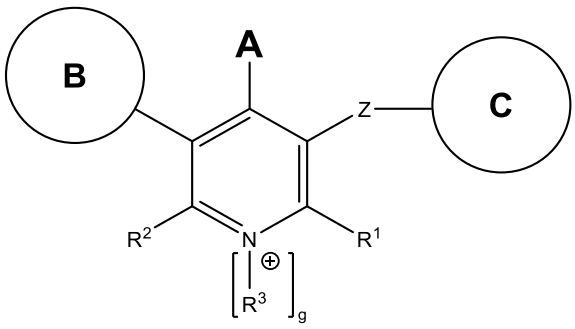
THAT WHICH IS CLAIMED:

1. A compound of Formula I:



I

,

or a pharmaceutically acceptable salt thereof, wherein:

g is 1 or 0;

Z is absent, -N(H)-C(=O)- or -C(=O)-NH-;

Ring B is phenyl or pyridinyl, each of which is mono-substituted with R^{B1} or di-substituted with one R^{B1} and one R^{B2}, wherein:

R^{B1} and R^{B2} are independently hydrogen, cyano, C_1-C_6 alkyl, halogen, halo-C_1-C_6 alkyl, hydroxy-C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, -O-C_2-C_6 alkenyl, -NH-$(CH_2)_{1\text{-}5}$-NH_2, -O-$(CH_2)_{q2}$-O-$(CH_2)_{r2}$-CH_3, or -C(O)-$NR^{Na}R^{Nb}$,

each R^{Na} and R^{Nb} is independently hydrogen or C_1-C_6 alkyl, and

q2 and r2 are independently an integer from 1 to 4;

Ring C is 4- to 10-membered monocyclic or bicyclic fused heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl, each of which is substituted with R^{C1}, R^{C2}, and R^{C3}, wherein:

said heterocyclyl or heteroaryl contains 1, 2, 3, or 4 ring heteroatoms selected from N, O, and S,

R^{C1} is hydrogen or is bonded to R^1, R^3, or R^6,

R^{C2} and R^{C3} are independently hydrogen, halogen, cyano, C_1-C_6 alkyl, hydroxy, -C(=O)NH_2, -O-C_2-C_6 alkenyl, -C_1-C_6 alkoxy, -NH-$(CH_2)_{1\text{-}5}$-NH_2, -O-piperidinyl, or -O-$(CH_2)_{qC}$-O-$(CH_2)_{rC}$-CH_3, and

qC and rC are independently an integer from 1 to 4;

R^1 is hydrogen or halogen, or

R^1 and Z together with the ring to which each is attached form a fused bicyclic ring, optionally substituted with one or two R^8, or

R^1 and R^{C1} together with the ring to which each is attached form a fused tricyclic ring;

R^2 is hydrogen or halogen, or

R^2 and R^{B1} together with the ring to which each is attached form a fused tricyclic ring;

R^3, if present, is a group covalently bound to R^{C1};

A is:

i. $-NR^4R^5$, wherein:

R^4 is optionally substituted C_1-C_6 alkyl, -NH-C_1-C_6 alkyl-NHR^{4a}, or -C_1-C_6 alkyl-NHR^{4a}, wherein the optional substituents are selected from the group consisting of halogen and hydroxy,

R^{4a} is hydrogen or methyl, and

R^5 is hydrogen or optionally substituted C_1-C_6 alkyl, wherein the optional substituents are selected from the group consisting of halogen and hydroxy, or

R^5 and R^{B1} together with the N to which R^5 is attached and Ring B to which R^{B1} is attached form a fused heterocyclyl, or

R^5 and R^{C1} together with the N to which R^5 is attached and Ring C to which R^{C1} is attached form a fused heterocyclyl, or

R^5 and R^8 together with the N to which R^5 is attached and the ring to which R^8 is attached form a fused heterocyclyl;

ii. spirocyclic, substituted with -NH-R^6 or R^S, wherein R^S is hydrogen or -C(=O)-C_1-C_6 alkyl; or

iii. -O-(C_3-C_8 cycloalkyl), 5- to 11-membered heterocyclyl, or 5- to 6-membered heteroaryl, each of which is mono-substituted with -NH-R^6 or di-substituted with one R^F and one R^G, wherein:

R^F is hydroxy, hydroxy-C_1-C_6 alkyl, nitro, -C(=O)H, -C_1-C_6 alkoxy, -C(=NH)-NH_2, -NH-C(=NH)-NH_2, -C(=O)-C_1-C_6 alkyl, -(C=O)-O-C_1-C_6 alkyl, or -(C_1-C_6 alkyl)$_x$-$NR^{F1}R^{F2}$,

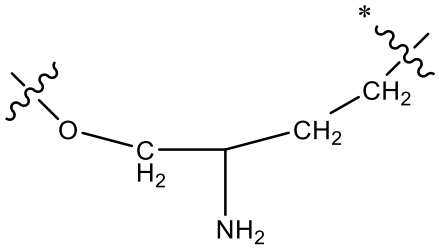
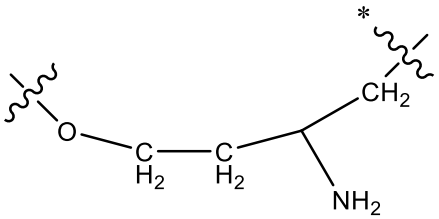
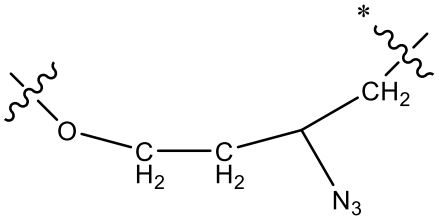
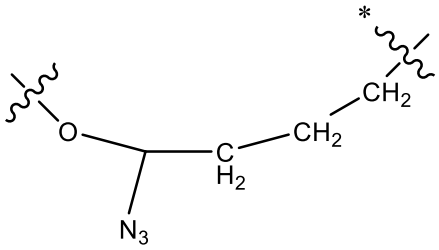
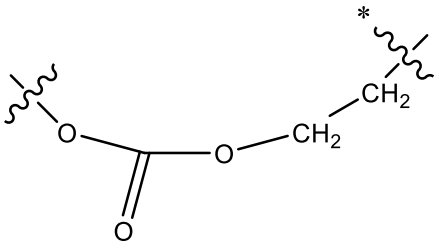
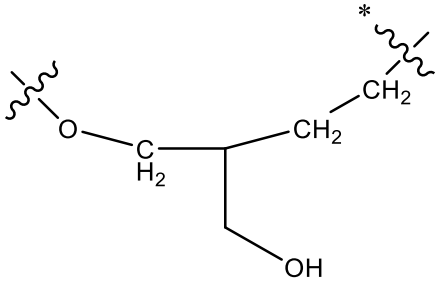
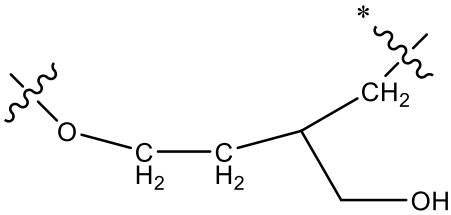
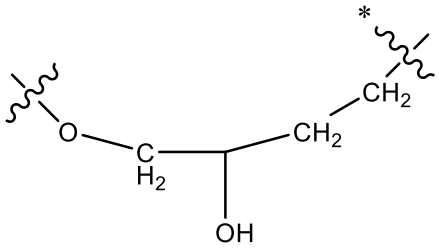
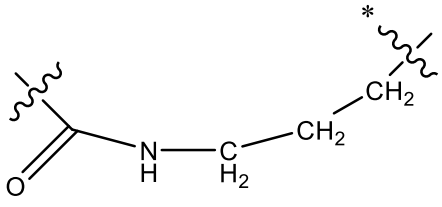
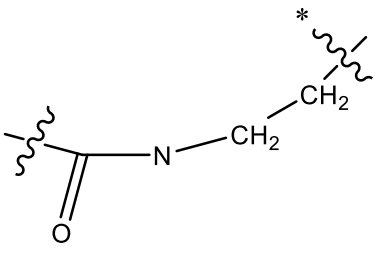
x is 0 or 1,

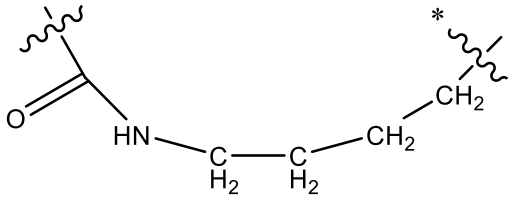
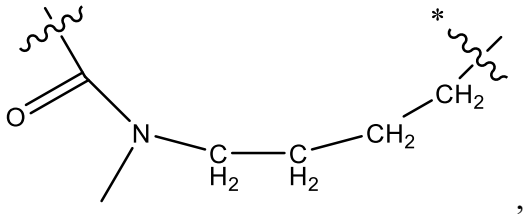
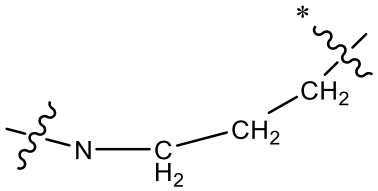
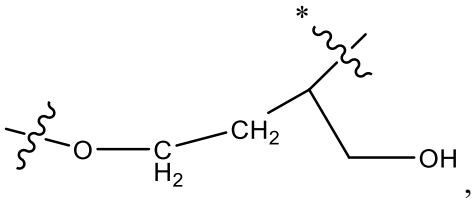
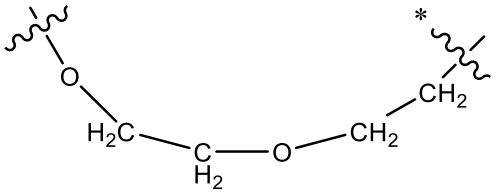
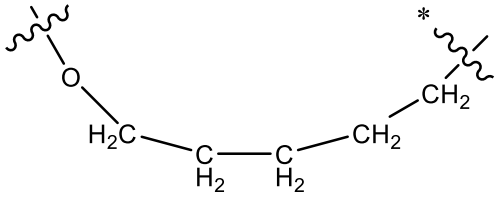
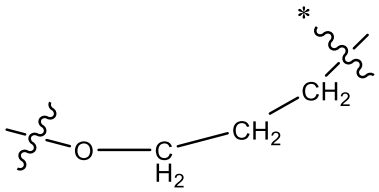
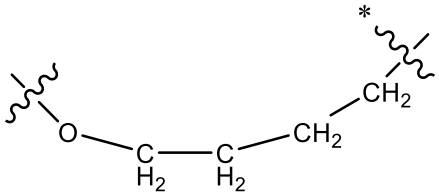
R^{F1} and R^{F2} are independently H, -(C=O)-O-C_1-C_6-alkyl, or C_1-C_6 alkyl, and R^G is hydrogen or -C_1-C_6 alkoxy; or

R^G together with R^{C1} form a -O-$(CH_2)_k$-O-, wherein k is an integer from 1 to 5; or

R^F and R^G together form carboxy; and

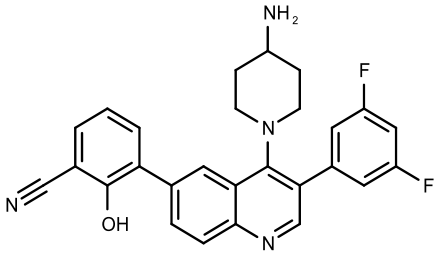
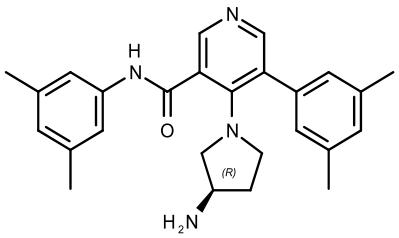
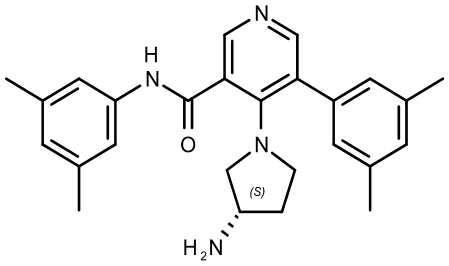
R^6 and R^{C1} form:


,

,

,

,

,

,

,

,

,

,

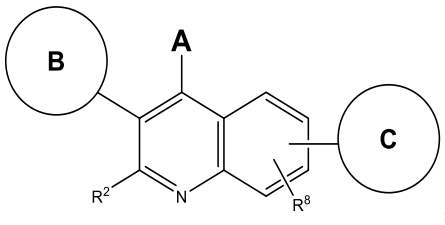

,

,

,

,

,

,

, or

,

wherein  represents the attachment point of R^6;

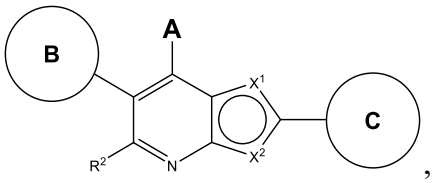
provided that the compound is not one of:


,

, and

.

