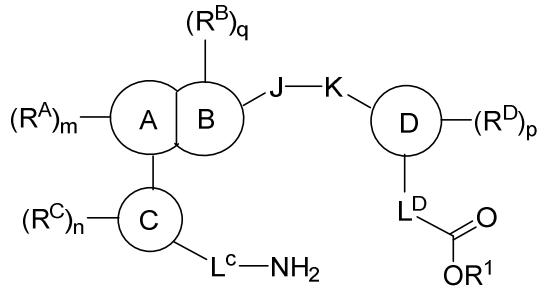
CLAIMS

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)–, –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^C represents a bond, $–CH_2–$, –CH(alkyl)–, –CH(cycloalkyl)–, –CH(hydroxyalkyl)–, –CH(haloalkyl)–, $–CH_2CH_2–$, $–CF_2–$, –CH(F)–, –CF(alkyl)–, –C(O)–, $–CD_2–$, or –CH(D)– ;

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

R^A represents H, halo, hydroxyl, cyano, amino, alkyl, alkoxyl, 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), –$CH_2N(Boc)$(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 represents H, –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), alkylaminoalkyl, alkylaminocycloalkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, (hydroxy)haloalkyl, or tosyl, or is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl, (cycloalkyl)alkyl, or heterocycloalkyl;

R^C represents H, halo, -OH, or amino, or is optionally substituted alkoxy, alkyl, cycloalkyl, heterocycloalkyl, or (heteroaryl)alkoxy;

R^D 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, alkoxyl, cycloalkyl, (cycloalkyl)alkyl, hydroxyalkyl, aminoalkyl, haloalkoxyl, 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:

J represents $–CH_2–$, –NH–, $–CH_2CH_2–$, or –C(O)–;

K represents a bond, –O–, –NH–, or –C(O)–;

wherein if J represents –NH–, then K is a bond or –C(O)–;

L^C represents $–CH_2–$, –CH(alkyl)–, or –CH(hydroxyalkyl)–;

R^A represents H, halo, hydroxyl, alkyl, alkoxyl, hydroxyalkyl, optionally substituted aryloxy, (aryloxy)alkyl, (heterocycloalkyl)alkoxy, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted (heterocycloalkyl)alkyl, –C(O)OH, $–NO_2$, $–CH_2NH$(optionally substituted alkyl), $–CH_2NH$((cycloalkyl)alkyl), –NH((cycloalkyl)alkyl), $–CH_2O$(optionally substituted aryl), –C(O)O(alkyl), –C(O)NH(optionally substituted alkyl), –C(O)NH((cycloalkyl)alkyl), –NHC(O)O(alkyl), or $–CH_2N(alkyl)_2$;

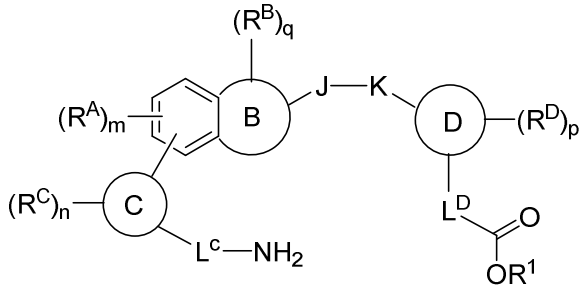
R^B represents H, –C(O)O(alkyl), alkyl, –C(O)OH, hydroxyalkyl, tosyl, heterocycloalkyl, $–C(O)NH_2$, or –C(O)NH(cycloalkyl);

R^C represents H or halo;

R^D represents H or halo, hydroxyl, alkyl, alkoxyl, $–NH_2$, $–C(O)NH_2$, –NHC(O)O(alkyl), or haloalkoxyl; and

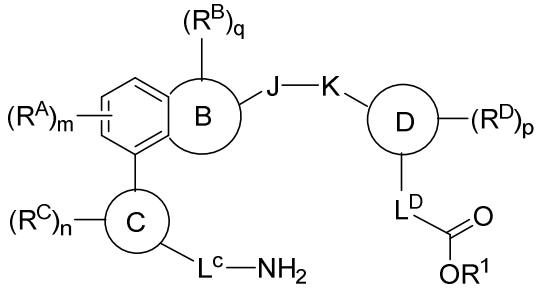
R^1 represents H or alkyl.

3. The compound of claim 1 or 2, having the structure of formula (Ia):



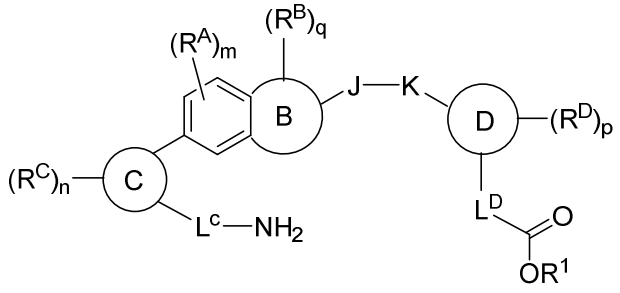
(Ia).

4. The compound of any one of claims 1-3, having the structure of formula (Ia-1):



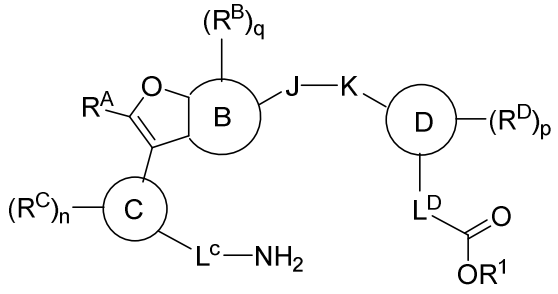
(Ia-1).

5. The compound of any one of claims 1-3, having the structure of formula (Ia-2):



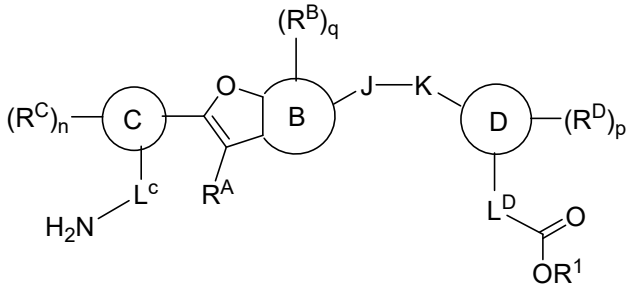
(Ia-2).

6. The compound of claim 1 or 2, having the structure of formula (Ib-1):



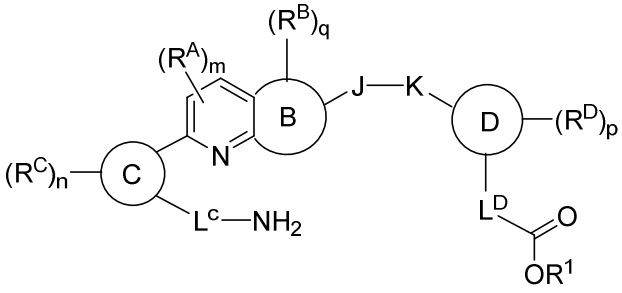
(Ib-1).

7. The compound of claim 1 or 2, having the structure of formula (Ib-2):



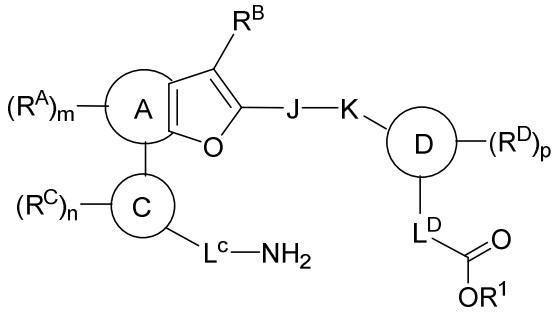
(Ib-2).

8. The compound of claim 1 or 2, having the structure of formula (Ic-1):



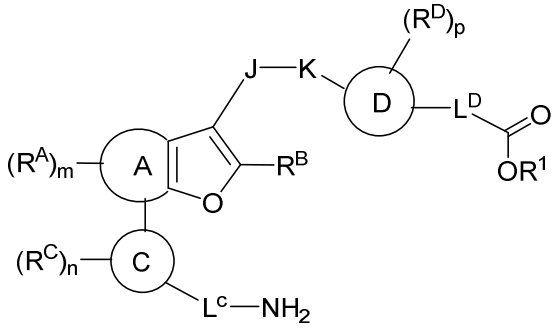
(Ic-1).

9. The compound of any one of claims 1-8, having the structure of formula (Id-1):



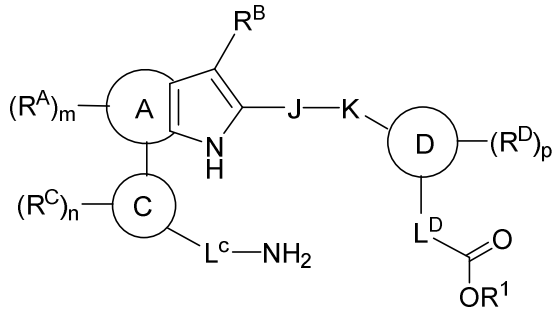
(Id-1).

10. The compound of any one of claims 1-8, having the structure of formula (Id-2):



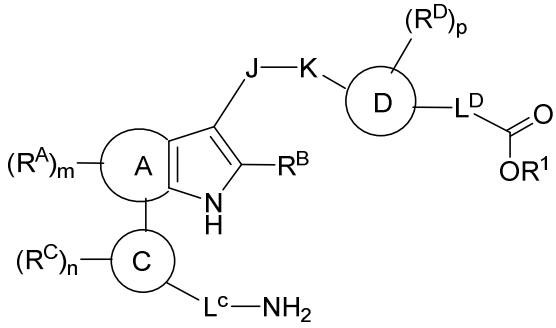
(Id-2).

11. The compound of any one of claims 1-8, having the structure of formula (Ie-1):



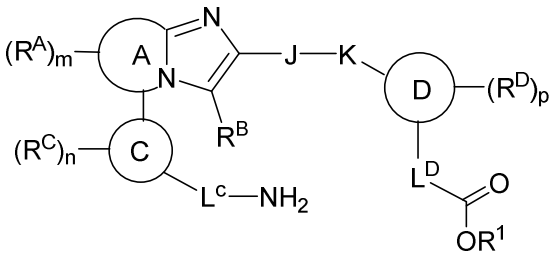
(Ie-1).

12. The compound of any one of claims 1-8, having the structure of formula (Ie-2):



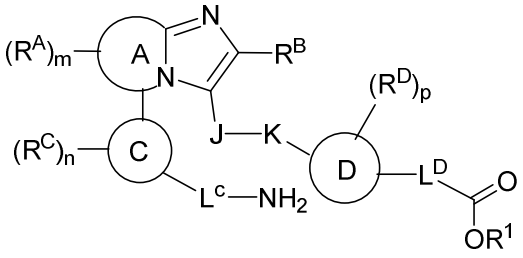
(Ie-2).

13. The compound of any one of claims 1-8, having the structure of formula (If-1):



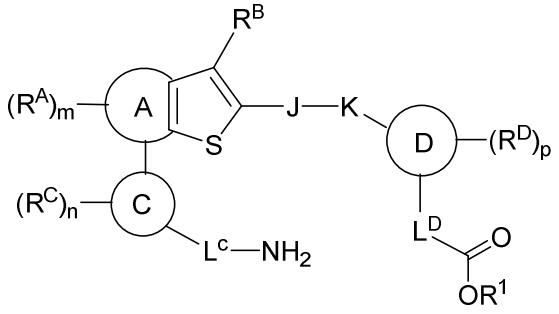
(If-1).

14. The compound of any one of claims 1-8, having the structure of formula (If-2):



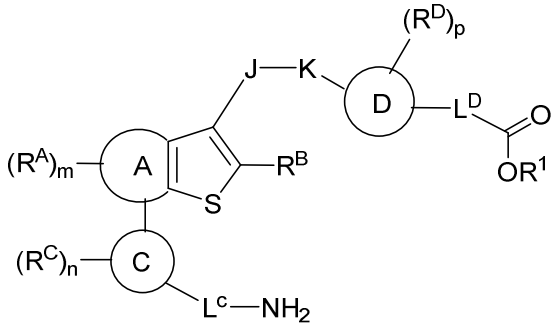
(If-2).

15. The compound of any one of claims 1-8, having the structure of formula (Ig-1):



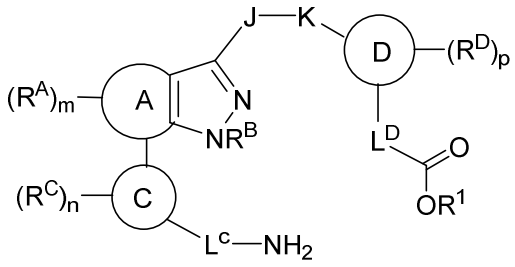
(Ig-1).

16. The compound of any one of claims 1-8, having the structure of formula (Ig-2):



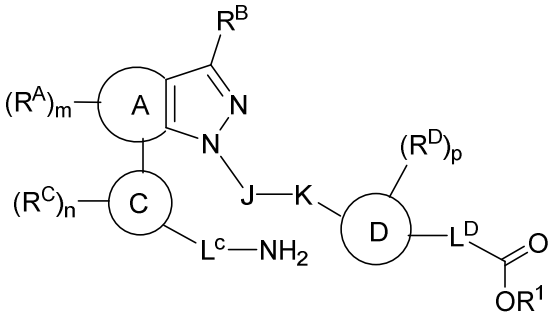
(Ig-2).

17. The compound of any one of claims 1-8, having the structure of formula (Ih-1):



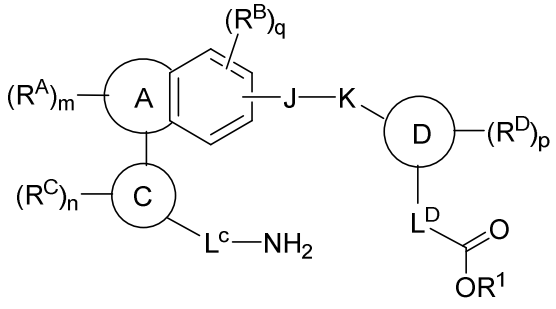
(Ih-1).

18. The compound of any one of claims 1-8, having the structure of formula (Ih-2):



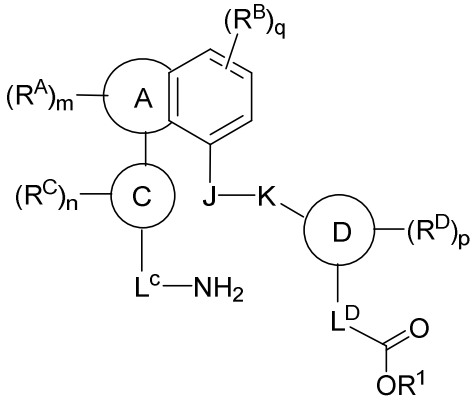
(Ih-2).

19. The compound of any one of claims 1-8, having the structure of formula (Ij):



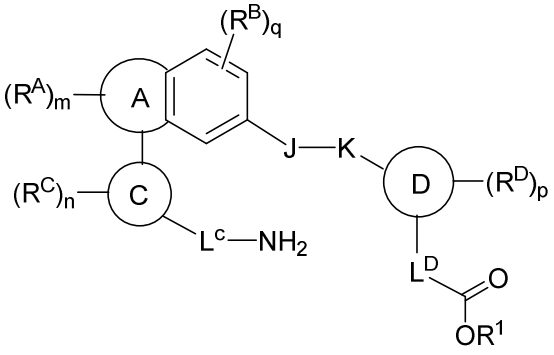
(Ij).

20. The compound of any one of claims 1-8 and 18, having the structure of formula (Ij-1):



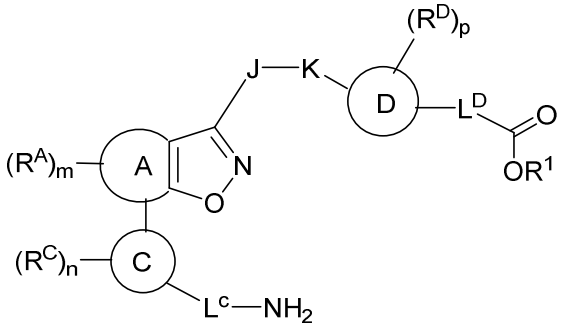
(Ij-1).

21. The compound of any one of claims 1-8 and 18, having the structure of formula (Ij-2):



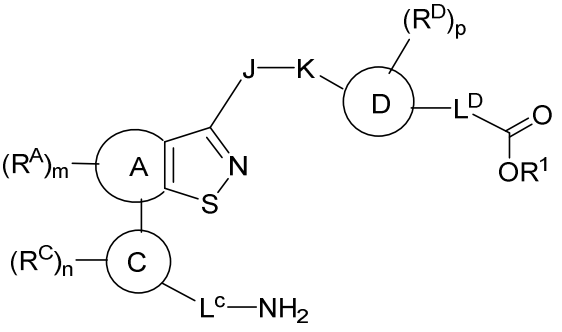
(Ij-2).

22. The compound of any one of claims 1-8, having the structure of formula (Ik):



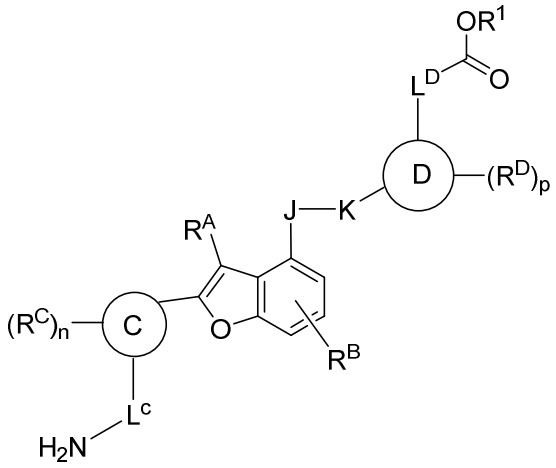
(Ik).

23. The compound of any one of claims 1-8, having the structure of formula (Im):



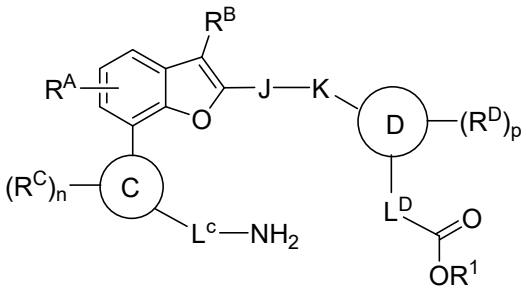
(Im).

24. The compound of claim 1 or 2, having the structure of formula (IIa):



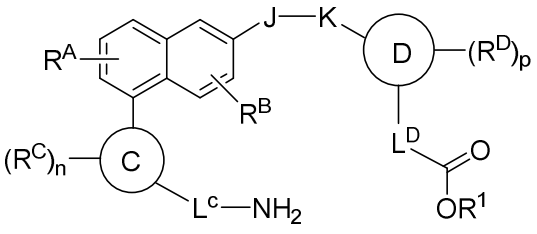
(IIa).

25. The compound of claim 1 or 2, having the structure of formula (IIb):



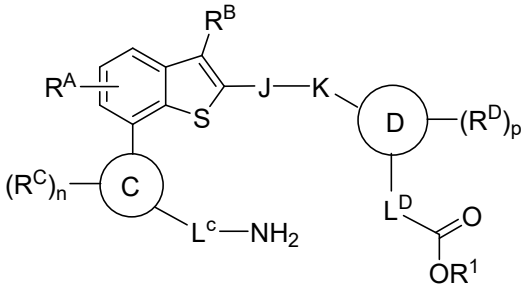
(IIb).

26. The compound of claim 1 or 2, having the structure of formula (IIc):



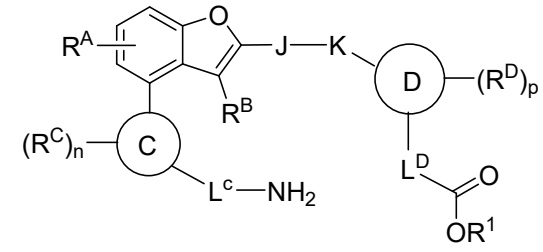
(IIc).

27. The compound of claim 1 or 2, having the structure of formula (IId):



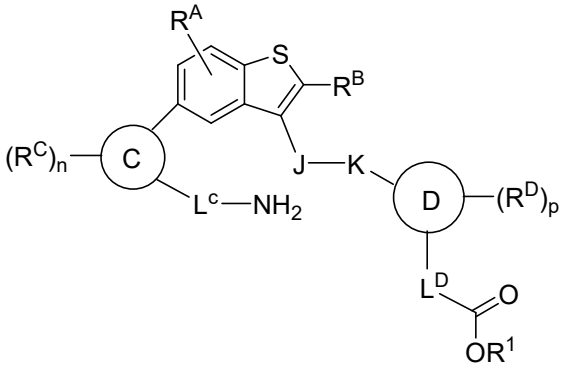
(IId).

28. The compound of claim 1 or 2, having the structure of formula (IIe):



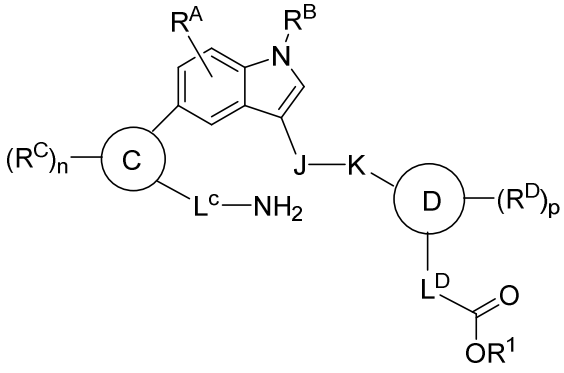
(IIe).

29. The compound of claim 1 or 2, having the structure of formula (IIf):



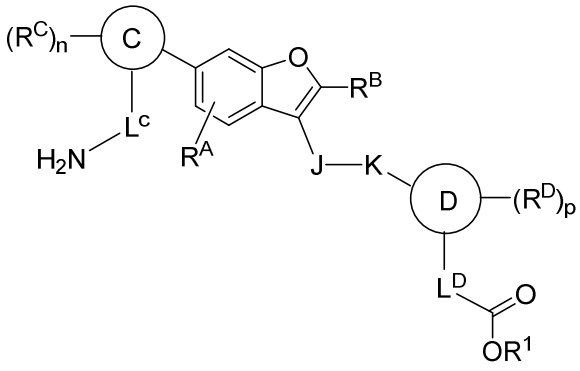
(IIf).

30. The compound of claim 1 or 2, having the structure of formula (IIg):



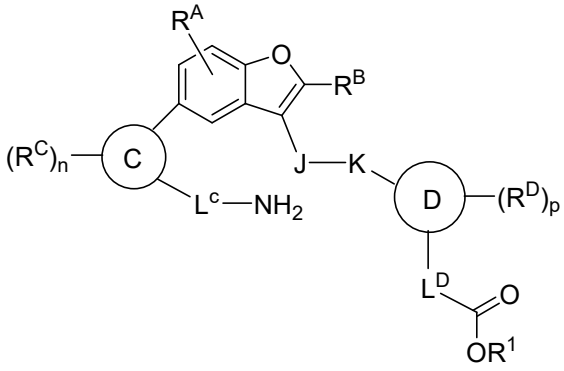
(IIg).

