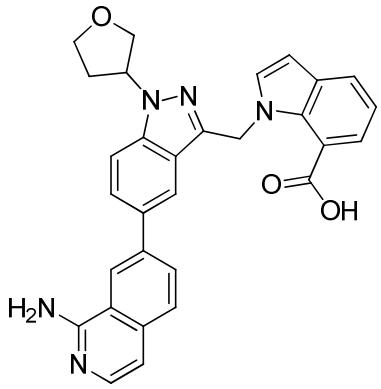
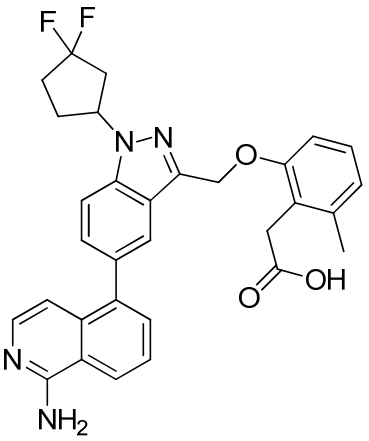
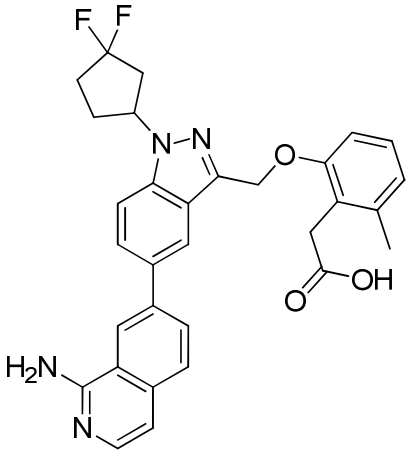
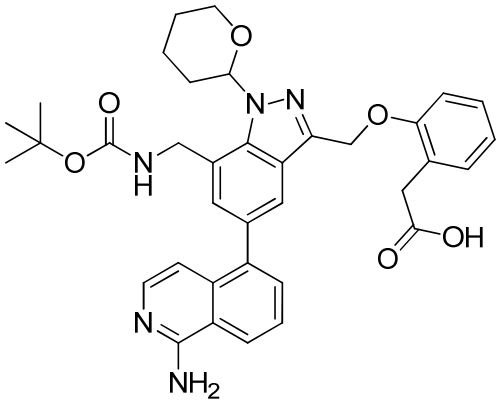
	
	
	
	

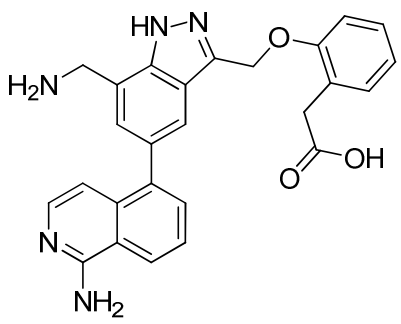
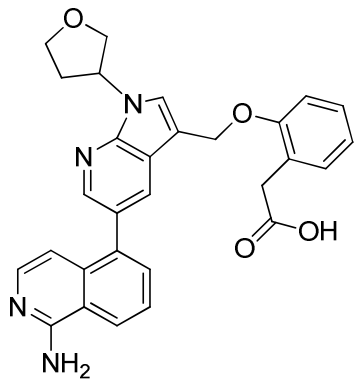
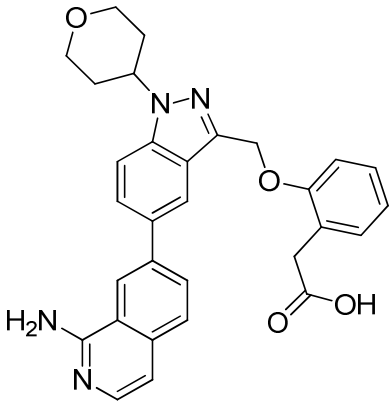
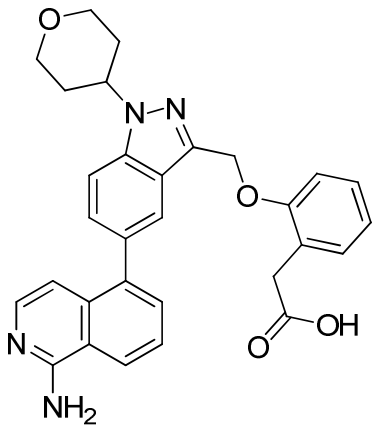
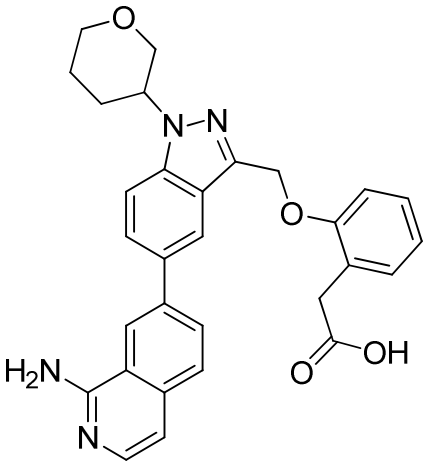
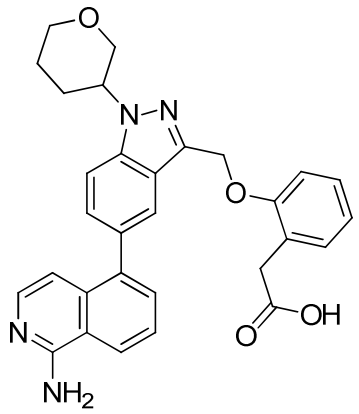
	
	
	
	

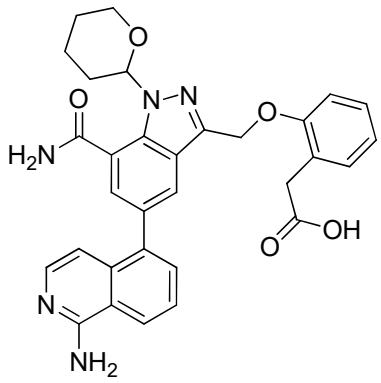
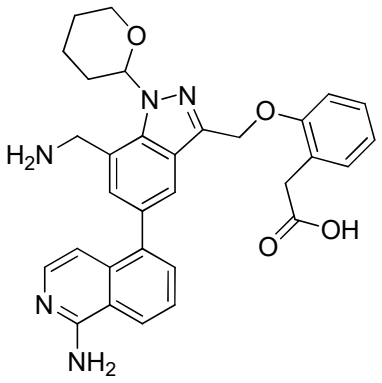
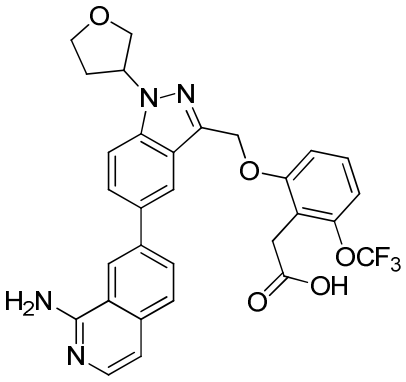
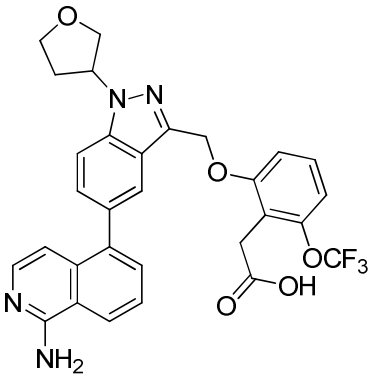
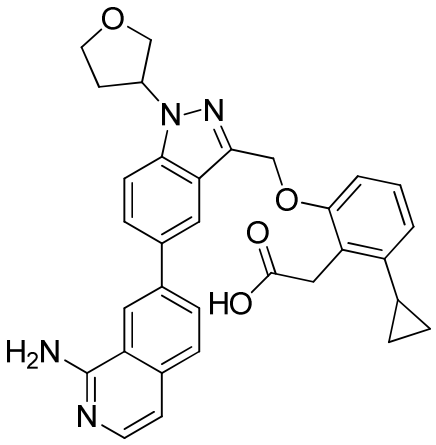
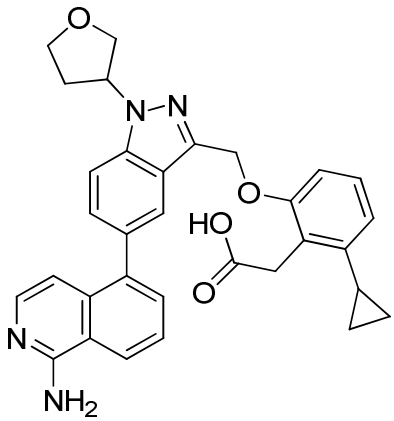
	
	
	
	

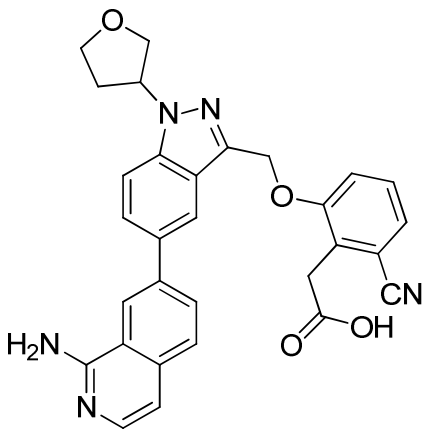
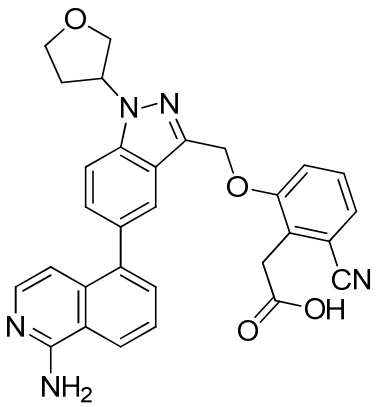
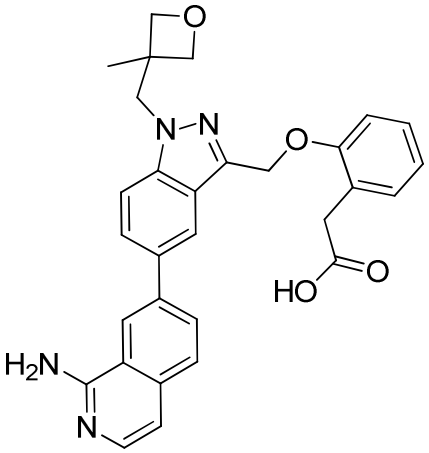
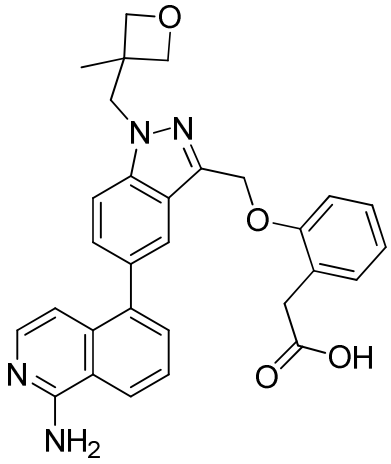
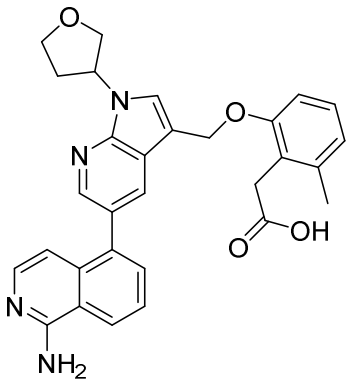
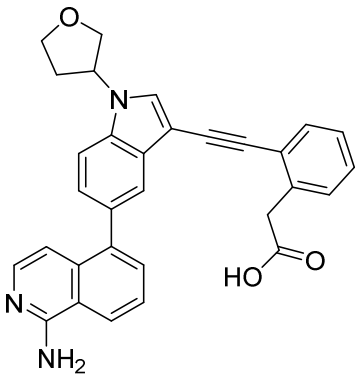
	
	
	
	

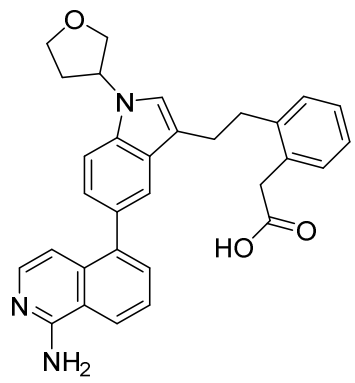
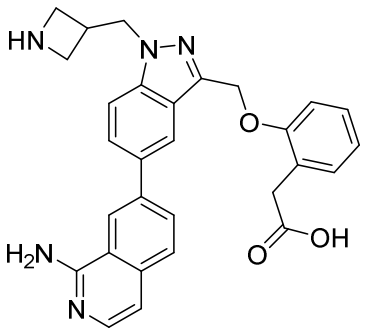
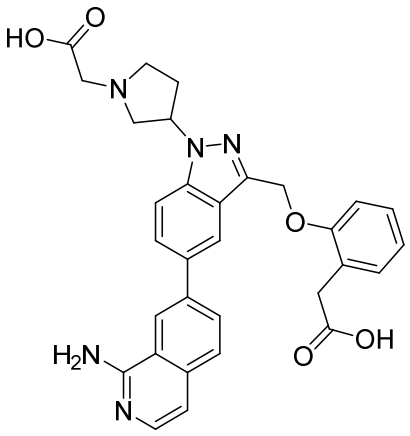
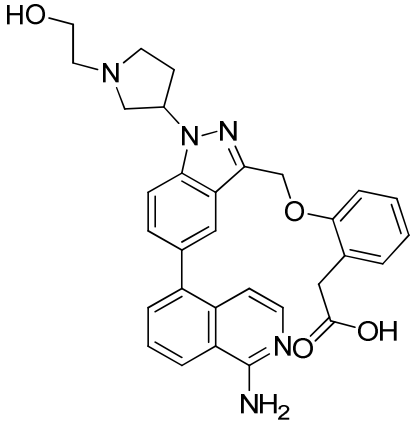
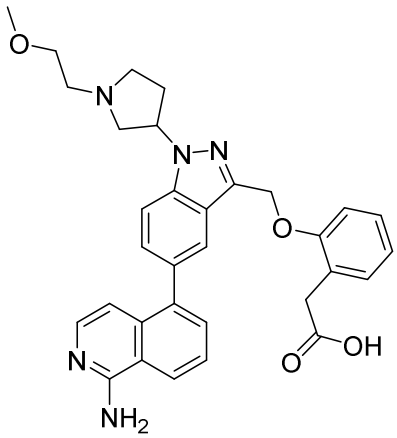
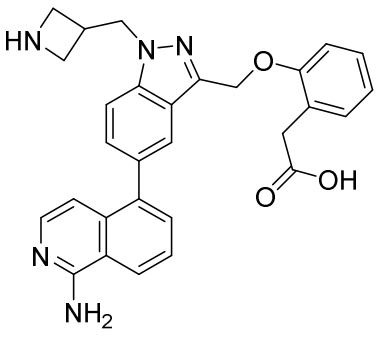
	
