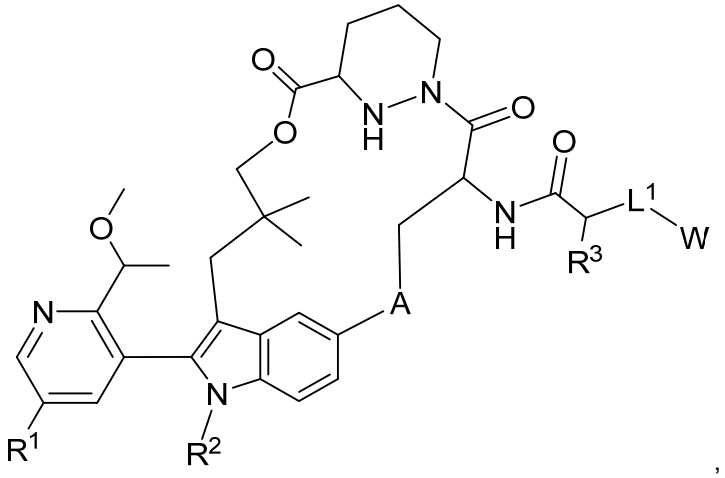
Claims

1. A compound, or pharmaceutically acceptable salt thereof, having the structure of Formula I:



Formula I

wherein A is optionally substituted 3 to 6-membered heterocycloalkylene, optionally substituted 3 to 6-membered cycloalkylene, optionally substituted 6-membered arylene, or optionally substituted 5 to 10-membered heteroarylene;

L^1 is absent or a linker;

W is a cross-linking group comprising a vinyl ketone, vinyl sulfone, ynone, or an alkynyl sulfone;

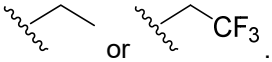
R^1 is hydrogen, optionally substituted 3 to 10-membered heterocycloalkyl, or optionally substituted C_1-C_6 heteroalkyl;

R^2 is optionally substituted C_1-C_6 alkyl; and

R^3 is optionally substituted C_1-C_6 alkyl or optionally substituted C_1-C_3 heteroalkyl.

2. The compound of claim 1, or pharmaceutically acceptable salt thereof, wherein A is optionally substituted thiazole-diyl, optionally substituted oxazole-diyl, optionally substituted morpholine-diyl, optionally substituted pyrrolidine-diyl, optionally substituted pyridine-diyl, optionally substituted azetidine-diyl, optionally substituted pyrazine-diyl, optionally substituted pyrimidine-diyl, optionally substituted piperidine-diyl, optionally substituted oxadiazole-diyl, optionally substituted thiadiazole-diyl, optionally substituted triazole-diyl, optionally substituted thiomorpholine-diyl, or optionally substituted phenylene.

3. The compound of claim 1 or 2, or pharmaceutically acceptable salt thereof, wherein R^2 is:



.

4. The compound of any one of claims 1 to 3, or pharmaceutically acceptable salt thereof, wherein R^3 is optionally substituted C_1-C_6 alkyl.

5. The compound of any one of claims 1 to 4, or pharmaceutically acceptable salt thereof, wherein A is optionally substituted 5 to 10-membered heteroarylene.

6. The compound of any one of claims 1 to 4, or pharmaceutically acceptable salt thereof, wherein A is optionally substituted phenylene.

7. The compound of any one of claims 1 to 4, or pharmaceutically acceptable salt thereof, wherein A is optionally substituted 3 to 6-membered heterocycloalkylene.

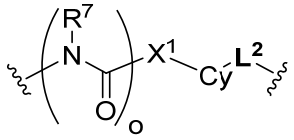
8. The compound of any one of claims 1 to 7, or pharmaceutically acceptable salt thereof, wherein the linker is the structure of Formula III:

$$A^1\text{-}(B^1)_f\text{-}(C^1)_g\text{-}(B^2)_h\text{-}(D^1)\text{-}(B^3)_i\text{-}(C^2)_j\text{-}(B^4)_k\text{–}A^2$$

Formula III,

wherein A^1 is a bond between the linker and $CH(R^3)$; A^2 is a bond between W and the linker; B^1, B^2, B^3, and B^4 each, independently, is selected from optionally substituted C_1-C_2 alkylene, optionally substituted C_1-C_3 heteroalkylene, O, S, and NR^N; each R^N is, independently, hydrogen, optionally substituted C_1–C_4 alkyl, optionally substituted C_2-C_4 alkenyl, optionally substituted C_2-C_4 alkynyl, optionally substituted 3 to 14-membered heterocycloalkyl, optionally substituted 6 to 10-membered aryl, or optionally substituted C_1-C_7 heteroalkyl; C^1 and C^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl; f, g, h, i, j, and k are each, independently, 0 or 1; and D^1 is optionally substituted C_1-C_{10} alkylene, optionally substituted C_2-C_{10} alkenylene, optionally substituted C_2-C_{10} alkynylene, optionally substituted 3 to 14-membered heterocycloalkylene, optionally substituted 5 to 10-membered heteroarylene, optionally substituted 3 to 8-membered cycloalkylene, optionally substituted 6 to 10-membered arylene, optionally substituted C_2-C_{10} polyethylene glycolene, or optionally substituted C_1-C_{10} heteroalkylene, or a chemical bond linking $A^1\text{-}(B^1)_f\text{-}(C^1)_g\text{-}(B^2)_h$- to -$(B^3)_i\text{-}(C^2)_j\text{-}(B^4)_k\text{–}A^2$.

9. The compound of any one of claims 1 to 8, or pharmaceutically acceptable salt thereof, wherein the linker has the structure of Formula IIIa:



Formula IIIa,

wherein o is 0 or 1;

R^7 is hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted 3 to 8-membered cycloalkylene, or optionally substituted 3 to 8-membered heterocycloalkylene;

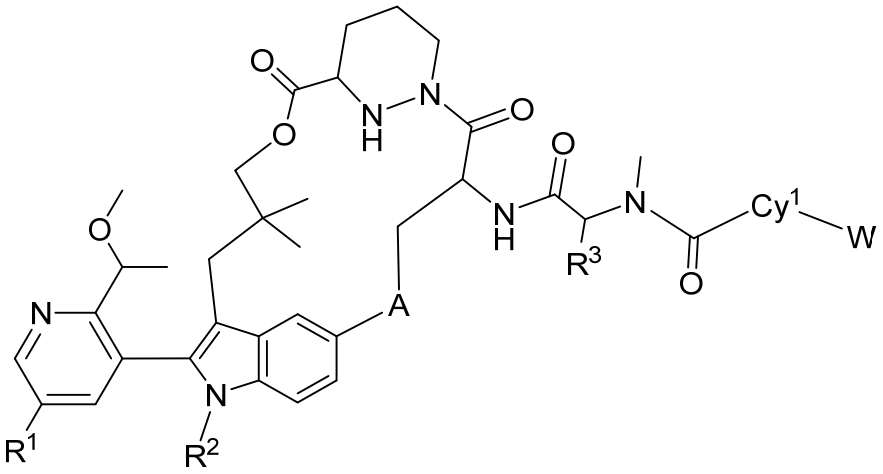
X^1 is absent, optionally substituted C_1-C_4 alkylene, O, NCH_3, or optionally substituted C_1-C_4 heteroalkylene;

Cy is optionally substituted 3 to 8-membered cycloalkylene, optionally substituted 3 to 12-membered heterocycloalkylene, optionally substituted 6-10 membered arylene, or optionally substituted 5 to 10-membered heteroarylene; and

L^2 is absent, -SO_2-, -NH-, optionally substituted C_1-C_4 alkylene, optionally substituted C_1-C_4 heteroalkylene, or optionally substituted 3 to 6-membered heterocycloalkylene.

10. The compound of any one of claims 1 to 9, or pharmaceutically acceptable salt thereof, wherein the compound is not a compound of Table 2.

11. The compound of any one of claims 1 to 10, or pharmaceutically acceptable salt thereof, having the structure of Formula II-5:



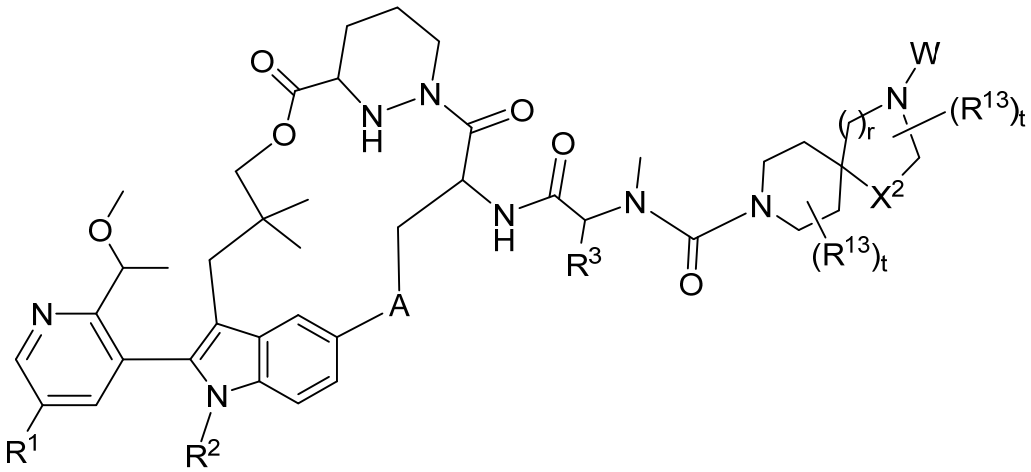
Formula II-5,

wherein Cy^1 is optionally substituted spirocyclic 8 to 11-membered heterocycloalkylene or optionally substituted bicyclic 7 to 9-membered heterocycloalkylene; and

wherein W comprises a vinyl ketone or a vinyl sulfone.

12. The compound of claim 11, or pharmaceutically acceptable salt thereof, wherein Cy^1 is optionally substituted spirocyclic 10 to 11-membered heterocycloalkylene.

13. The compound of claim 12, or pharmaceutically acceptable salt thereof, having the structure of Formula II-5a:



Formula II-5a,

wherein X^2 is O, $C(R^{11})_2$, NR^{12}, S, or SO_2.

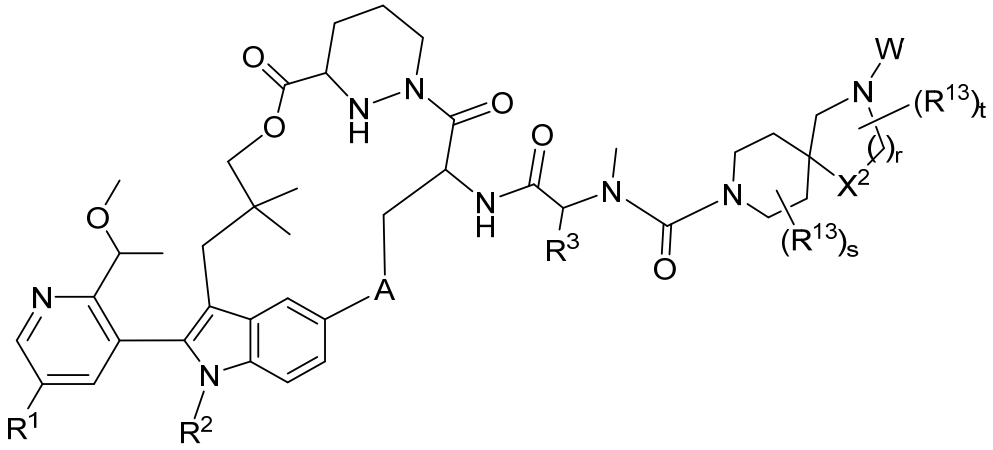
r is 1 or 2;

each t is, independently, 0, 1, or 2;

R^{11} and R^{12} are each, independently, hydrogen, optionally substituted C_1-C_4 alkyl, optionally substituted C_2-C_4 heteroalkyl, or optionally substituted 3 to 5-membered cycloalkyl; and

each R^{13} is, independently, -CH_3.

14. The compound of claim 12, or pharmaceutically acceptable salt thereof, having the structure of Formula II-5b:



Formula II-5b,

wherein X^2 is O, $C(R^{11})_2$, NR^{12}, S, or SO_2.

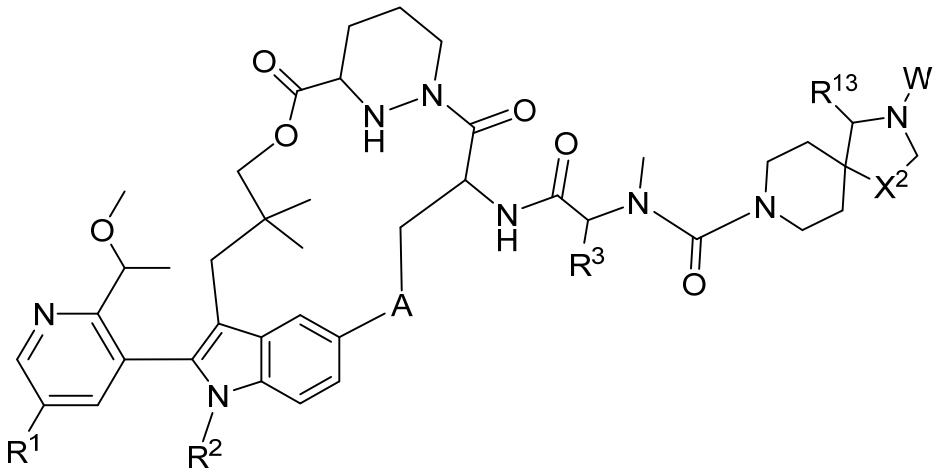
r is 1 or 2;

s and t are each, independently, 0, 1, or 2;

R^{11} and R^{12} are each, independently, hydrogen, optionally substituted C_1-C_4 alkyl, optionally substituted C_2-C_4 heteroalkyl, optionally substituted 3- to 6- membered heterocycloalkyl, or optionally substituted 3 to 5-membered cycloalkyl; and

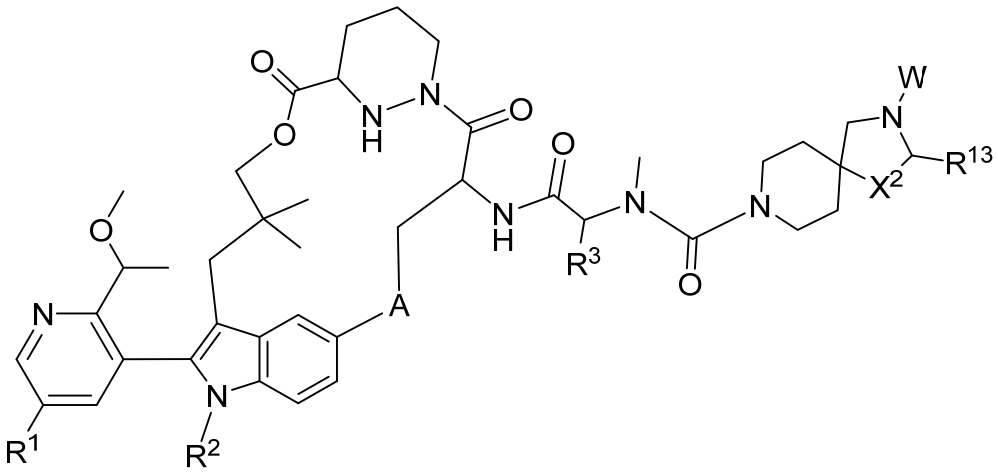
each R^{13} is, independently, -CH_3, F, or two R^{13} attached to the same atom combine with the atom to which they are attached to form an optionally substituted C_3-C_6 cycloalkyl, or two R^{13} attached to the same atom combine with the atom to which they are attached to form an optionally substituted 3- to 6-membered heterocycloalkyl.

15. The compound of claim 13 or 14, or pharmaceutically acceptable salt thereof, having the structure of Formula II-5c:



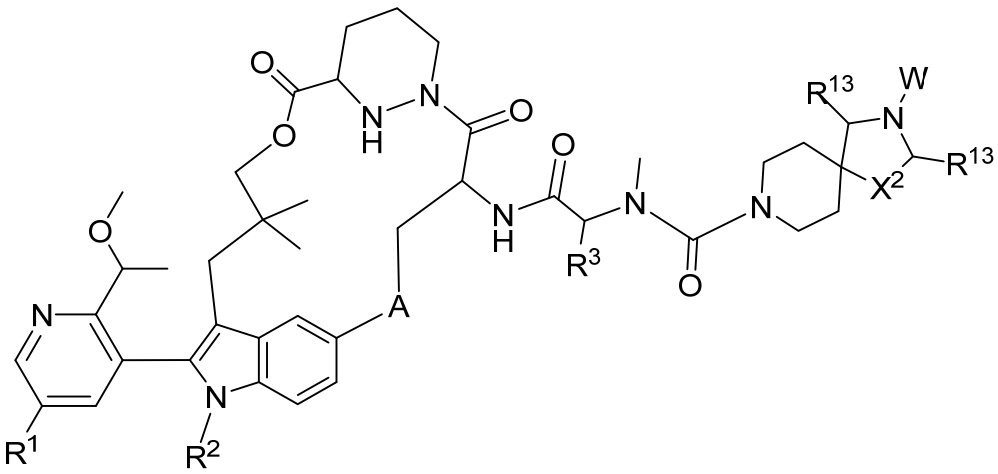
Formula II-5c.

16. The compound of claim 13 or 14, or pharmaceutically acceptable salt thereof, having the structure of Formula II-5d:



Formula II-5d.

17. The compound of claim 13 or 14, or pharmaceutically acceptable salt thereof, having the structure of Formula II-5e:



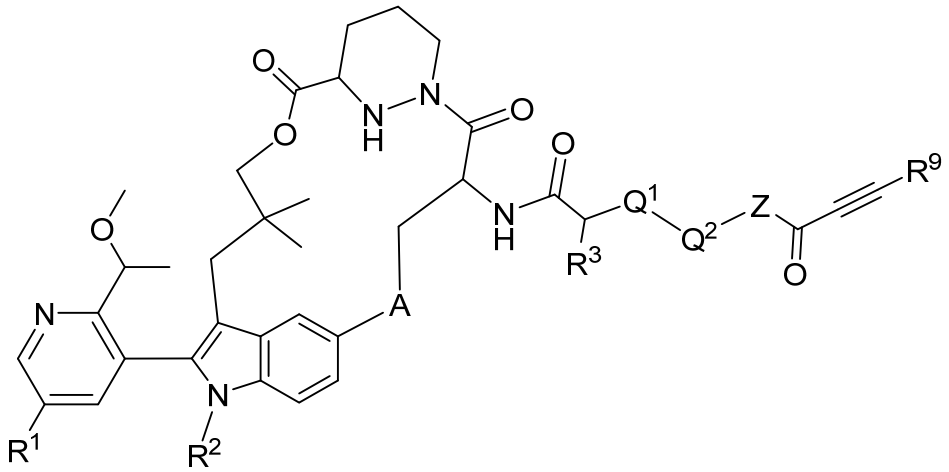
Formula II-5e.

18. The compound of any one of claims 1 to 17, or pharmaceutically acceptable salt thereof, wherein W is a cross-linking group comprising a vinyl ketone.

19. The compound of any one of claims 1 to 17, or pharmaceutically acceptable salt thereof, wherein W is a cross-linking group comprising a vinyl sulfone.

20. The compound of any one of claims 1 to 17, or pharmaceutically acceptable salt thereof, wherein W is a cross-linking group comprising an ynone.

21. The compound of claim 20, or pharmaceutically acceptable salt thereof, having the structure of Formula II-6:



Formula II-6,

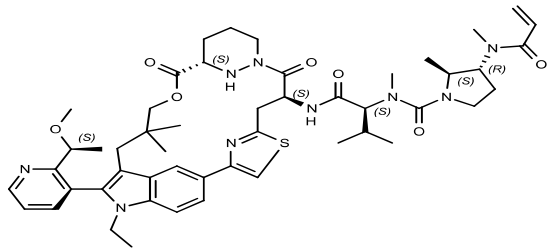
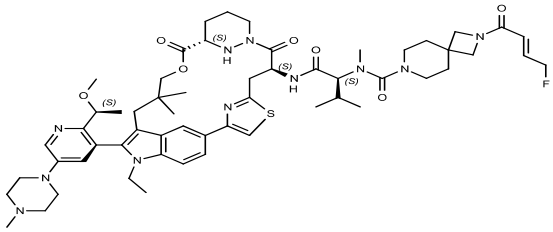
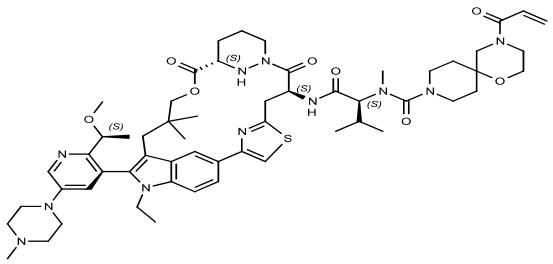
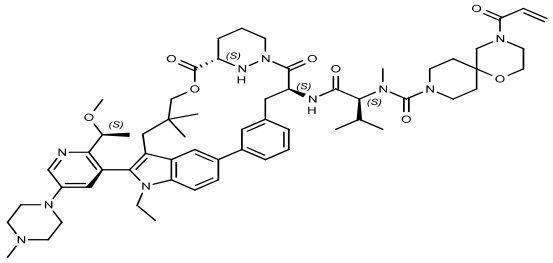
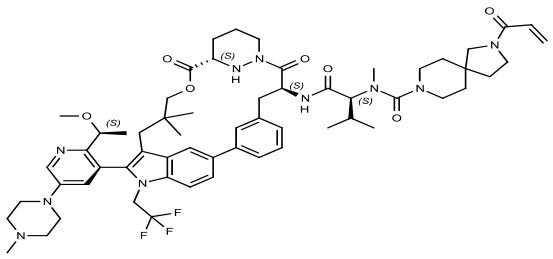
wherein Q^1 is CH_2, NR^N, or O;

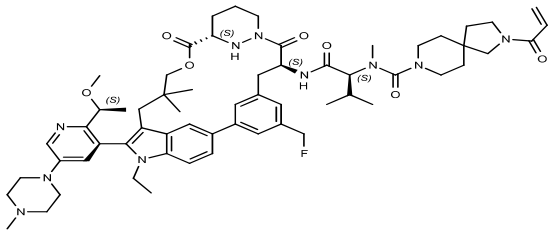
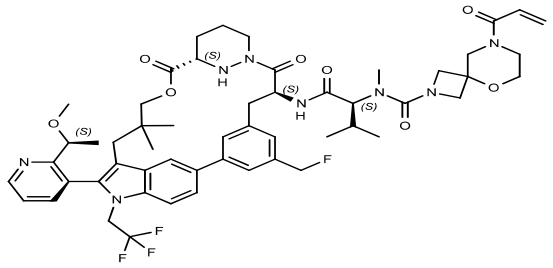
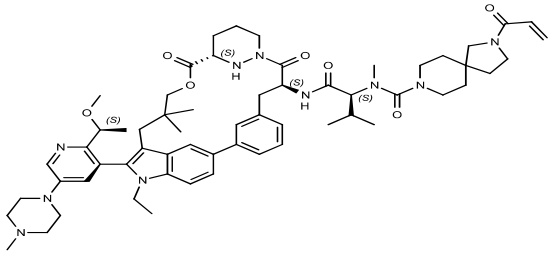
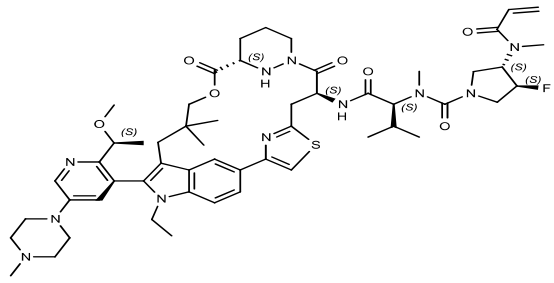
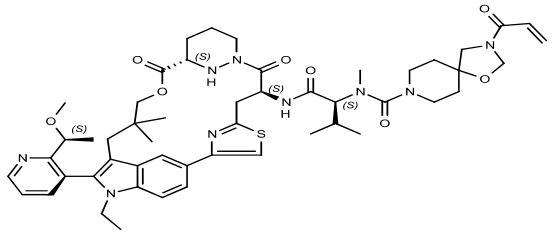
Q^2 is CO, NR^N, or O; and

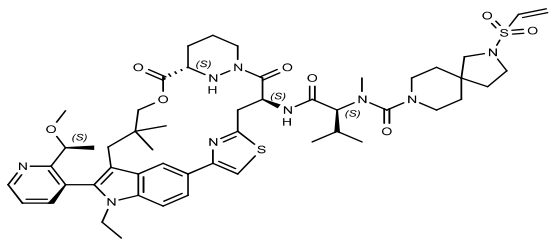
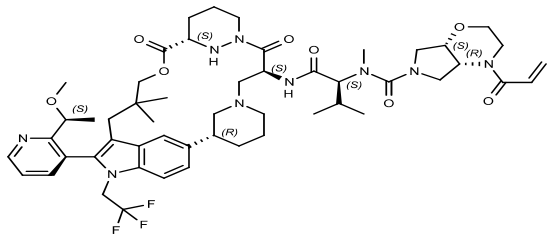
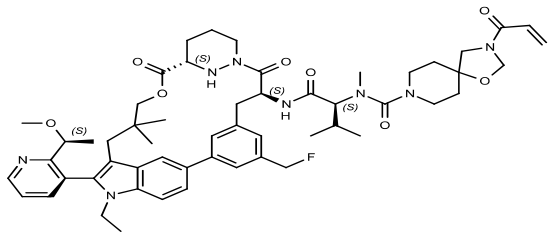
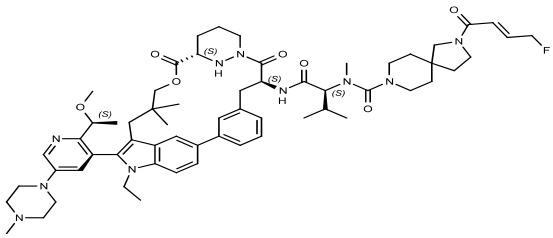
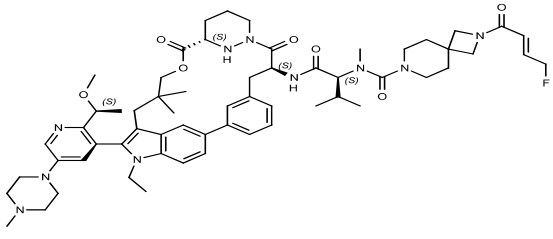
Z is optionally substituted 3 to 6-membered heterocycloalkylene or optionally substituted 5 to 10-membered heteroarylene; or

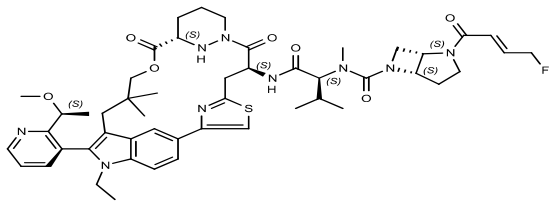
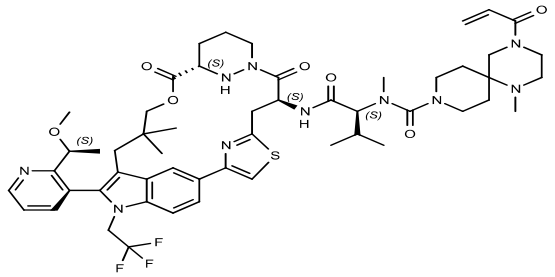
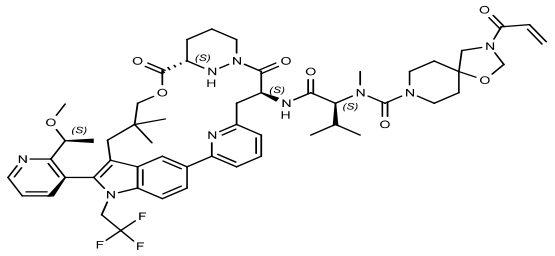
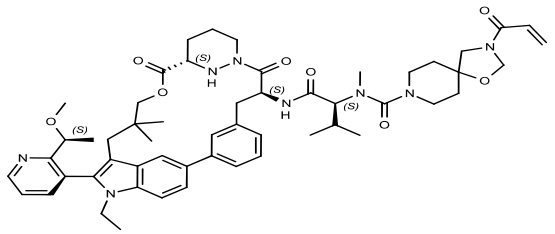
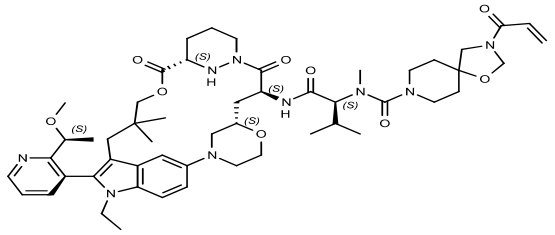
wherein Q^1-Q^2-Z is an optionally substituted 9 to 10-membered spirocyclic heterocycloalkylene.