31. The compound of claim 1 or 2, having the structure of formula (IIh):



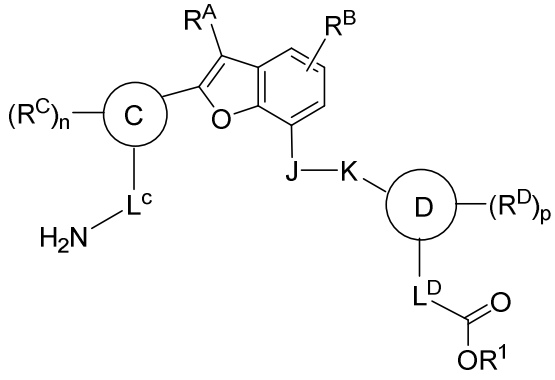
(IIh).

32. The compound of claim 1 or 2, having the structure of formula (IIj):



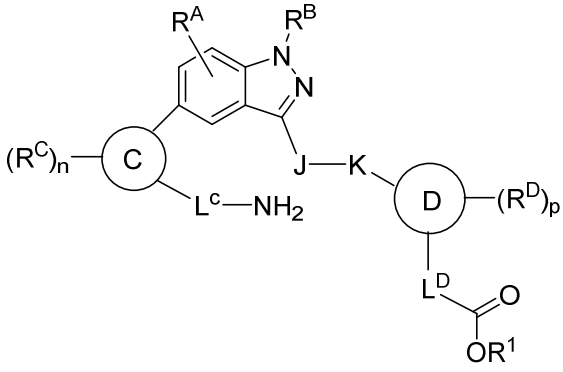
(IIj).

33. The compound of claim 1 or 2, having the structure of formula (IIk):



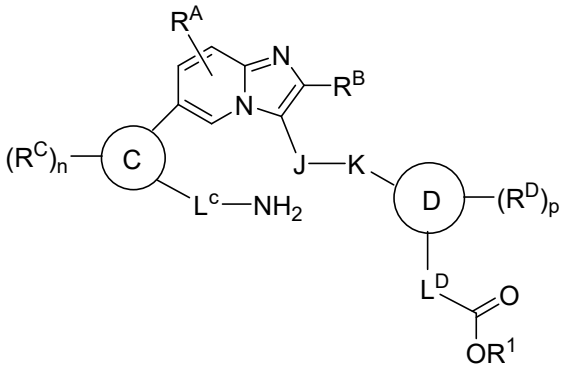
(IIk).

34. The compound of claim 1 or 2, having the structure of formula (IIm):



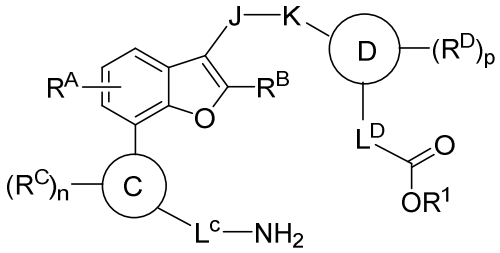
(IIm).

35. The compound of claim 1 or 2, having the structure of formula (IIn):



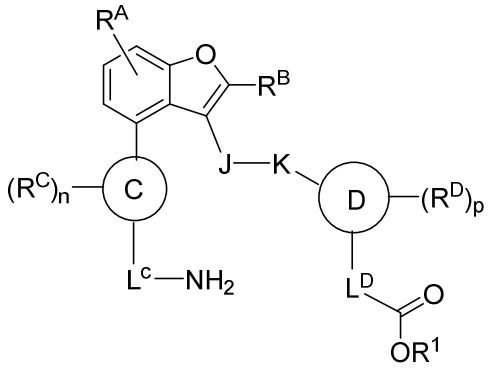
(IIn).

36. The compound of claim 1 or 2, having the structure of formula (IIo):



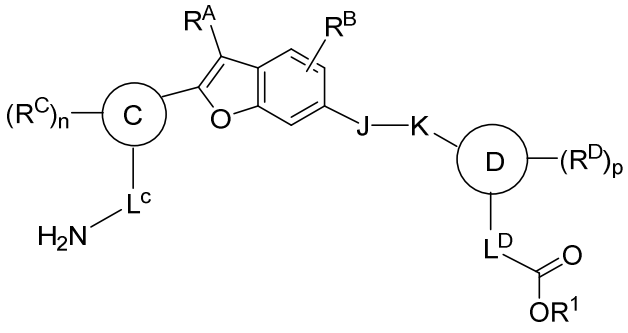
(IIo).

37. The compound of claim 1 or 2, having the structure of formula (IIp):



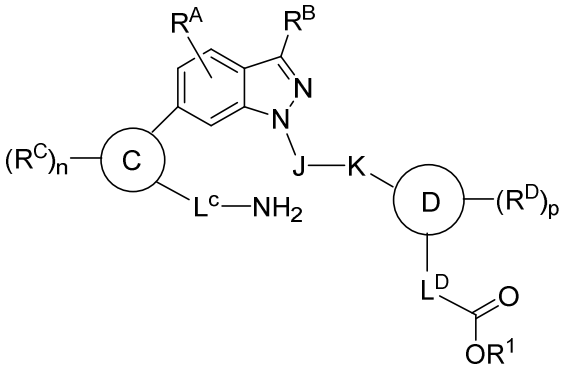
(IIp).

38. The compound of claim 1 or 2, having the structure of formula (IIq):



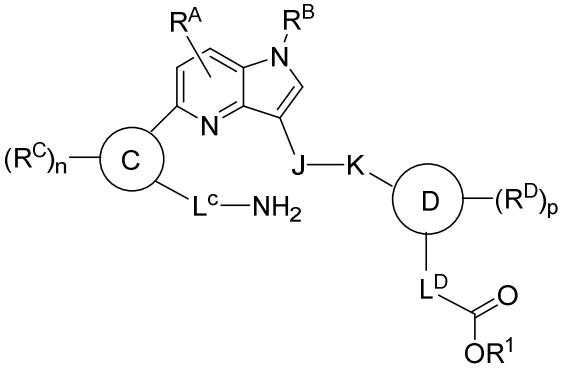
(IIq).

39. The compound of claim 1 or 2, having the structure of formula (IIr):



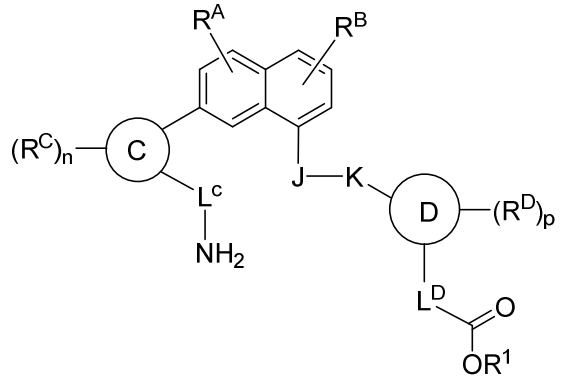
(IIr).

40. The compound of claim 1 or 2, having the structure of formula (IIs):



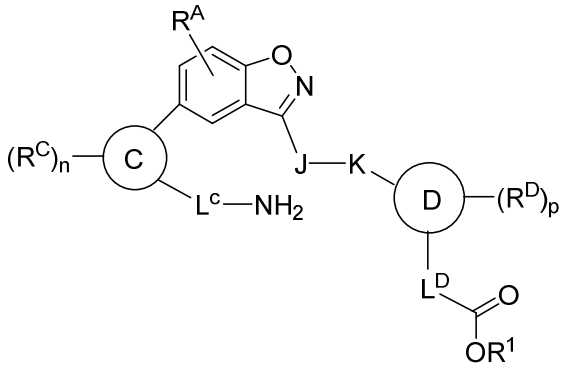
(IIs).

41. The compound of claim 1 or 2, having the structure of formula (IIt):



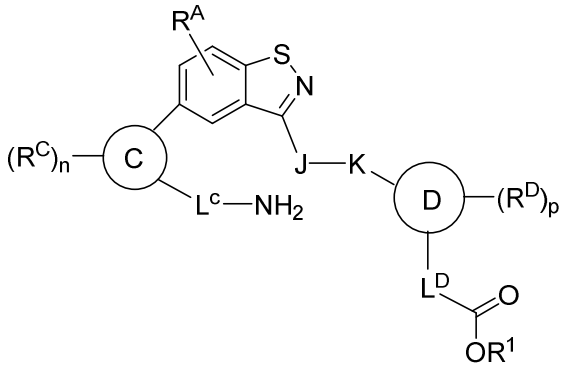
(IIt).

42. The compound of claim 1 or 2, having the structure of formula (IIu):



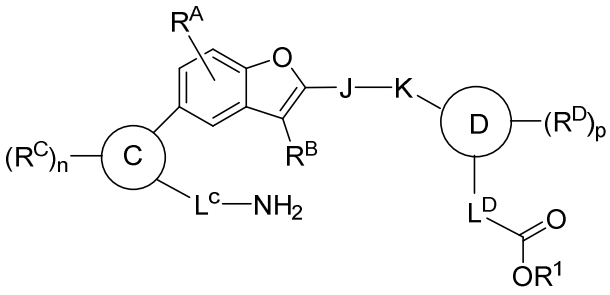
(IIu).

43. The compound of claim 1 or 2, having the structure of formula (IIv):



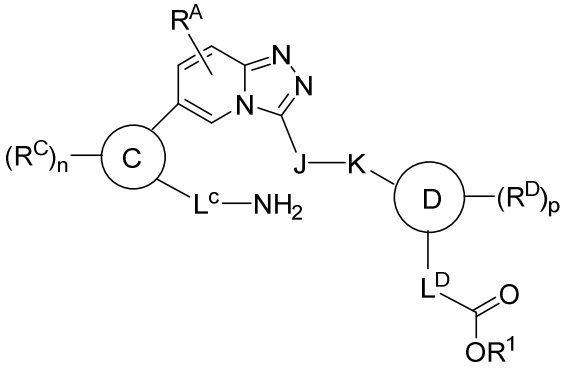
(IIv).

44. The compound of claim 1 or 2, having the structure of formula (IIw):



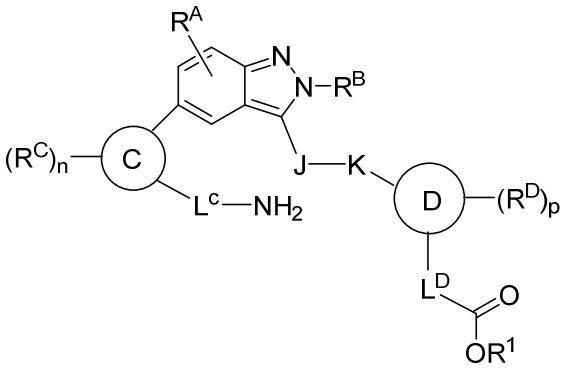
(IIw).

45. The compound of claim 1 or 2, having the structure of formula (IIx):



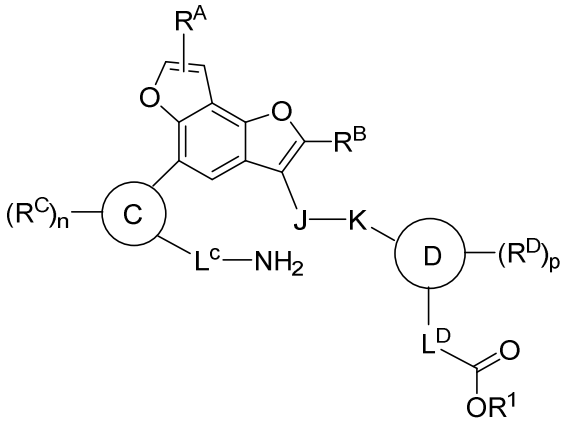
(IIx).

46. The compound of claim 1 or 2, having the structure of formula (IIy):



(IIy).

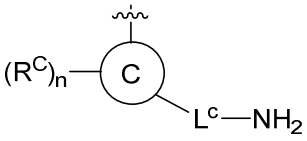
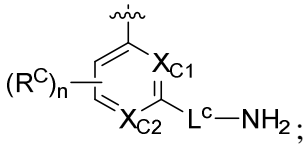
47. The compound of claim 1 or 2, having the structure of formula (IIz):



(IIz).

48. The compound of any one of claims 1-47, wherein ring  represents a 6-membered aryl or heteroaryl.

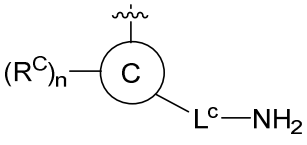
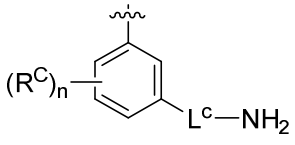
49. The compound of any one of claims 1-48, wherein:

 represents ;

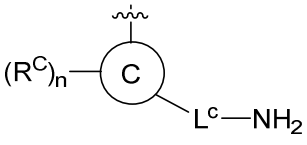
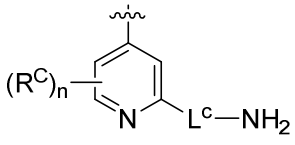
X_{C1} represents CH or N; and

X_{C2} represents CH or N.

50. The compound of any one of claims 1-49, wherein

 represents .

51. The compound of any one of claims 1-49, wherein

 represents .

52. The compound of any one of claims 1-51, wherein L^C represents $–CH_2–$.

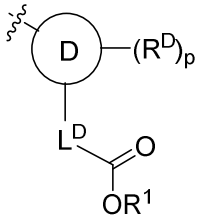
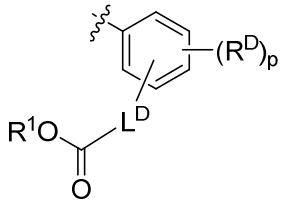
53. The compound of any one of claims 1-52, wherein R^C represents H.

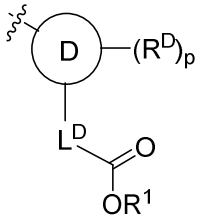
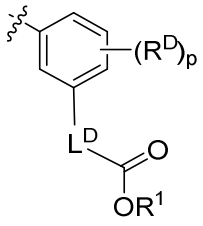
54. The compound of any one of claims 1-52, wherein R^C represents halo, preferably F.

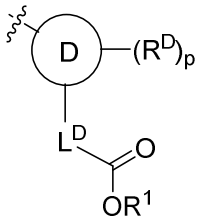
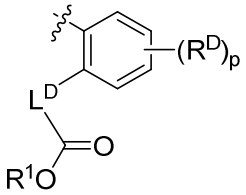
55. The compound of any one of claims 1-54, wherein –J–K– represents $–CH_2–$, –NH–, $–CH_2$-O–, $–CH_2CH_2$-O–, –C(O)-NH–, or –NHC(O)–.

56. The compound of any one of claims 1-54, wherein –J–K– represents $–CH_2$-O– or –C(O)-NH–.

57. The compound of any one of claims 1-56, wherein ring  is aryl.

58. The compound of any one of claims 1-57, wherein  represents .

59. The compound of any one of claims 1-58, wherein  represents .

60. The compound of any one of claims 1-58, wherein  represents .

61. The compound of any one of claims 1-60, wherein R^1 is H.

62. The compound of any one of claims 1-61, wherein L^D represents $–CH_2–$, $–CH_2CH_2–$, or a bond.

63. The compound of any one of claims 1-62, wherein L^D represents $–CH_2–$.

64. The compound of any one of claims 1-63, wherein R^D represents H, halo, hydroxyl, alkyl, or alkoxyl.

65. The compound of any one of claims 1-64, wherein R^D represents H.

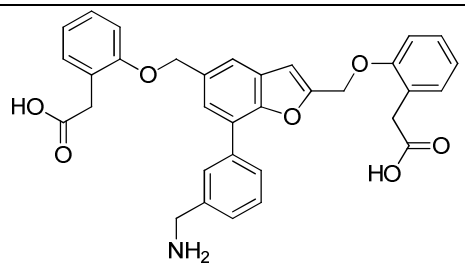
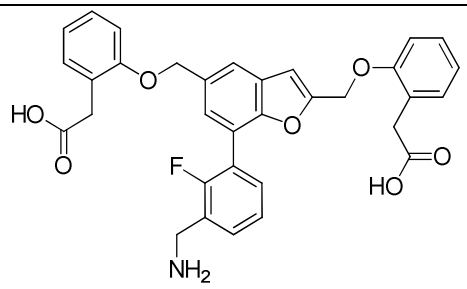
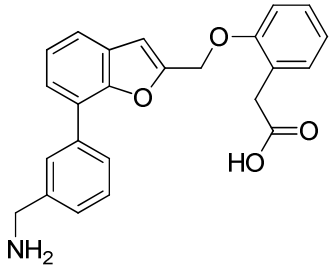
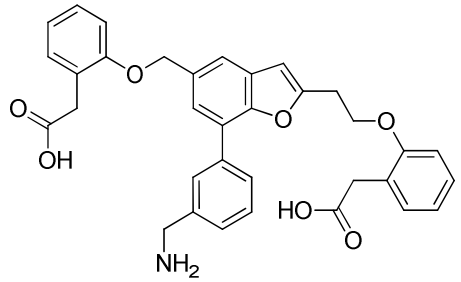
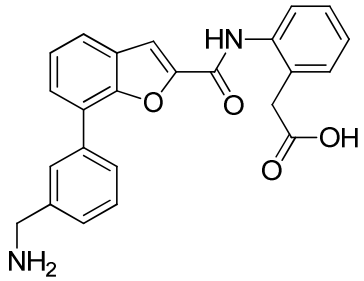
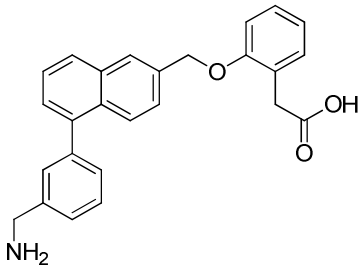
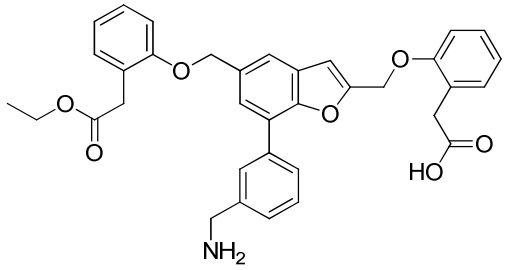
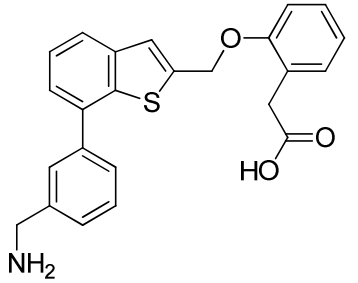
66. The compound of any one of claims 1-65, wherein R^B represents H, alkyl, or –C(O)OH.

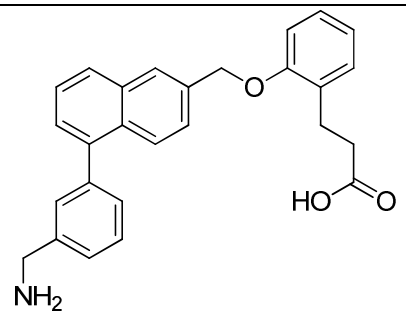
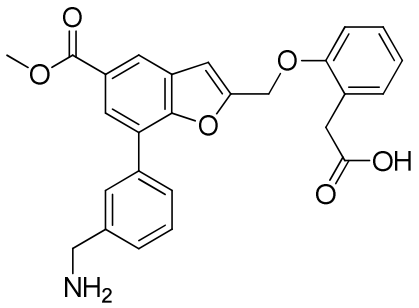
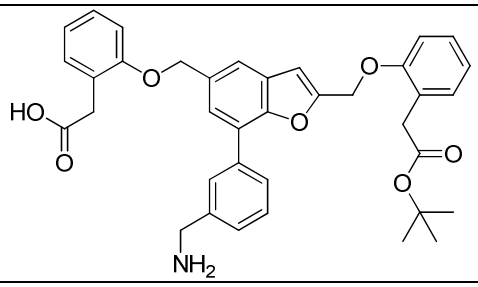
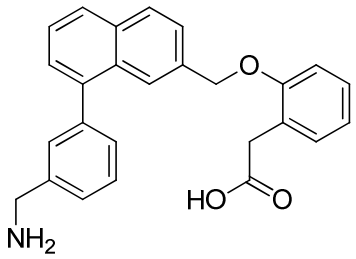
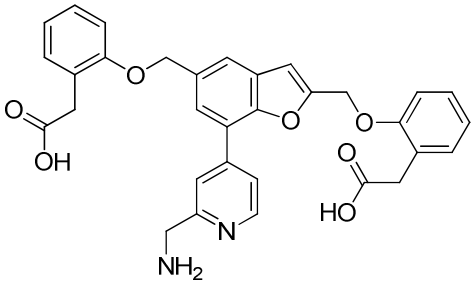
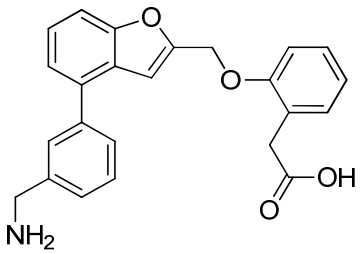
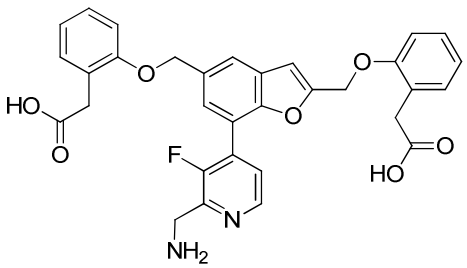
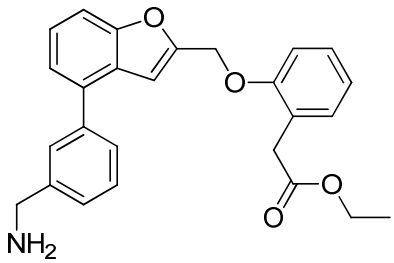
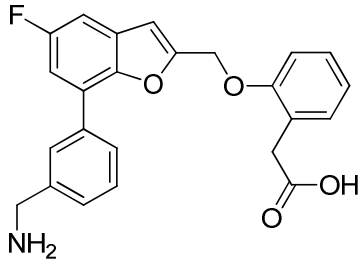
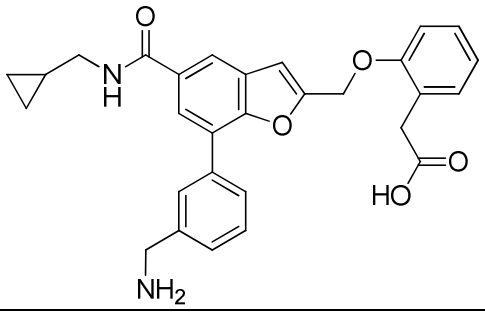
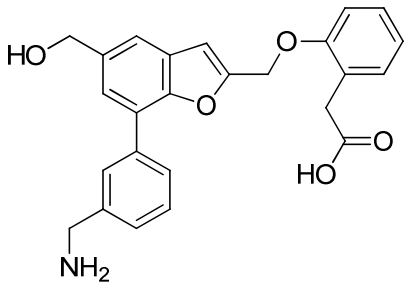
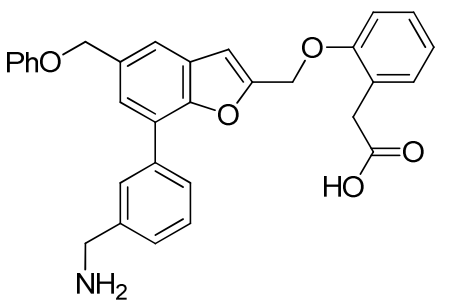
67. The compound of any one of claims 1-66, wherein R^B represents H.

