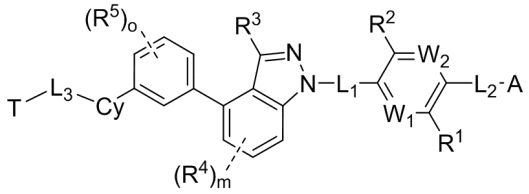
CLAIMS

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof, a prodrug, an isotopic derivative, an isomer, a solvate, or a metabolite thereof



Formula (I)

wherein L_1 is selected from $-CR^AR^B-$ and -C(O)-;

L_2, L_3 is selected from $-(CR^CR^D)_p$, $-(CR^CR^D)_p-NR^a-(CR^CR^D)_q-$, $-(CR^CR^D)_p-O-(CR^CR^D)_q-$ and -C(O)-;

W_1, W_2 each independently represents CR^L or N;

R^1 each independently represents hydrogen, halogen, nitro, cyano or $-NR^aR^b$, or C_1-C_6 alkyl, C_3-C_6 cycloalkyl , -O(C_1-C_6 alkyl), -O(C_0-C_6 alkylene)(C_3-C_6 cycloalkyl) or -O(C_0-C_6 alkylene)(3-6 membered heterocycloalkyl) substituted with 0, 1, 2 or 3 substituents; wherein the substituents are selected from $-OR^a$, cyano, oxo, halogen, C_1-C_6 alkyl, -(C_1-C_6 alkylene)OR^a, cyano C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl , $-C(O)R^a$, -(C_1-C_6 alkylene)$C(O)R^a$, $-C(O)OR^a$, -(C_1-C_6 alkyl)$C(O)OR^a$, $-NR^aR^b$, -(C_1-C_6 alkylene)NR^aR^b,$-C(O)NR^aR^b$, $-SO_2R^a$, $-C(O)NR^aSO_2R^b$ and $-NR^aC(O)R^b$;

R^2, R^3, R^4, R^5 each independently represent hydrogen, halogen, nitro, cyano, $-NR^aR^b$, $-SO_2R^a$, $-S(O)R^a$, $-P(O)R^aR^b$, C_1-C_6 alkyl, -O(C_1-C_6 alkyl), -O(C_3-C_6 cycloalkyl), halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl;

Cy represents benzene ring or six-membered heteroaryl substituted by 0, 1, 2 or 3 R^6, wherein the six-membered heteroaryl may optionally contain 1 or 2 nitrogen atoms; wherein the R^6 represents hydrogen, halogen, nitro, cyano, $-NR^aR^b$, $-SO_2R^a$, $-S(O)R^a$ or $-P(O)R^aR^b$ or C_1-C_6 alkyl, C_3-C_6 cycloalkyl , -O(C_1-C_6 alkyl), -O(C_0-C_6 alkylene)(C_5-C_{10} aryl), -O(C_0-C_6 alkylene)(5-10 membered heteroaryl), -O(C_0-C_6 alkylene)(C_3-C_6 cycloalkyl) or -O(C_0-C_6 alkylene)(3-6

membered heterocycloalkyl) substituted with 0, 1, 2 or 3 substituents; wherein the substituents are selected from -OR^a, cyano, oxo, halogen, C_1-C_6 alkyl, -(C_1-C_6 alkylene)OR^a, cyano C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl , -$C(O)R^a$, -(C_1-C_6 alkylene)$C(O)R^a$, -$C(O)OR^a$, -(C_1-C_6 alkylene)$C(O)OR^a$, -NR^aR^b, -(C_1-C_6 alkylene)NR^aR^b, -$C(O)NR^aR^b$, -SO_2R^a, -$C(O)NR^aSO_2R^b$ or -$NR^aC(O)R^b$;

wherein R^L represents hydrogen, C_1-C_6 alkyl, -$O(C_1$-C_6 alkyl), -$O(C_3$-C_6 cycloalkyl), halogen, nitro, cyano, -NR^aR^b, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl;

T, A each independently represent -(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-(C_3-C_{12} cycloalkyl), -(C_0-C_6 alkylene)-(3-12 membered heterocycle), -(C_0-C_6 alkylene)-(C_6-C_{10} aryl) or -(C_0-C_6 alkylene)-(5-10 membered heteroaryl) substituted with 0, 1, 2 or 3 substituents, wherein the substituents are selected from cyano, oxo, halogen, C_1-C_6 alkyl, -(C_0-C_6 alkylene)OR^a, cyano C_1-C_6 alkyl, halo(C_1-C_6 alkyl), C_3-C_8 cycloalkyl , -(C_0-C_6 alkylene)$C(O)R^a$, -(C_0-C_6 alkylene)$C(O)OR^a$, -(C_0-C_6 alkenyl)$C(O)OR^a$, -(C_0-C_6 alkylene)NR^aR^b, -$C(O)NR^aR^b$, -$NR^aSO_2R^b$, -$C(O)NR^aSO_2R^b$ and -$NR^aC(O)R^b$;

wherein R^A, R^B each independently represent hydrogen, C_1-C_6 alkyl, -(C_0-C_3 alkylene)(C_3-C_{12} cycloalkyl), -(C_0-C_3 alkylene)(3-12 membered heterocycle), halo(C_1-C_6 alkyl) or halogen, or R^A and R^B together with their co-attached carbon atom form a 3-6 membered ring;

R^C, R^D each independently represent hydrogen, C_1-C_6 alkyl, -(C_0-C_3 alkylene)(C_3-C_{12} cycloalkyl), -(C_0-C_3 alkylene)(3-12 membered heterocycle), halo(C_1-C_6 alkyl) or halogen, or R^C and R^D together with their co-attached carbon atom form a 3-6 membered ring;

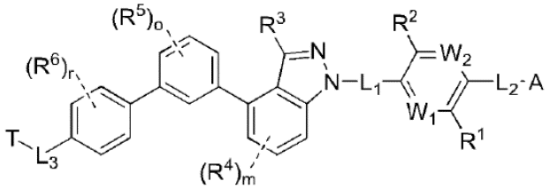
R^a, R^b each independently represent hydrogen, C_1-C_6 alkyl, halo(C_1-C_6 alkyl), -(C_0-C_6 alkylene)OH, -(C_0-C_3 alkylene)(C_3-C_{12} cycloalkyl), -(C_0-C_3 alkylene)(3-12 membered heterocycle), -(C_0-C_3 alkylene)(C_6-C_{10} aryl), -(C_0-C_3 alkylene)(5-10 membered heteroaryl) or halo(C_1-C_6 alkyl), or R^a and R^b together with their co-attached atom form a 3-6 membered ring;

wherein m, o each independently represent 0, 1 or 2; and

wherein p, q each independently represent 0, 1, 2 or 3.

2. The compound of Formula (I) or a pharmaceutically acceptable salt thereof, a prodrug, an

isotopic derivative, an isomer, a solvate, or a metabolite thereof according to claim 1, wherein the compound of Formula (I) having the following structure of Formula (II):

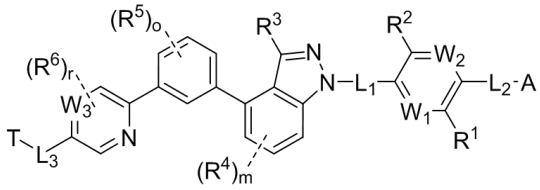


Formula (II)

wherein R^1, R^2, R^3, R^4, R^5, R^6, L_1, L_2, L_3, T, A, W_1, W_2, m, o are as defined in claim 1;

and wherein r represents 0, 1, 2 or 3.

3. The compound of Formula (I) or a pharmaceutically acceptable salt thereof, a prodrug, an isotopic derivative, an isomer, a solvate, or a metabolite thereof according to claim 1, wherein the compound of Formula (I) having the following structure of Formula (III):



Formula (III)

wherein R^1, R^2, R^3, R^4, R^5, R^6, L_1, L_2, L_3, T, A, W_1, W_2, m, o as defined in claim 1;

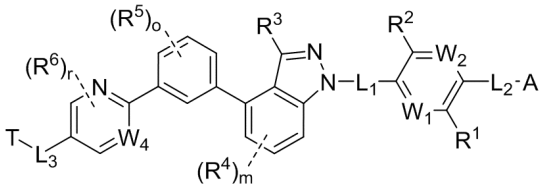
wherein W_3 represents CR^M or N;

wherein R^M represents hydrogen, C_1-C_6 alkyl, -O(C_1-C_6 alkyl), -O(C_3-C_6 cycloalkyl), halogen, nitro, cyano, -NR^aR^b, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl;

wherein r represents 0, 1 or 2.

4. The compound of Formula (I) or a pharmaceutically acceptable salt thereof, a prodrug, an isotopic derivative, an isomer, a solvate, or a metabolite thereof according to claim 1, wherein the

compound of Formula (I) having the following structure of Formula (IV):



Formula (IV)

wherein R^1, R^2, R^3, R^4, R^5, R^6, L_1, L_2, L_3, T, A, W_1, W_2, m, o as defined in claim 1;

wherein W_4 represents CR^N or N;

wherein R^N represents hydrogen, C_1-C_6 alkyl, -O(C_1-C_6 alkyl), -O(C_3-C_6 cycloalkyl), halogen, nitro, cyano, -NR^aR^b, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl;

wherein r represents 0, 1 or 2.

5. The compound according to any one of claims 1-4, wherein L_1 is selected from -CR^AR^B-, and wherein R^A and R^B are each independently selected from hydrogen, halogen, C_1-C_6 alkyl and halo(C_1-C_6 alkyl), preferably are hydrogen; and/or wherein L_2 and L_3 are each independently selected from -CR^CR^D- and -CR^CR^D -NR^a- $(CR^CR^D)_q$-, wherein q is selected from 0, 1 or 2, and wherein R^C, R^D are each independently selected from hydrogen, halogen, C_1-C_6 alkyl and halo(C_1-C_6 alkyl) , preferably are hydrogen; R^a is each independently selected from hydrogen, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) and -(C_0-C_3 alkylene)C_3-C_{12} cycloalkyl.

~~6. The compound according to any one of claims 1-4, wherein L_2 and L_3 are each independently selected from -CR^CR^D- and -CR^CR^D -NR^a- $(CR^CR^D)_q$-, wherein q is selected from 0, 1 or 2, and wherein R^C, R^D are each independently selected from hydrogen, halogen, C_1-C_6 alkyl and halo(C_1-C_6 alkyl) , preferably are hydrogen; R^a is each independently selected from hydrogen, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) and -(C_0-C_3 alkylene)C_3-C_{12} cycloalkyl.~~

~~7~~6. The compound of Formula (I) or a pharmaceutically acceptable salt thereof, a prodrug, an

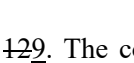
isotopic derivative, an isomer, a solvate, or a metabolite thereof according to any one of claims 1-~~6~~5, wherein W_1, W_2 each independently represents CH or N; and/or wherein W_3 represents CH or N; and/or wherein W_4 represents CH or N.