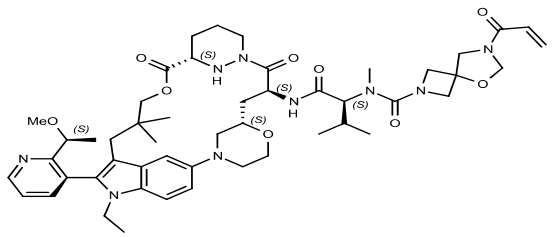
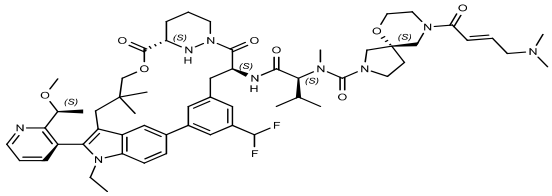
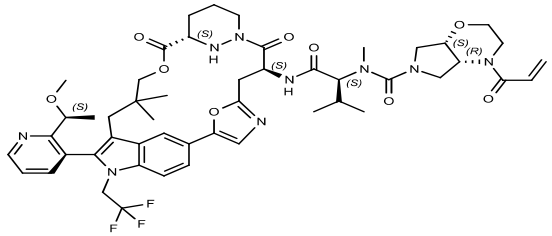
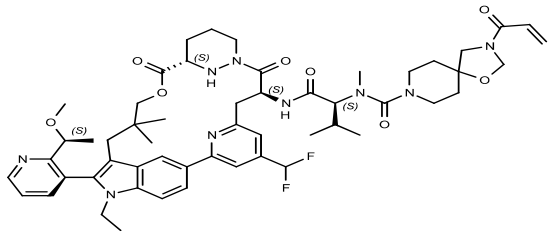
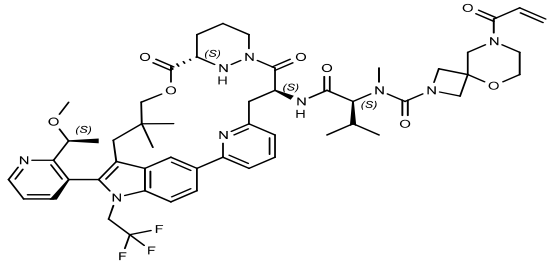
22. A compound, or a pharmaceutically acceptable salt thereof, selected from the following compounds:

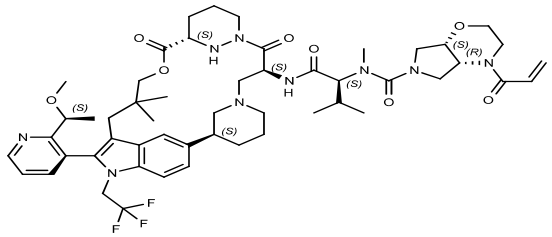
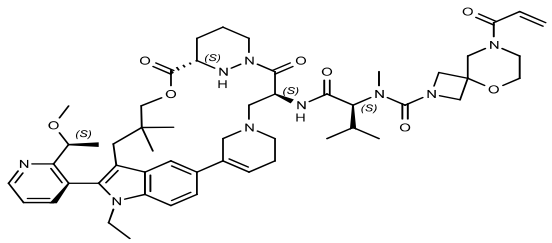
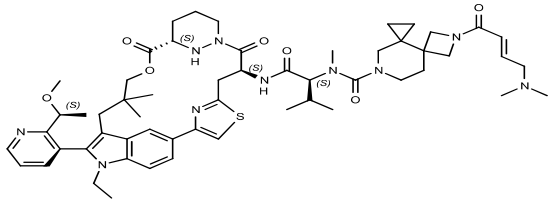
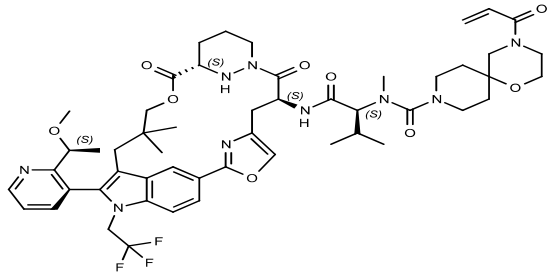
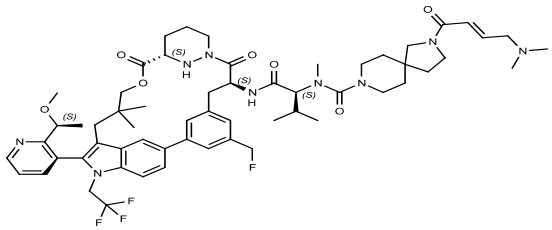
x#	Structure
1	
2	
3	
4	
5	