2. A compound having a structure of Formula Ia or Ib:



Ia



Ib

wherein:

Ring B is phenyl or pyridinyl, each of which is mono-substituted with R^{B1} or di-substituted with one R^{B1} and one R^{B2}, wherein:

R^{B1} and R^{B2} are independently hydrogen, cyano, C_1-C_6 alkyl, halogen, halo-C_1-C_6 alkyl, hydroxy-C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, -O-C_2-C_6 alkenyl, -NH-$(CH_2)_{1\text{-}5}$-NH_2, -O-$(CH_2)_{q2}$-O-$(CH_2)_{r2}$-CH_3, or -C(O)-$NR^{Na}R^{Nb}$,

each R^{Na} and R^{Nb} is independently hydrogen or C_1-C_6 alkyl, and

q2 and r2 are independently an integer from 1 to 4;

Ring C is 4- to 10-membered monocyclic or bicyclic fused heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl, each of which is substituted with R^{C1}, R^{C2}, and R^{C3}, wherein:

said heterocyclyl or heteroaryl contains 1, 2, 3, or 4 ring heteroatoms selected from N, O, and S,

R^{C1} is hydrogen, is bonded to R^6, or is as further defined,

R^{C2} and R^{C3} are independently hydrogen, halogen, cyano, C_1-C_6 alkyl, hydroxy, -C(=O)NH_2, -O-C_2-C_6 alkenyl, -C_1-C_6 alkoxy, -NH-$(CH_2)_{1\text{-}5}$-NH_2, -O-piperidinyl, or -O-$(CH_2)_{qC}$-O-$(CH_2)_{rC}$-CH_3, and

qC and rC are independently an integer from 1 to 4;

R^2 is hydrogen or halogen, or

R^2 and R^{B1} together with the ring to which each is attached form a fused tricyclic ring;

A is:

i. $-NR^4R^5$, wherein:

R^4 is optionally substituted C_1-C_6 alkyl, -NH-C_1-C_6 alkyl-NHR^{4a}, or -C_1-C_6 alkyl-NHR^{4a}, wherein the optional substituents are selected from the group consisting of halogen and hydroxy,

R^{4a} is hydrogen or methyl, and

R^5 is hydrogen or optionally substituted C_1-C_6 alkyl, wherein the optional substituents are selected from the group consisting of halogen and hydroxy, or

R^5 and R^{B1} together with the N to which R^5 is attached and Ring B to which R^{B1} is attached form a fused heterocyclyl, or

R^5 and R^{C1} together with the N to which R^5 is attached and Ring C to which R^{C1} is attached form a fused heterocyclyl, or

R^5 and R^8 together with the N to which R^5 is attached and the ring to which R^8 is attached form a fused heterocyclyl;

ii. spirocyclic, substituted with -NH-R^6 or R^S, wherein R^S is hydrogen or -C(=O)-C_1-C_6 alkyl; or

iii. -O-(C_3-C_8 cycloalkyl), 5- to 11-membered heterocyclyl, or 5- to 6-membered heteroaryl, each of which is mono-substituted with -NH-R^6 or di-substituted with one R^F and one R^G, wherein:

R^F is hydroxy, hydroxy-C_1-C_6 alkyl, nitro, -C(=O)H, -C_1-C_6 alkoxy, -C(=NH)-NH_2, -NH-C(=NH)-NH_2, -C(=O)-C_1-C_6 alkyl, -(C=O)-O-C_1-C_6 alkyl, or -(C_1-C_6 alkyl)$_x$-$NR^{F1}R^{F2}$,

x is 0 or 1,

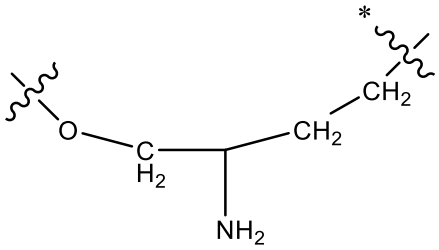
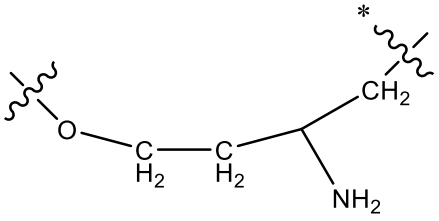
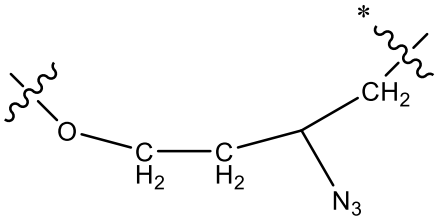
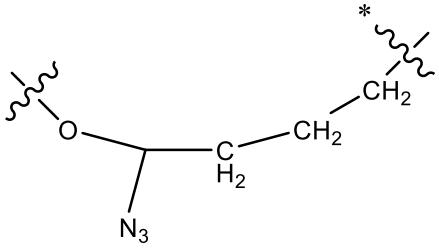
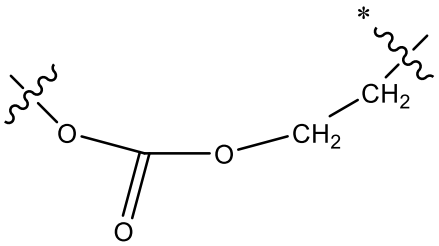
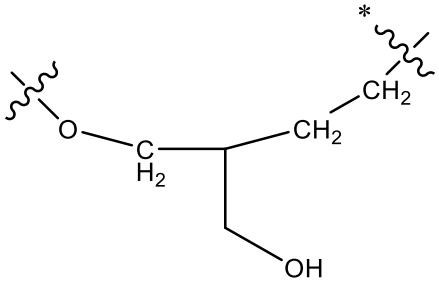
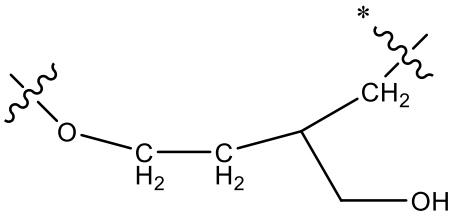
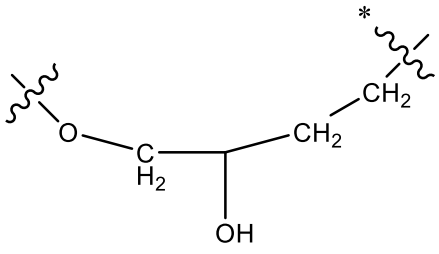
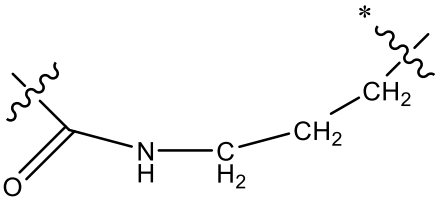
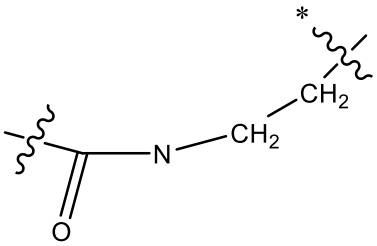
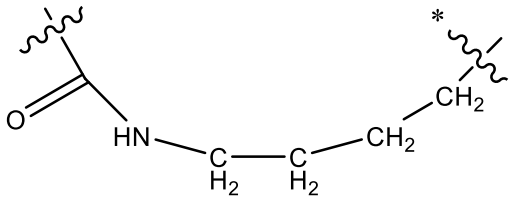
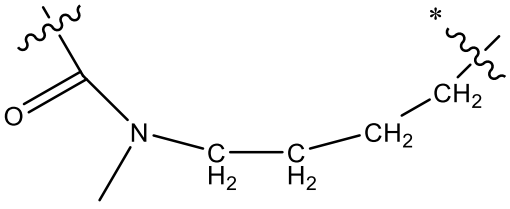
R^{F1} and R^{F2} are independently H, -(C=O)-O-C_1-C_6-alkyl, or C_1-C_6 alkyl, and

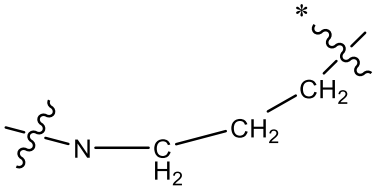
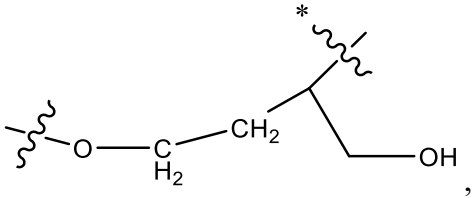
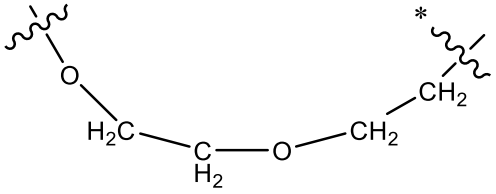
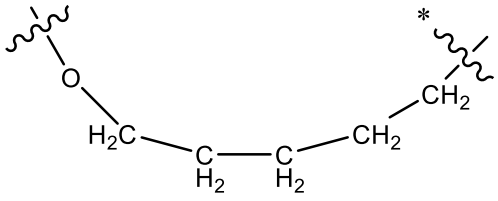
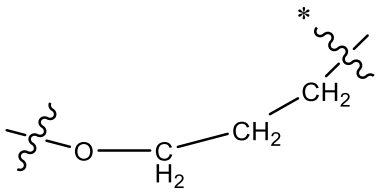
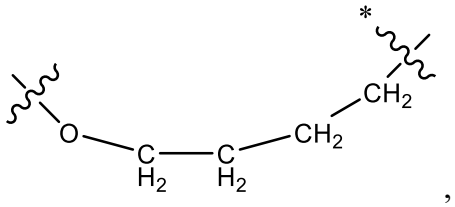
R^G is hydrogen or -C_1-C_6 alkoxy; or

R^G together with R^{C1} form a -O-(CH_2)$_k$-O-, wherein k is an integer from 1 to 5; or

R^F and R^G together form carboxy; and

R^6 and R^{C1} form:


,

,

,

,

,

,

,

,

,

,

,

,


,

,

,

,

, or

,

wherein  represents the attachment point of R^6;

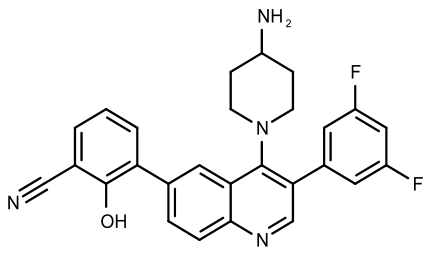
X^1 and X^2 are independently O, N, N-R^8, S, or C-R^8;

R^8 is as defined in (i), or

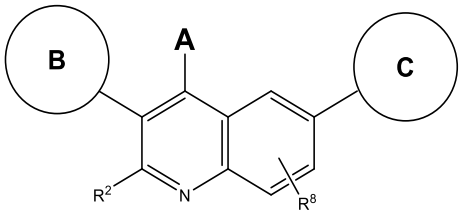
R^8 is hydrogen, optionally substituted C_1-C_6 alkyl, or -C(=O)OR^{8a}, wherein the optional substituents are selected from the group consisting of halogen, -NH_2, and hydroxy; and

R^{8a} is hydrogen or C_1-C_6 alkyl;

provided that the compound is not:

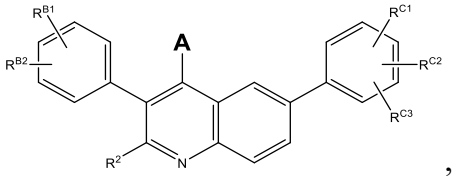

.

