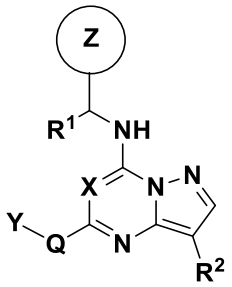
Claims

1. Use of a compound having the general formula I



Formula **I**

or an enantiomer, stereoisomeric form, mixture of enantiomers, diastereomer, mixture of diastereomers, racemate or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a DNA-virus infection in a subject, said DNA-virus preferably being selected from *Herpesviridae* and *Papillomaviridae*;

wherein in said compound

X is, independently at each occurrence, selected from CH and N;

Q is either absent or independently, at each occurrence, selected from the group consisting of -NH-, -NH(CH_2)-, -NH(CH_2)$_2$-, -NH(C=O)-, -NHSO_2-, -O-, -O(CH_2)-, -(C=O)-, –(C=O)NH- and -(C=O)(CH_2)-;

Y is, independently at each occurrence, selected from the group consisting of halogen, C1-C3 haloalkyl, C3-C8 cycloalkyl, aryl, heteroaryl, heterocyclyl, -S(=O)$_2$R^3, C1-C6 alkyl and C1-C6 alkyl substituted with one or two of –OR^5, –N(R^5)R^5, aryl, heteroaryl and heterocyclyl;

Wherein C3-C8 cycloalkyl is optionally substituted with one or two of R^3, R^4 and -(C=O)R^5, wherein heterocyclyl is optionally substituted with one or two of R^3, R^4 and -(C=O)R^5, and wherein aryl or heteroaryl is optionally substituted with one or two of R^3, C1-C6 alkyl, –OR^5, -N(R^5)R^5, -(C=O)R^5, halogen, heteroaryl and heterocyclyl;

R^1 is, at each occurrence, independently selected from the group consisting of hydrogen and methyl;

R^2 is, at each occurrence, independently selected from the group consisting of halogen, C1-C6 alkyl, C3-C10 cycloalkyl, -CN, $-(C=O)CH_3$ and C1-C3 haloalkyl, any of which is optionally substituted;

R^3 is either absent or independently, at each occurrence, selected from the group consisting of hydrogen, $-OR^5$, halogen, C1-C3 haloalkyl, -CN, $-N(R^5)R^5$, (=O), $-NH(C=O)R^5$, $-(C=O)NH_2$, $-S(=O)_2N(R^5)R^5$, aryl, heteroaryl, heterocyclyl, C1-C6 alkyl and C1-C6 alkyl substituted with $-OR_5$, $-NH_2$ or $-S(=O)_2N(R^5)R^5$;

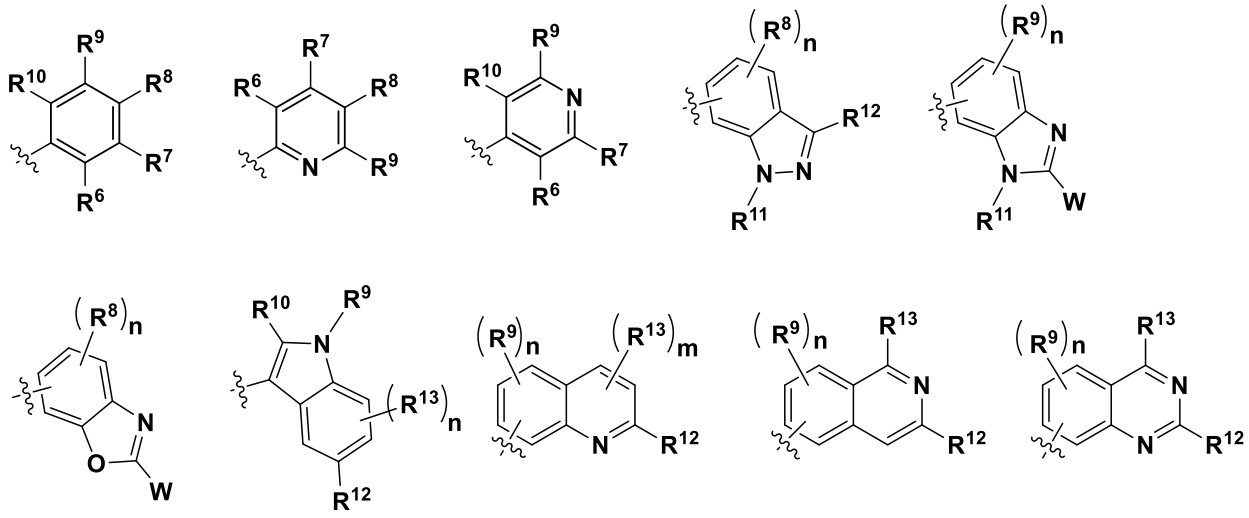
R^4 is, independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C1-C3 haloalkyl, -CN, $-OR^5$, $-N(R^5)R^5$, (=O), $S(=O)_2N(R^5)R^5$, aryl, heteroaryl, heterocyclyl, C1-C6 alkyl and C1-C6 alkyl substituted with –OH, $-NH_2$ or $-S(=O)_2N(R^5)R^5$;

wherein both R^3 and R^4 are (=O) if attached to a single sulfur atom that forms part of Y being a heterocycle;

or wherein R^3 and R^4, together with the structure to which they are attached, form an aromatic ring, a heteroaromatic ring, a saturated or unsaturated heterocyclic ring, or a fused or bridged ring structure of any of an aromatic ring, a heteroaromatic ring, and a saturated or unsaturated heterocyclic ring;

R^5 is, at each occurrence, independently selected from the group consisting of hydrogen, C1-C6 alkyl, C3-C6 cycloalkyl, C1-C3 haloalkyl, heteroaryl, heterocyclyl, heteroaryl substituted with one or two of halogen, $-OR^{11}$, $-N(R^{11})R^{11}$, C1-C6 alkyl and C1-C6 alkyl substituted with -OH, $-NH_2$; heterocyclyl substituted with one or two of halogen, $-OR^{11}$, $-N(R^{11})R^{11}$, C1-C6 alkyl and C1-C6 alkyl substituted with -OH or $-NH_2$;

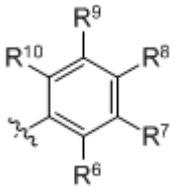
Z is any structure of the following group **A**;

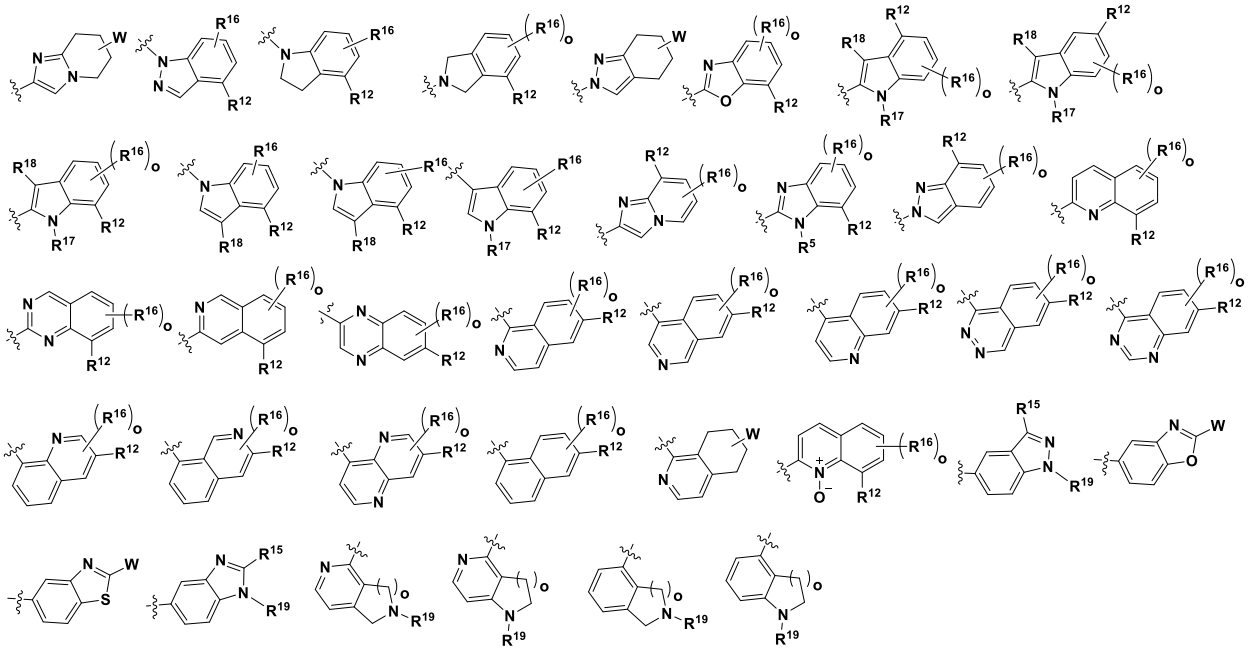


Group **A**

Wherein n= 1, 2, or 3; m= 1, or 2;

R^6 and R^7 are, at each occurrence, independently selected from the group consisting of hydrogen, -NH(C=O)R^{14}, -NHR^{14}, -OR^{14} and any structure of the following group **B**, with the

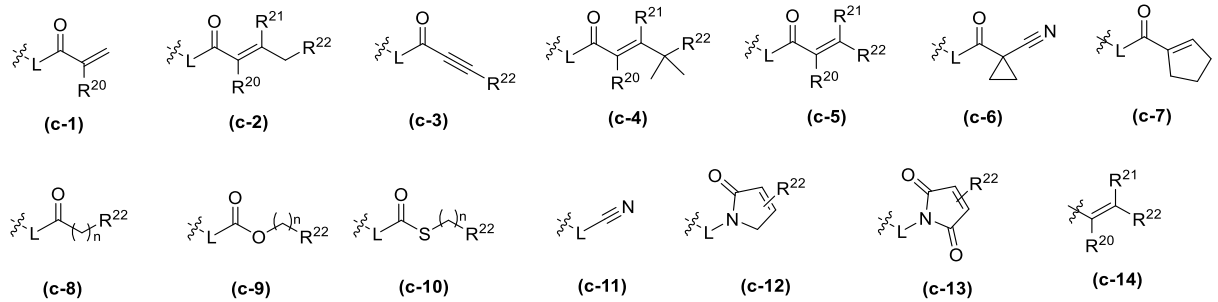
proviso that, when Z is  , one of R^6 and R^7 is not H;



Group **B**

wherein o is, independently at each occurrence, selected from 1, 2 and 3;

W is any structure of the following group **C**;



Group **C**

L is absent or, at each occurrence, independently selected from the group consisting of -O- and –NH-;

wherein n is, independently at each occurrence, selected from 1, 2 and 3;

R^8, R^9 and R^{10} are, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, -OR^5, -CN and C1-C6 alkyl substituted with -OH, -OR^5 or -NHR^5;

R^{11} is, at each occurrence, independently selected from the group consisting of hydrogen, C1-C6 alkyl, C3-C10 cycloalkyl and W, as defined above;

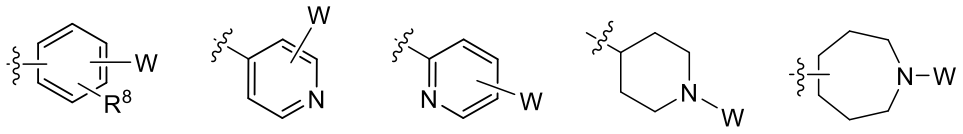
R^{12} is, at each occurrence, independently selected from hydrogen and W, as defined above;

Wherein if R^{11} is W, R^{12} is hydrogen;

R^{13} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-NH_2$, $-OR^5$, -CN and W, as defined above;

Wherein if R^{13} is W, R^{12} is hydrogen;

R^{14} is any structure of group **D**;



Group **D**

R^{15} is, at each occurrence, independently selected from hydrogen and W, as defined above;

R^{16} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-NH_2$, $-OR^5$, -CN and W, as defined above;

Wherein if R^{16} is W, R^{12} is hydrogen;

R^{17} is, at each occurrence, independently selected from the group consisting of hydrogen, C1-C6 alkyl and C1-C3 haloalkyl;

R^{18} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-NH_2$, $-OR^5$ and -CN;

R^{19} is, at each occurrence, independently selected from the group consisting of hydrogen, C1-C6 alkyl, C3-C10 cycloalkyl and W, as defined above;

Wherein if R^{19} is W, R^{15} is hydrogen;

R^{20} and R^{21} are, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-OR^5$, heterocyclyl and -CN;

R^{22} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C3-C10 cycloalkyl, $-N(R^5)_2$, $-NR^{19}R^{20}$, $-NR^{19}CH_2(CO)NH_2$, heterocyclyl, $-OR^5$ and –CN.