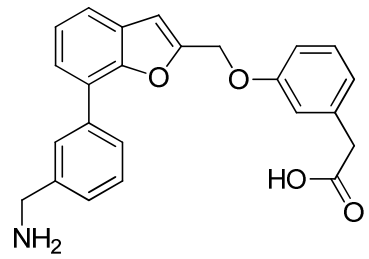
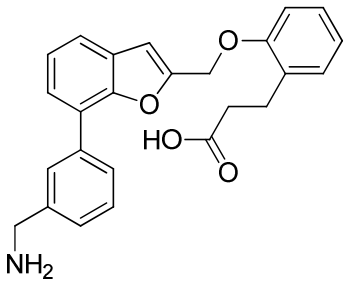
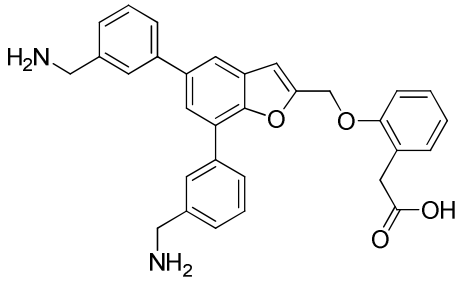
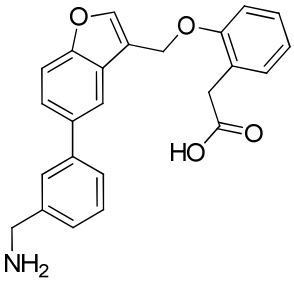
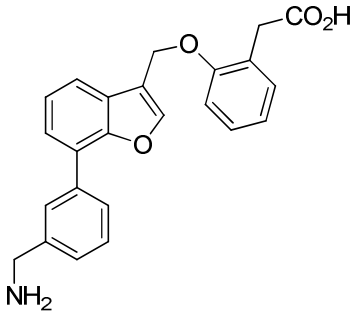
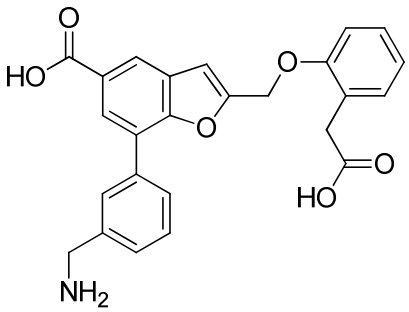
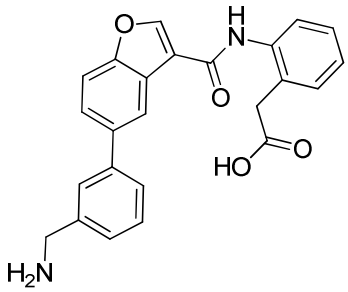
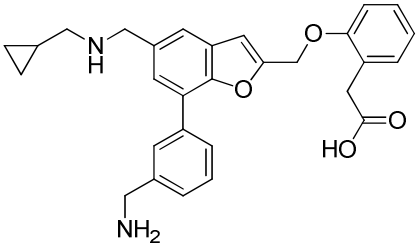
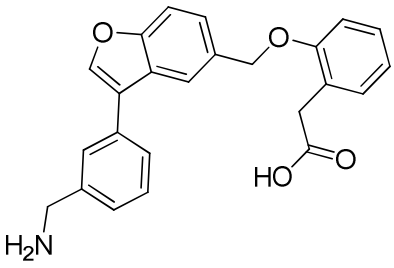
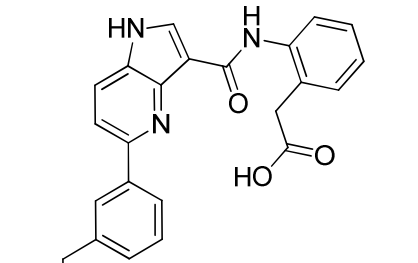
68. The compound of any one of claims 1-67, wherein R^A represents H, alkyl, alkoxyl, or –CH_2O(optionally substituted aryl).

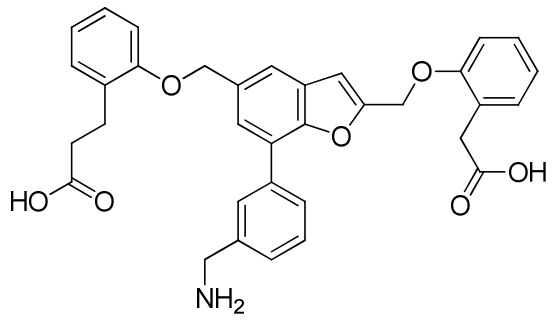
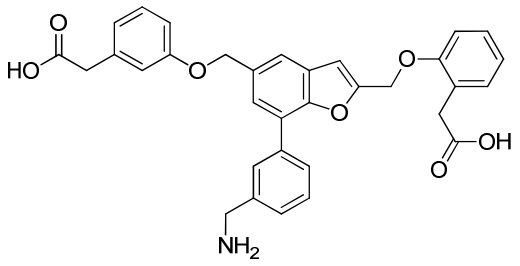
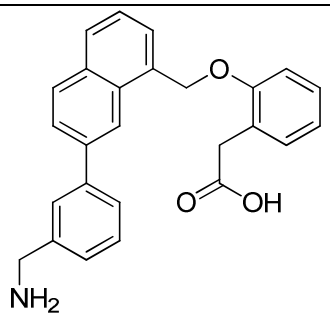
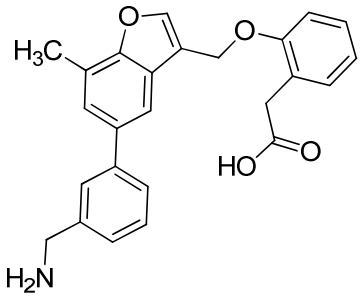
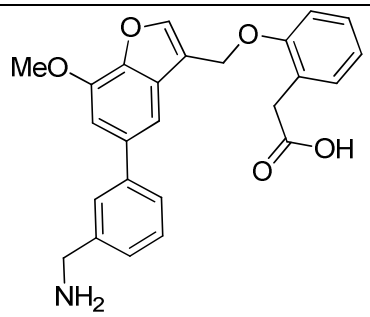
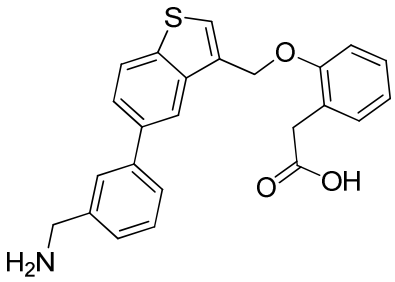
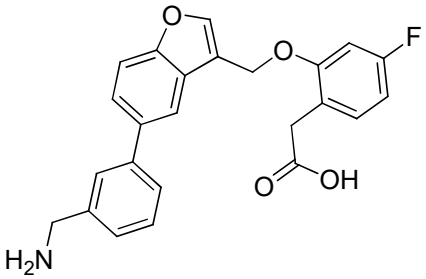
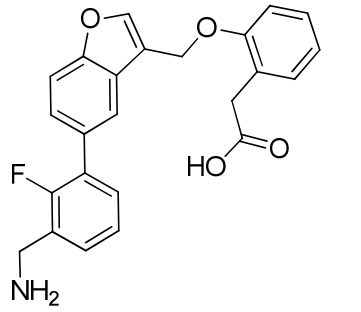
69. The compound of any one of claims 1-68, wherein R^A represents H.

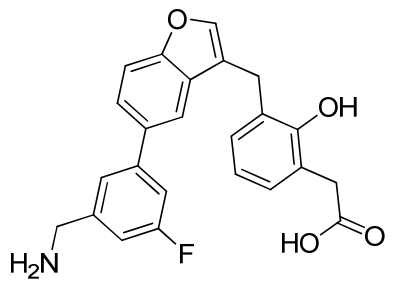
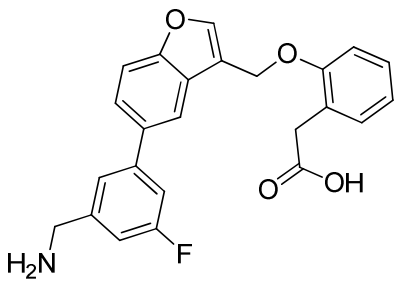
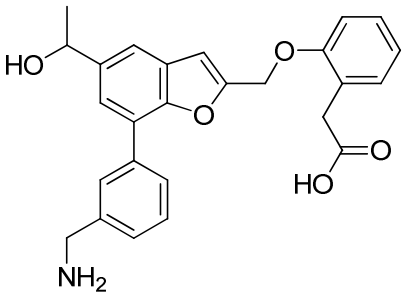
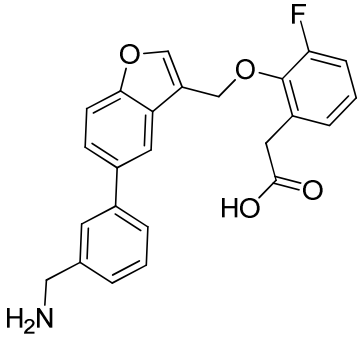
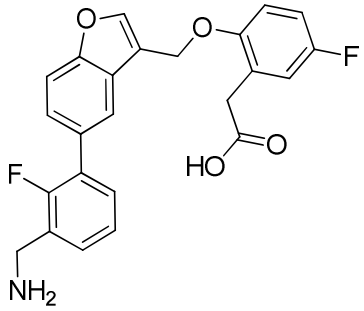
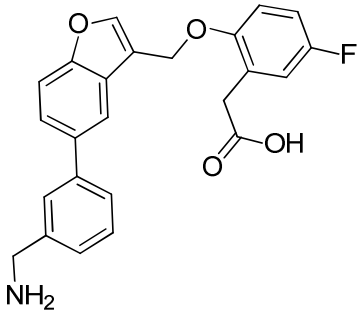
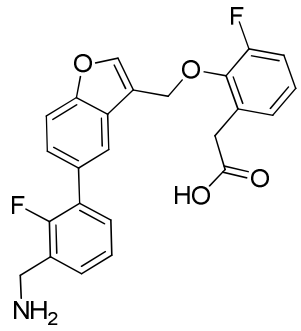
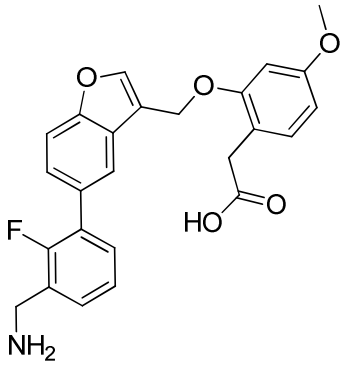
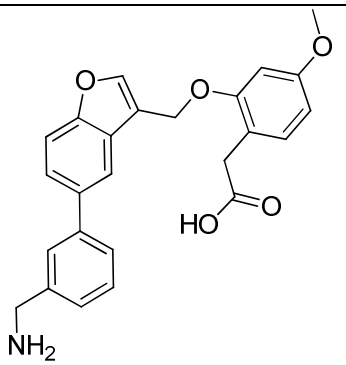
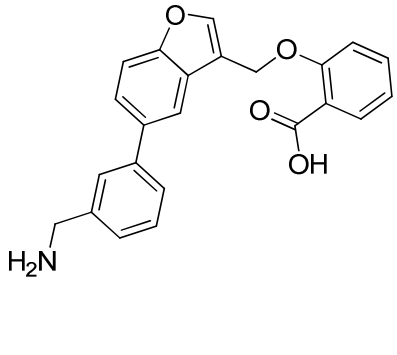
70. The compound of claim 1, selected from the following table:

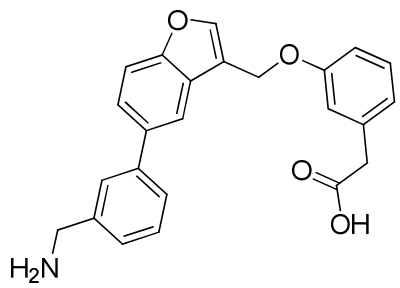
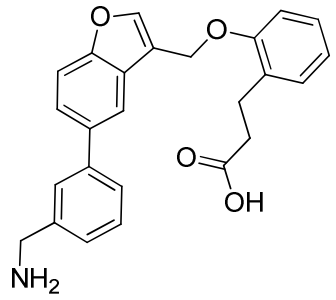
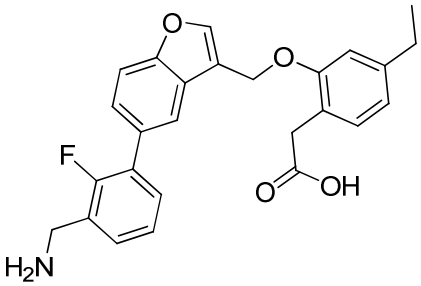
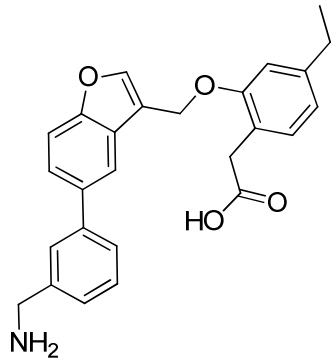
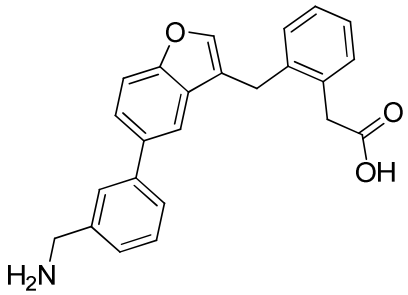
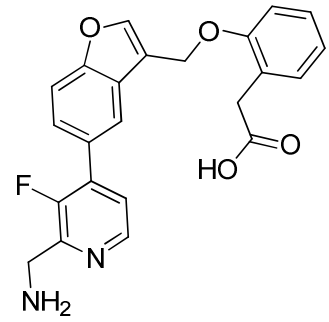
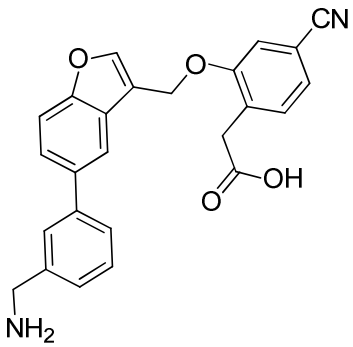
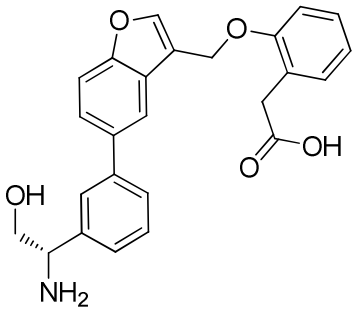
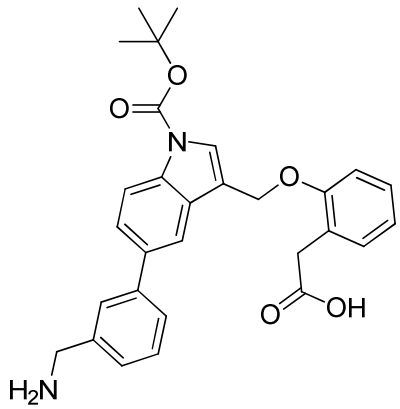
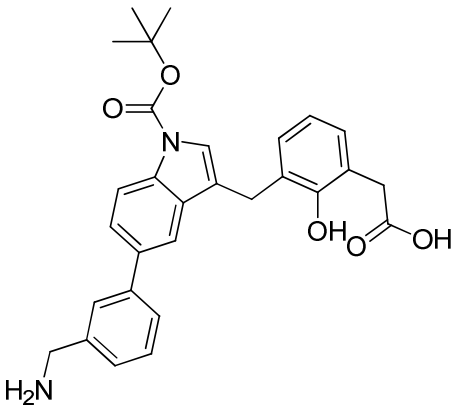
	
	
	
	

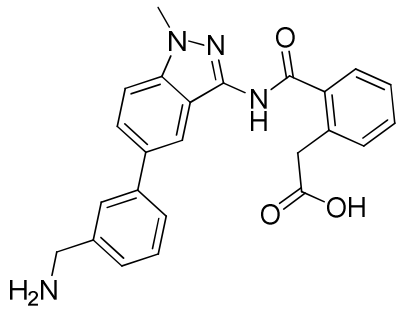
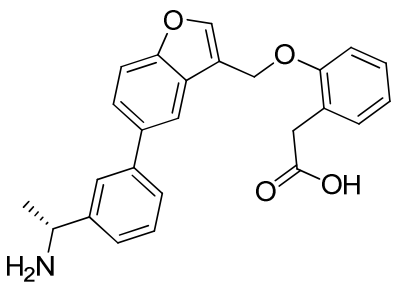
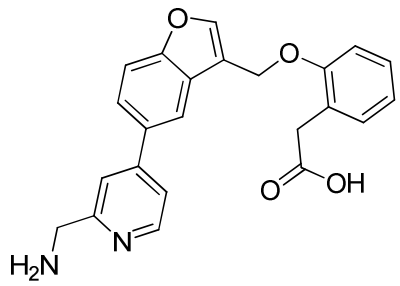
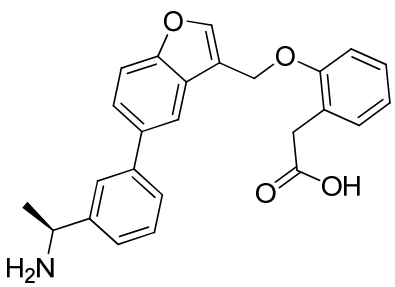
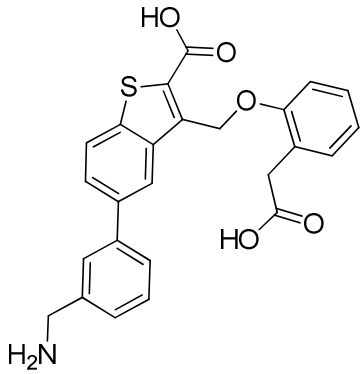
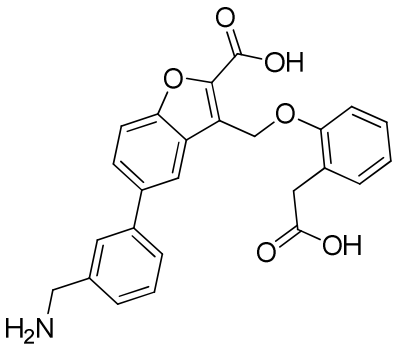
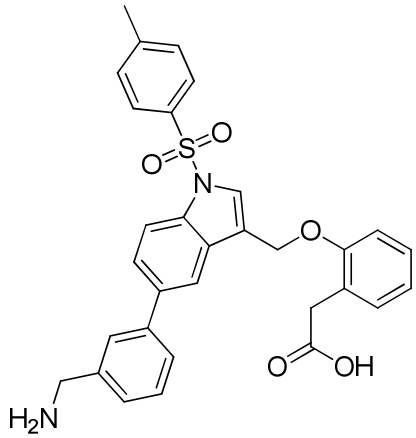
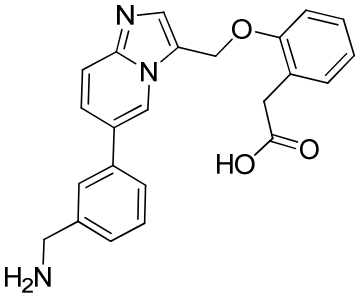
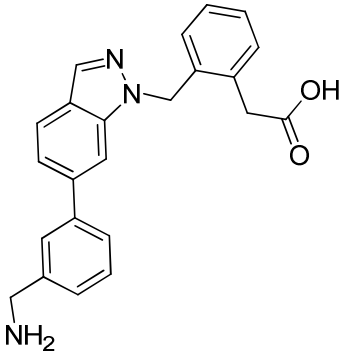
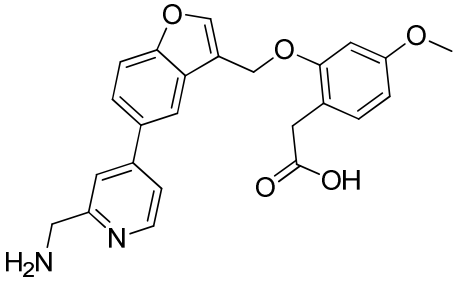
	
	
	
	
	
	

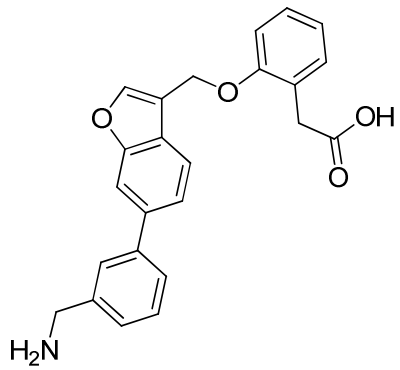
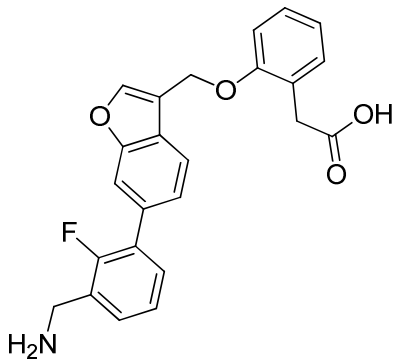
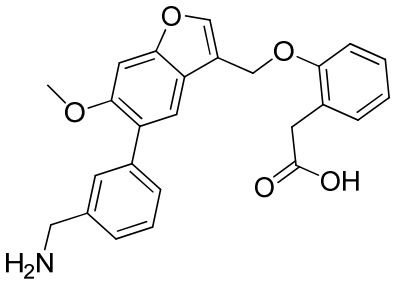
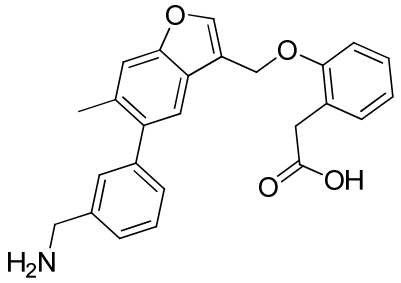
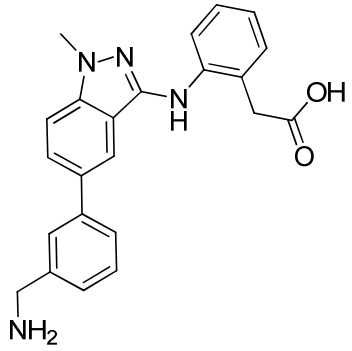
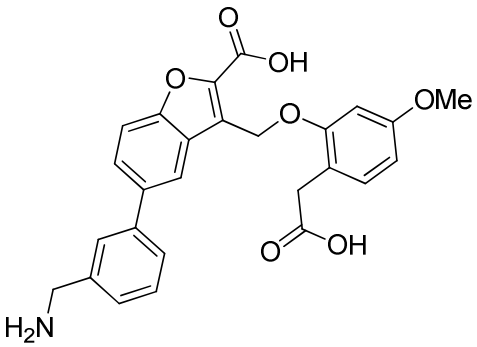
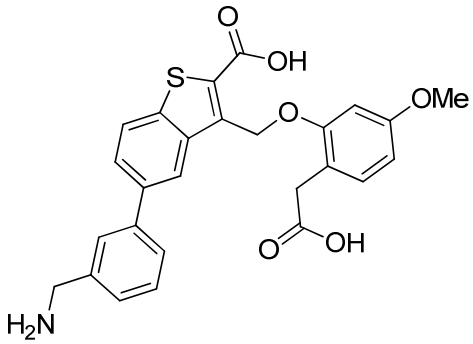
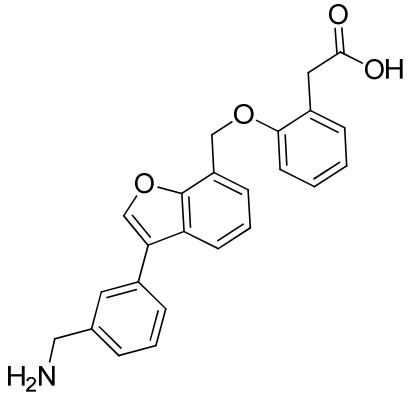
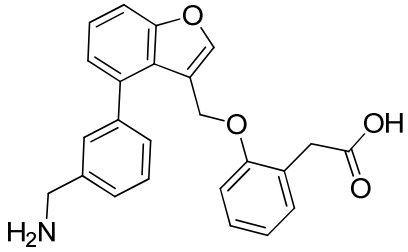
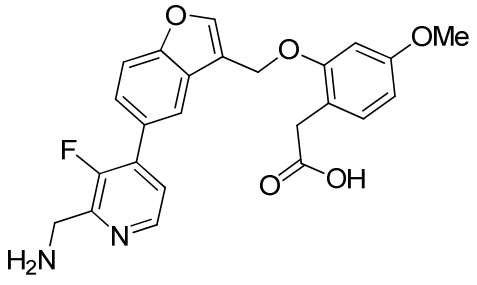
	