3. The compound of claim 2, having a structure of Formula Ia-1, Ia-2, Ia-3, or Ib-1:



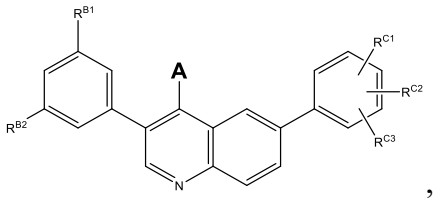
Ia-1

,



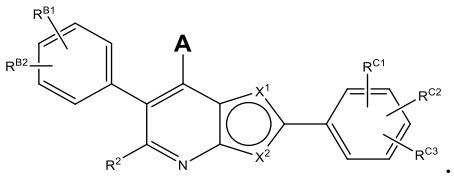
Ia-2

,



Ia-3

,



Ib-1

.

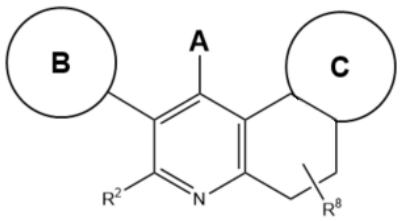
4. The compound of any one of claims 1-3, wherein R^{B1} and R^{B2} are independently C_1-C_6 alkyl, halogen, or C_1-C_6 alkoxy.

5. The compound of claim 2, wherein

Ring B is phenyl di-substituted with R^{B1} and R^{B2}; and

Ring C is 4- to 10-membered monocyclic or bicyclic heterocyclyl.

6. The compound of claim 1, having a structure of Formula Ic:



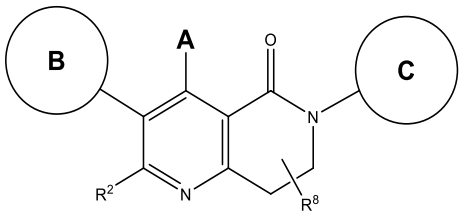
Ic

,

wherein R^8 is hydrogen.

7. The compound of claim 6, wherein Ring C is 8- to 10- membered heteroaryl substituted with R^{C2} and R^{C3}, and Ring B is phenyl di-substituted with R^{B1} and R^{B2}.

8. The compound of claim 1, having a structure of Formula Id:



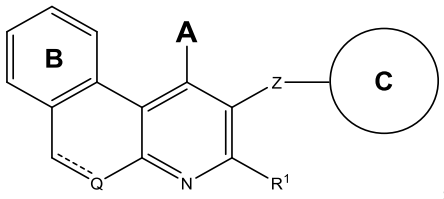
Id

,

wherein R^8 is hydrogen.

9. The compound of claim 8, wherein Ring C is phenyl substituted with R^{C1}, R^{C2}, and R^{C3}, and Ring B is phenyl di-substituted with R^{B1} and R^{B2}.

10. The compound of claim 1, having a structure of Formula Ie:



Ie

,

wherein:

Q is O or CH_2 and ------ is a single bond, or

Q is N and ------ is a double bond;

R^1 is hydrogen or halogen; and

Ring B is phenyl substituted with R^{B2}.

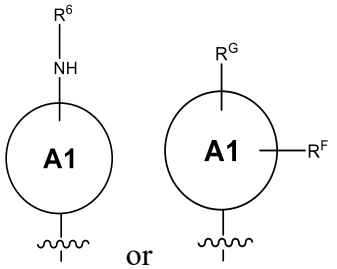
11. The compound of claim 10, wherein R^1 is hydrogen.

12. The compound of claim 10 or 11, wherein Ring C is 8- to 10- membered heteroaryl substituted with R^{C1}, R^{C2}, and R^{C3}.

13. The compound of any one of claims 10-12, wherein Q is N and ------ is a double bond; or wherein Q is O and ------ is a single bond.

14. The compound of any one of claims 1-13, wherein A is 5- to 11-membered heterocyclyl or 5- to 6-membered heteroaryl, each of which is mono-substituted with -NH-R^6 or di-substituted with one R^F and one R^G.

15. The compound of claim 14, wherein A has the structure:

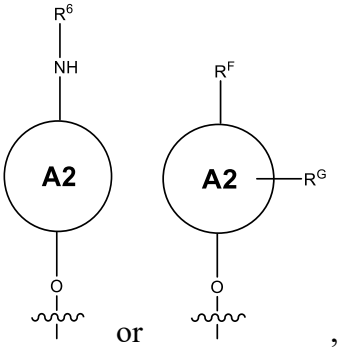


or ,

wherein Ring A1 is 5- to 6-membered heteroaryl or 5- to 6-membered heterocyclyl.

16. The compound of any one of claims 1-13, wherein A is -O-(C_3-C_8 cycloalkyl) which is mono-substituted with -NH-R^6 or di-substituted with one R^F and one R^G.

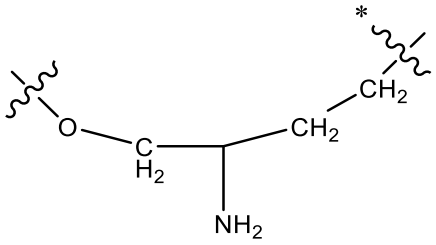
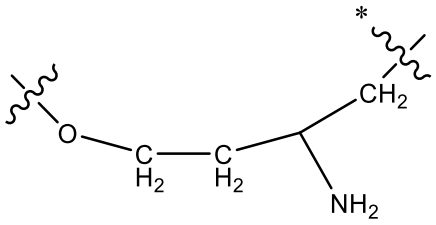
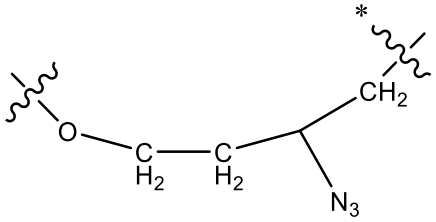
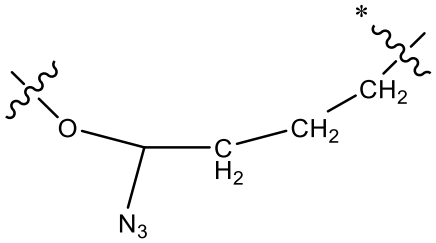
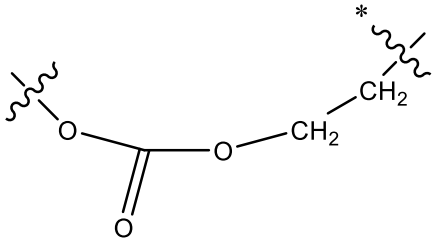
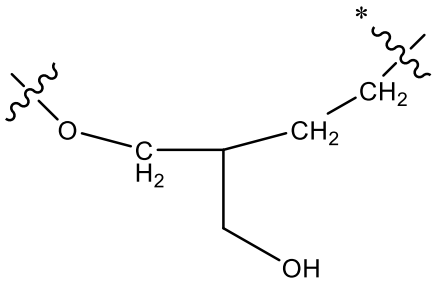
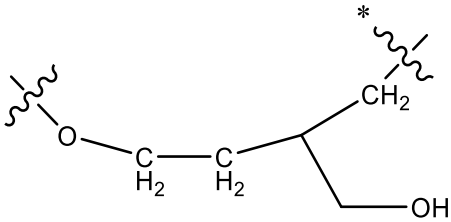
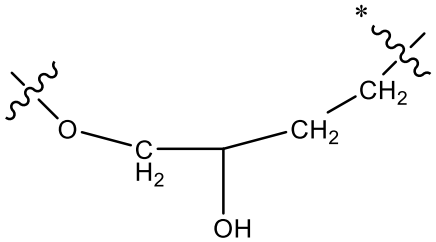
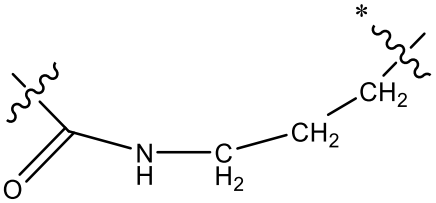
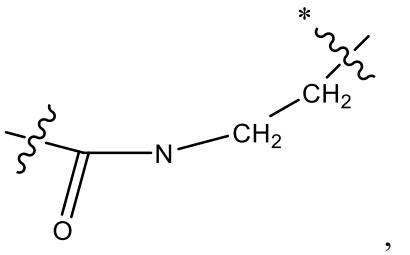
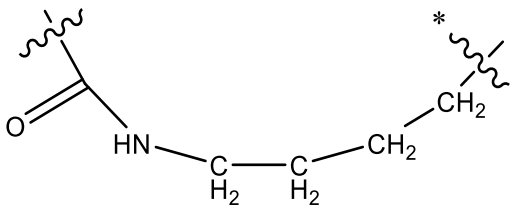
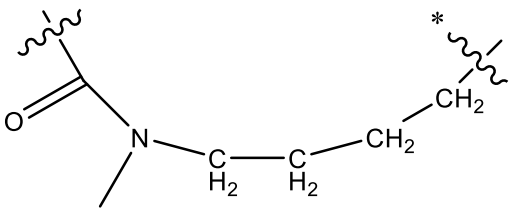
17. The compound of claim 16, wherein A has the structure:

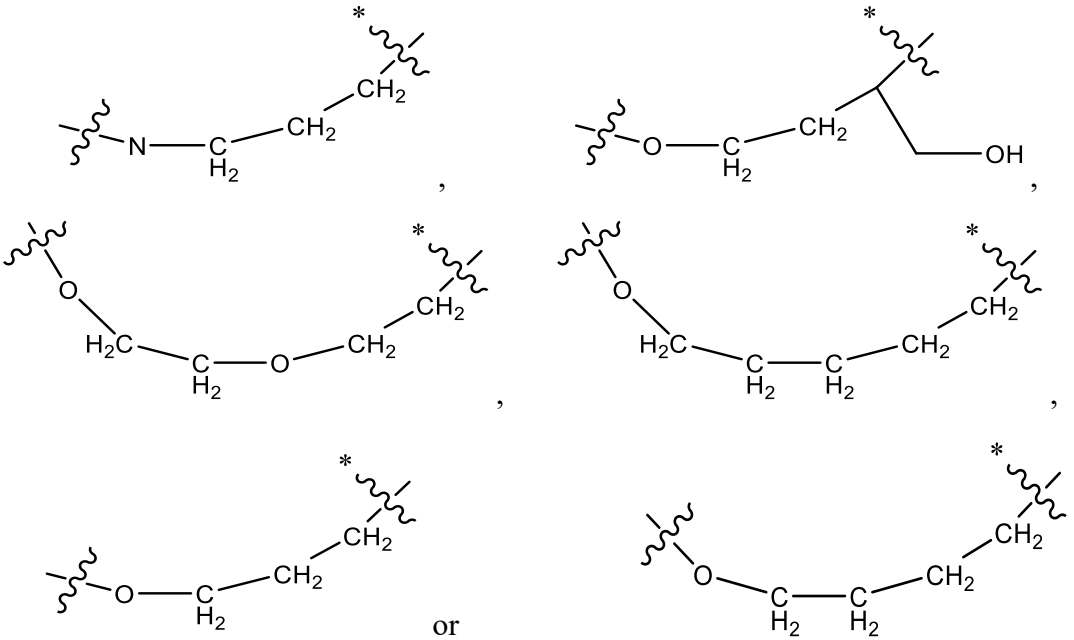


or ,

wherein Ring A2 is C_4-C_6 cycloalkyl.