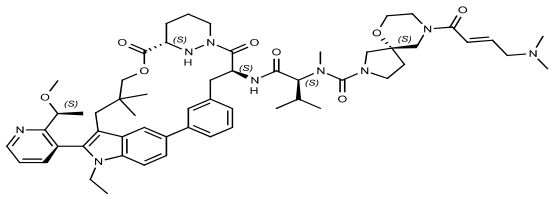
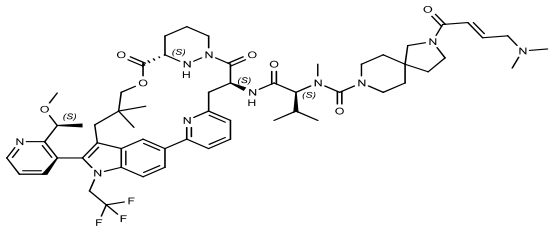
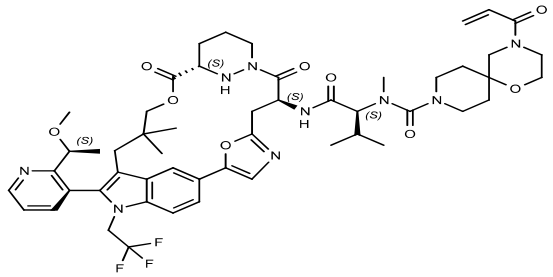
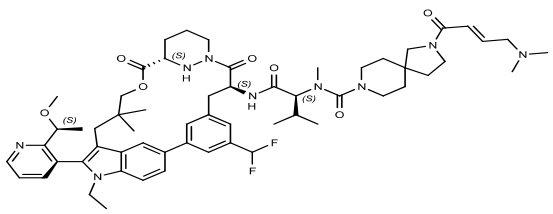
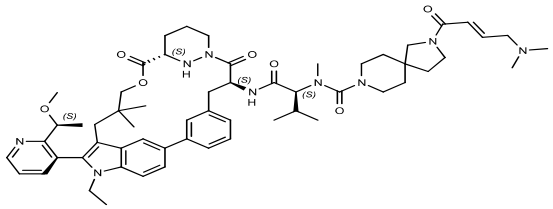
x#	Structure
6	
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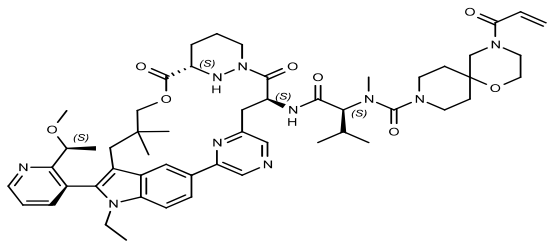
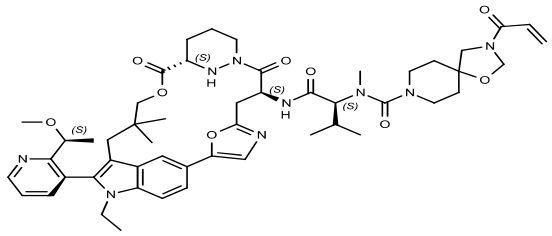
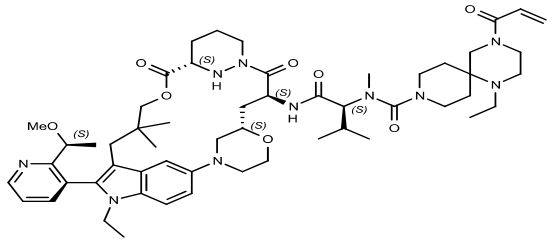
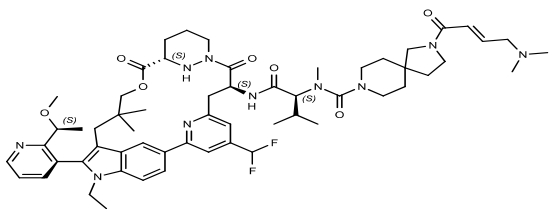
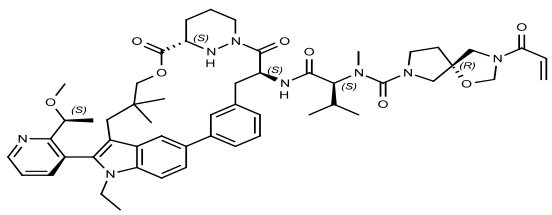
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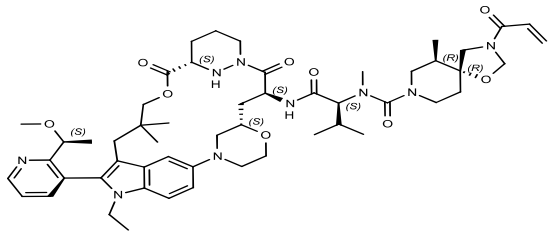
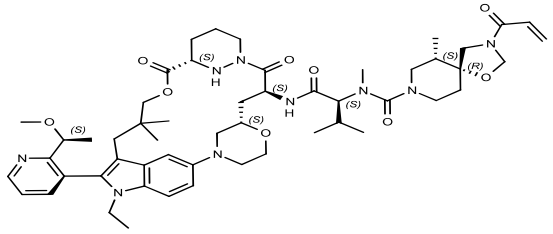
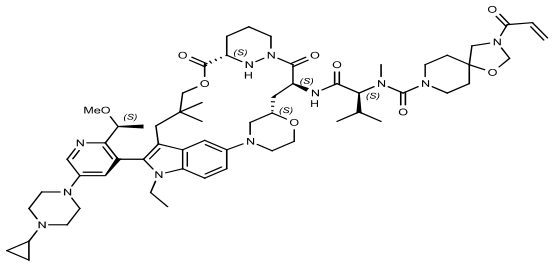
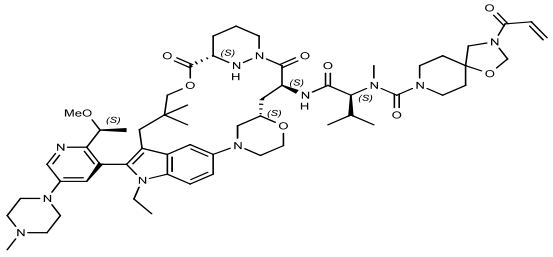
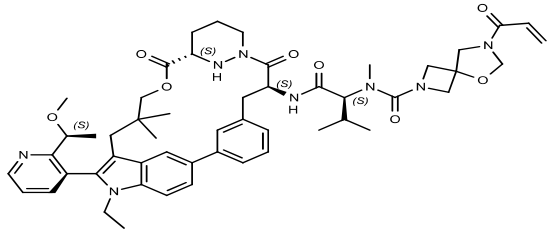
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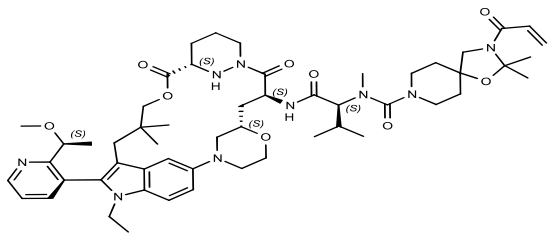
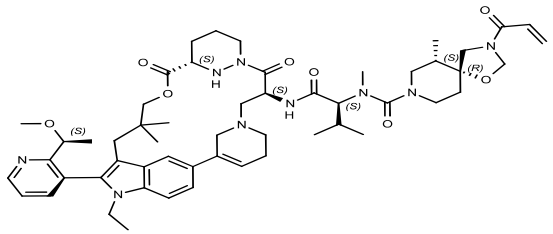
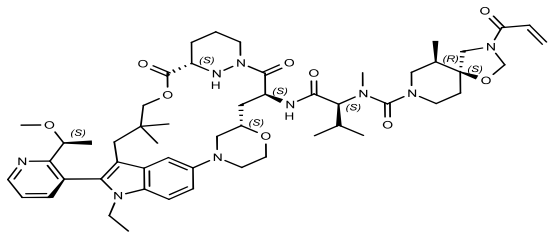
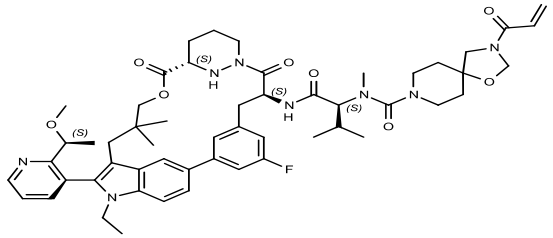
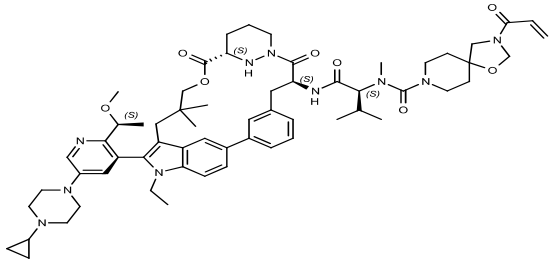
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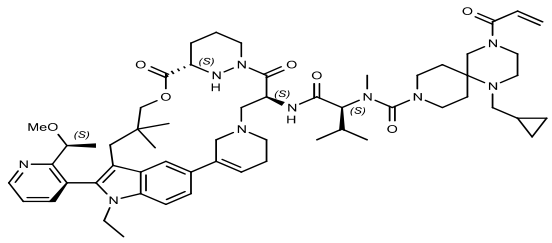
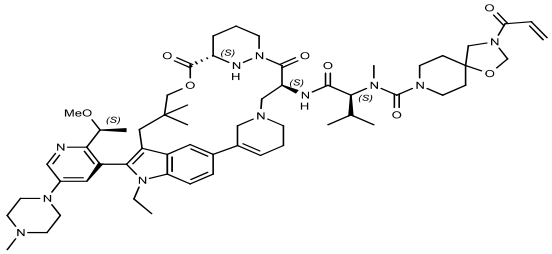
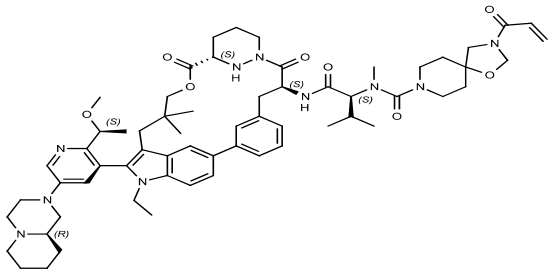
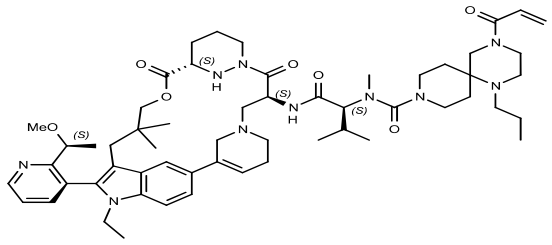
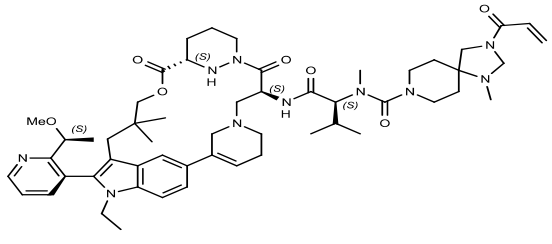
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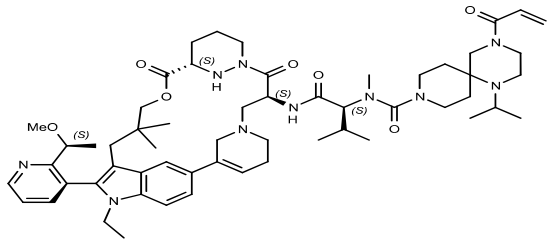
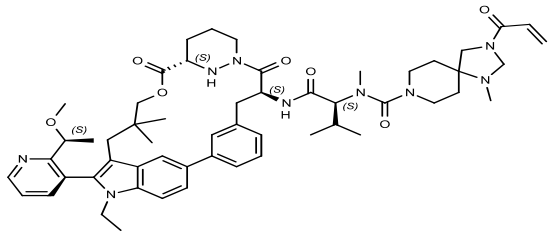
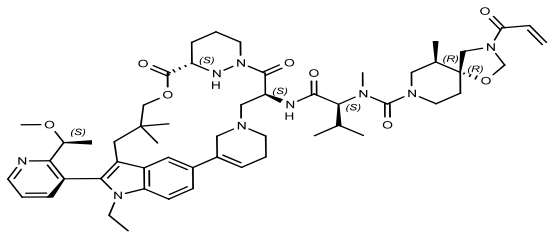
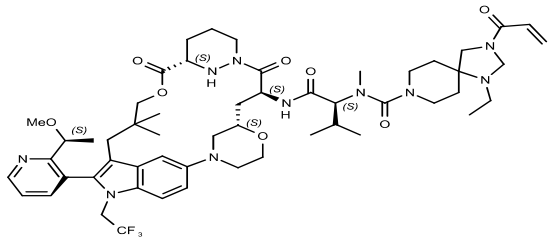
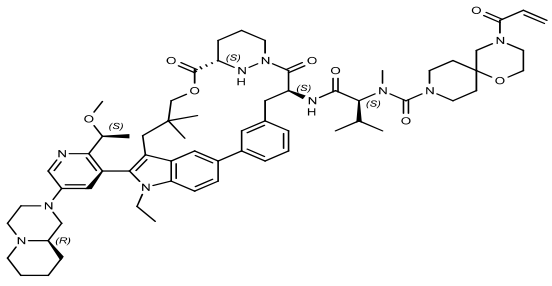
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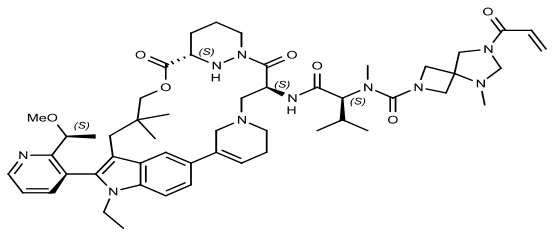
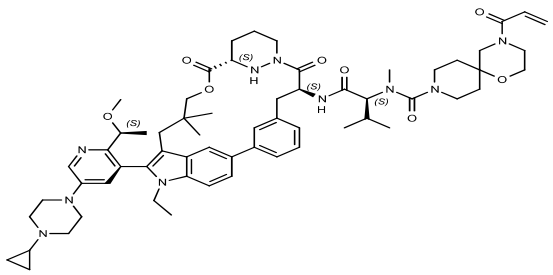
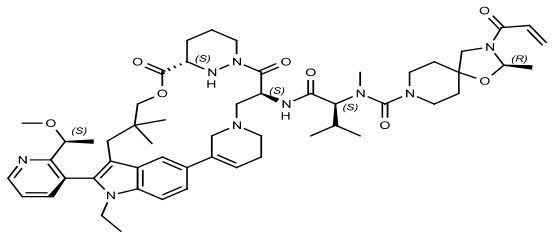
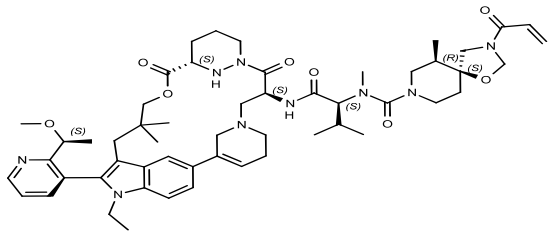
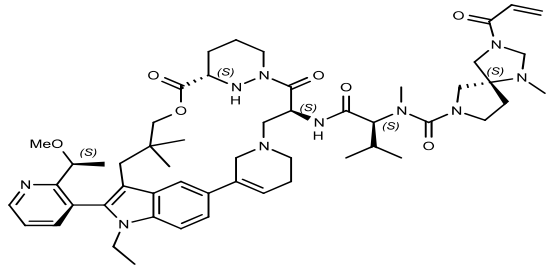
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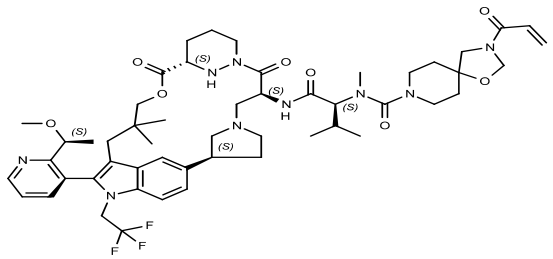
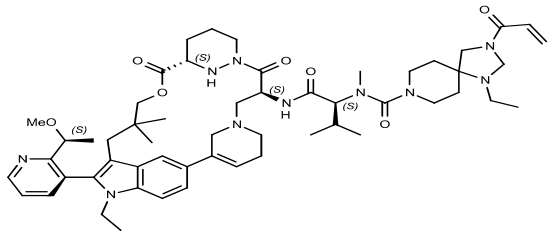
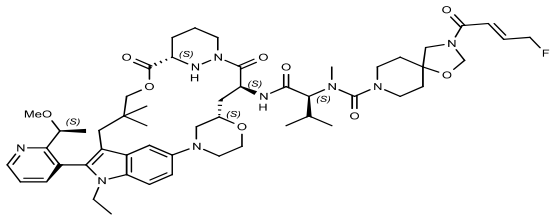
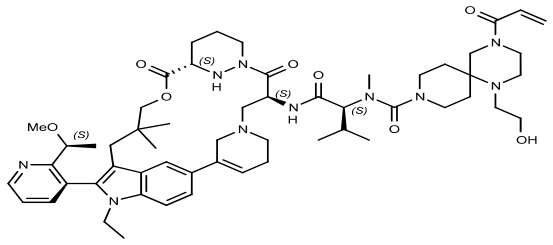
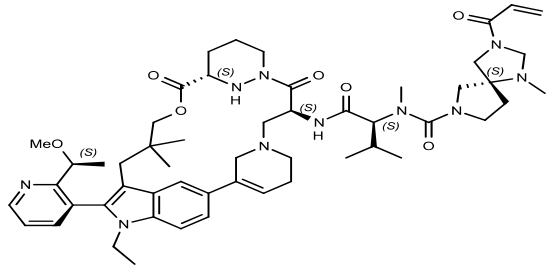
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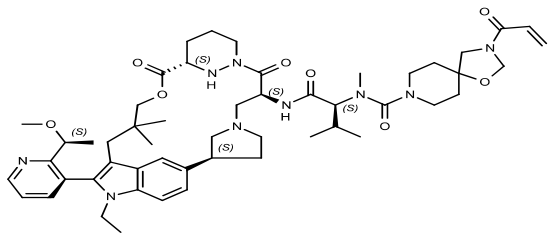
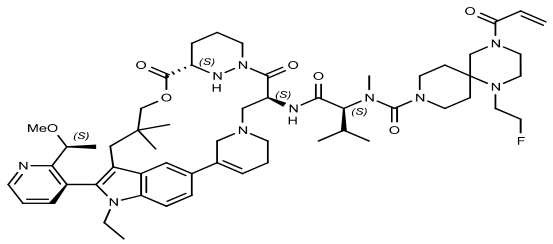
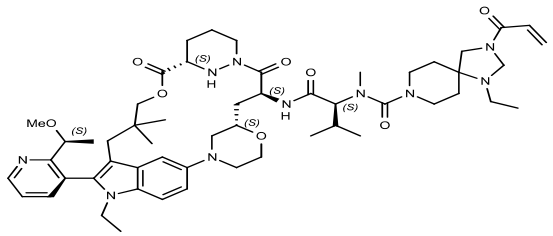
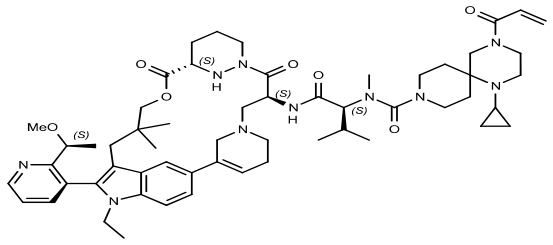
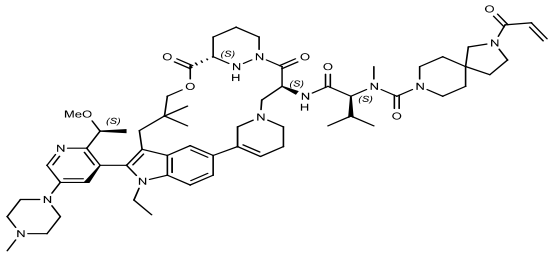
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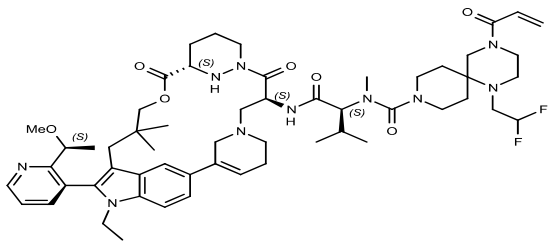
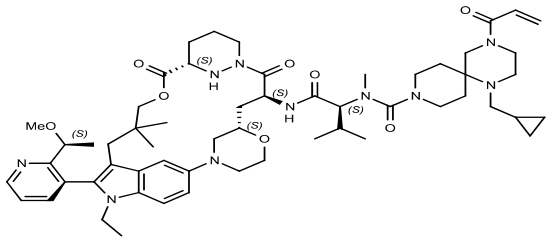
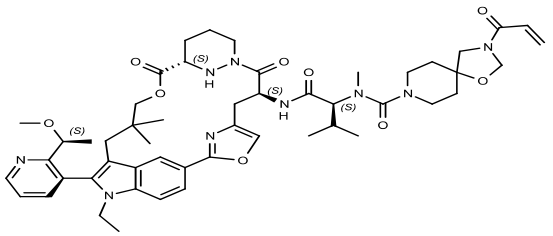
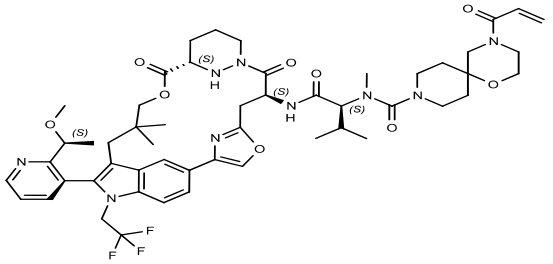
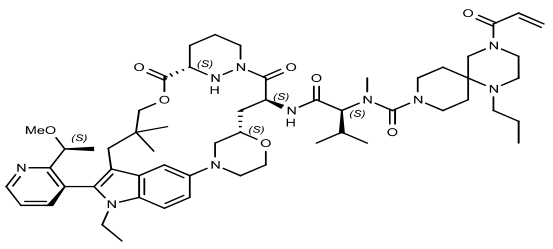
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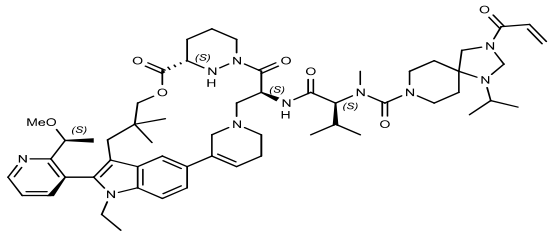
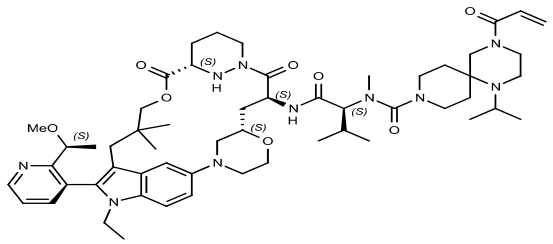
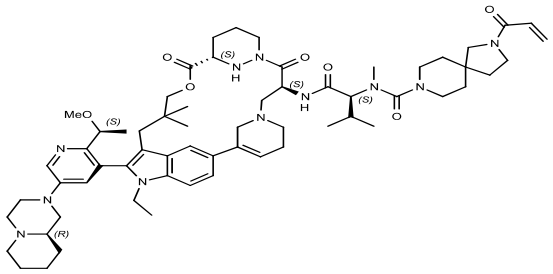
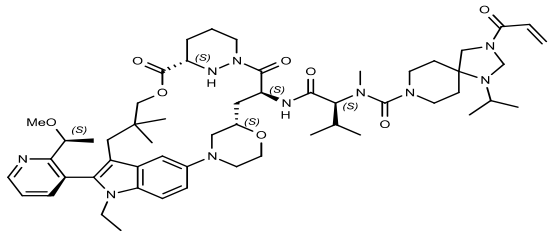
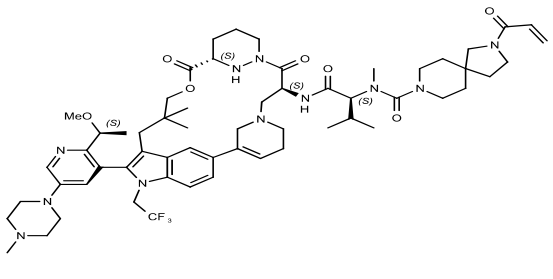
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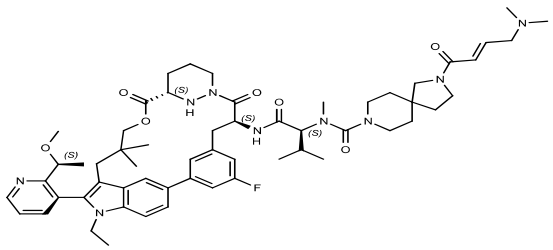
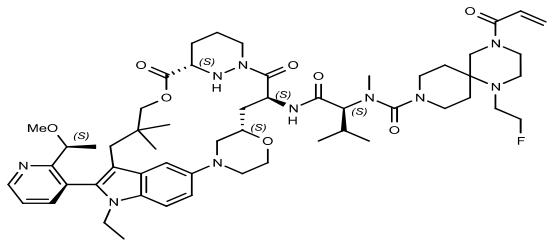
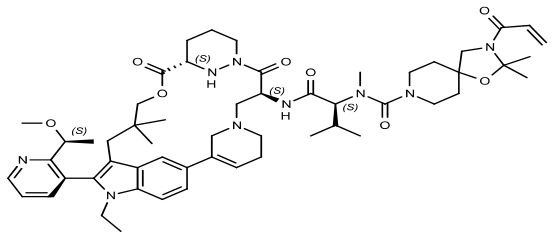
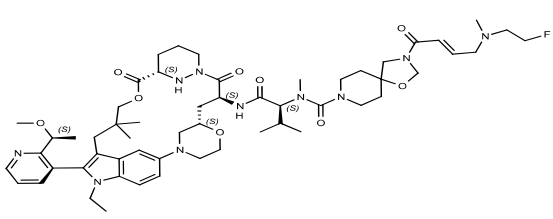
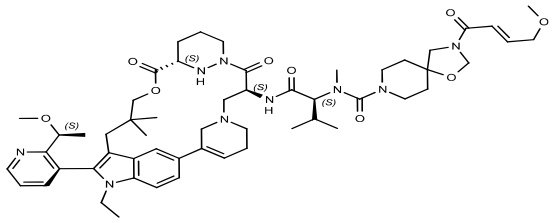
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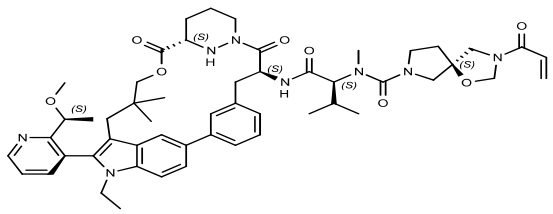
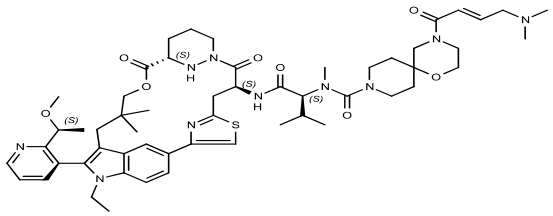
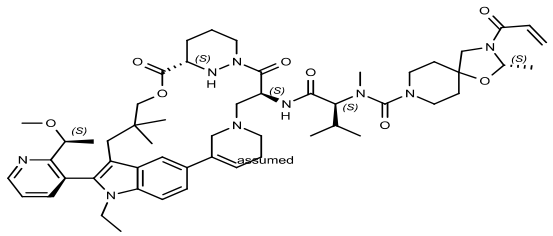
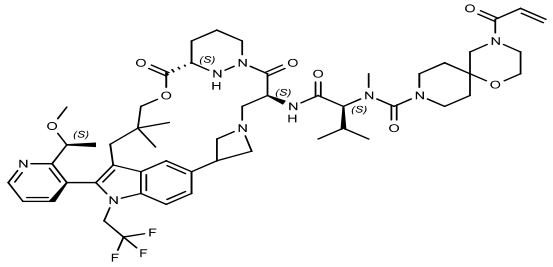
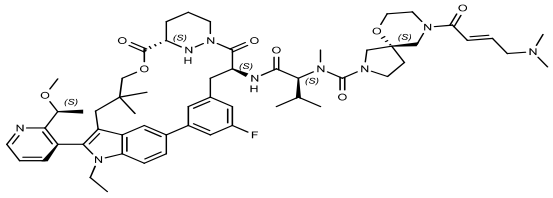
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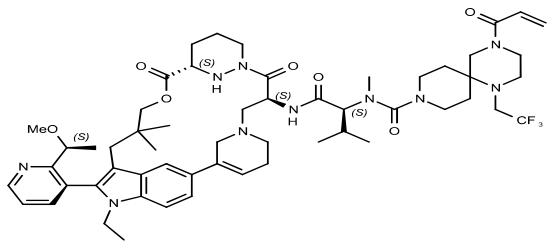
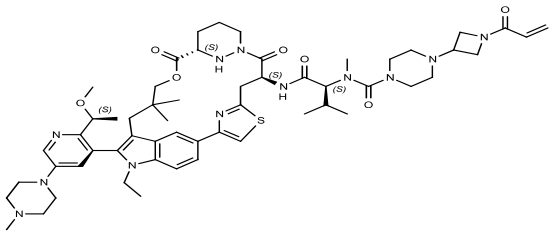
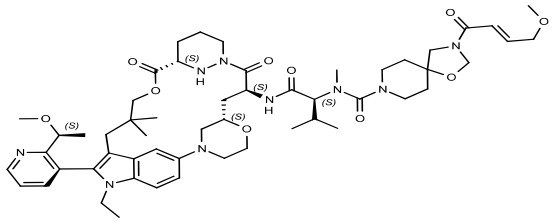
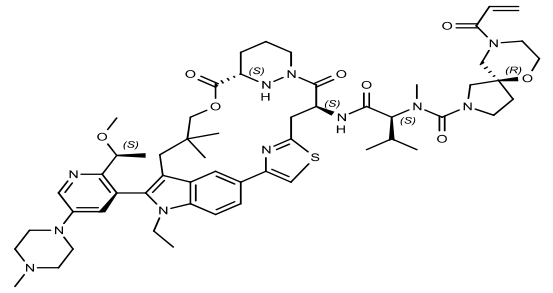
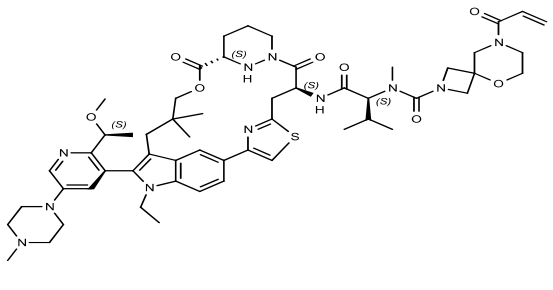