2. The use according to claim 1, wherein said DNA-virus infection is a *Herpesviridae* infection, and said *Herpesviridae* infection is an infection by a member from a *Herpesviridae* subfamily, such subfamily being selected from *Alphaherpesvirinae*, *Betaherpesvirinae*, and *Gammaherpesvirinae*, wherein preferably said member is selected from human *Herpes-simplex-virus-1 (HSV-1)*, human *Herpes-simplex-virus-2 (HSV-2)*, *Varicella zoster virus*, *human cytomegalovirus* (*HCMV*), and *Epstein-Barr-Virus (EBV)*.

3. The use according to any of claims 1 – 2, wherein said DNA-virus infection is a *Herpesviridae* infection, and said *Herpesviridae* infection is an infection by human cytomegalovirus (HCMV).

4. The use according to any of claims 1 – 2, wherein said DNA-virus infection is a *Herpesviridae* infection, and said *Herpesviridae* infection is an infection by human *Herpes-simplex-virus-1 (HSV-1)*.

5. The use according to any of claims 1 – 2, wherein said DNA-virus infection is a *Herpesviridae* infection, and said *Herpesviridae* infection is an infection by Epstein-Barr-Virus (*EBV*).

6. The use according to any of claims 1 – 5, wherein said DNA-virus infection is a *Herpesviridae* infection by a virus that is resistant against nucleobase analogues or nuceloside analogues or inhibitors of viral DNA synthesis.

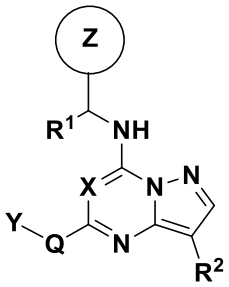
7. The use according to claim 6, wherein said DNA-virus infection is a *human cytomegalovirus (HCMV)* infection by an HCM virus (*HCMV*), or is a human *Herpes-simplex-virus-1 (HSV-1)* infection or a human *Herpes-simplex-virus-2 (HSV-2)* infection, or is a Epstein-Barr-Virus (*EBV*), wherein said *HCMV*, said *HSV-1,* said *HSV-2* and said *EBV* is resistant against a nucleobase analogue, in particular a guanine analogue, preferably against ganciclovir, aciclovir and/or penciclovir, or against an inhibitor of viral DNA synthesis, in particular an inhibitor of pUL97 kinase activity, more particularly maribavir; or wherein said *HCMV*, said *HSV-1* and said *HSV-2* is resistant against a nucleoside analogue, in particular selected from analogues of deoxyadenosine, adenosine, deoxycytidine, guanosine, deoxyguanosine, thymidine, deoxythymidine, and/or deoxyuridine, wherein, preferably, said nucleoside analogue is selected from didanosine, vidarabine, galidesivir, remdesivir, cytarabine, gemcitabine, emtricitabine, lamivudine, zalcitabine, abacavir, entecavir, stavudine, telbivudine, zidovudine, idoxuridine, and trifluridine.

8. The use according to claim 1, wherein said DNA-virus infection is a *Papillomaviridae* infection, and said *Papillomaviridae* infection is an infection by a human papillomavirus (HPV), selected from alphapapillomavirus, betapapillomavirus and gammapapillomavirus, wherein, preferably, said human papillomavirus is selected from alphapapillomavirus, in particular types HPV-6, HPV-16, HPV-2, HPV-7, HPV-10, HPV-18, HPV-26, HPV-32, HPV-34, HPV-53, HPV-61, HPV-71, HPV-cand90, and the respective subtypes of the foregoing ; wherein, more preferably, said human papillomavirus is selected from types HPV-6 and HPV-16, and corresponding subtypes of HPV-6, namely subtypes HPV-6, HPV-11, HPV-13, HPV-44 and HPV-74; and corresponding subtypes of HPV-16, namely HPV-16, HPV-31, HPV-33, HPV-35, HPV-52, HPV58, and HPV-67.

9. The use according to claim 8, wherein the medicament is for the treatment and/or prevention of a cancer caused by or associated with HPV, said cancer being selected from cervical cancer, oropharyngeal cancer, anal cancer, penile cancer, vaginal cancer and vulvar cancer.

10. The use according to claim 9, wherein the subject is a non-responder, or fails to respond adequately, to HPV-vaccination, or is a subject who cannot be vaccinated against HPV.

11. The use according to any of the foregoing claims, comprising administration of a compound having the general formula I



Formula **I**

As defined in any of the foregoing claims, to a subject having, or suspected of having, a *Herpesviridae* infection or a *Papillomaviridae* infection.

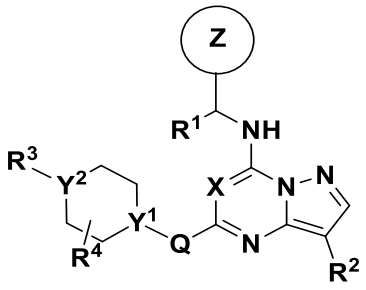
12. The use according to any of the foregoing claims, wherein said compound is to be administered at an early stage of infection in said subject and/or prior to onset of any symptoms in said subject.

13. The use according to any of the foregoing claims, wherein said subject is a non-responder to a previous course of treatment with a nucleobase analogue or a nucleoside analogue or an inhibitor of viral DNA synthesis, in particular an inhibitor of pUL97 kinase activity.

14. The use according to any of the foregoing claims, wherein said compound is to be administered systemically or topically.

15. The use according to any of the foregoing claims, wherein said compound is a compound

having the general formula Ia



Formula **Ia**

wherein

X is, independently at each occurrence, selected from CH and N;

Y^1 is, independently at each occurrence, selected from CH, C(OH) and N;

Y^2 is, independently at each occurrence, selected from CH, C(OH) and N;

Q is absent or, at each occurrence, independently selected from the group consisting of -NH-, -NH(CH_2)-, -NH(C=O)-, -$NHSO_2$-, -O-, -O(CH_2)-, -(C=O)- and -(C=O)(CH_2)-;

R^1 is, at each occurrence, independently selected from the group consisting of hydrogen and methyl;

R^2 is, at each occurrence, independently selected from the group consisting of halogen, C1-C6 alkyl, C3-C10 cycloalkyl, -CN, -(C=O)CH_3 and C1-C3 haloalkyl, any of which is optionally substituted;

R^3 is either absent or independently, at each occurrence, selected from the group consisting of hydrogen, -OR^5, halogen, C1-C3 haloalkyl, -CN, -N(R^5)R^5, (=O), -NH(C=O)R^5, -(C=O)NH_2, -S(=O)$_2$N(R^5)R^5, aryl, heteroaryl, heterocyclyl, C1-C6 alkyl and C1-C6 alkyl substituted with –OR_5, -NH_2 or -S(=O)$_2$N(R^5)R^5;

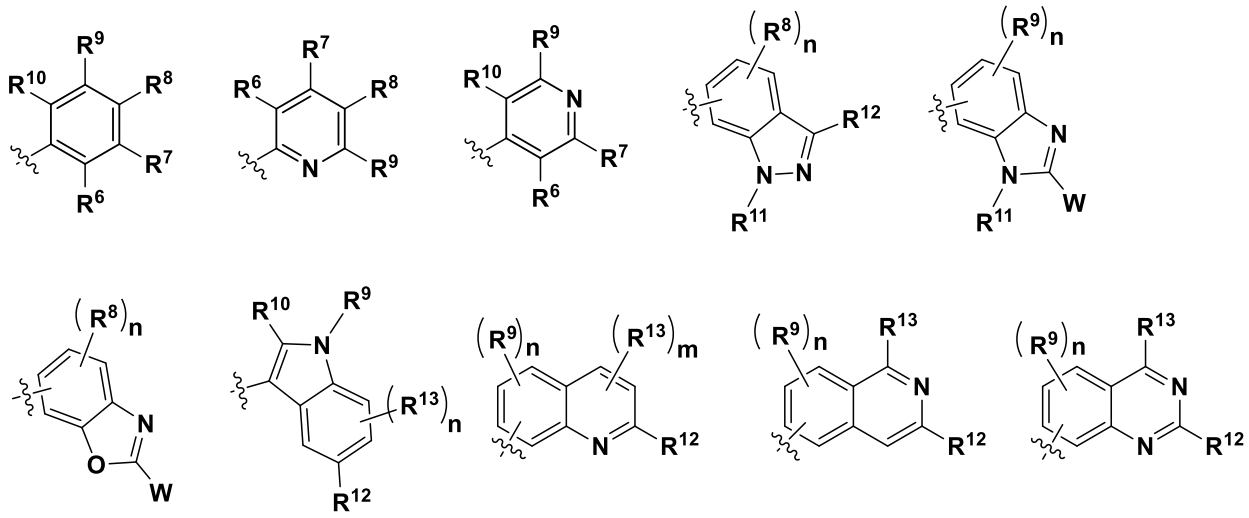
R^4 is, independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C1-C3 haloalkyl, -CN, -OR^5, -N(R^5)R^5, (=O), S(=O)$_2$N(R^5)R^5, aryl, heteroaryl, heterocyclyl, C1-C6 alkyl and C1-C6 alkyl substituted with –OH, -NH_2 or -S(=O)$_2$N(R^5)R^5;

wherein both R^3 and R^4 are (=O) if attached to a single sulfur atom that forms part of Y being a heterocycle;

or wherein R^3 and R^4, together with the structure to which they are attached, form an aromatic ring, a heteroaromatic ring, a saturated or unsaturated heterocyclic ring, or a fused or bridged ring structure of any of an aromatic ring, a heteroaromatic ring, and a saturated or unsaturated heterocyclic ring;

R^5 is, at each occurrence, independently selected from the group consisting of hydrogen, C1-C6 alkyl, C3-C6 cycloalkyl, C1-C3 haloalkyl, heteroaryl, heterocyclyl, heteroaryl substituted with one or two of halogen, $-OR^{11}$, $-N(R^{11})R^{11}$, C1-C6 alkyl and C1-C6 alkyl substituted with -OH, $-NH_2$;heterocyclyl substituted with one or two of halogen, $-OR^{11}$, $-N(R^{11})R^{11}$, C1-C6 alkyl and C1-C6 alkyl substituted with -OH or $-NH_2$;

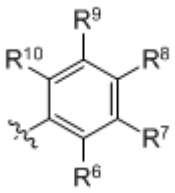
Z is any structure of the following group A;

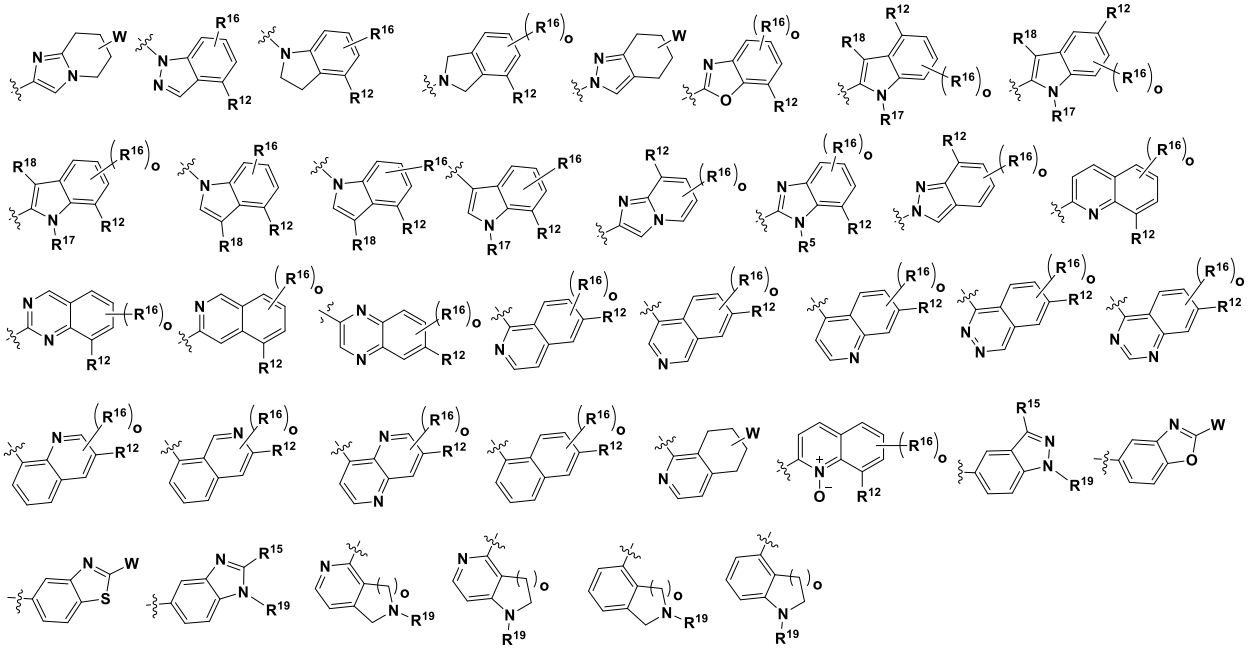


Group **A**

wherein n= 1, 2, or 3; m= 1, or 2;