~~8. The compound according to any one of claims 3, 5 or 6, wherein W_3 represents CH or N.~~

~~9. The compound according to any one of claims 4-6, wherein W_4 represents CH or N.~~

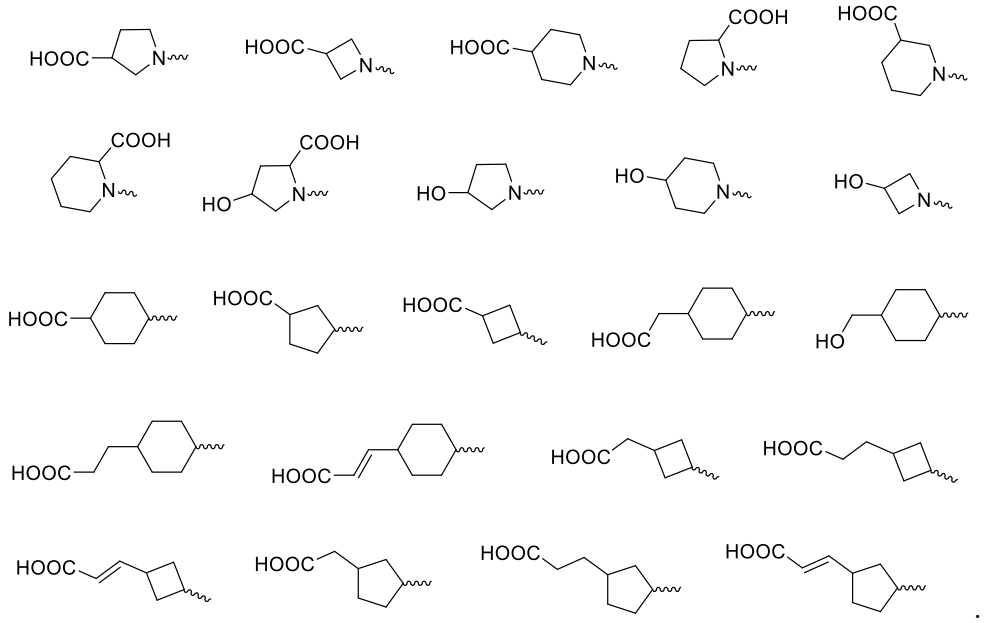
~~10~~7. The compound according to any one of claims 1-~~9~~6, wherein T, A each independently represent -(C_1-C_6 alkyl), -(C_0-C_6 alkylene)-(C_3-C_{12} cycloalkyl) or -(C_0-C_6 alkylene)-(3-12 membered heterocycle) substituted with 0, 1, 2 or 3 substituents, and wherein the substituents are selected from cyano, oxo, halogen, C_1-C_6 alkyl, -(C_0-C_6 alkylene)OR^a, cyano C_1-C_6 alkyl, halo(C_1-C_6 alkyl), C_3-C_8 cycloalkyl, -(C_0-C_6 alkylene)$C(O)R^a$, -(C_0-C_6 alkylene)$C(O)OR^a$, -(C_0-C_6 alkenyl)$C(O)OR^a$, -(C_0-C_6 alkylene)NR^aR^b, -$C(O)NR^aR^b$, -$NR^aSO_2R^b$, -$C(O)NR^aSO_2R^b$ and -$NR^aC(O)R^b$, wherein R^a and R^b each independently represent hydrogen, C_1-C_6 alkyl or halo(C_1-C_6 alkyl).

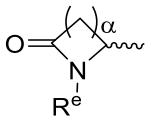
~~11~~8. The compound of claim ~~10~~7, wherein T, A each independently represents C_1-C_6 alkyl, C_3-C_{12} cycloalkyl or 3-12 membered heterocycle substituted with 0, 1 or 2 substituents, wherein the substituents are selected from cyano, oxo, -OR^a, -(C_0-C_6 alkylene)$C(O)OR^a$, -(C_0-C_6 alkenyl)$C(O)OR^a$, -$NR^aSO_2R^b$, -$C(O)NR^aSO_2R^b$ and -$NR^aC(O)R^b$, wherein R^a and R^b each independently represent hydrogen, C_1-C_6 alkyl or halo(C_1-C_6 alkyl).

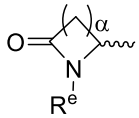
~~12~~9. The compound of claim ~~11~~8, wherein T, A each independently represents ,  optionally substituted with 0, 1 or 2 substituents, wherein the substituents are selected from C_1-C_6 alkyl, -OR^a, -(C_0-C_6 alkylene)$C(O)OR^a$ and -(C_0-C_6 alkenyl)$C(O)OR^a$, wherein R^a

represents hydrogen or C_1-C_6 alkyl, preferably are hydrogen, wherein α represents 1, 2 or 3.

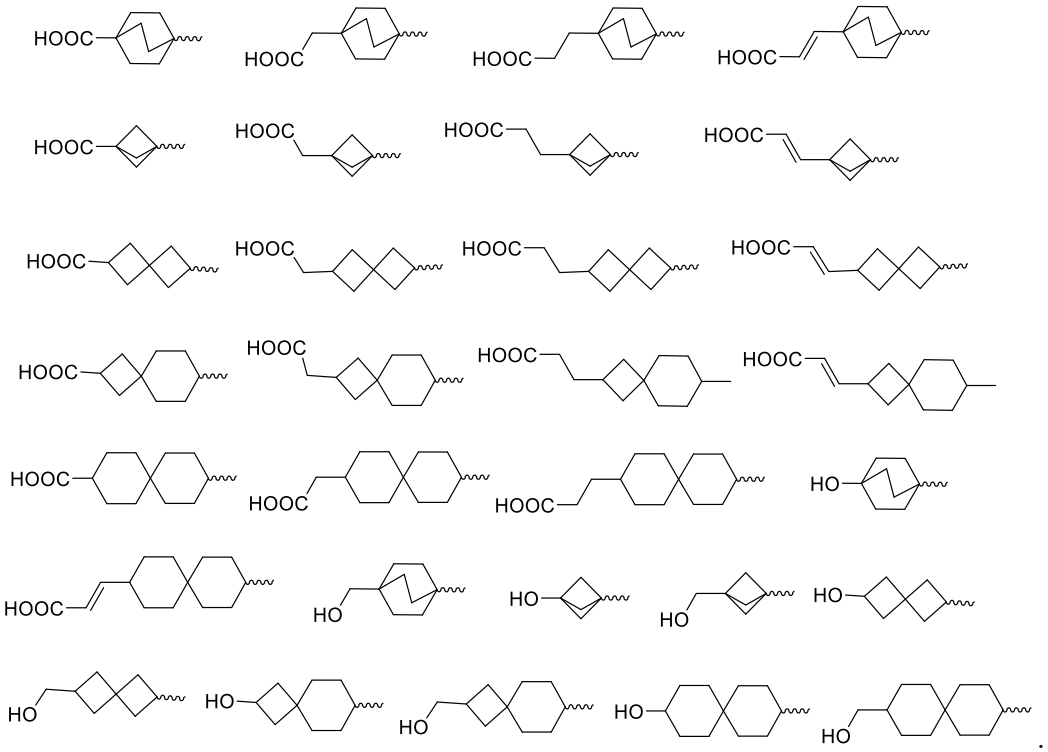
~~13~~10. The compound of claim ~~12~~9, wherein T, A each independently represents the following groups:



~~14~~11. The compound of claim ~~11~~8, wherein T, A each independently represent  optionally substituted with 0, 1 or 2 substituents:, wherein the substituents are selected from: C_1-C_6 alkyl, -OR^a and halogen, wherein R^e, R^a each independently represent hydrogen or C_1-C_6 alkyl;wherein α represents 1, 2 , 3 or 4.

~~15~~12. The compound of claim ~~14~~11, wherein T, A each independently represents , wherein R^e represents hydrogen or C_1-C_6 alkyl; wherein α represents 1, 2, 3 or 4.

~~16~~13. The compound of claim ~~11~~8, wherein T, A each independently represents:



~~17~~14. The compound according to any one of claims 1-~~16~~13, wherein R^1 represents -O(C_1-C_6 alkyl), -O(C_0-C_6 alkylene)(C_5-C_{10} aryl), -O(C_0-C_6 alkylene)(5-10 membered heteroaryl), -O(C_0-C_6 alkylene)(C_3-C_6 cycloalkyl) or -O(C_0-C_6 alkylene)(3-6 membered heterocycloalkyl) substituted with 0, 1, 2 or 3 substituents; wherein the substituents are selected from: cyano, oxo, halogen, cyano C_1-C_6 alkyl and C_1-C_6 haloalkyl; and/or wherein R^2 represents hydrogen, halogen, nitro, cyano, -SO_2R^a, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl; wherein R^a represents hydrogen, C_1-C_6 alkyl or halo(C_1-C_6 alkyl); and/or wherein R^3, R^4 each independently represent hydrogen, halogen, nitro or cyano; and/or wherein R^5 represents hydrogen, halogen, nitro, cyano, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl; and/or wherein R^6 represents hydrogen, halogen, nitro, cyano, -SO_2R^a, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl or -O(C_1-C_6 alkyl), -O(C_0-C_6 alkylene)(C_5-C_{10} aryl), -O(C_0-C_6 alkylene)(5-10 membered heteroaryl), -O(C_0-C_6 alkylene)(C_3-C_6 cycloalkyl) or -O(C_0-C_6 alkylene)(3-6 membered heterocycloalkyl) substituted with 0, 1, 2 or 3 substituents; wherein the substituents are selected from: cyano, oxo, halogen, cyano C_1-C_6 alkyl

and C_1-C_6 haloalkyl.