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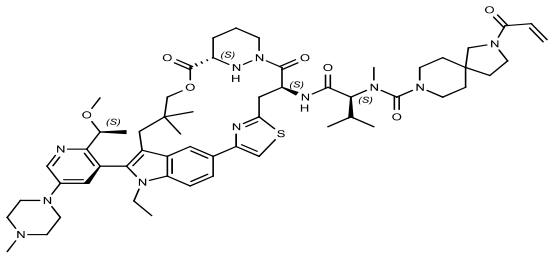
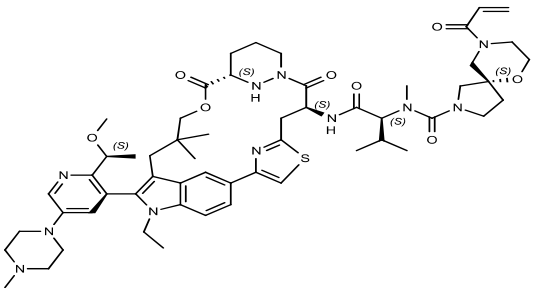
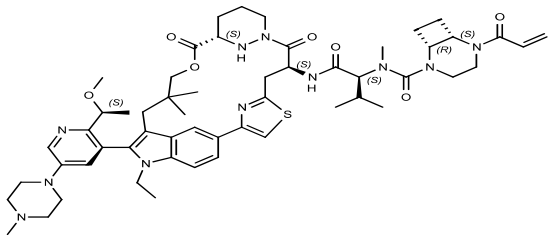
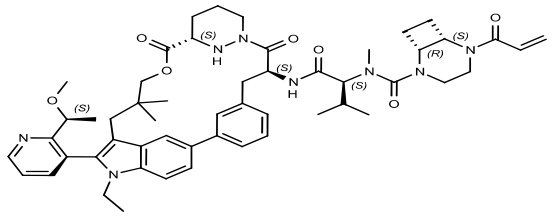
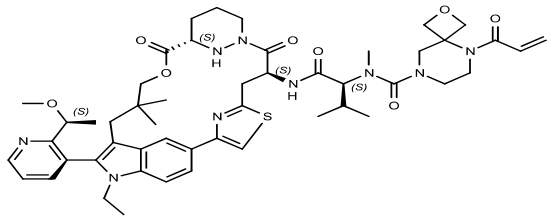
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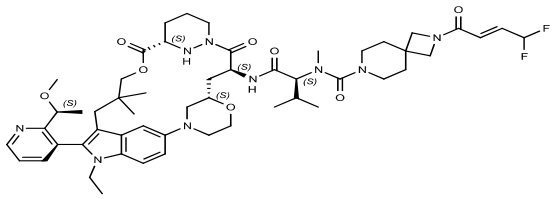
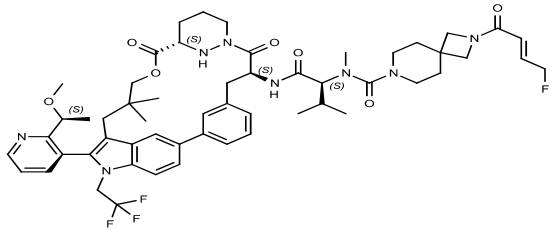
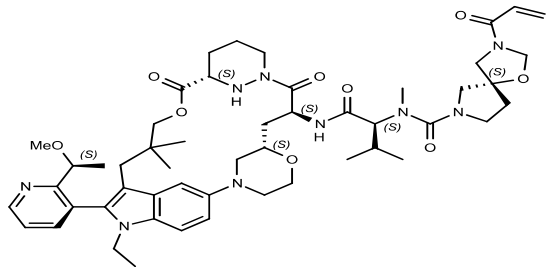
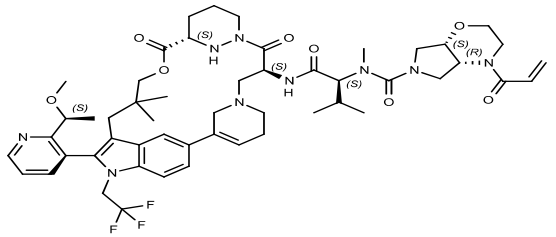
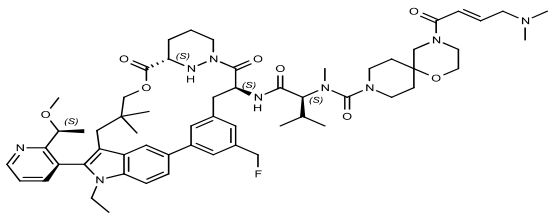
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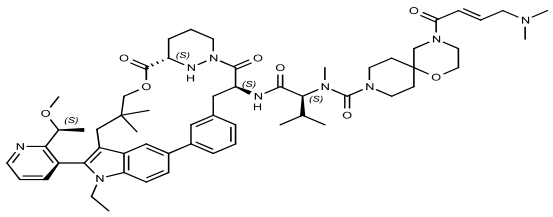
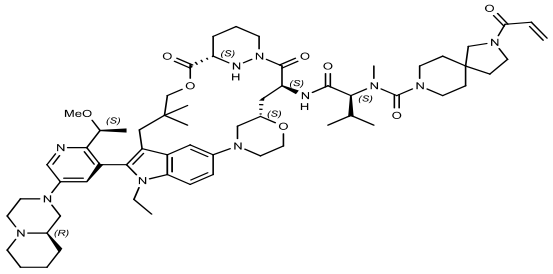
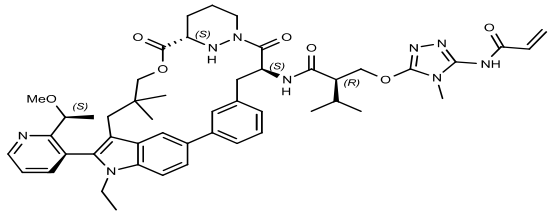
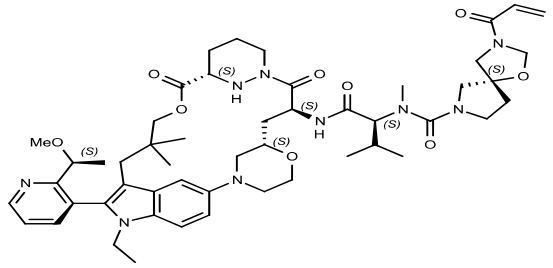
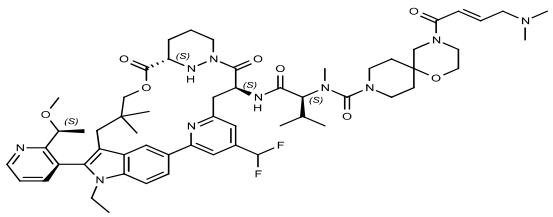
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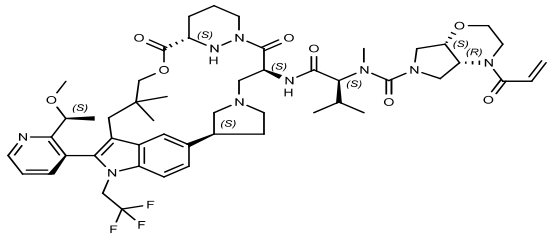
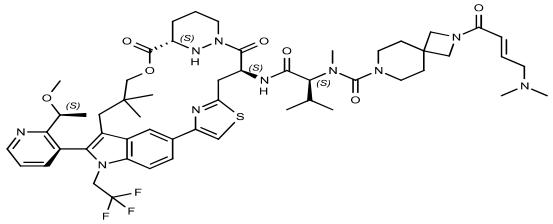
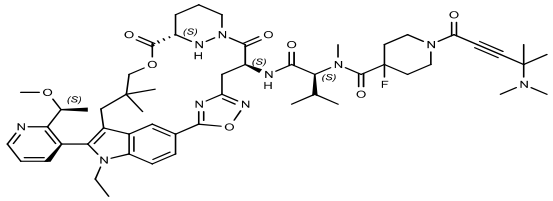
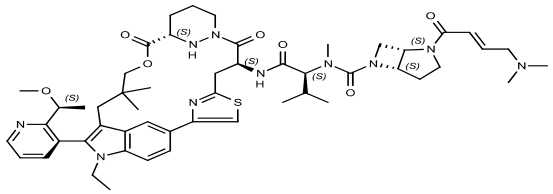
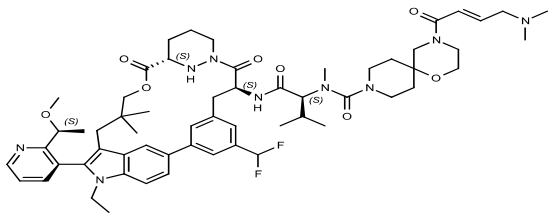
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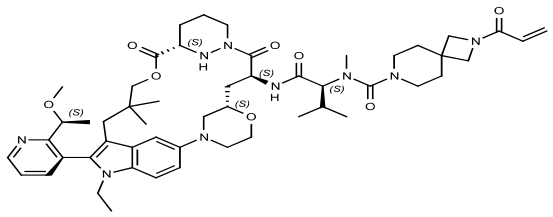
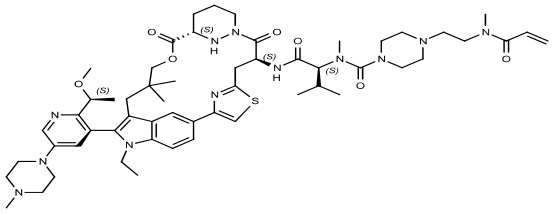
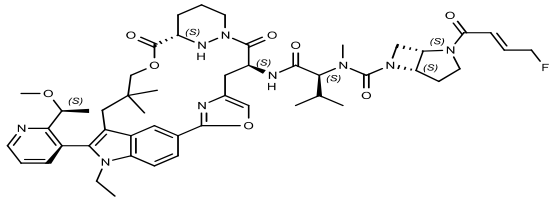
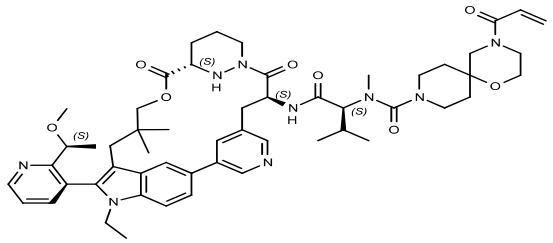
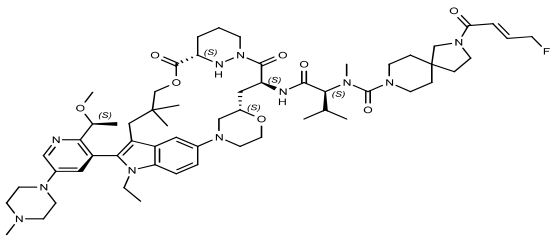
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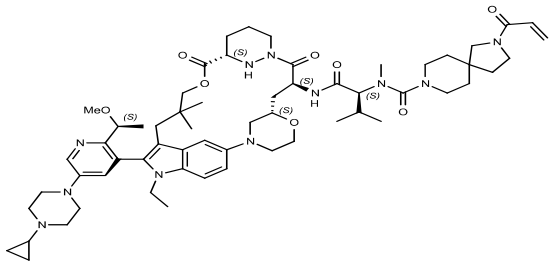
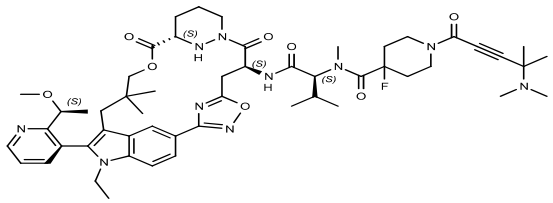
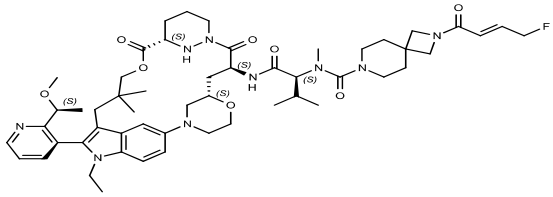
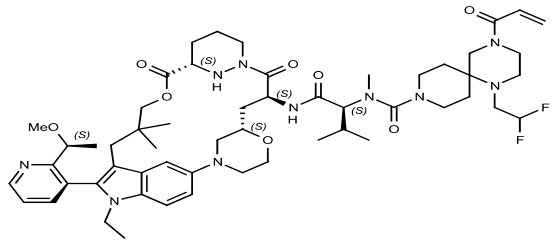
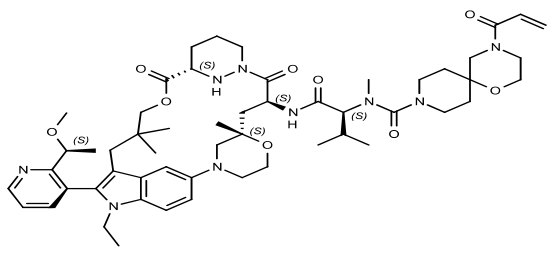
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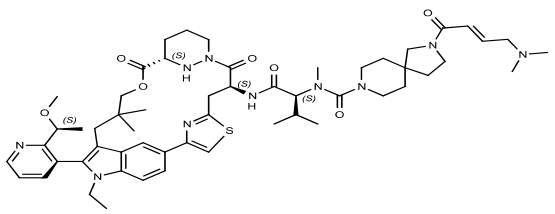
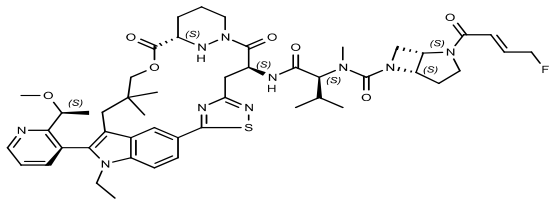
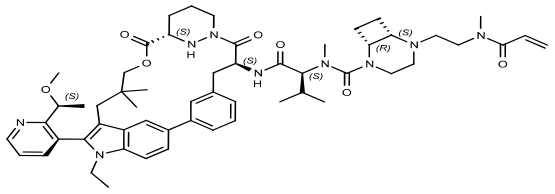
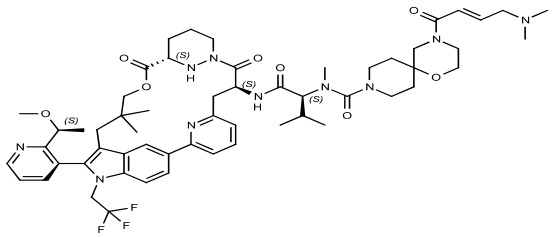
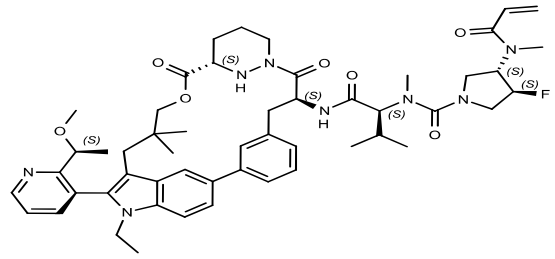
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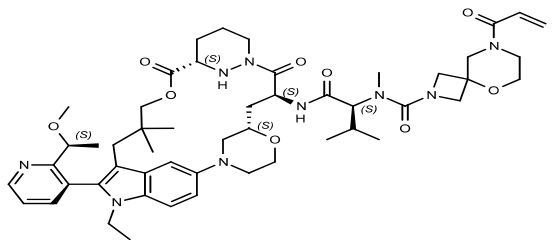
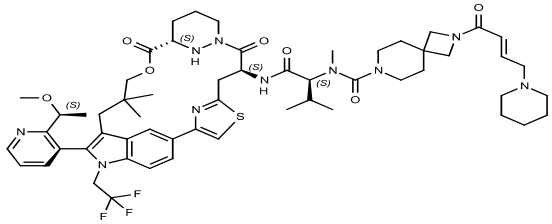
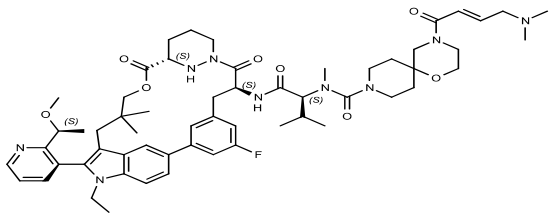
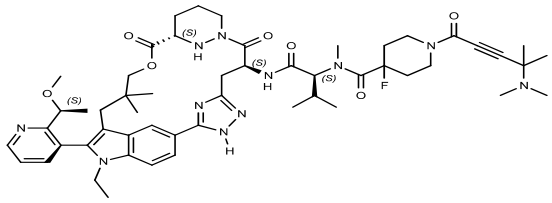
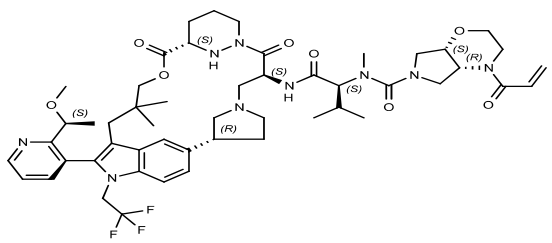
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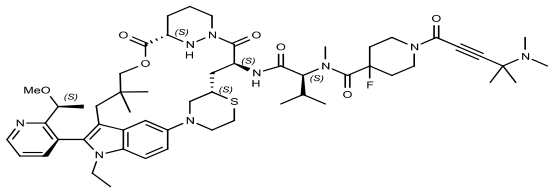
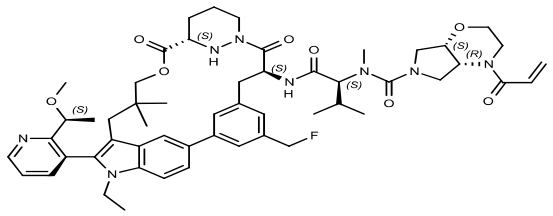
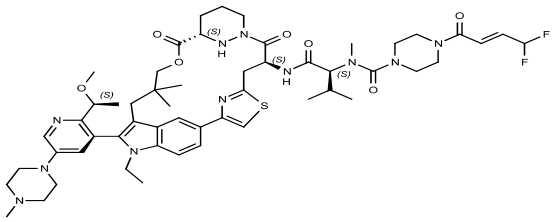
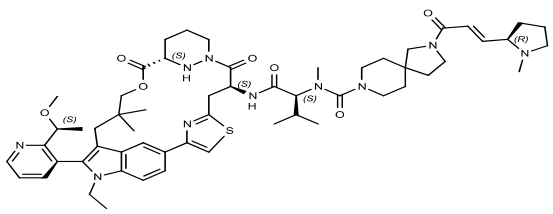
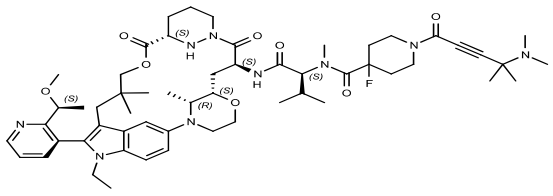
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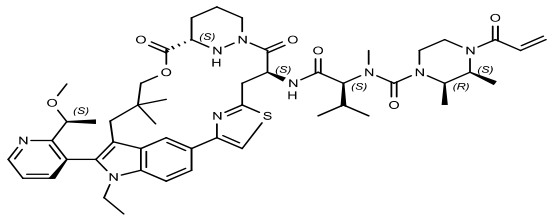
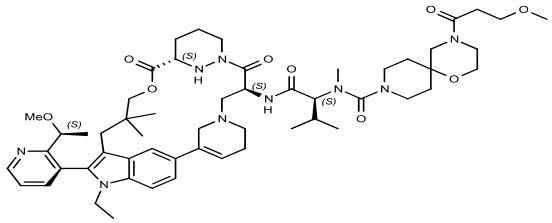
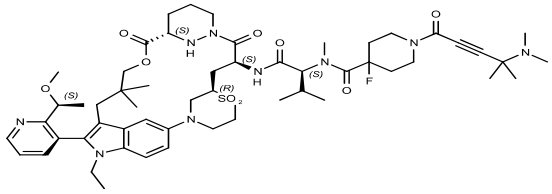
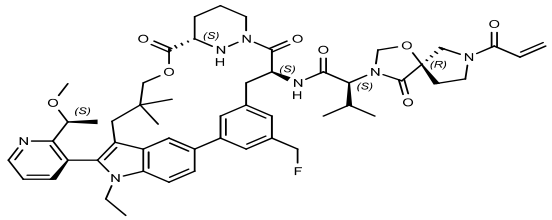
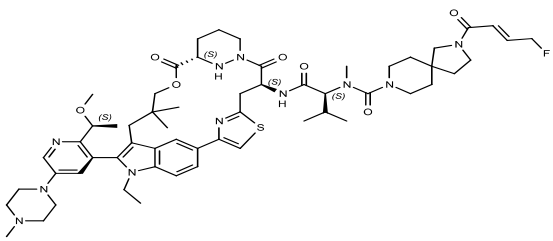
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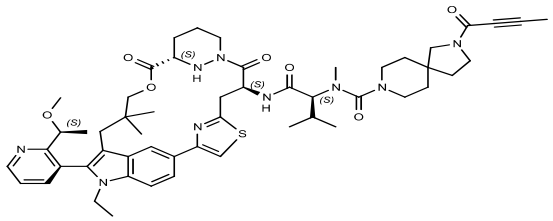
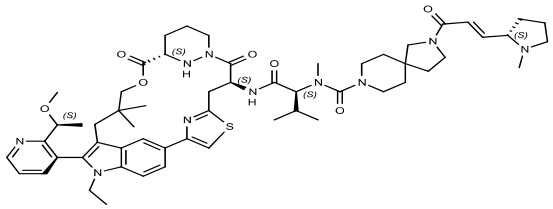
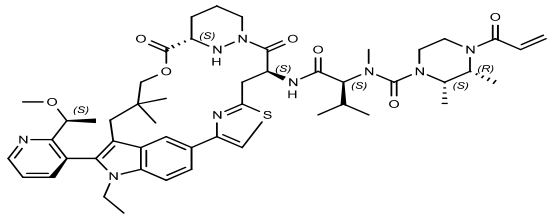
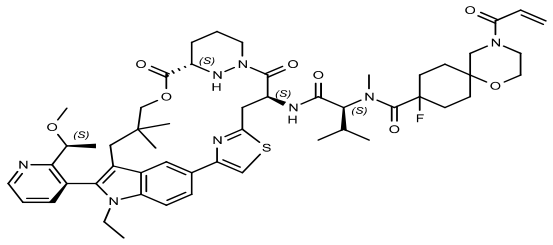
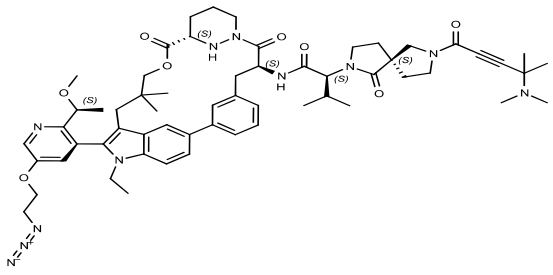
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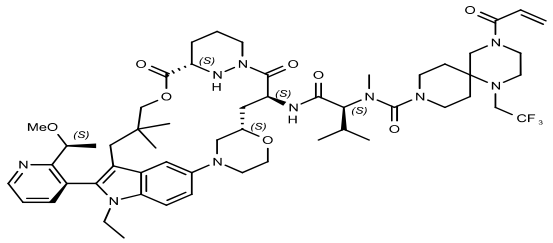
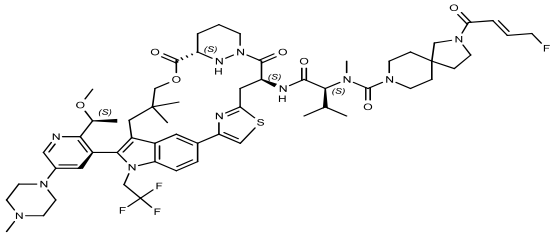
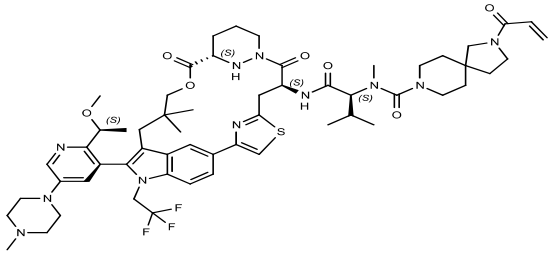
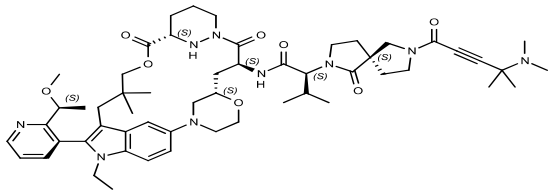
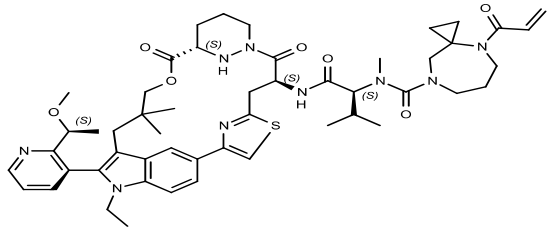
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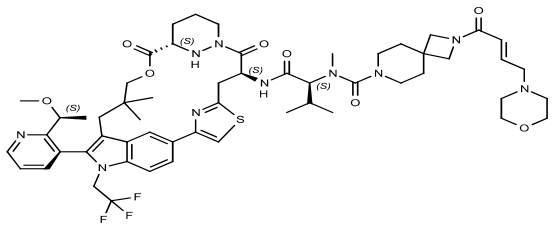
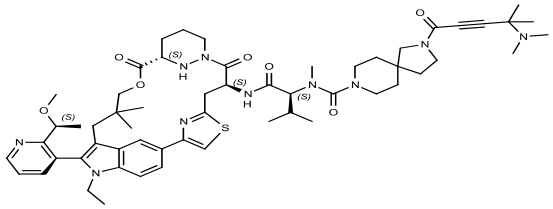
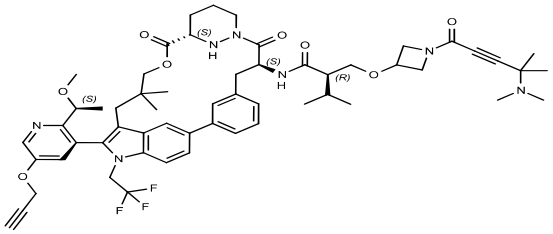
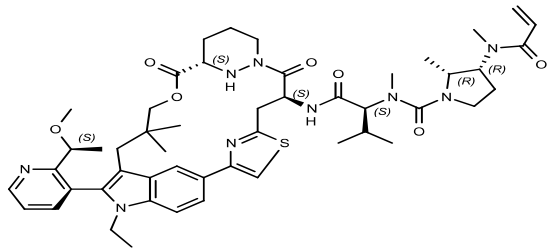
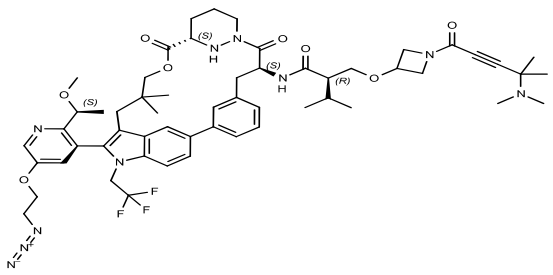
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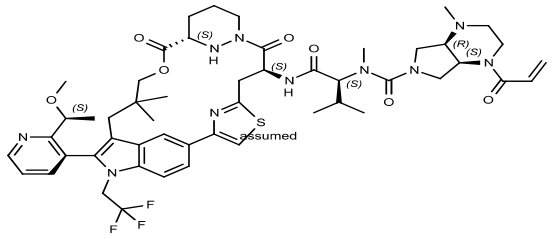
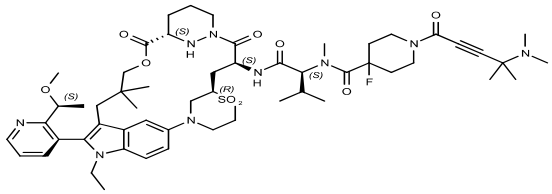
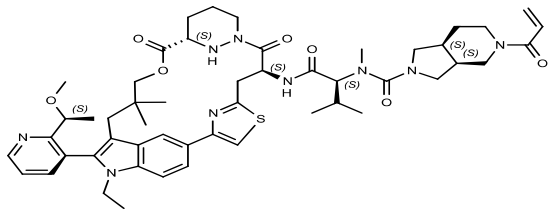
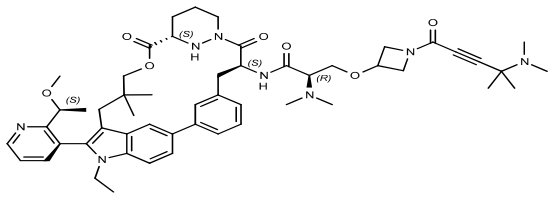
