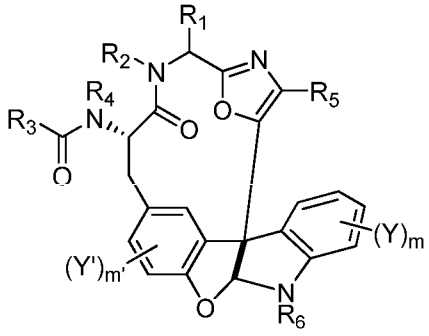
Claims

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt or conjugate thereof; wherein:

R^1 is optionally substituted C1-C4 alkyl;

R^2 is H, or optionally substituted C1-C4 alkyl;

R^3 is C1-C12 alkyl, C1-C12 heteroalkyl, C2-C12 alkenyl, C2-C12 heteroalkenyl, C3-C8 cycloalkyl, C3-C8 heterocyclyl, C4-C12 cycloalkylalkyl, C4-C12 heterocyclylalkyl, C6-C12 aryl, C5-C12 heteroaryl, C7-C14 arylalkyl, or C6-C14 heteroarylalkyl, each of which may be optionally substituted;

R^4 is H, or optionally substituted C1-C4 alkyl;

R^5 is optionally substituted C6-C12 aryl or optionally substituted C5-C12 heteroaryl;

R^6 is H, or optionally substituted C1-C4 alkyl;

each Y and Y' is independently halo, OH, C1-C4 alkoxy, or C1-C8 alkyl, C2-C8 alkenyl, C2-C8 alkynyl, C6-C12 aryl, or C7-C14 arylalkyl, or a heteroform of one of these, each of which may be optionally substituted;

m is 0-4; and

m' is 0-3.

2. The compound of claim 1 wherein:

R^1 is isopropyl or t-butyl;

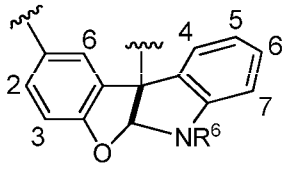
R^2, R^4 and R^6 are independently H or methyl;

R^3 is a substituted methyl of the general formula ($-CR^aR^bR^c$) wherein R^a is OH, OR, CH_2OR, SR, and NR_2, where each R is independently H, optionally halogenated C1-C4 alkyl, or optionally fluorinated C1-C4 acyl; and each of R^b and R^c is independently C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C3-C8 cycloalkylalkyl, C6-C12 aryl, C7-C14 arylalkyl, or a heteroform of one of these, each of which may be optionally substituted; or R^b

and R^c may be taken together with the carbon to which they are attached to form a C3-C8 cycloalkyl or a C3-C8 heterocyclyl ring, which may be optionally substituted;

R^5 is an optionally substituted oxazole or thiazole ring;

Y is at one or more of positions 4, 5, 6 and 7, and Y' is at one or more of positions 2, 3 and 6, wherein the positions are as indicated in formula II:



(II),

wherein R^6 is as defined in formula (I), and Y and Y' is each independently halo, OH, C1-C4 alkoxy, or C1-C8 alkyl, C2-C8 alkenyl, C2-C8 alkynyl, C6-C12 aryl, or C7-C14 arylalkyl, or a heteroform of one of these, each of which may be optionally substituted, ;

m is 3, 2, 1 or 0; and

m' is 2, 1 or 0.

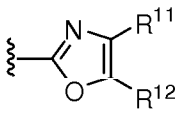
3. The compound of claim 1 wherein:

R^1 is isopropyl or t-butyl;

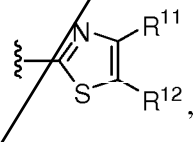
R^2, R^4 and R^6 are H;

R^3 is a substituted methyl of the general formula ($-CR^aR^bR^c$) wherein R^a is OH; and each of R^b and R^c is independently C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C3-C8 cycloalkylalkyl, C6-C12 aryl, C7-C14 arylalkyl, or a heteroform of one of these, each of which may be optionally substituted; or R^b and R^c may be taken together with the carbon to which they are attached to form a C3-C8 cycloalkyl or a C3-C8 heterocyclyl ring, which may be optionally substituted;

R^5 is an optionally substituted oxazole or thiazole ring:



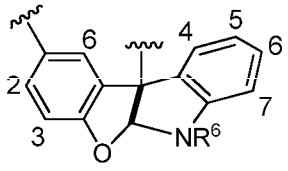
or



,

wherein R^{11} and R^{12} are indepently halo, nitro, cyano, C1-C4 alkyl, C1-C4 alkoxy, $COOR^8$, or $CONR^9{}_2$, C6-C12 aryl or C5-C12 heteroaryl, each of which may be optionally substituted;

Y is at one or more of positions 4, 5, 6 and 7, and Y' is at one or more of positions 2, 3 and 6, wherein the positions are as indicated in formula II:



(II),

wherein R6 is as defined in formula (I), and each Y and Y' is independently Cl or F;

m is 3, 2, 1 or 0; and

m' is 2, 1 or 0.

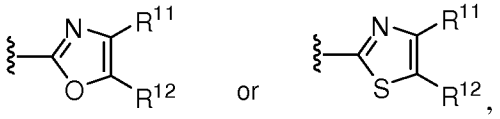
4. The compound of claim 1 wherein:

R^1 is isopropyl or t-butyl;

R^2, R^4 and R^6 are H;

R^3 is a substituted methyl of the general formula ($-CR^aR^bR^c$) wherein R^a is OH; and R^b and R^c are H and isopropyl or t-butyl, respectively

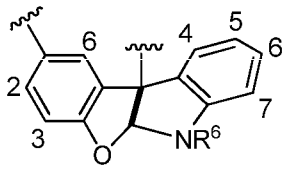
R^5 is an optionally substituted oxazole or thiazole ring:



,

wherein R^{11} is halo, nitro, cyano, C1-C4 alkyl, C1-C4 alkoxy, $COOR^8$, or $CONR^9_2$, C6-C12 aryl or C5-C12 heteroaryl, each of which may be optionally substituted, and R^{12} is H;

Y is at position 5 or 7, Y' is at position 2 or 3, wherein the positions are as indicated in formula II:



(II),

wherein R6 is as defined in formula (I), and each Y and Y' is independently Cl or F;

m is 2, 1 or 0; and

m' is 1 or 0.

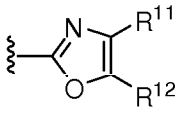
5. The compound of claim 1 wherein:

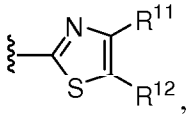
R^1 is isopropyl or t-butyl;

R^2, R^4 and R^6 are H;

R^3 is a substituted methyl of the general formula ($-CR^aR^bR^c$) wherein R^a is OH; and R^b and R^c are H and isopropyl or t-butyl, respectively

R^5 is an optionally substituted oxazole or thiazole ring:

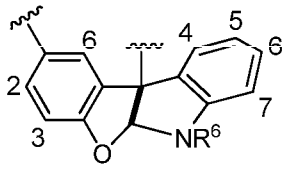


or


,

wherein R^{11} is halo, nitro, cyano, C1-C4 alkyl, C1-C4 alkoxy, $COOR^8$, or $CONR^9{}_2$, C6-C12 aryl or C5-C12 heteroaryl, each of which may be optionally substituted, and R^{12} is H;

Y is at position 5 or 7, wherein the positions are as indicated in formula II:



(II),

wherein R6 is as defined in formula (I), and Y is Cl or F;

m is 1; and

m' is 0.

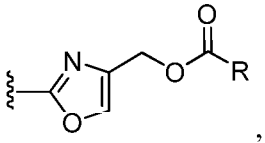
6. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



,

wherein R is H, C1-C4 alkyl or C1-C4 alkyloxy, particulary methyl, H, or methoxy;

Y is F or Cl, at position 5 or 7,

m is 0 or 1, and

m' is 0.

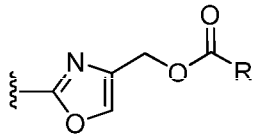
7. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



,

wherein R is H, methyl, or methoxy;

Y is F or Cl, at position 5 or 7,

m is 0 or 1, and

m' is 0.

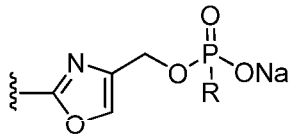
8. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



,

wherein R is H, C1-C4 alkyl,

Y is F or Cl, at postion 5 or 7,

m is 0 or 1, and

m' is 0.