~~18. The compound according to any one of claims 1-16, wherein R^2 represents hydrogen, halogen, nitro, cyano, $-SO_2R^a$, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl; wherein R^a represents hydrogen, C_1-C_6 alkyl or halo(C_1-C_6 alkyl).~~

~~19. The compound according to any one of claims 1-16, wherein R^3, R^4 each independently represent hydrogen, halogen, nitro or cyano.~~

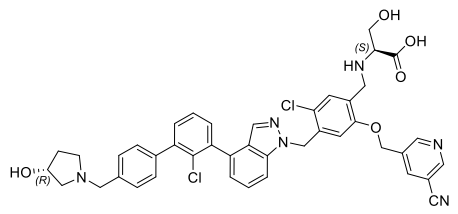
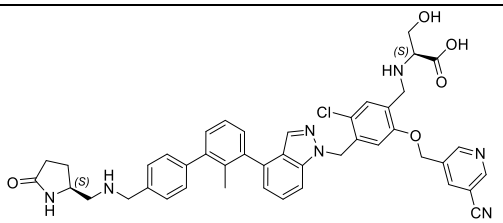
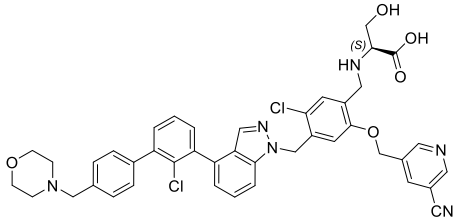
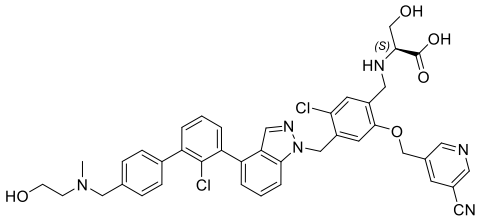
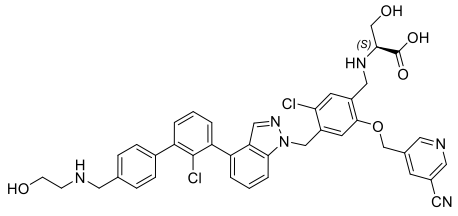
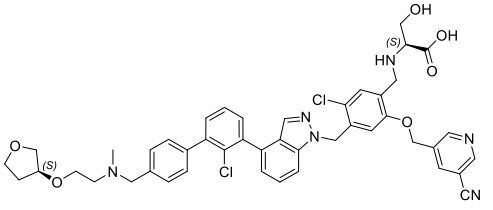
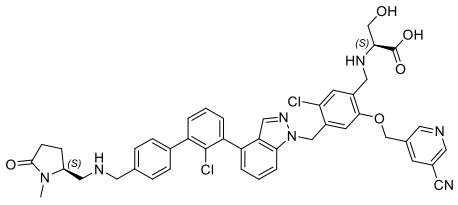
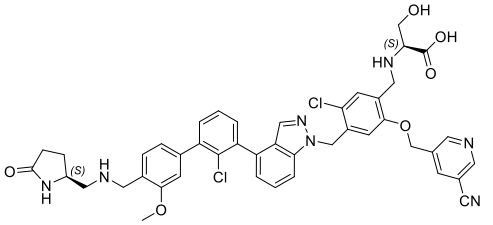
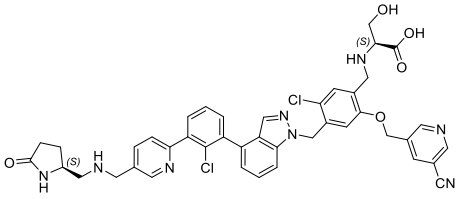
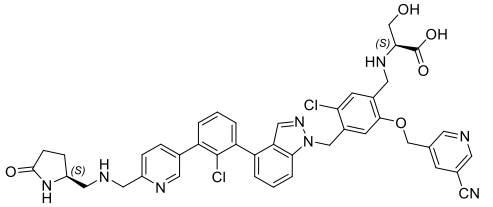
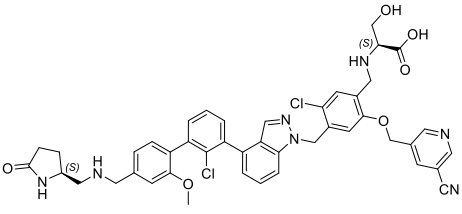
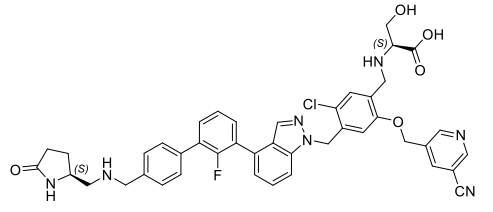
~~20. The compound according to any one of claims 1-16, wherein R^5 represents hydrogen, halogen, nitro, cyano, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl.~~

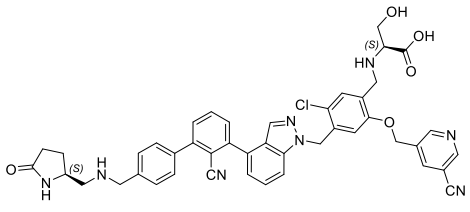
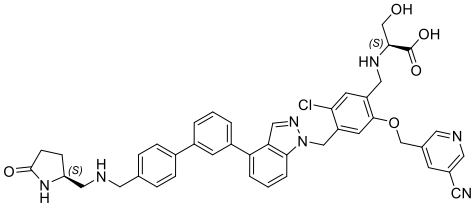
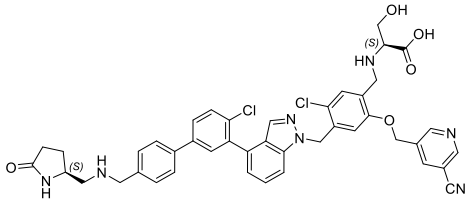
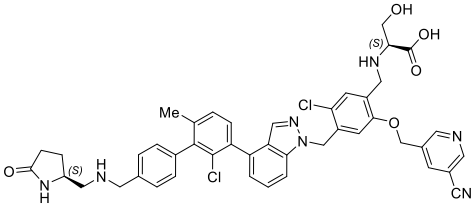
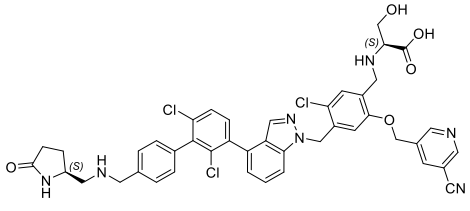
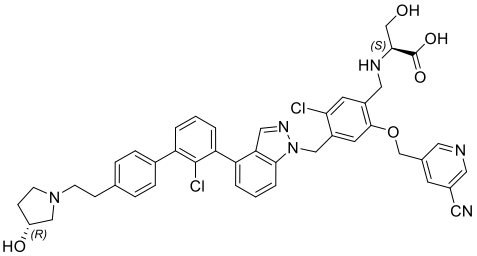
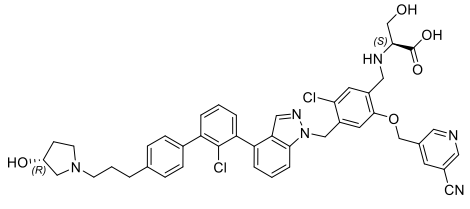
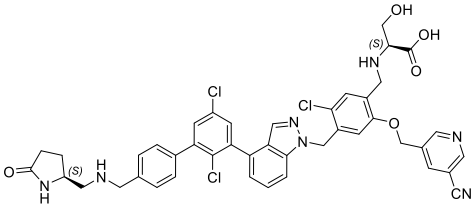
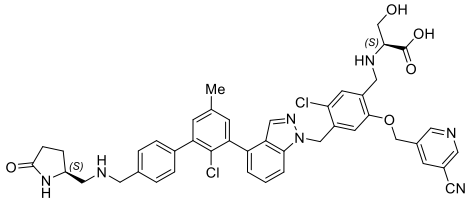
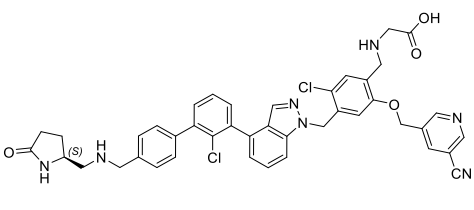
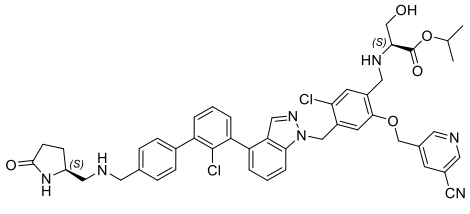
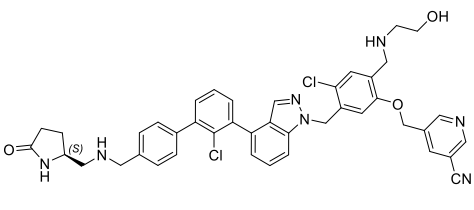
~~21. The compound according to any one of claims 1-16, wherein R^6 represents hydrogen, halogen, nitro, cyano, $-SO_2R^a$, C_1-C_6 alkyl, halo(C_1-C_6 alkyl) or C_3-C_6 cycloalkyl or $-O(C_1$-C_6 alkyl), $-O(C_0$-C_6 alkylene)(C_5-C_{10} aryl), $-O(C_0$-C_6 alkylene)(5-10 membered heteroaryl), $-O(C_0$-C_6 alkylene)(C_3-C_6 cycloalkyl) or $-O(C_0$-C_6 alkylene)(3-6 membered heterocycloalkyl) substituted with 0, 1, 2 or 3 substituents; wherein the substituents are selected from: cyano, oxo, halogen, cyano C_1-C_6 alkyl and C_1-C_6 haloalkyl.~~

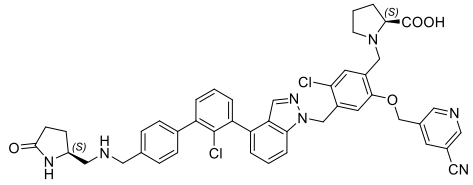
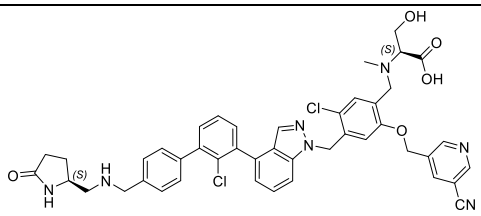
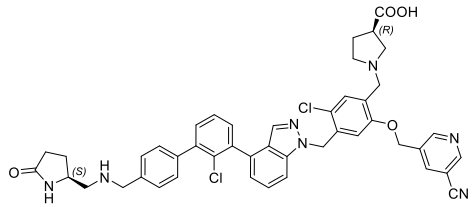
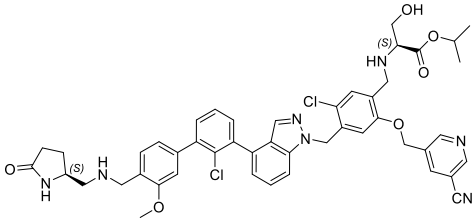
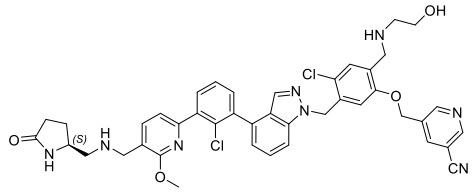
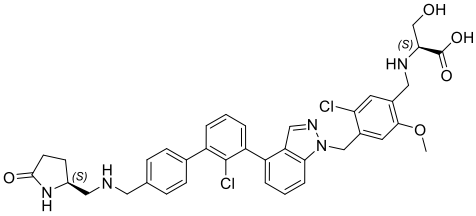
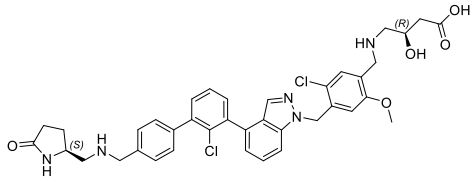
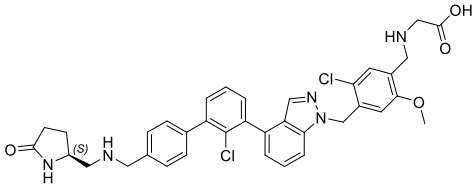
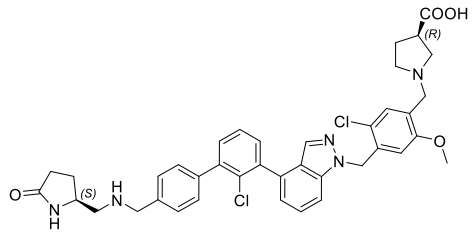
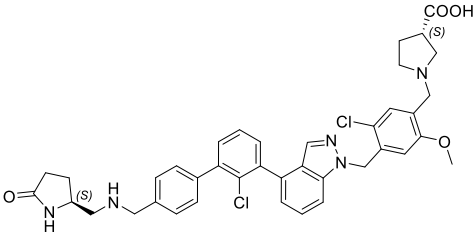
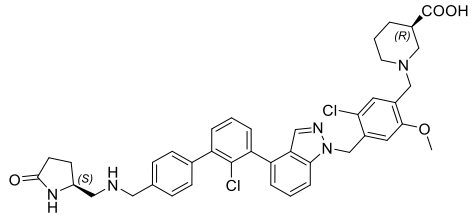
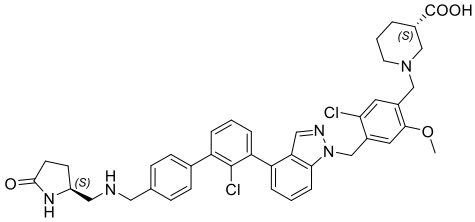
~~22~~15. The compound according to any one of claims 1-~~21~~14, R^L represents hydrogen or halogen; and/or R^M, R^N each preferably independently represents hydrogen.