	
	
	
	

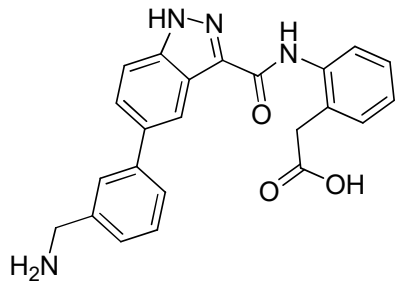
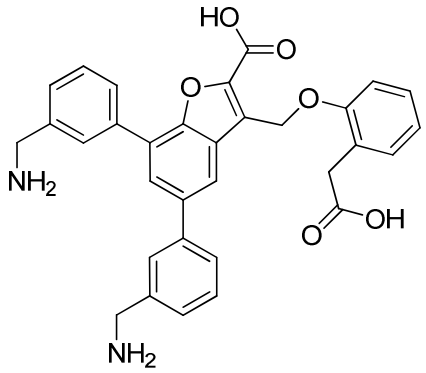
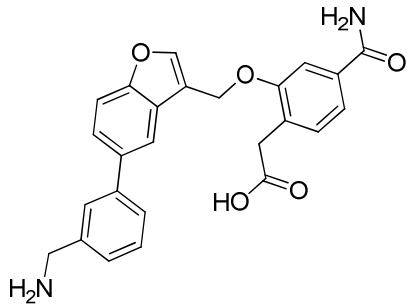
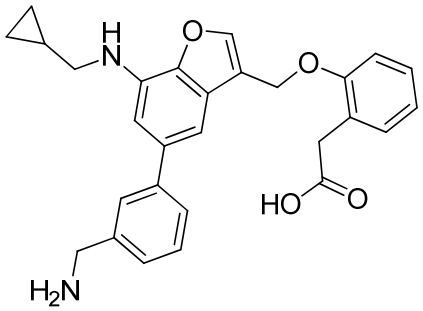
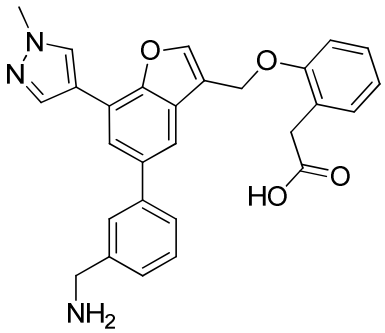
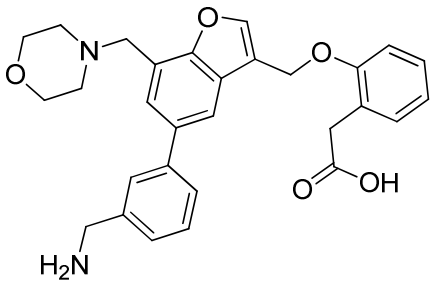
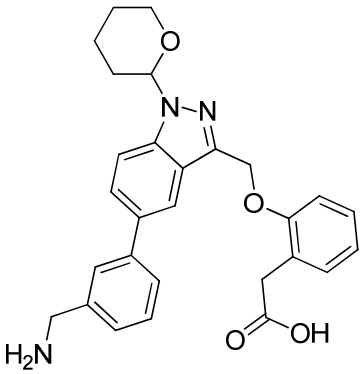
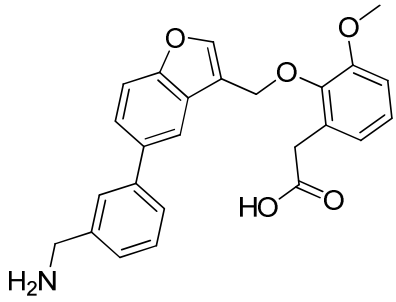
	
	
	
	

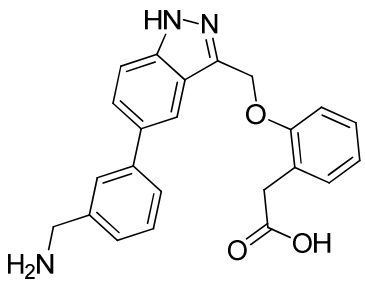
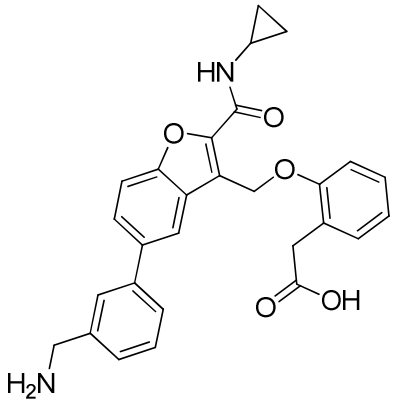
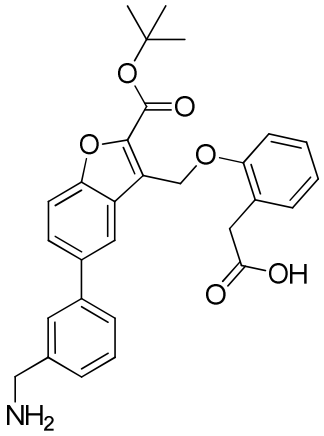
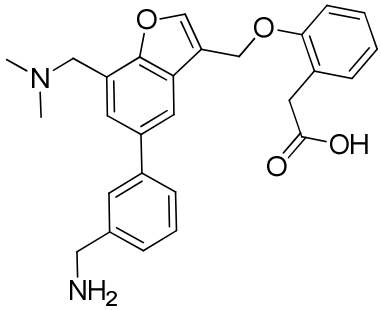
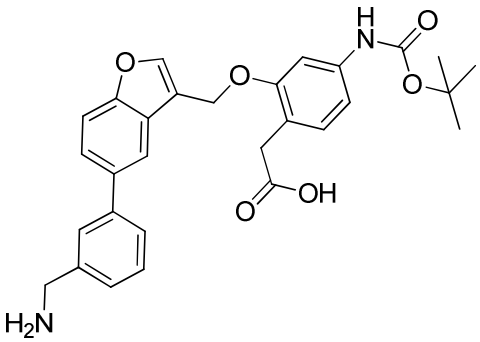
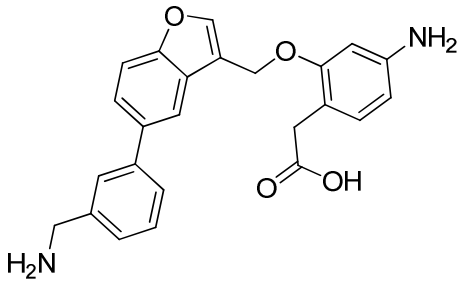
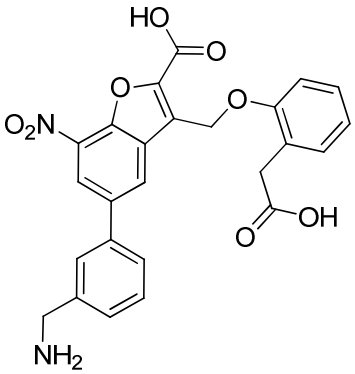
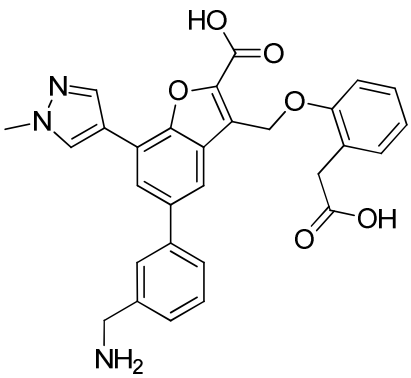
	
	
	
	
	

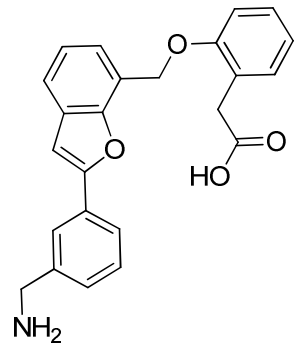
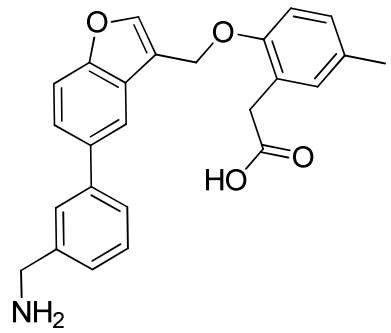
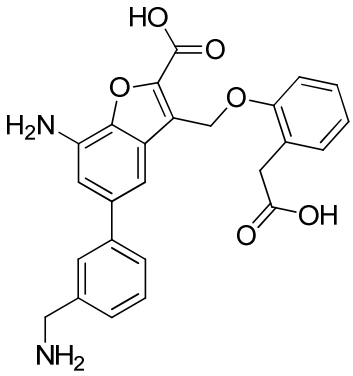
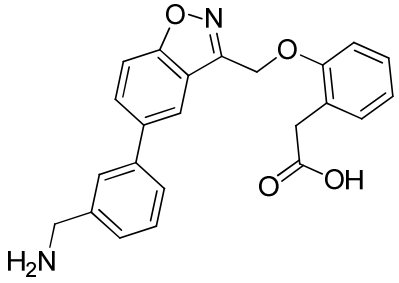
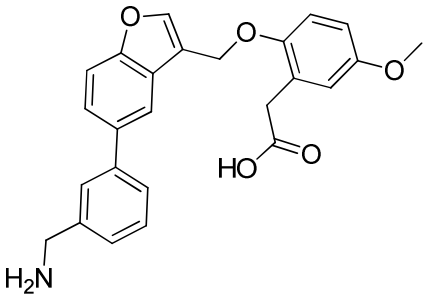
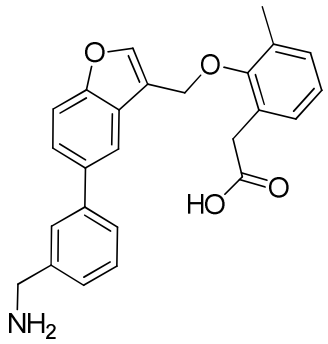
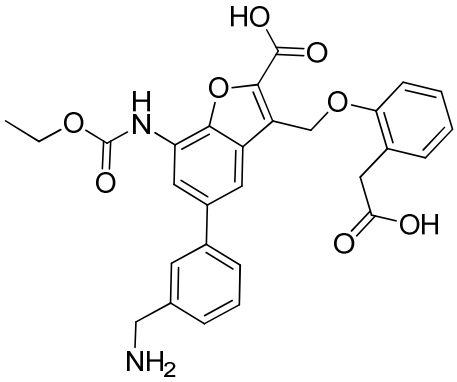
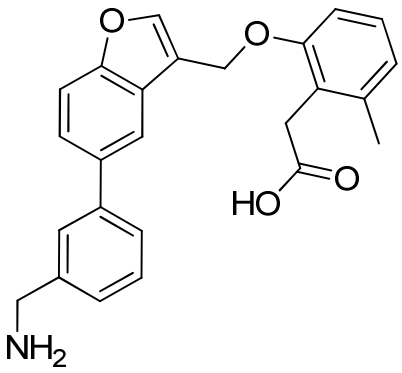
	
	
	
	
	

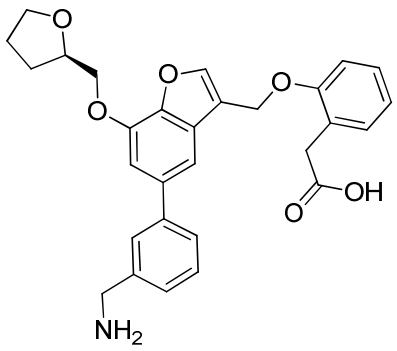
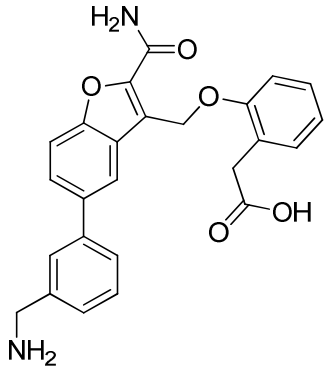
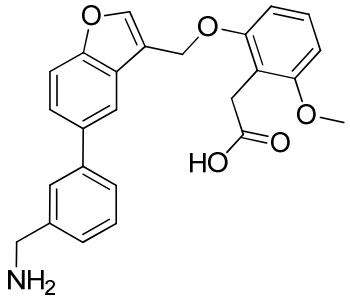
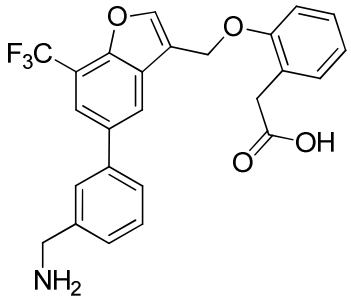
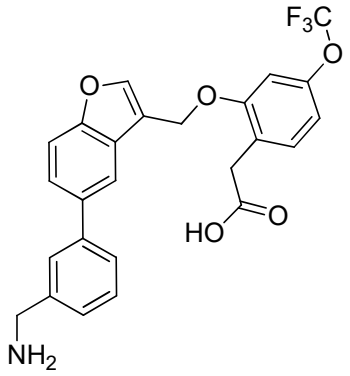
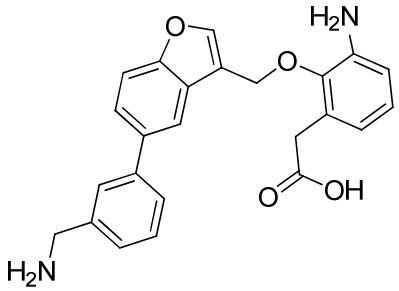
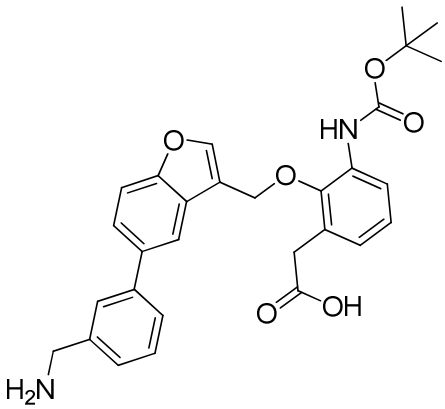
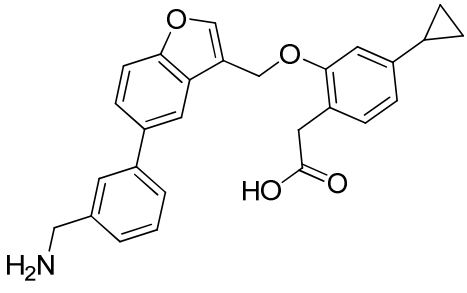
	
	
	
	
	

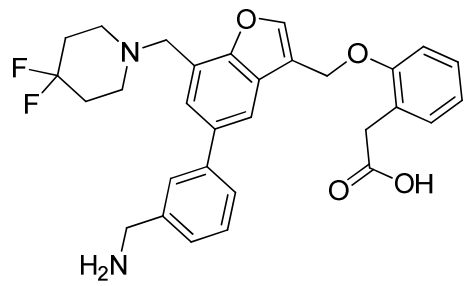
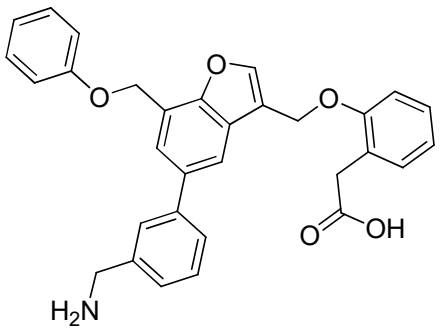
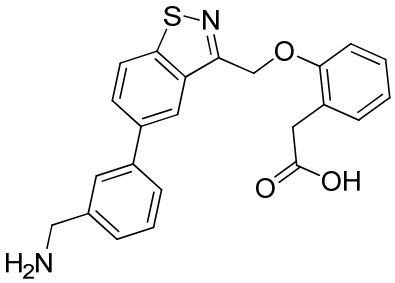
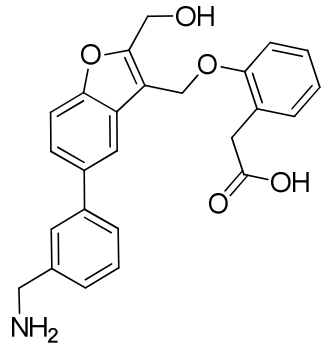
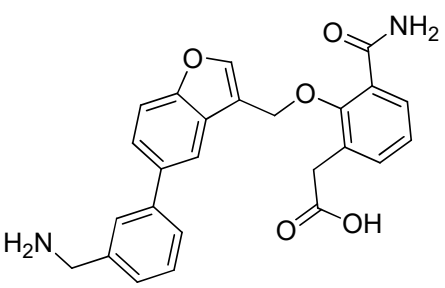
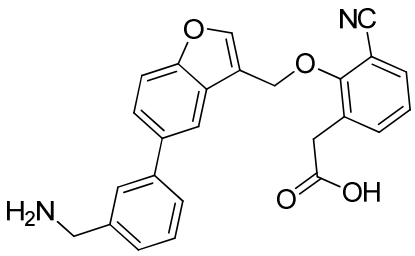
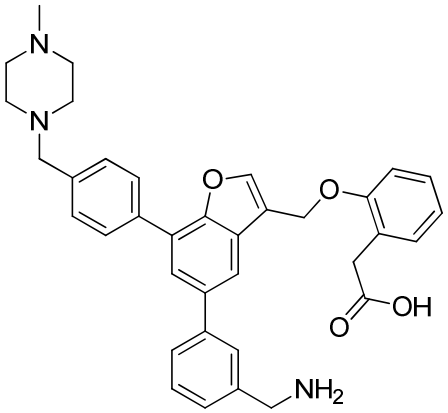
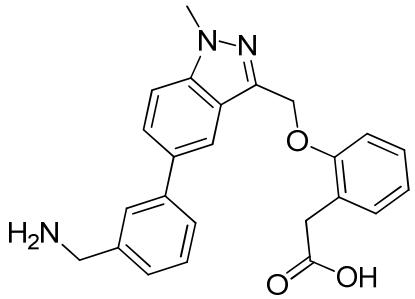
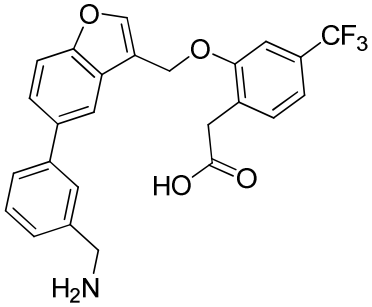
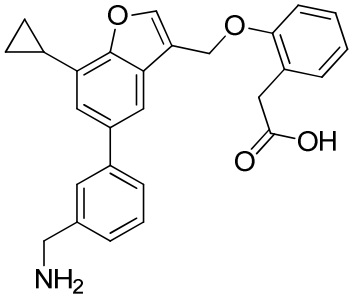
	
	
	
	
	

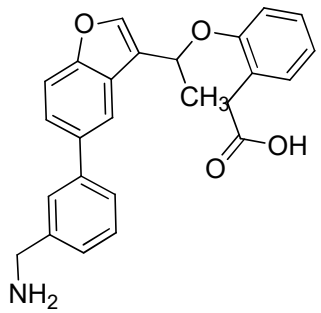
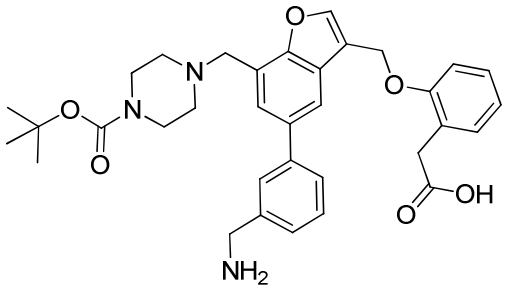
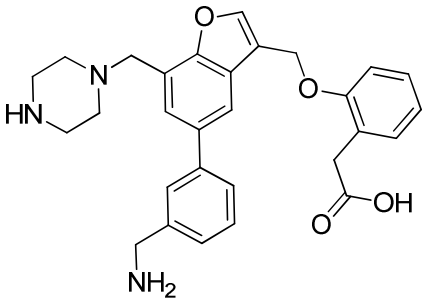
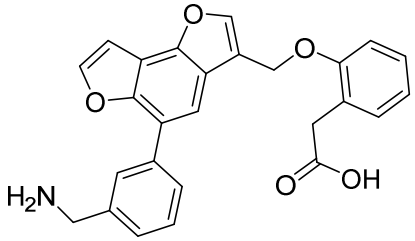
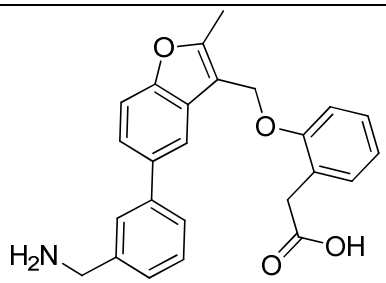
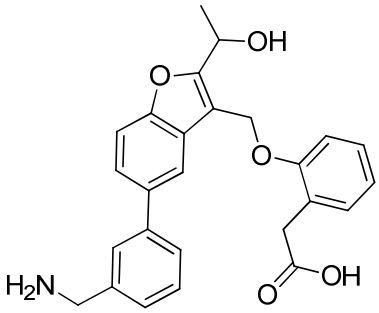
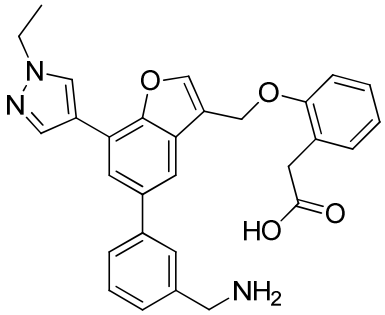
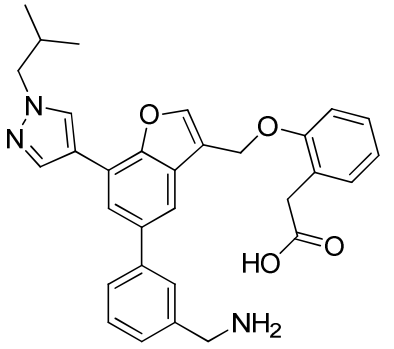
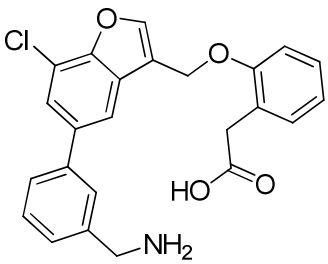
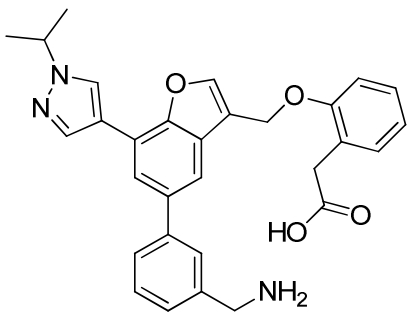
	