	
	
	

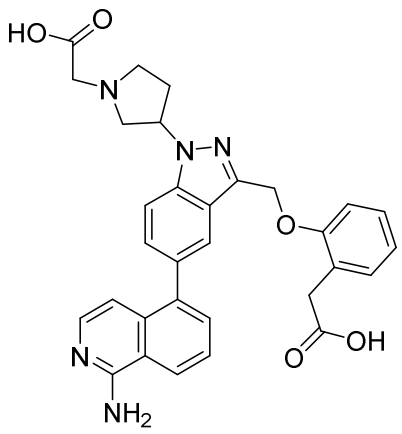
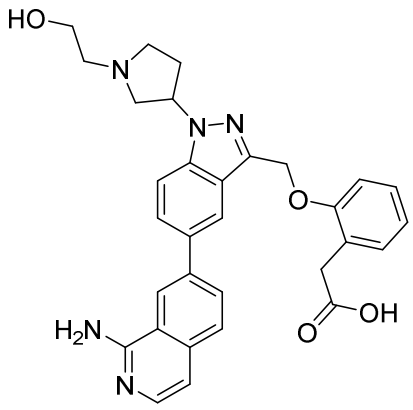
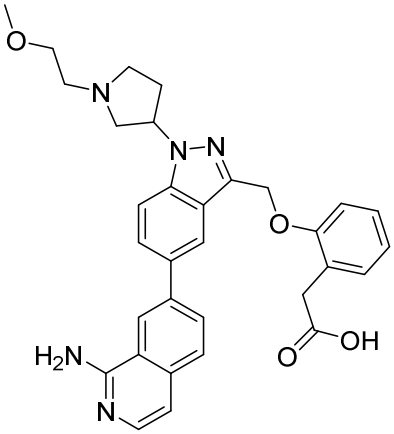
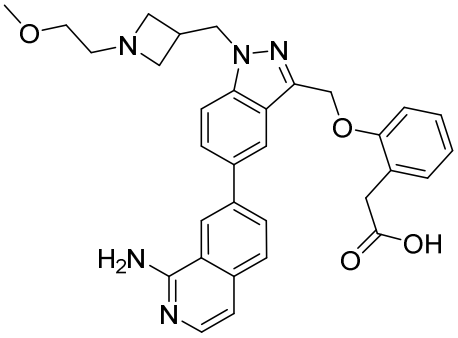
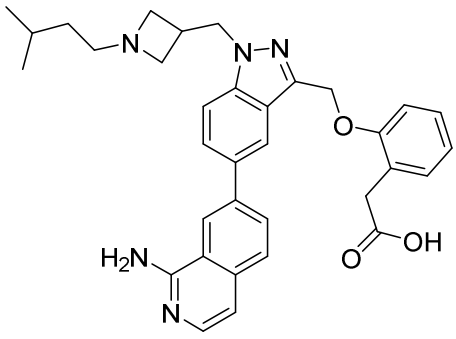
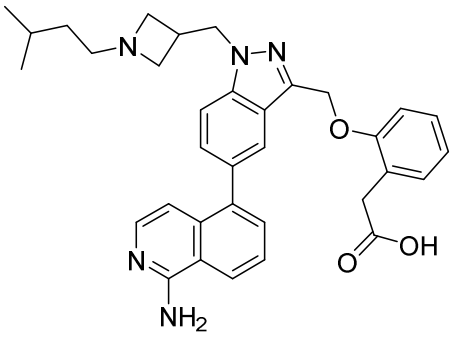
	
	
	

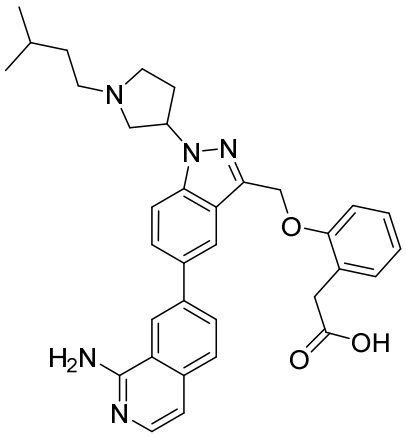
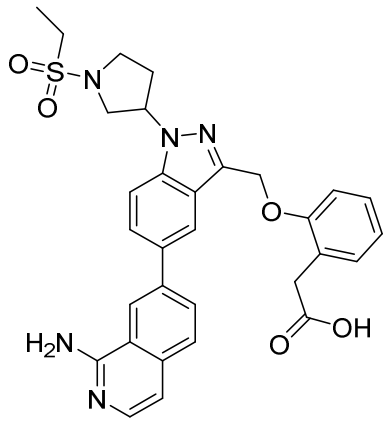
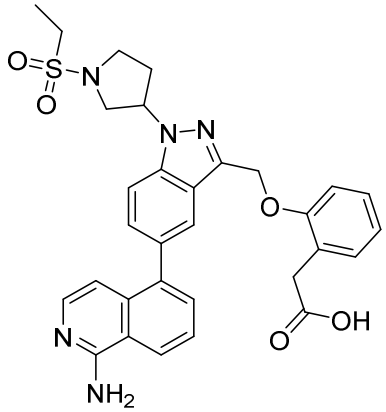
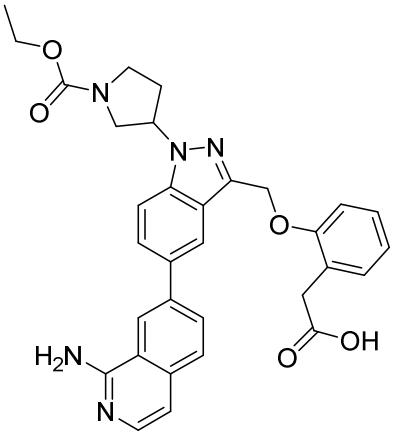
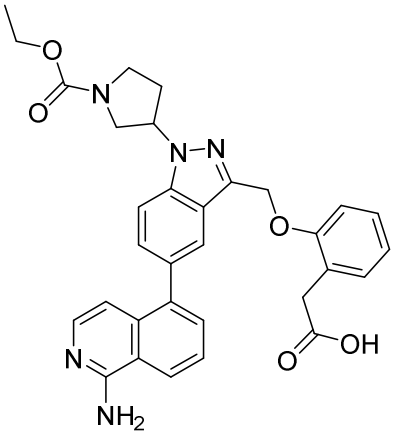
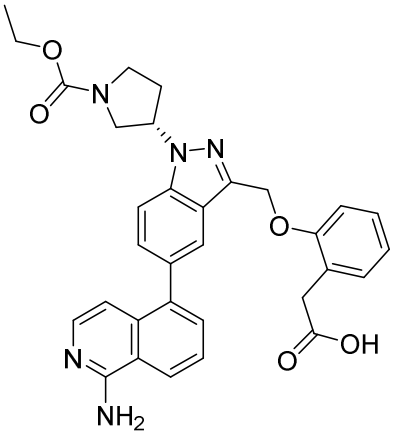
	
	
	

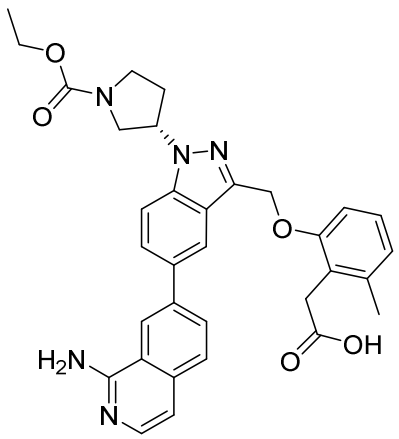
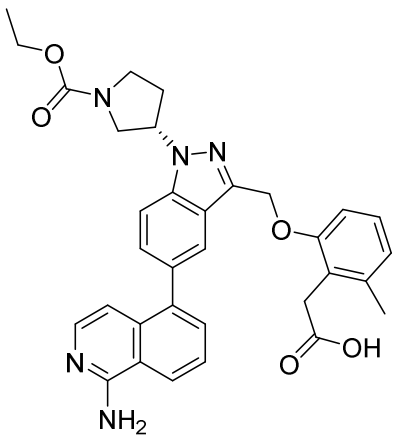
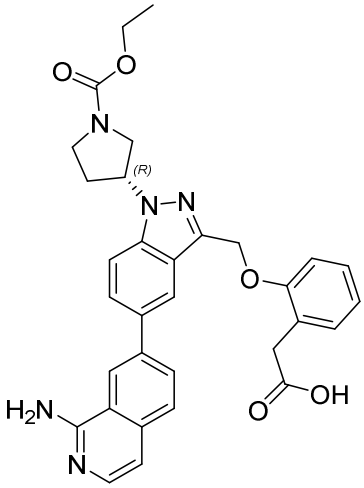
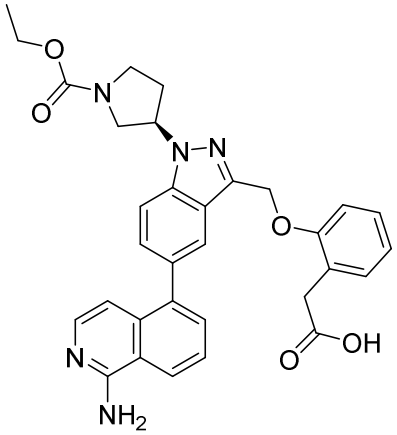
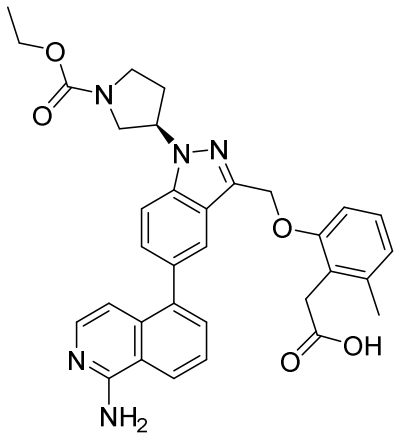
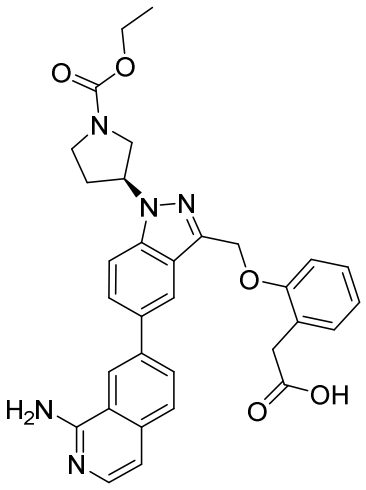
	
	
	

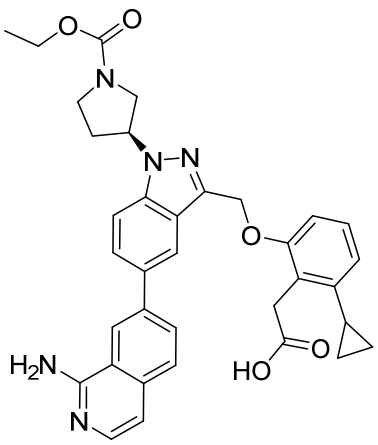
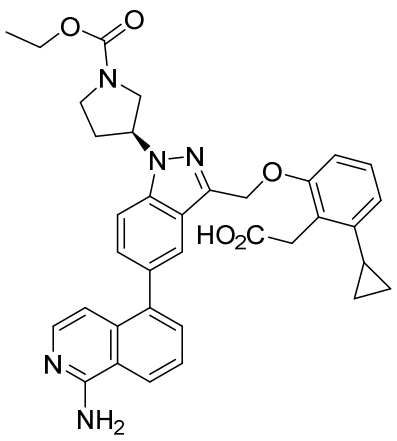
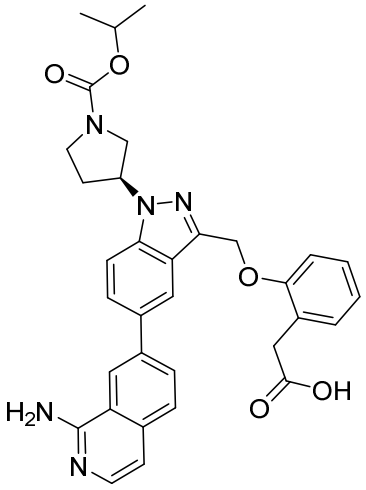
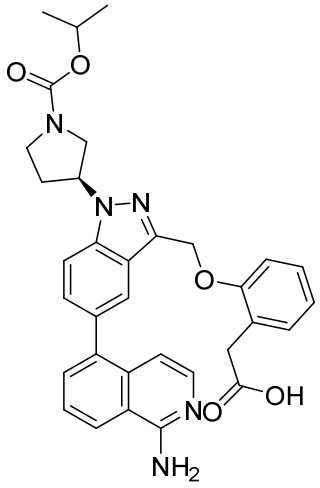
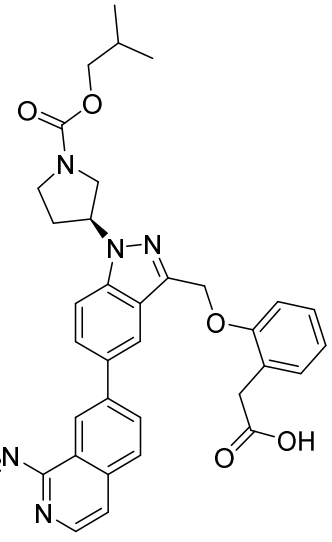
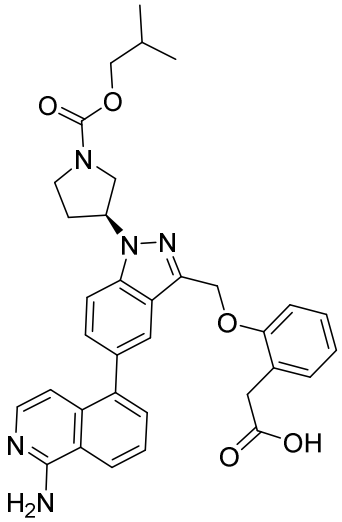
	