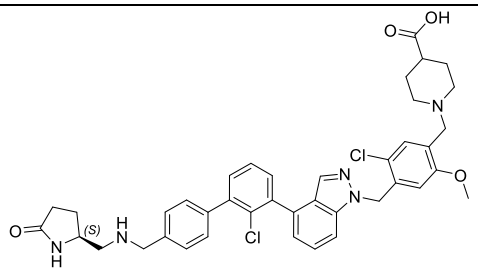
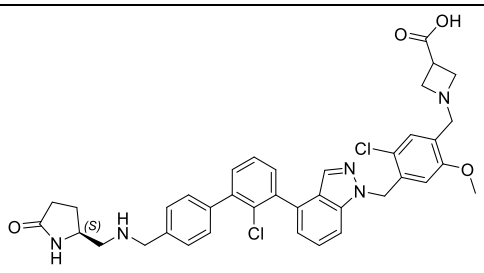
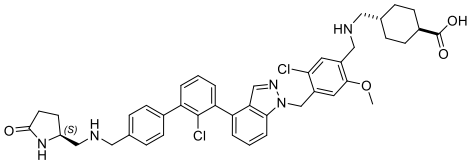
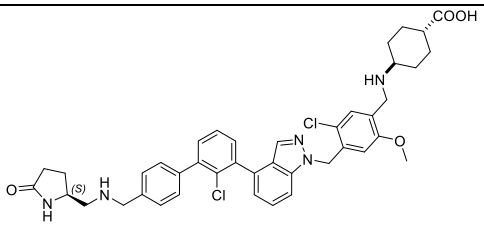
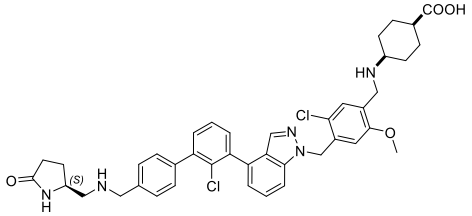
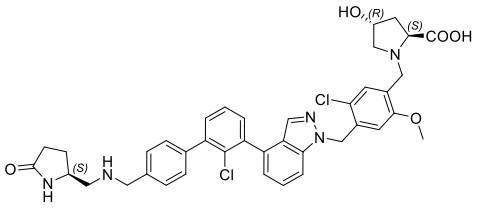
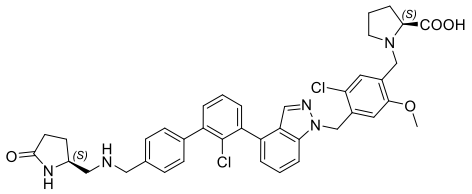
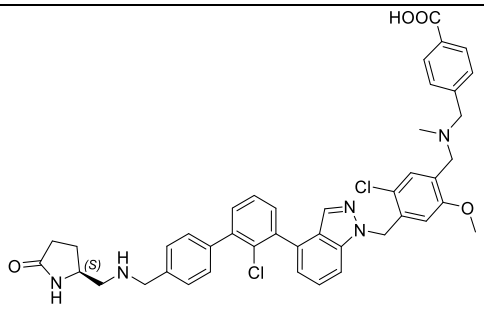
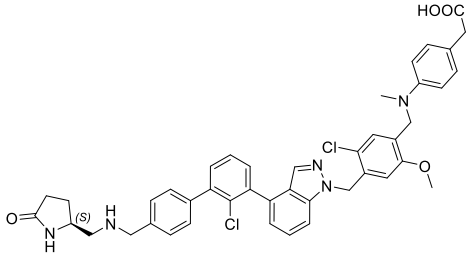
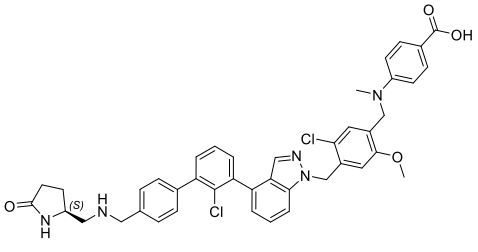
~~23. The compound according to any one of claims 3-21, R^M, R^N each preferably independently represents hydrogen.~~

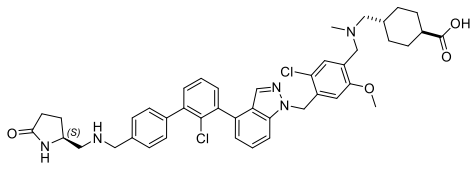
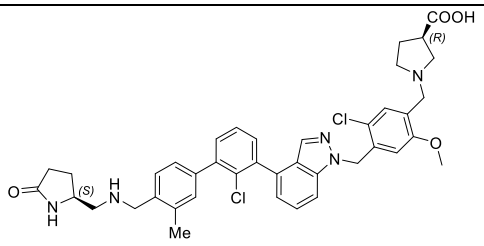
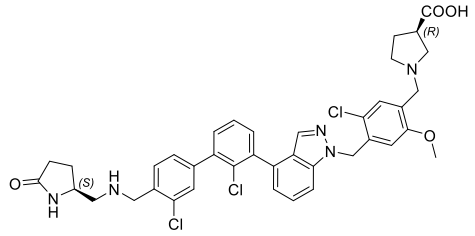
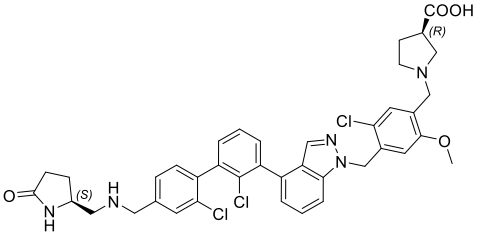
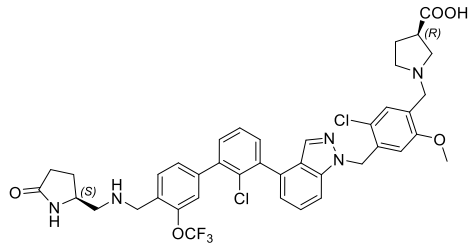
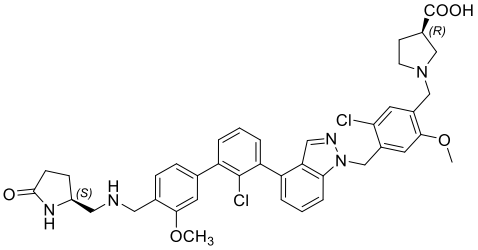
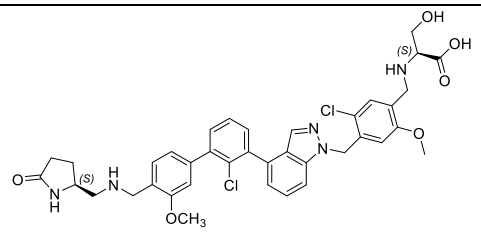
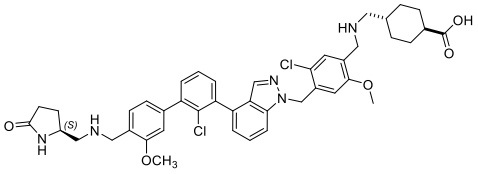
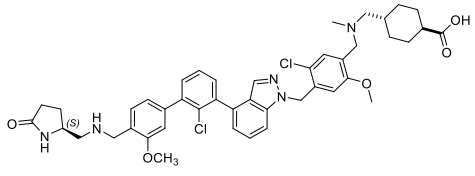
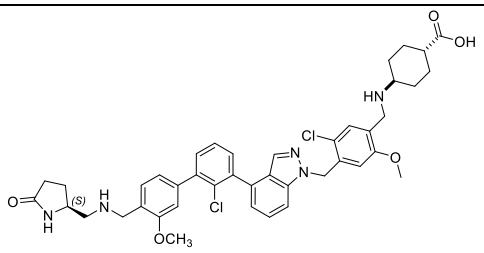
~~24~~16. Compounds having the following structures:

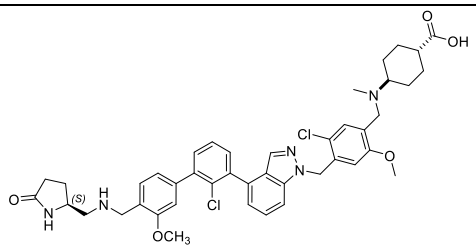
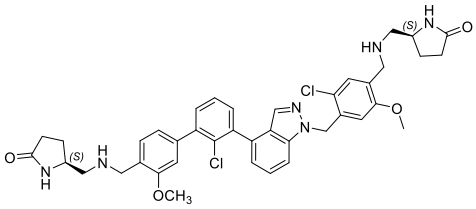
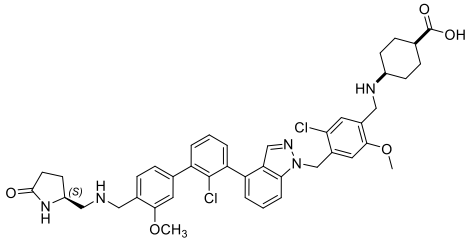
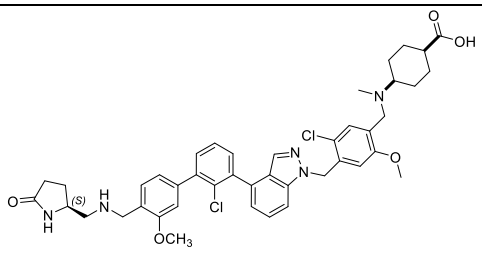
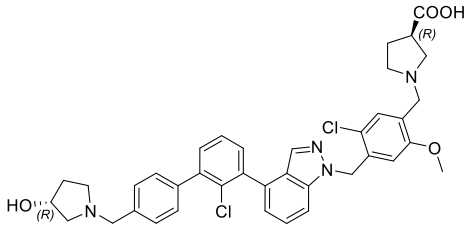
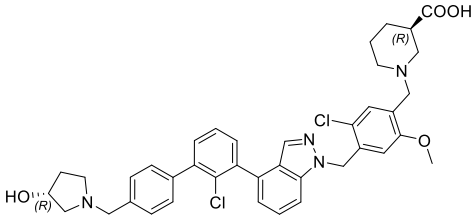
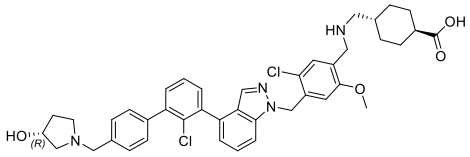
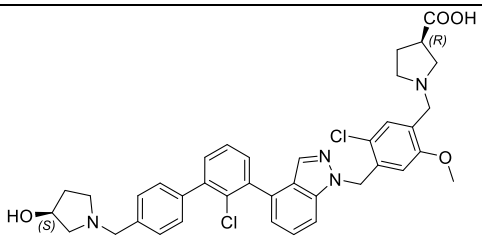
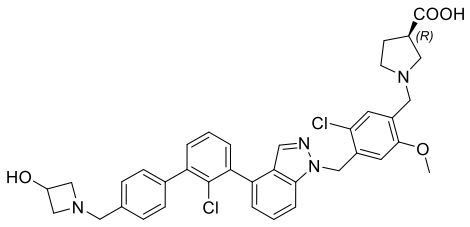
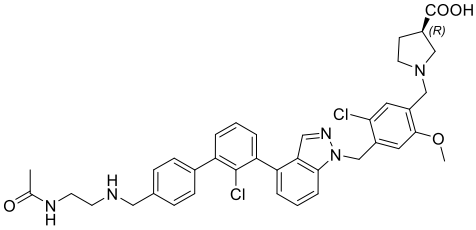
	
	
	
	
	
	

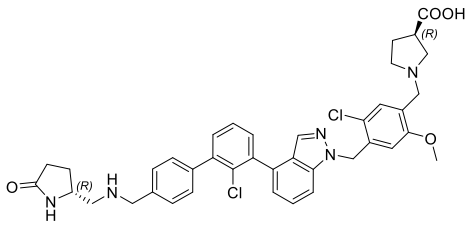
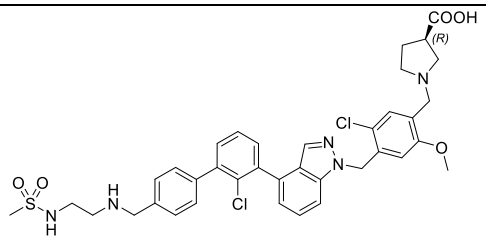
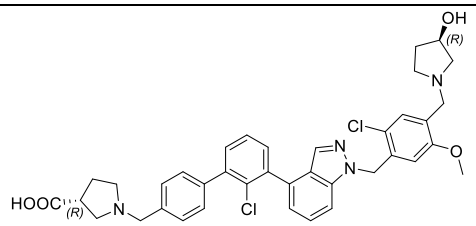
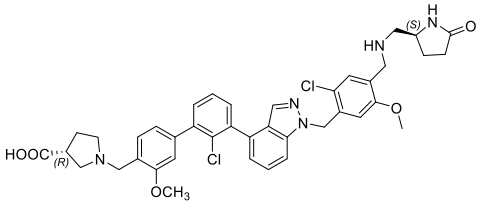
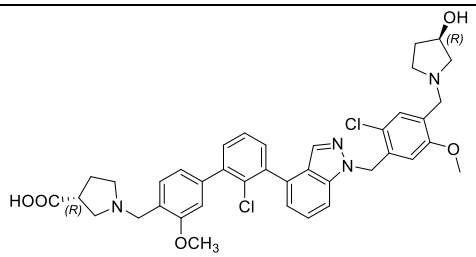
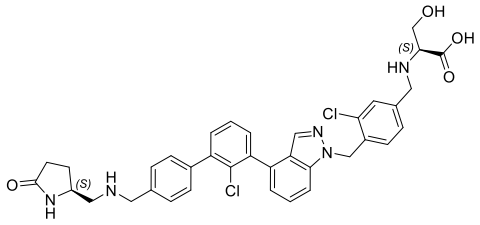
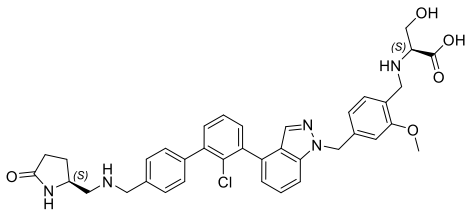
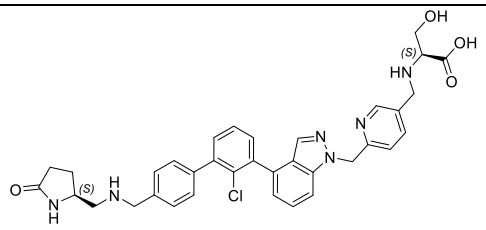
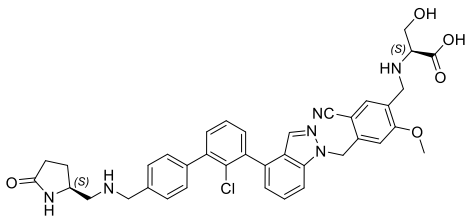
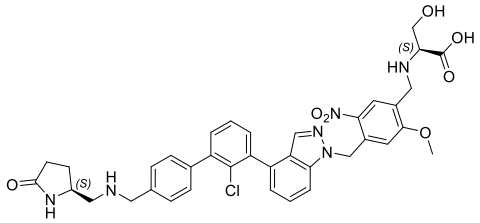
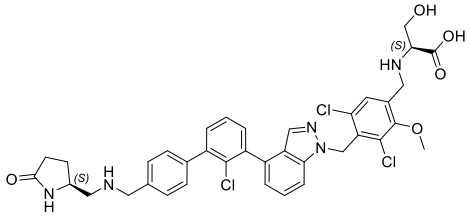
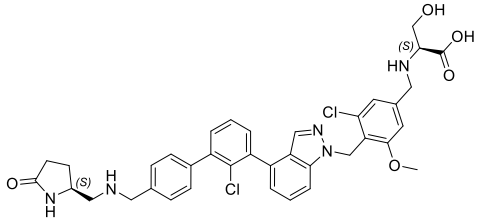
	
	
	
	
	
	

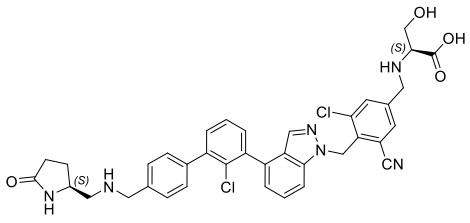
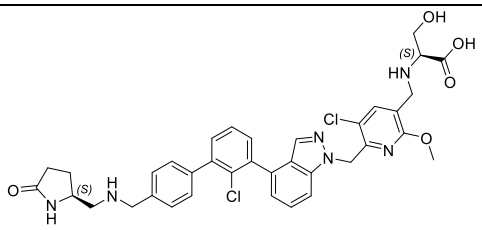
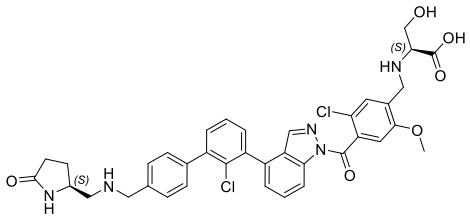
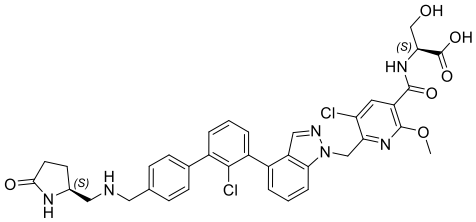
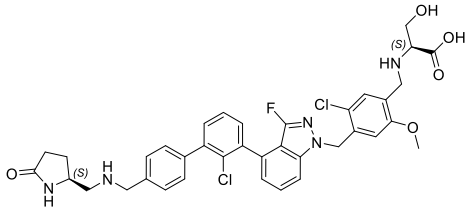
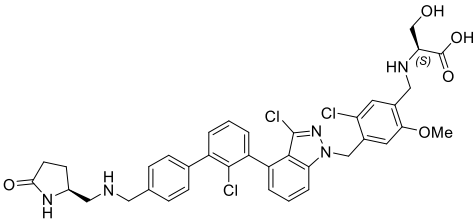
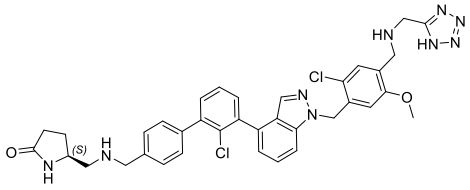
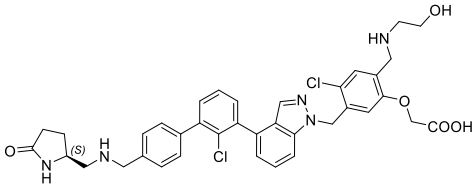
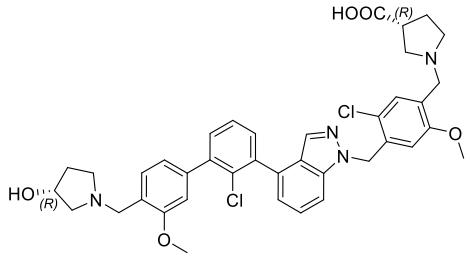
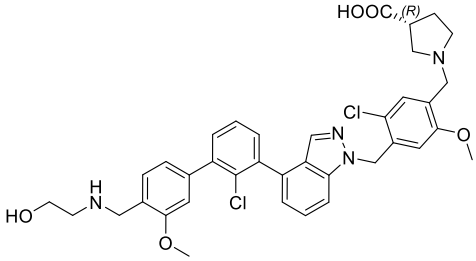
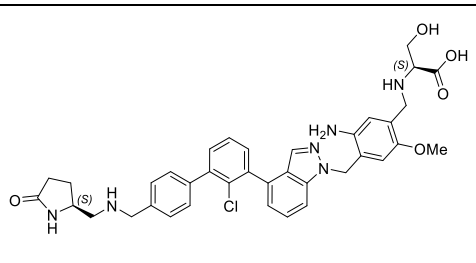
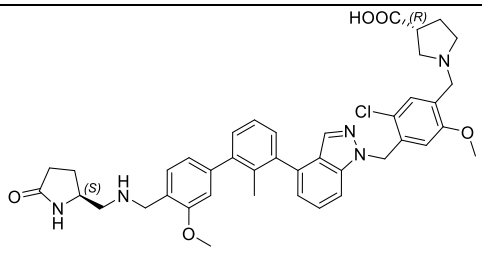
	
	
	
	
	
	