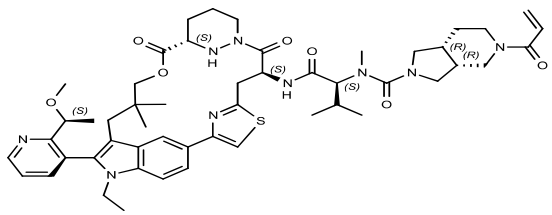
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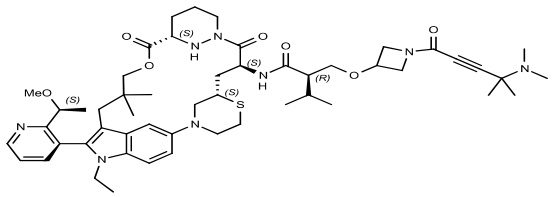
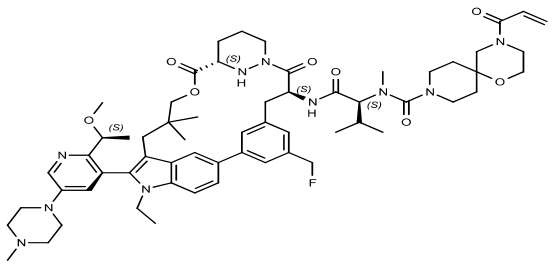
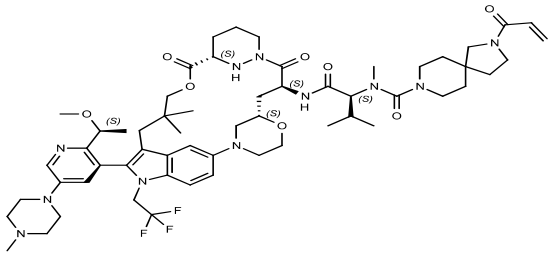
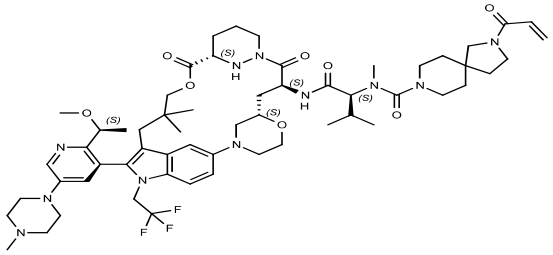
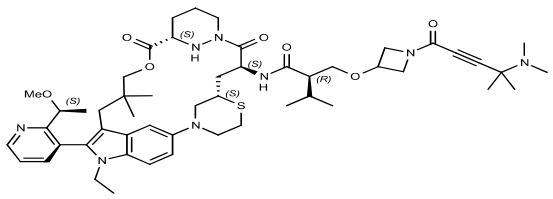
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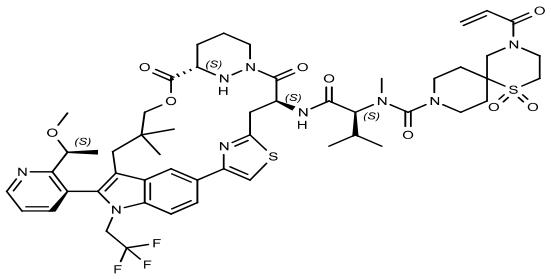
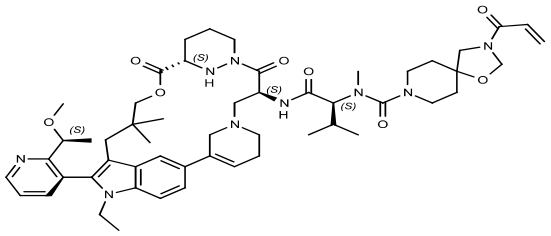
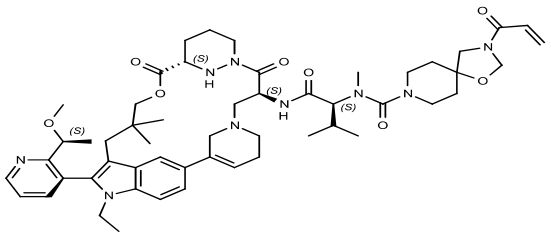
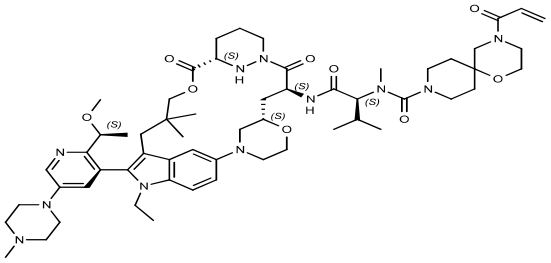
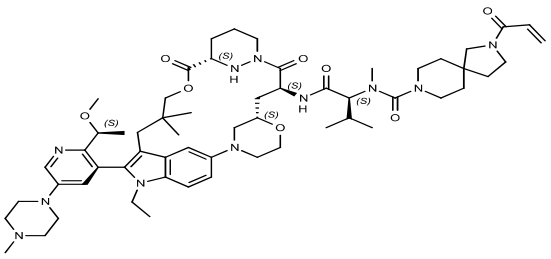
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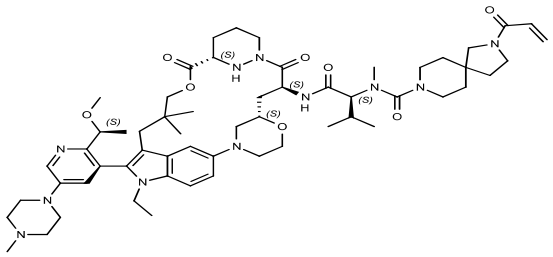
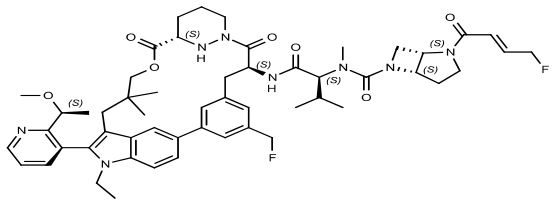
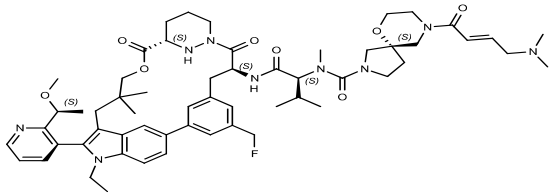
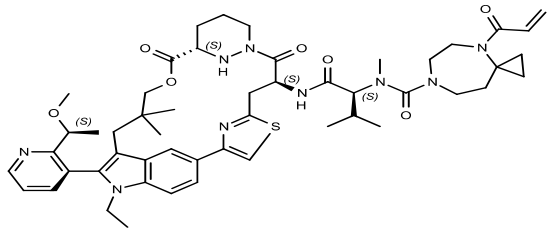
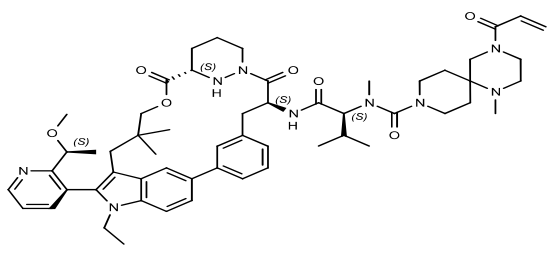
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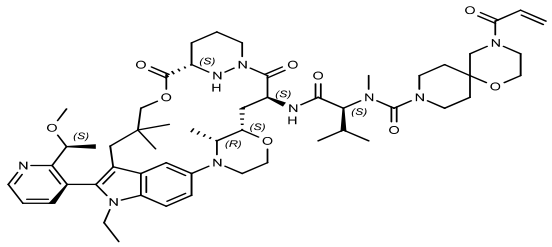
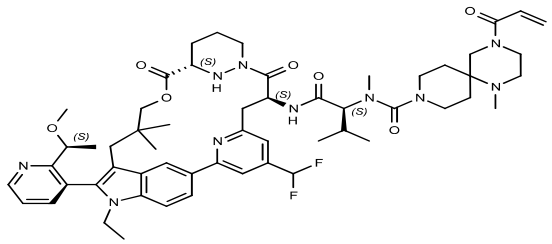
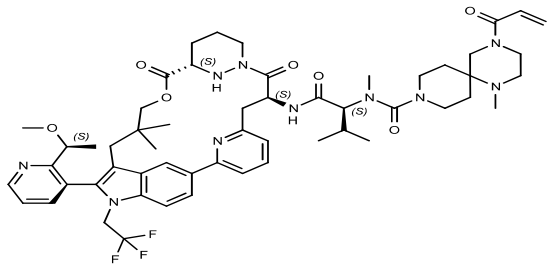
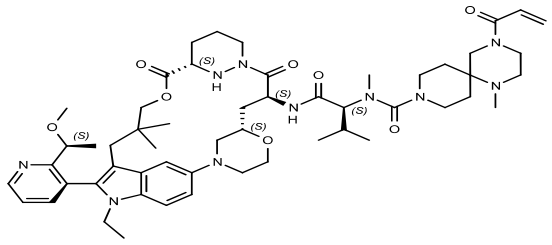
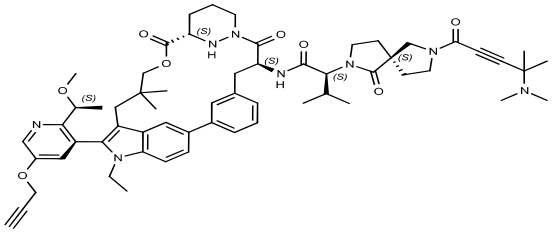
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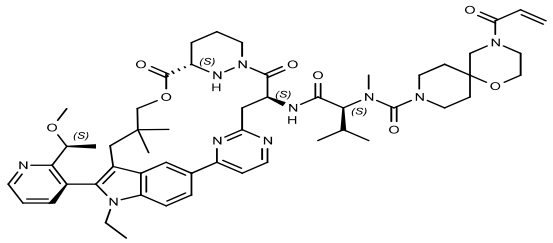
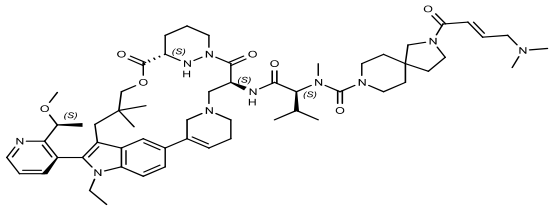
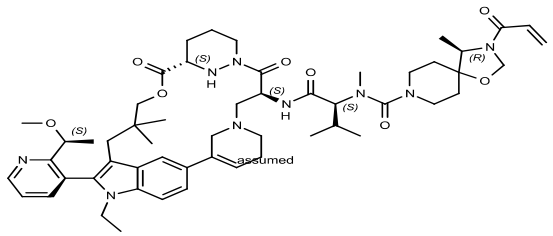
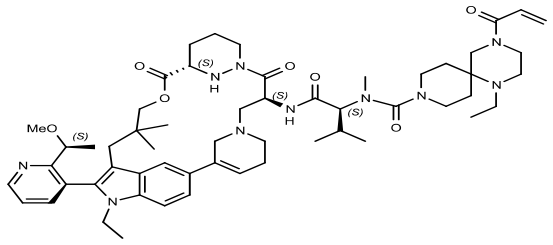
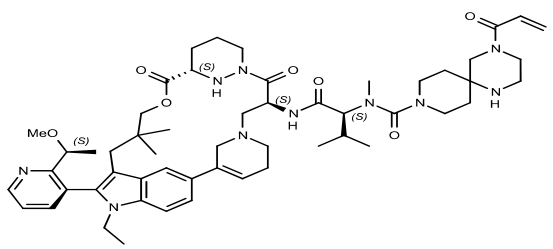
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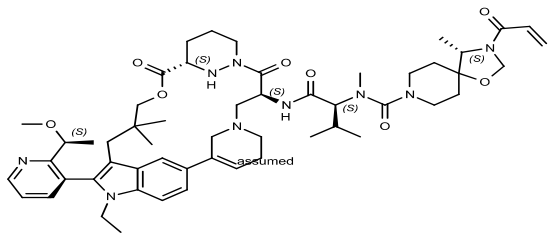
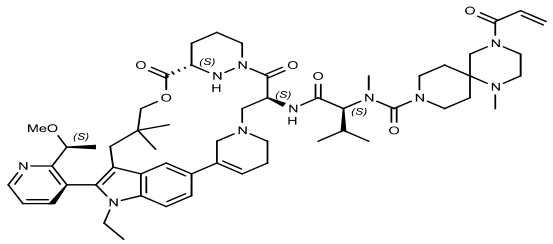
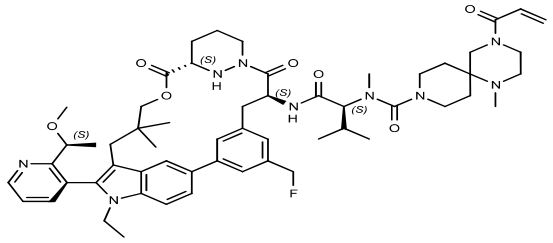
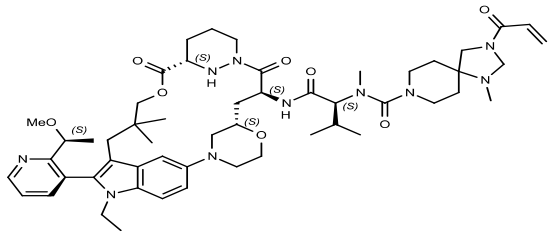
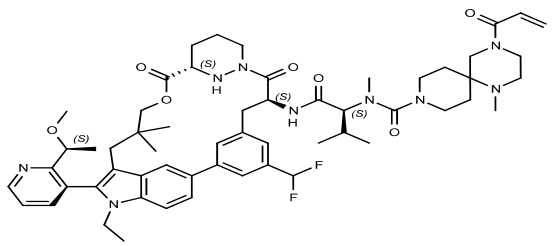
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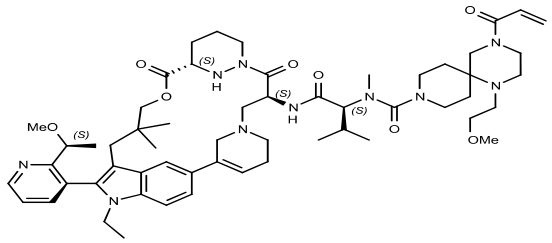
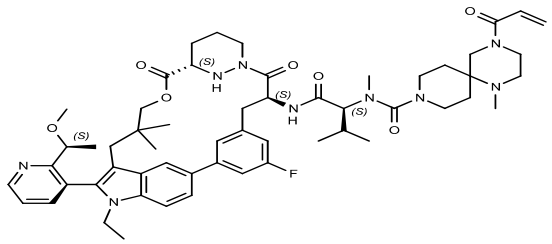
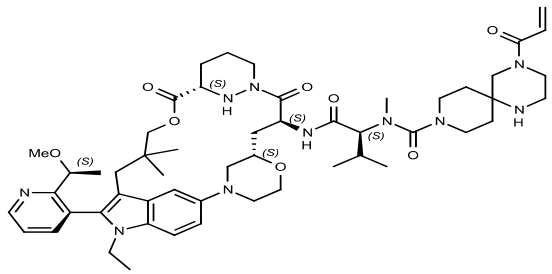
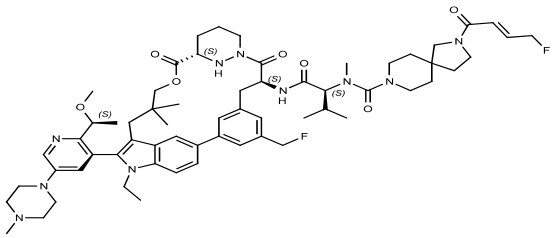
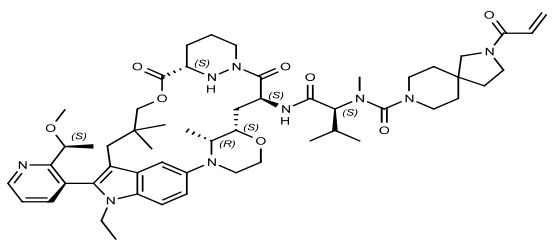
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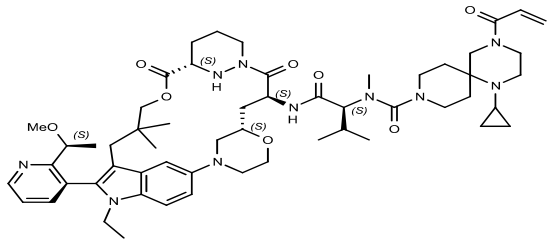
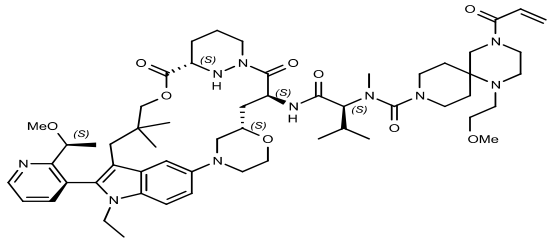
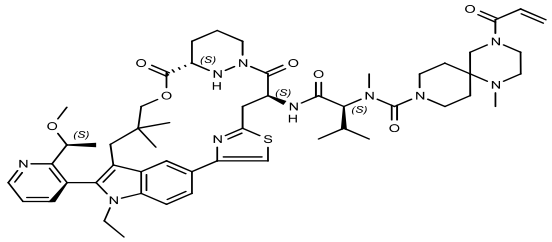
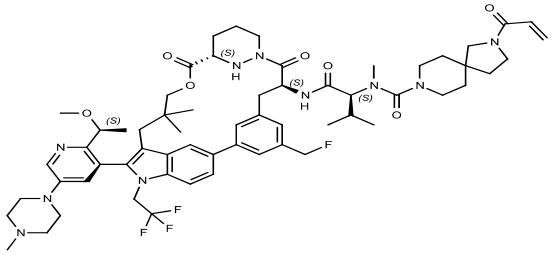
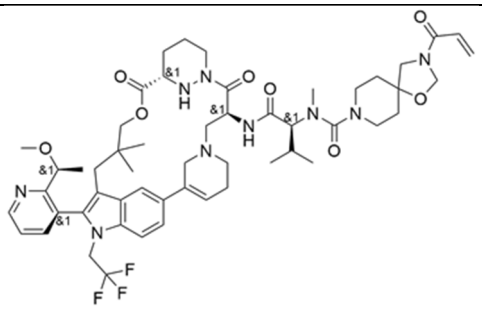
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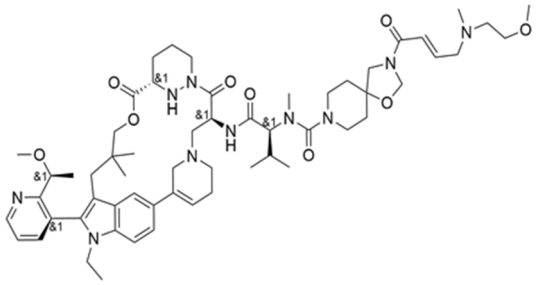
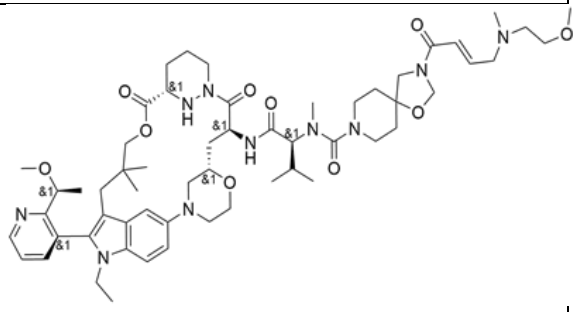
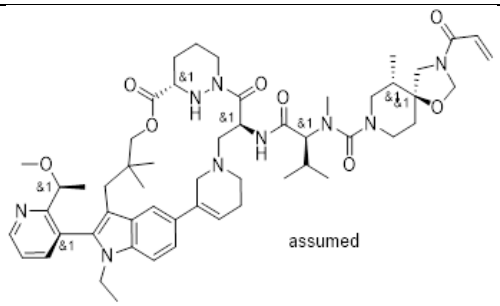
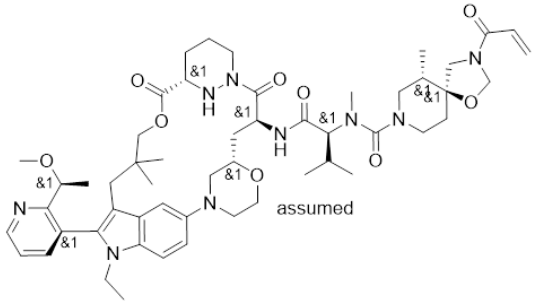
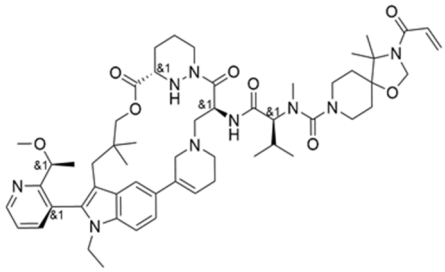
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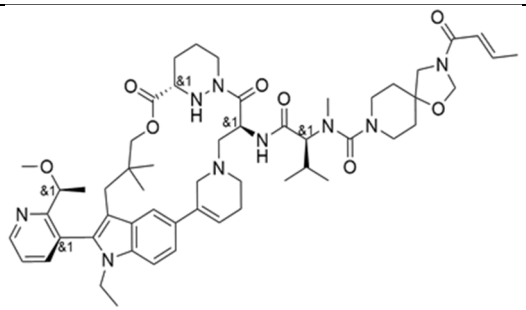
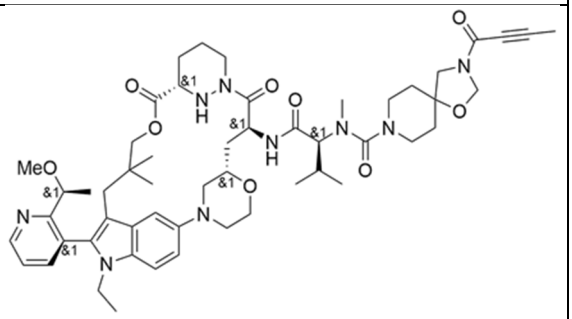
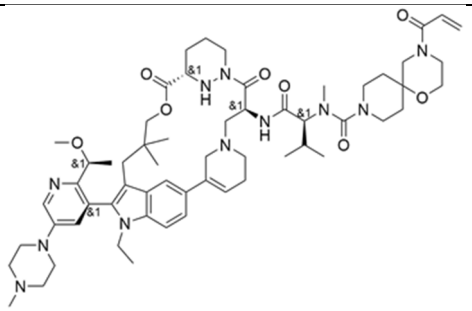
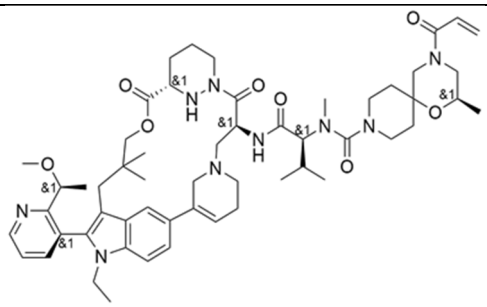
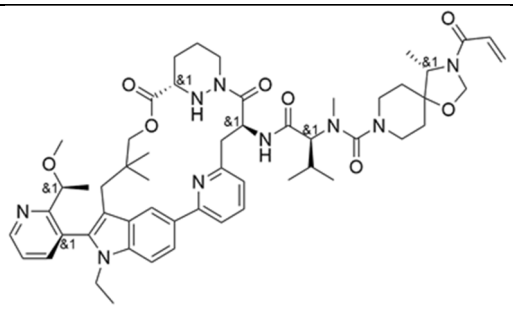
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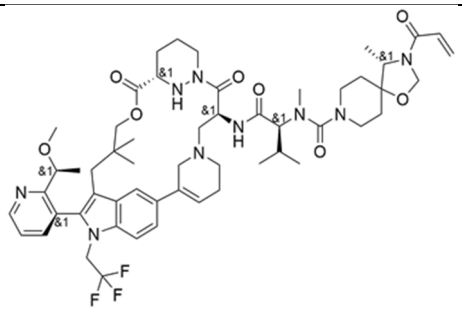
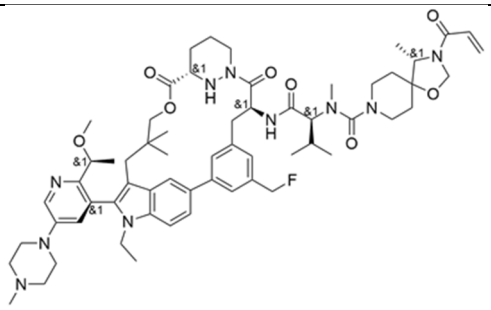
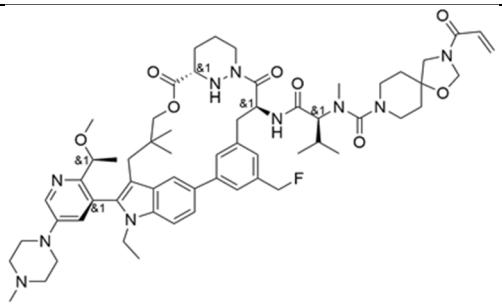
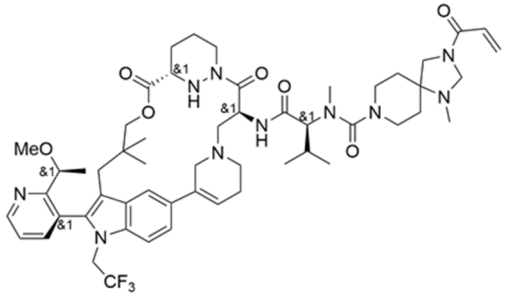
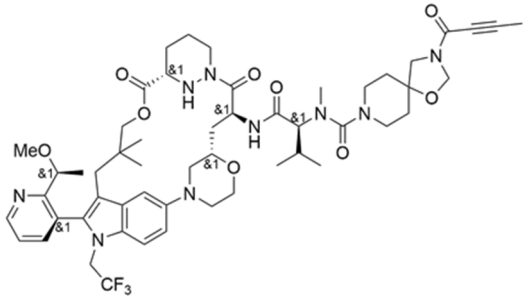
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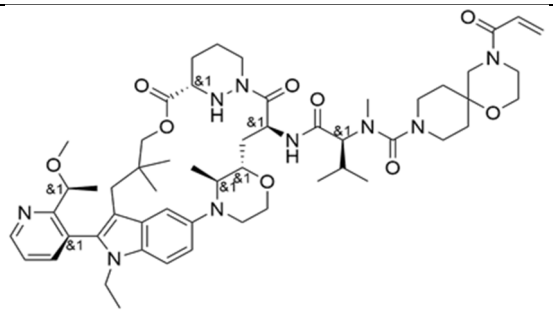
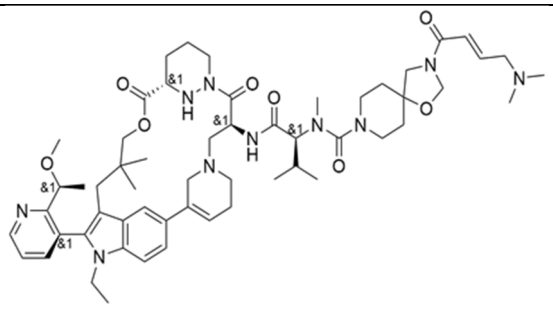
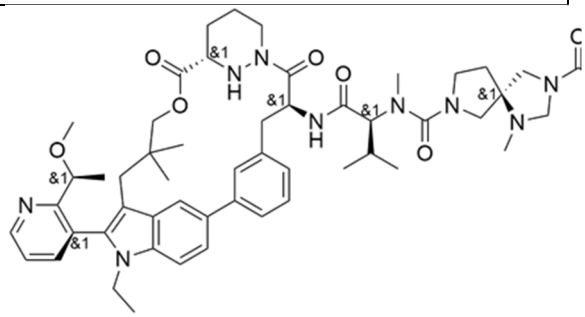
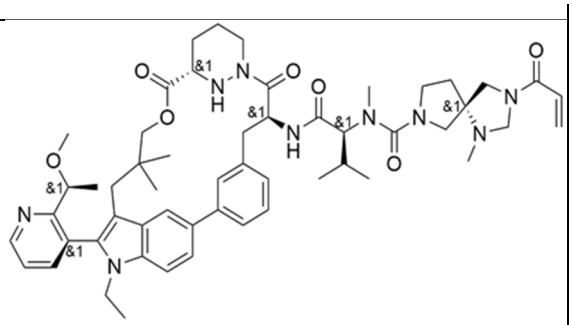
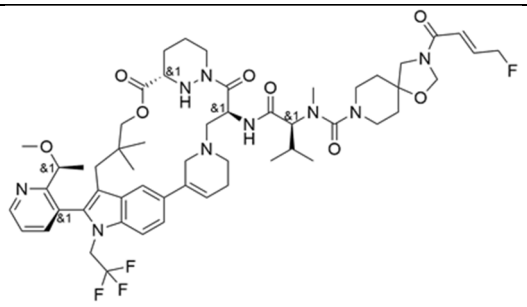
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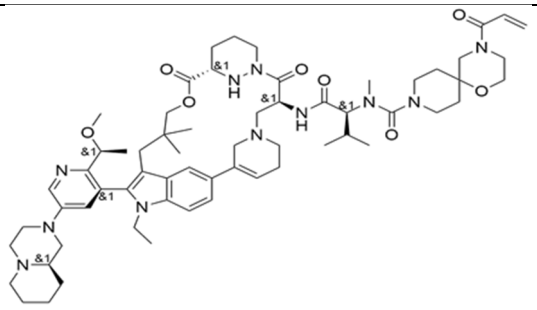
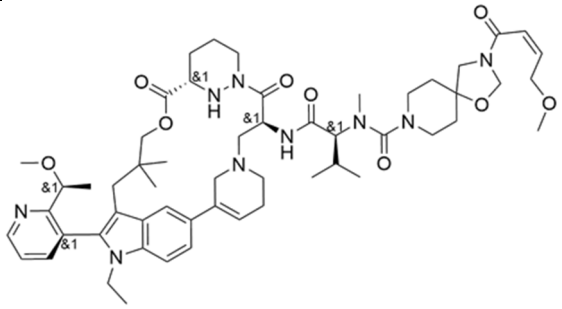
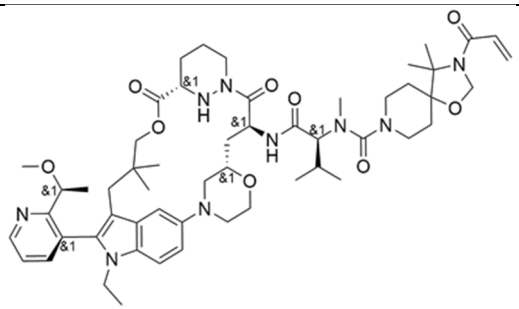
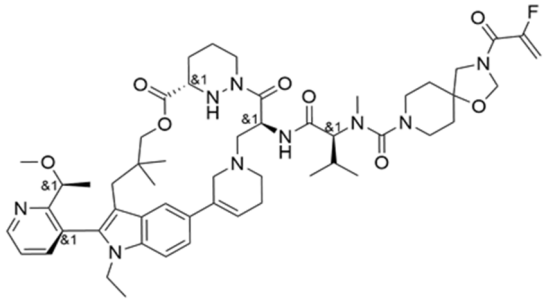
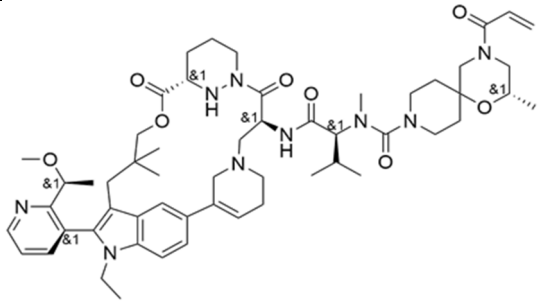
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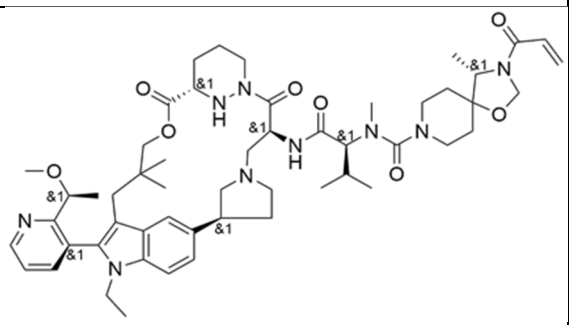
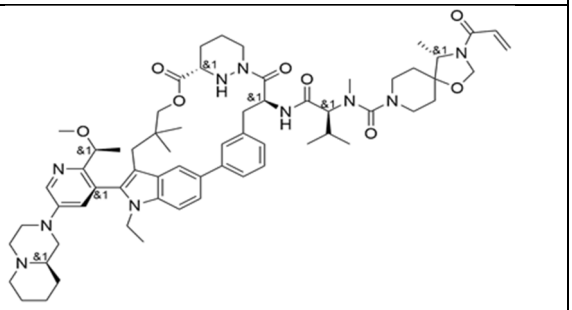
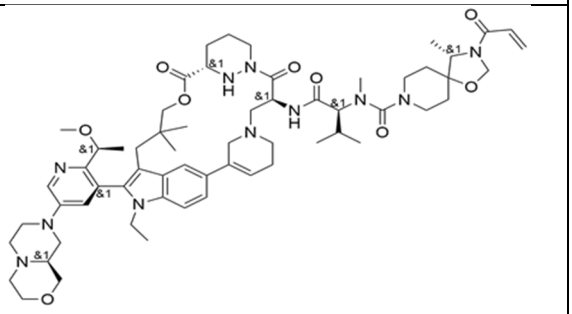