R^6 and R^7 are, at each occurrence, independently selected from the group consisting of hydrogen, $-NH(C=O)R^{14}$, $-NHR^{14}$, $-OR^{14}$ and any structure of the following group **B**, with the

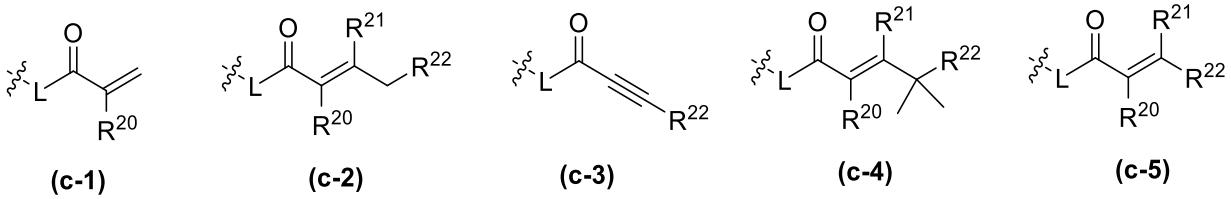
proviso that, when Z is  , one of R6 and R7 is not H;



Group **B**

wherein o= 1, 2 or 3;

W is any structure of the following group **C**;



(c-1) **(c-2)** **(c-3)** **(c-4)** **(c-5)**

Group **C**

L is absent or, at each occurrence, independently selected from the group consisting of -O- and –NH-;

R^8, R^9 and R^{10} are, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, -OR^5, -CN and C1-C6 alkyl substituted with -OH, -OR^5 or -NHR^5;

R^{11} is, at each occurrence, independently selected from the group consisting of hydrogen,

C1-C6 alkyl, C3-C10 cycloalkyl and W, as defined above;

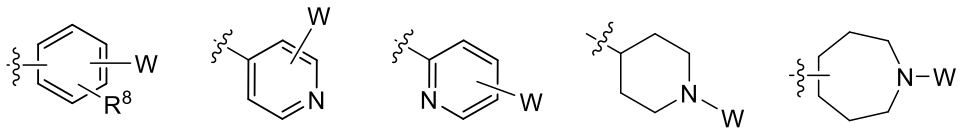
R^{12} is, at each occurrence, independently selected from hydrogen and W, as defined above;

wherein if R^{11} is W, R^{12} is hydrogen;

R^{13} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-NH_2$, $-OR^5$, -CN and W, as defined above;

wherein if R^{13} is W, R^{12} is hydrogen;

R^{14} is any structure of group **D**;



Group **D**

R^{15} is, at each occurrence, independently selected from hydrogen and W, as defined above;

R^{16} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-NH_2$, $-OR^5$, -CN and W, as defined above;

wherein if R^{16} is W, R^{12} is hydrogen;

R^{17} is, at each occurrence, independently selected from the group consisting of hydrogen, C1-C6 alkyl and C1-C3 haloalkyl;

R^{18} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-NH_2$, $-OR^5$ and -CN;

R^{19} is, at each occurrence, independently selected from the group consisting of hydrogen, C1-C6 alkyl, C3-C10 cycloalkyl and W, as defined above;

wherein if R^{19} is W, R^{15} is hydrogen;

R^{20} and R^{21} are, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C1-C3 haloalkyl, $-OR^5$, heterocyclyl and -CN;

R^{22} is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, C1-C6 alkyl, C3-C10 cycloalkyl, $-N(R^5)_2$, $-NR^{19}R^{20}$, heterocyclyl, $-OR^5$ and -CN;

16. The use according to any of the foregoing claims,

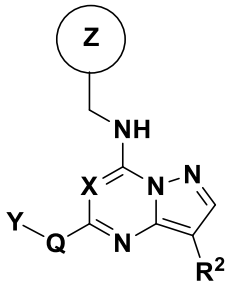
wherein at least one of Z, R^6, R^7, R^{11}, R^{12}, R^{13}, R^{15}, R^{16} and R^{19} is W, as defined in claim 1, or is a structure containing W, as defined in claim 1.

17. The use according to any of the foregoing claims,

wherein exactly one of Z, R^6, R^7, R^{11}, R^{12}, R^{13}, R^{15}, R^{16} and R^{19} is W, as defined in claim 1, or is a structure containing W, as defined in claim 1.

18. The use according to any of the foregoing claims,

wherein R^1 is hydrogen and the compound has the general formula II

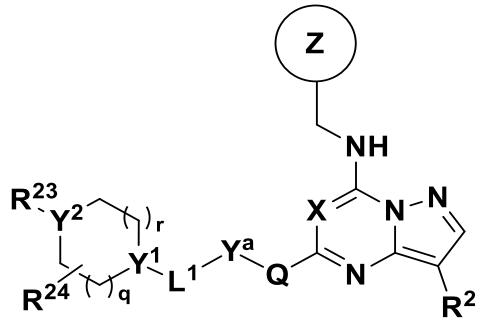


Formula **II**

wherein X, Y, Z, R^2 and Q are as defined in claim 1.

19. The use according to any of the foregoing claims,

wherein said compound has the general formula III



Formula **III**

wherein X, Z, R^2 and Q are as defined in claim 1, and

Y^a is either absent or independently, at each occurrence, selected from the group consisting of aryl, heteroaryl, heterocyclyl, aryl substituted with one or two of C1-C6 alkyl, $-OR^5$, $-N(R^5)R^5$, and halogen, heteroaryl substituted with one or two of C1-C6 alkyl, $-OR^5$, $-N(R^5)R^5$ and halogen, heterocyclyl substituted with one or two of R^{23} and R^{24};

R^{23} is either absent or independently, at each occurrence, selected from the group consisting of hydrogen, $-OR^5$, halogen, $-N(R^5)R^5$, $-NH(C=O)R^5$, $-(C=O)NH_2$, aryl, heteroaryl, heterocyclyl, C1-C6 alkyl and C1-C6 alkyl substituted with -OH or $-NH_2$;

R^{24} is, independently, at each occurrence, selected from the group consisting of hydrogen, halogen, $-OR^5$, $-N(R^5)R^5$, (=O), aryl, heteroaryl, heterocyclyl, C1-C6 alkyl and C1-C6 alkyl substituted with -OH or $-NH_2$,;

wherein R^5 is as defined in claim 1;

L^1 is either absent or independently, at each occurrence, selected from the group consisting of -NH-, $-NH(CH_2)-$, -NH(C=O)-, $-NHSO_2-$, -O-, $-O(CH_2)-$, -(C=O)-, –(C=O)NH- and $-(C=O)(CH_2)-$;

Y^1 is, independently at each occurrence, selected from CH, C(OH) and N;

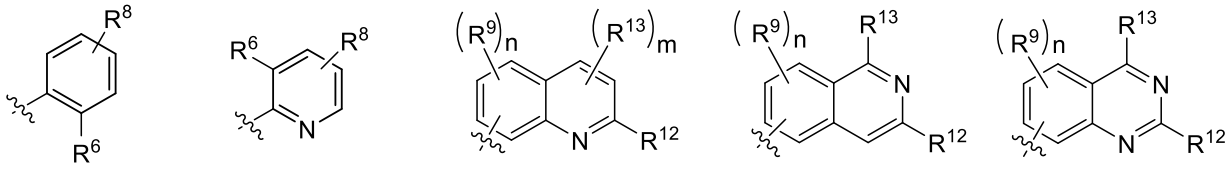
Y^2 is, independently at each occurrence, selected from CH, C(OH), O and N;

q is, independently at each occurrence, selected from 0, 1 and 2;

r is, independently at each occurrence, selected from 0, 1, 2 and 3.

20. The use according to any of the foregoing claims,

wherein Z is Z^1, and Z^1 is any structure of the following group **E**;



Group **E**

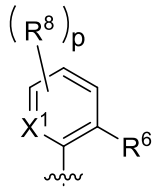
wherein m is, independently at each occurrence, selected from 1 and 2; and
n is as defined in claim 1;

R^8, R^9, R^{12} and R^{13} are as defined in claim 1;

R^6 is any structure of group B as defined in claim 1.

21. The use according to any of the foregoing claims,

wherein

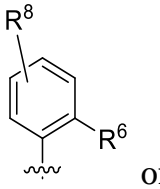
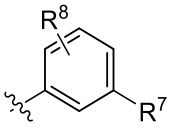
Z is 

p is, independently at each occurrence, selected from 0, 1, 2 and 3;
X^1 is, independently at each occurrence, selected from CR^8 and N;

R^6 is any structure of group **B**, as defined in claim 1; and
R^8 is as defined in claim 1.

22. The use according to any of the foregoing claims,

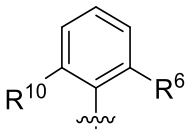
wherein

Z is  or Z is 

wherein R^6 – R^8 are as defined in claim 1.

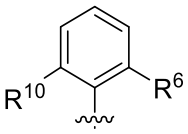
23. The use according to any of the foregoing claims,

wherein

Z is 

wherein R^6 and R^{10} are as defined in claim 1.

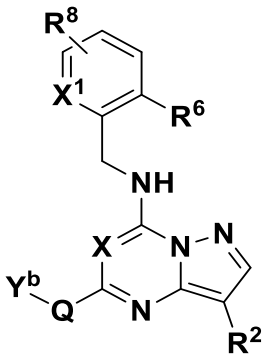
24. The use according to any of the foregoing claims, in particular according to claim 1, claim 15, claim 18 or claim 19,

wherein R^1 is hydrogen, Z is 

and wherein R^6 and R^{10} are as defined in claim 1.

25. The use according to any of claims 1 - 23,

wherein said compound has the general formula IV

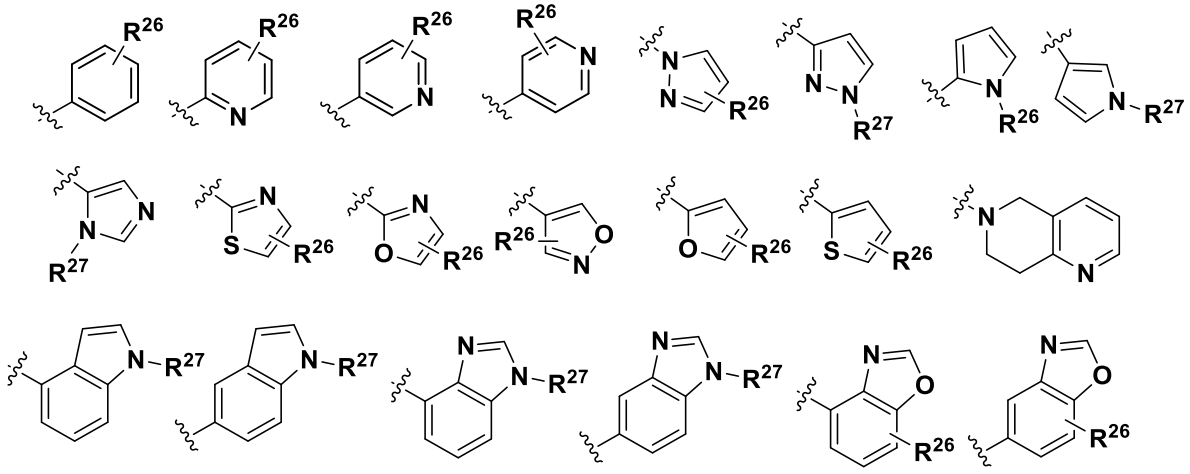


Formula **IV**

wherein X, X^1, R^6, R^8 and Q are as defined in claim 1, and

X^1 is as defined in claim 21;

wherein Y^b is any structure of the following group F;



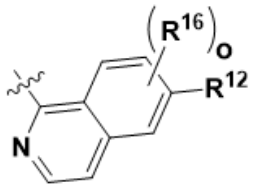
Group **F**

R^{26} and R^{27} is either absent or independently, at each occurrence, selected from the group consisting of hydrogen, $-OR^5$, halogen, $-N(R^5)R^5$, $-NH(C=O)R^5$, $-(C=O)NH_2$, aryl, heteroaryl, heterocyclyl, C1-C6 alkyl and C1-C6 alkyl substituted with -OH or $-NH_2$;

wherein R^5 is as defined in claim 1.