	
	
	

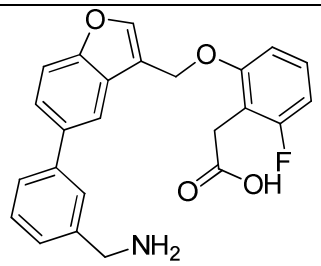
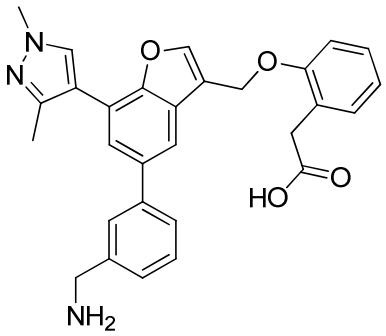
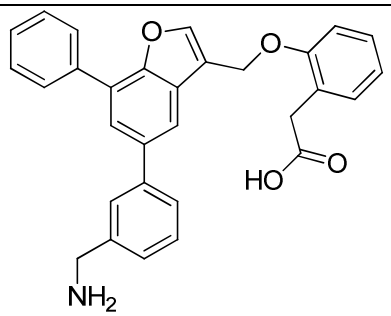
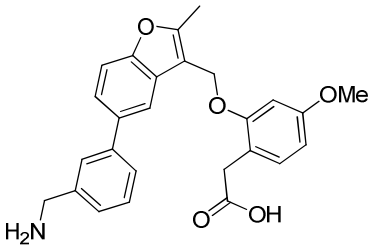
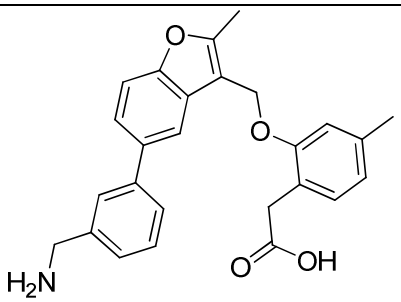
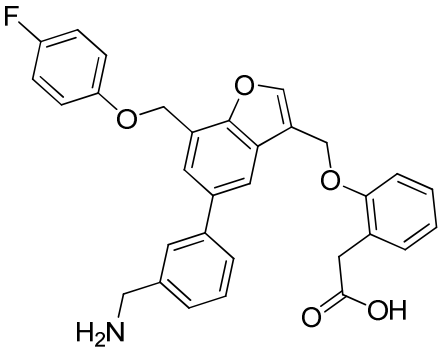
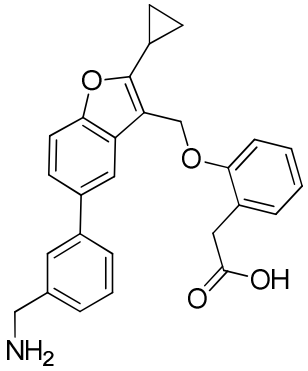
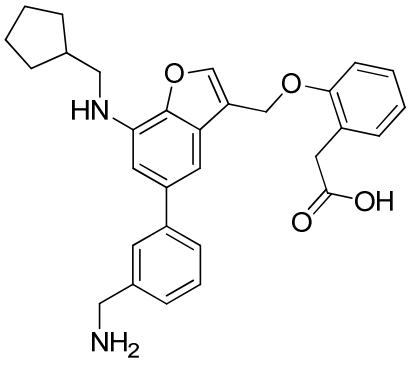
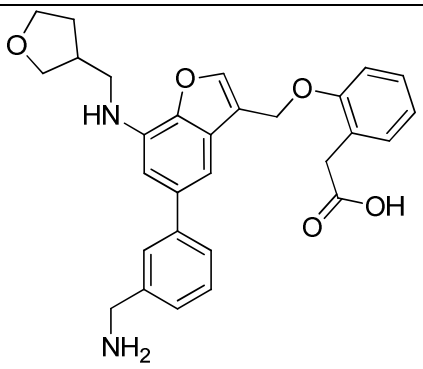
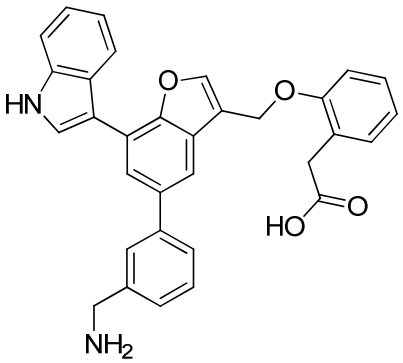
	
	
	
	

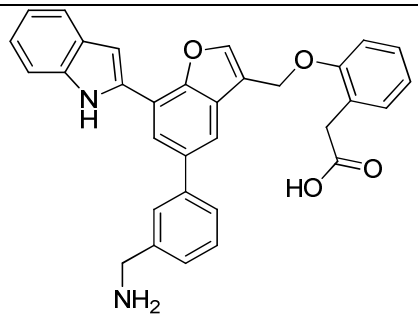
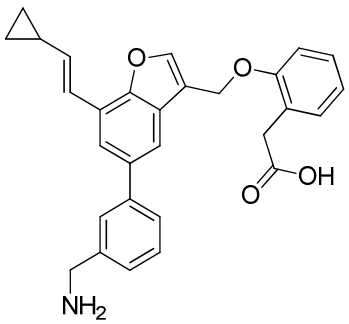
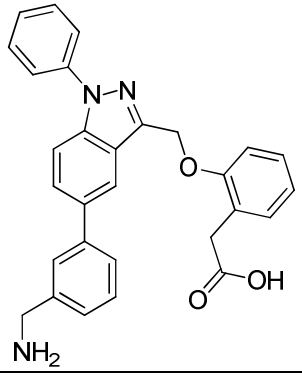
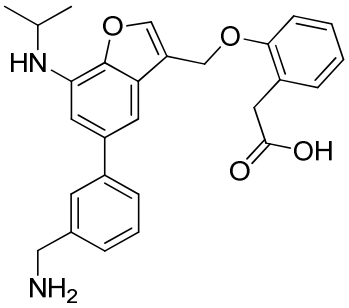
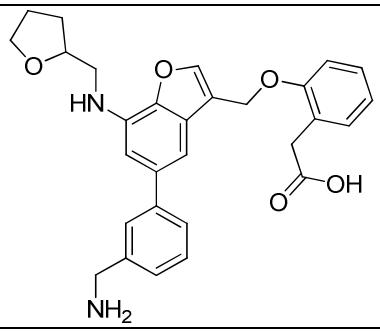
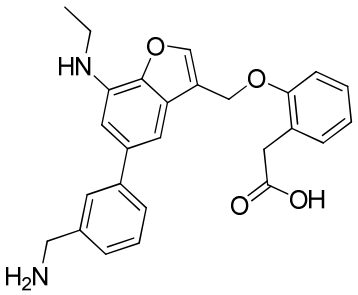
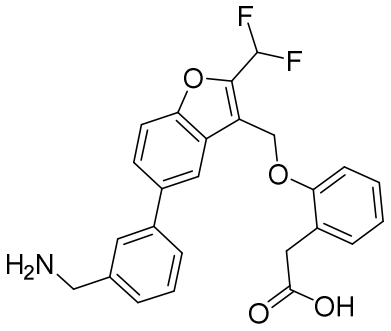
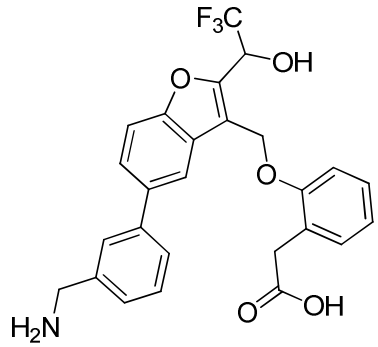
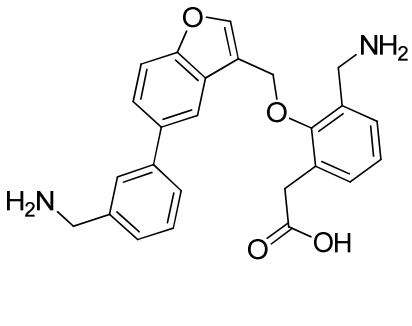
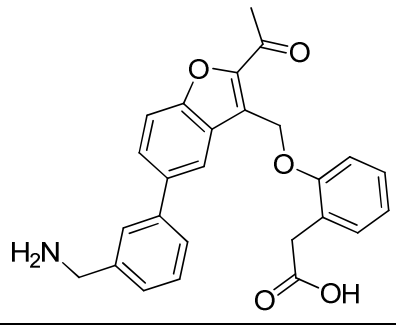
	
	
	
	

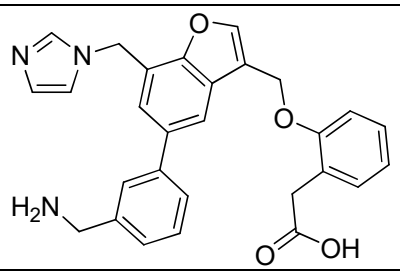
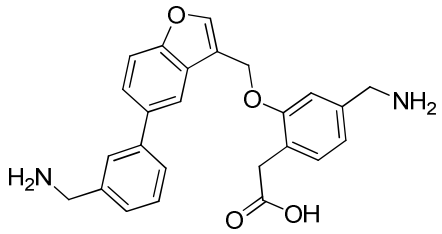
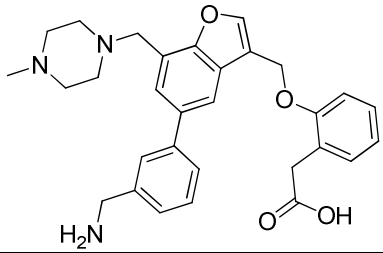
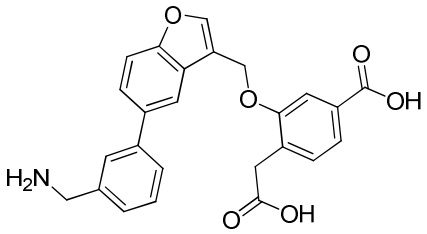
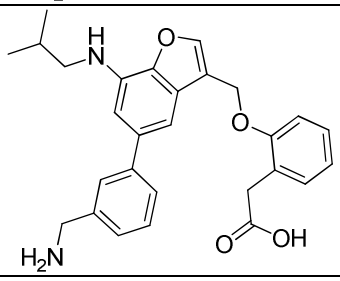
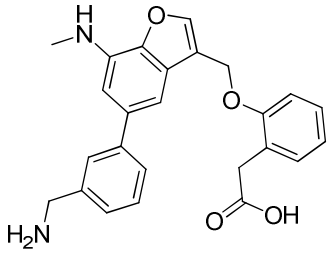
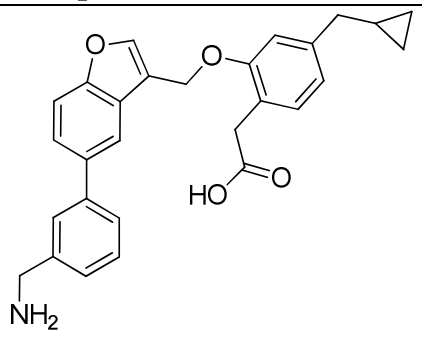
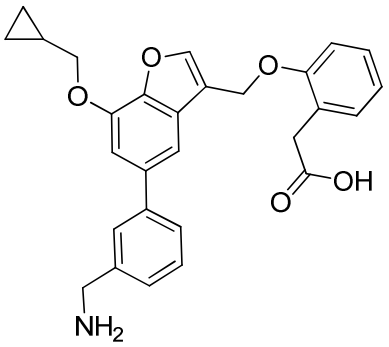
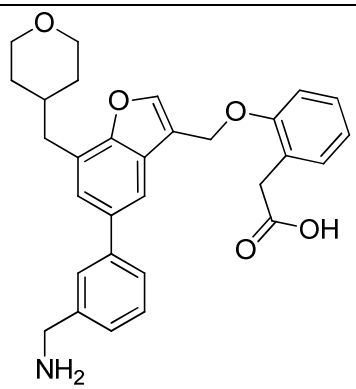
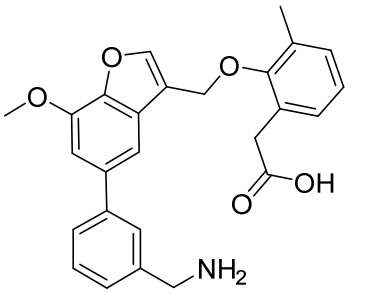
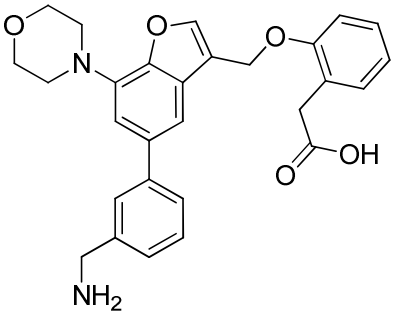
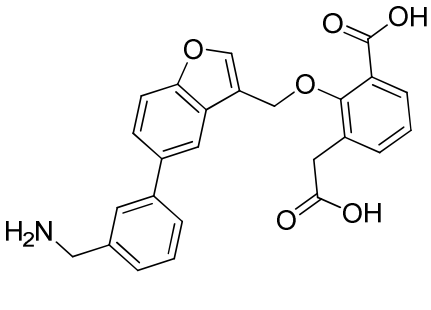
	
	
	
	

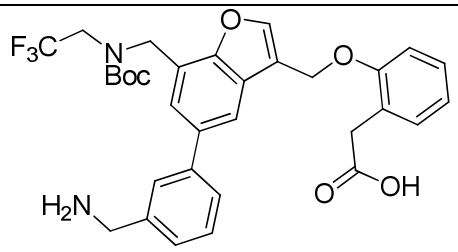
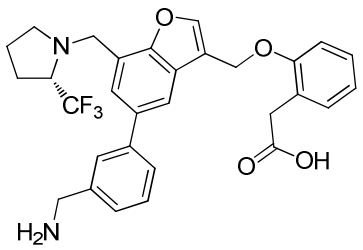
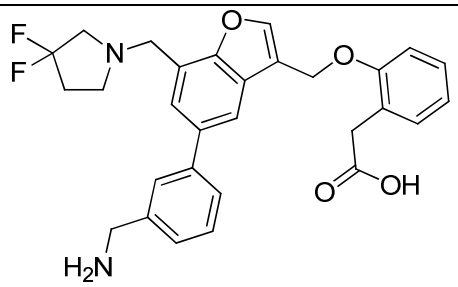
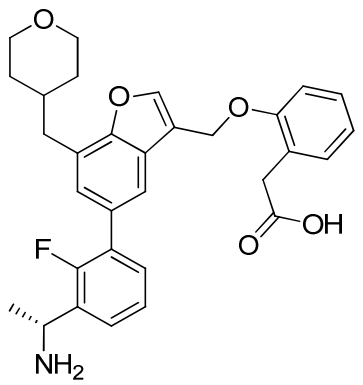
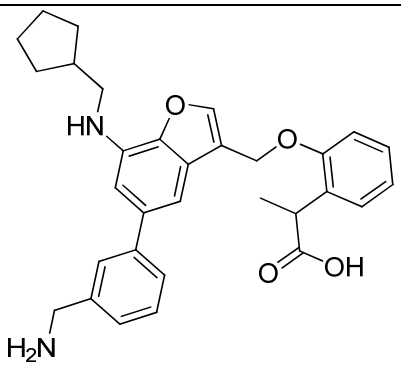
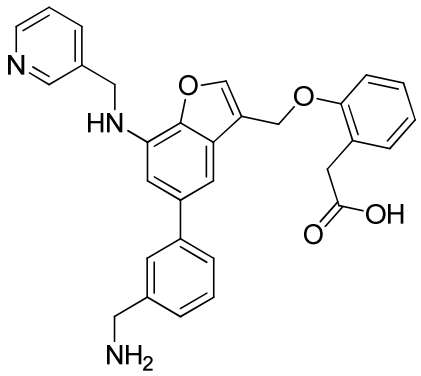
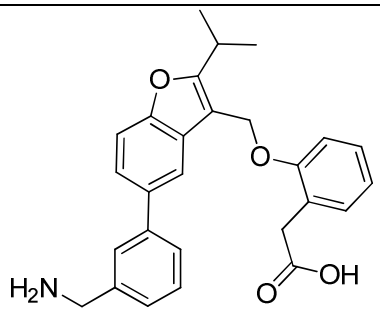
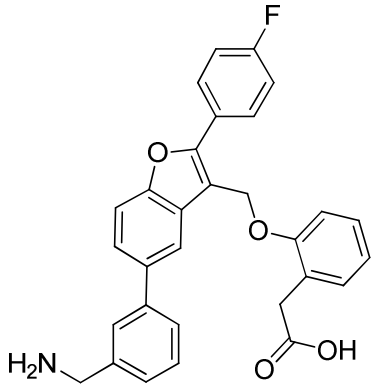
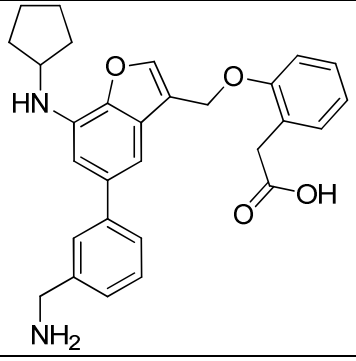
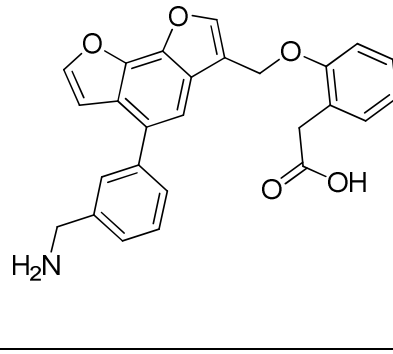
	
	
	
	
	

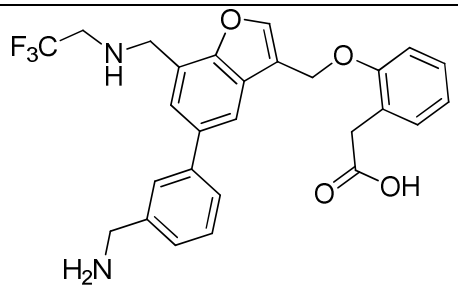
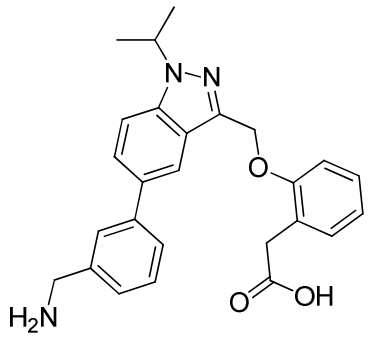
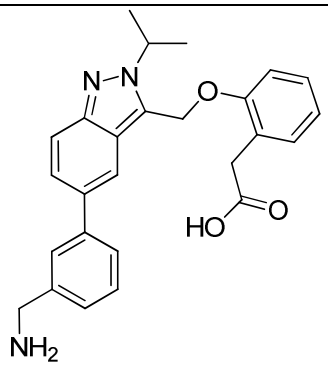
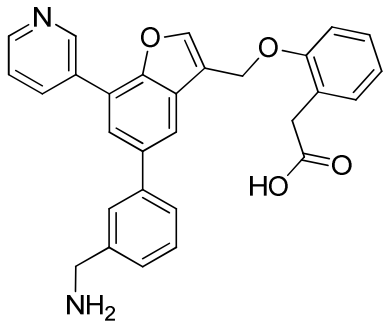
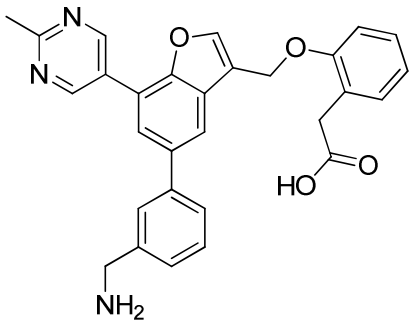
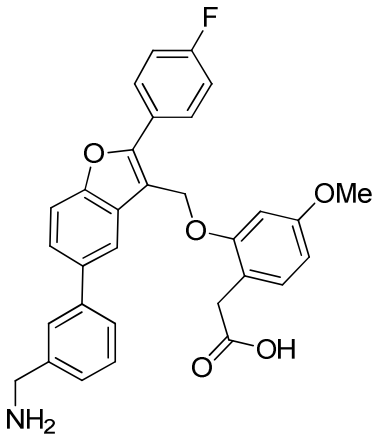
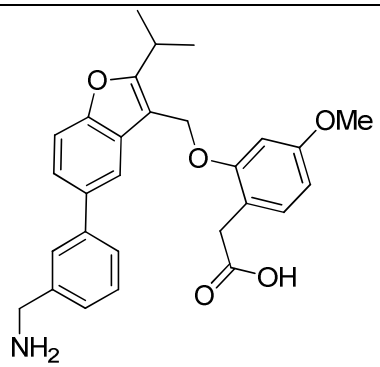
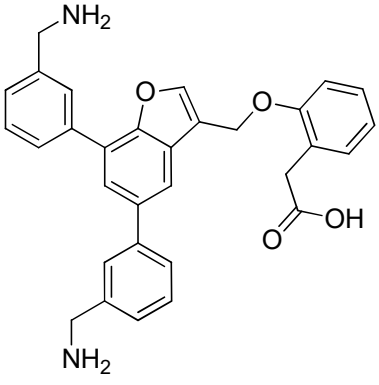
	
	
	
	
	