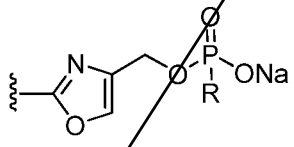
9. The compound of claim 1 wherein

R^1 is C1-C4 alkyl, particulary isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



,

wherein R is H or methyl,

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

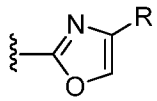
10. The compound of claim 1 wherein:

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



wherein R is hydroxyl or C1-C4 alcohol, or C1-C4 ketone,

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

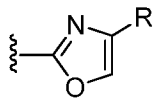
11. The compound of claim 1 wherein:

R^1 is C1-C4 alkyl, particulary isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



wherein R is hydroxyl, hydroxy methyl, 1-hydroxy ethyl or 1-hydroxy isopropyl, and

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

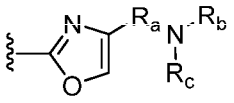
12. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



,

wherein Ra is optionally substituted C0-C4 alkyl, Rb and Rc are independently H, C1-C8 alkyl, C2-C8 alkenyl, C6-C12 aryl, or a heteroform of one of these, each of which may be optionally substituted,

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

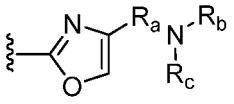
13. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



,

wherein Ra is C0 or C1 alkyl, Rb is H, and Rc is H, methyl, methyl ester, methyl sulfonyl or phenyl sulfonyl, and

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

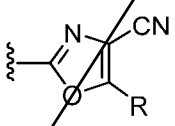
14. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



wherein R is H, C1-C8 alkyl, C2-C8 alkenyl, C6-C12 aryl, or a heteroform of one of these, each of which may be optionally substituted,

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

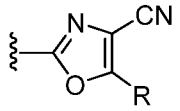
15. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



wherein R is H, methyl, or NHAc,

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

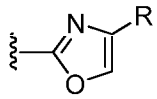
16. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula ($-CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



wherein R is a C3-C8 heterocyclyl, C4-C12 heterocyclylalkyl, C5-C12 heteroaryl, or C6-C14 heteroarylalkyl, each of which may be optionally substituted,

Y is F or Cl at postion 5 or 7,

m is 0 or 1, and

m' is 0.

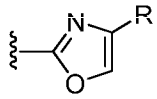
17. The compound of claim 1 wherein

R^1 is isopropyl or t-butyl,

R^2, R^4 and R^6 are H,

R^3 is a substituted methyl of the formula (-$CR^aR^bR^c$) wherein R^a is OH, R^b is H, and R^c is isopropyl or t-butyl,

R^5 is



wherein R is an optionally substituted oxazole, oxazoline, thiazole, thiazoline, pyrazole, pyrazoline, imidazole, imidazoline, pyrrole, pyrroline, isoxazole, isoxazoline, isothiazole, isothiazoline, oxadiazole, thiadiazole, triazole or tetrazole ring,

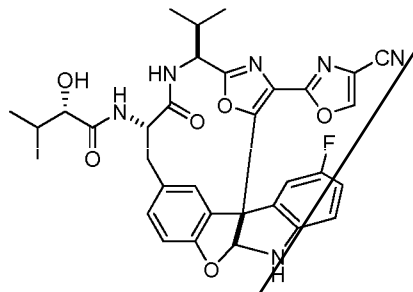
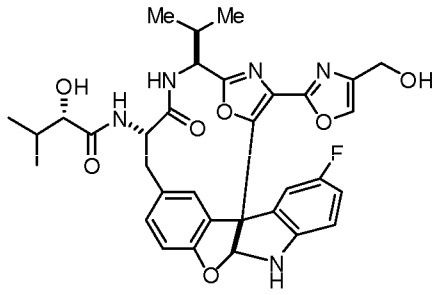
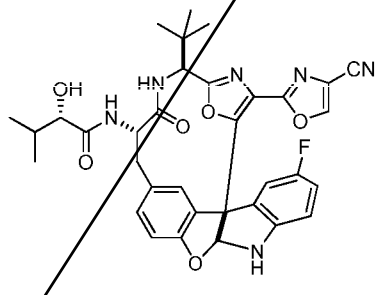
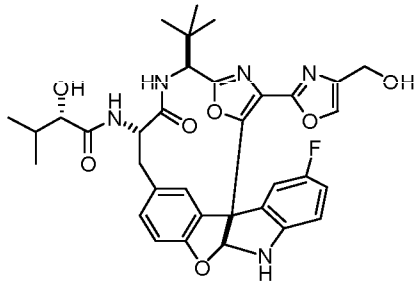
Y is F or Cl at postion 5 or 7,

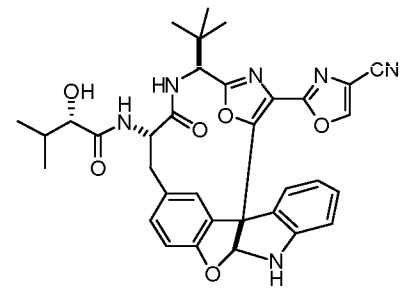
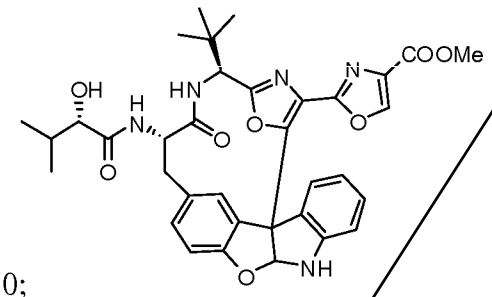
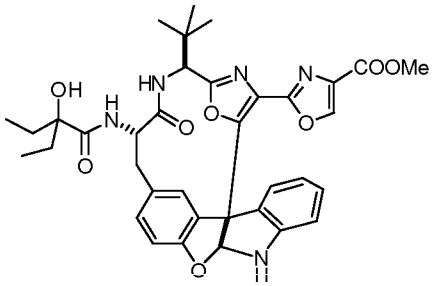
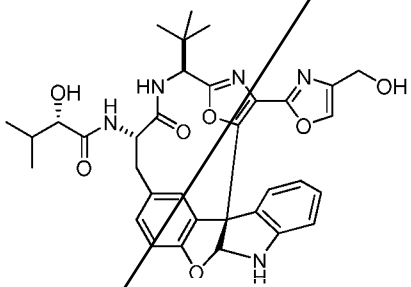
m is 0 or 1, and

m' is 0.

18. A compound of Table 1, or a pharmaceutically acceptable salt or conjugate thereof.

19. A compound selected from the group consisting of:

86; 	81; 
87; 	85; 

 62;	 50;
 63;	 57;

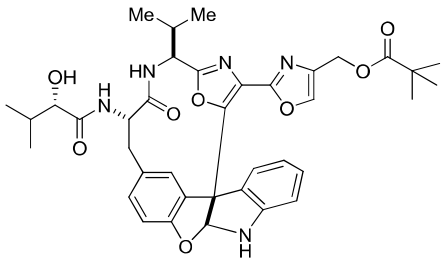
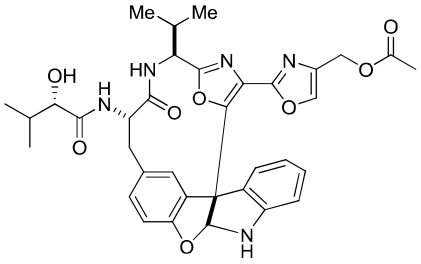
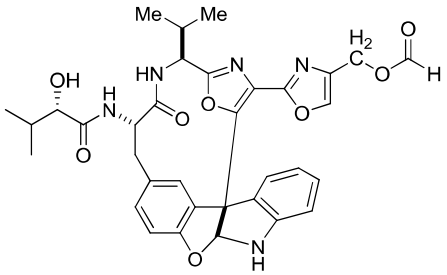
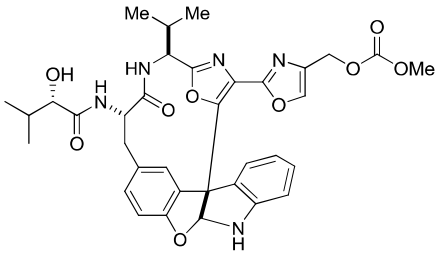
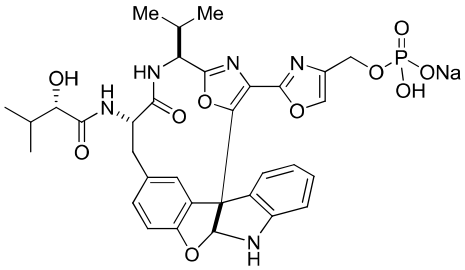
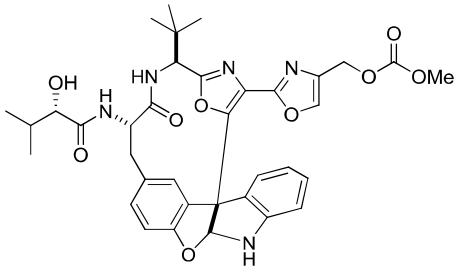
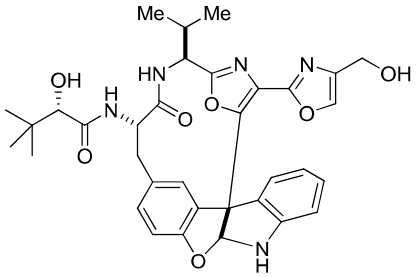
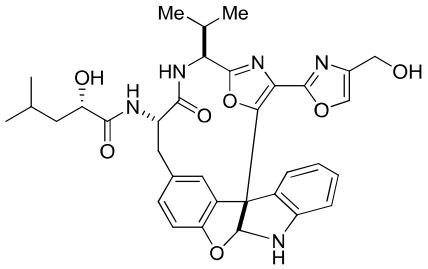
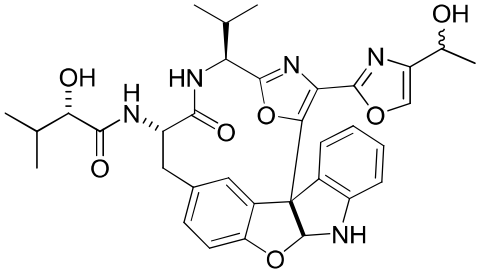
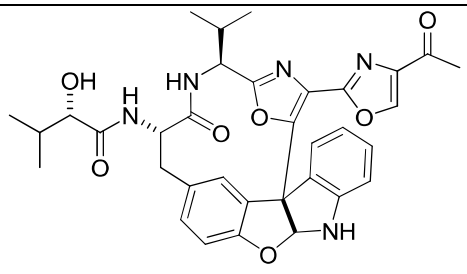
or a pharmaceutically acceptable salt or conjugate thereof.