26. The use according to any of the foregoing claims, wherein R^2 is C1 –C6 alkyl or C1-C3 haloalkyl.

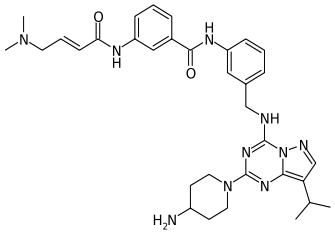
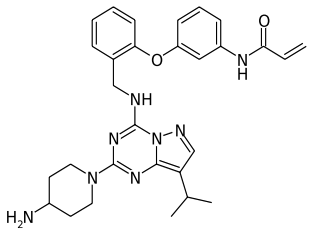
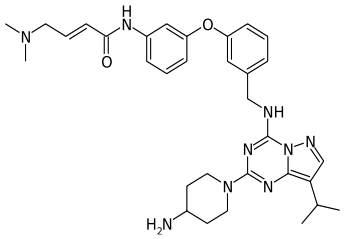
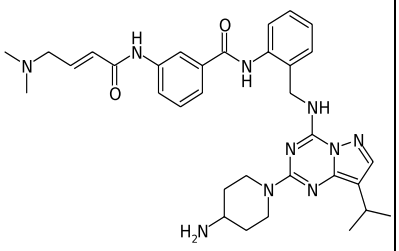
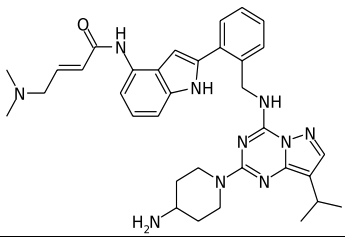
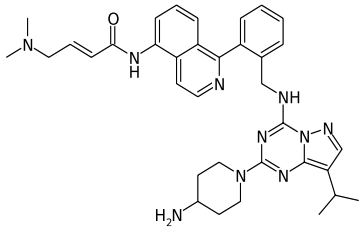
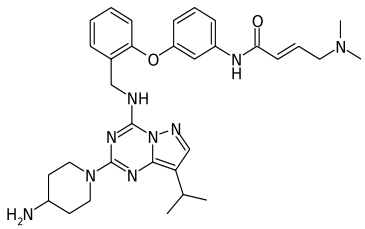
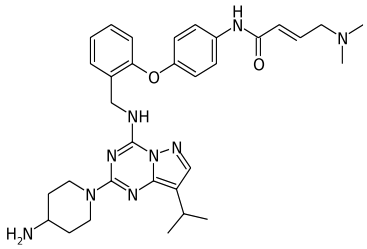
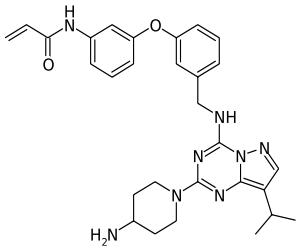
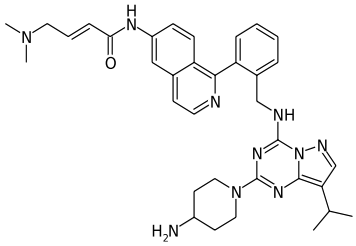
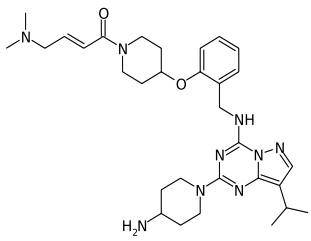
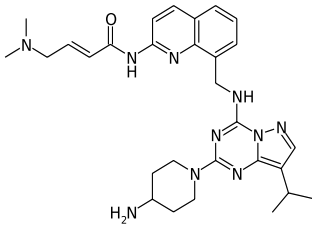
27. The use according to any of the foregoing claims, wherein R^6 is

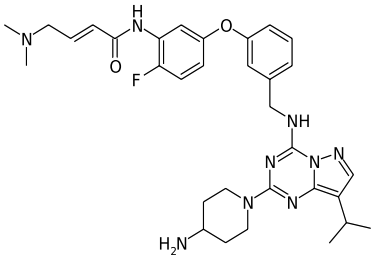
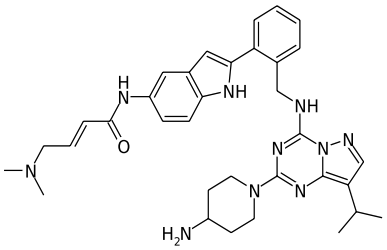
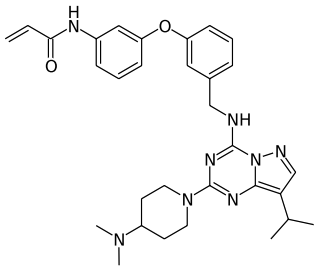
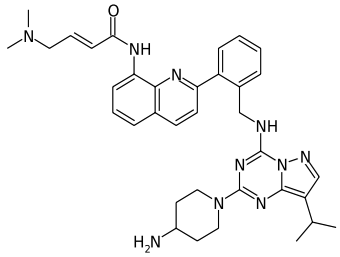
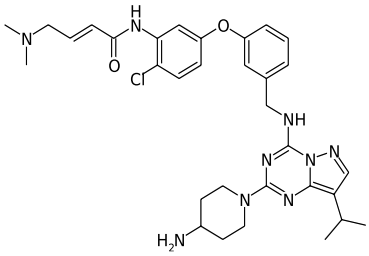
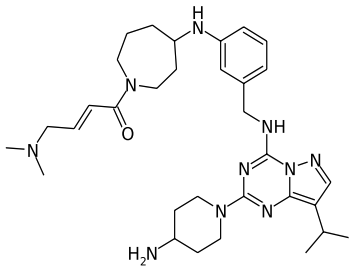
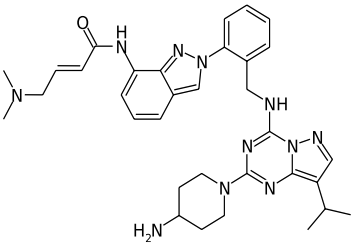
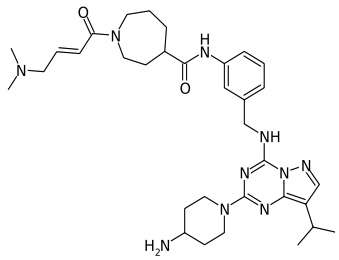
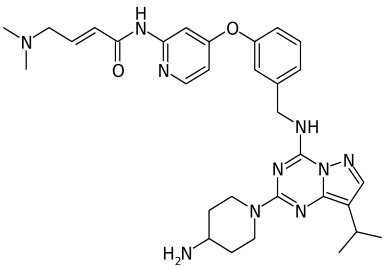
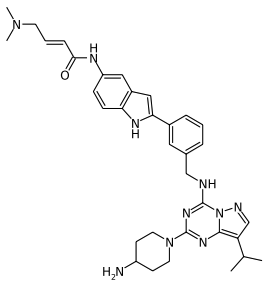
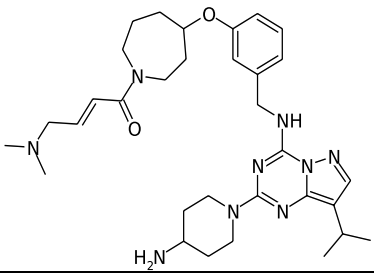
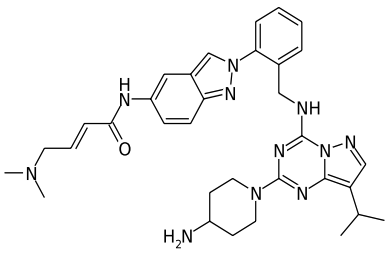


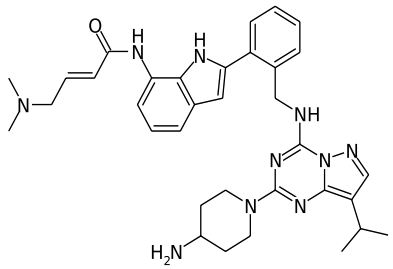
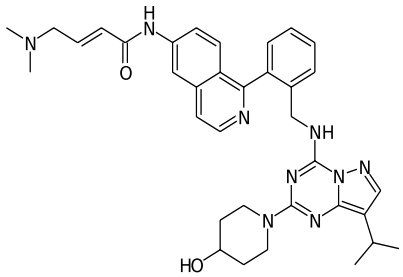
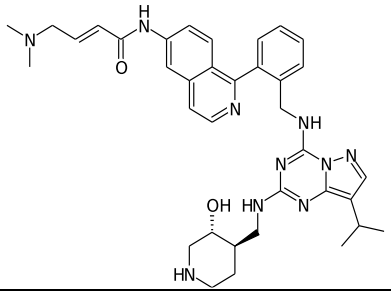
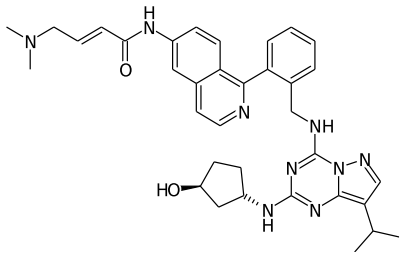
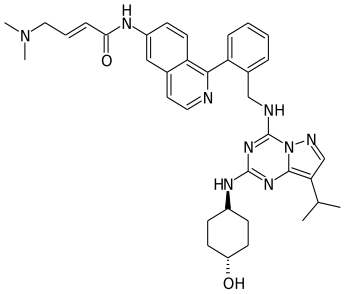
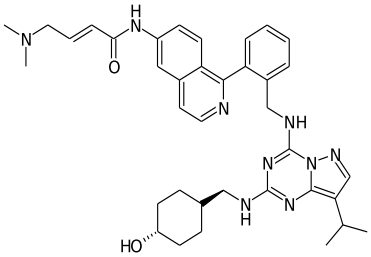
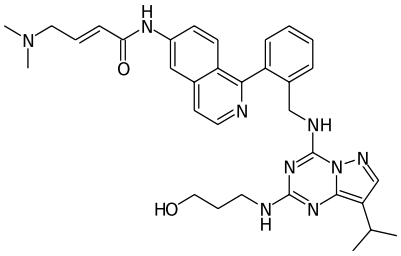
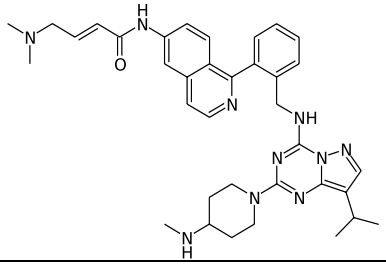
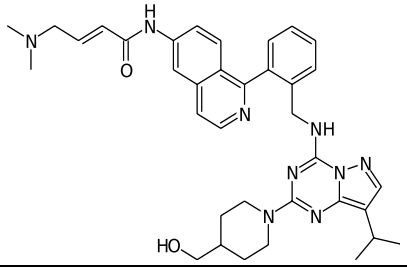
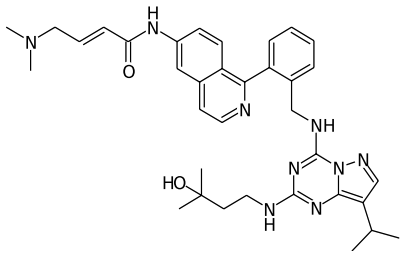
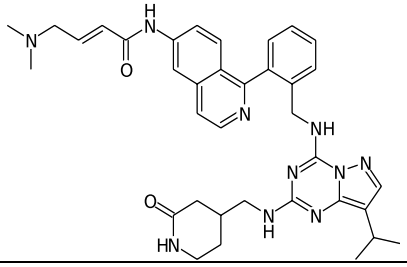
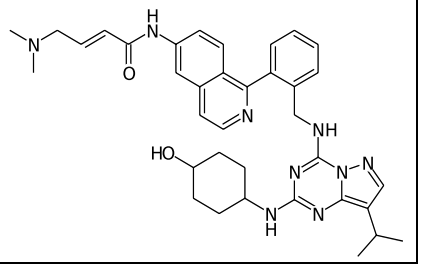
.