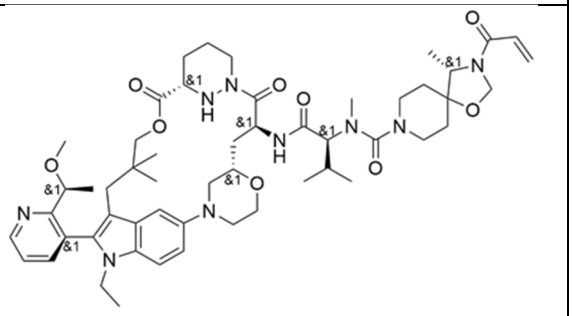
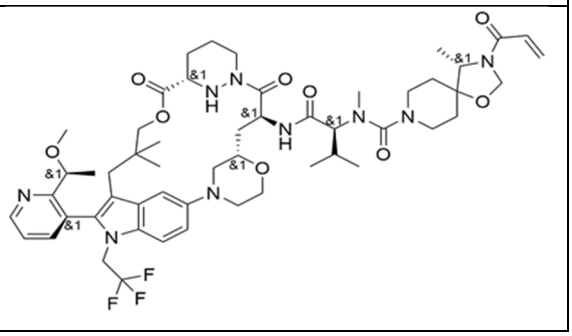
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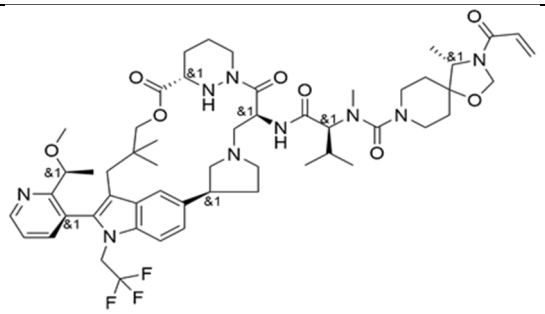
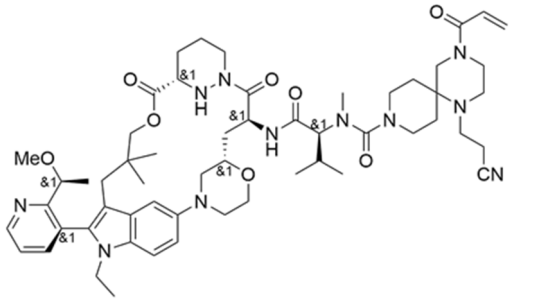
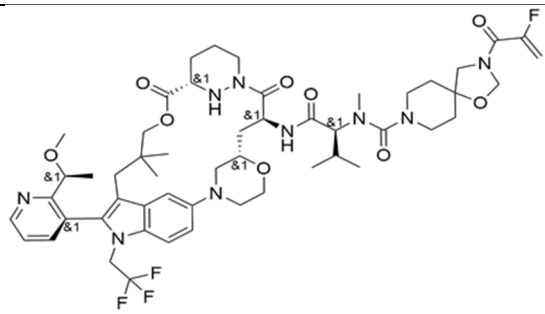
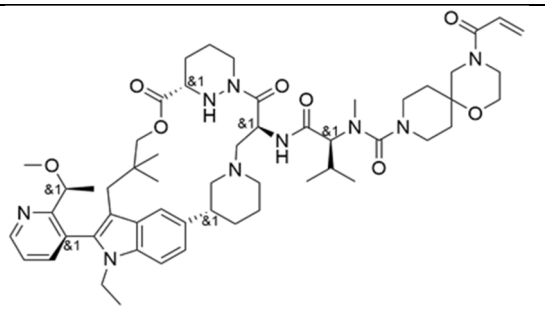
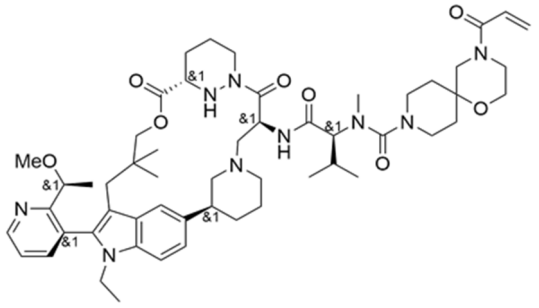
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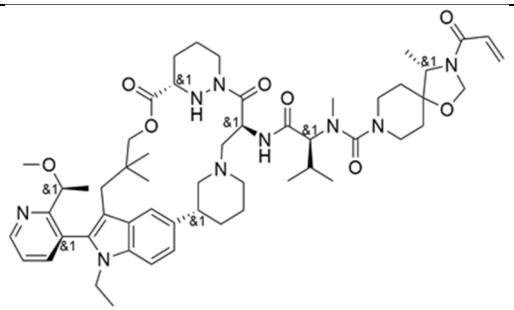
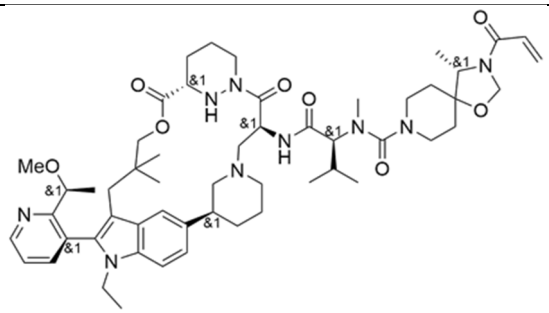
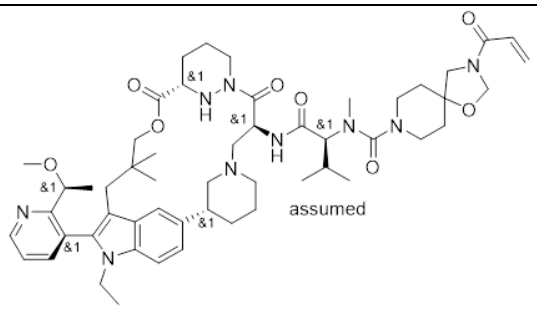
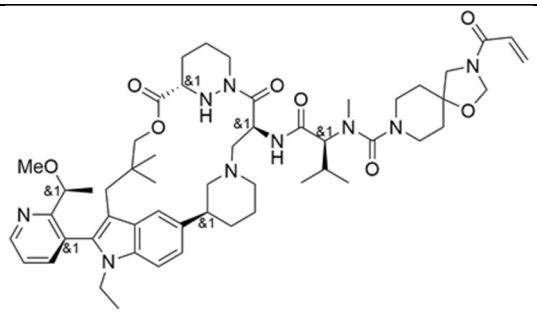
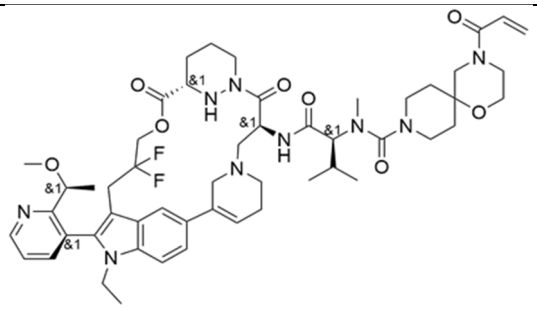
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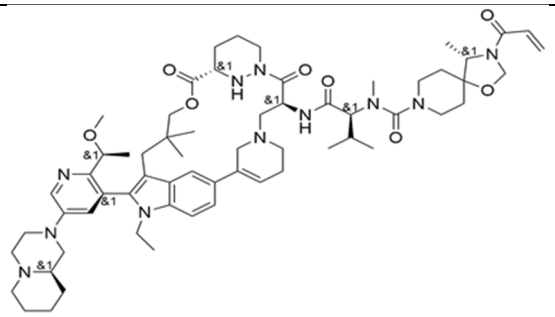
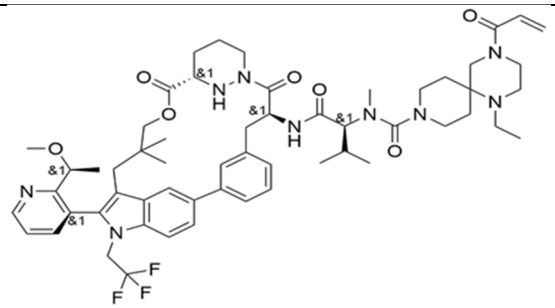
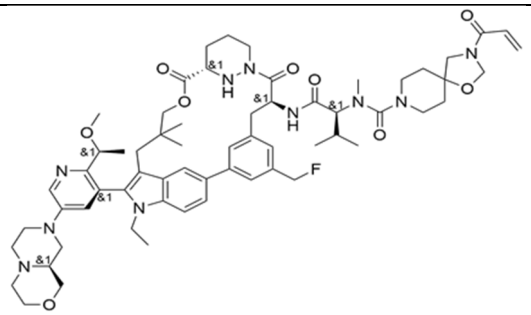
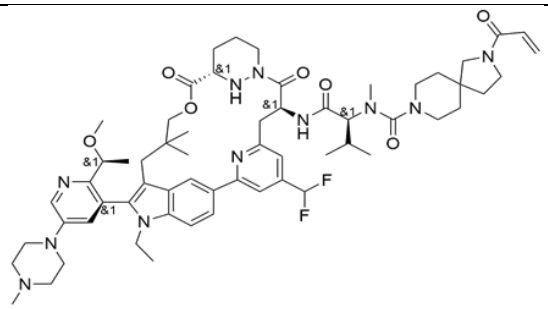
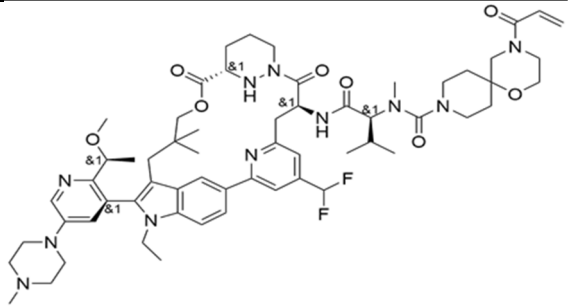
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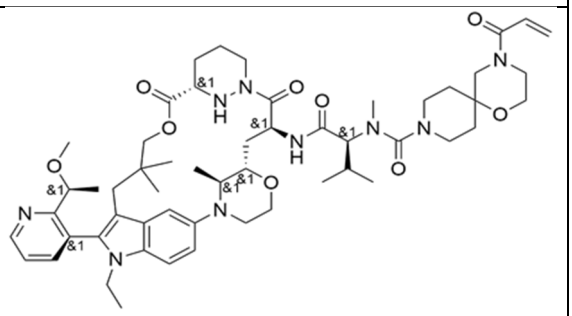
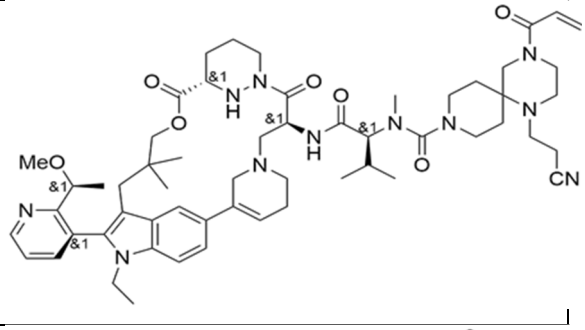
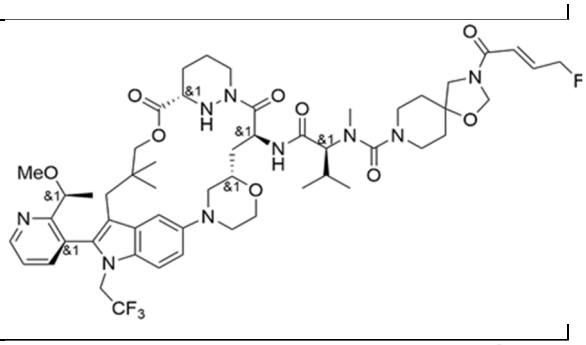
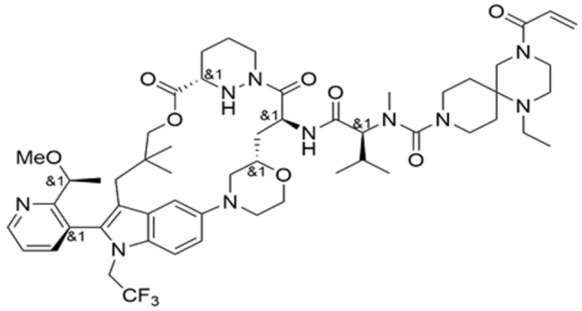
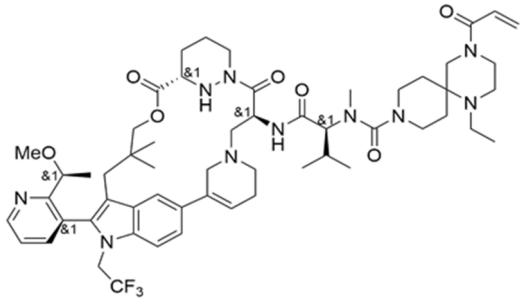
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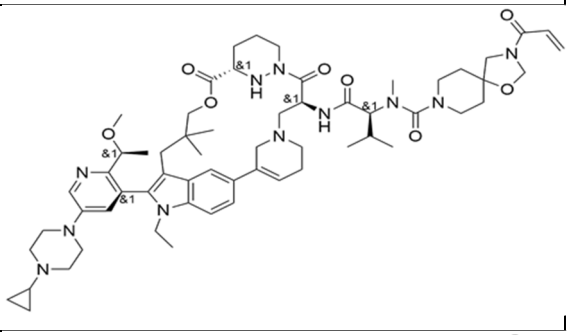
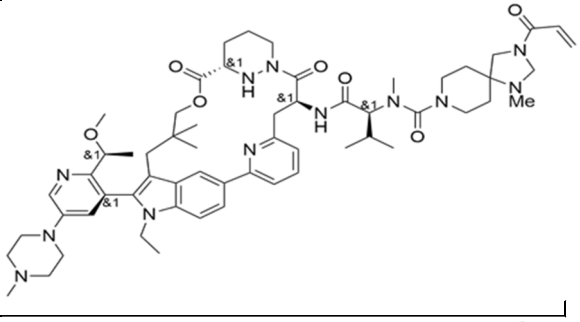
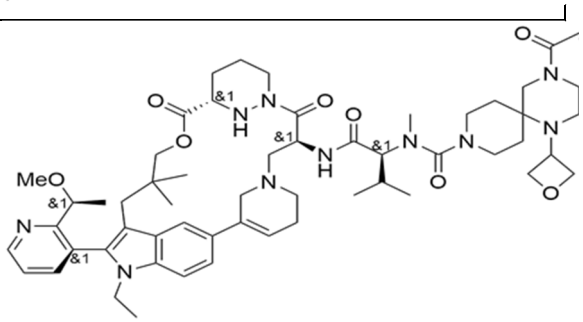
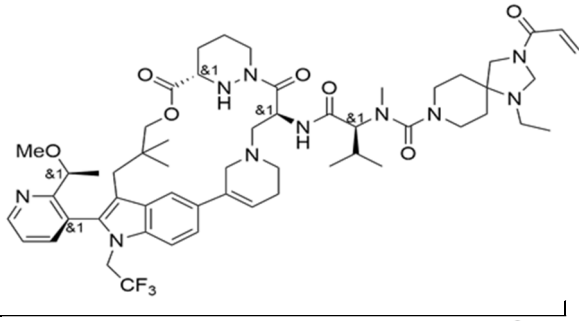
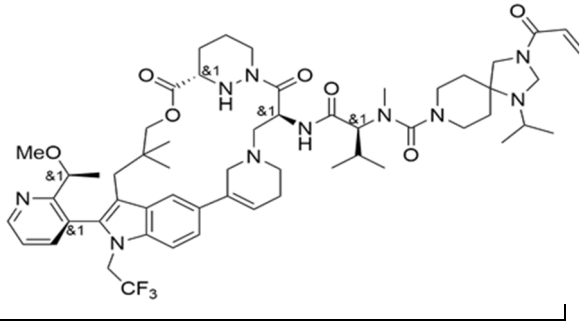
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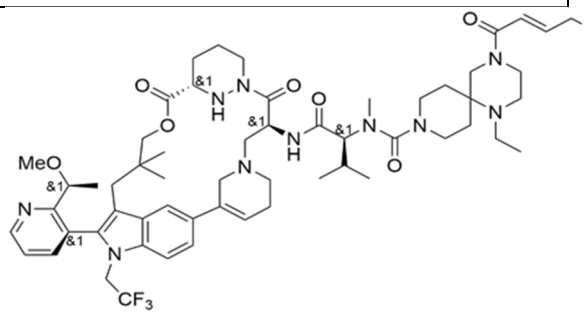
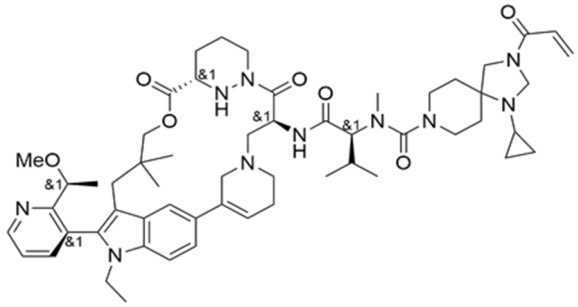
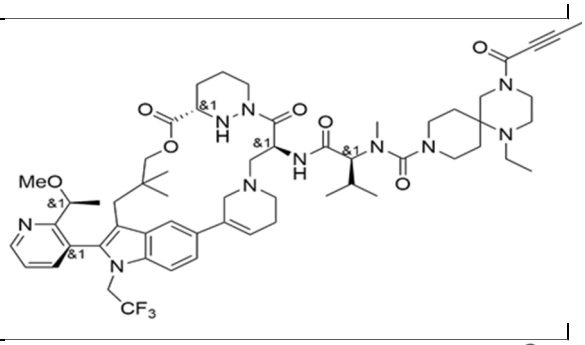
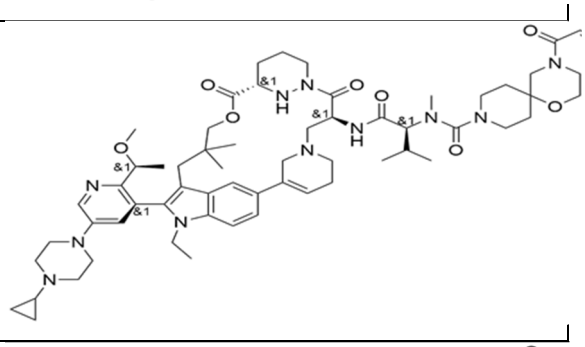
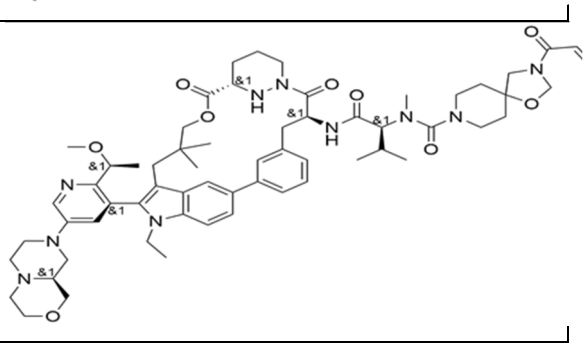
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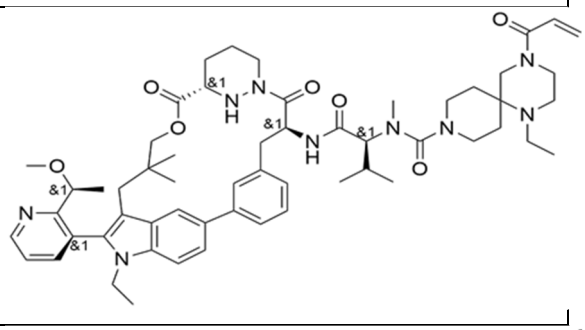
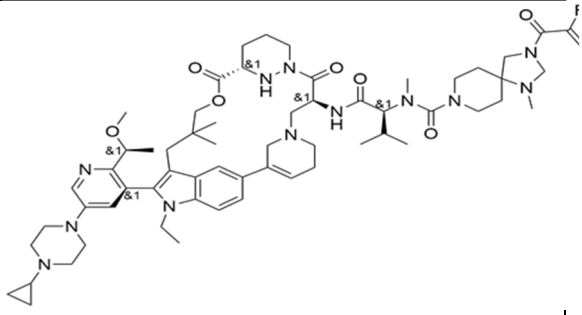
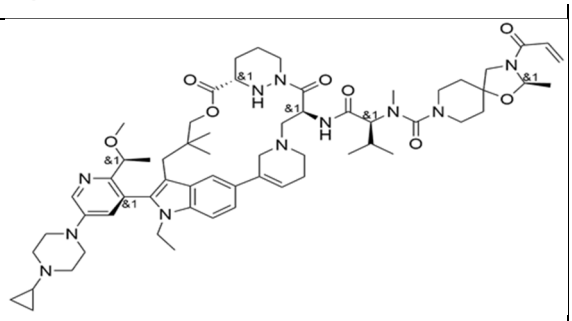
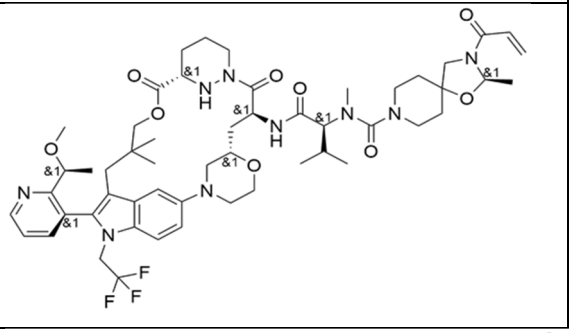
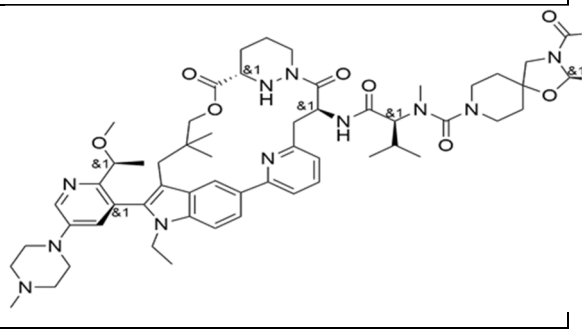
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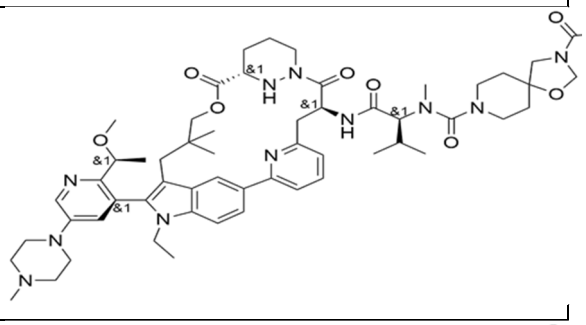
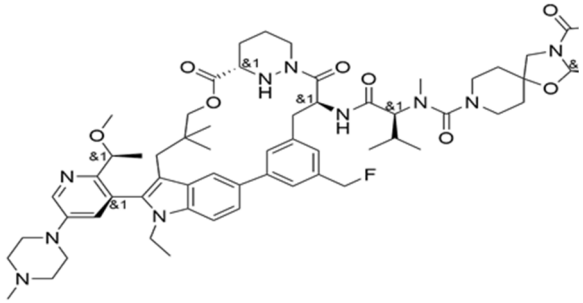
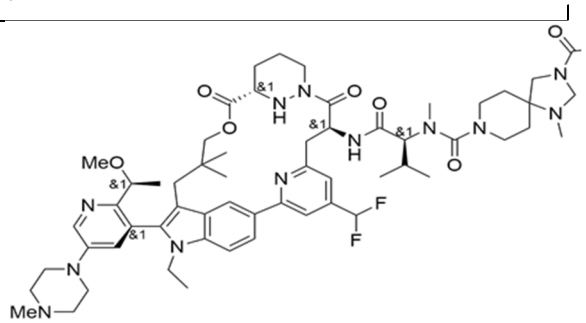
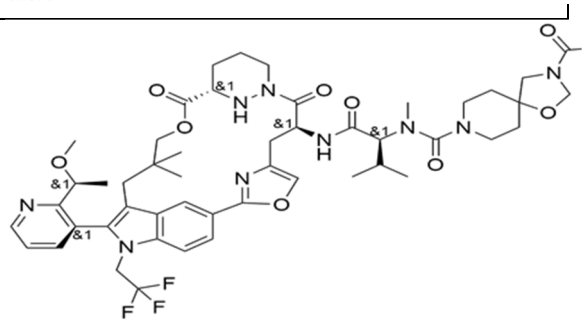
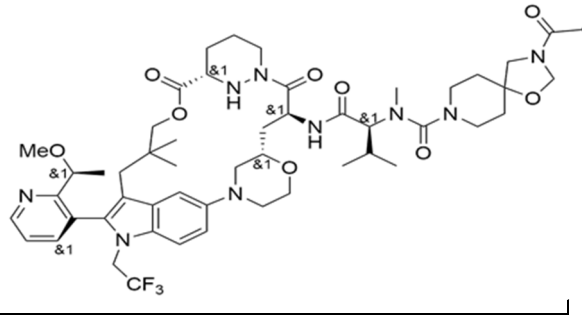
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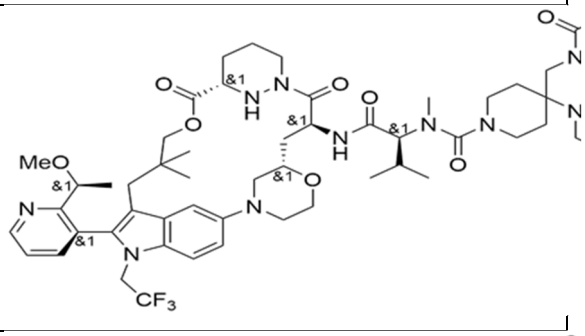
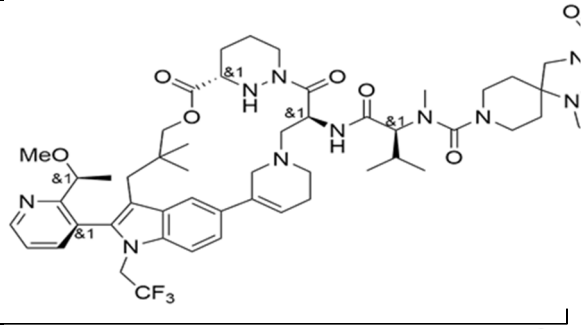
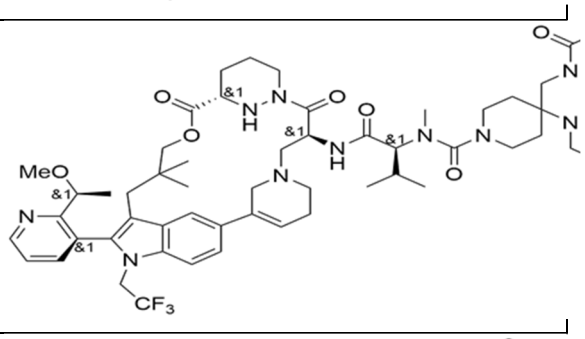
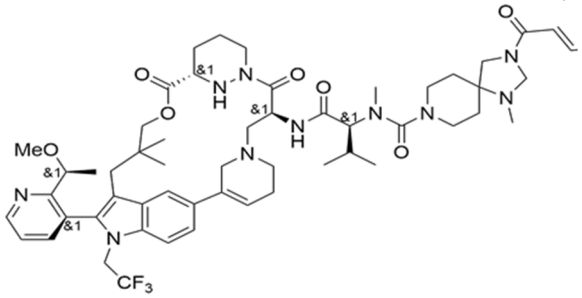
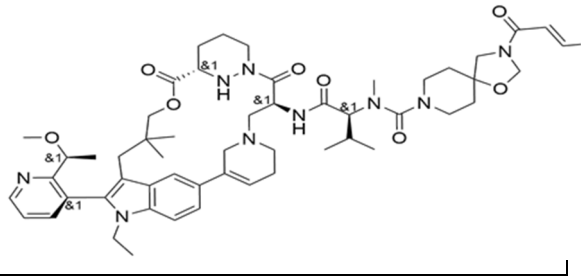
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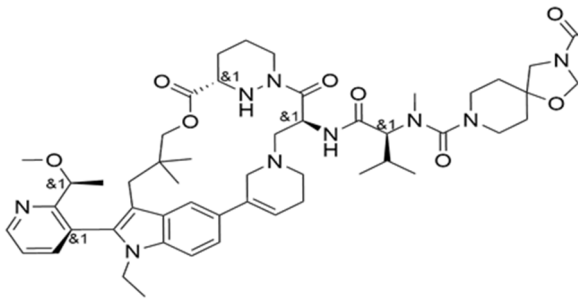
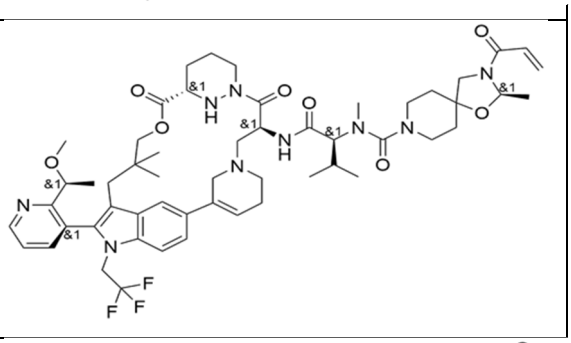
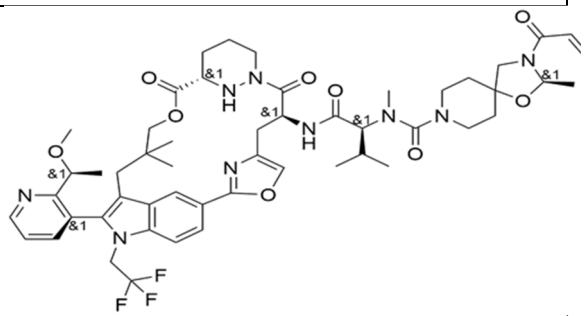
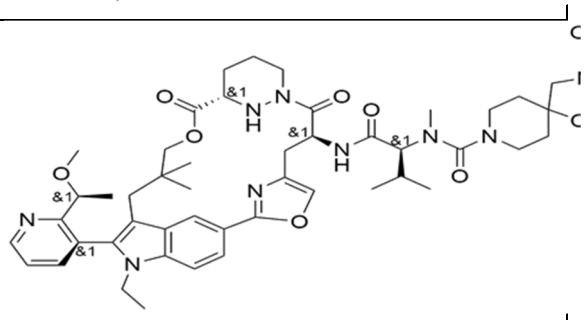
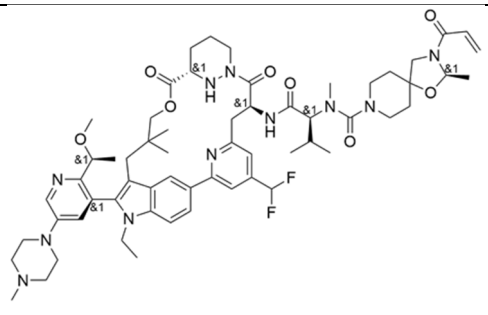
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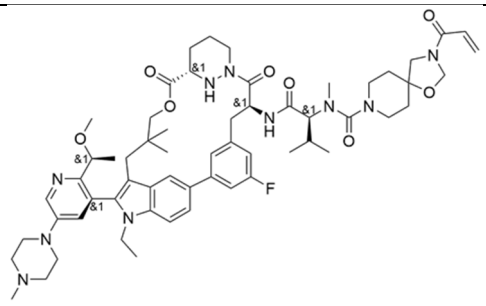
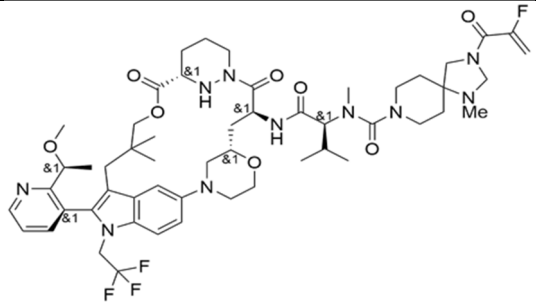
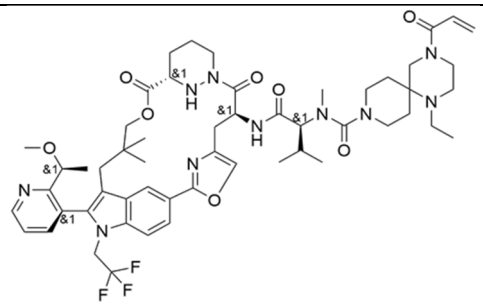
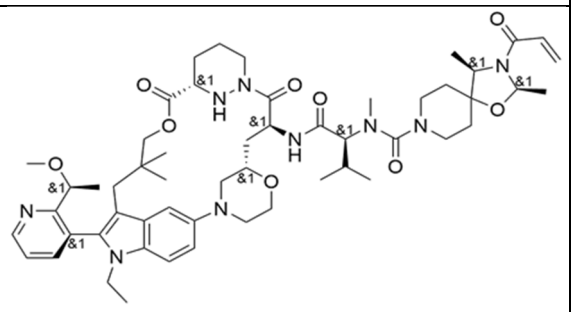
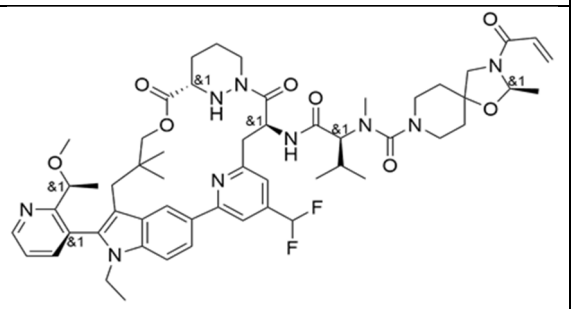
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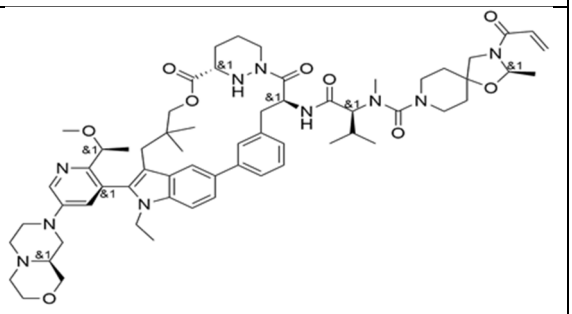
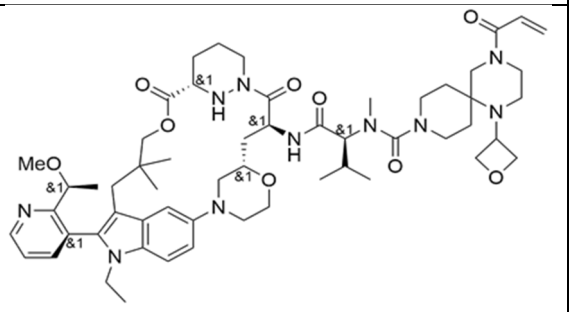
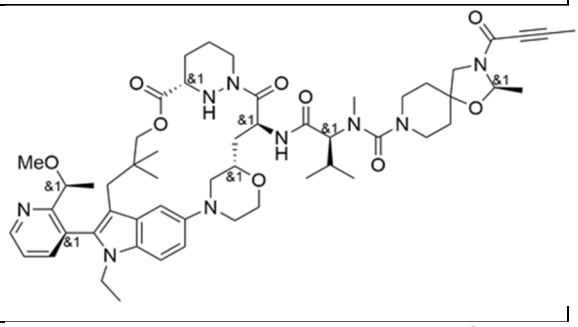
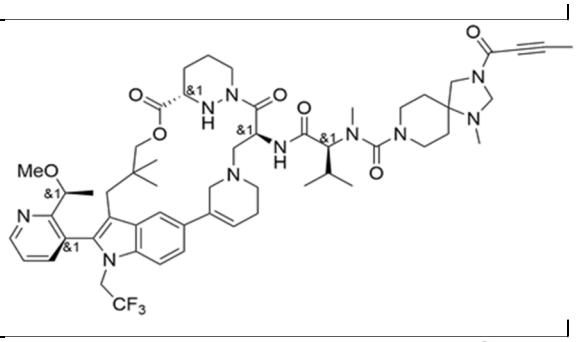
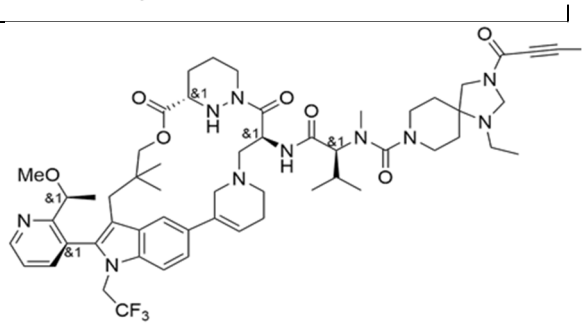
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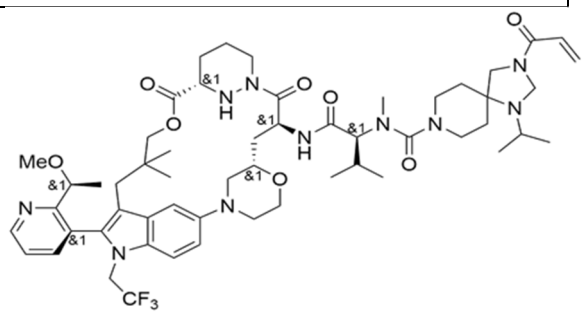
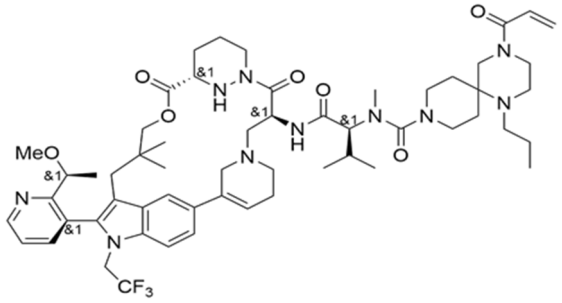
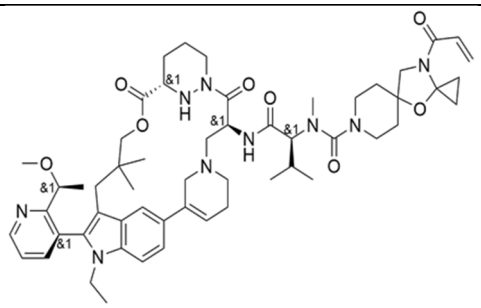
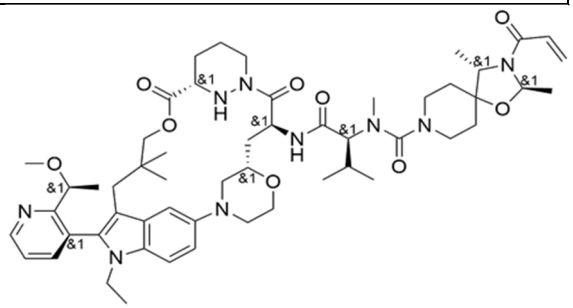
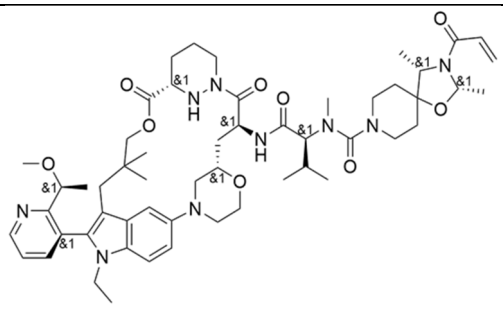
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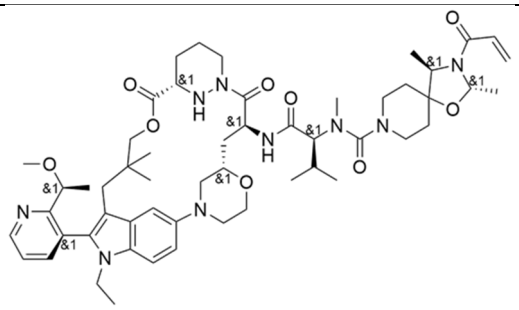