18. The compound of any one of claims 14-17, wherein R^6 and R^{C1} form:

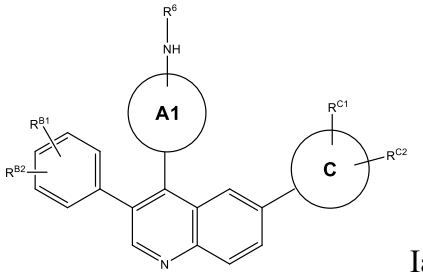

,

,

,

,

,

,

,

,

,

,

,

,



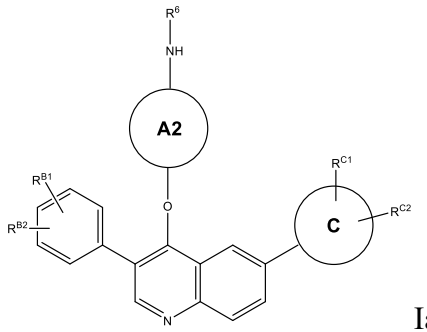
or

wherein  represents the attachment point of R^6.

19. The compound of claim 18, having a structure of Formula Ia-4 or Ia-5:



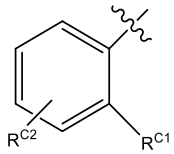
Ia-4

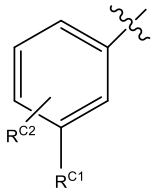


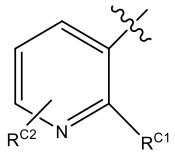
Ia-5,

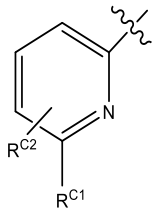
wherein Ring A1 is 5- to 6-membered heteroaryl or 5- to 6-membered heterocyclyl; and Ring A2 is C_4-C_6 cycloalkyl.

20. The compound of claim 19, wherein Ring C to which R^{C1} is attached has the structure:



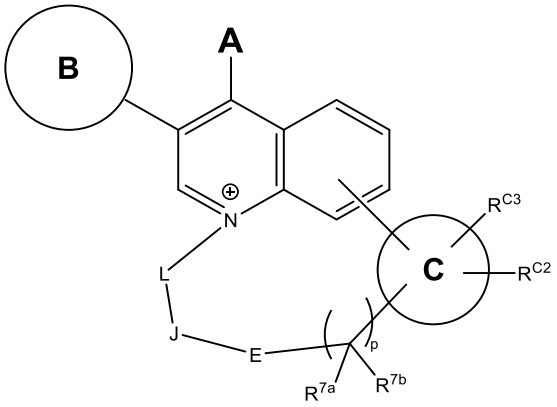
,


,


or


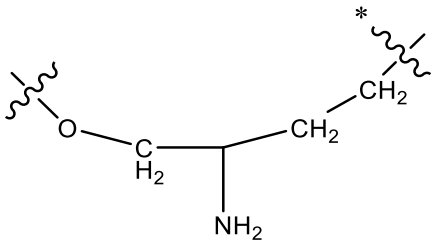
.

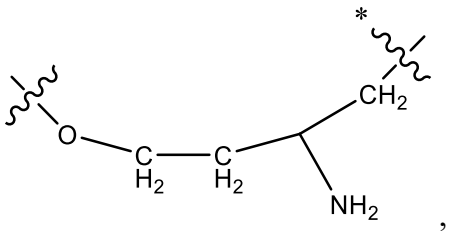
21. The compound of claim 1, having a structure of Formula I-2:

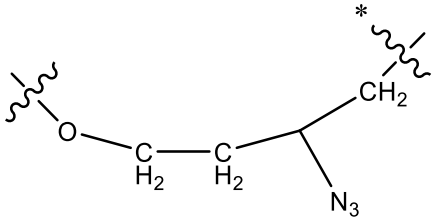


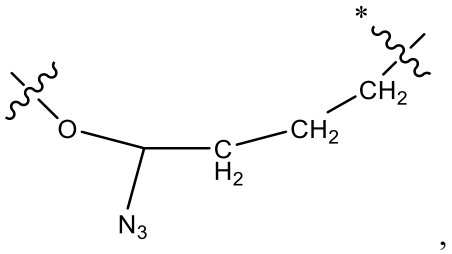
I-2
;

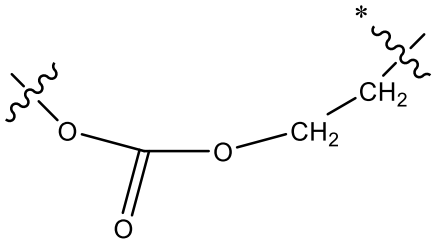
wherein -L-J-E-$(CR^{7a}R^{7b})_p$- form:

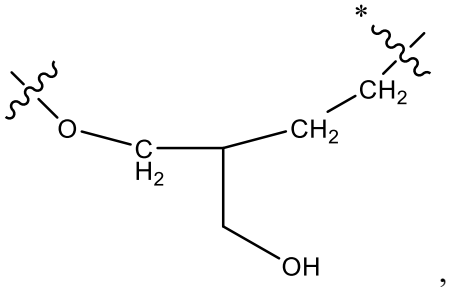


,


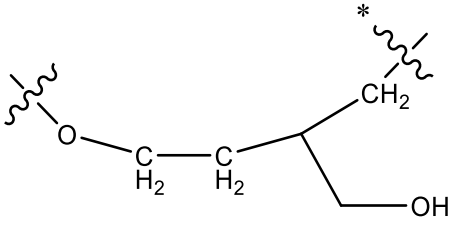
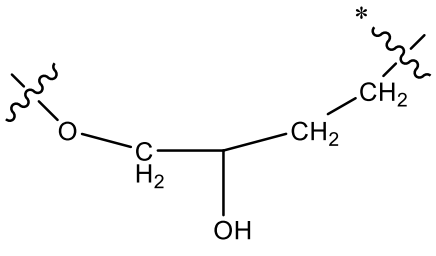
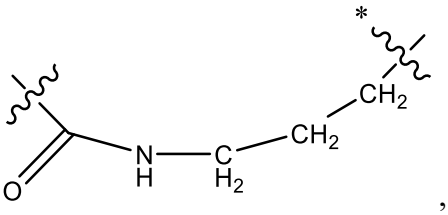
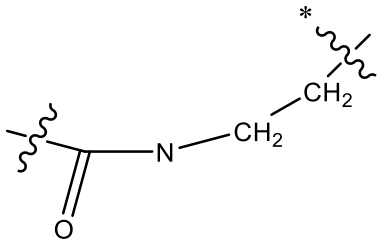
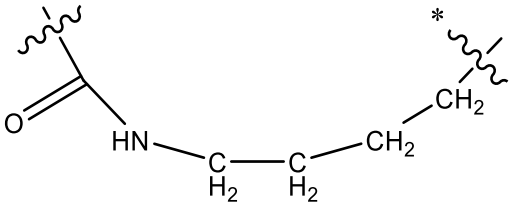
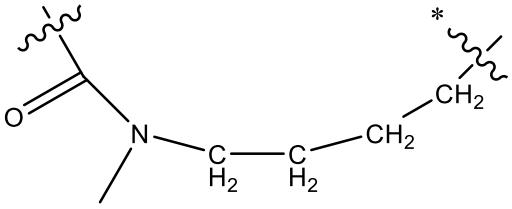
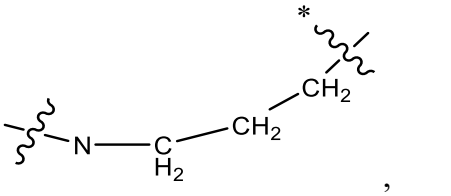
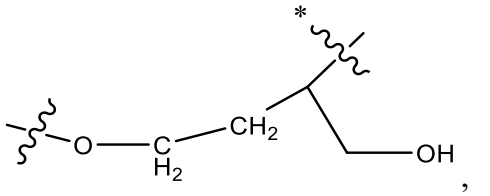
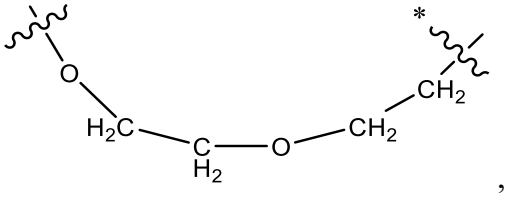
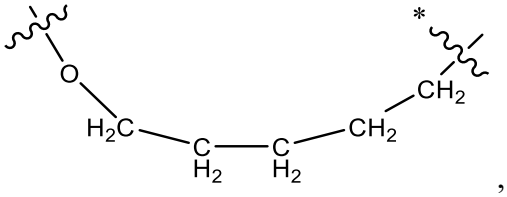
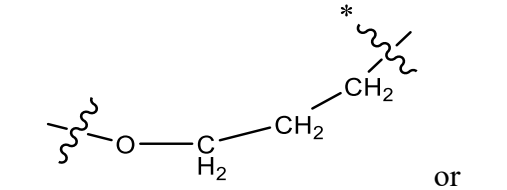
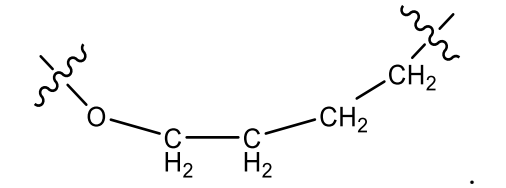
,