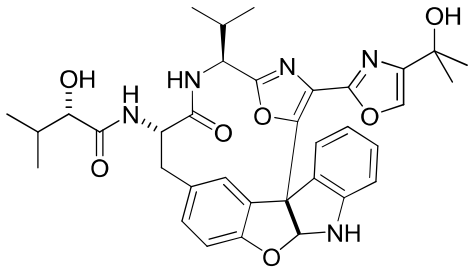
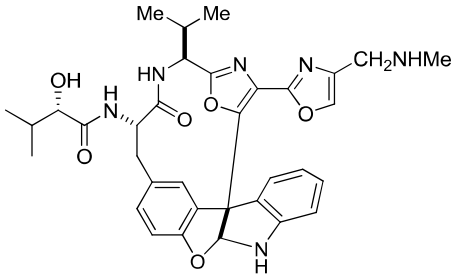
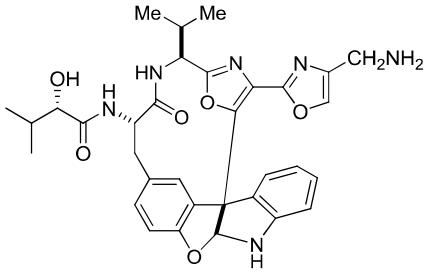
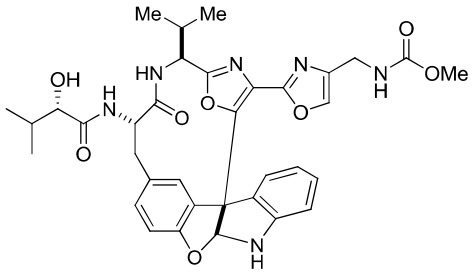
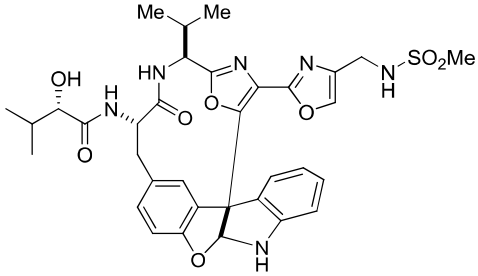
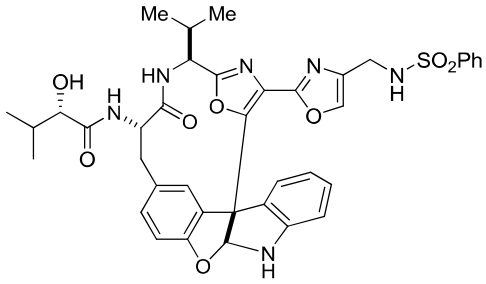
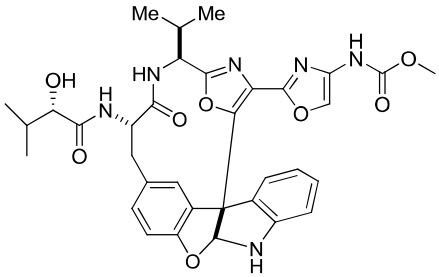
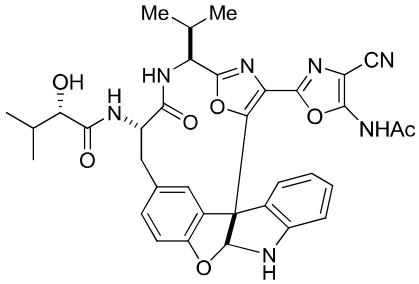
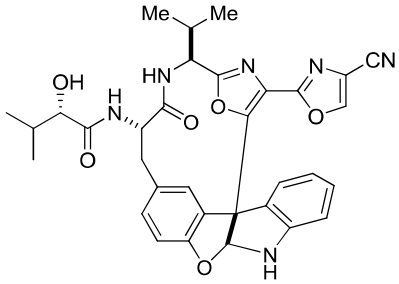
20. A pharmaceutical composition comprising the compound of claim 1 in unit dosage form with at least one pharmaceutically acceptable excipient.

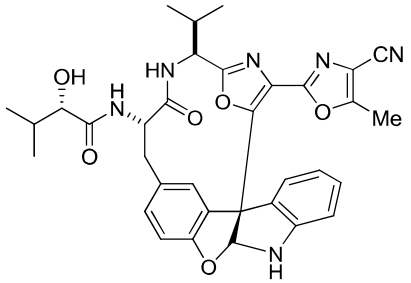
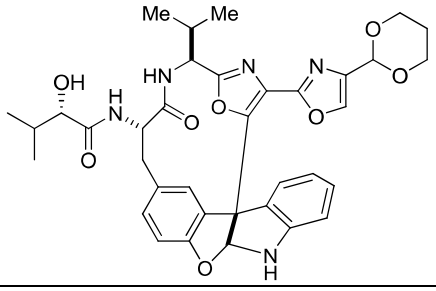
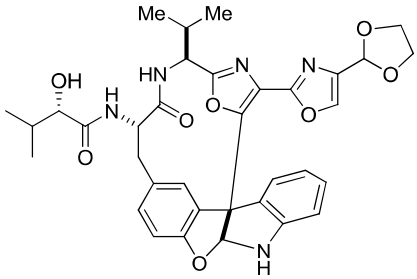
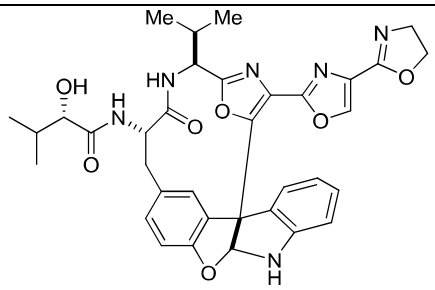
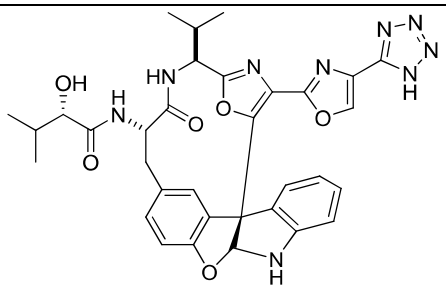
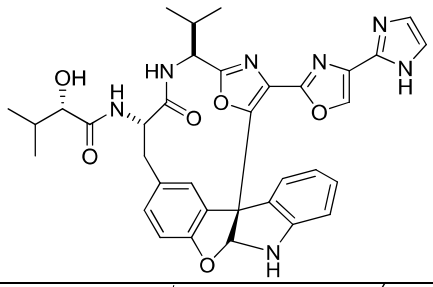
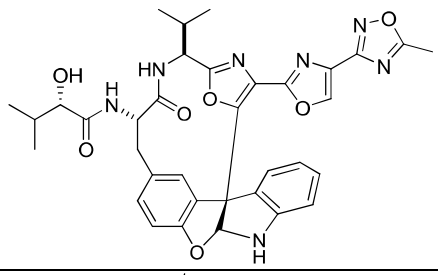
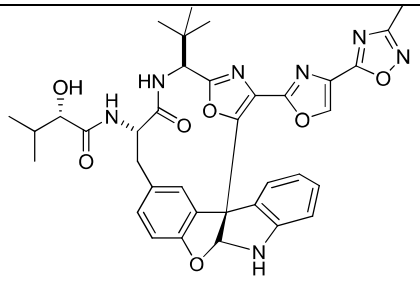
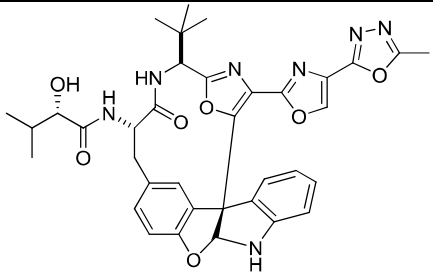
21. A method of using a compound of claim 1 comprising comprising administering to a subject in need thereof a therapeutically effective amount of the compound.