	
	

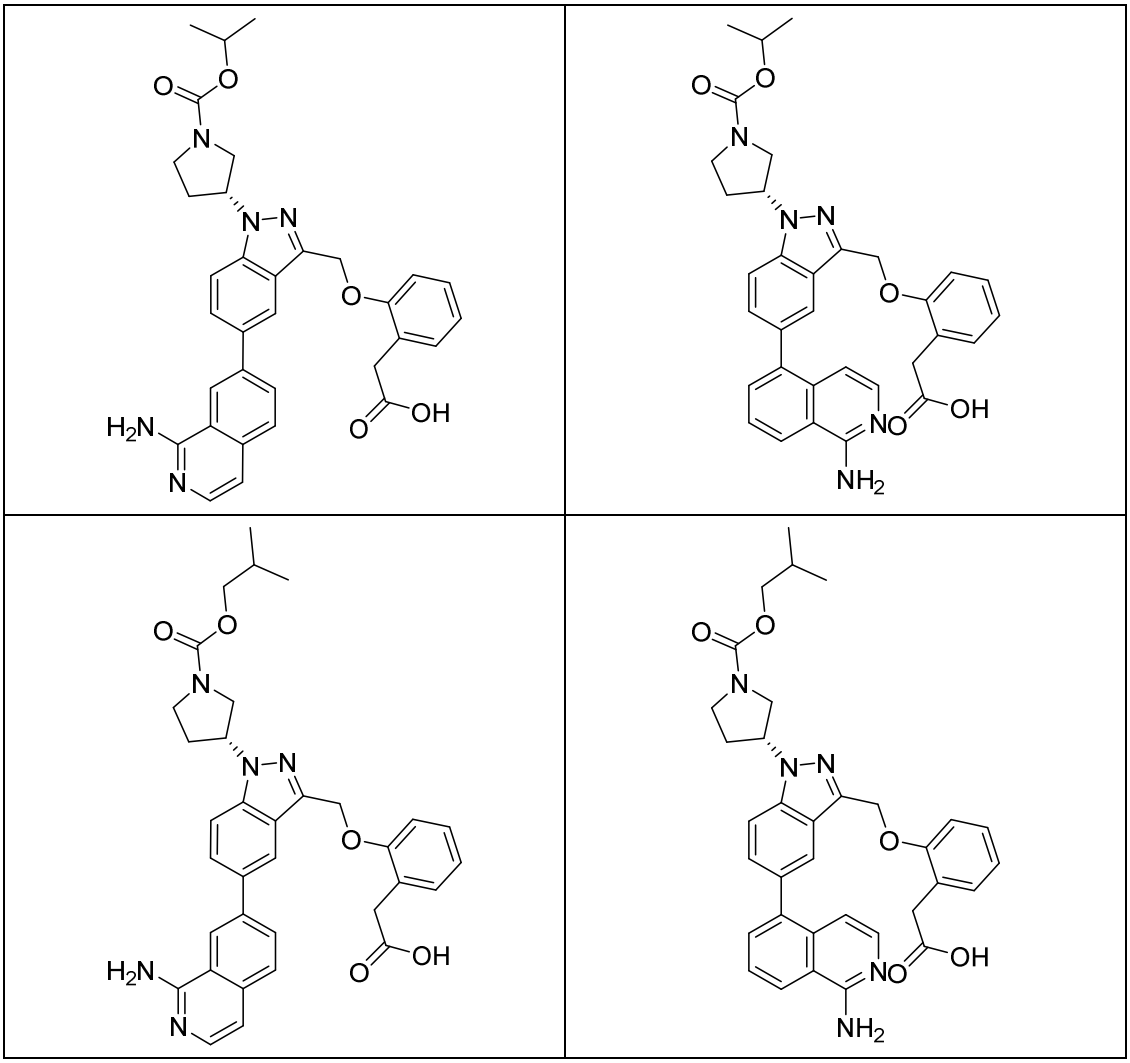
	
	
	

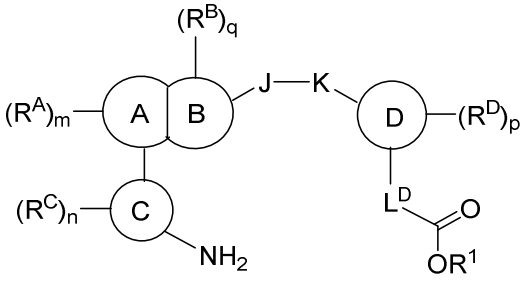
	
	
	



.

28. A compound of formula (III), or a pharmaceutically acceptable salt thereof:



(III);

wherein:

ring  is arylene or heteroarylene;

ring  is cycloalkylene, heterocycloalkylene, cycloalkenylene, or heterocycloalkenylene;

ring  is fused to ring  at two and only two adjacent positions;

ring  is a bicyclic ring system, where the ring attached to ring  is aryl or heteroaryl;

ring  is aryl or heteroaryl;

J represents $–CH_2–$, –NH–, $–CH_2CH_2–$, –C(O)–, –C≡C–, –O–, –S–, –S(O)–, $–SO_2–$, –N(alkyl)–, –CH(alkyl)–, –CH(aryl)–, $–C(alkyl)_2–$, –CH(cycloalkyl)–, or ;

K represents a bond, –O–, –NH–, –C(O)–, $–CH_2–$, –S–, –S(O)–, $–SO_2–$, –N(alkyl)–, –CH(alkyl)–, or –CH(cycloalkyl)–;

wherein at least one of J and K is a bond, –C(O)–, $–CH_2–$, $–CH_2CH_2–$, –CH(alkyl)–, or –CH(aryl)–;

L^D represents $–CH_2–$, $–CH_2CH_2–$, $–CF_2–$, –CH(F)–, $–CD_2–$, –CH(D)–, –CH(OH)–, –CH(alkyl)–, –CH(cycloalkyl)–, $–CHNH_2–$, –CH(NH(alkyl))–, –CH(NH(cycloalkyl))–, or a bond;

R^A, independently for each occurrence, represents H, halo, hydroxyl, cyano, amino, alkyl, optionally substituted alkoxy, hydroxyalkyl, optionally substituted aryloxy, (aryloxy)alkyl, (cycloalkyl)alkoxy, (heterocycloalkyl)alkoxy, optionally substituted (heteroaryl)alkoxy, haloalkyl, haloalkoxy, (hydroxy)haloalkyl, alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl, optionally substituted (cycloalkyl)alkenyl, optionally substituted heterocycloalkyl, optionally substituted (heterocycloalkyl)alkyl, –C(O)OH, $–C(O)NH_2–$, $–C(O)N(alkyl)_2–$, $–CH_2C(O)OH$, $–NO_2$, $–CH_2NH$(optionally substituted alkyl), $–CH_2N$(Boc),

–CH_2N(Boc)(optionally substituted alkyl), –CH_2NH((cycloalkyl)alkyl), –CH_2N(alkyl)(cycloalkyl), –CH_2N(alkyl)((cycloalkyl)alkyl), –NH(optionally substituted alkyl), –NH(cycloalkyl), –NH((cycloalkyl)alkyl), –NH((heterocycloalkyl)alkyl), –$N(alkyl)_2$, –N(alkyl)((cycloalkyl)alkyl, –N(alkyl)((heterocycloalkyl)alkyl, –NH(heteroarylalkyl), –CH_2O(optionally substituted aryl), –C(O)O(alkyl), –C(O)NH(optionally substituted alkyl), –C(O)NH((cycloalkyl)alkyl), –NHC(O)O(alkyl), or –$CH_2N(alkyl)_2$;

R^B, independently for each occurrence, represents H, oxo, –C(O)O(alkyl), halogen, cyano, amino, –C(O)OH, –$CH_2C(O)OH$, –$C(O)NH_2$, –C(O)NH(cycloalkyl), –C(O)NH(alkyl), –C(O)NH(aryl), -C(O)NH(heteroaryl), –C(O)(alkyl), -$S(O)_2$alkyl, alkylaminoalkyl, alkylaminocycloalkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, (hydroxy)haloalkyl, or tosyl, or is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl, spirocycloalkyl, halocycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, spiroheterocycloalkyl, or (heterocycloalkyl)alkyl; or two adjacent occurrences of R^B taken together with the intervening atoms form an aromatic ring; or two geminal occurrences of R^B taken together with the atom to which they are attached form an optionally substituted spirocycloalkyl or a spiroheterocycloalkyl;

R^C, independently for each occurrence, represents H, halo, -OH, cyano, or amino, or is optionally substituted alkoxy, haloalkoxy, alkyl, cycloalkyl, heterocycloalkyl, or (heteroaryl)alkoxy;

R^D, independently for each occurrence, represents H, halo, hydroxyl, cyano, –NH_2, -NH(Ac), -NH(alkyl), -$N(alkyl)_2$, -NH(CO)(alkyl), –CH_2NH_2, -CH_2NHC(O)(alkyl), –$C(O)NH_2$, –C(O)OH, or –NHC(O)O(alkyl), or is optionally substituted alkyl, alkoxy, cycloalkyl, (cycloalkyl)alkyl, hydroxyalkyl, aminoalkyl, haloalkoxy, or haloalkyl;

R^1 represents H or optionally substituted alkyl; and

m, n, p, and q are each independently 0, 1, or 2.

29. The compound of claim 28, wherein ring (B) is cycloalkylene or heterocycloalkylene.

30. The compound of claim 28 or 29, wherein:

ring  is arylene;

ring  is cycloalkylene;

ring  is fused to ring  at two and only two adjacent positions;

ring  is a bicyclic ring system, where the ring attached to ring  is aryl;

ring  is aryl;

J represents –O–;

K represents a bond;

L^D represents $–CH_2–$;

R^A, independently for each occurrence, represents H, halo, alkyl, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted cycloalkyl;

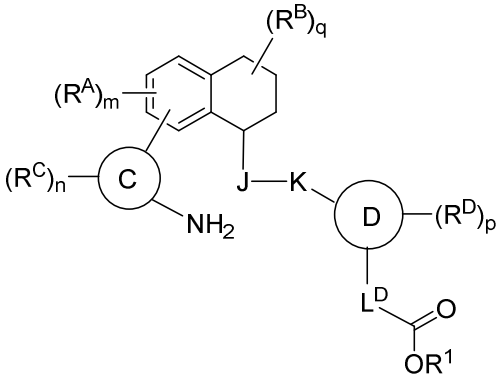
R^B, independently for each occurrence, represents H, or two adjacent occurrences of R^B taken together with the intervening atoms form an aromatic ring; or two geminal occurrences of R^B taken together with the atom to which they are attached form an optionally substituted spirocycloalkyl or a spiroheterocycloalkyl;

R^C represents H;

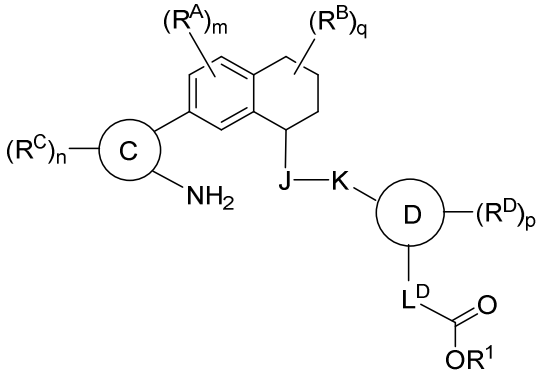
R^D represents H or optionally substituted alkyl;

R^1 represents H.

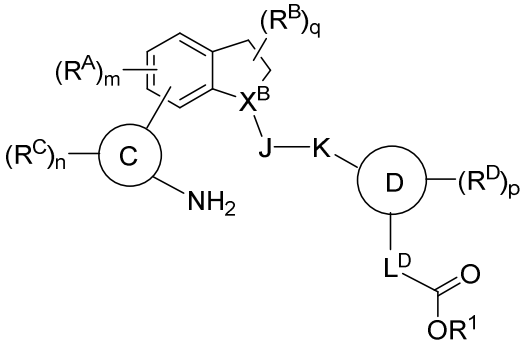
31. The compound of any one of claims 28-30, having the structure of formula (IIIa), (IIIa-1), (IIIb), (IIIb-1), (IIIc), (IIIc-1), (IIId), or (IIId-1):



(IIIa);

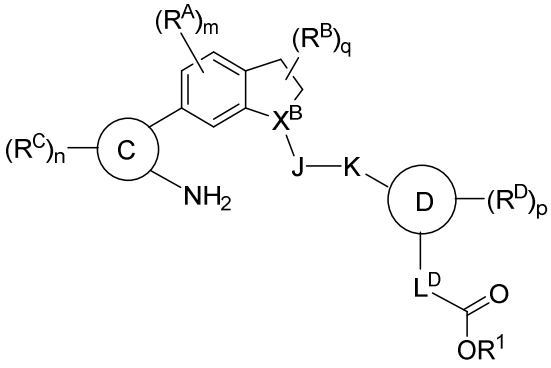


(IIIa-1);



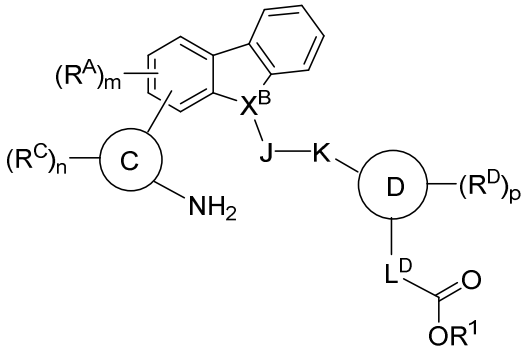
(IIIb);

wherein X^B represents CH or N;