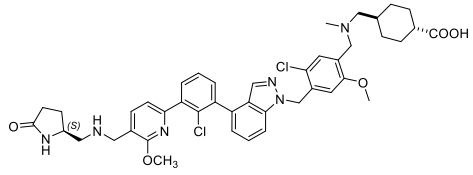
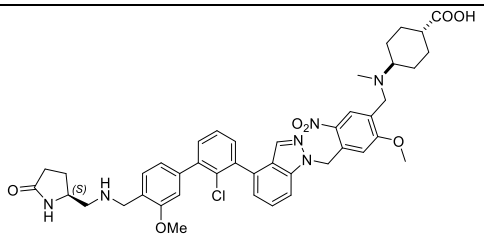
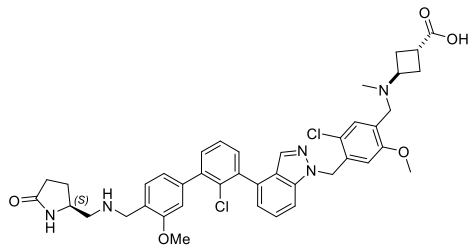
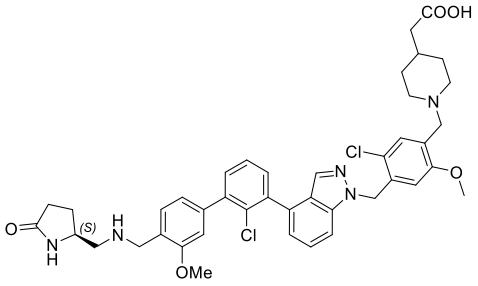
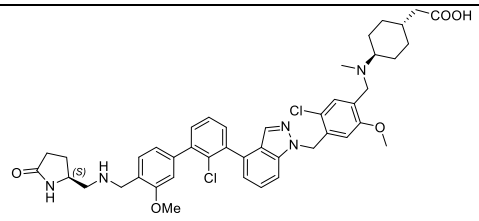
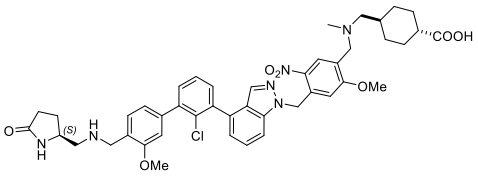
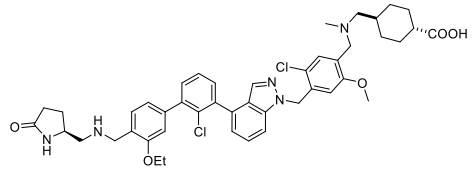
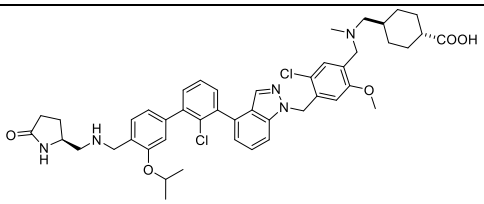
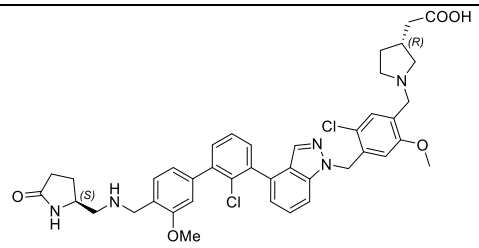
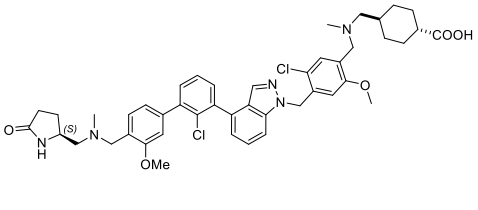
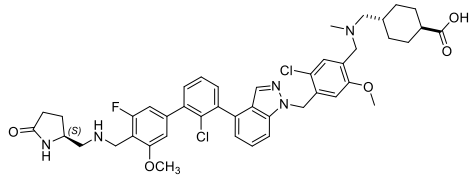
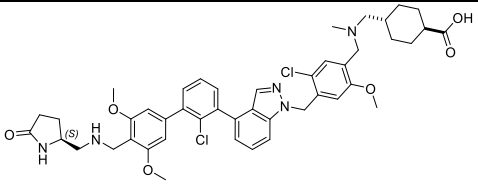
	
	
	
	
	

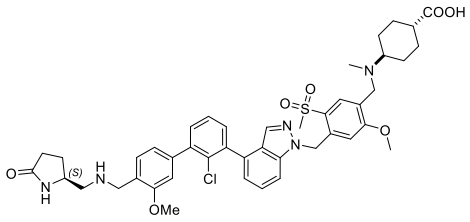
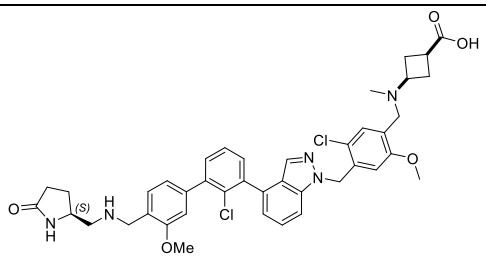
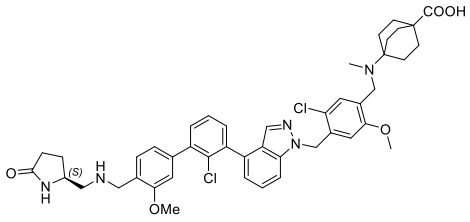
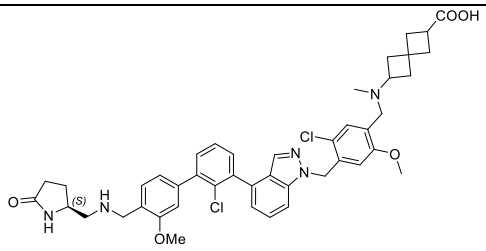
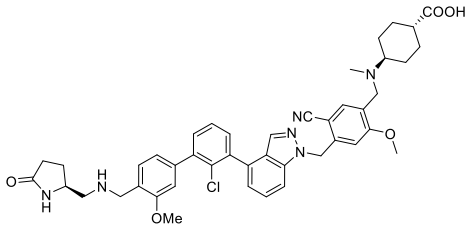
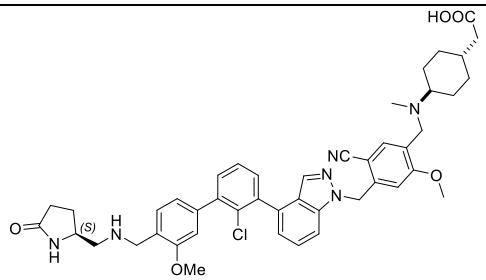
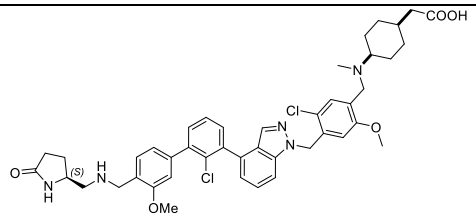
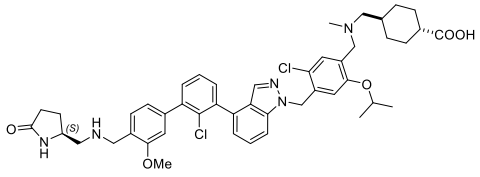
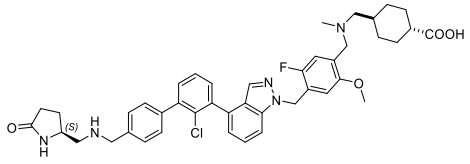
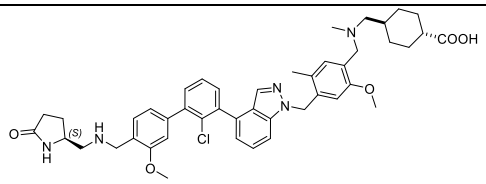
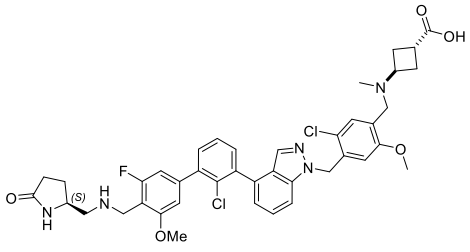
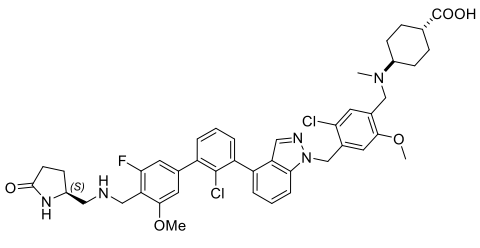
	
	
	
	
	

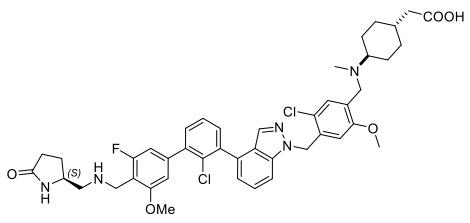
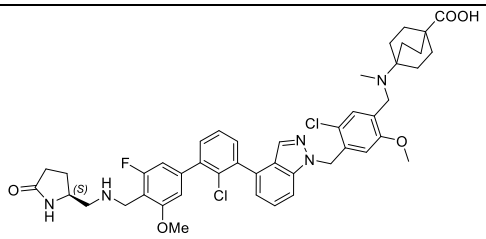
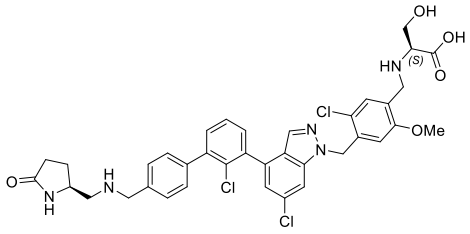
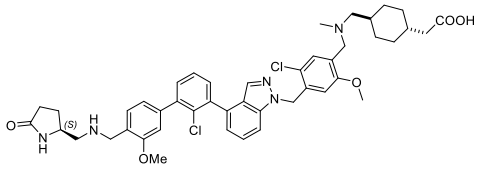
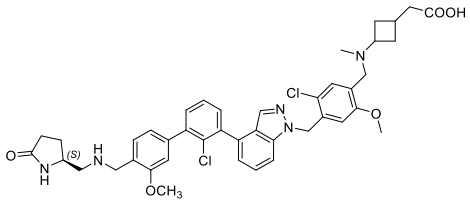
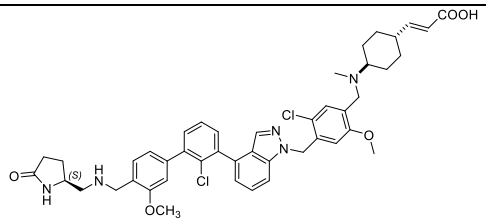
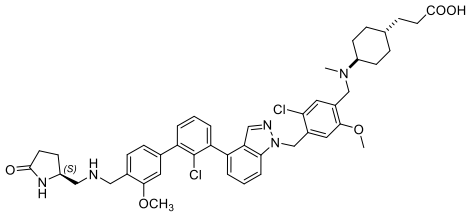
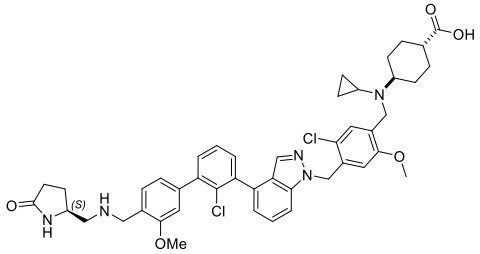
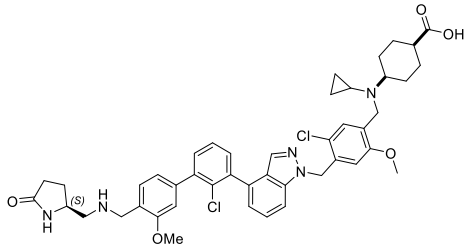
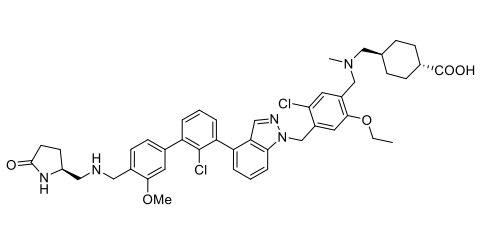
	