,


,


,


,

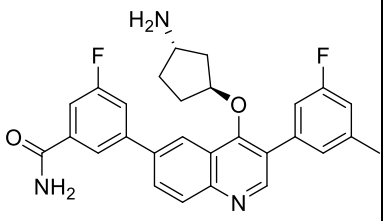
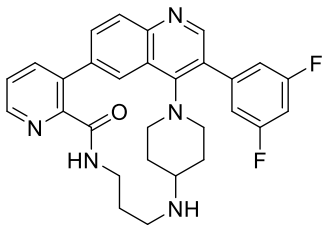
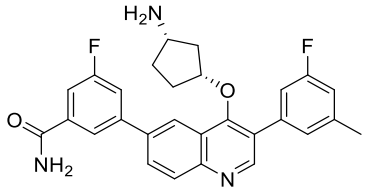
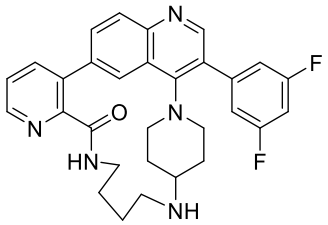
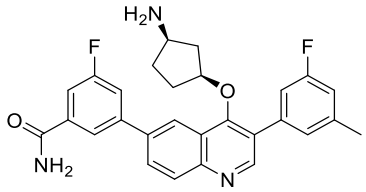
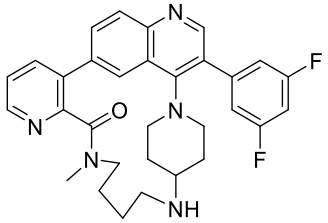
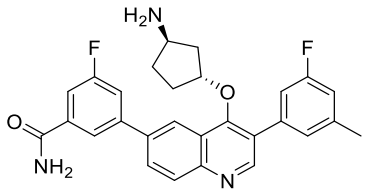
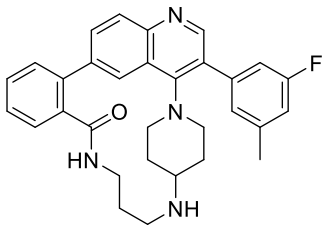
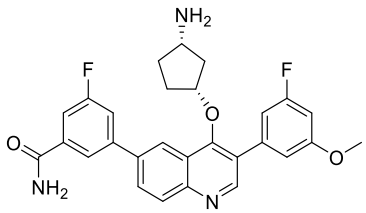
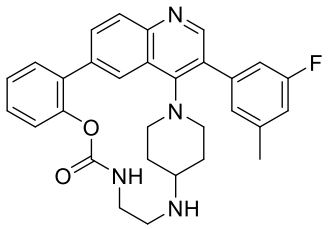
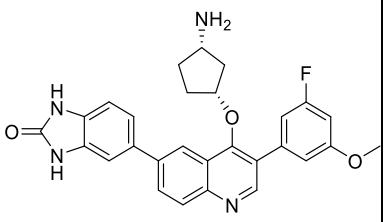
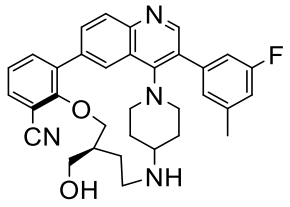
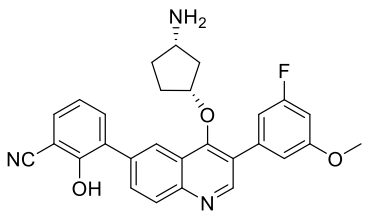
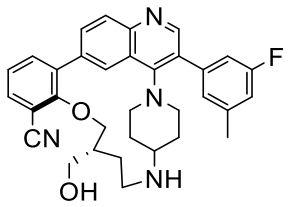

,

,

,

,

,

,

,

,

,

,

,

,

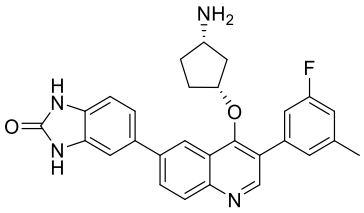
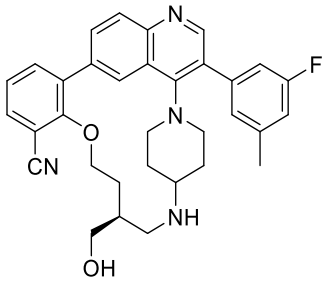
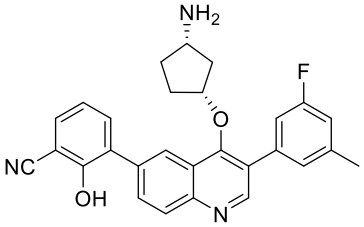
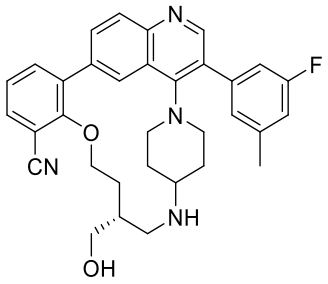
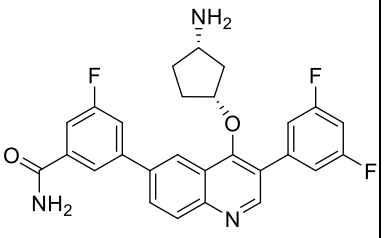
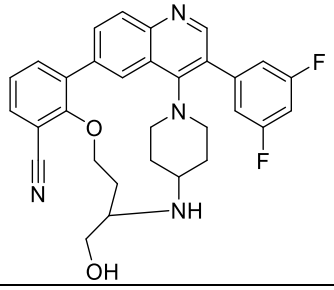
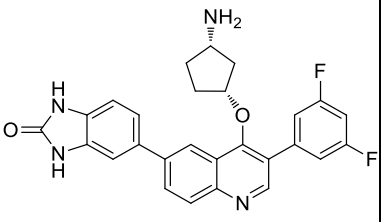
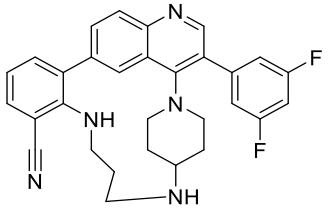
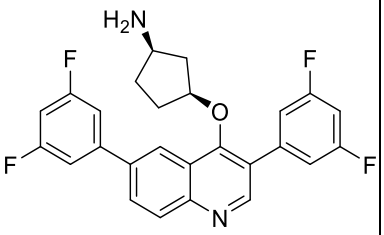
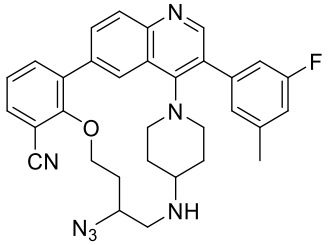
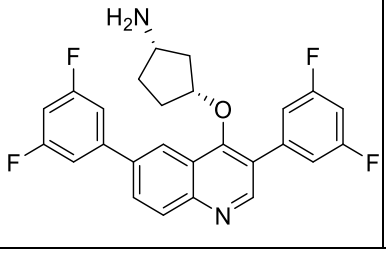
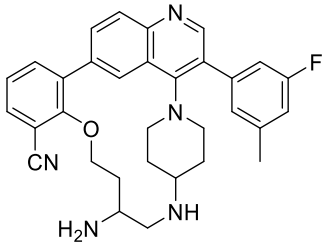
or

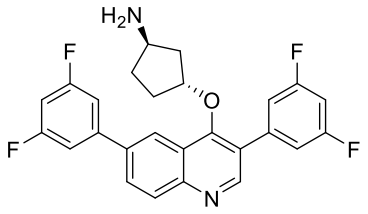
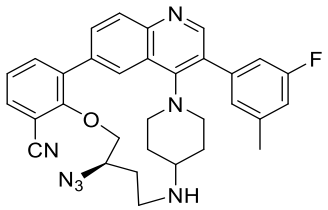
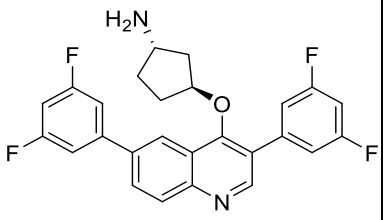
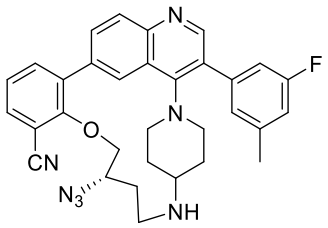
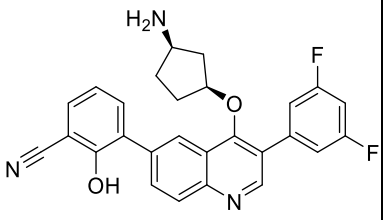
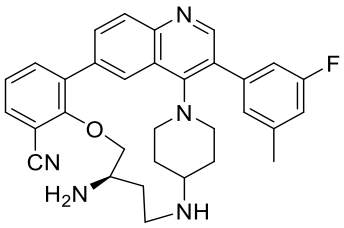
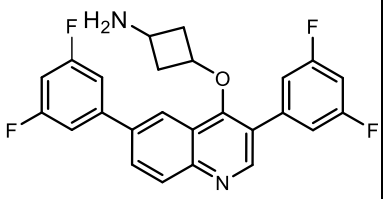
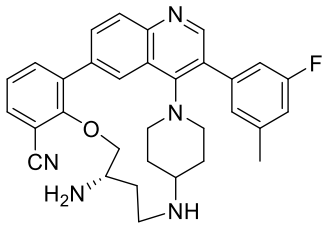
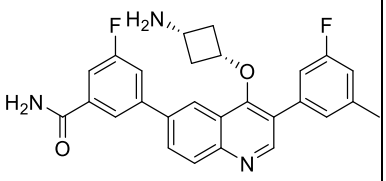
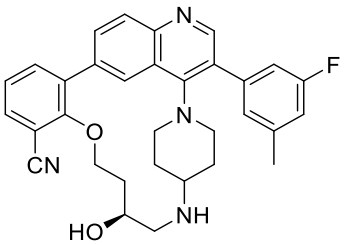
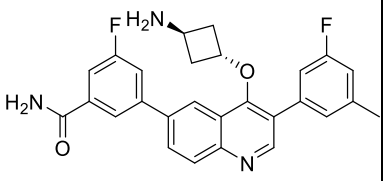
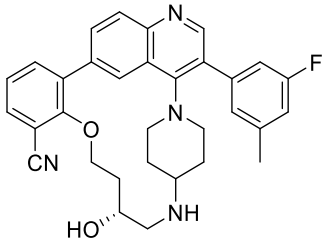
.

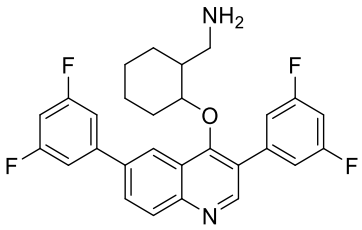
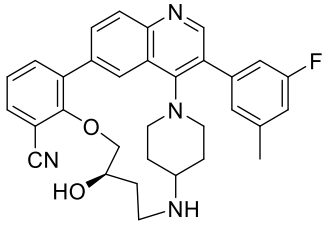
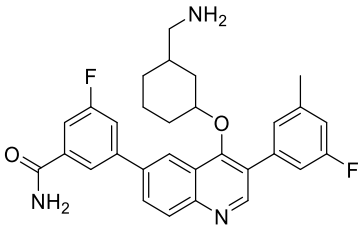
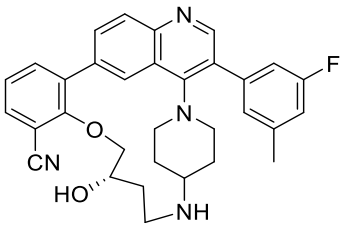
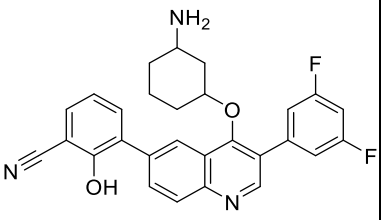
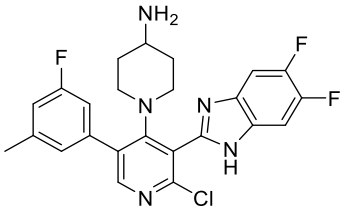
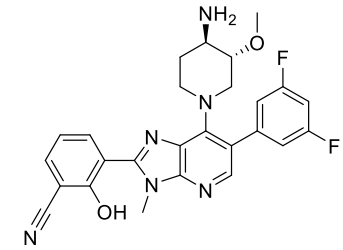
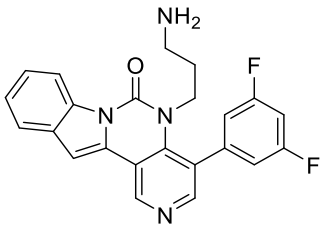
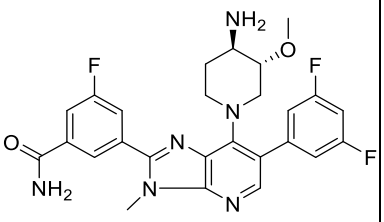
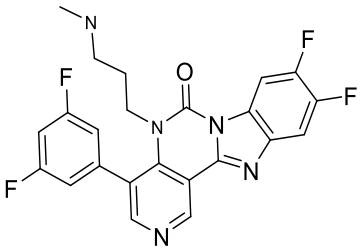
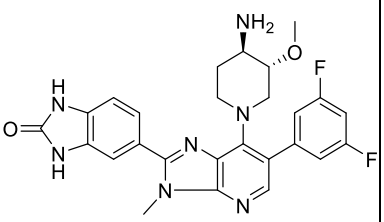
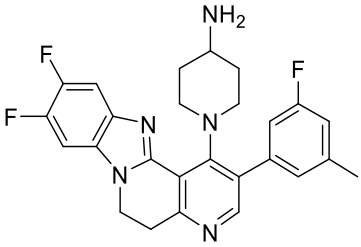
22. The compound of claim 21, wherein Ring B is phenyl di-substituted with R^{B1} which is halogen and R^{B2} which is halogen or C_1-C_6 alkyl.