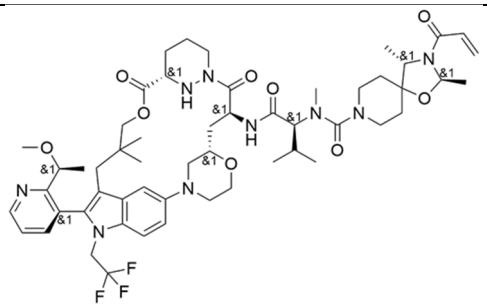
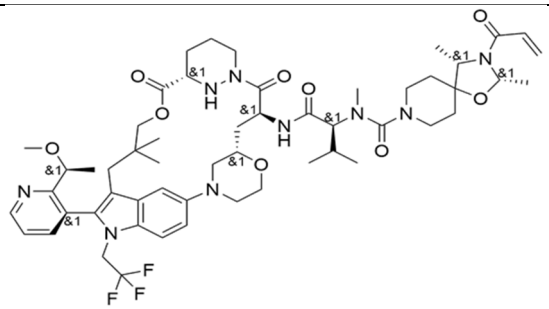
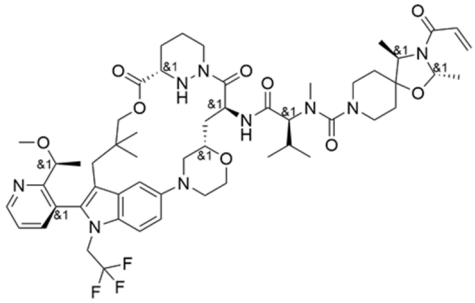
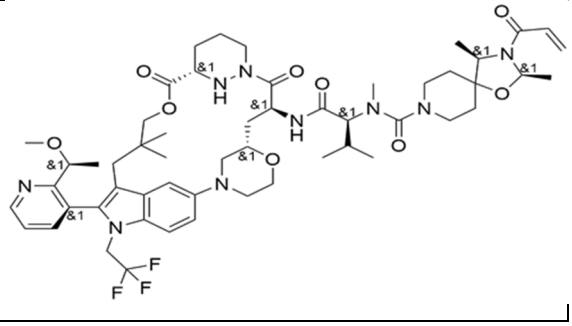
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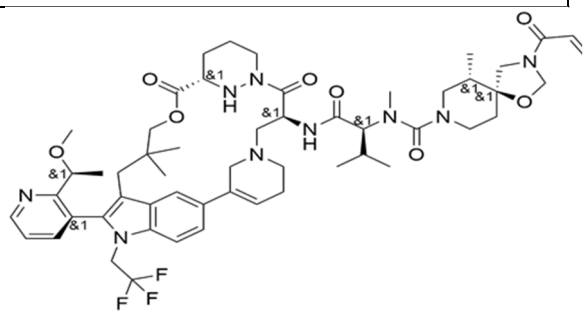
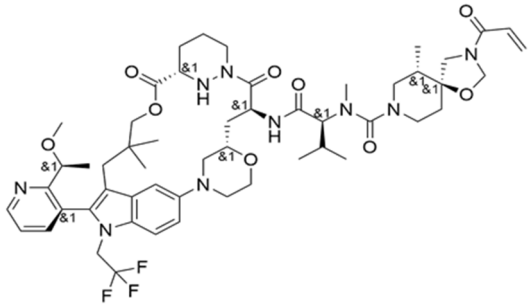
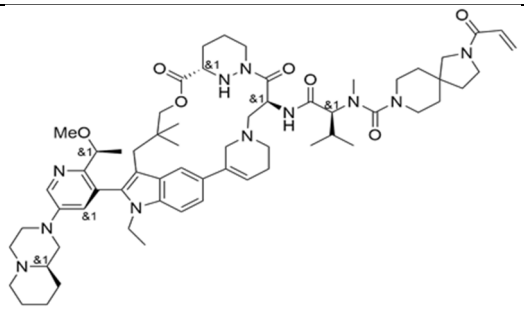
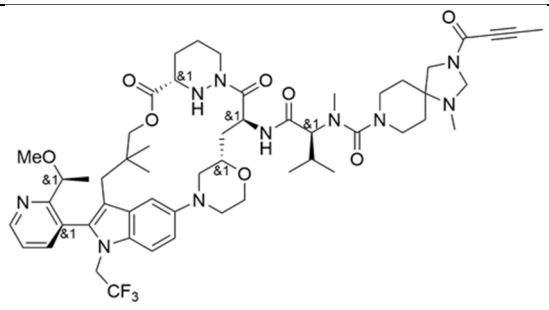
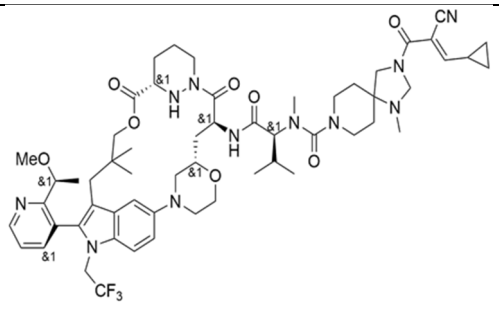
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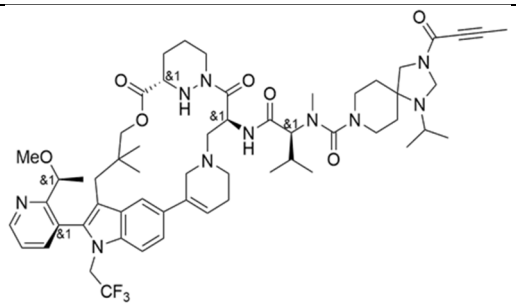
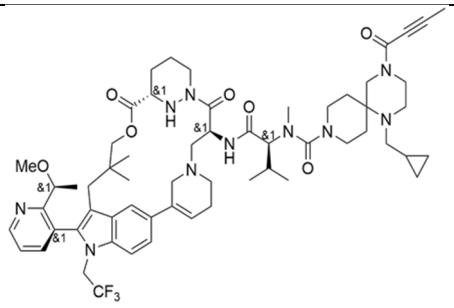
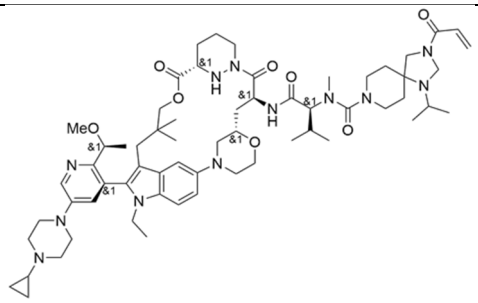
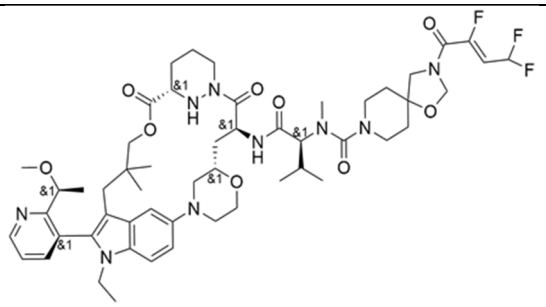
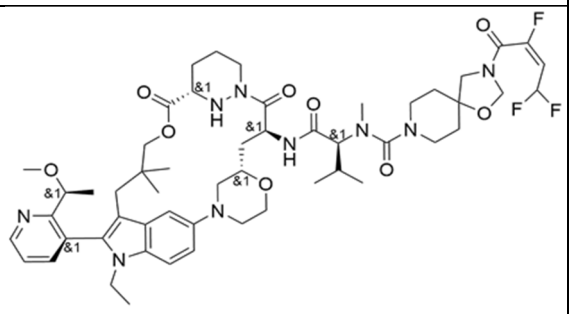
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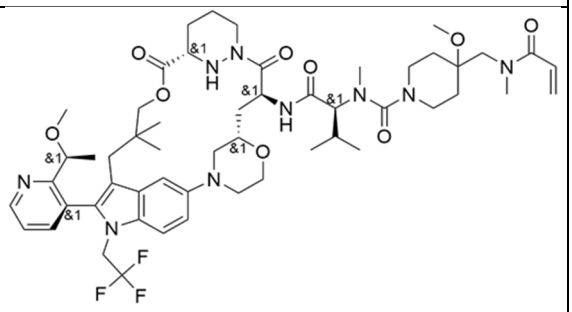
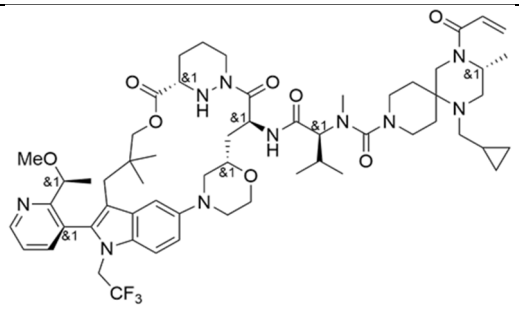
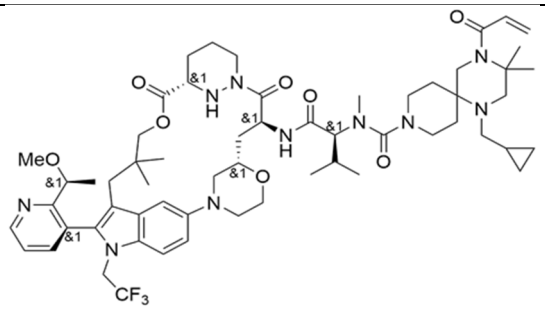
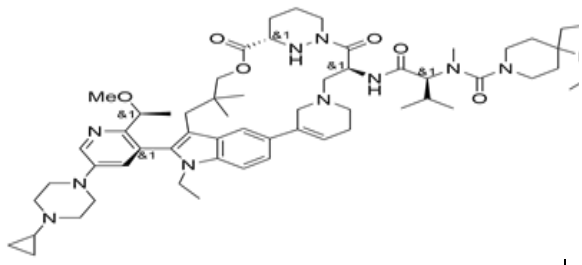
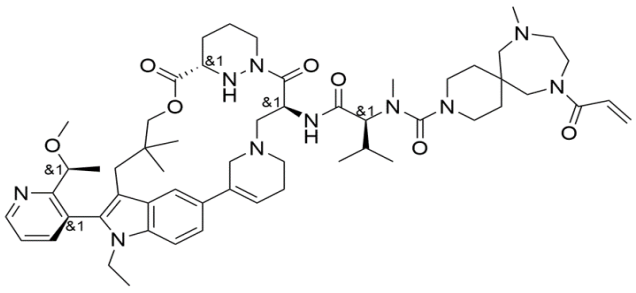
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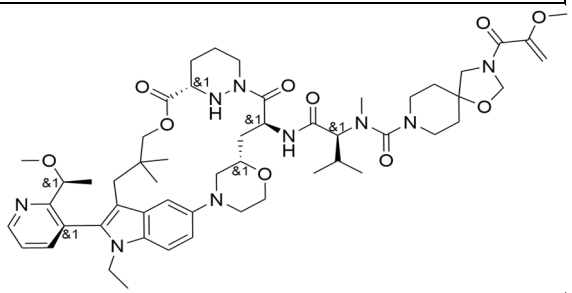
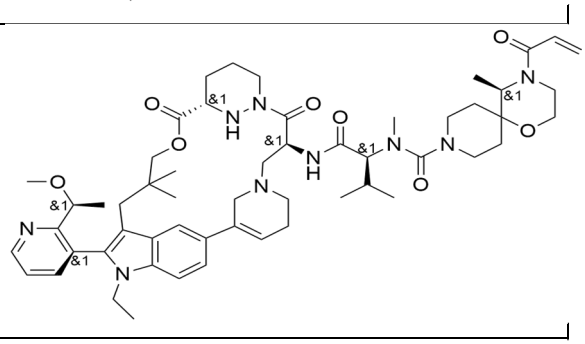
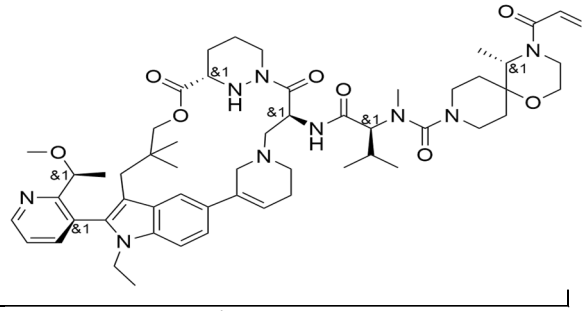
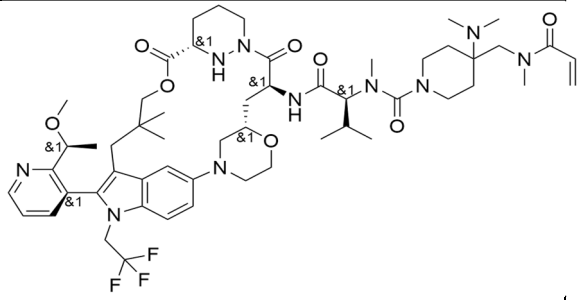
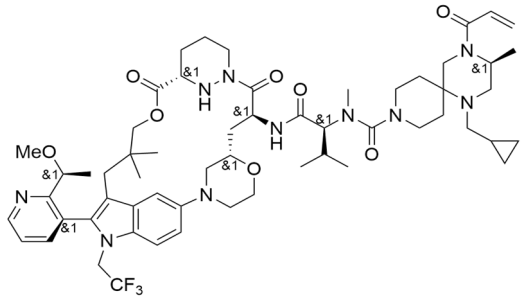
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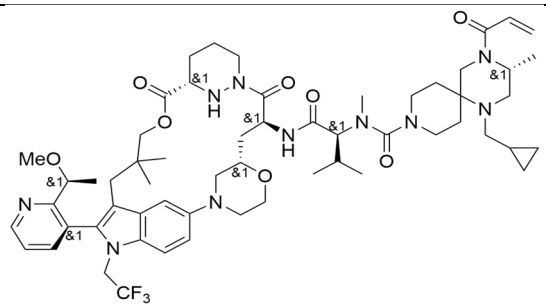
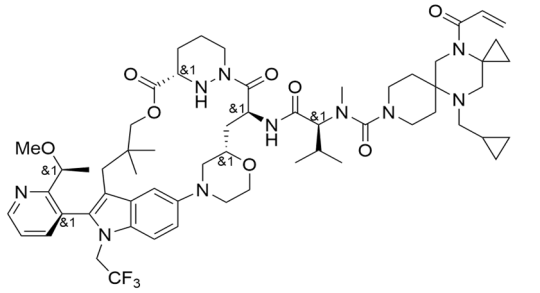
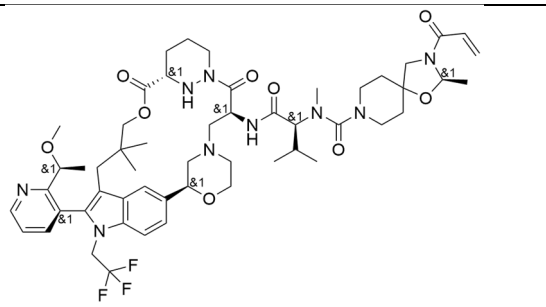
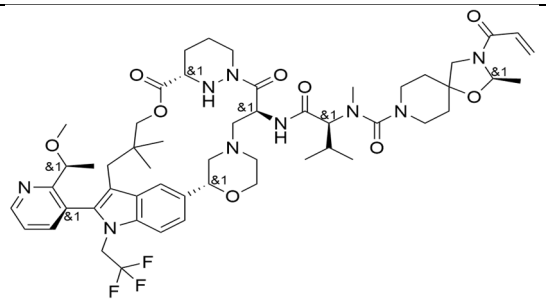
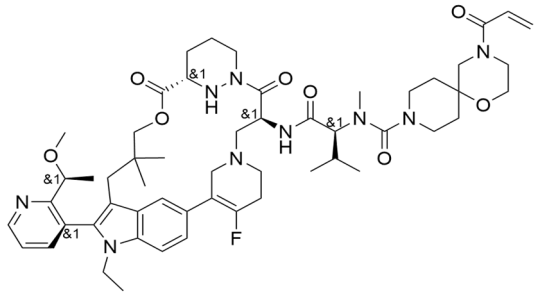
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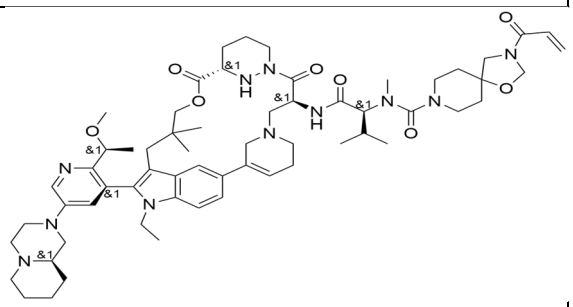
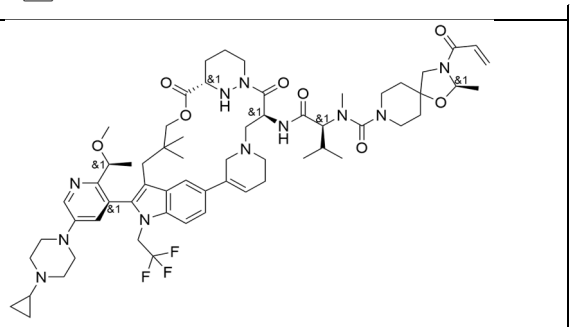
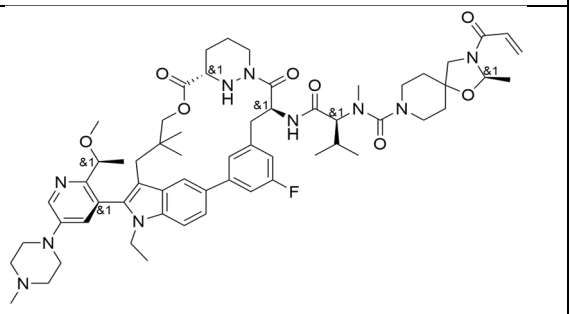
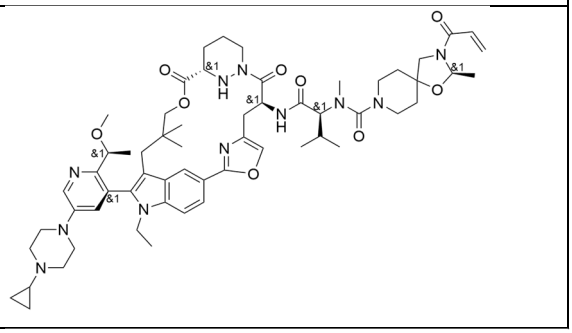
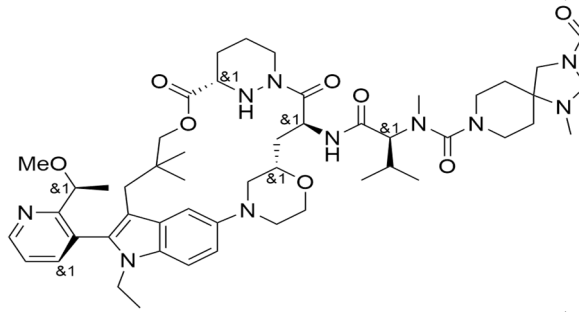
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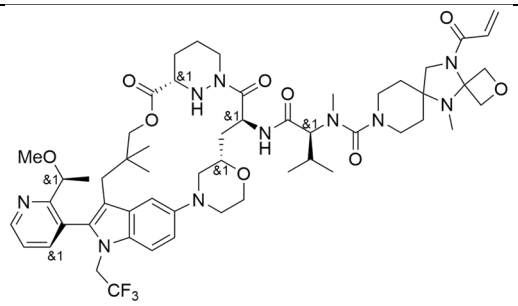
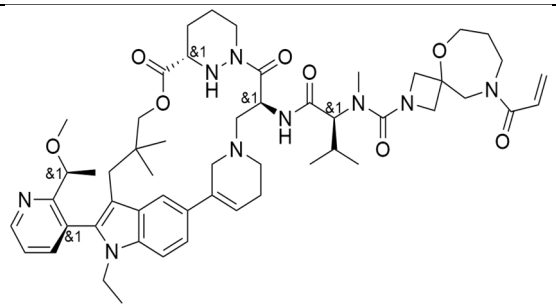
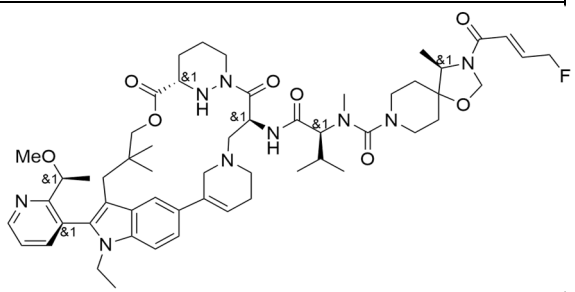
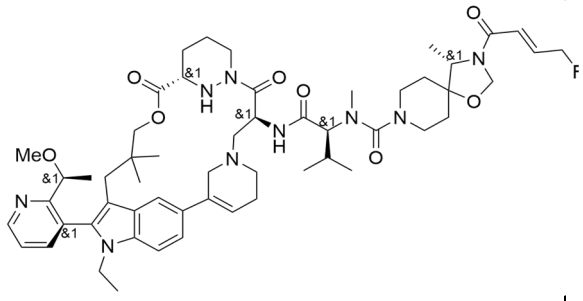
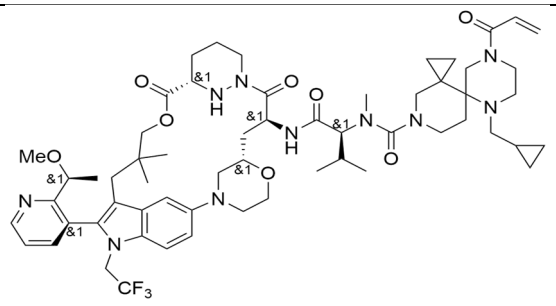
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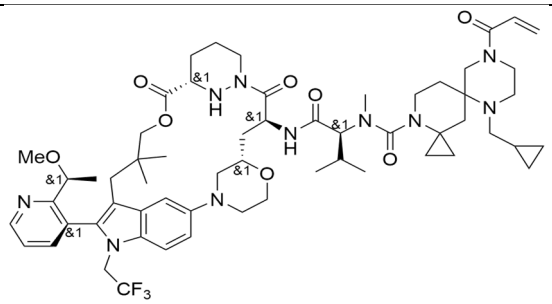
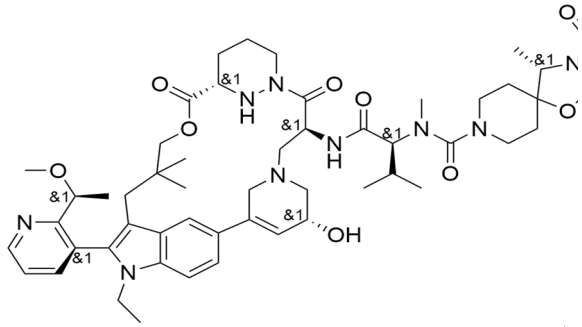
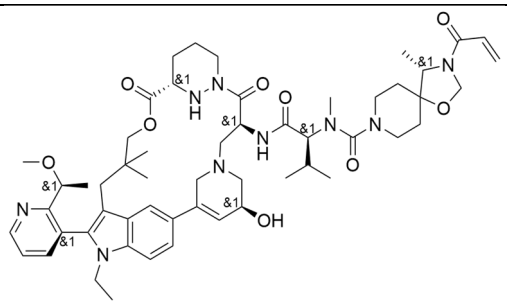
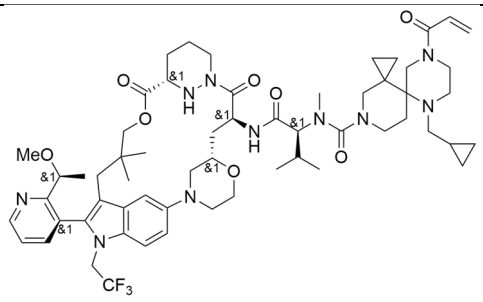
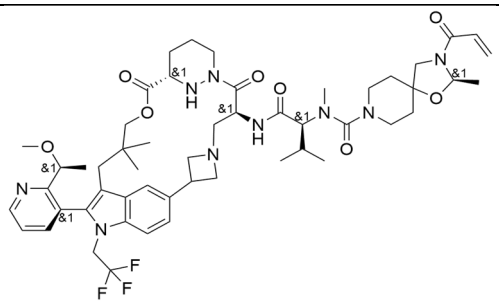
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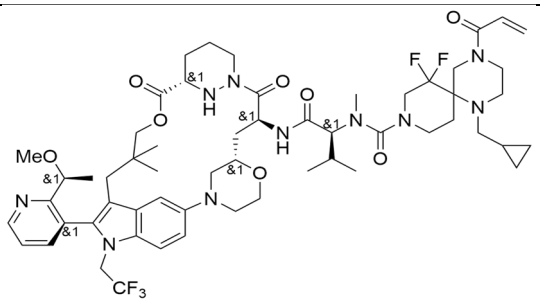
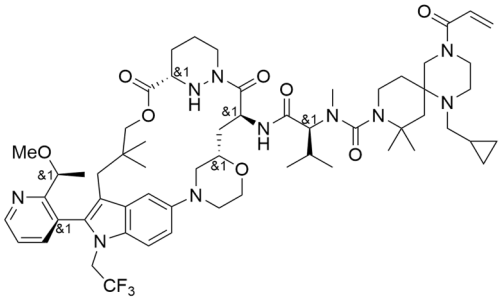
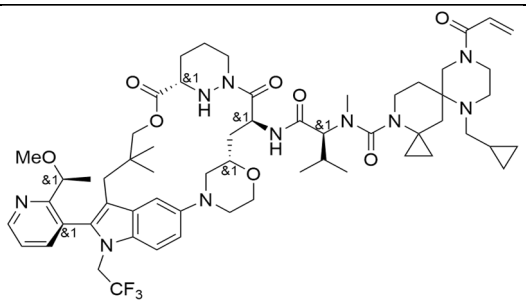
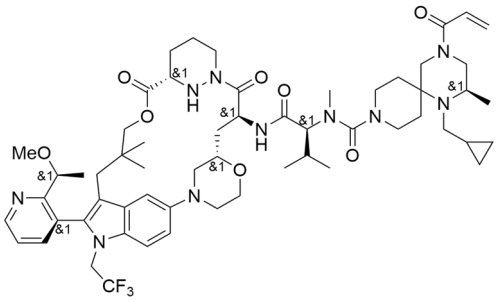
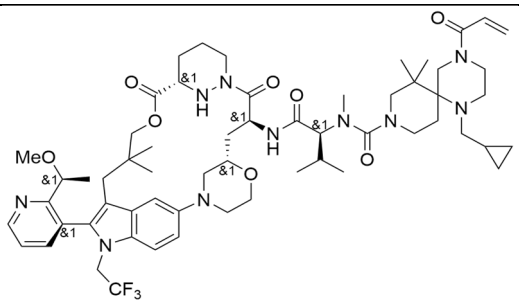
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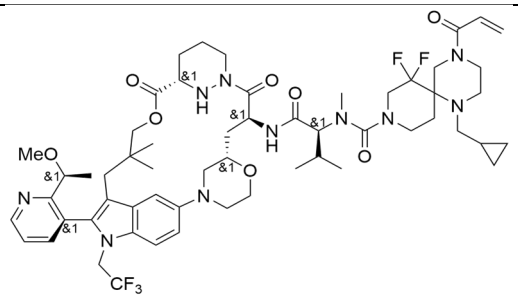
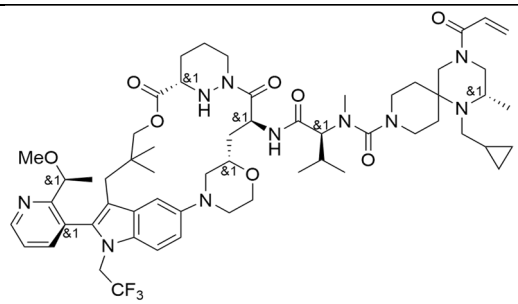
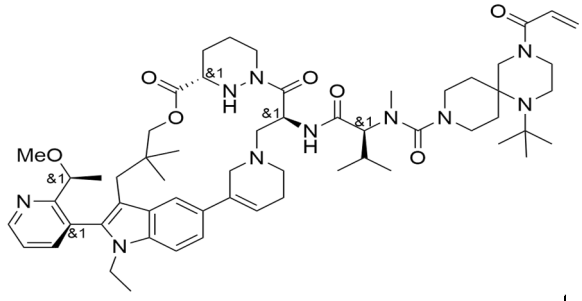
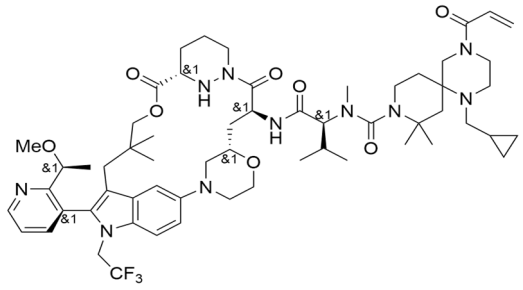
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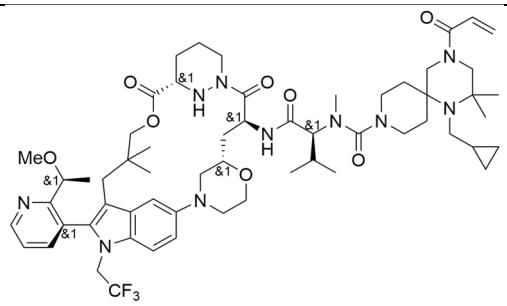
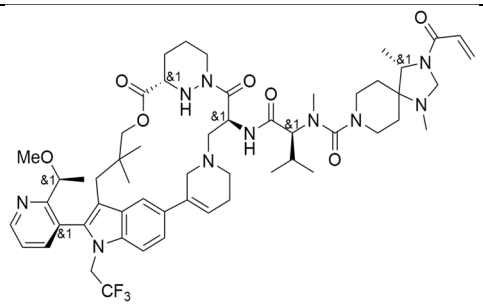
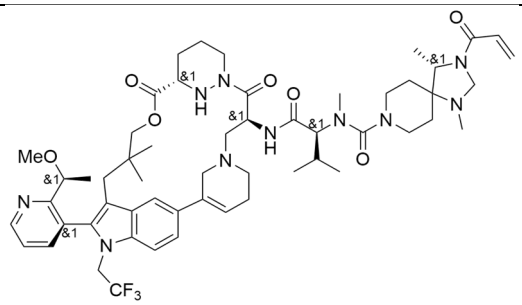
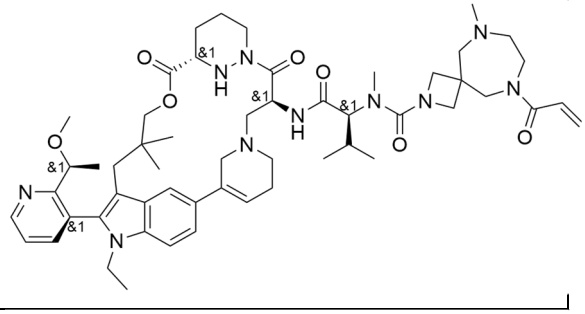
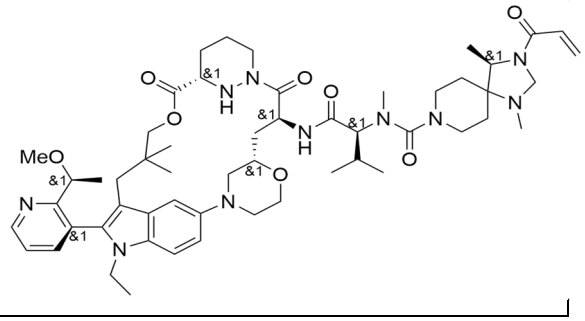
x#	Structure
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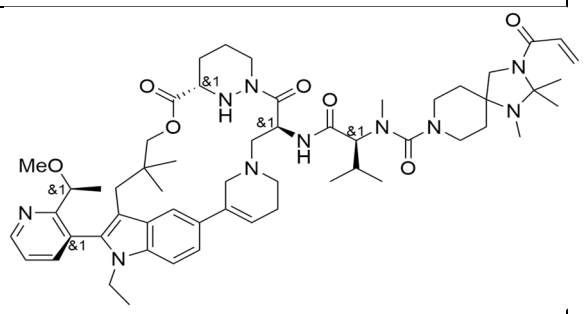
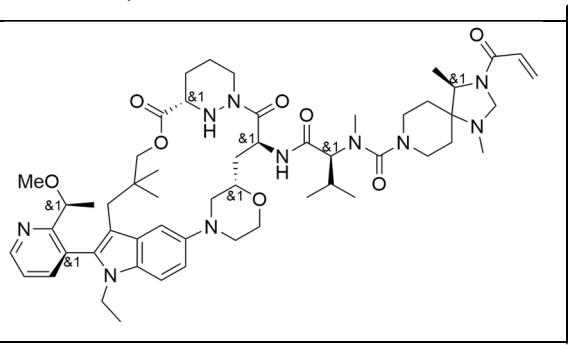
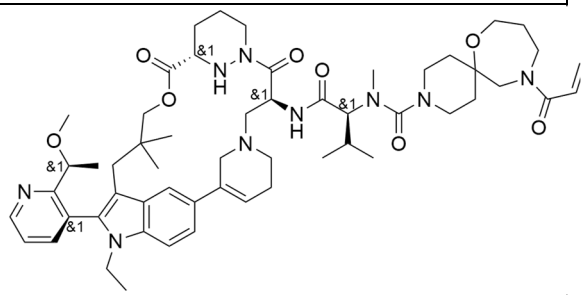
x#	Structure
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x#	Structure
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x#	Structure
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x#	Structure
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x#	Structure
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23. A pharmaceutical composition comprising a compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