	
	
	
	

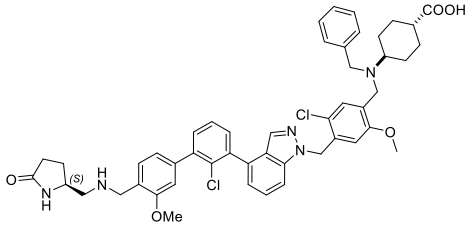
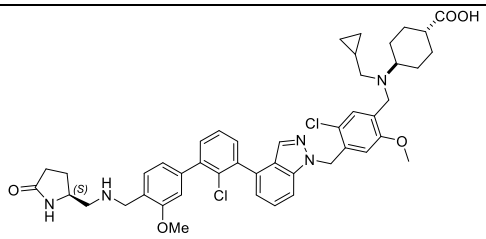
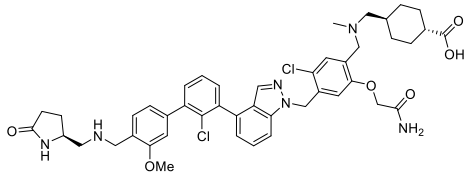
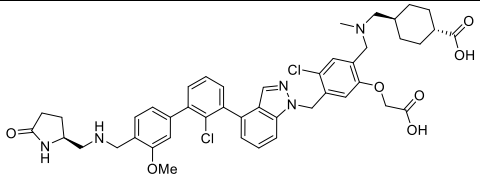
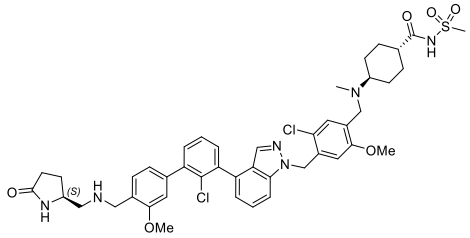
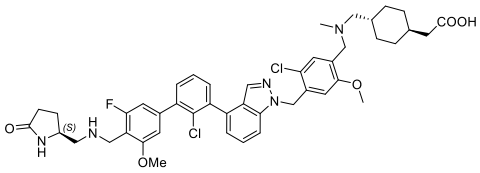
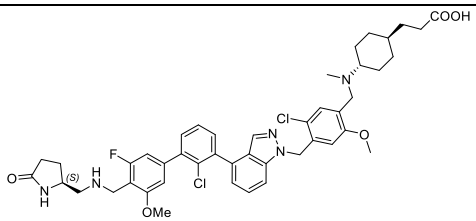
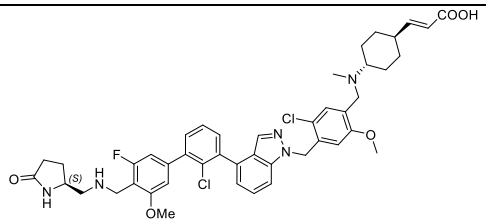
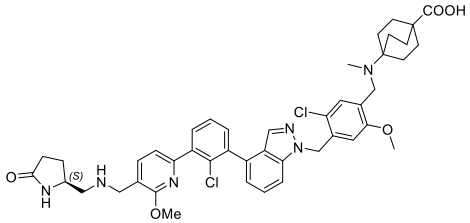
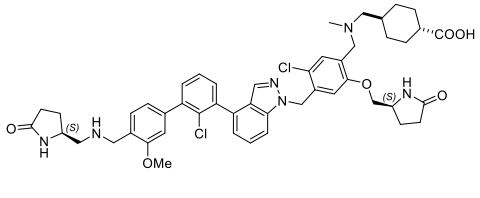
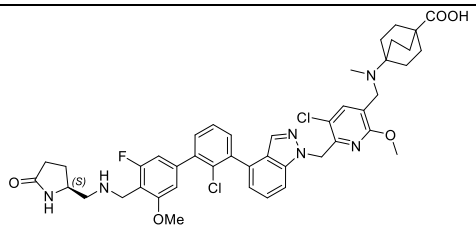
	
	
	
	
	
	

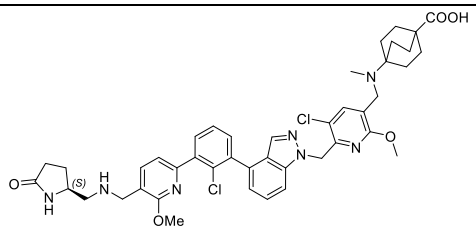
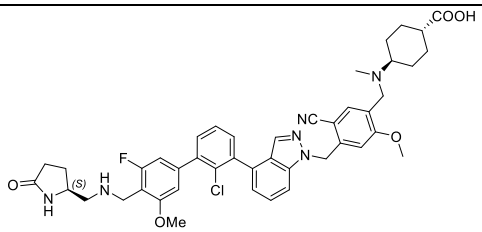
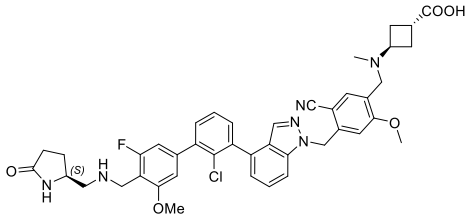
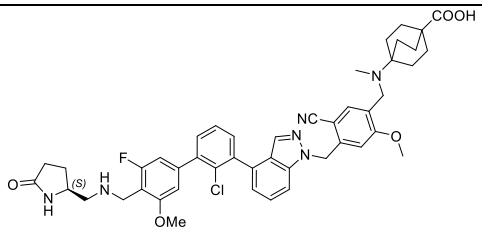
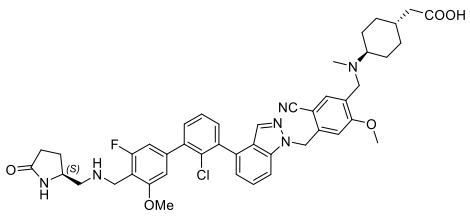
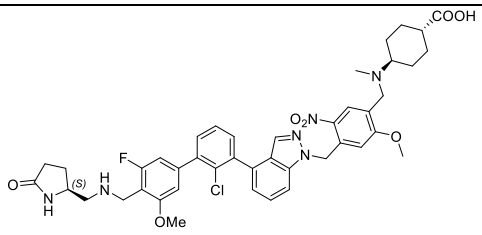
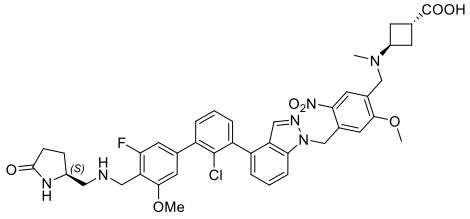
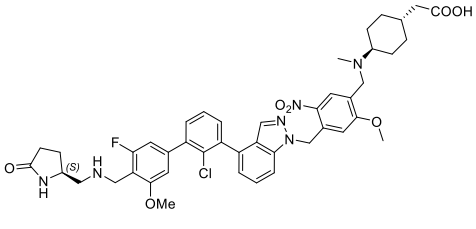
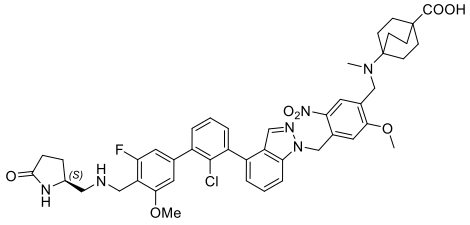
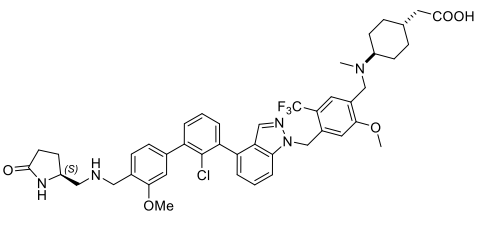
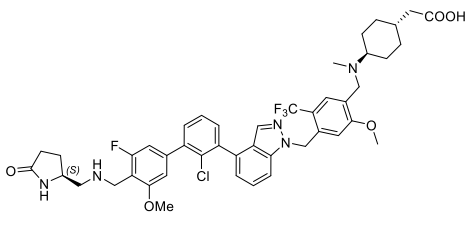
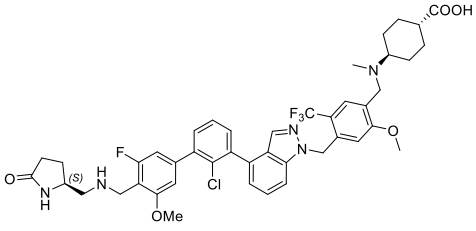
	
	
	
	
	
	