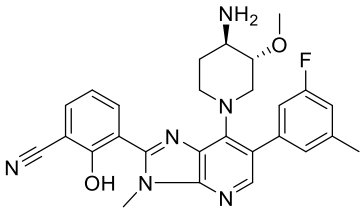
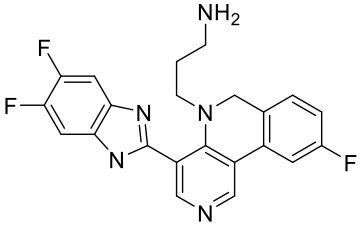
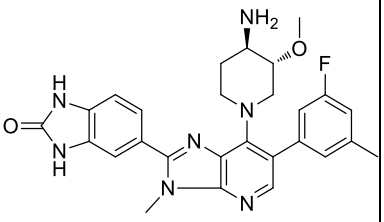
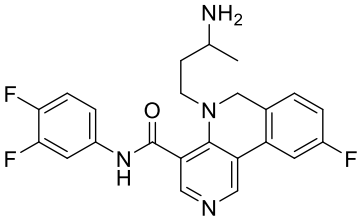
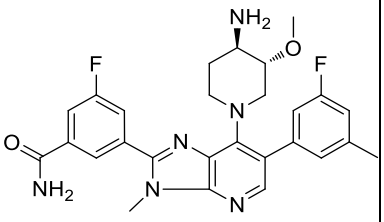
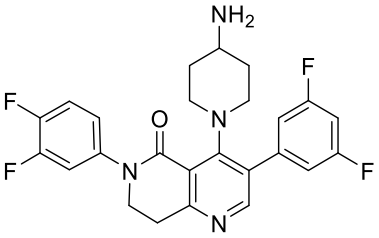
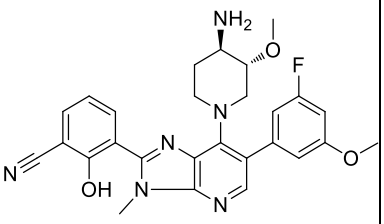
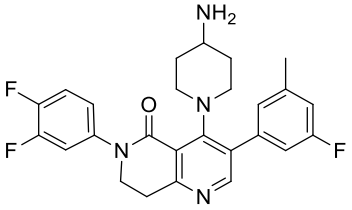
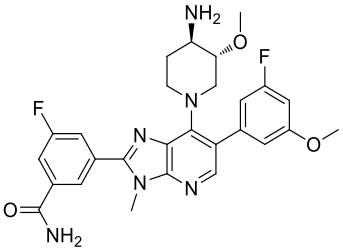
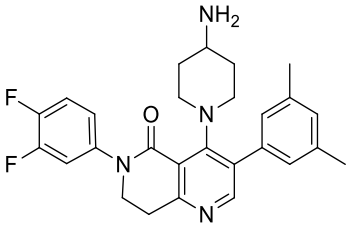
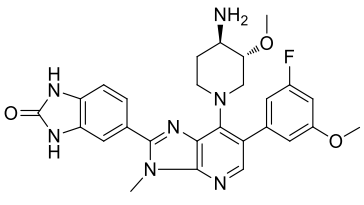
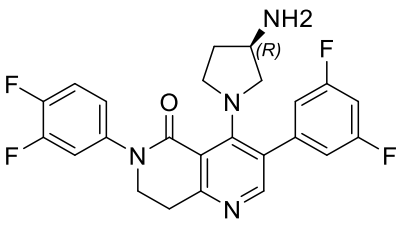
23. A compound as shown below,

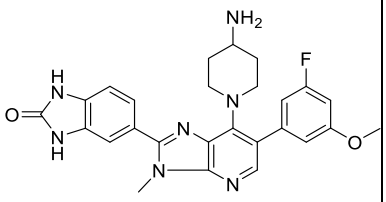
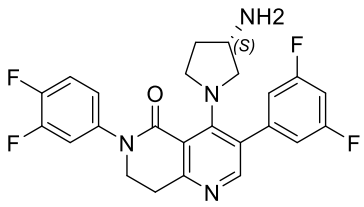
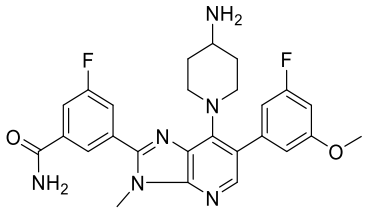
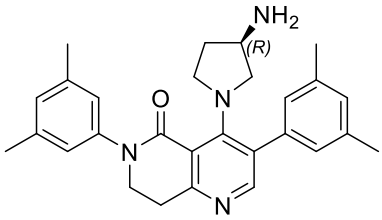
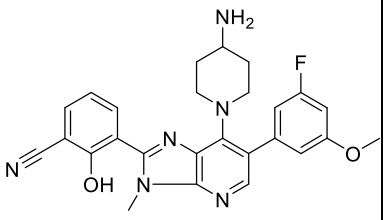
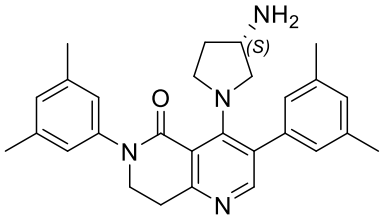
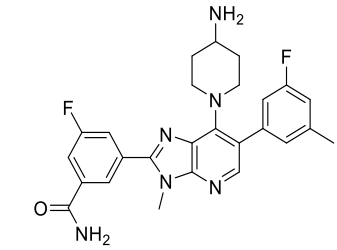
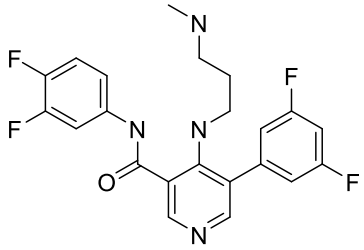
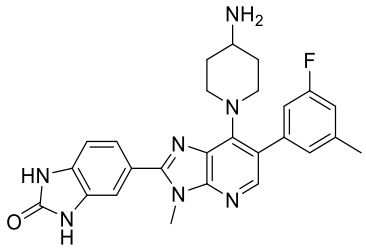
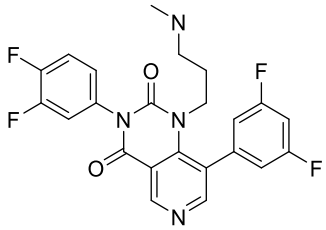
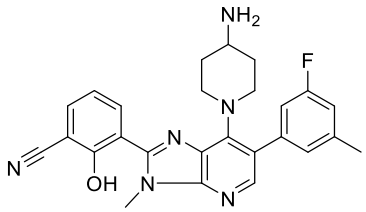
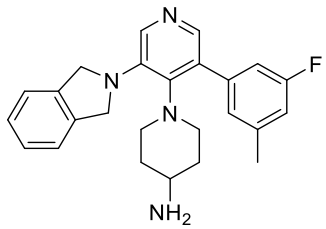
Cpd. No.	Structure	Cpd. No.	Structure
1		**83**	
2		**84**	
3		**85**	
4		**86**	
5		**87**	
6		**88***	
7		**89***	

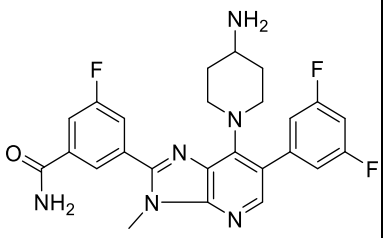
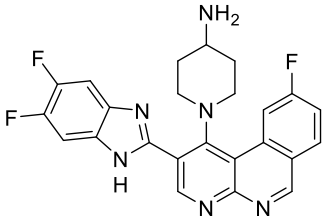
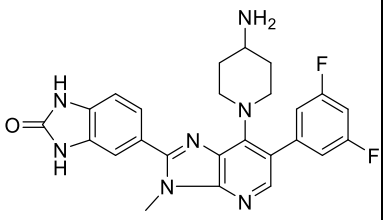
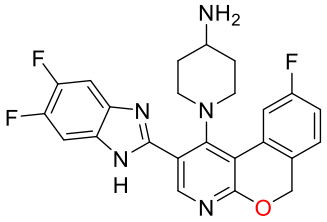
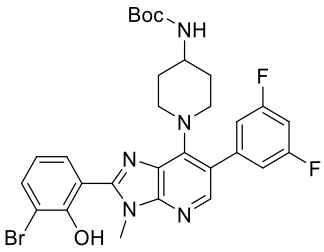
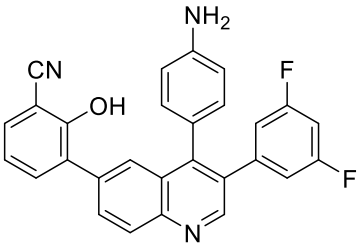
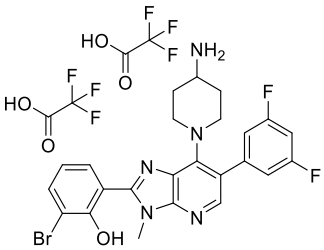
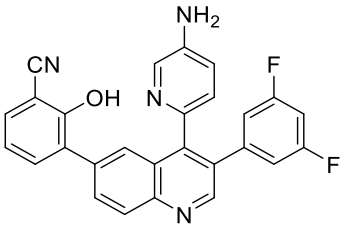
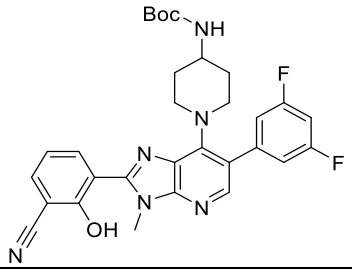
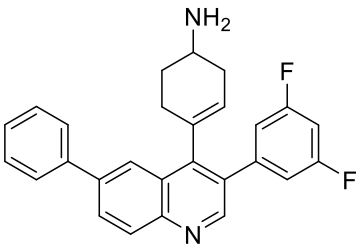
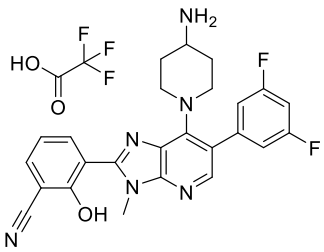
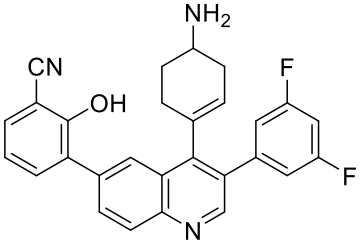
Cpd. No.	Structure	Cpd. No.	Structure
8		**90***	
9		**91***	
10		**92**	
11		**93**	
12		**94**	
13		**95**	