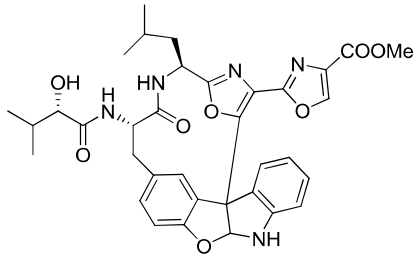
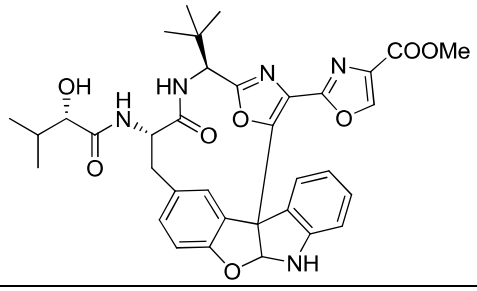
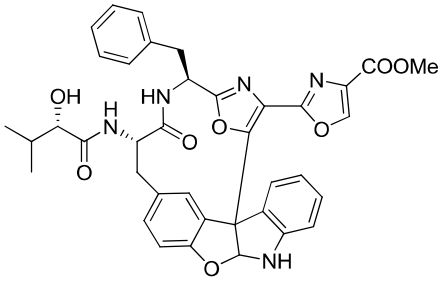
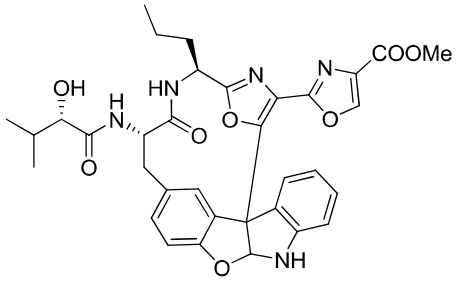
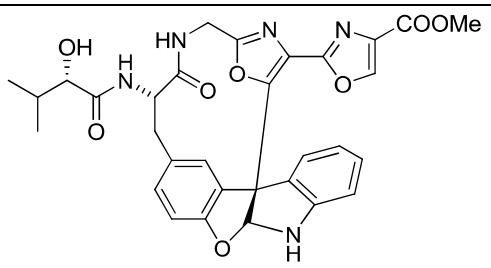
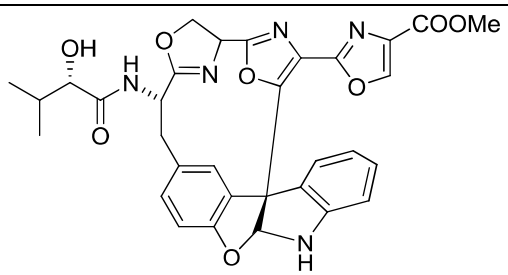
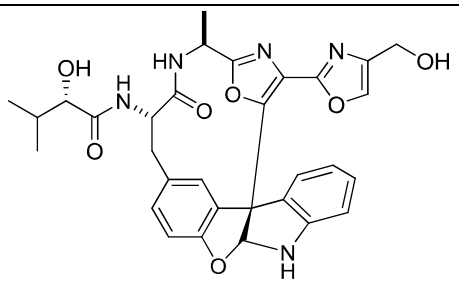
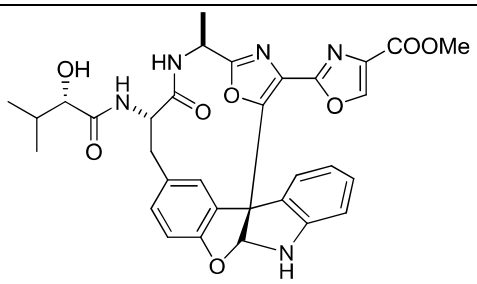
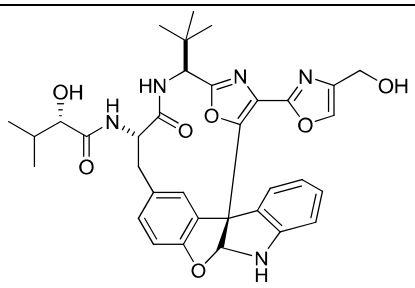
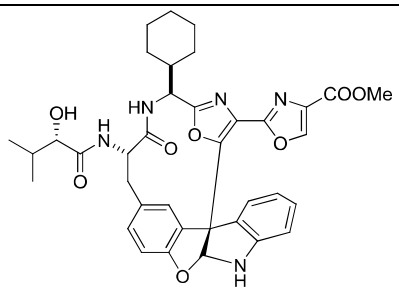
Claims

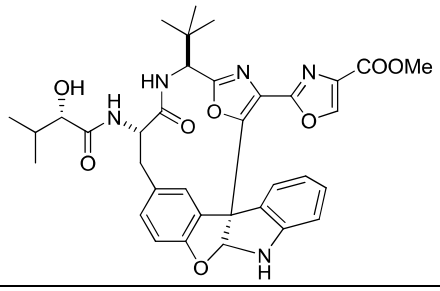
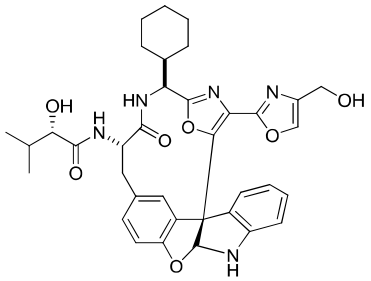
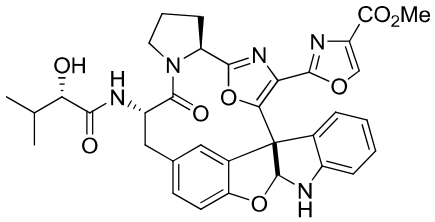
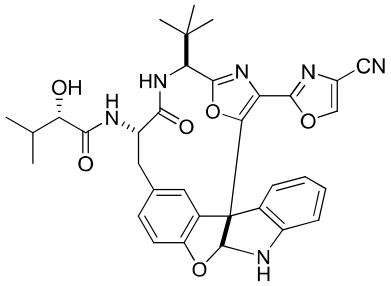
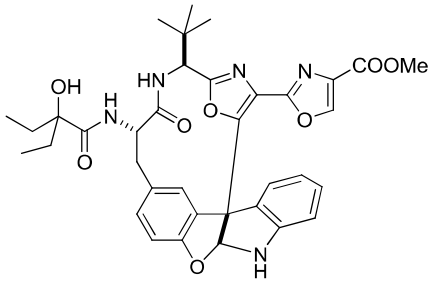
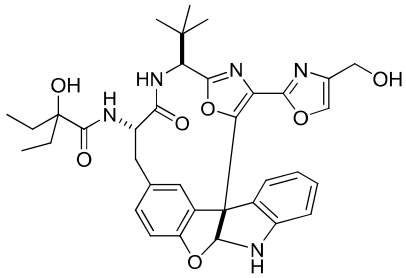
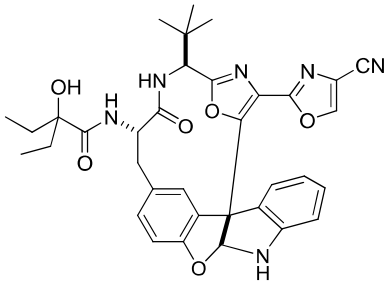
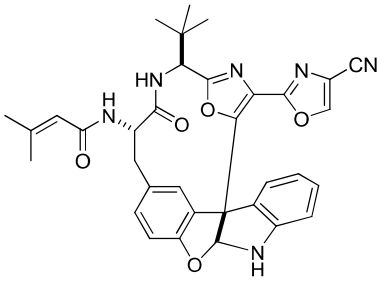
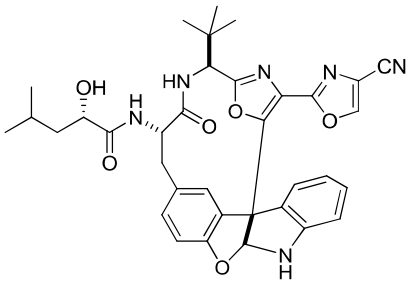
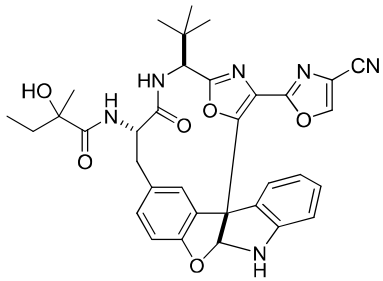
1. A compound of the following table, or a pharmaceutically acceptable salt thereof:

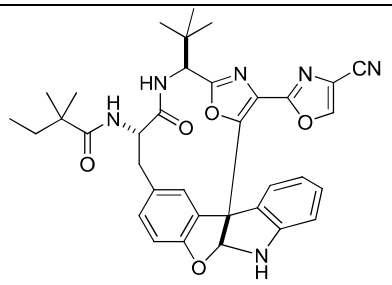
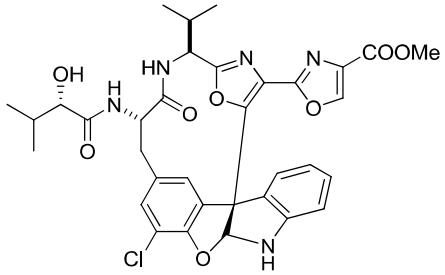
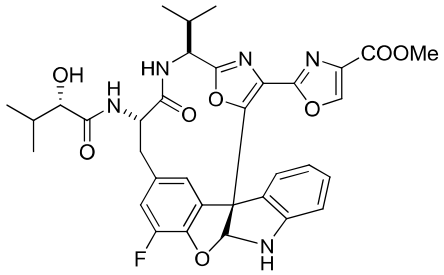
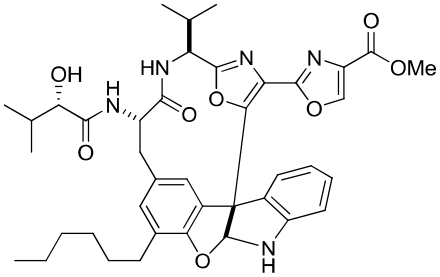
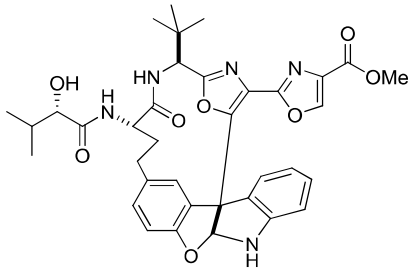
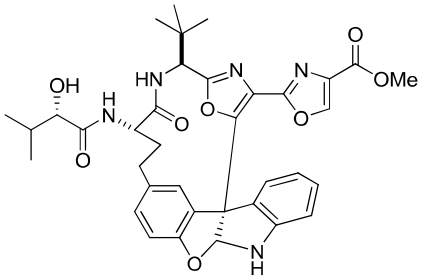
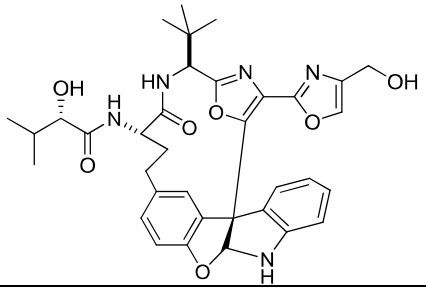
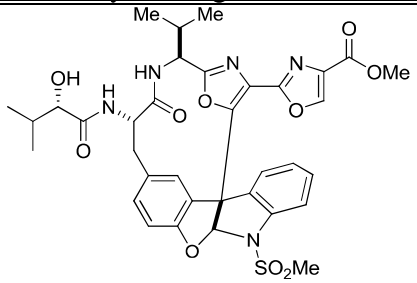
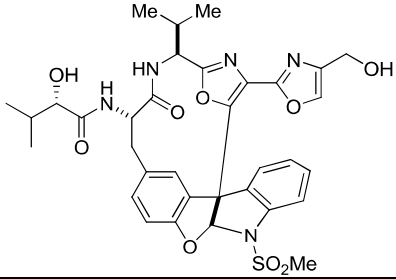
I. Oxazole, 4 oxazoyl analogs with esters other than methyl ester in position 4.			
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23		24	
25		26	
II. Oxazole, 4 oxazoyl analogs with alcohol or ketone in position 4			
27		28	
29		30	

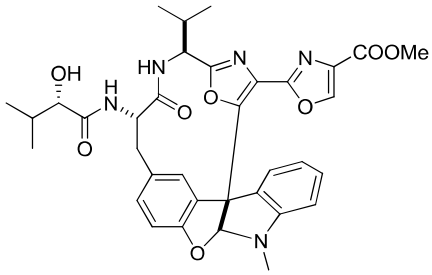
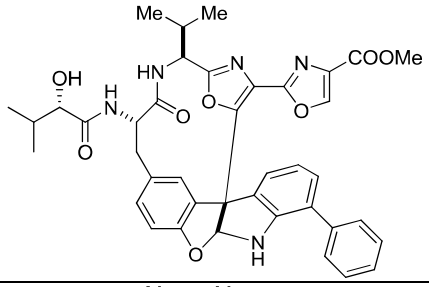
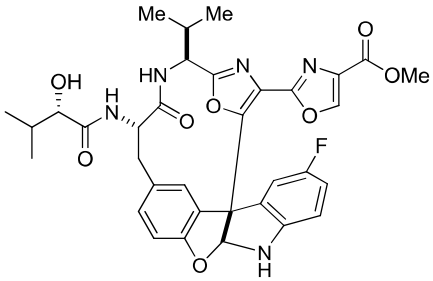
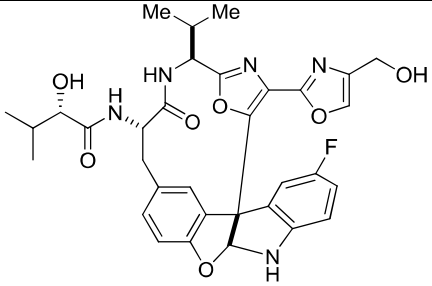
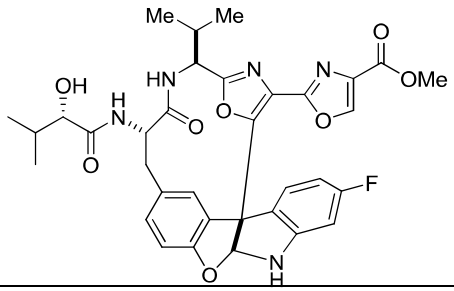
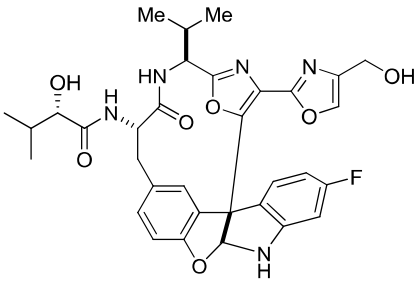
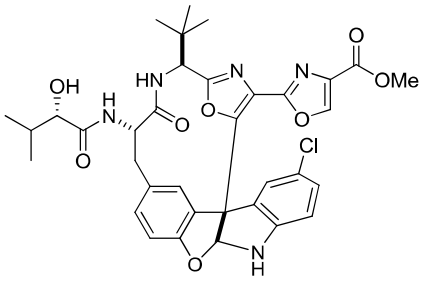
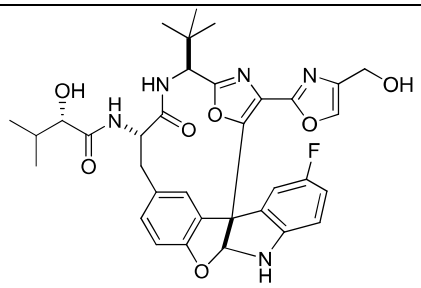
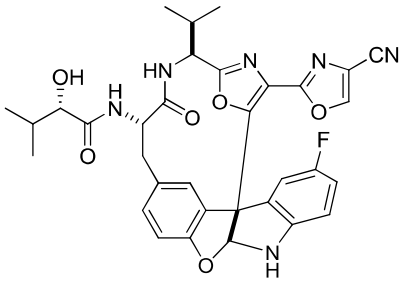
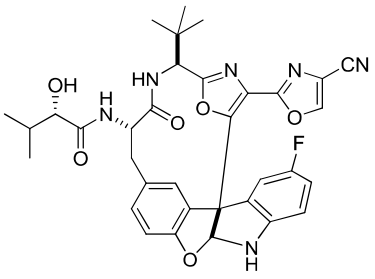
31			
III. Oxazole, 4 oxazoyl analogs with amide, amine, carbamate or sulfonamide in position 4			
32		33	
34		35	
36		37	
IV. Oxazole, 4 oxazoyl analogs with cyano-group in position 4			
38		39	