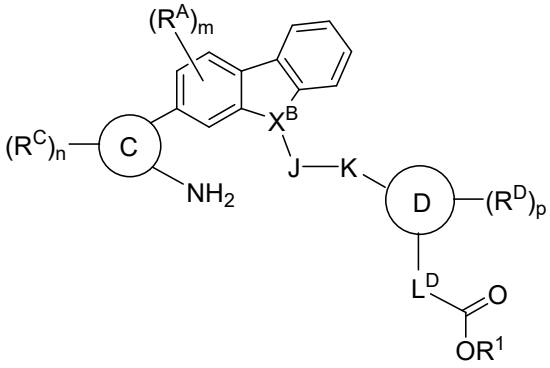
(IIIb-1);

wherein X^B represents CH or N;



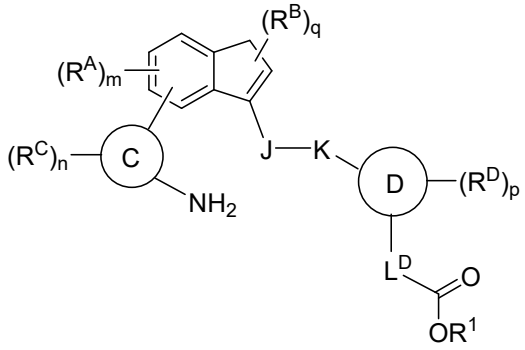
(IIIc);

wherein X^B represents CH or N;

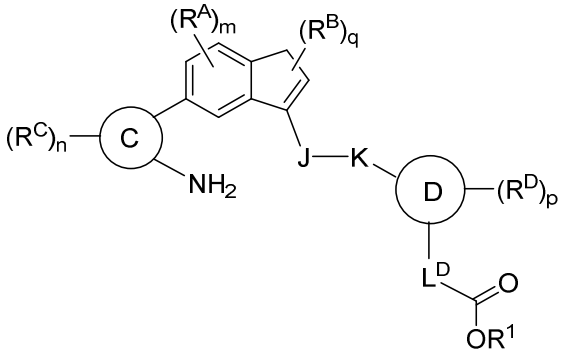


(IIIc-1);

wherein X^B represents CH or N;

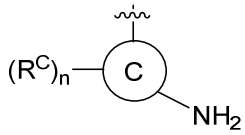
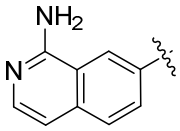
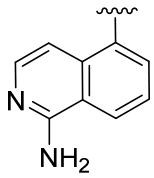


(IIId); or



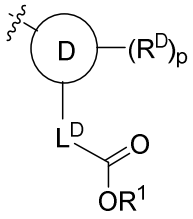
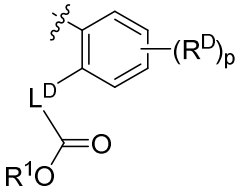
(IIId-1).

32. The compound of any one of claims 28-31, wherein ring  is a bicyclic ring system, where the ring attached to ring  is aryl.

33. The compound of any one of claims 28-31, wherein  represents  or .

34. The compound of any one of claims 28-33, wherein R^C represents H.

35. The compound of any one of claims 28-34, wherein –J–K– represents –O–.

36. The compound of any one of claims 28-35, wherein  represents .

37. The compound of any one of claims 28-36, wherein R^1 is H.

38. The compound of any one of claims 28-37, wherein L^D represents $–CH_2–$.

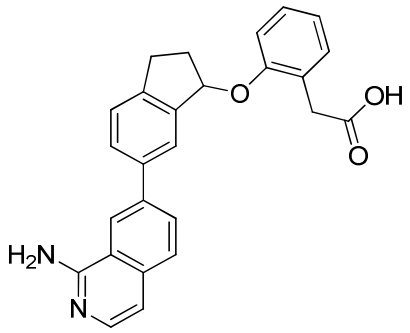
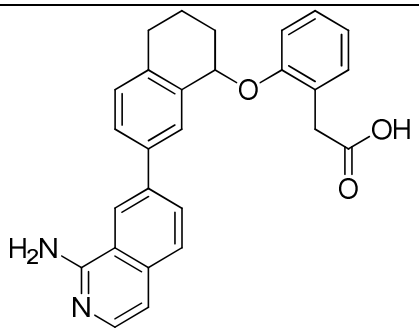
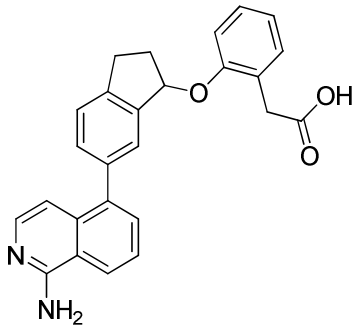
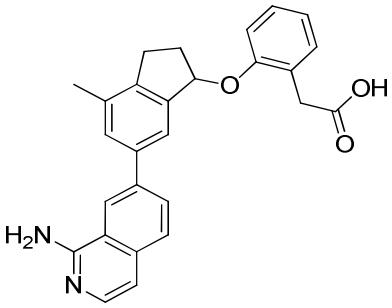
39. The compound of any one of claims 28-38, wherein R^D, independently for each occurrence, represents H or alkyl.

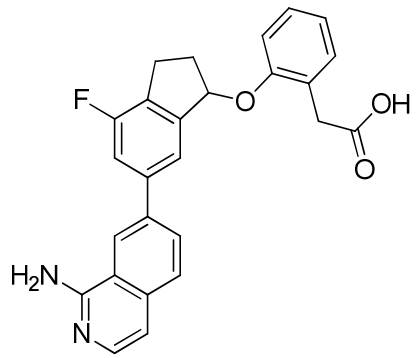
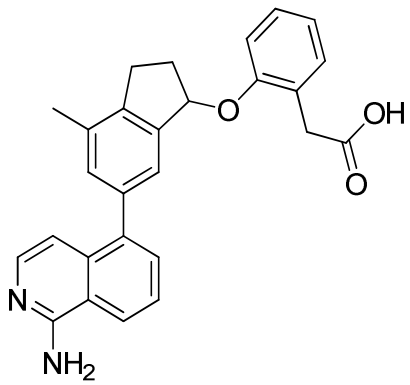
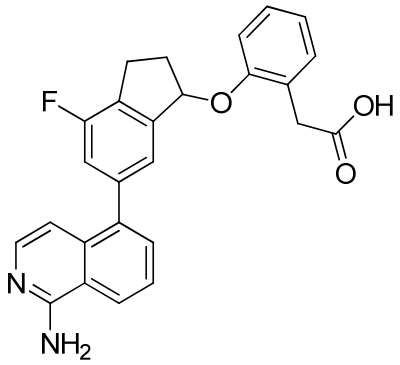
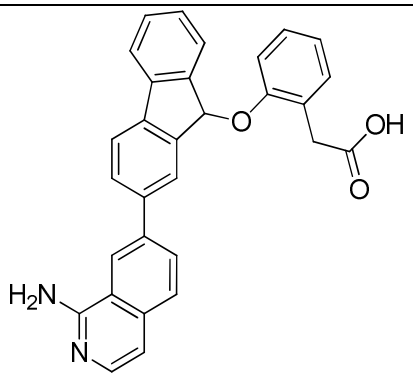
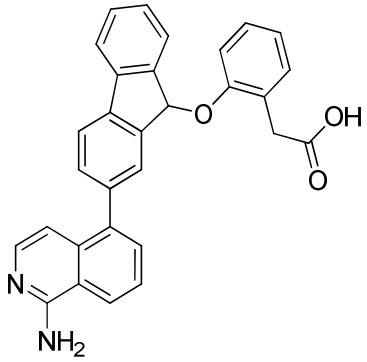
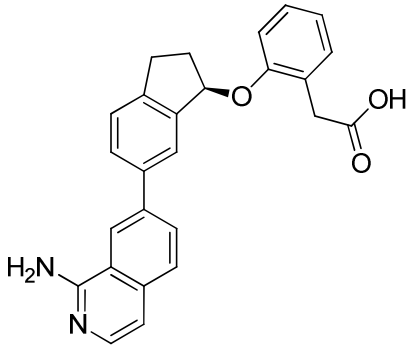
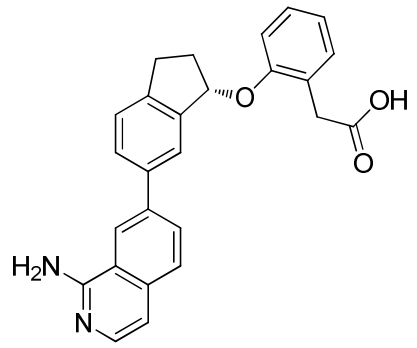
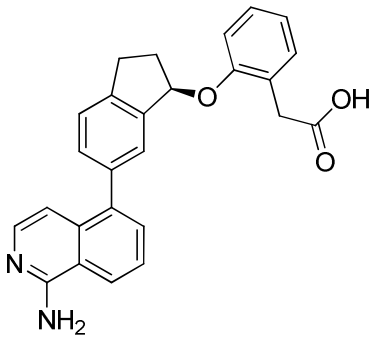
40. The compound of any one of claims 28-39, wherein two geminal occurrences of R^B taken together with the atom to which they are attached form an optionally substituted spirocycloalkyl or a spiroheterocycloalkyl; or
R^B represents H.

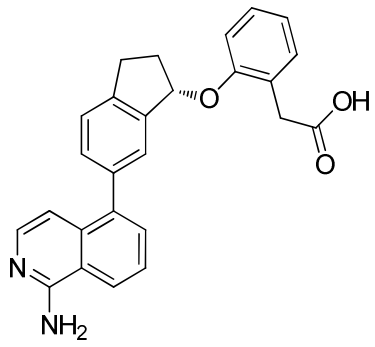
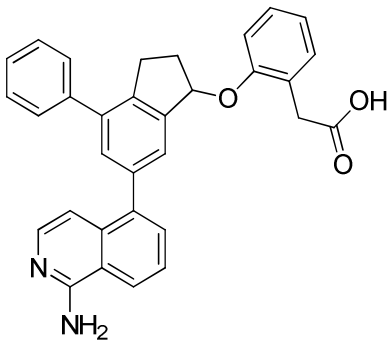
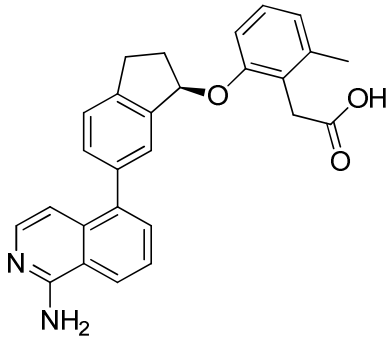
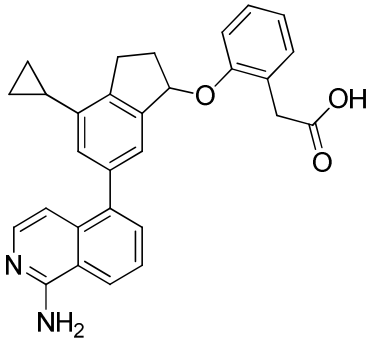
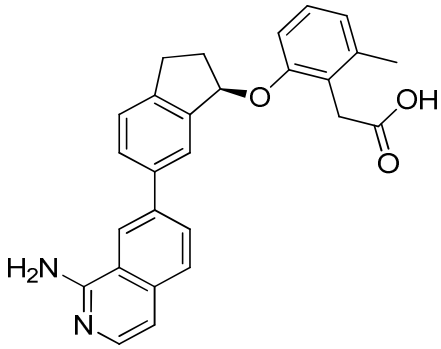
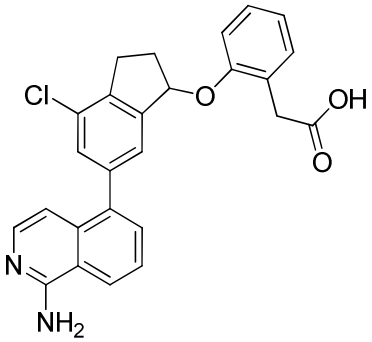
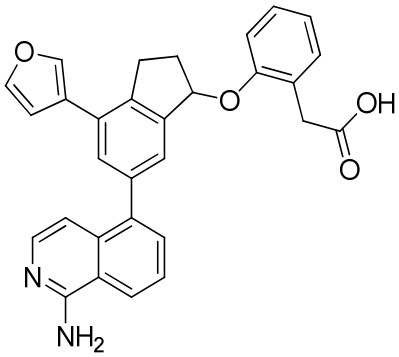
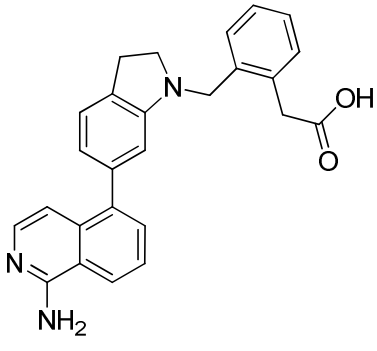
41. The compound of any one of claims 28-40, wherein two geminal occurrences of R^B taken together with the atom to which they are attached form a substituted spiroheterocycloalkyl.