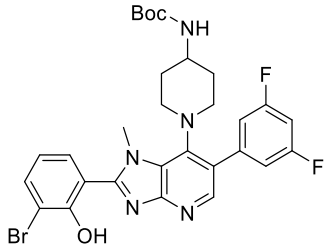
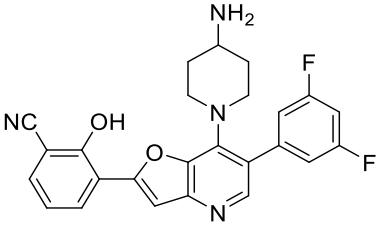
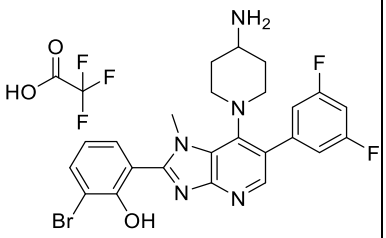
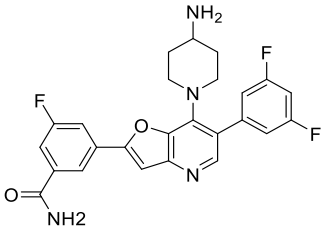
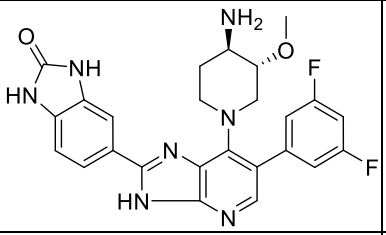
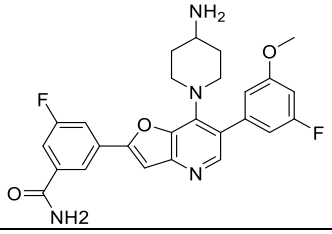
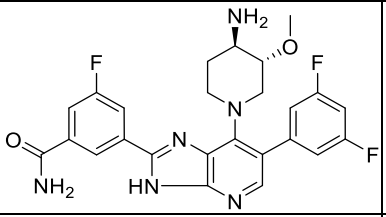
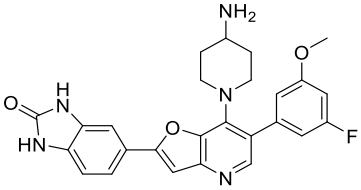
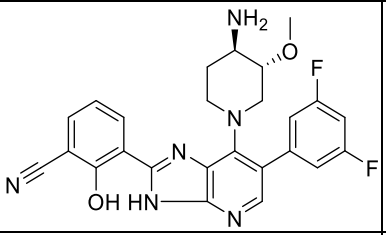
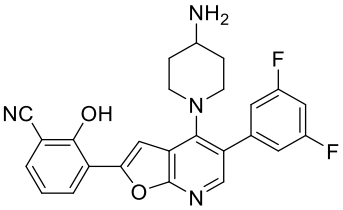
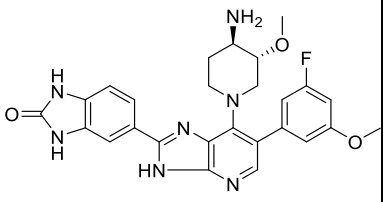
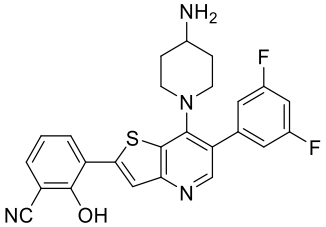
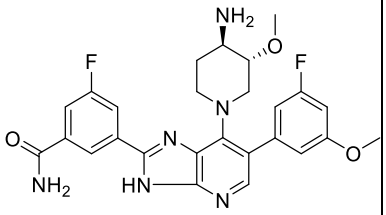
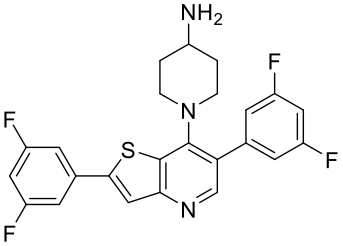
Cpd. No.	Structure	Cpd. No.	Structure
14		**96***	
15		**97***	
16		**98***	
17		**99***	
18		**100***	
19		**101***	

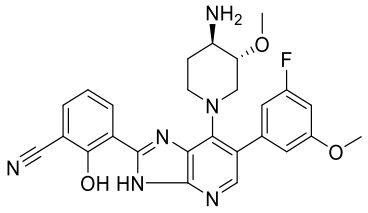
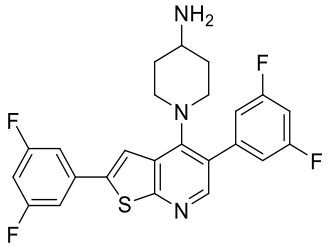
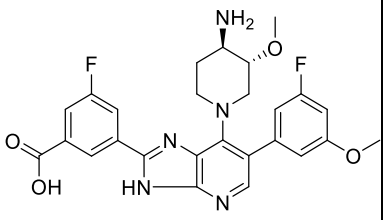
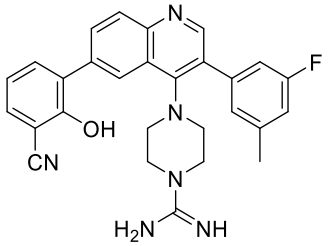
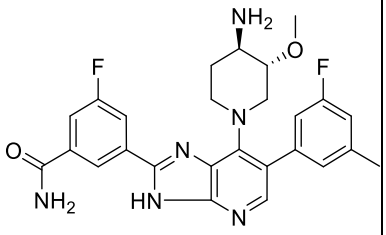
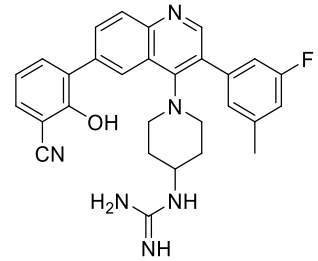
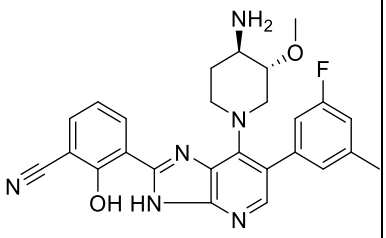
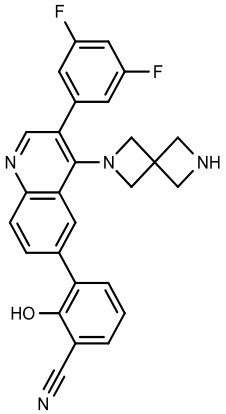
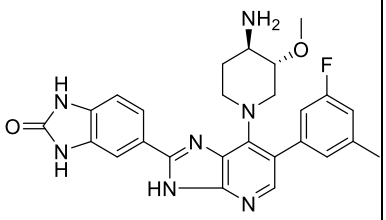
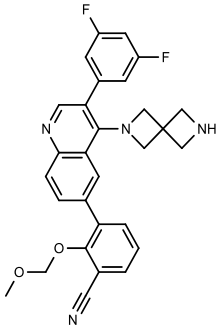
Cpd. No.	Structure	Cpd. No.	Structure
20		**102***	
21		**103***	
22		**104**	
23		**105**	
24		**106**	
25		**107**	

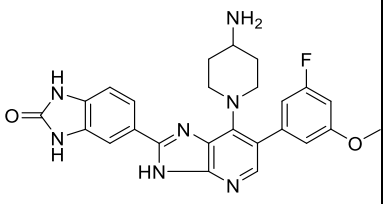
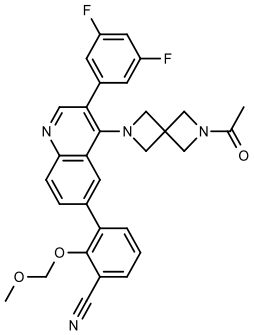
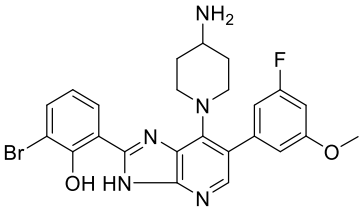
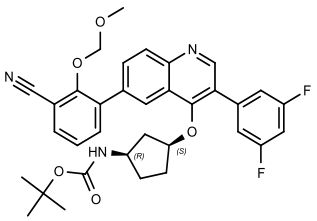
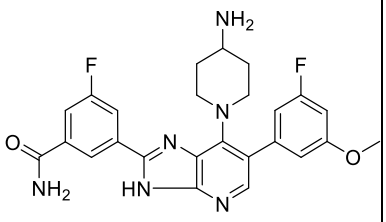
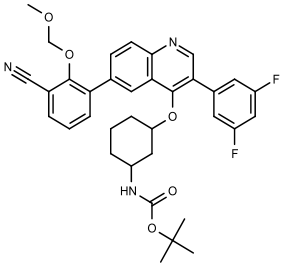
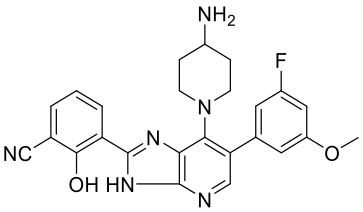
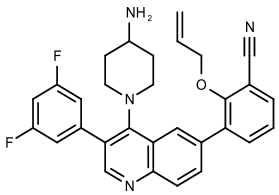
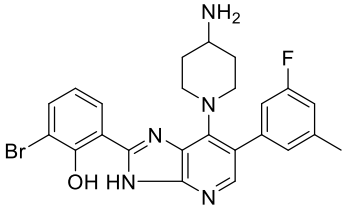
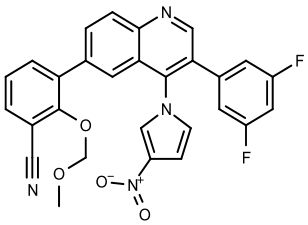
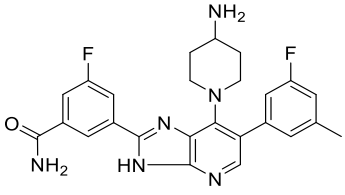
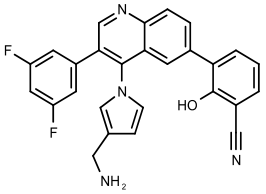
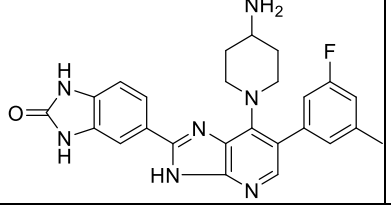
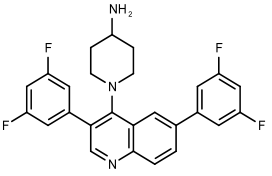
Cpd. No.	Structure	Cpd. No.	Structure
26		**108**	
27		**109**	
28		**110**	
29		**111**	
30		**112**	
31		**113**	