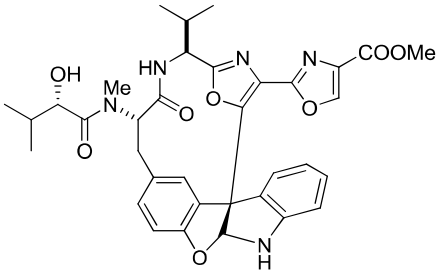
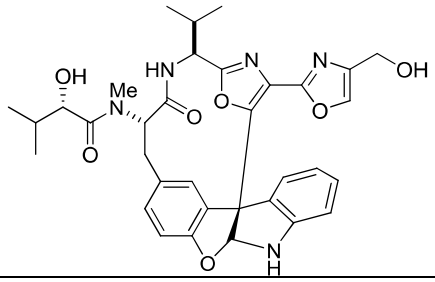
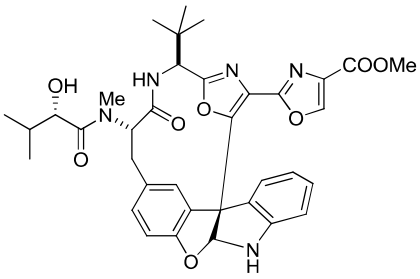
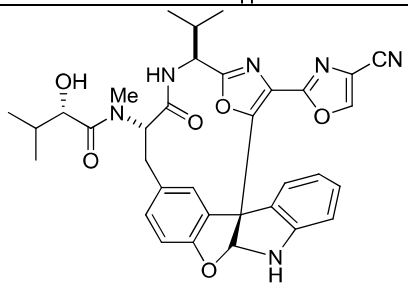
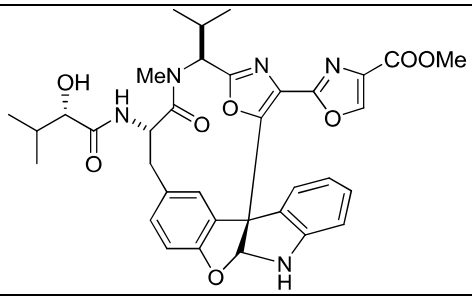
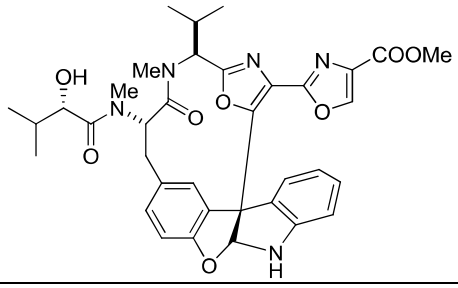
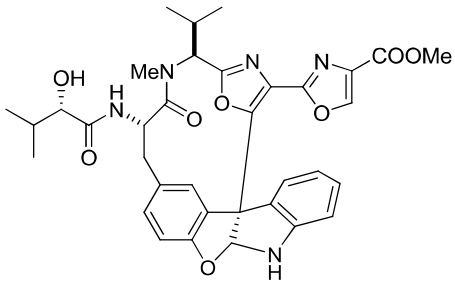
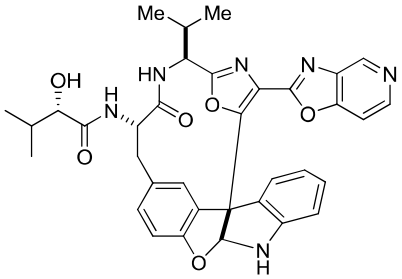
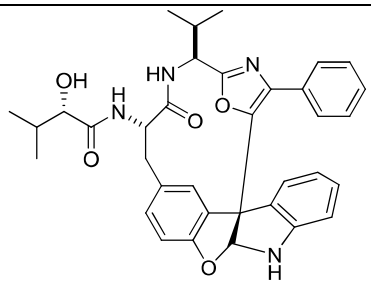
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V. Oxazole, 4 oxazoyl analogs with heterocycles in position 4			
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43		44	
45		46	
47		48	
VI. Oxazole, 4 oxazoyl analogs with substituents replacing isopropyl group			

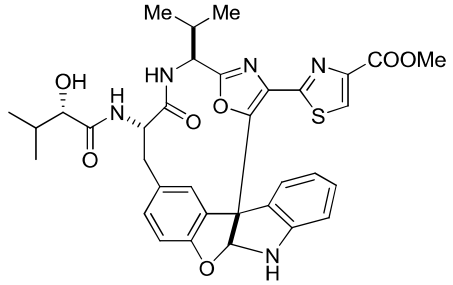
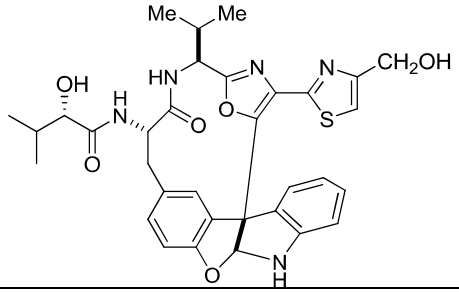
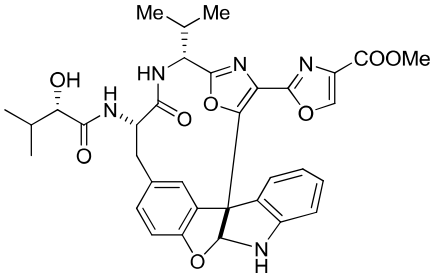
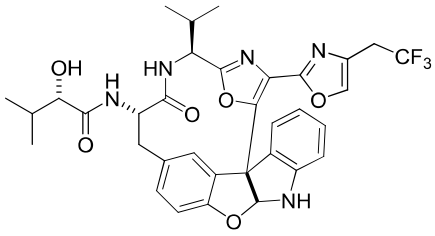
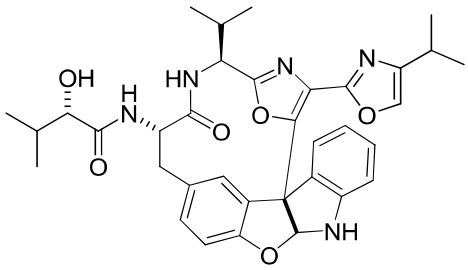
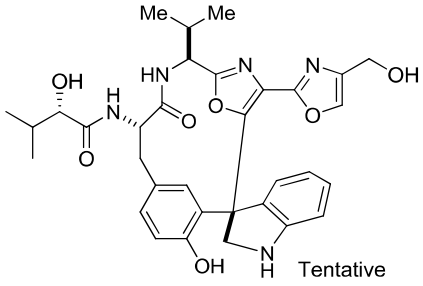
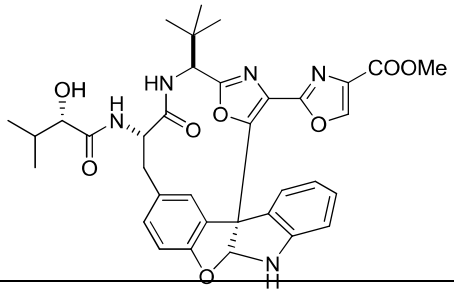
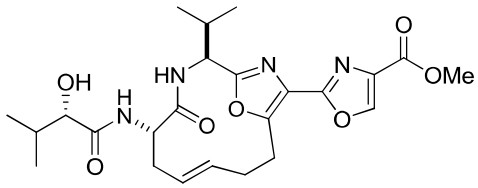
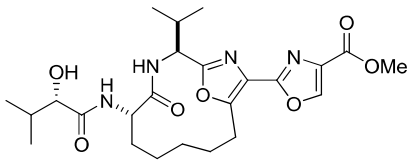
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67		68	