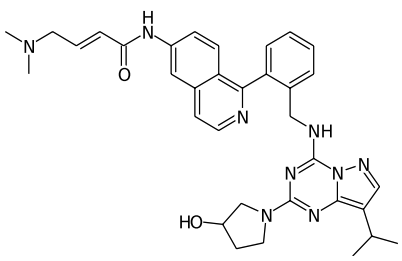
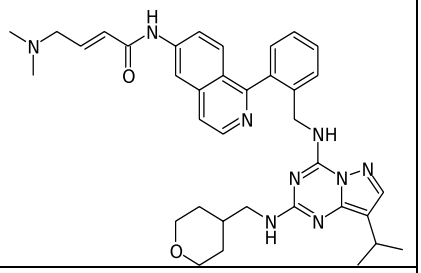
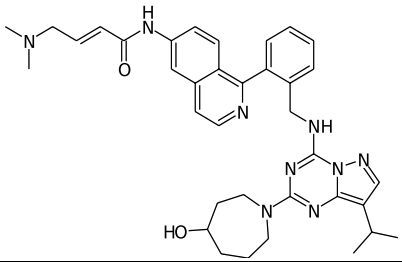
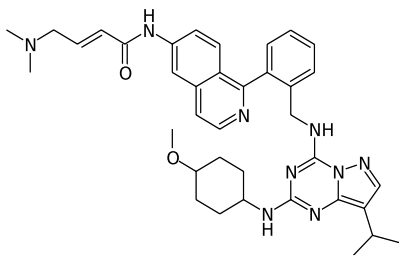
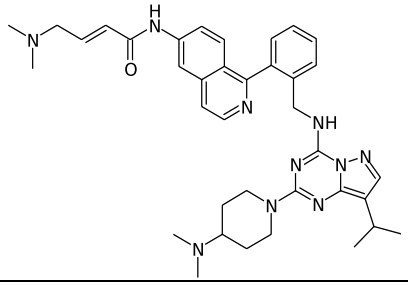
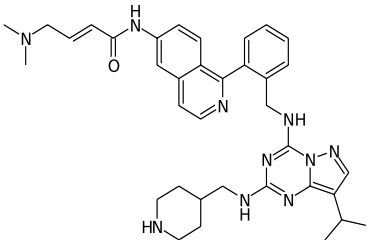
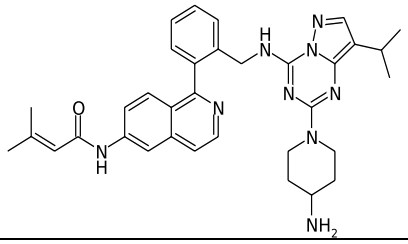
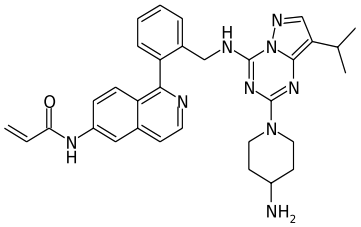
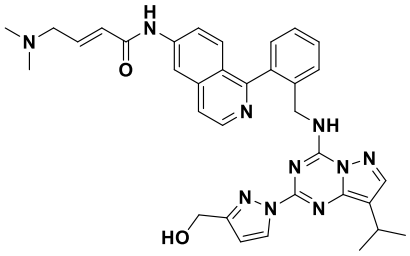
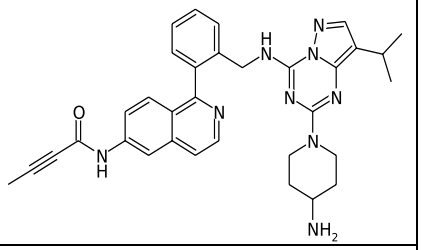
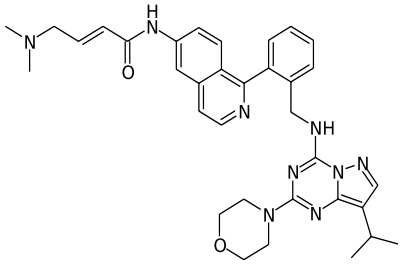
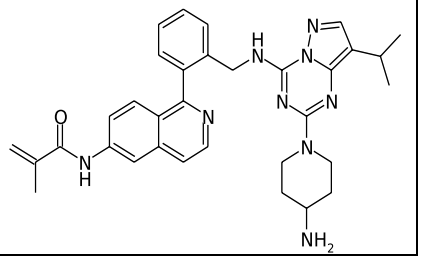
28. The use according to claim 27, wherein R^{16} is hydrogen; o is 1; R^{12} is W; W is (c-1) or (c-2) or (c-3), preferably (c-1); L is –NH-; R^{20} and R^{21} are, independently, at each occurrence, hydrogen, halogen, or C1-C6 alkyl, wherein, preferably, R^{20} is halogen; wherein R^{22} is hydrogen, halogen, C1-C6 alkyl, $-N(R^5)_2$, $-NR^{19}R^{20}$, wherein, preferably, R^{22} is $-N(R^5)_2$ or $-NR^{19}R^{20}$.

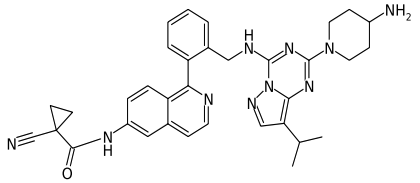
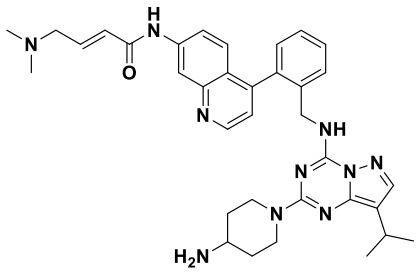
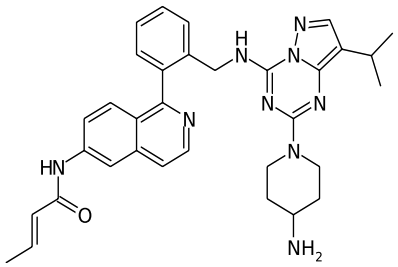
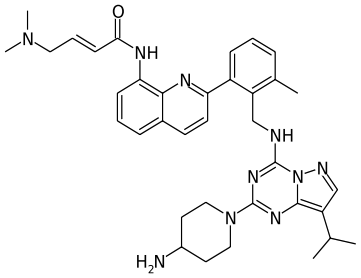
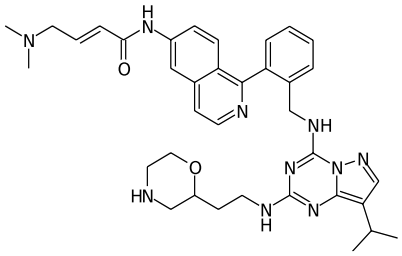
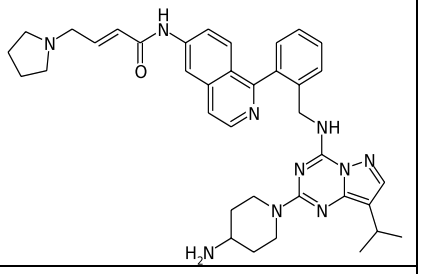
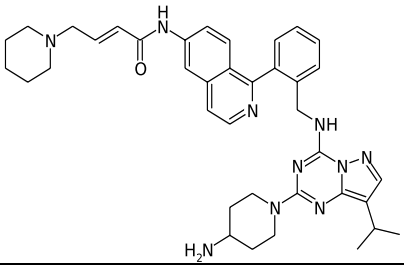
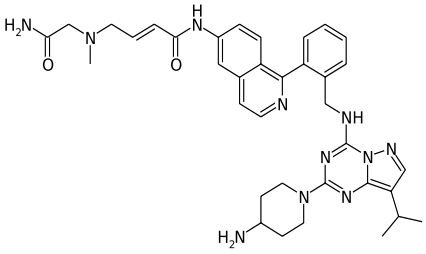
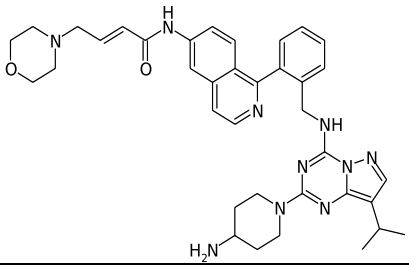
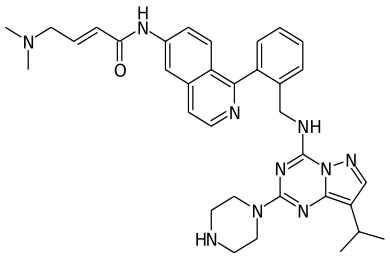
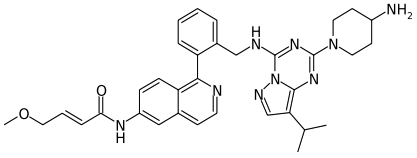
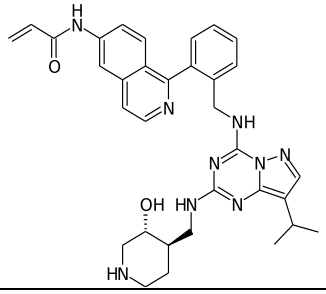
29. The use according to any of claims 1 – 28, wherein said compound is a compound having a structure selected from structures 1 – 216, as defined in the following table:

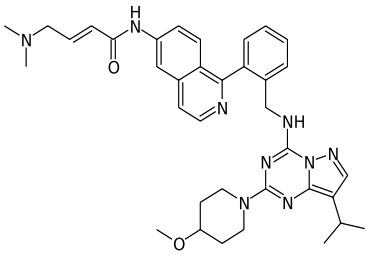
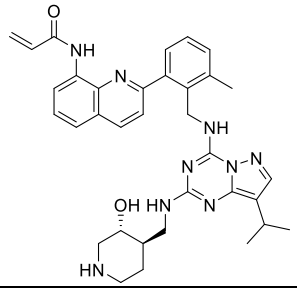
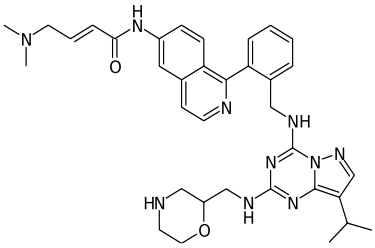
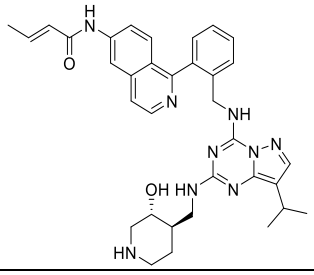
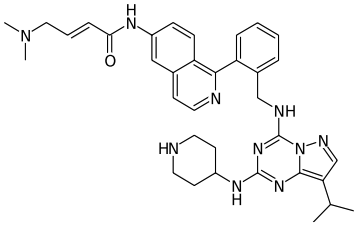
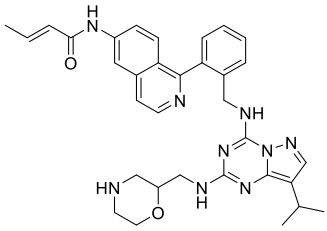
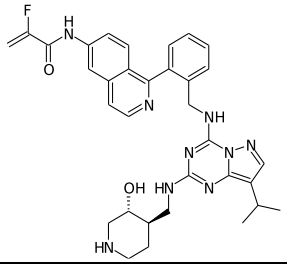
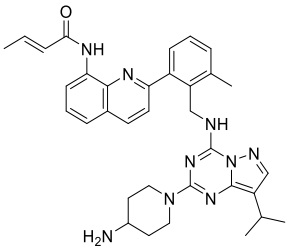
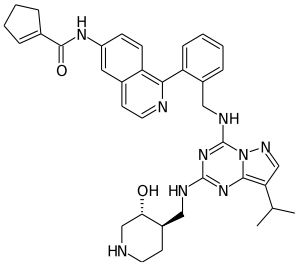
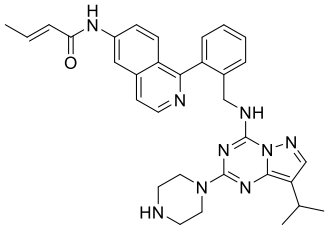
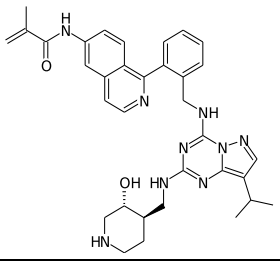
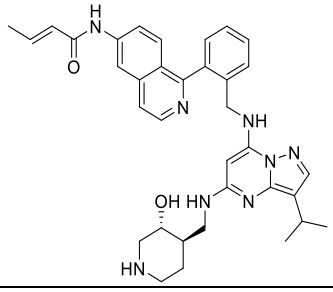
#cpds	Structure	#cpds	Structure
1		7	
2		8	
3		9	
4		10	
5		11	
6		12	