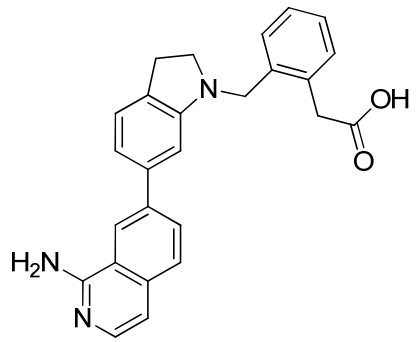
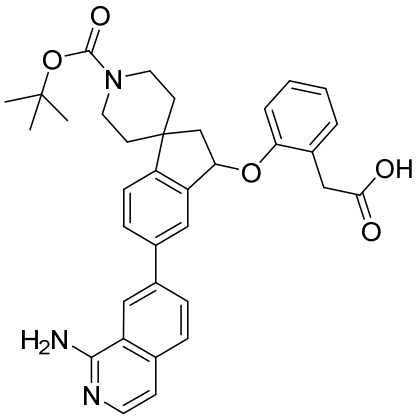
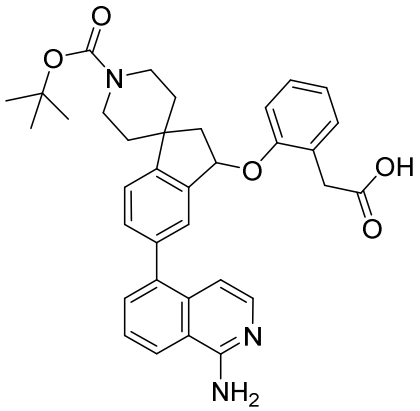
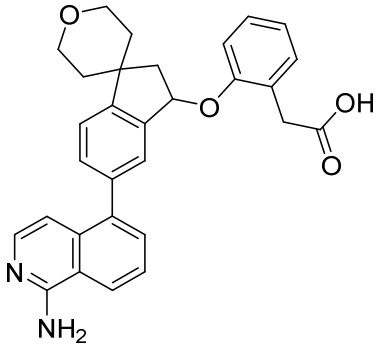
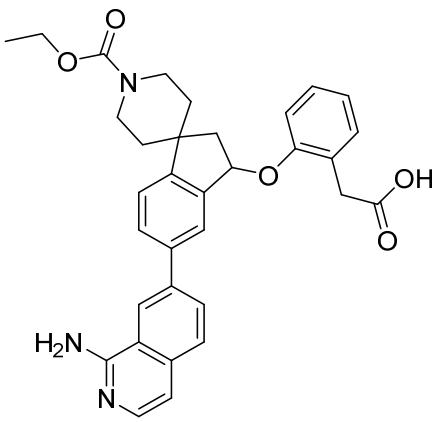
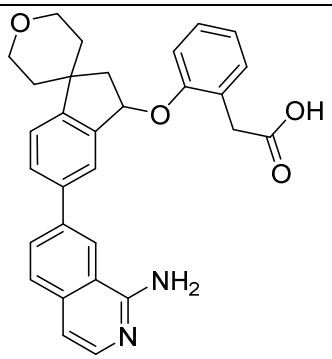
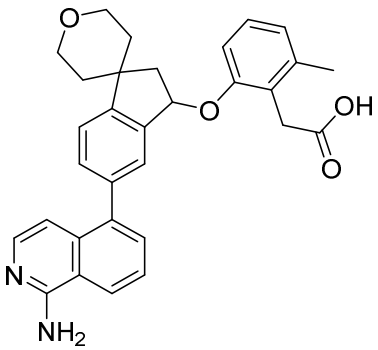
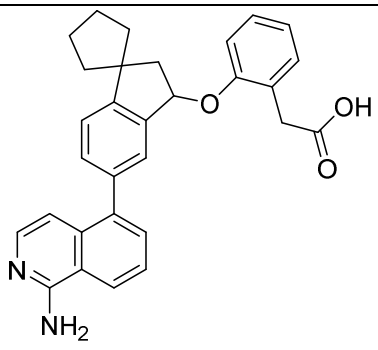
42. The compound of any one of claims 28-41, wherein R^A represents H.

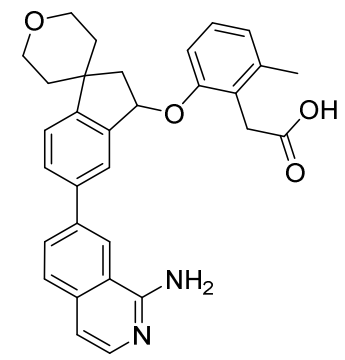
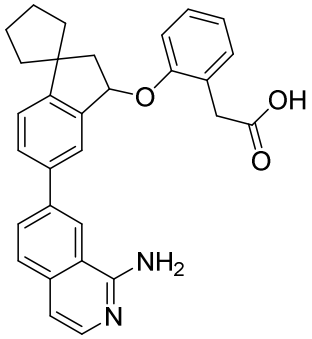
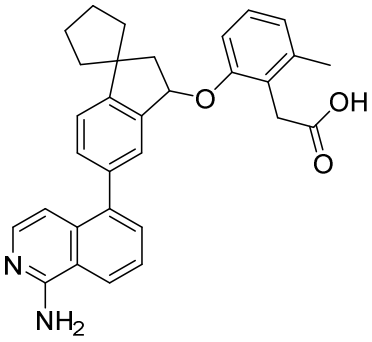
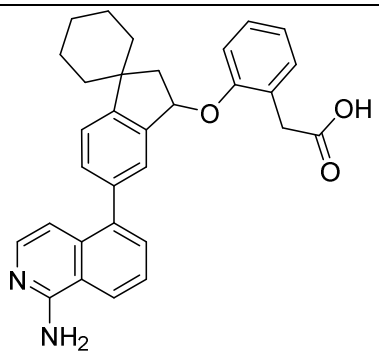
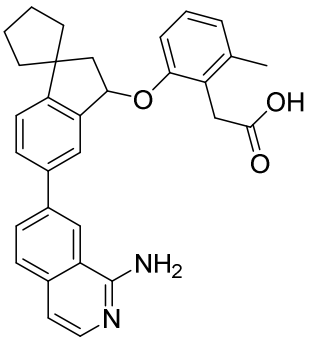
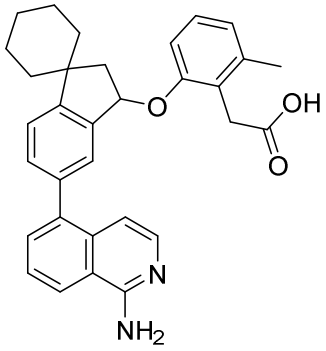
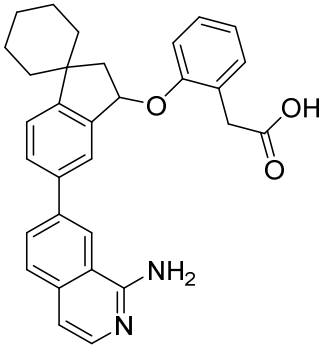
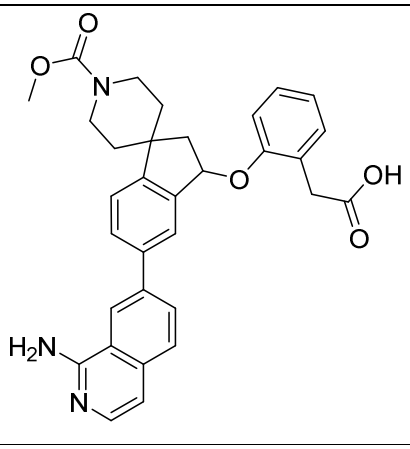
43. The compound of claim 28, selected from the following table:

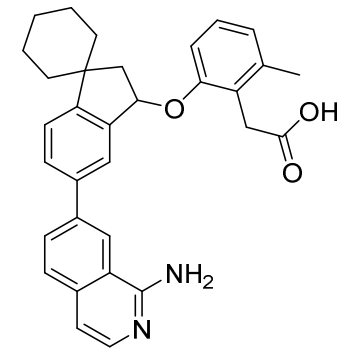
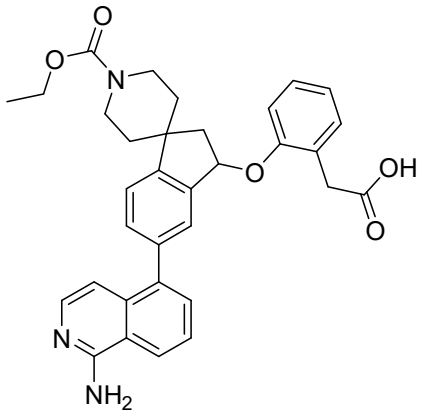
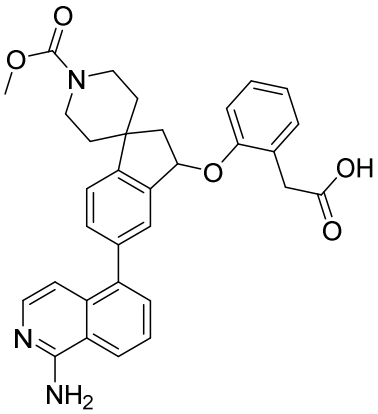
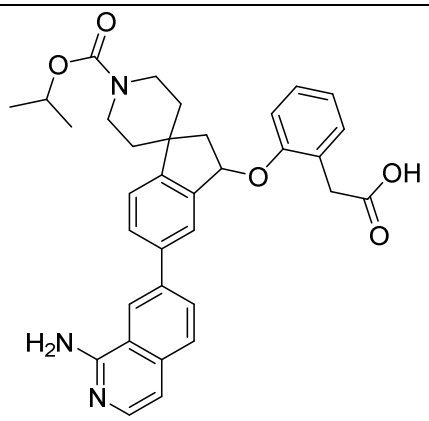
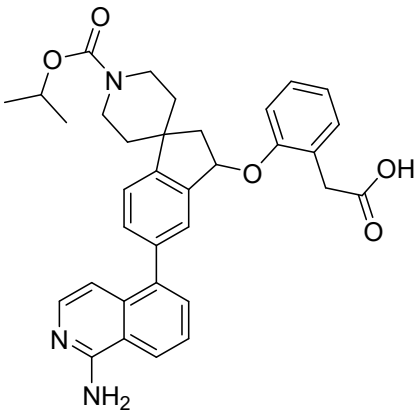
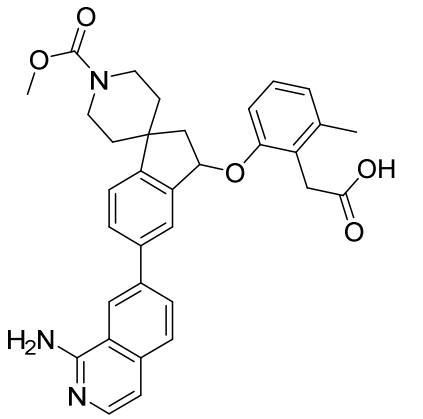
	
	

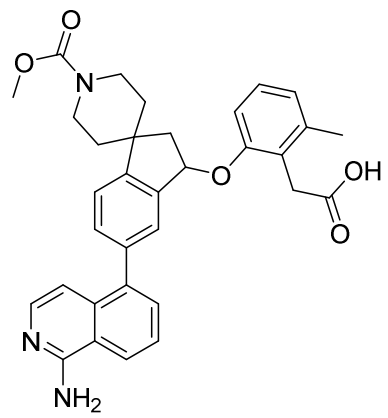
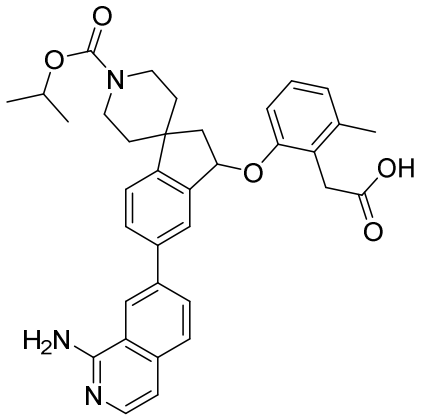
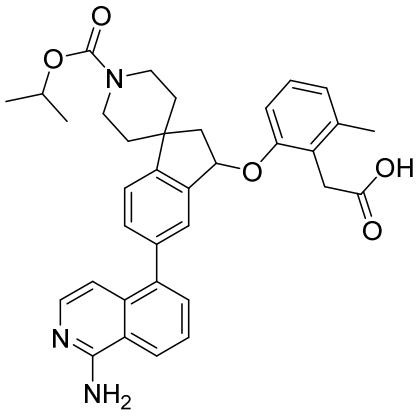
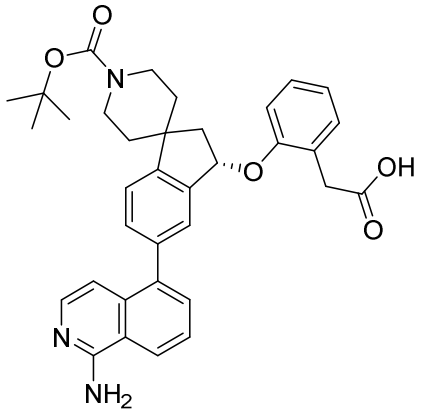
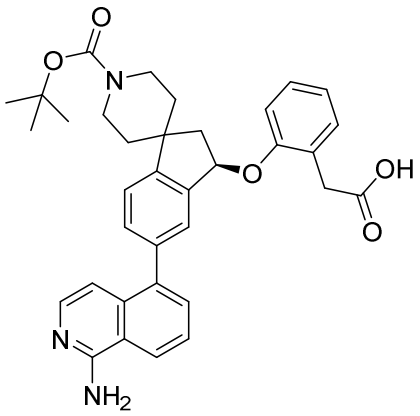
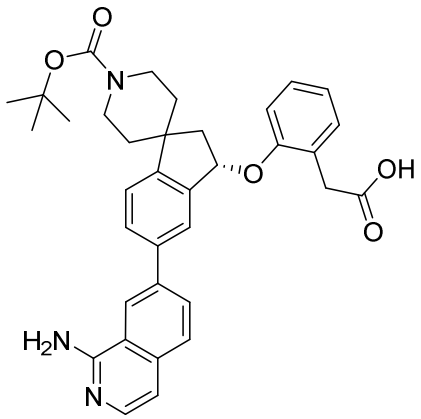
	
	
	
	