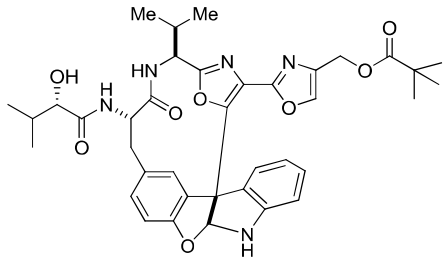
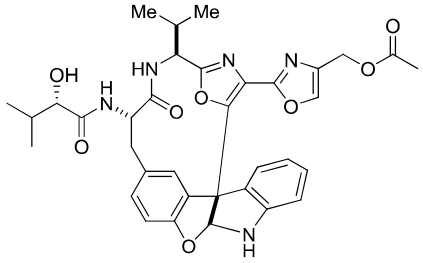
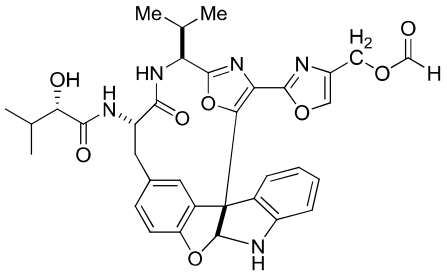
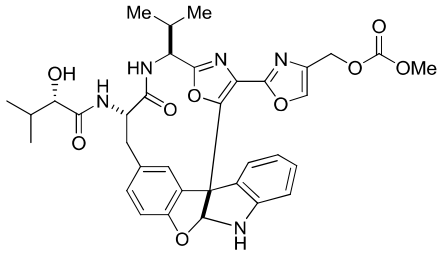
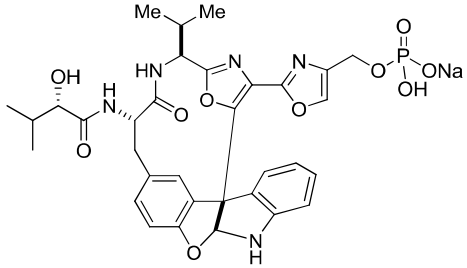
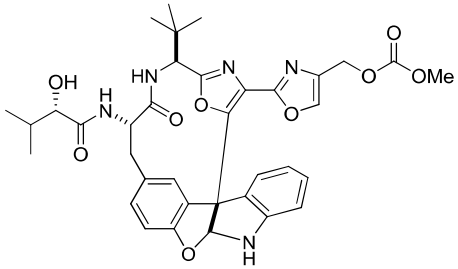
69			
VII. Oxazole, 4 oxazoyl analogs with variations in tyrosine moiety			
70		71	
72		73	
74		75	
VIII. Oxazole, 4 oxazoyl analogs with variations in indoline moiety			
76		77	

78		79	
80		81	
82		83	
84		85	
86		87	
IX. Oxazole, 4 oxazoyl analogs with N-Methyl group in side chain and/or macrocyclic moiety			

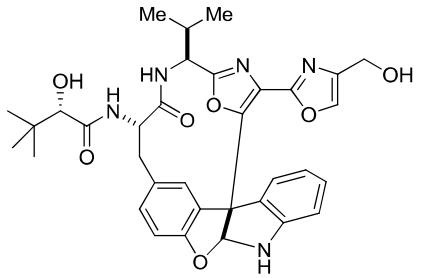
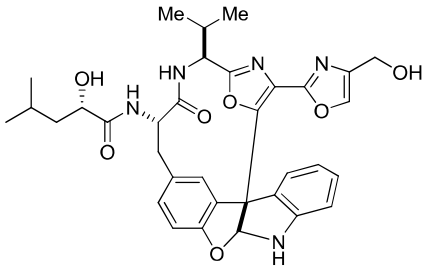
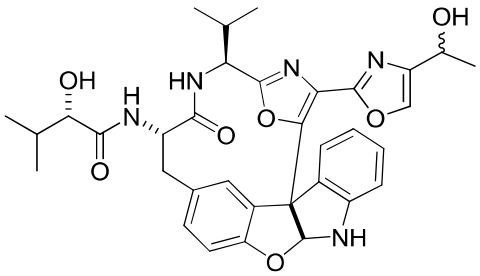
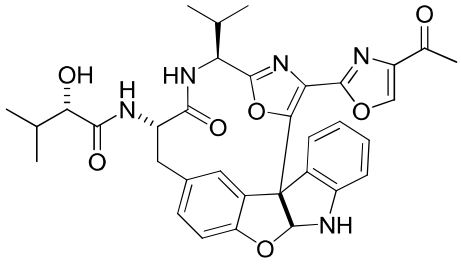
88		89	
90		91	
92		93	
94			
X. Oxazole, 4-aryl (non-oxazole) analogs			
95		96	

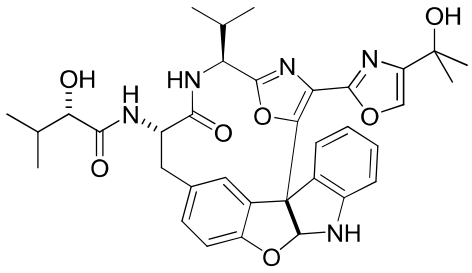
97		98	
XI. Oxazole, 4 oxazoyl analogs			
99		100	
101		102	 Tentative
103		104	
105			

2. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

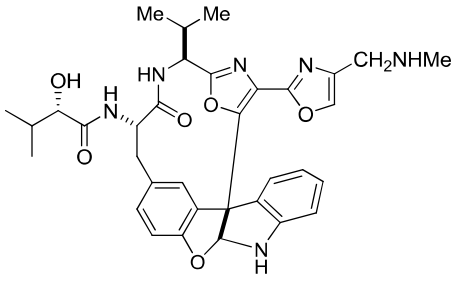
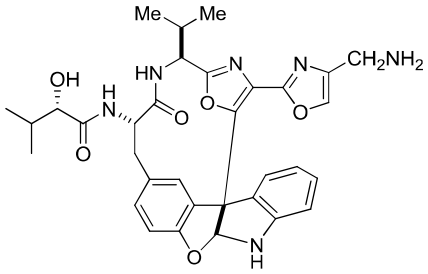
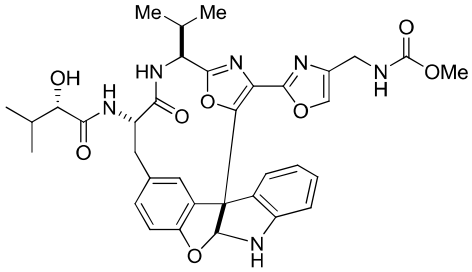
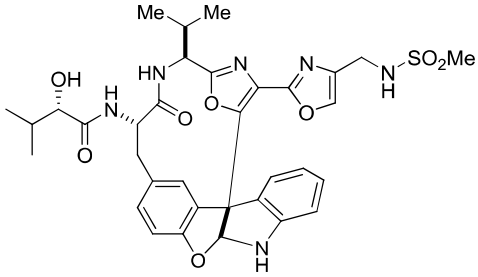
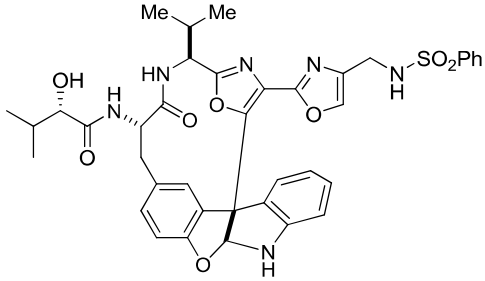
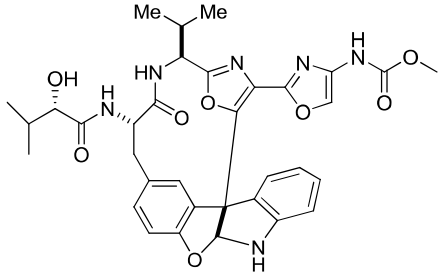
I. Oxazole, 4 oxazoyl analogs with esters other than methyl ester in position 4.			
21		22	
23		24	
25		26	

3. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

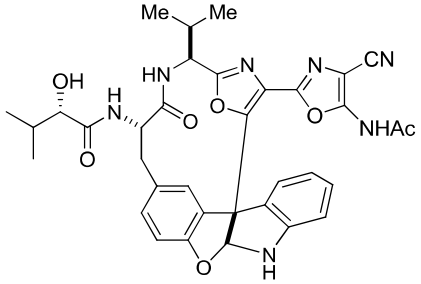
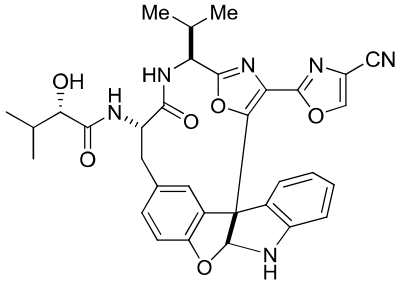
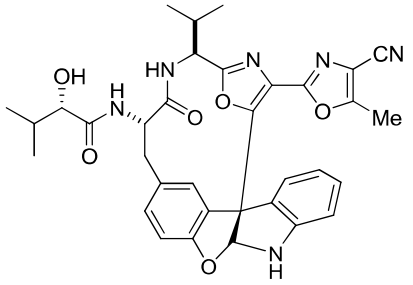
II. Oxazole, 4 oxazoyl analogs with alcohol or ketone in position 4			
27		28	
29		30	