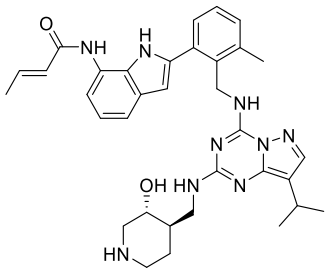
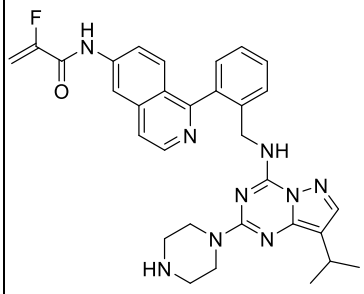
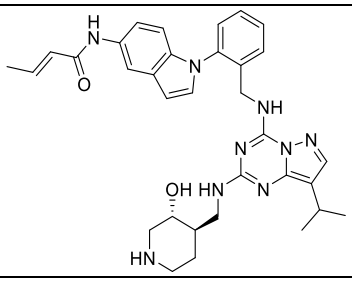
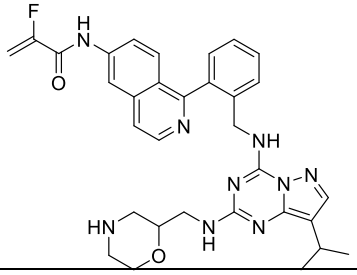
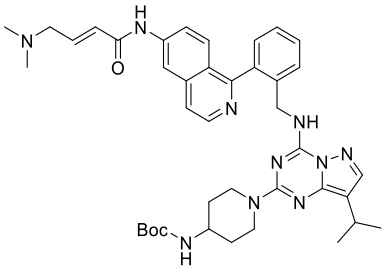
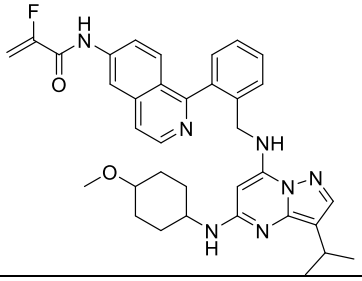
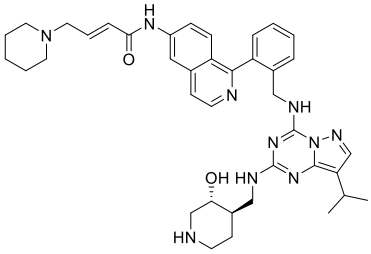
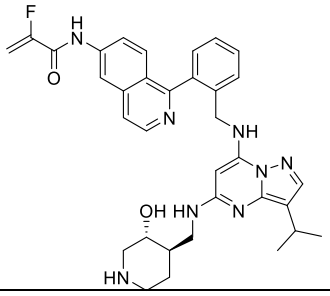
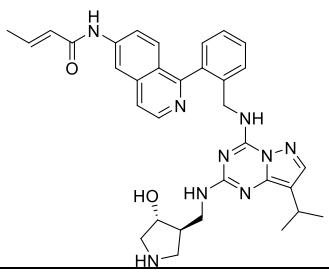
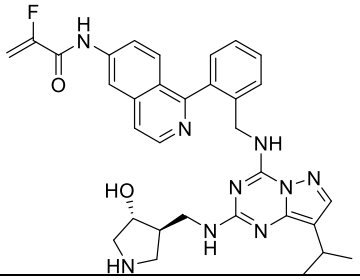
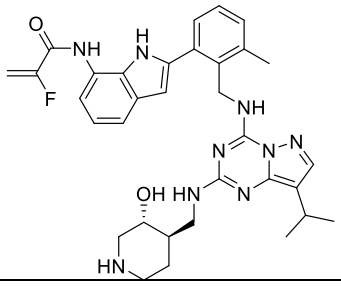
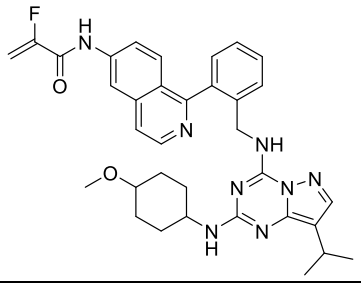
13		19	
14		20	
15		21	
16		22	
17		23	
18		24	

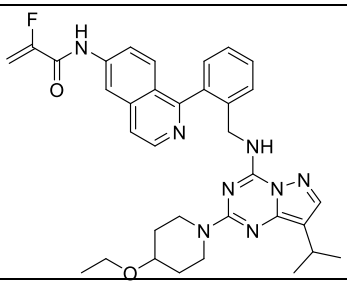
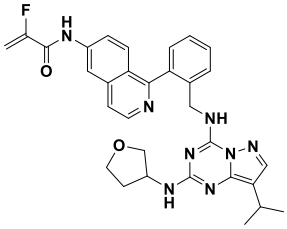
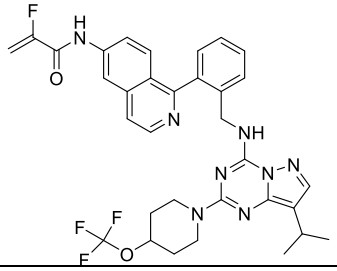
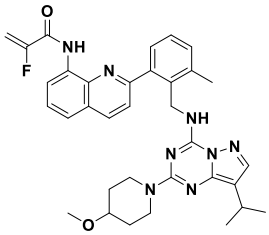
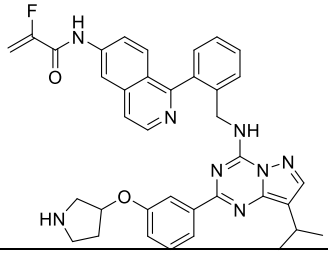
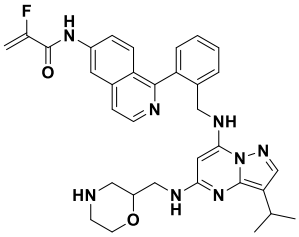
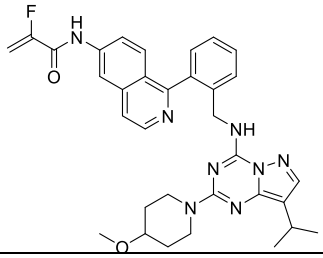
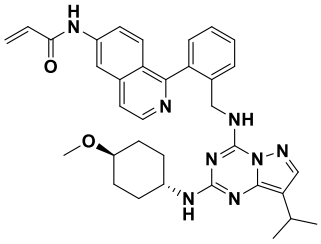
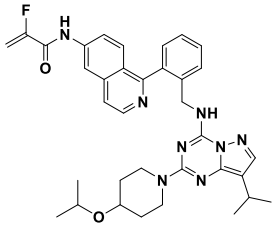
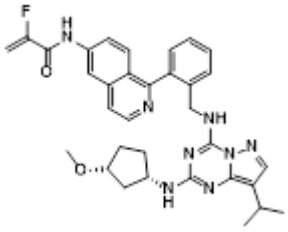
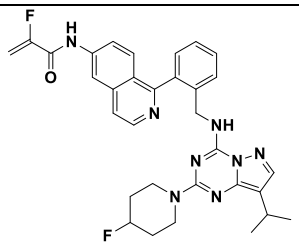
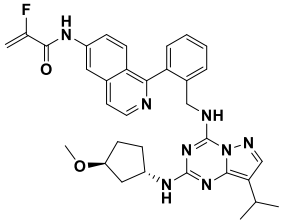
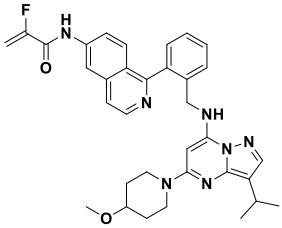
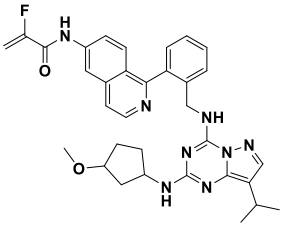
25		31	
26		32	
27		33	
28		34	
29		35	
30		36	

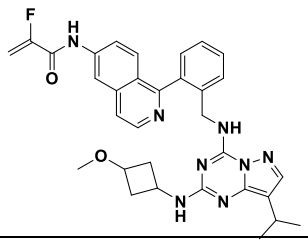
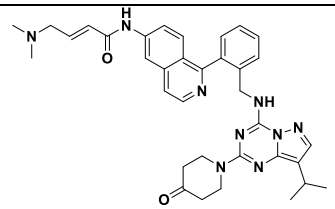
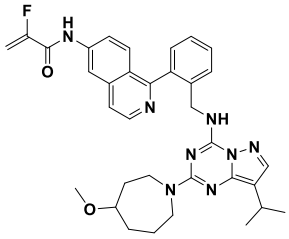
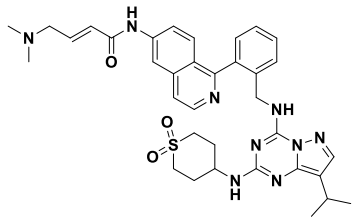
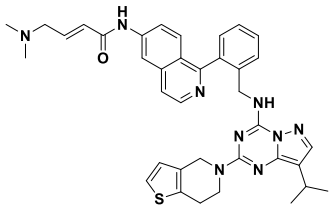
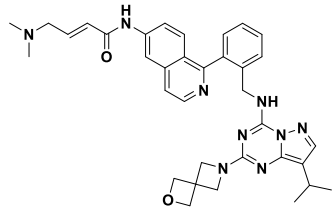
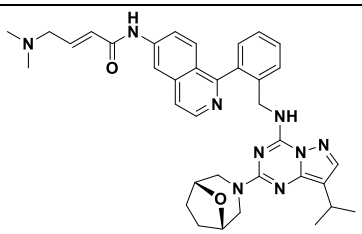
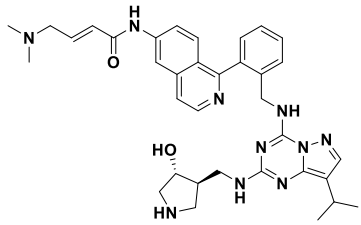
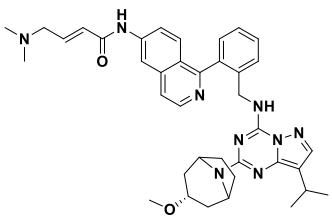
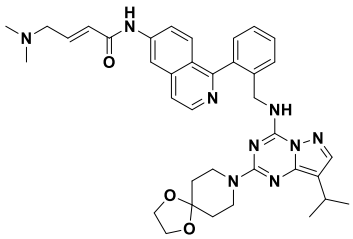
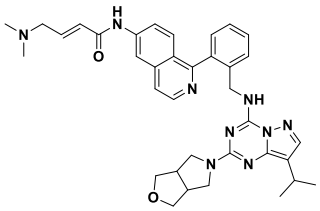
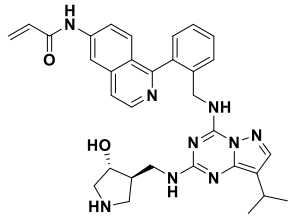
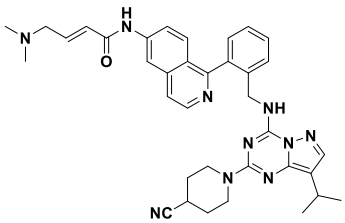
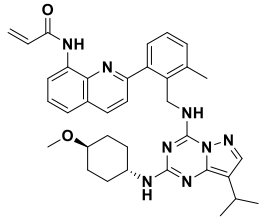
37		43	
38		44	
39		45	
40		46	
41		47	
42		48	