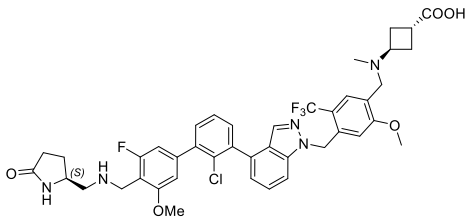
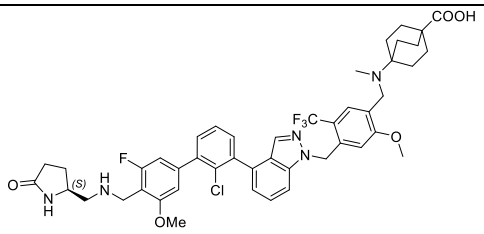
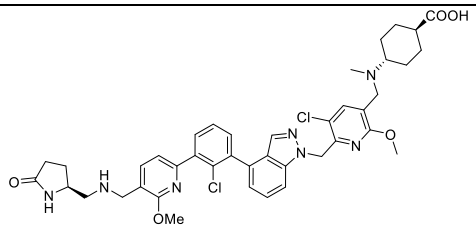
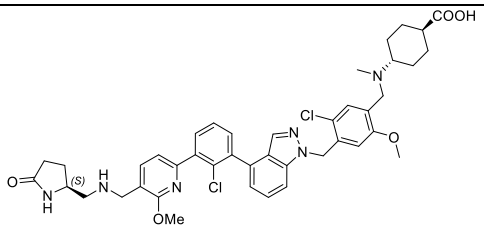
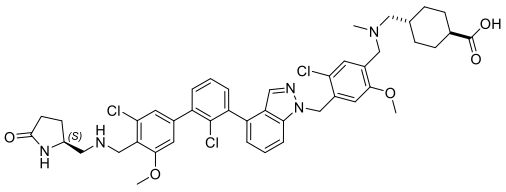
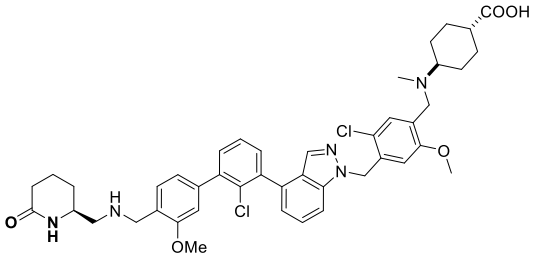
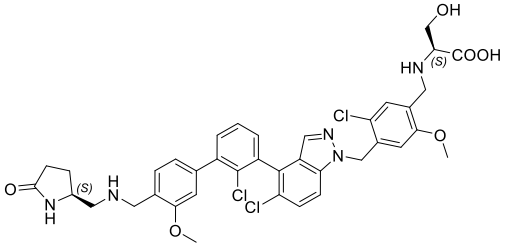
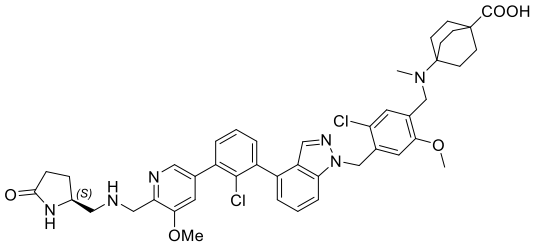
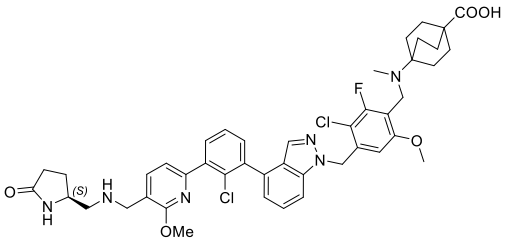
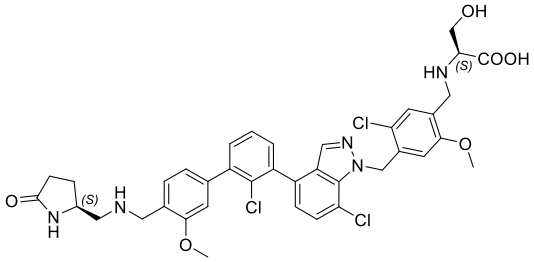
	
	
	
	
	
	
	

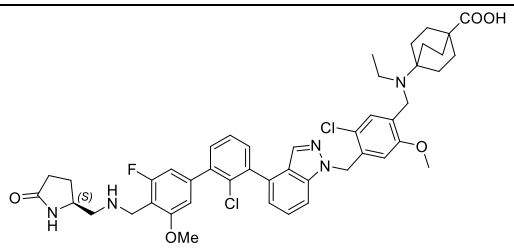
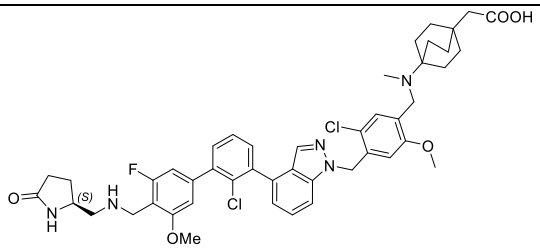
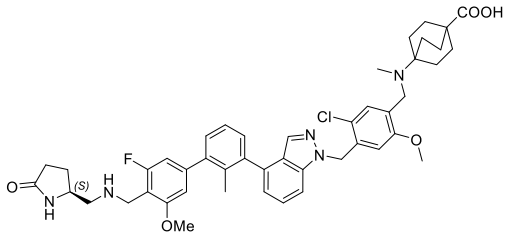
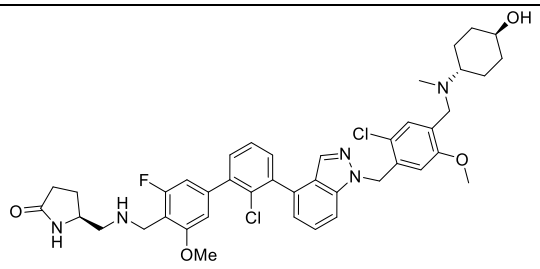
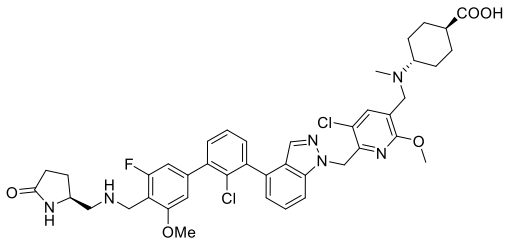
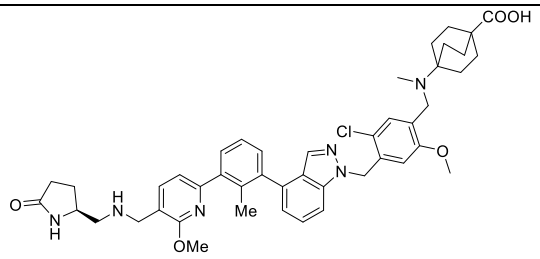
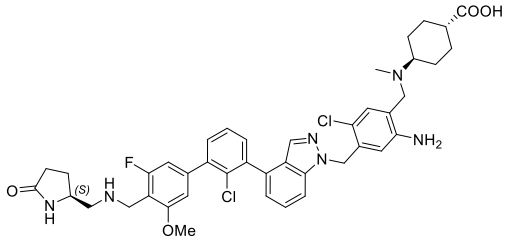
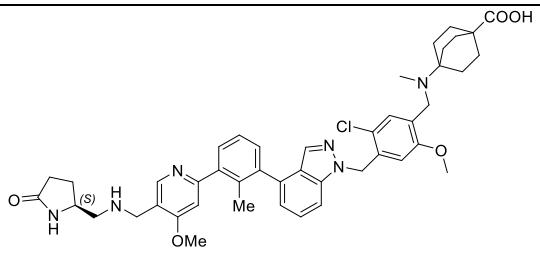
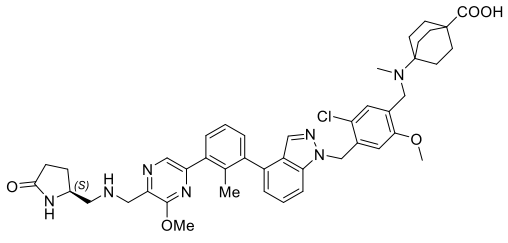
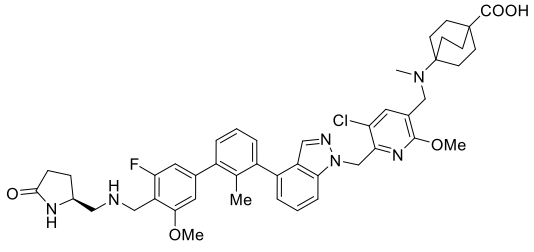
	
	
	
	
	
	

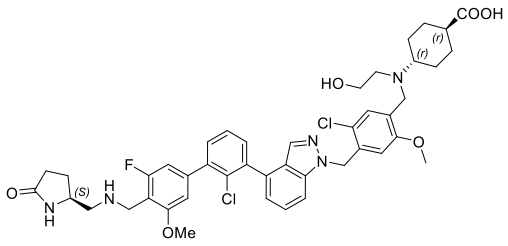
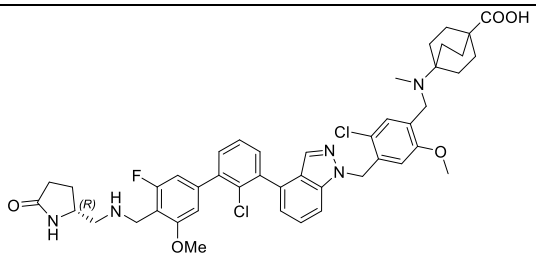
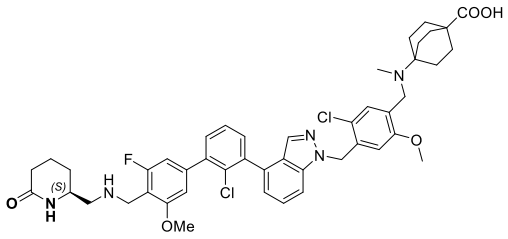
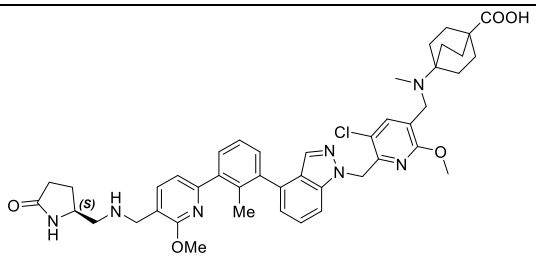
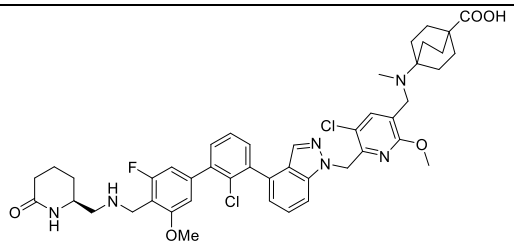
	
	
	
	
	

~~25~~17. A pharmaceutical composition, comprising a compound according to any one of claims 1 to ~~24~~ 16 and optionally a pharmaceutically acceptable carrier.

~~26~~18. Use of the compound according to any one of claims 1 to ~~24~~ 16 or the pharmaceutical composition of claim ~~25~~ 17 in the manufacture of a medicament for the prevention or treatment of a disease or condition responsive to inhibition of the binding of PD-L1 to PD-1.

~~27~~19. The use according to claim ~~26~~18, wherein the disease or condition is selected from tumors, cancers, viral infections, inflammation-related diseases and autoimmune diseases.

~~28. A method of treating a disease or condition responsive to inhibition of PD-L1 binding to PD-1, comprising administering the compound of any one of claims 1 or 24 or the pharmaceutical~~

~~composition of claim 25 to a mammal in need thereof.~~

~~29. A method of inhibiting the binding of PD-L1 to PD-1, comprising exposing the compound of any of claims 1 or 24 or the pharmaceutical composition of claim 25 to the PD-L1 and/or PD-1.~~