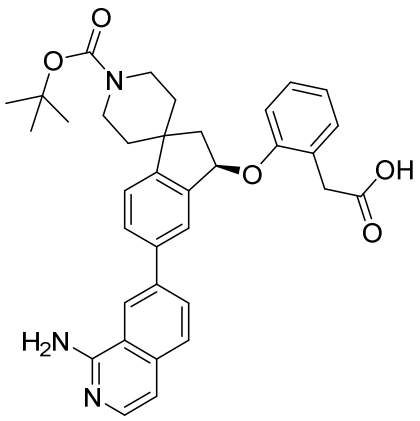
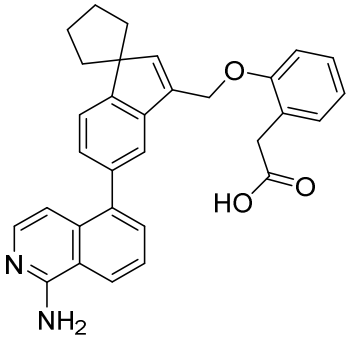
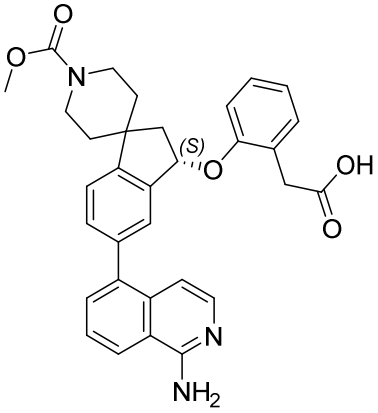
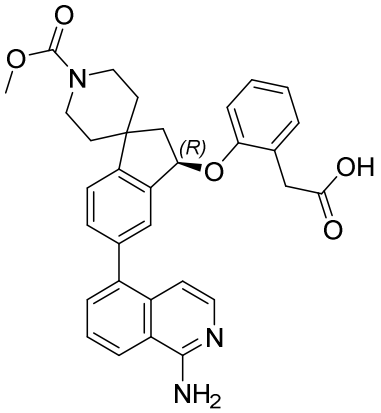
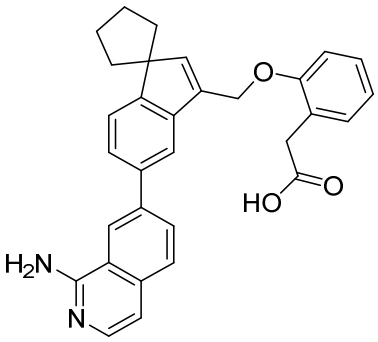
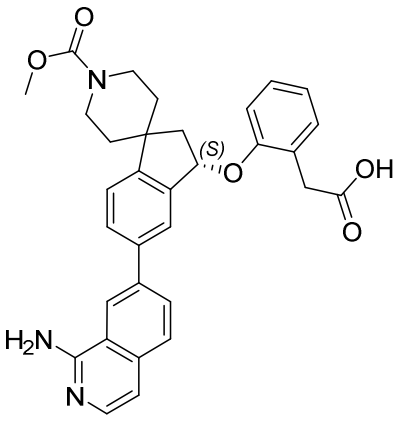
	
	
	
	

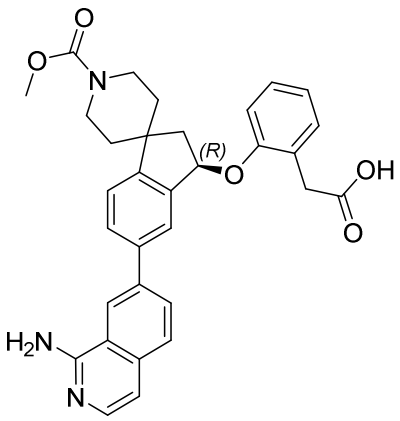
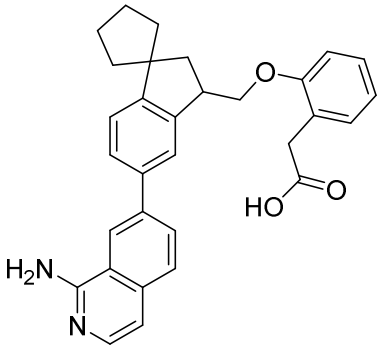
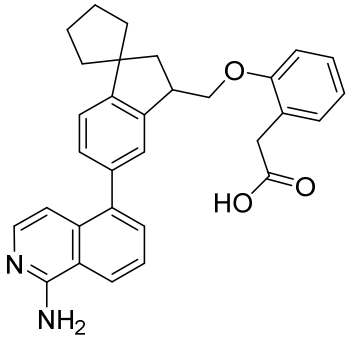
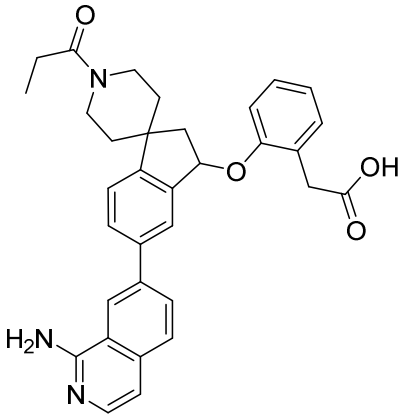
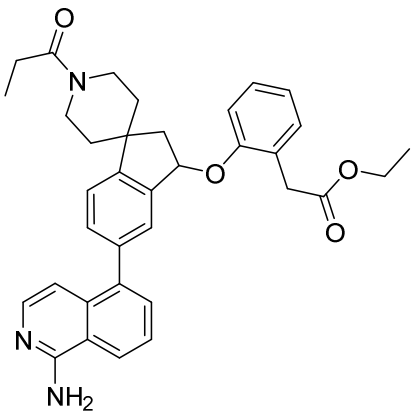
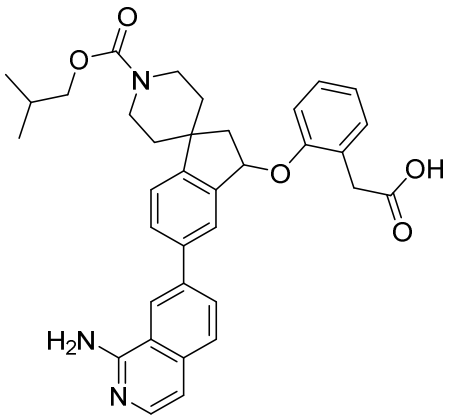
	
	
	
	

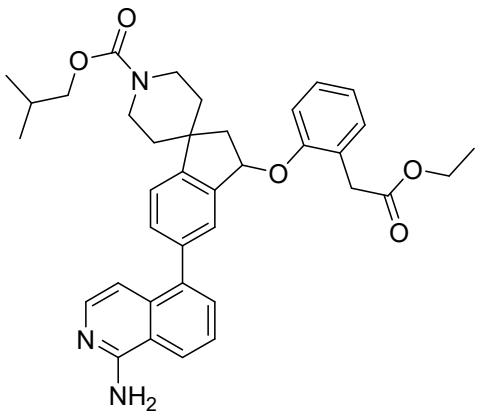
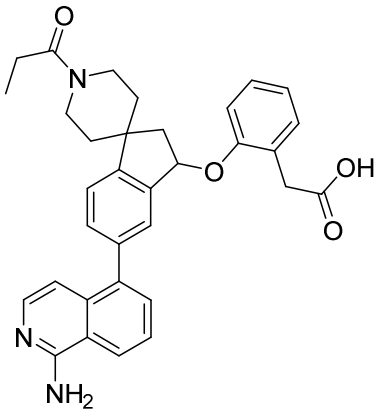
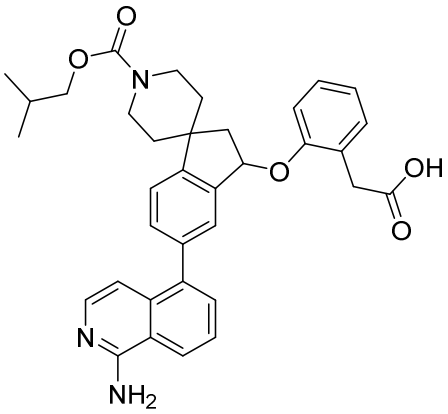
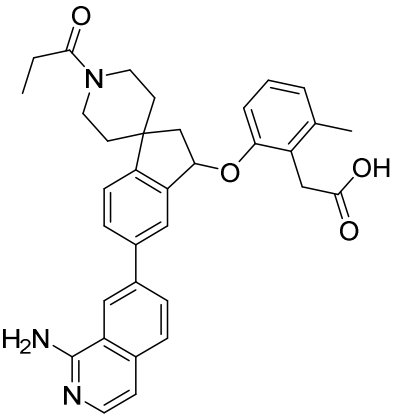
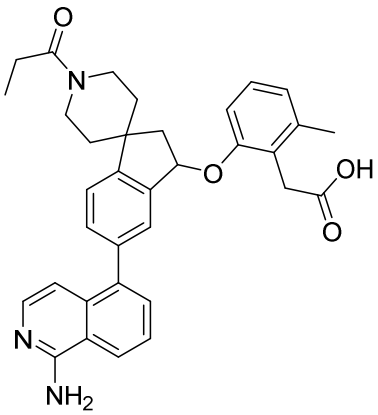
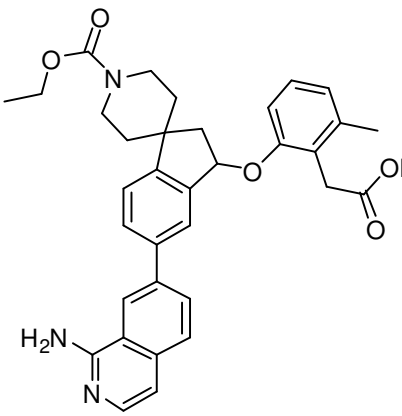
	
	
	
	

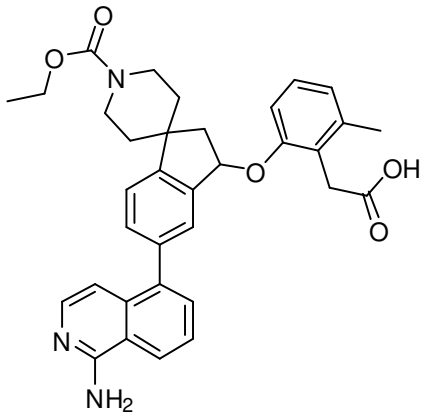
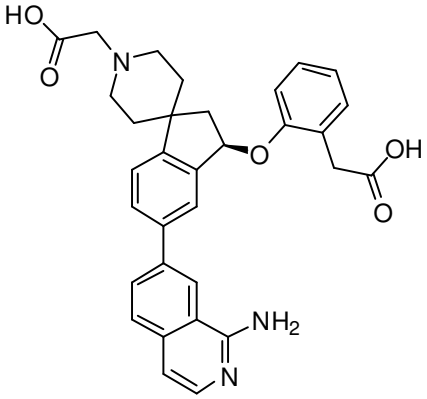
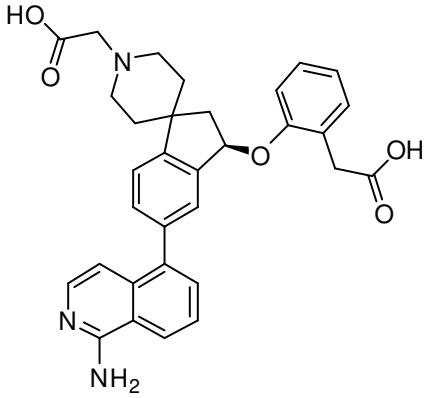
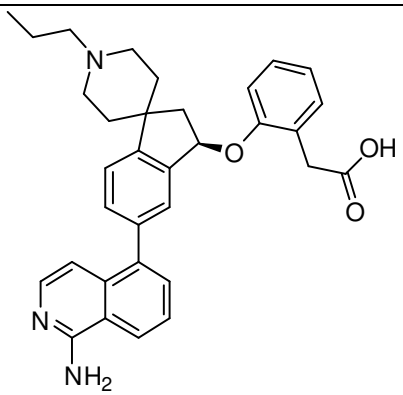
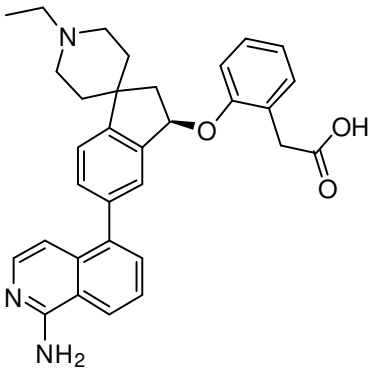
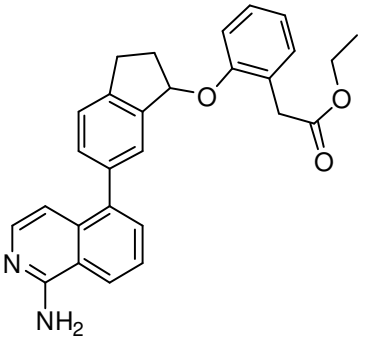
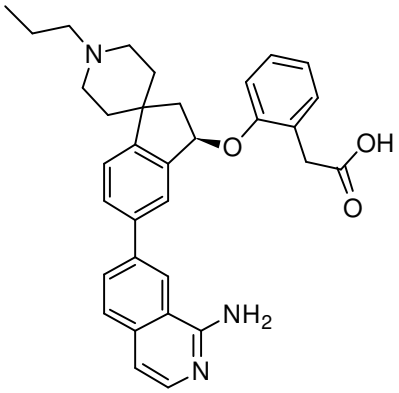
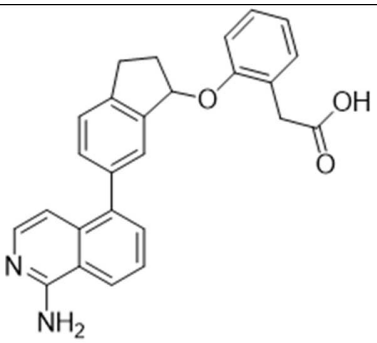
	
	
	