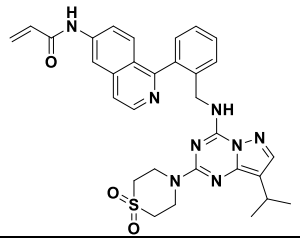
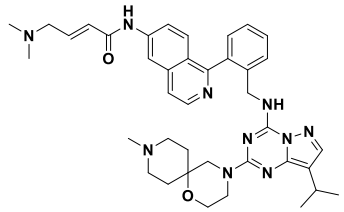
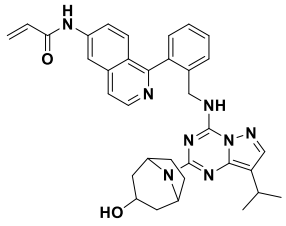
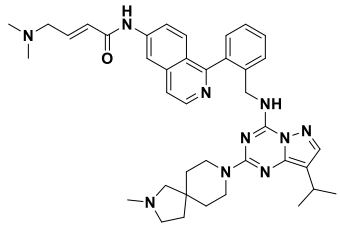
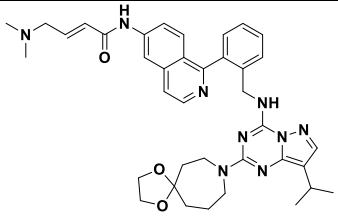
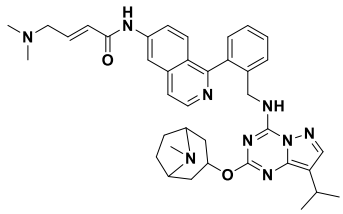
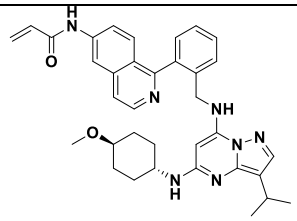
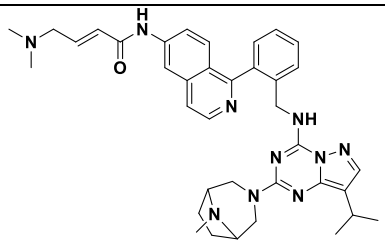
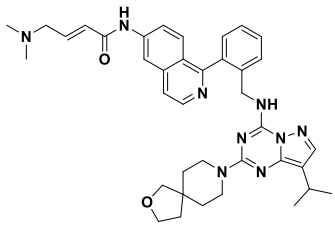
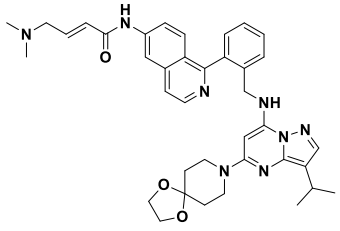
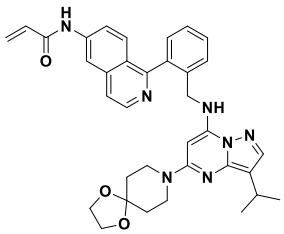
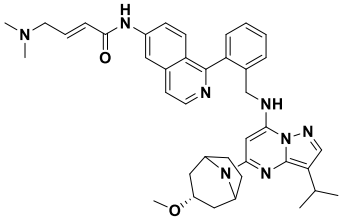
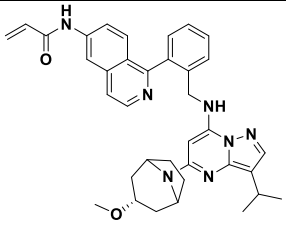
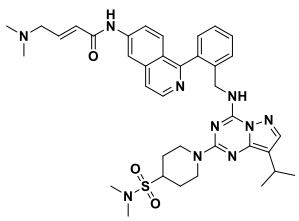
49		55	
50		56	
51		57	
52		58	
53		59	
54		60	

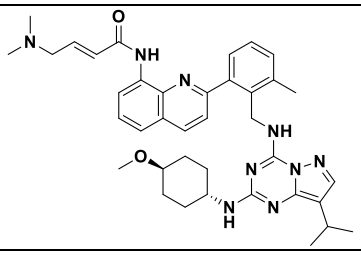
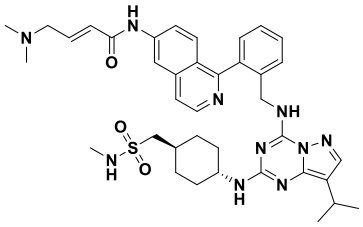
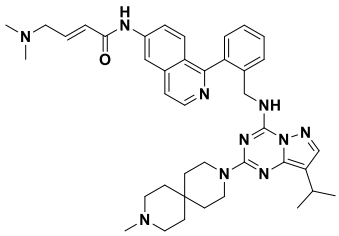
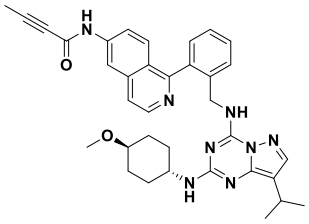
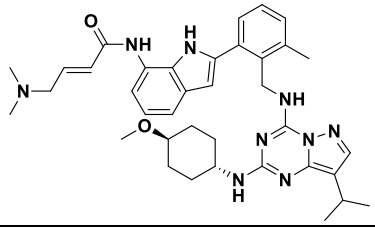
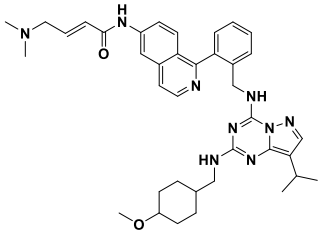
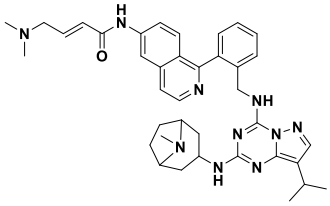
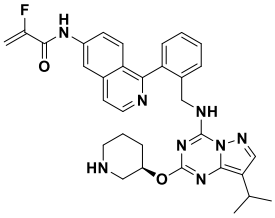
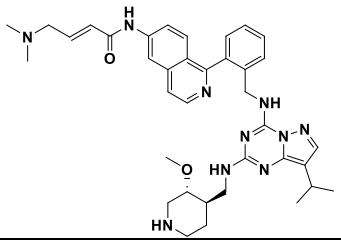
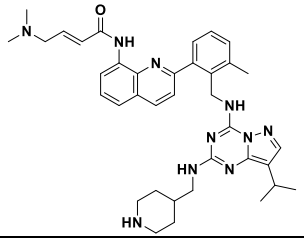
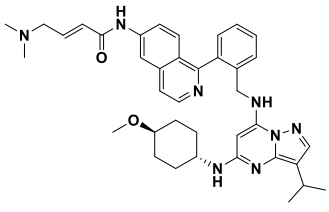
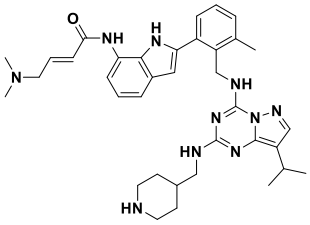
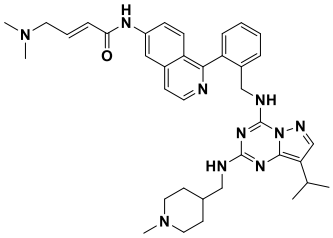
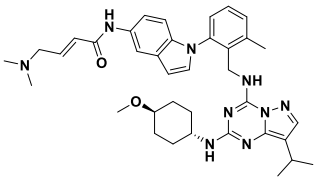
61		67	
62		68	
63		69	
64		70	
65		71	
66		72	

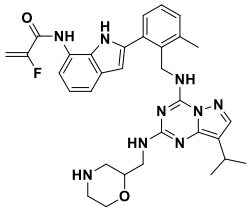
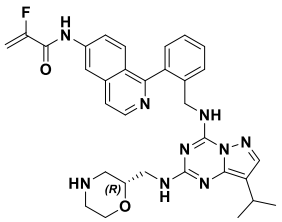
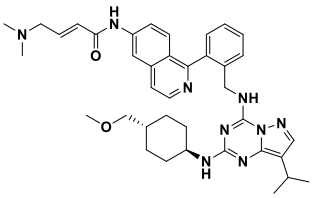
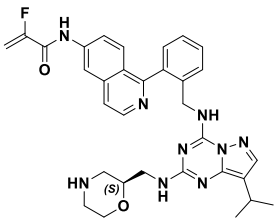
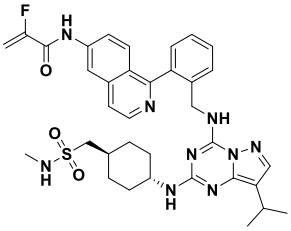
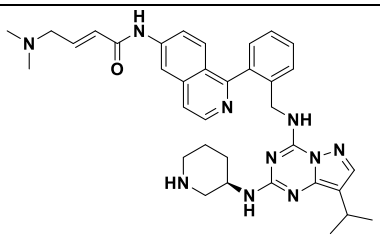
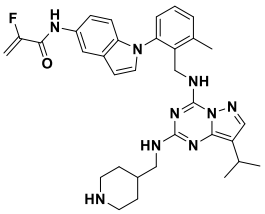
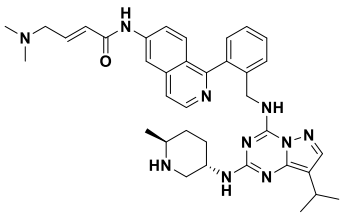
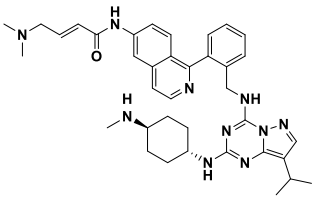
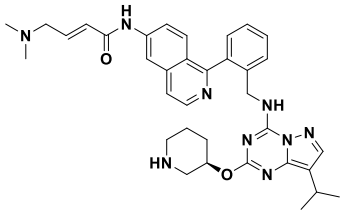
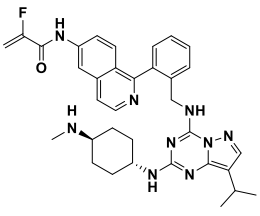
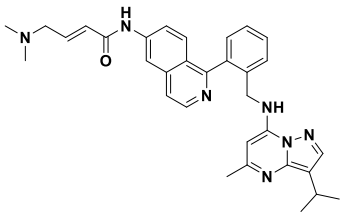
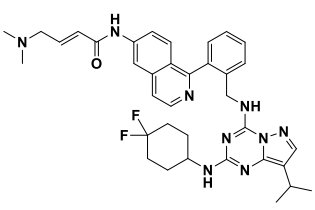
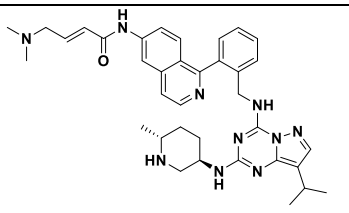
73		79	
74		80	
75		81	
76		82	
77		83	
78		84	

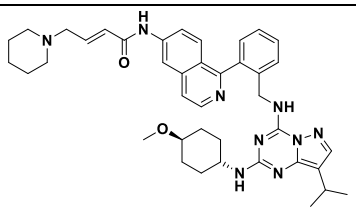
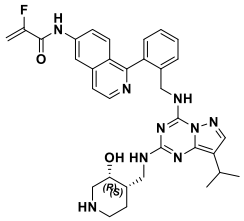
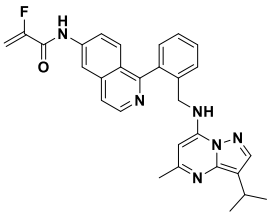
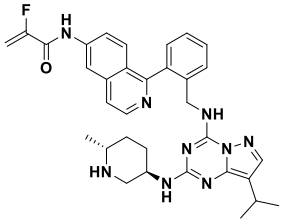
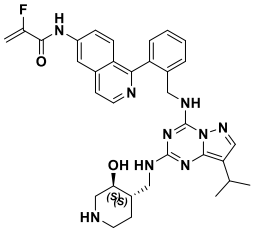
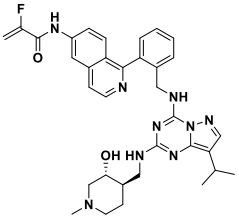
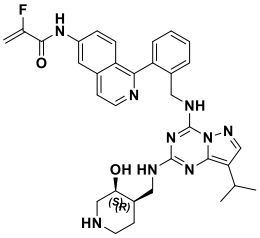
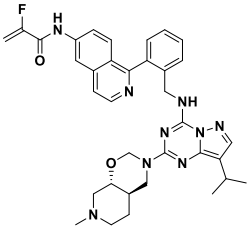
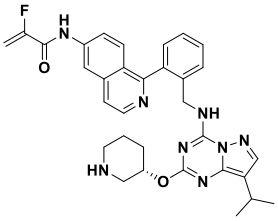
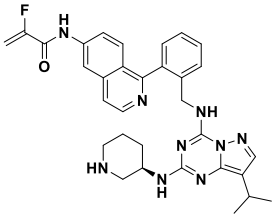
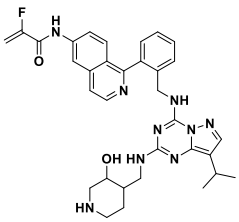
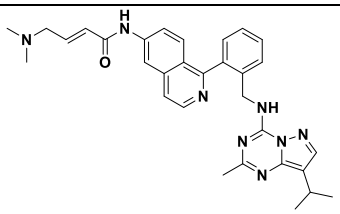
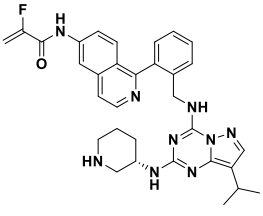
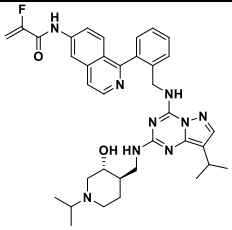
85		92	
86		93	
87		94	
88		95	
89		96	
90		97	
91		98	