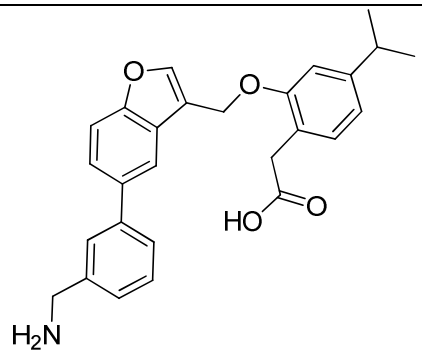
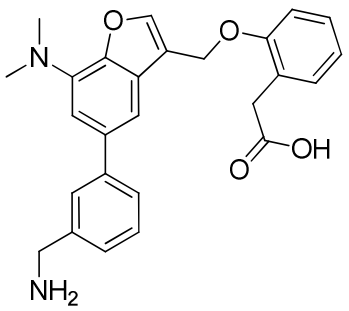
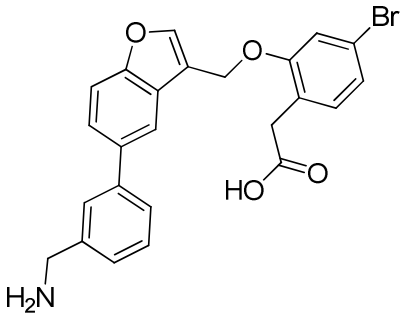
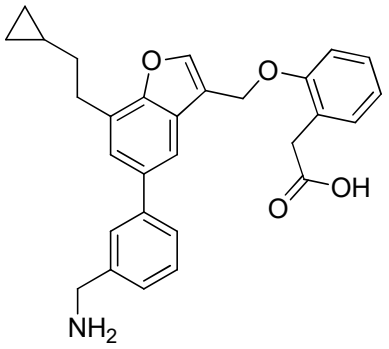
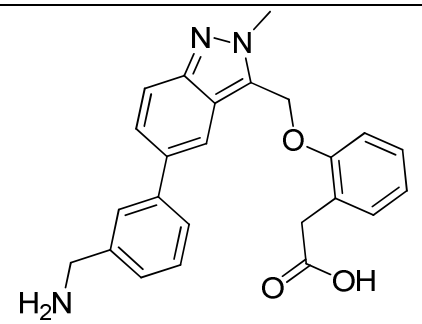
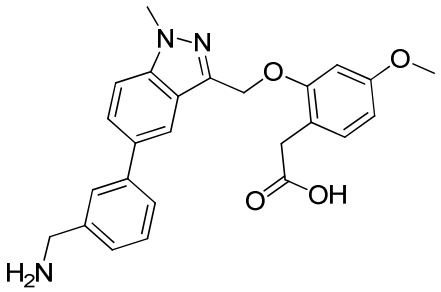
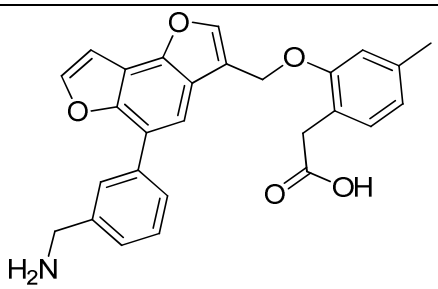
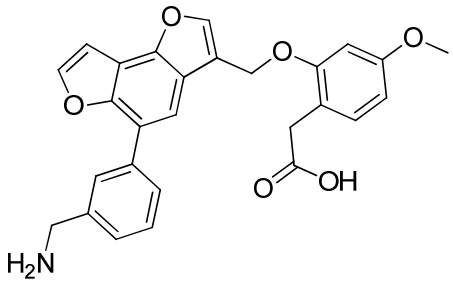
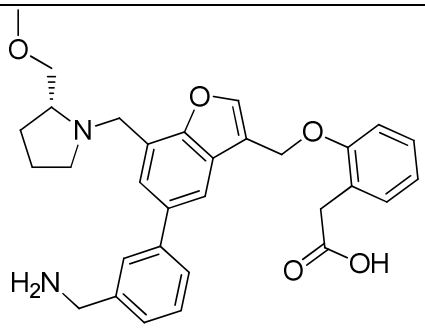
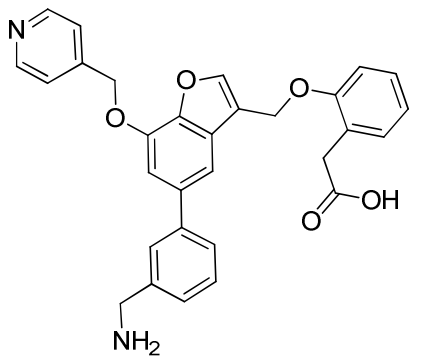
	
	
	
	
	

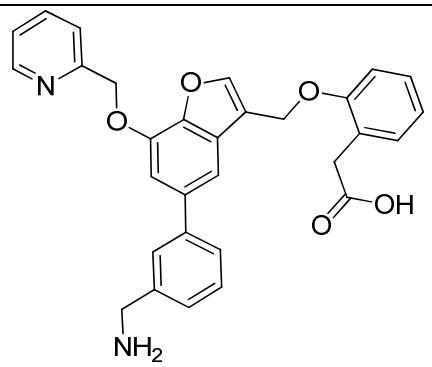
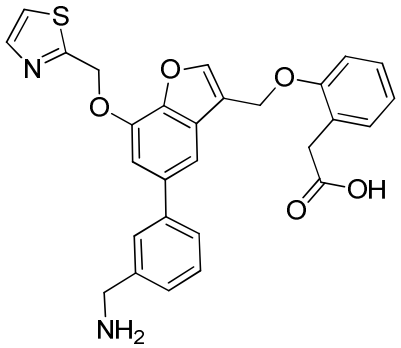
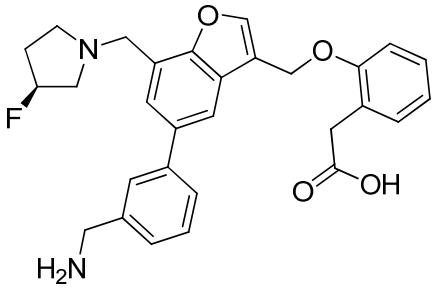
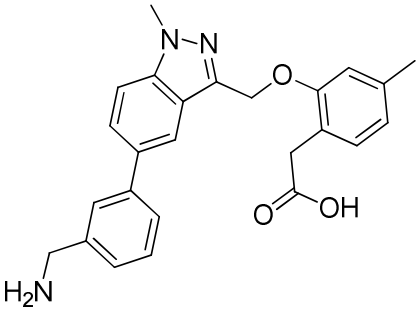
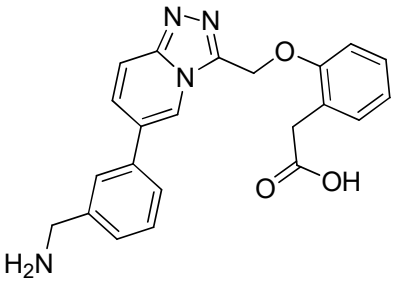
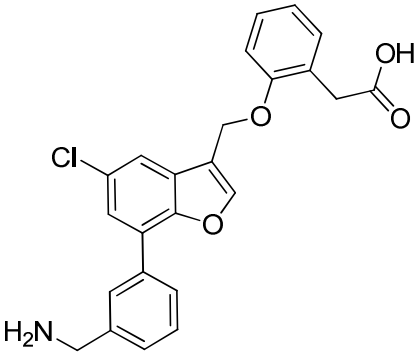
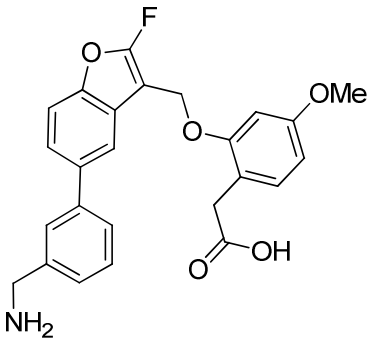
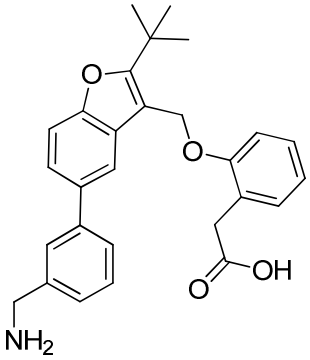
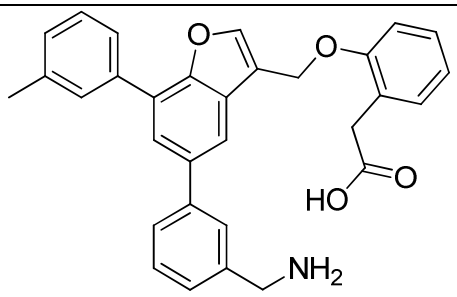
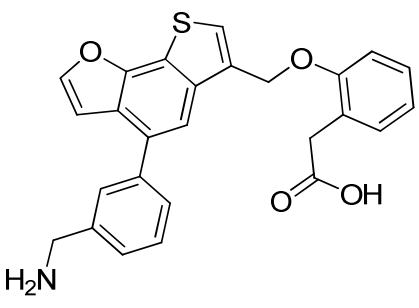
	
	
	
	
	

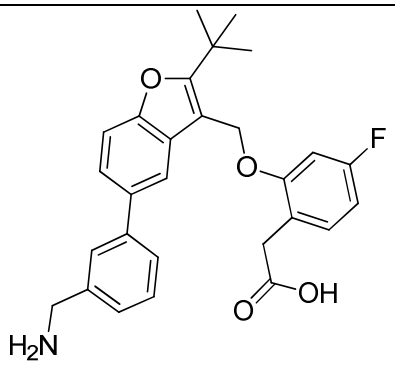
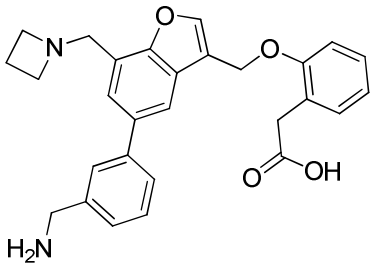
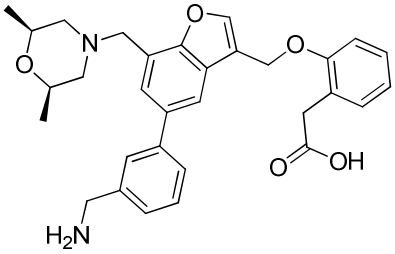
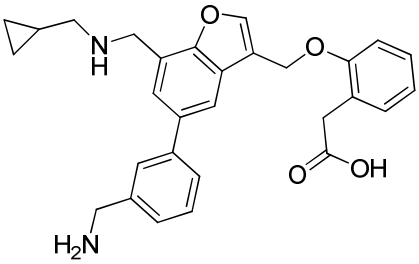
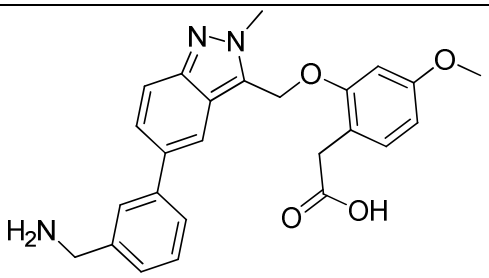
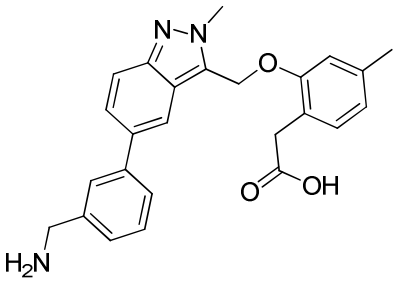
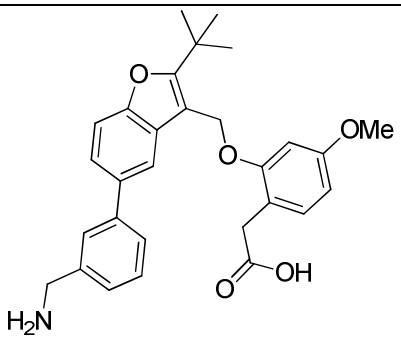
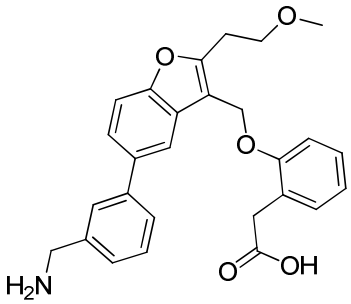
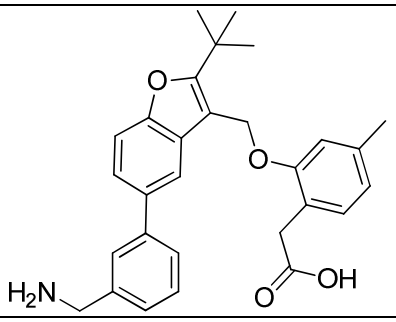
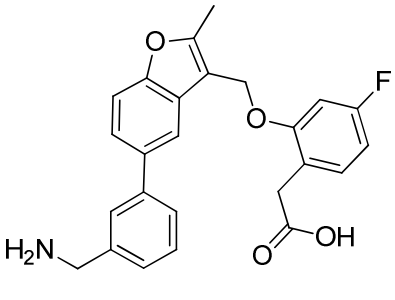
	
	
	
	
	
	

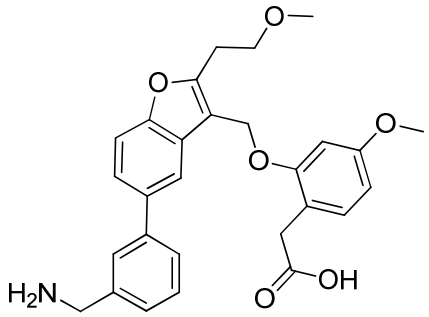
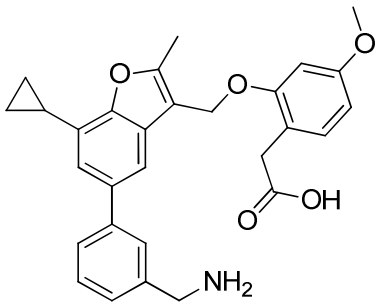
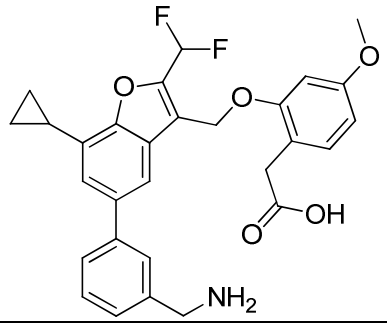
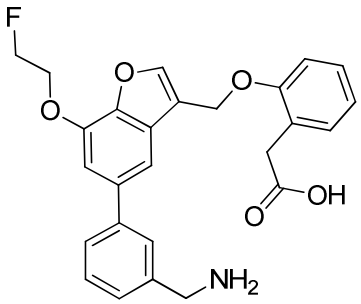
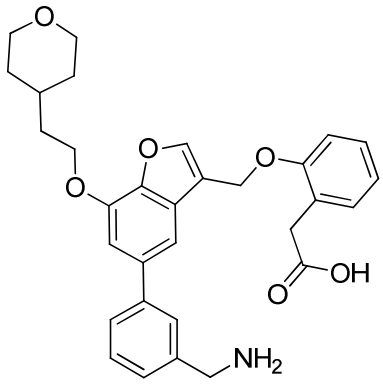
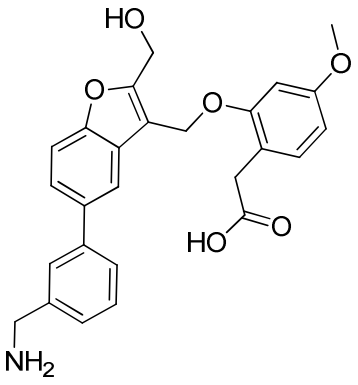
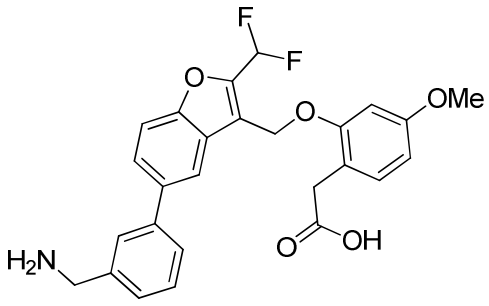
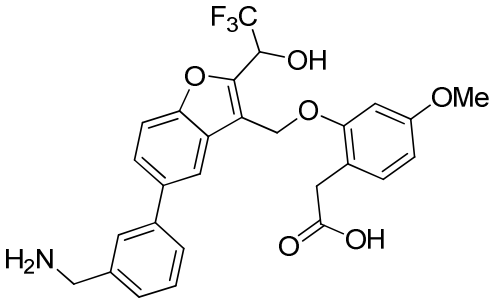
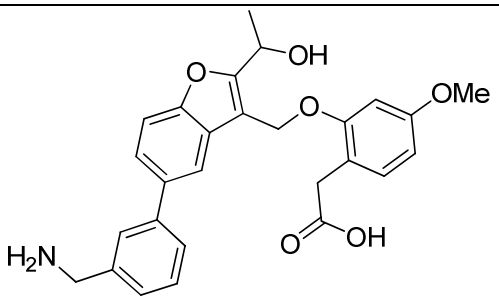
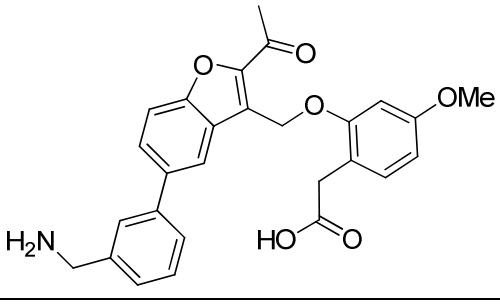
	
	
	
	
	

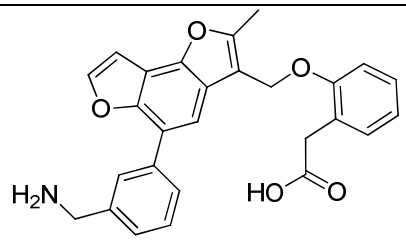
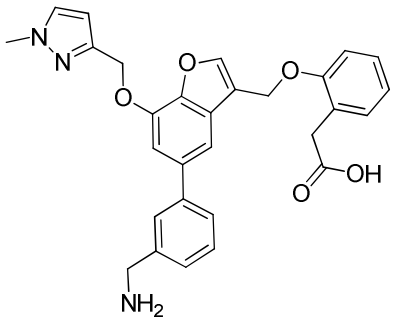
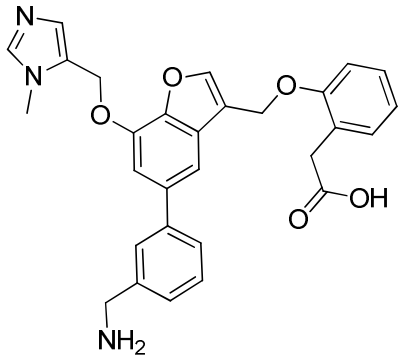
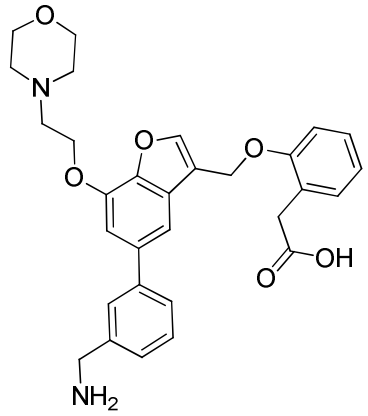
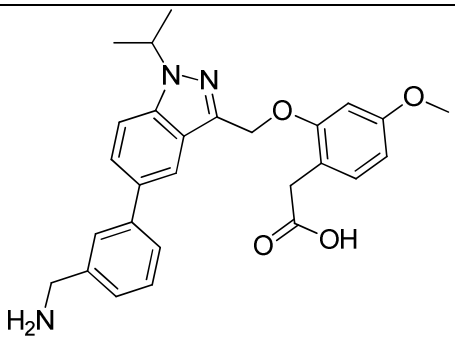
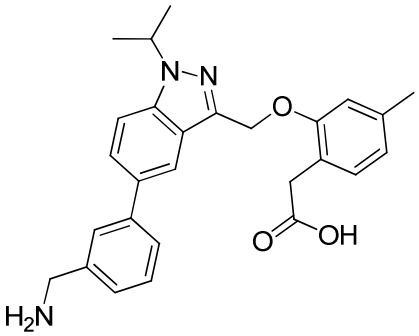
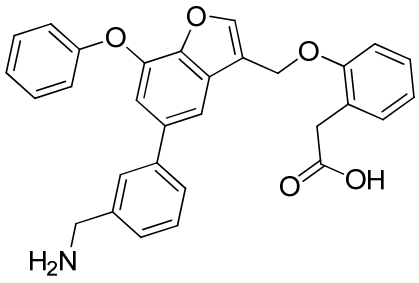
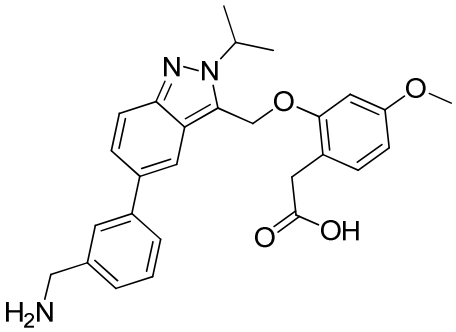
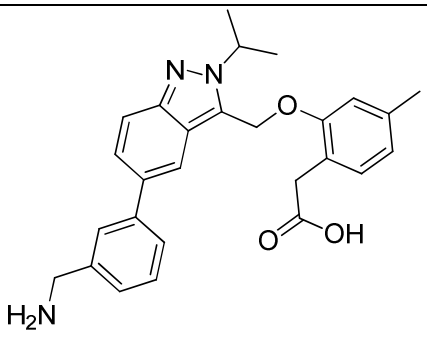
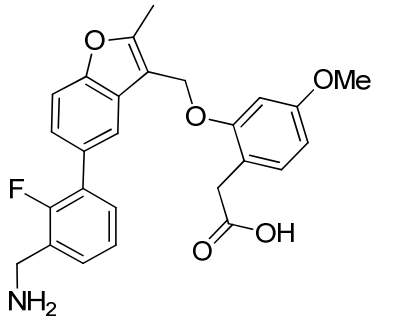
	
	
	
	