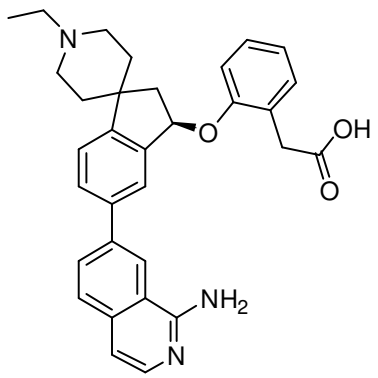
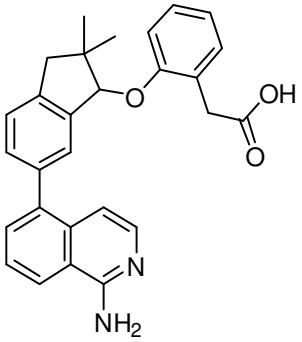
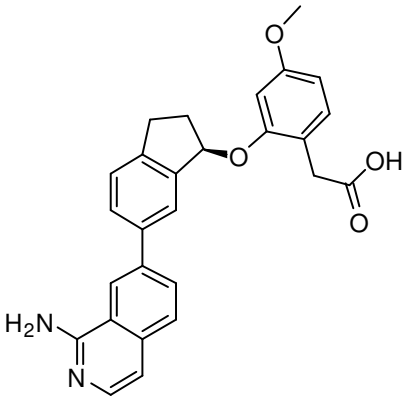
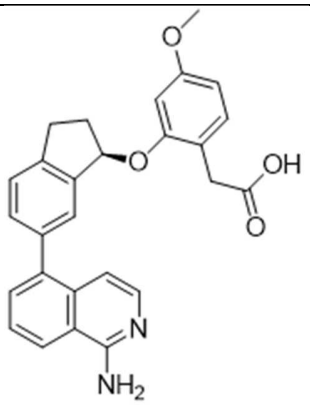
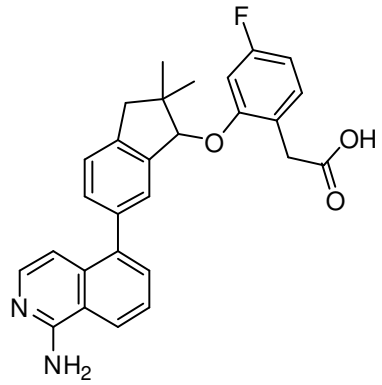
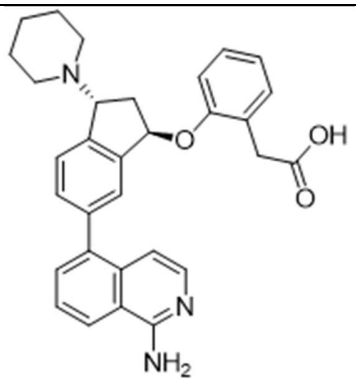
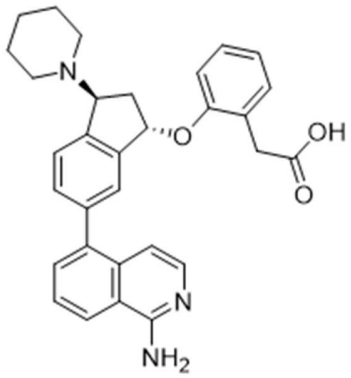
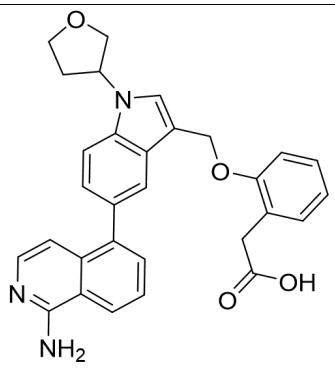
	
	
	

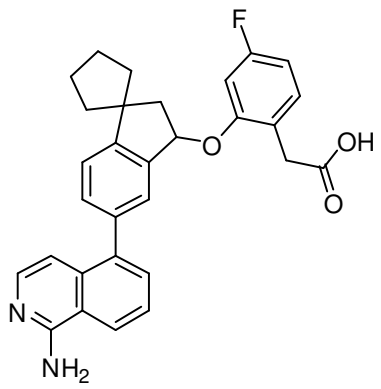
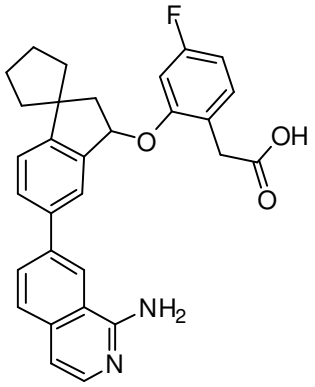
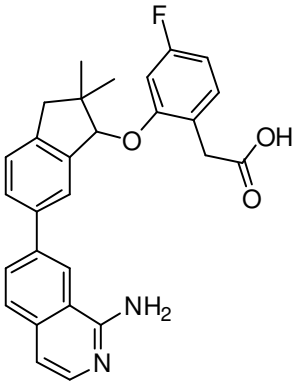
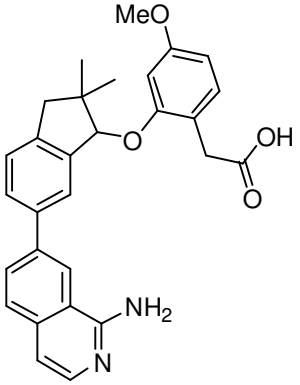
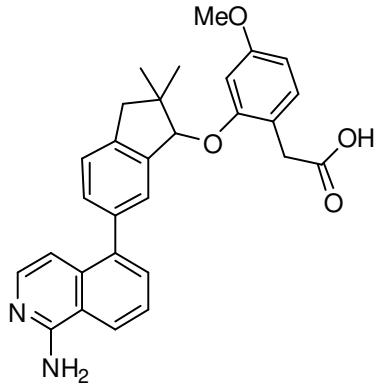
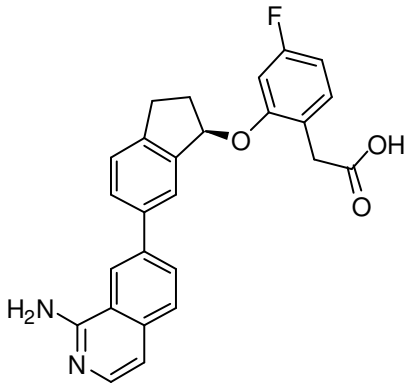
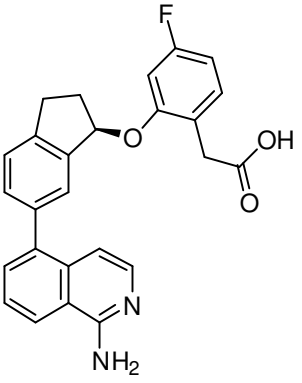
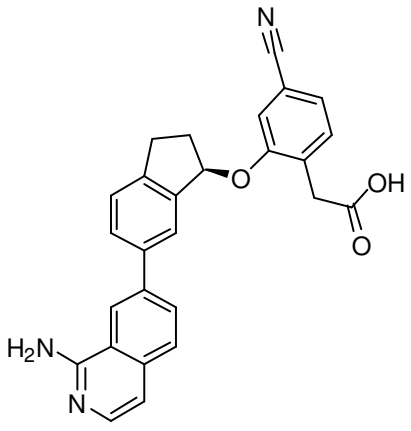
	
	
	

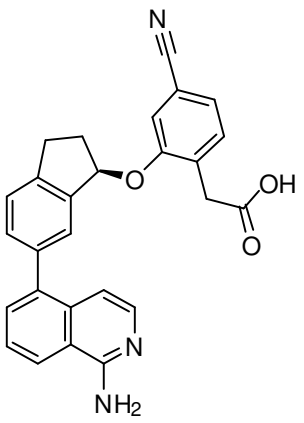
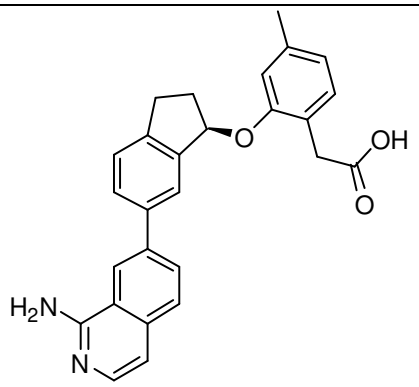
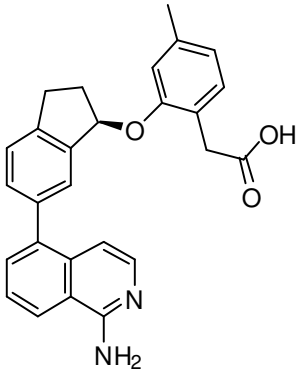
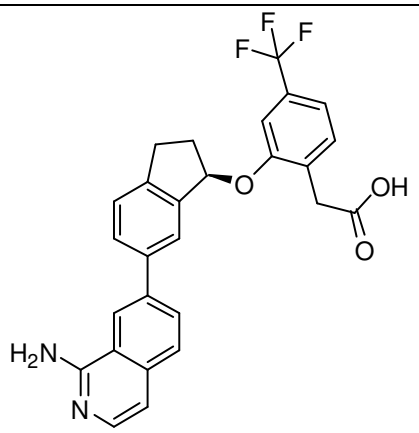
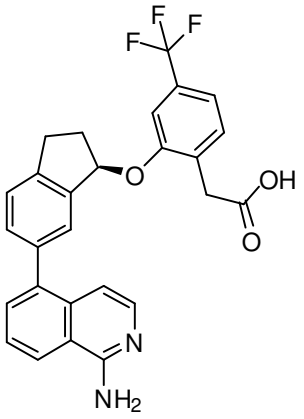
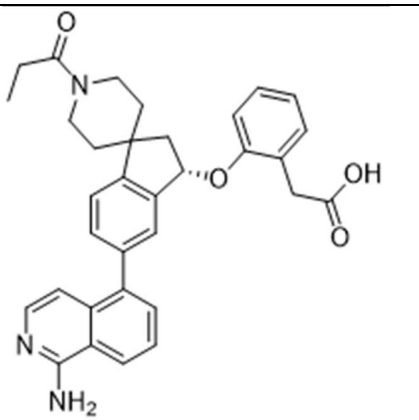
	
	
	

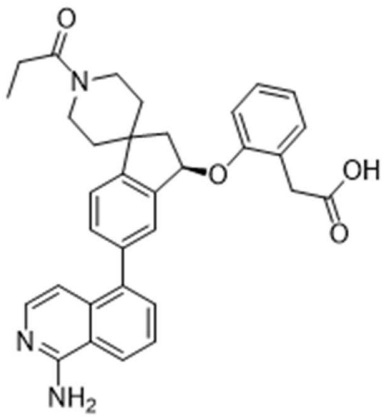
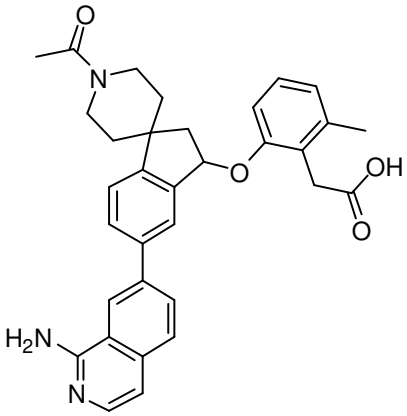
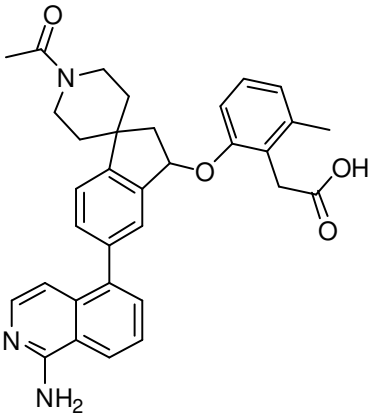
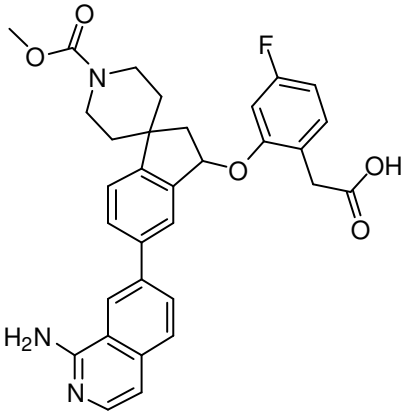
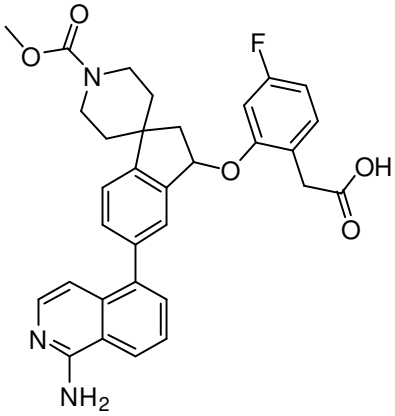
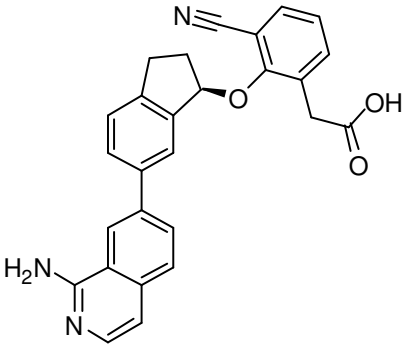
	
	
	

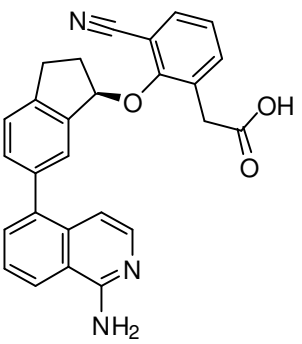
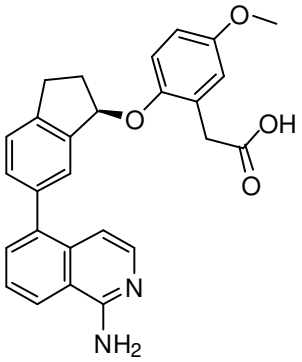
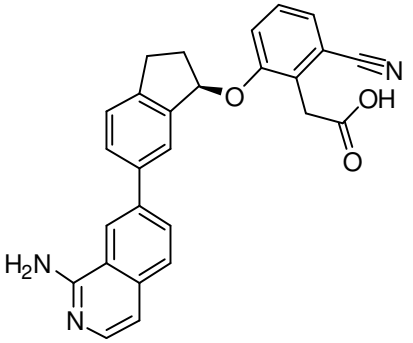
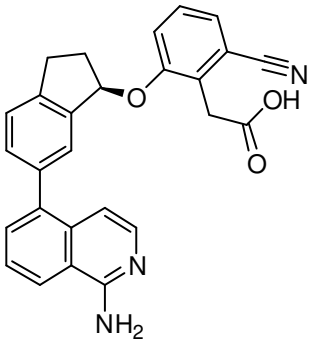
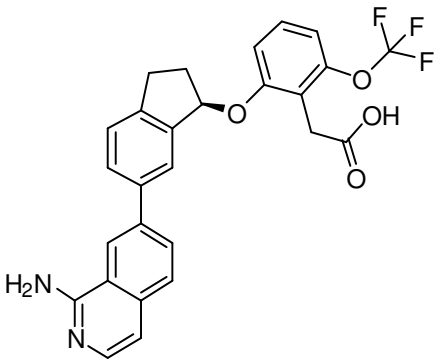
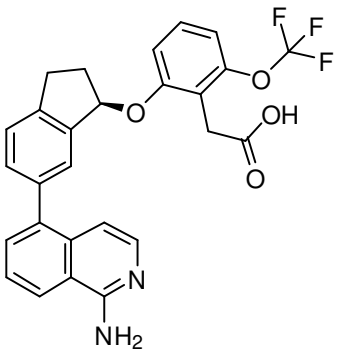
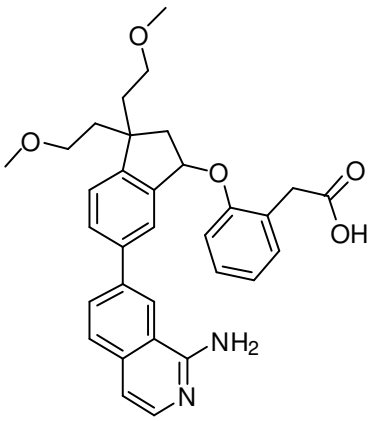
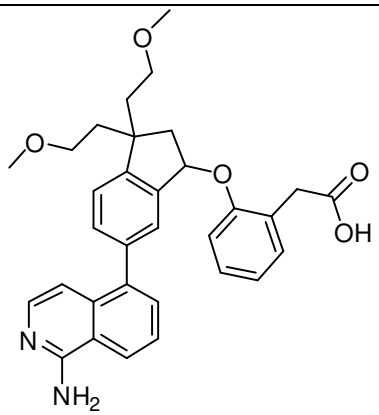
	