24. A conjugate, or salt thereof, comprising the structure of Formula V:

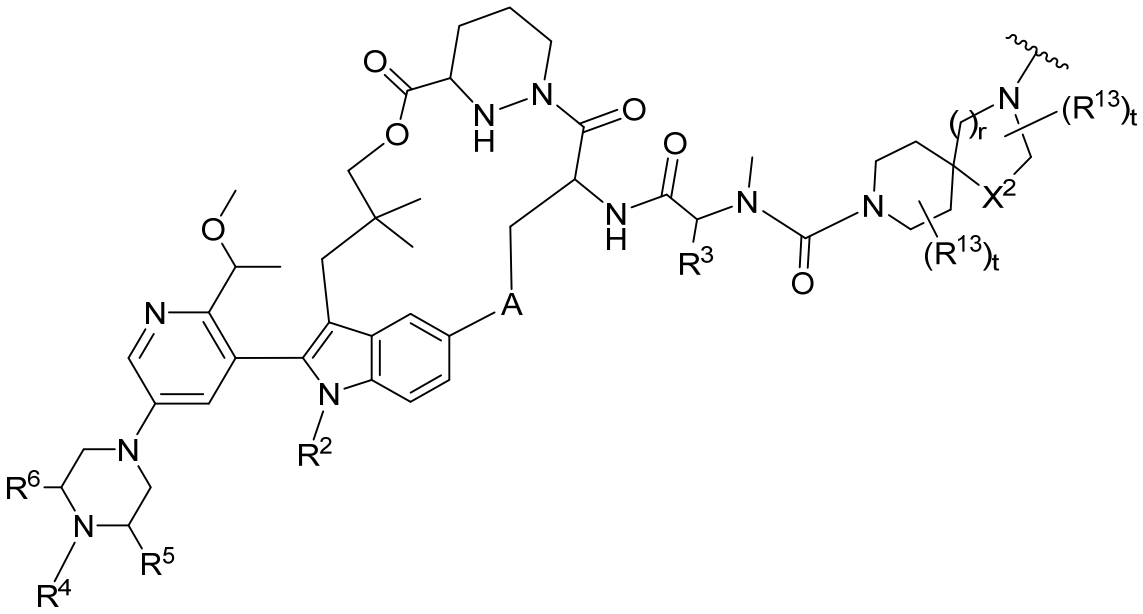
M-L-P

Formula V,

wherein L is a linker;

P is a monovalent organic moiety; and

M has the structure of Formula VIa:



Formula VIa,

wherein A is optionally substituted 3 to 6-membered heterocycloalkylene, optionally substituted 3 to 6-membered cycloalkylene, optionally substituted 6-membered arylene, or optionally substituted 5 to 10-membered heteroarylene;

R^2 is optionally substituted C_1-C_6 alkyl;

R^3 is optionally substituted C_1-C_6 alkyl or optionally substituted C_1-C_3 heteroalkyl;

X^2 is O, $C(R^{11})_2$, NR^{12}, S, or SO_2;

r is 1 or 2;

each t is, independently, 0, 1, or 2;

R^{11} and R^{12} are each, independently, hydrogen, optionally substituted C_1-C_4 alkyl, optionally substituted C_2-C_4 heteroalkyl, or optionally substituted 3 to 5-membered cycloalkyl;

each R^{13} is, independently, $-CH_3$; and

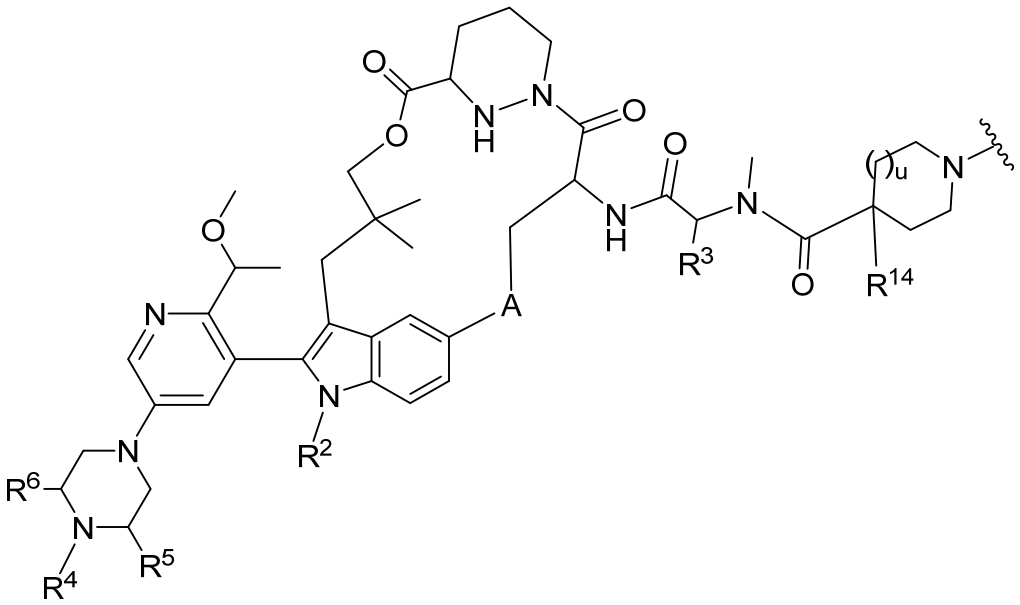
R^4, R^5, and R^6 are each independently selected from hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted 3 to 6-membered cycloalkyl, optionally substituted 3 to 6-membered heterocycloalkyl; or

R^4 and R^5 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl; or

R^4 and R^6 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl;

or

M has the structure of Formula VIb:



Formula VIb,

wherein A is optionally substituted 3 to 6-membered heterocycloalkylene, optionally substituted 3 to 6-membered cycloalkylene, optionally substituted 6-membered arylene, or optionally substituted 5 to 10-membered heteroarylene;

R^2 is optionally substituted C_1-C_6 alkyl;

R^3 is optionally substituted C_1-C_6 alkyl or optionally substituted C_1-C_3 heteroalkyl;

R^{14} is fluoro, hydrogen, or C_1-C_3 alkyl;

u is 0 or 1; and

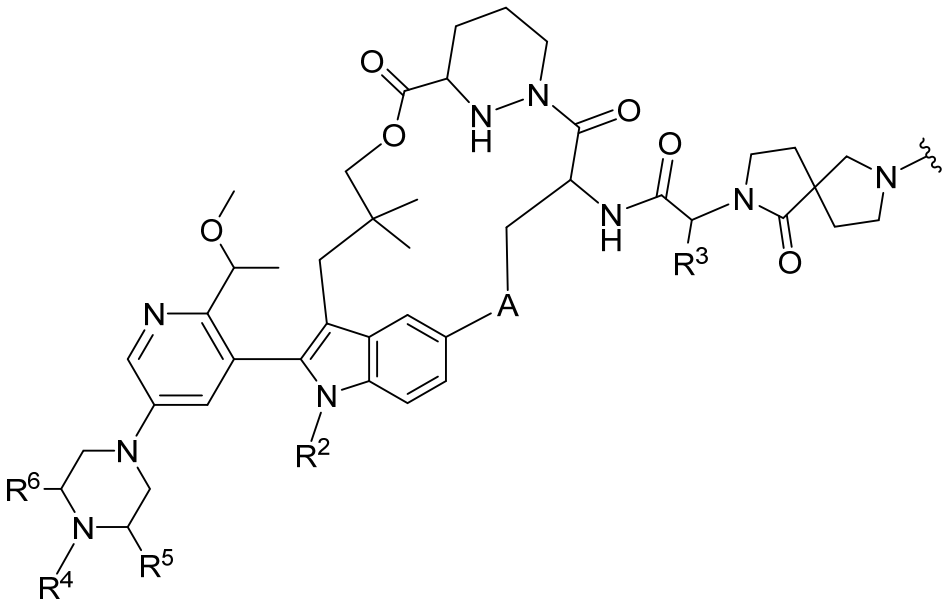
R^4, R^5, and R^6 are each independently selected from hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted 3 to 6-membered cycloalkyl, optionally substituted 3 to 6-membered heterocycloalkyl; or

R^4 and R^5 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl; or

R^4 and R^6 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl;

or

M has the structure of Formula VIc:



Formula VIc,

wherein A is optionally substituted 3 to 6-membered heterocycloalkylene, optionally substituted 3 to 6-membered cycloalkylene, optionally substituted 6-membered arylene, or optionally substituted 5 to 10-membered heteroarylene;

R^2 is optionally substituted C_1-C_6 alkyl;

R^3 is optionally substituted C_1-C_6 alkyl or optionally substituted C_1-C_3 heteroalkyl; and

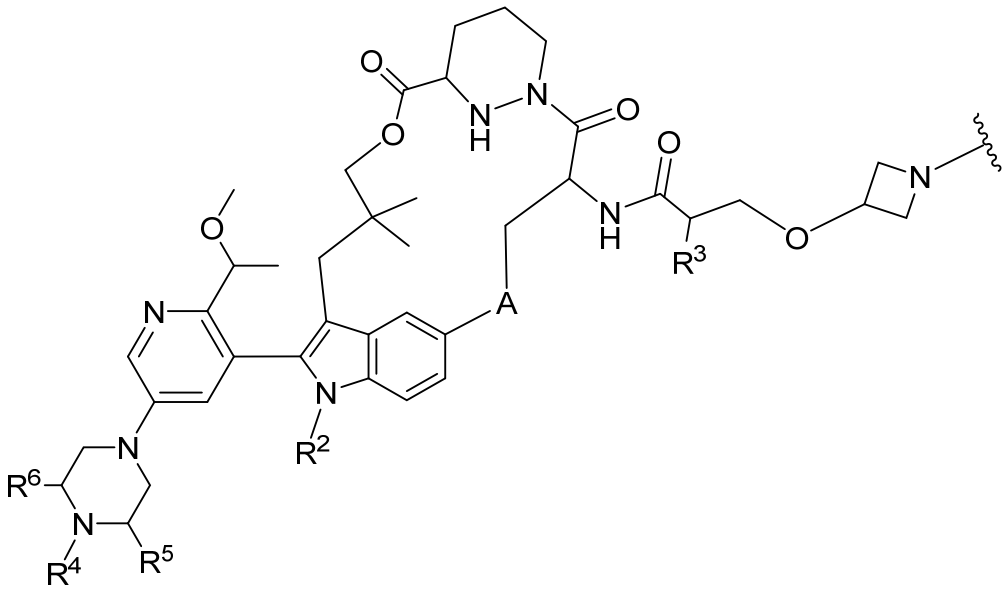
R^4, R^5, and R^6 are each independently selected from hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted 3 to 6-membered cycloalkyl, optionally substituted 3 to 6-membered heterocycloalkyl; or

R^4 and R^5 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl; or

R^4 and R^6 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl;

or

M has the structure of Formula VId:



Formula VId,

wherein A is optionally substituted 3 to 6-membered heterocycloalkylene, optionally substituted 3 to 6-membered cycloalkylene, optionally substituted 6-membered arylene, or optionally substituted 5 to 10-membered heteroarylene;

R^2 is optionally substituted C_1-C_6 alkyl;

R^3 is optionally substituted C_1-C_6 alkyl or optionally substituted C_1-C_3 heteroalkyl; and

R^4, R^5, and R^6 are each independently selected from hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted 3 to 6-membered cycloalkyl, optionally substituted 3 to 6-membered heterocycloalkyl; or

R^4 and R^5 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl; or

R^4 and R^6 combine with the atoms to which they are attached to form an optionally substituted 3 to 8-membered cycloalkyl or an optionally substituted 3 to 8-membered heterocycloalkyl.

25. Use of a compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 23 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

26. The use of claim 25, wherein the cancer is pancreatic cancer, colorectal cancer, non-small cell lung cancer, or endometrial cancer.

27. The use of claim 25 or 26, wherein the cancer comprises a Ras mutation.

28. Use of a compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 23 in the manufacture of a medicament for treating a

Ras protein-related disorder in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

29. An *in-vitro* or *ex-vivo* method of inhibiting a Ras protein in a cell, the method comprising contacting the cell with an effective amount of a compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 23.