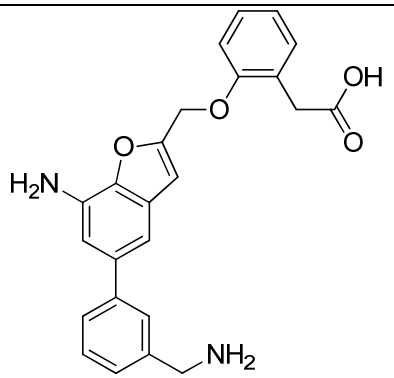
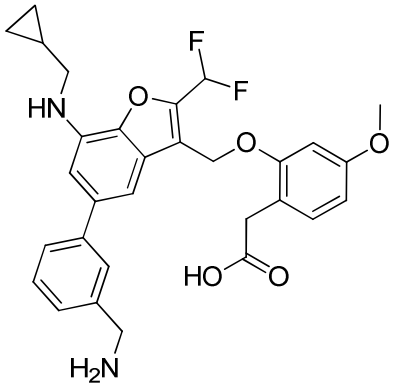
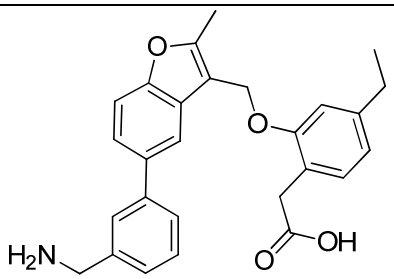
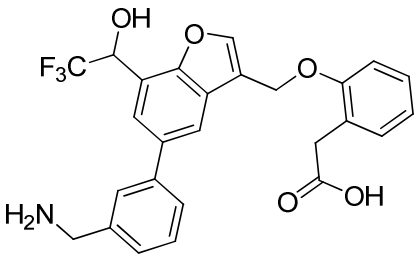
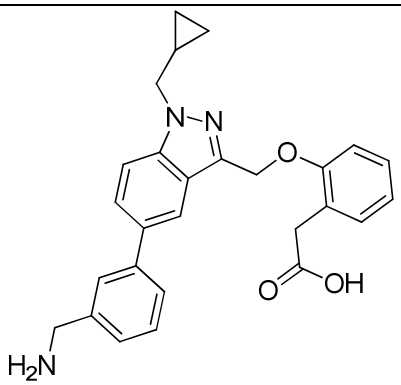
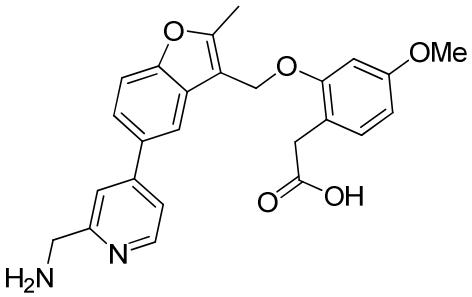
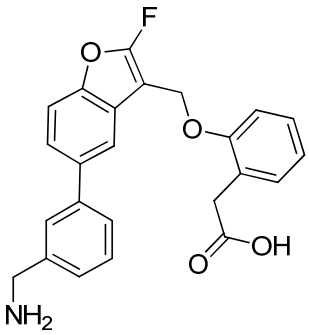
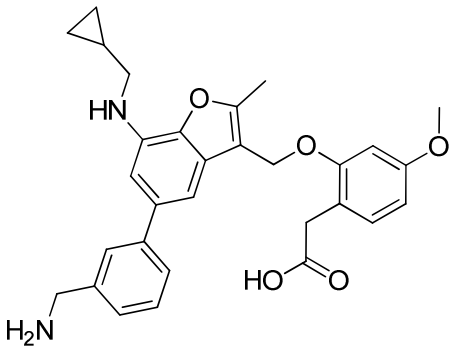
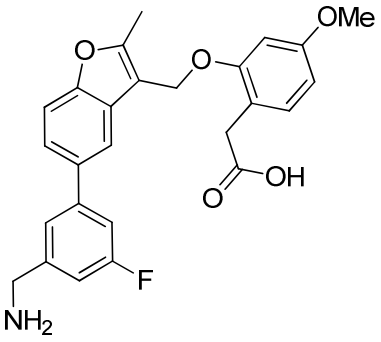
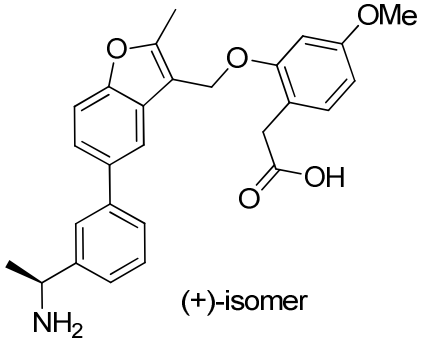
	
	
	
	
	

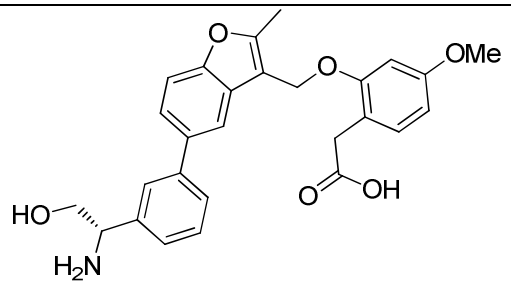
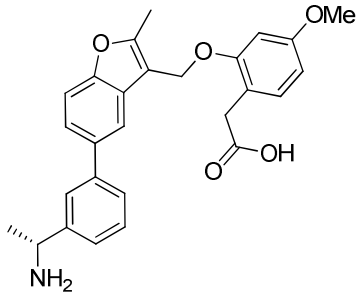
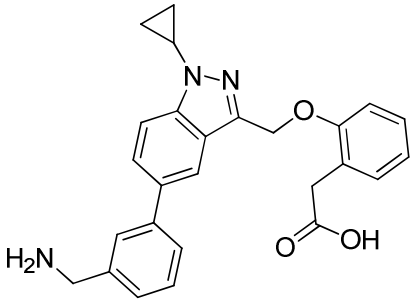
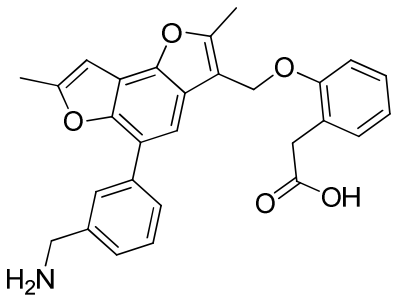
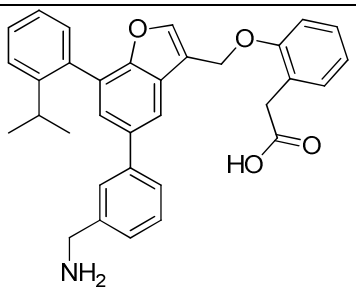
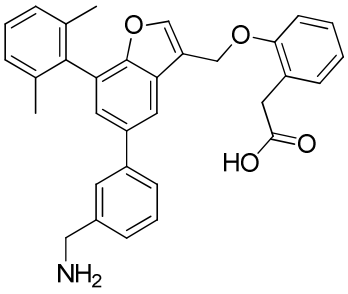
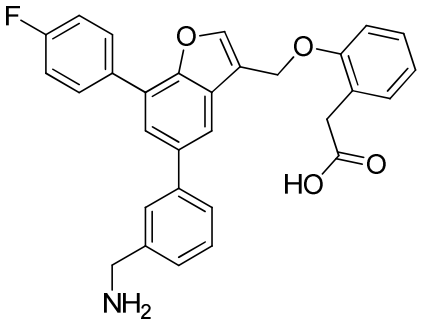
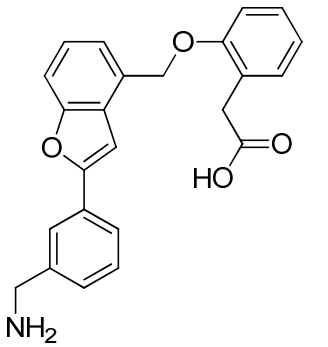
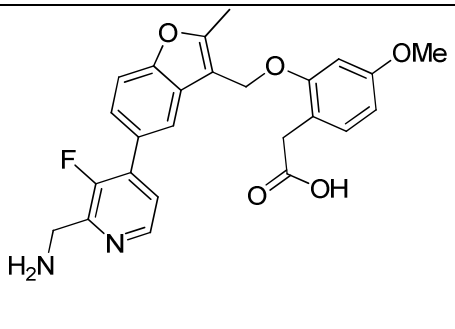
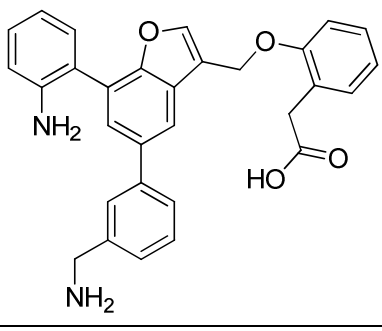
	
	
	
	
	

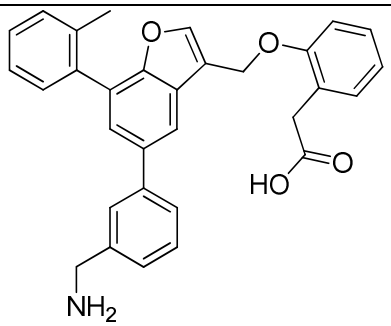
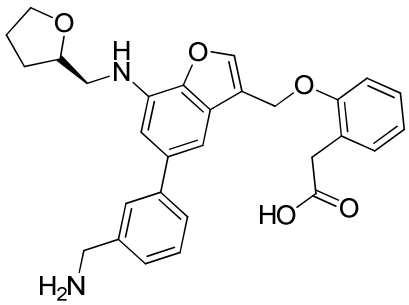
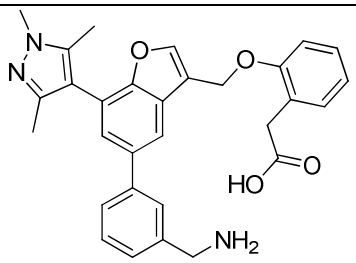
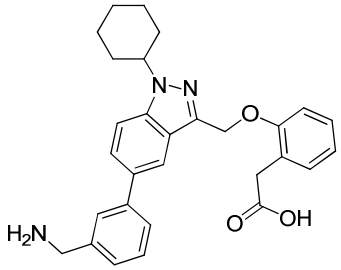
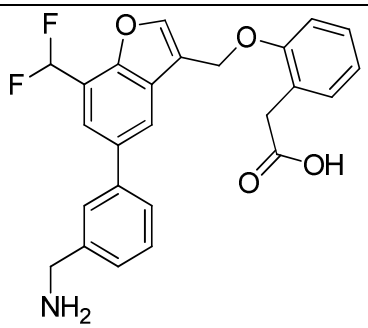
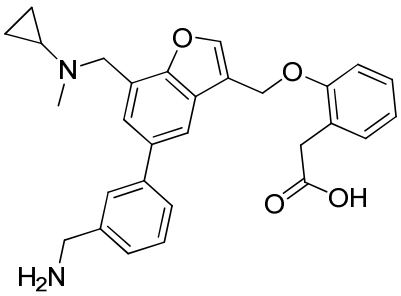
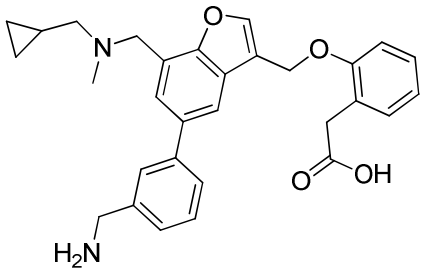
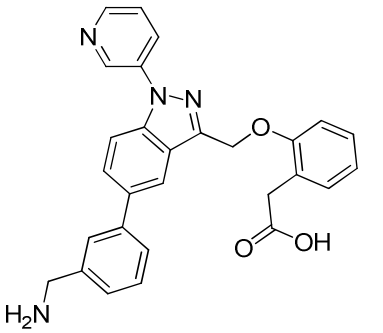
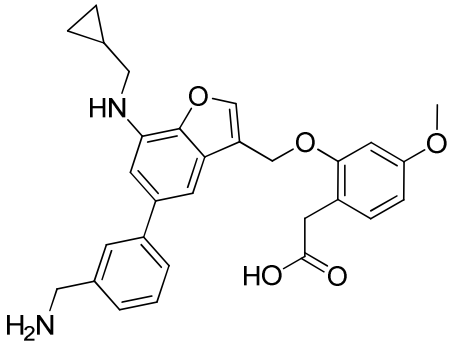
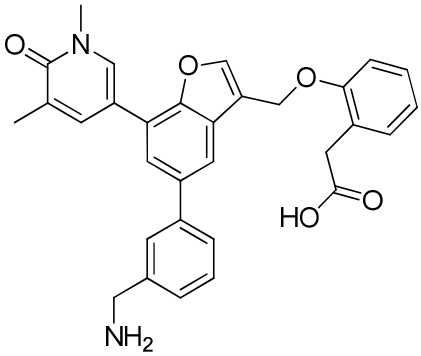
	
	
	
	
	

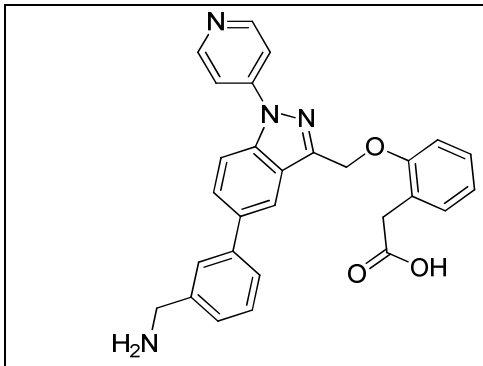
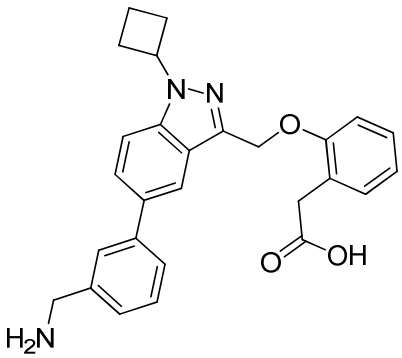
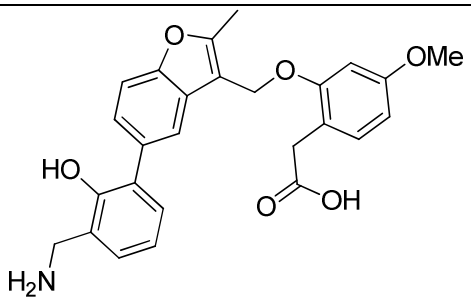
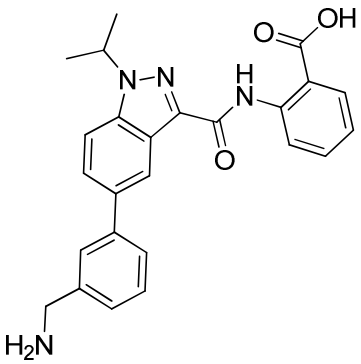
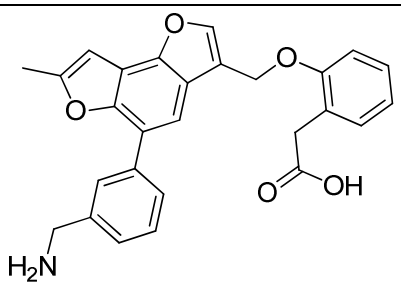
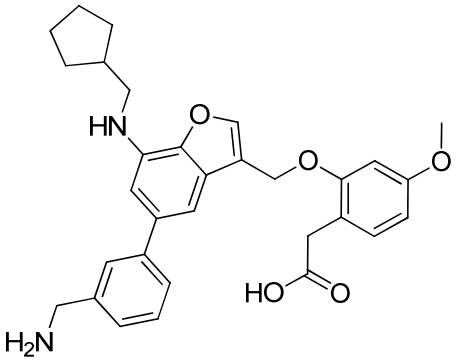
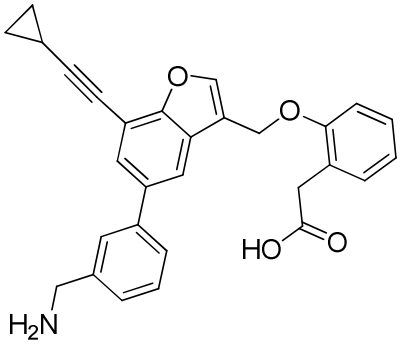
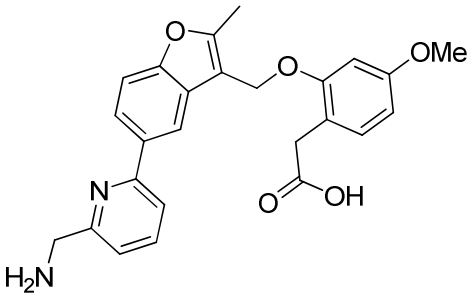
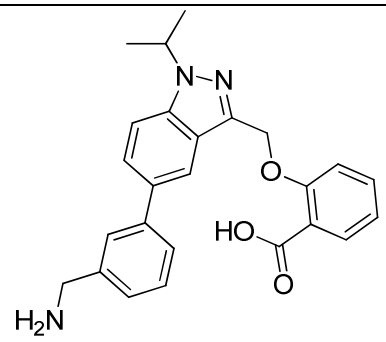
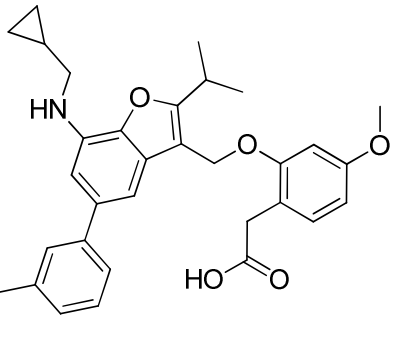
	
	
	
	
	

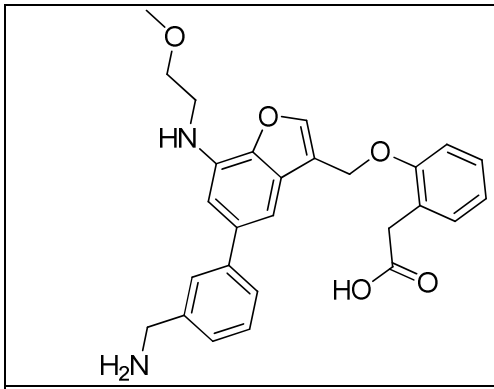
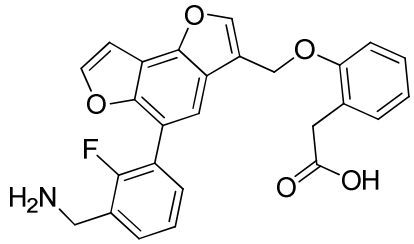
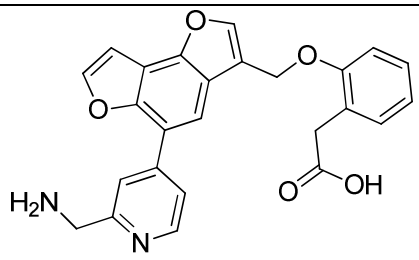
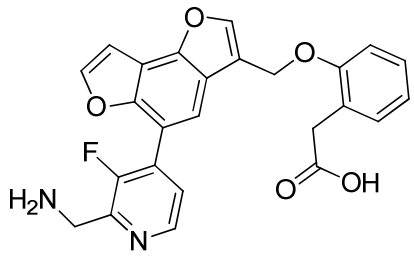
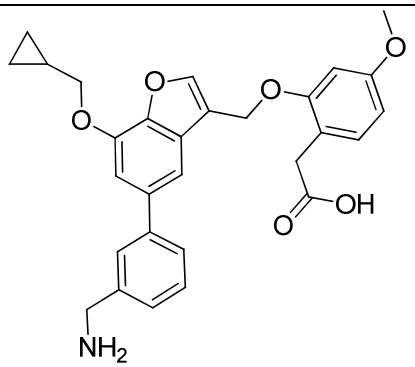
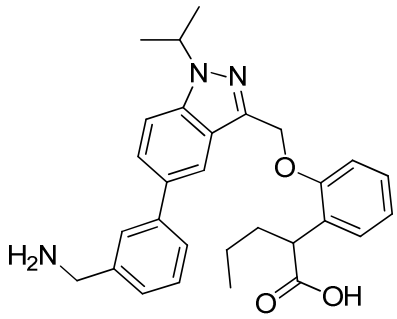
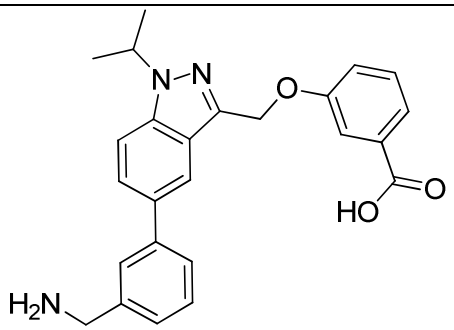
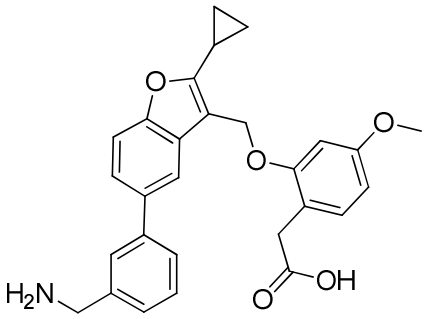
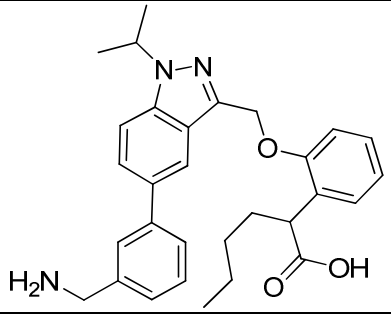
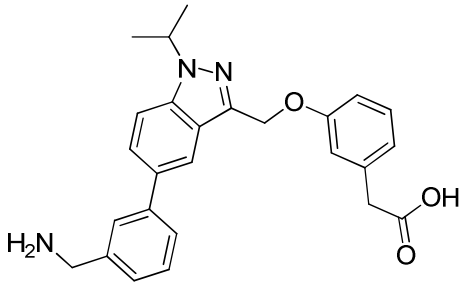
	
	
	
	
	

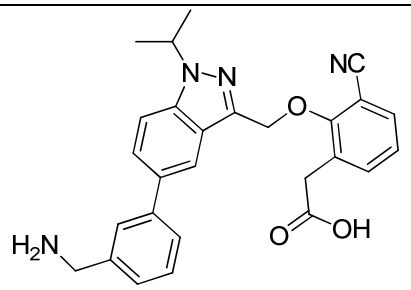
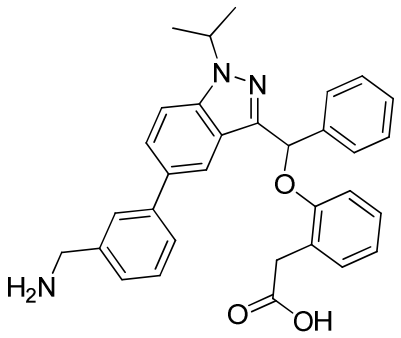
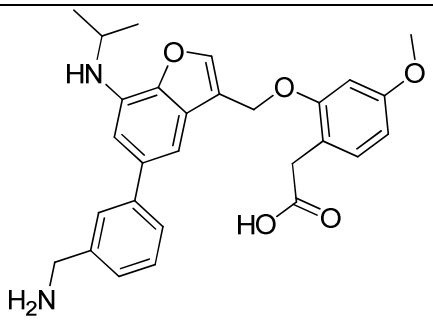
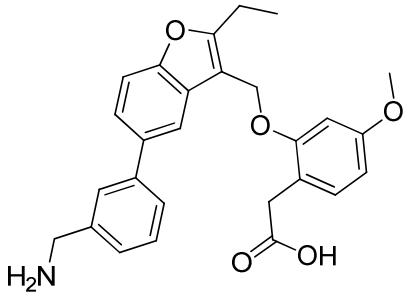
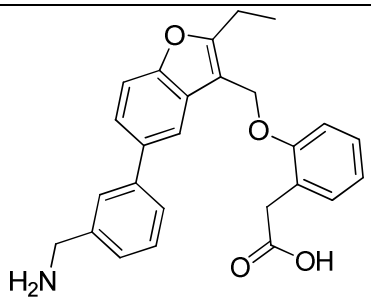
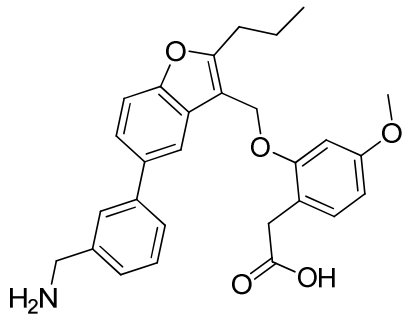
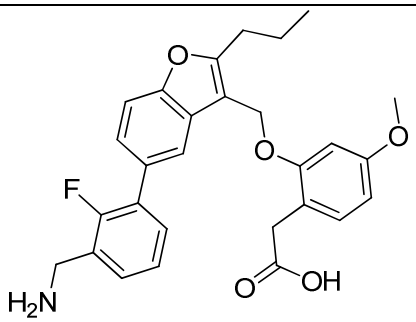
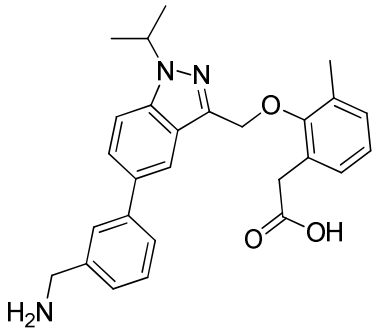
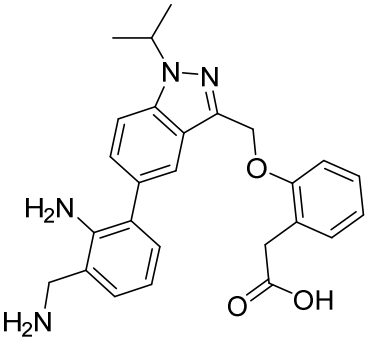
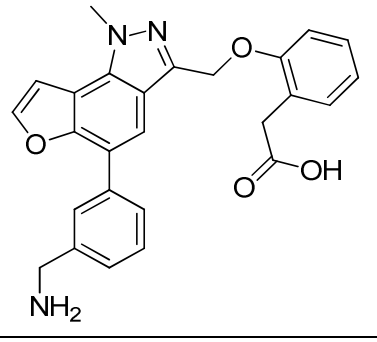
	