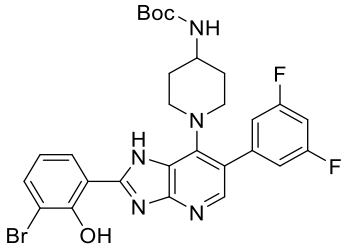
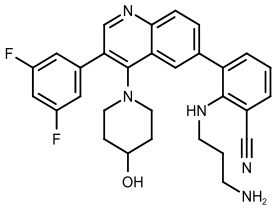
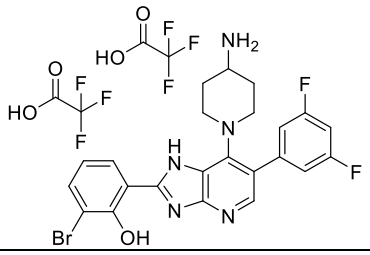
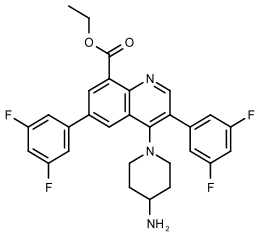
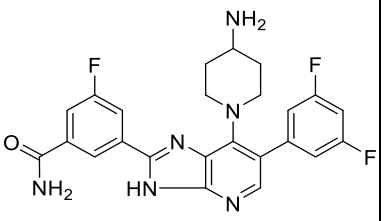
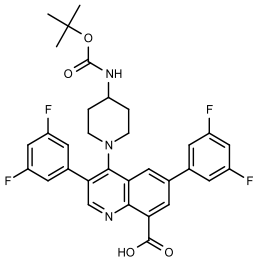
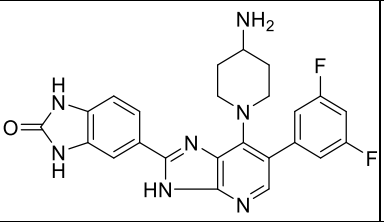
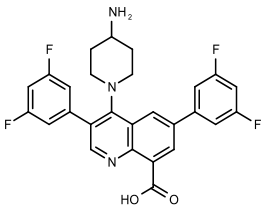
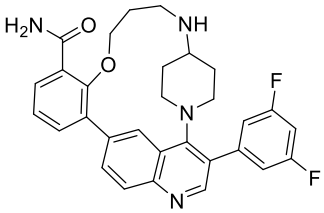
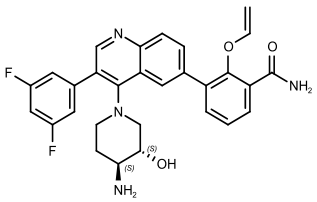
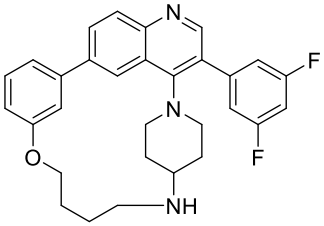
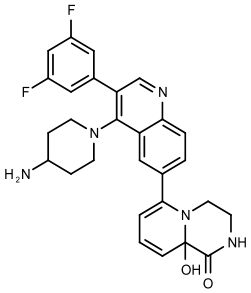
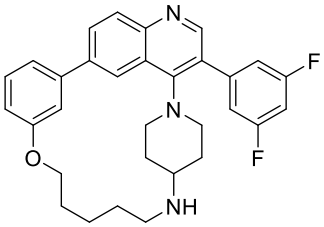
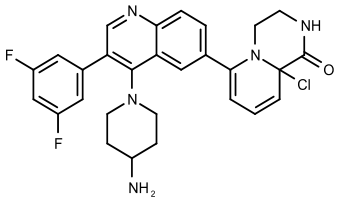
Cpd. No.	Structure	Cpd. No.	Structure
32		**114**	
33		**115**	
34		**116**	
35		**117**	
36		**118**	
37		**119**	

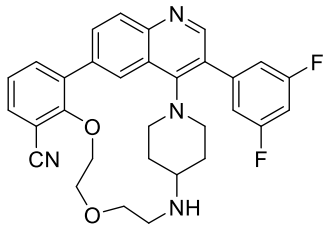
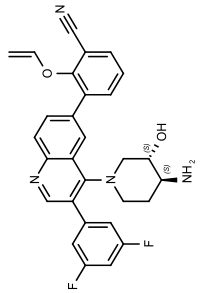
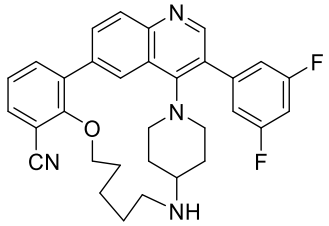
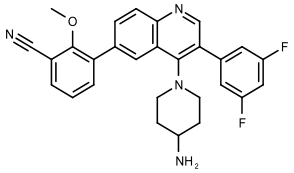
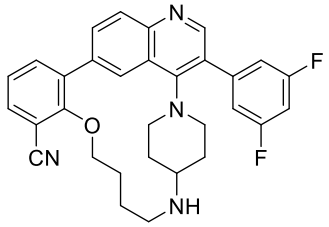
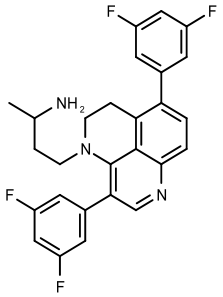
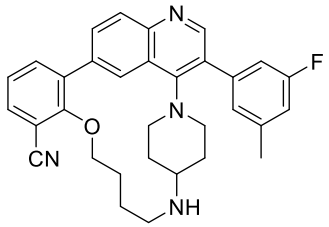
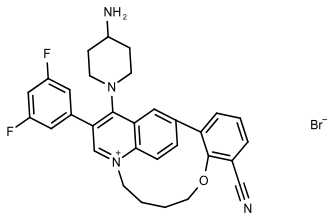
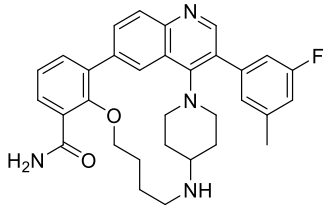
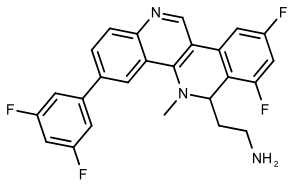
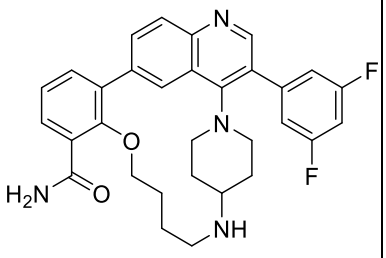
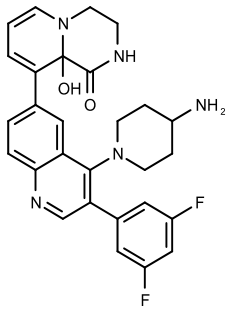
Cpd. No.	Structure	Cpd. No.	Structure
38		**120**	
39		**121**	
40		**122**	
41		**123**	
42		**124**	
43		**125**	

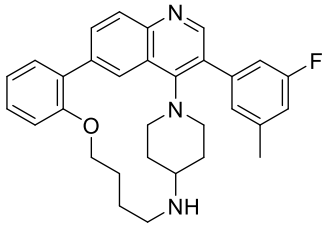
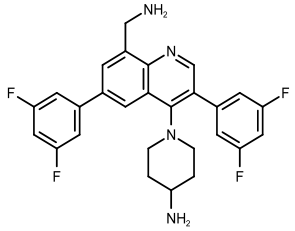
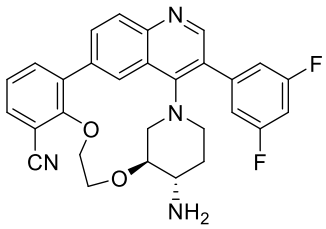
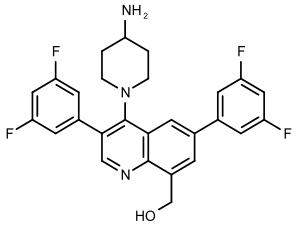
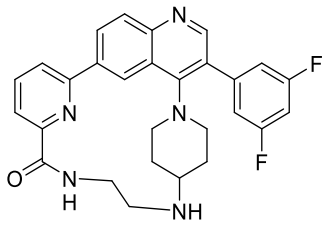
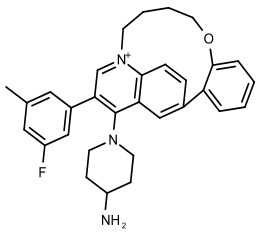
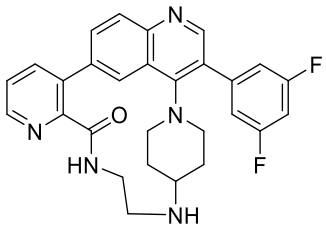
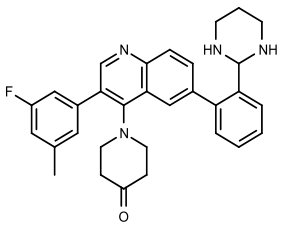
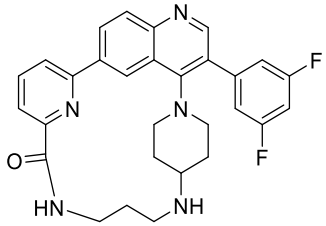
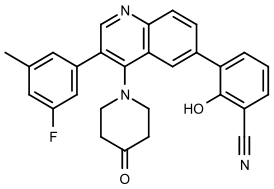
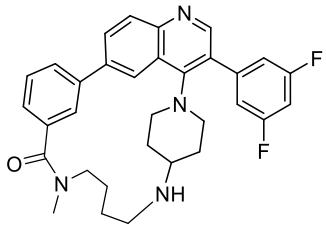
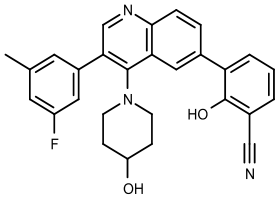
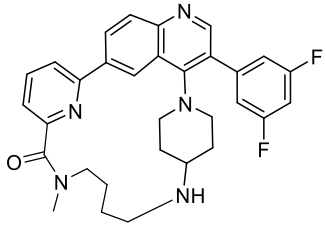
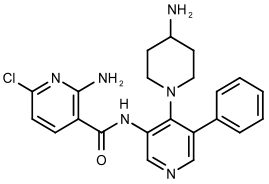
Cpd. No.	Structure	Cpd. No.	Structure
44		**127**	
45		**128**	
46		**129**	
47		**130**	
48		**131**	
49		**132**	
50		**133**	

Cpd. No.	Structure	Cpd. No.	Structure
51		**134**	
52		**135**	
53		**136**	
54		**137**	
55		**138**	

Cpd. No.	Structure	Cpd. No.	Structure
56		**139**	
57		**140**	
58		**141**	
59		**142**	
60		**143**	
61		**144**	
62		**145**	

Cpd. No.	Structure	Cpd. No.	Structure
63		**146**	
64		**147**	
65		**148**	
66		**149**	
67		**150**	
68		**151**	
69		**152**	

Cpd. No.	Structure	Cpd. No.	Structure
70		**153**	
71		**154**	
72		**155**	
73		**156**	
74		**157**	
75		**158**	

Cpd. No.	Structure	Cpd. No.	Structure
76		**159**	
77		**160**	
78		**161**	
79		**162**	
80		**163**	
81		**164**	
82		**165**	

or pharmaceutically acceptable salt thereof.

24. A pharmaceutical composition comprising a compound of any one of claims 1-23, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

25. Use of a compound of any one of claims 1-23 or the pharmaceutical composition of claim 24 in the preparation of a medicament for treating a disease associated with somatostatin, wherein the disease is diabetes, diarrhea, inflammatory bowel disease, irritable bowel syndrome, cancer, acromegaly, depression, chronic atrophic gastritis, Crohn's disease, ulcerative colitis, retinopathy, arthritis, restenosis, neuroendocrine tumors (NETs), or pain.