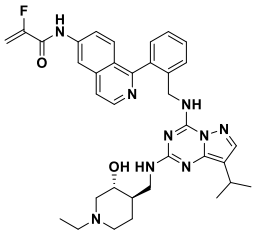
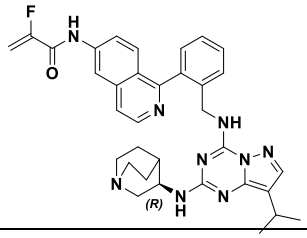
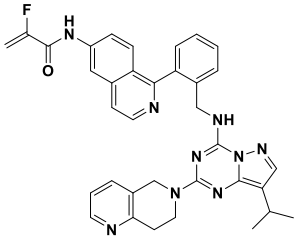
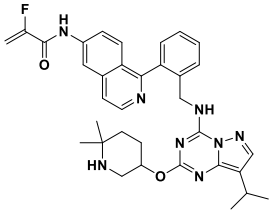
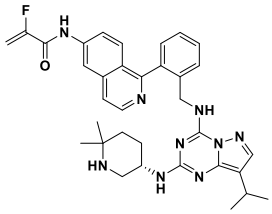
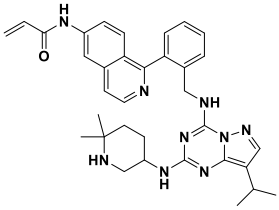
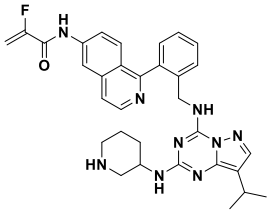
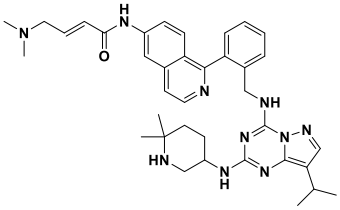
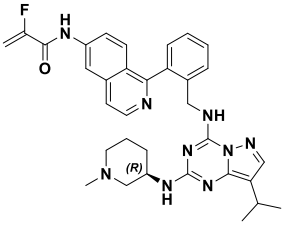
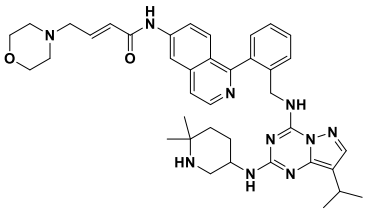
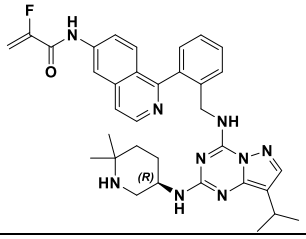
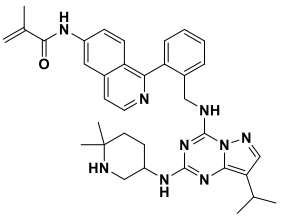
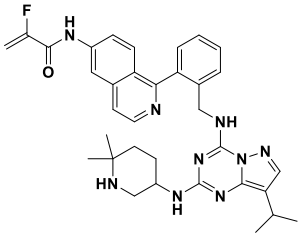
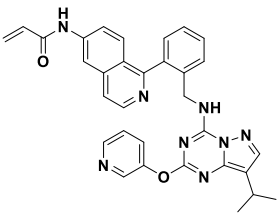
99		106	
100		107	
101		108	
102		109	
103		110	
104		111	
105		112	

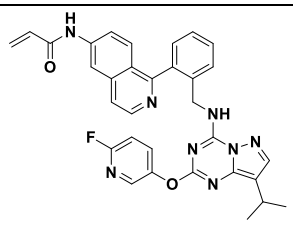
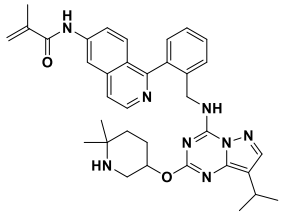
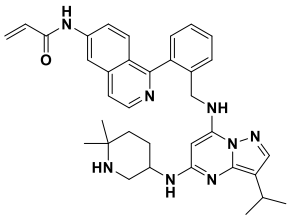
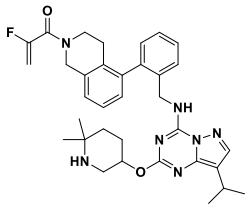
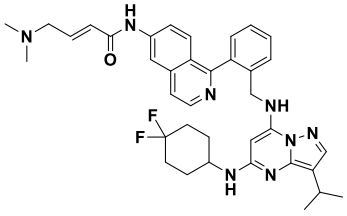
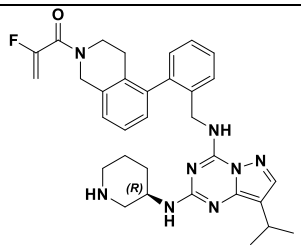
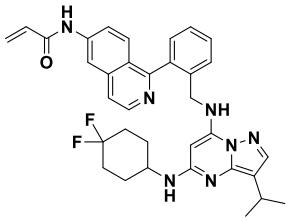
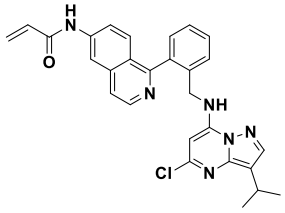
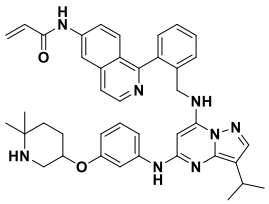
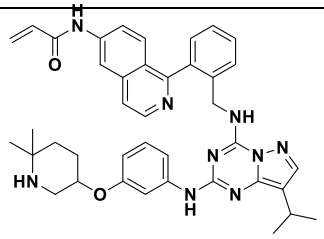
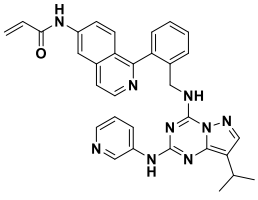
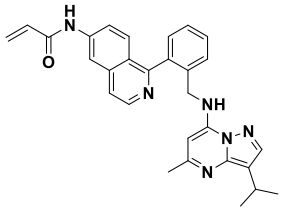
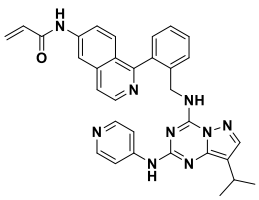
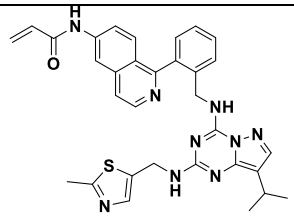
113		120	
114		121	
115		122	
116		123	
117		124	
118		125	
119		126	

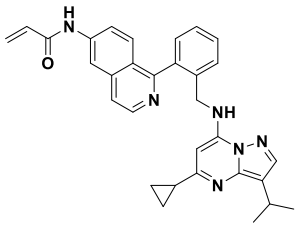
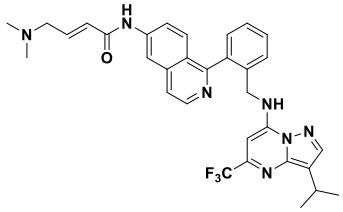
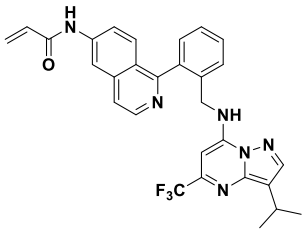
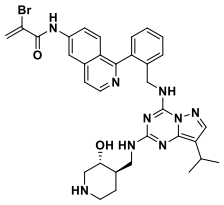
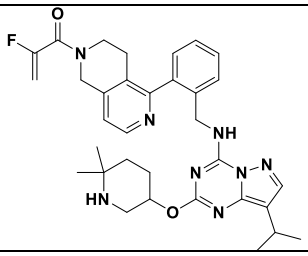
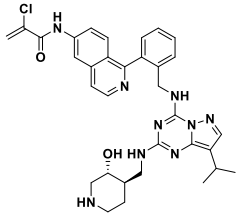
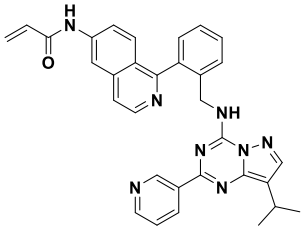
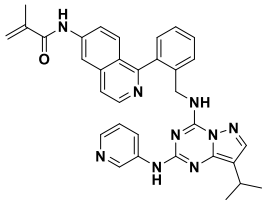
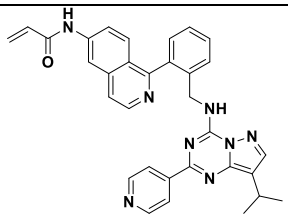
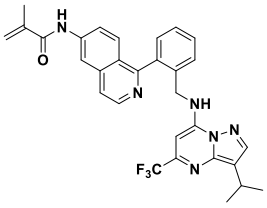
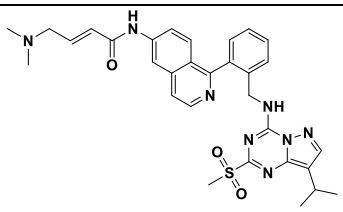
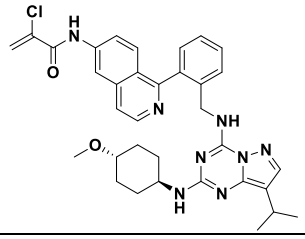
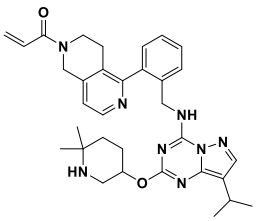
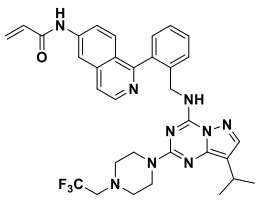
127		134	
128		135	
129		136	
130		137	
131		138	
132		139	
133		140	

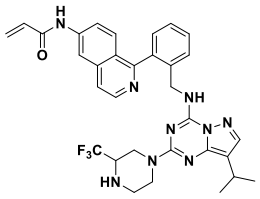
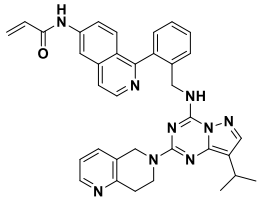
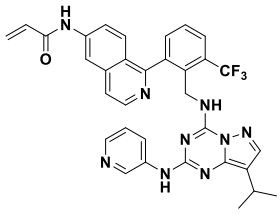
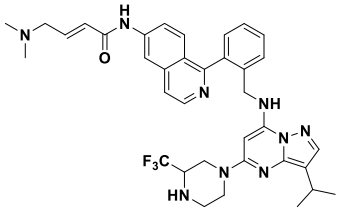
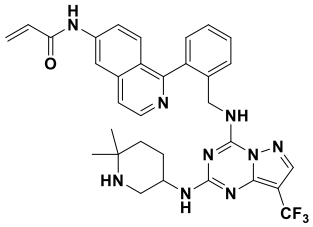
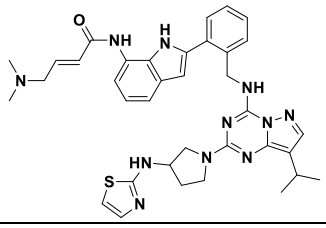
141		148	
142		149	
143		150	
144		151	
145		152	
146		153	
147		154	

155		162	
156		163	
157		164	
158		165	
159		166	
160		167	
161		168	

169		176	
170		177	
171		178	
172		179	
173		180	
174		181	
175		182	

183		190	
184		191	
185		192	
186		193	
187		194	
188		195	
189		196	

197		204	
198		205	
199		206	
200		207	
201		208	
202		209	
203		210	

211		
212		
213		
214		
215		
216		

30. The use according to any of claims 1 – 29, wherein said compound is a compound having a structure selected from structures 44, 64, 95, 134, 147, 164, 174, 175, 177, and 178, as defined in claim 29, wherein, preferably, said compound is a compound having a structure selected from structures 64, 134, 164, 174, 175, 177 and 178, as defined in claim 29, wherein, more preferably, said compound is a compound having a structure selected from 174, 175 and 177, as defined in claim 29.