	
	
	

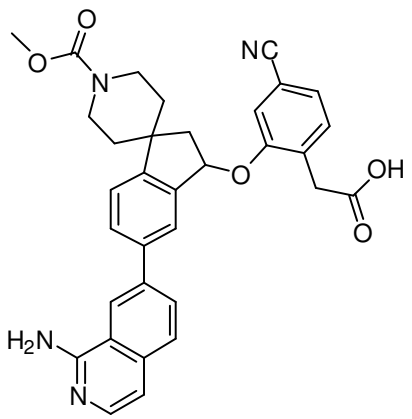
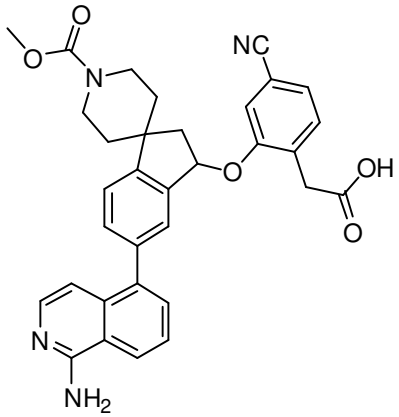
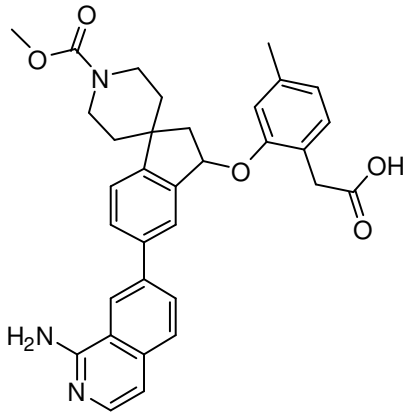
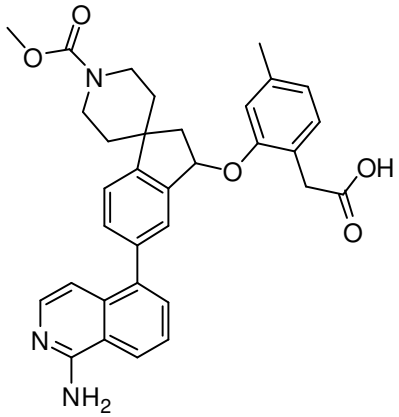
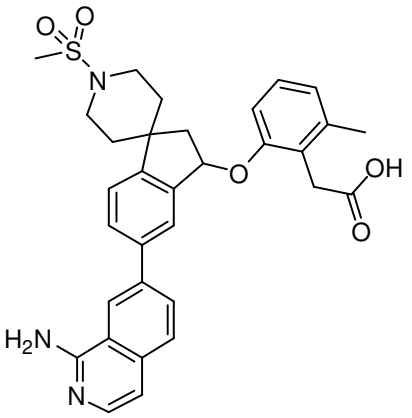
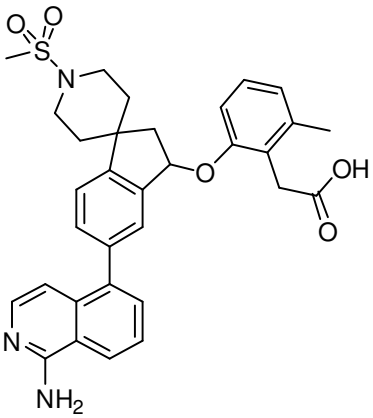
	
	
	
	

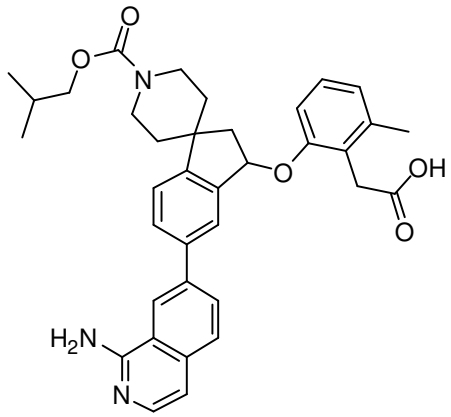
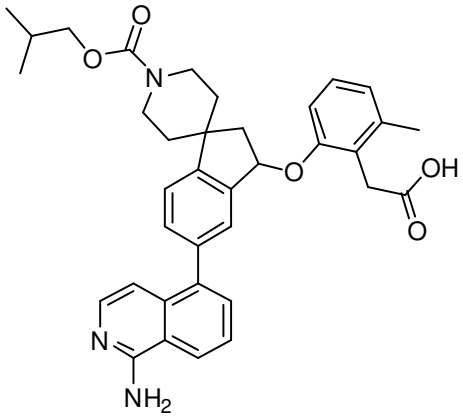
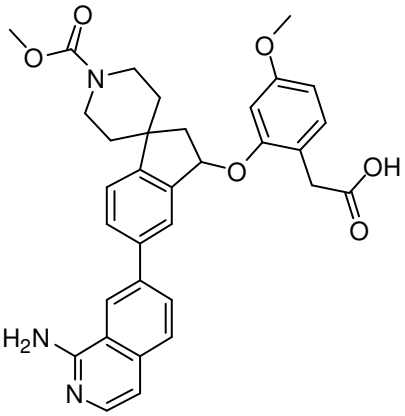
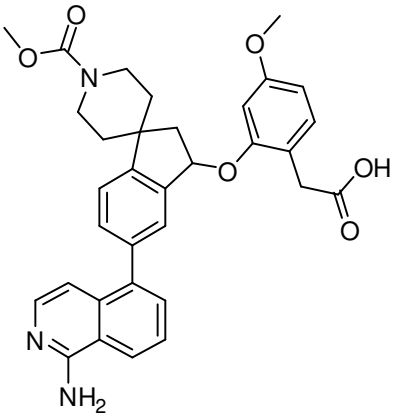
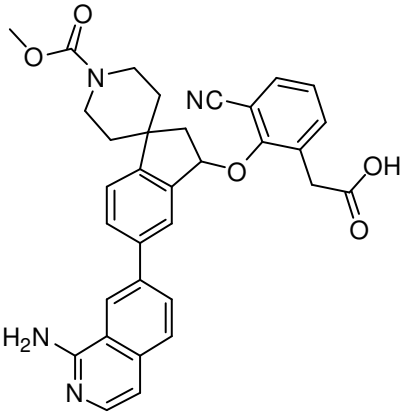
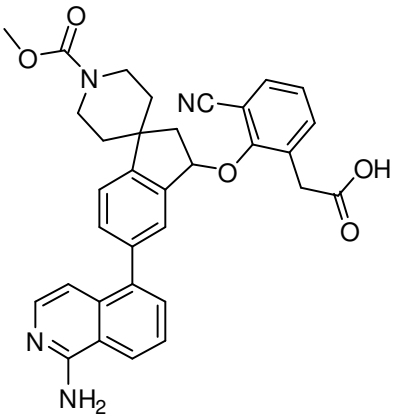
	
	
	
	

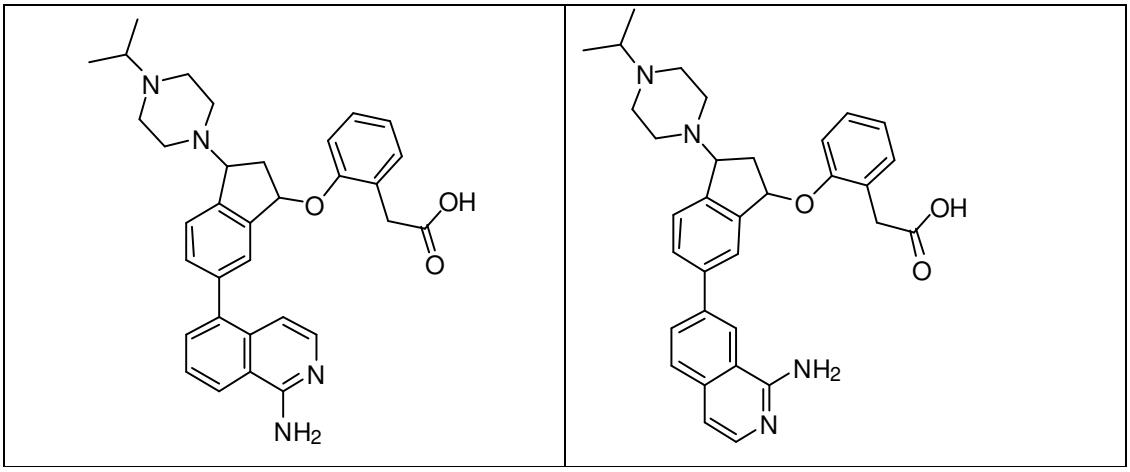
	
	
	



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44. A pharmaceutical composition, comprising a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

45. Use of a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a disease or condition characterized by aberrant kallikrein activity.

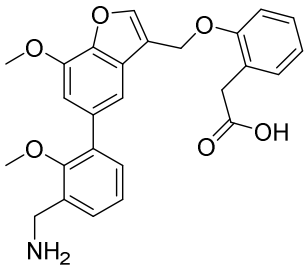
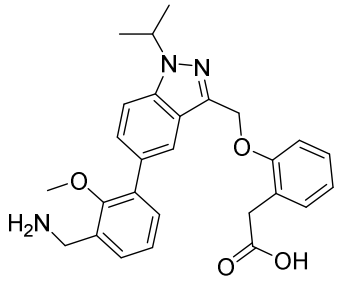
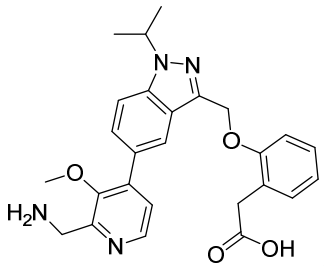
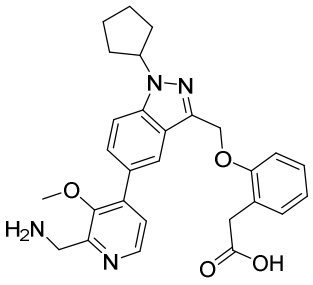
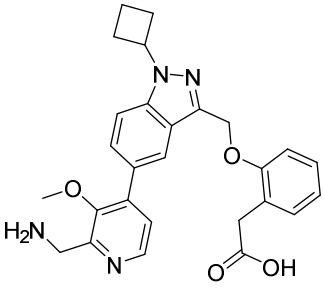
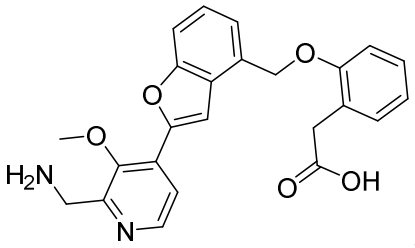
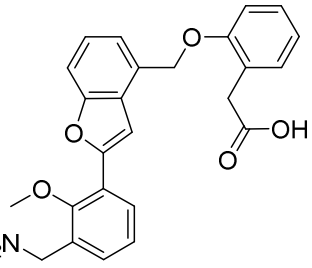
46. The use of claim 45, wherein the disease or condition is characterized by aberrant kallikrein-related peptidase 5 (KLK5) activity.

47. The use of claim 45 or 46, wherein the disease or condition is Netherton Syndrome.

48. The use of claim 45 or 46, wherein the disease or condition is selected from the group consisting of hypersensitivity of the immune system (atopy), hyper IgE syndrome, allergies (including allergies to food and airborne agents), asthma, allergic asthma, chronic inflammation, rhinitis, conjunctivitis, angioedema, eosinophilia, eosinophilic esophagitis, growth delay, failure to thrive, trichorrhexis invaginata (TI), respiratory tract infections, systemic infections, and gastrointestinal disorders.

49. The use of claim 45 or 46, wherein the disease or condition is cancer, wherein the cancer is selected from the group consisting of ovarian cancer, breast cancer, prostate cancer, bladder cancer, cervical cancer, glioblastoma multiforme, and neuroblastoma.

50. Use of a compound, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a disease or condition characterized by aberrant kallikrein activity; wherein the compound is selected from the group consisting of:


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and .

51. The use of claim 50, wherein the disease or condition is Netherton Syndrome.

52. The use of claim 50, wherein the disease or condition is selected from the group consisting of rhinitis, conjunctivitis, angioedema, eosinophilia, eosinophilic esophagitis, growth delay, failure to thrive, trichorrhexis invaginata (TI), respiratory tract infections, systemic infections and gastrointestinal disorders.

53. The use of claim 50, wherein the disease or condition is selected from the group consisting of hypersensitivity of the immune system (atopy), hyper IgE syndrome, allergies (including allergies to food and airborne agents), asthma, allergic asthma, and chronic inflammation.

54. The use of claim 50, wherein the disease or condition is cancer, wherein the cancer is selected from the group consisting of ovarian cancer, breast cancer, prostate cancer, bladder cancer, cervical cancer, glioblastoma multiforme, and neuroblastoma.

55. A compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, for use in treating or preventing a disease or condition characterized by aberrant kallikrein activity.