	
	
	
	 (+)-isomer

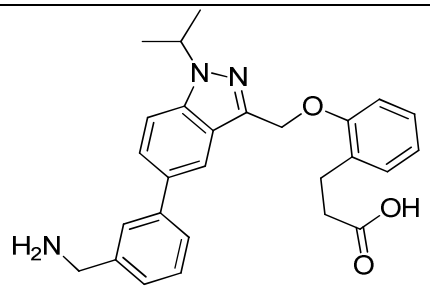
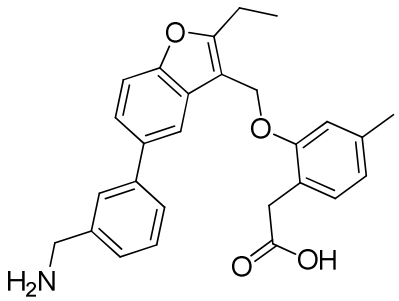
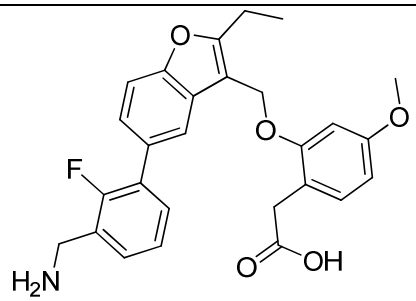
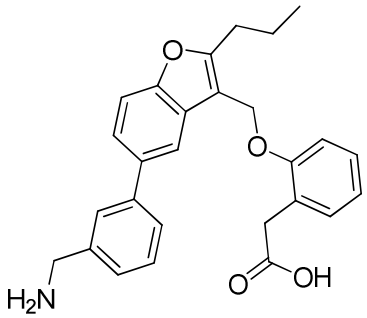
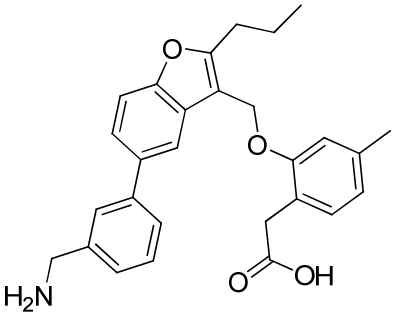
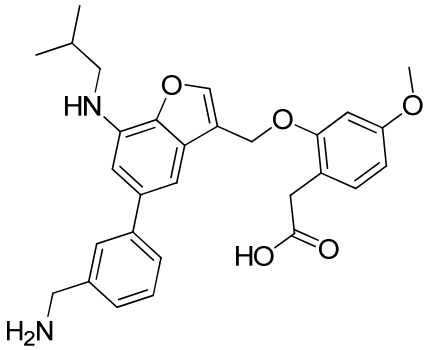
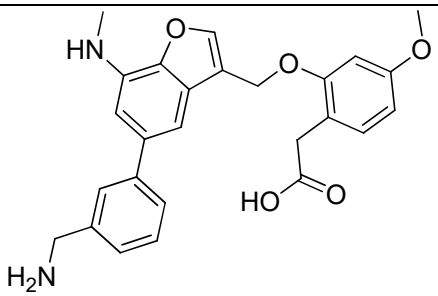
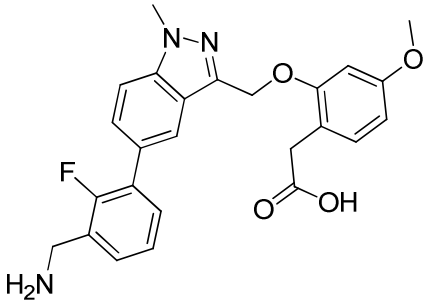
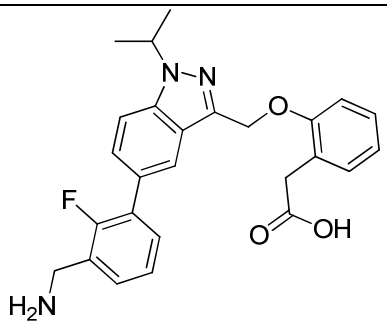
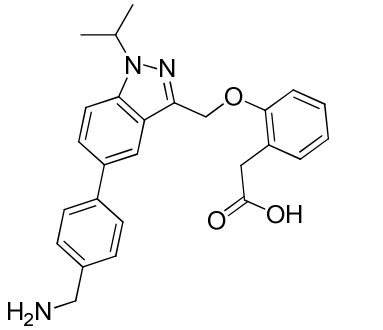
 (+)-isomer	
	
	
	
	

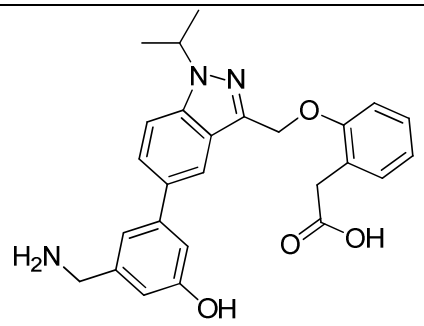
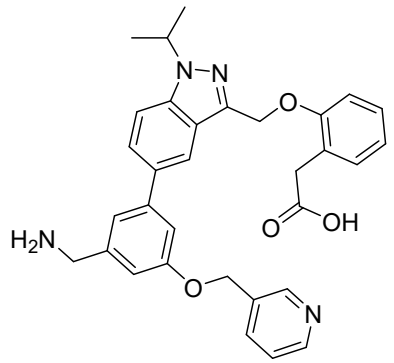
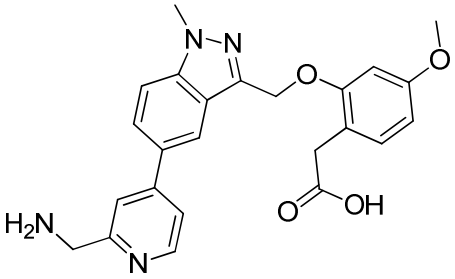
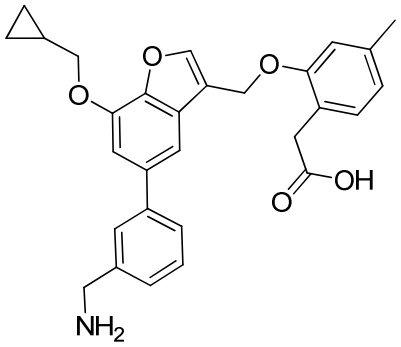
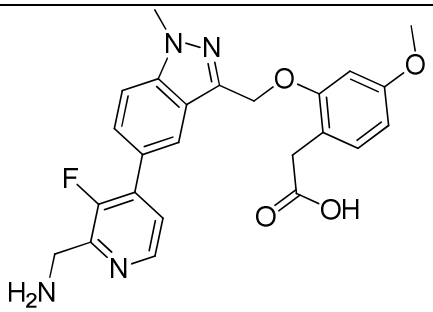
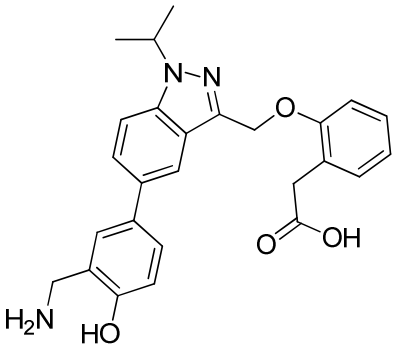
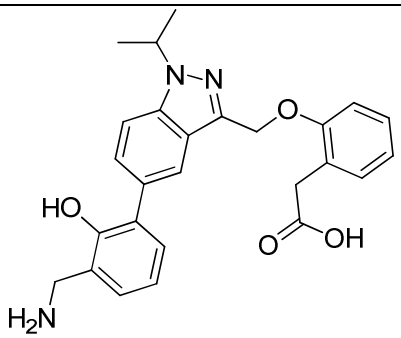
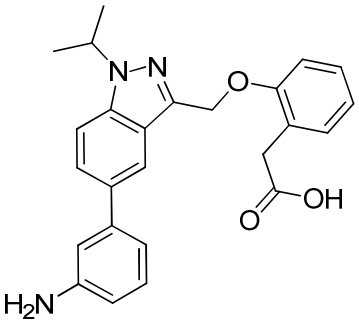
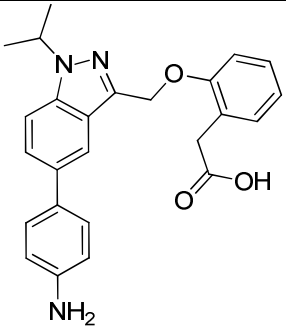
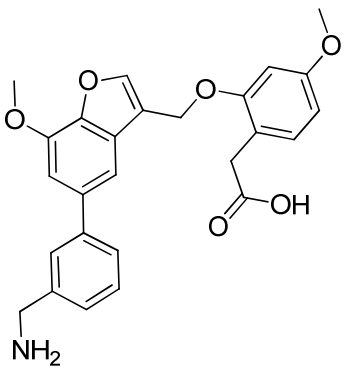
	
	
	
	
	

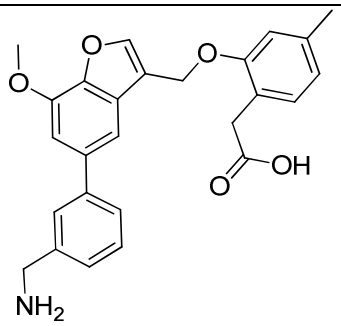
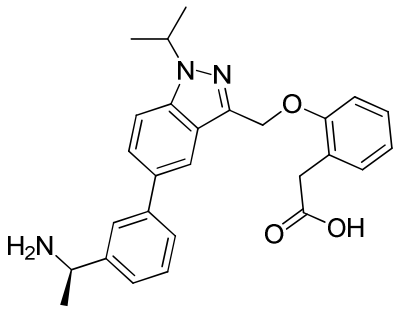
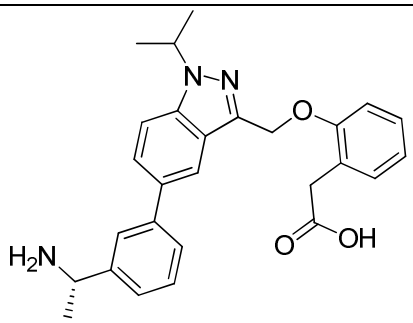
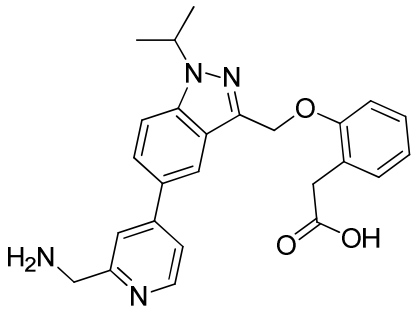
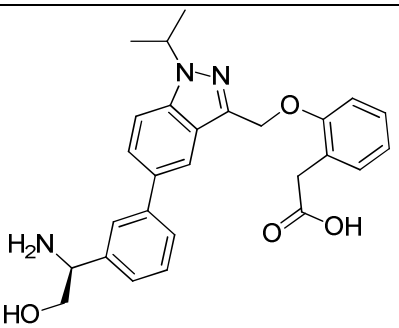
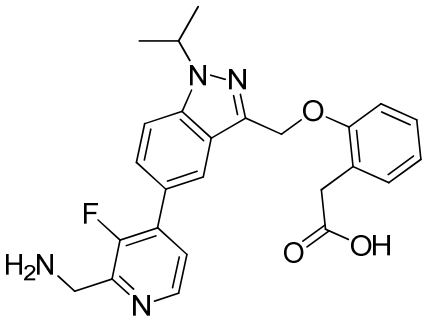
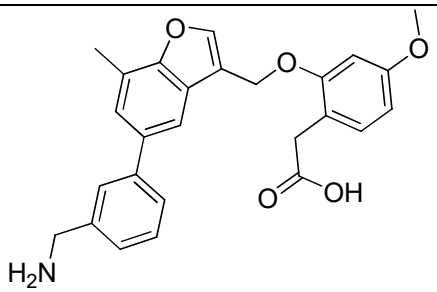
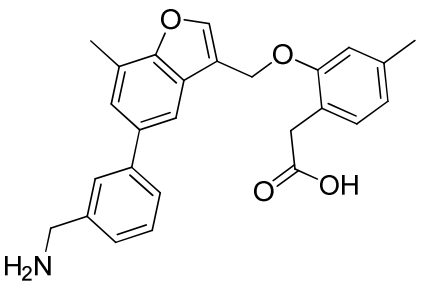
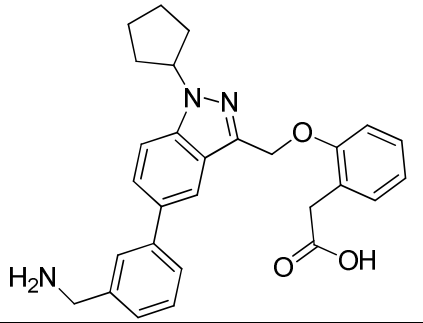
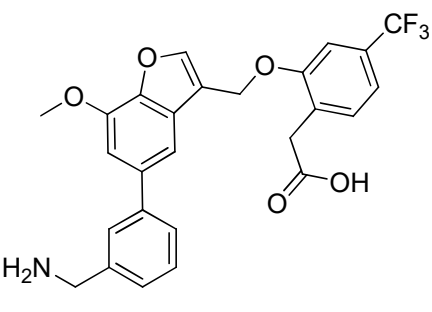
	
	
	
	
	

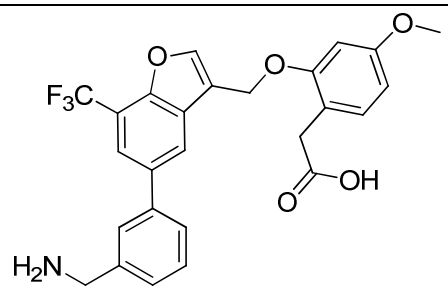
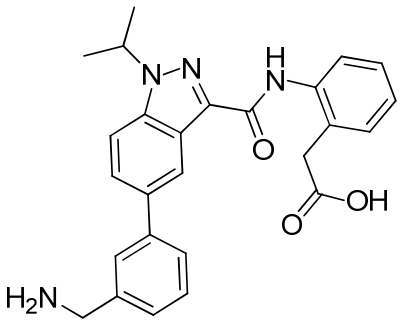
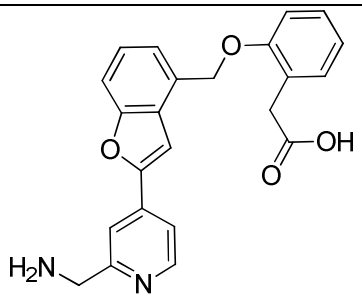
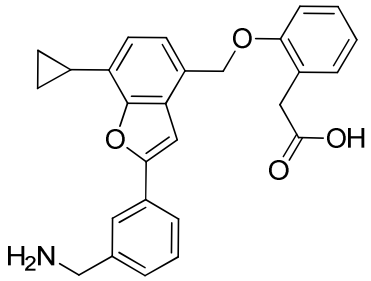
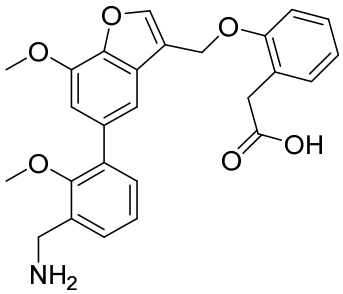
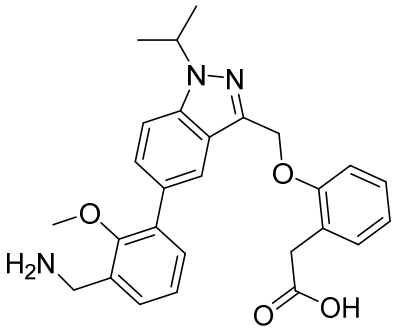
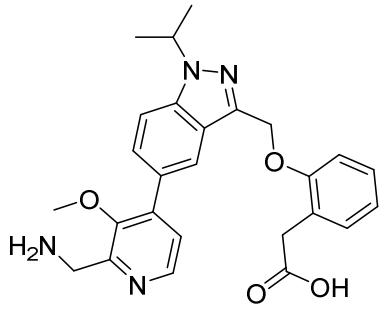
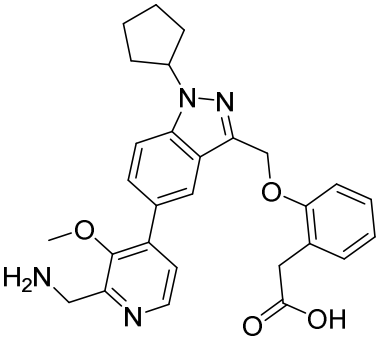
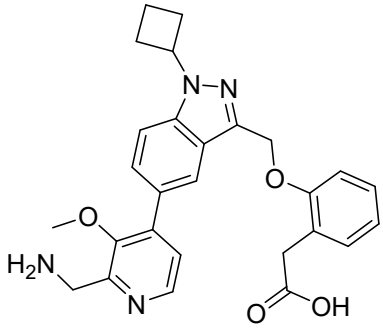
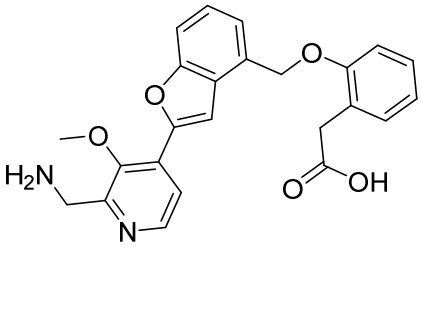
	
	
	
	
	

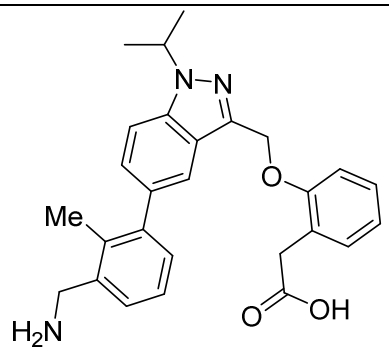
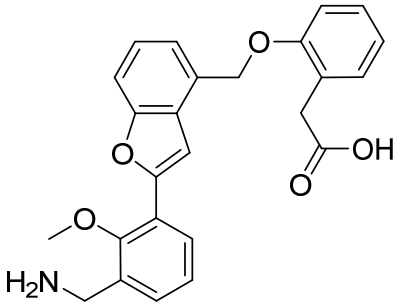
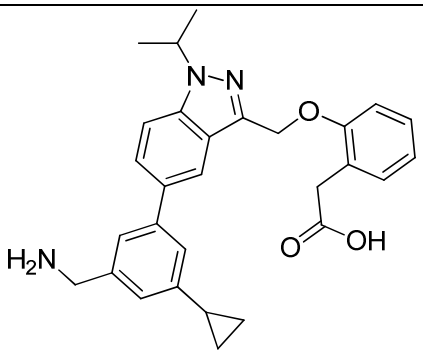
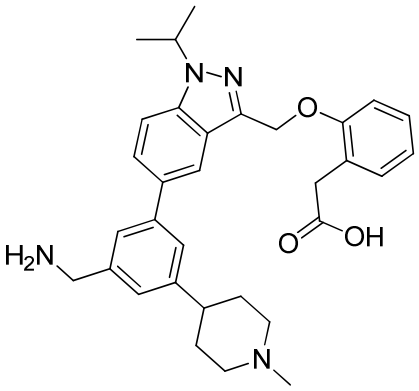
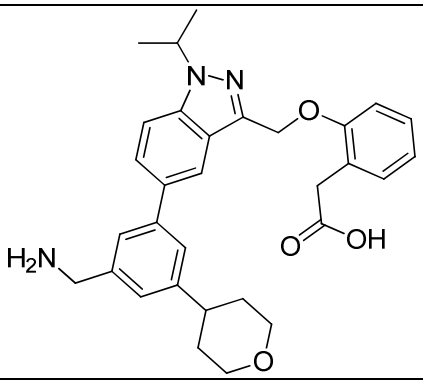
	
	
	
	
	

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71. A compound of any one of claims 1-70, or a pharmaceutically acceptable salt thereof for use in therapy.

72. Use of a compound of any one of claims 1-70, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a disease or condition characterized by aberrant complement system activity.

73. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is an immunological disorder.

74. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is a disease of the central nervous system.

75. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is a neurodegenerative disease or neurological disease.

76. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is a renal disease.

77. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is a cardiovascular disease.

78. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is selected from the group consisting of paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, organ transplant rejection, myasthenia gravis, neuromyelitis optica, membranoproliferative glomerulonephritis, dense-deposit disease, cold agglutinin disease, and catastrophic antiphospholipid syndrome.

79. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is selected from the group consisting of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), warm autoimmune hemolytic anemia, IgA nephropathy, C3 glomerulonephritis, and focal segmental glomerulosclerosis.

80. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is a hematological disorder.

81. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is an ocular disorder or an eye disorder.

82. The use of claim 72, wherein the disease or condition characterized by aberrant complement system activity is macular degeneration, age-related macular degeneration (AMD), macular edema, diabetic macular edema, choroidal

neovascularization (CNV), uveitis, Behcet's uveitis, proliferative diabetic retinopathy, non-proliferative diabetic retinopathy, glaucoma, hypertensive retinopathy, a corneal neovascularization disease, post-corneal transplant rejection, a corneal dystrophic disease, an autoimmune dry eye disease, Stevens-Johnson syndrome, Sjogren's syndrome, an environmental dry eye disease, Fuchs' endothelial dystrophy, retinal vein occlusion, or post-operative inflammation.