31			

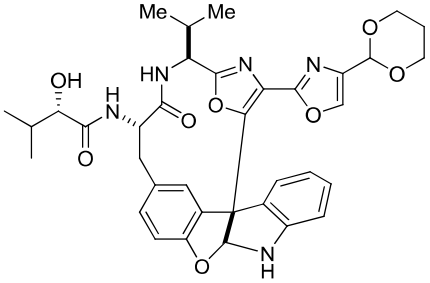
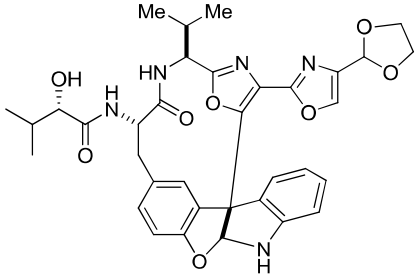
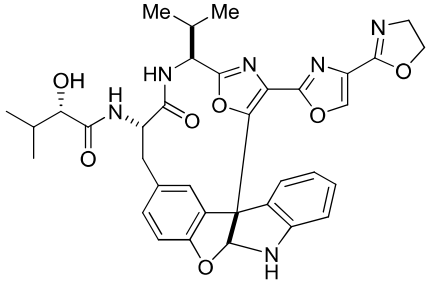
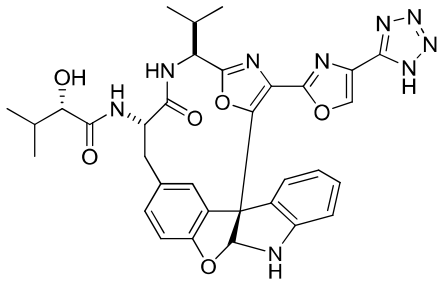
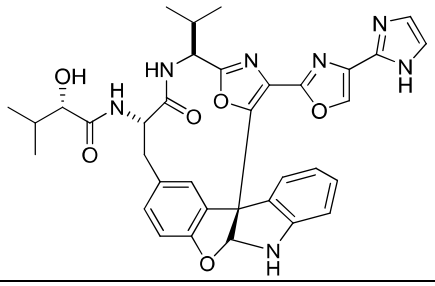
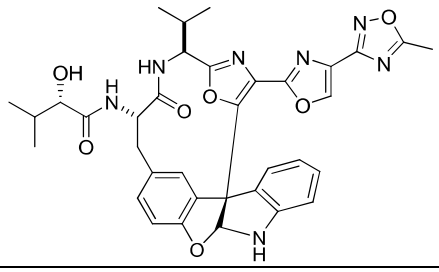
4. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

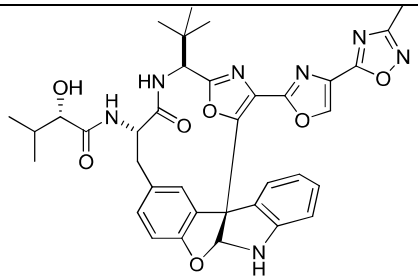
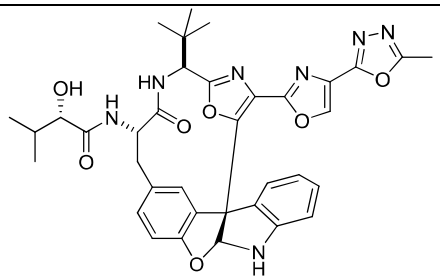
32		33	
34		35	
36		37	

5. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

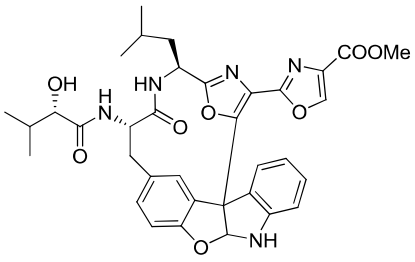
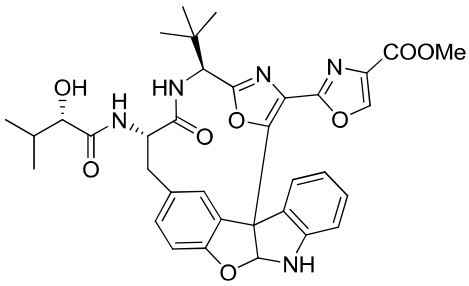
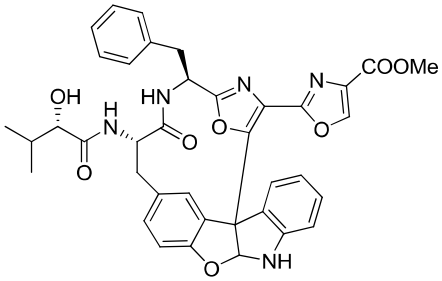
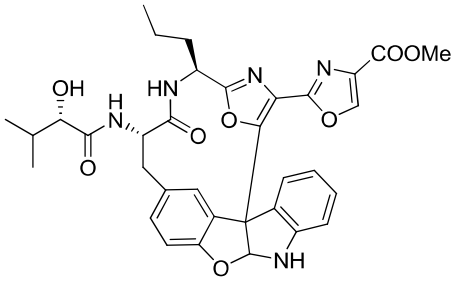
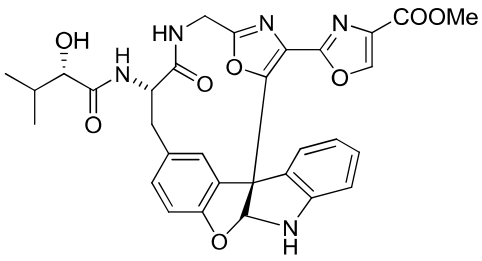
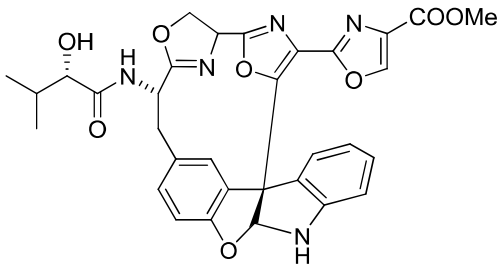
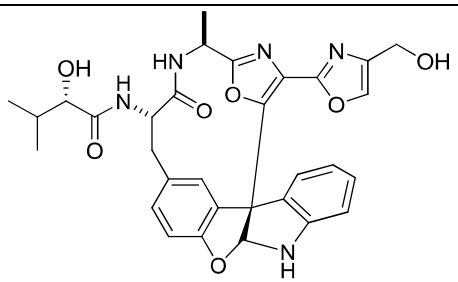
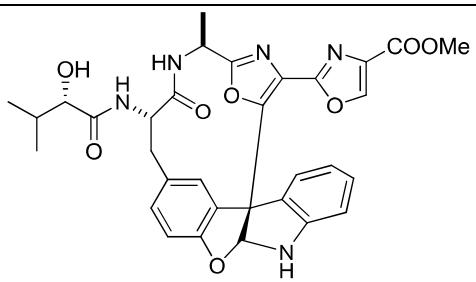
IV. Oxazole, 4 oxazoyl analogs with cyano-group in position 4			
38		39	
40			

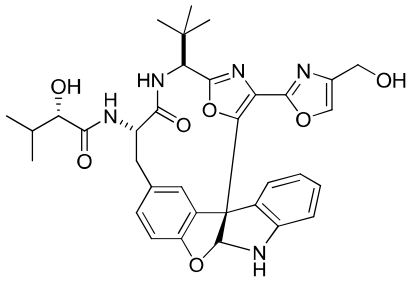
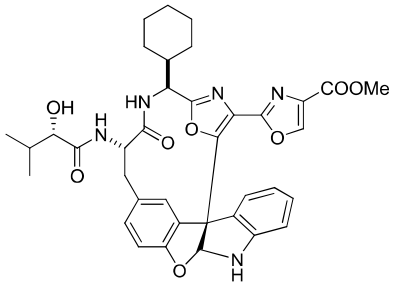
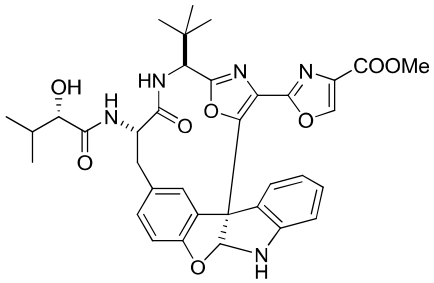
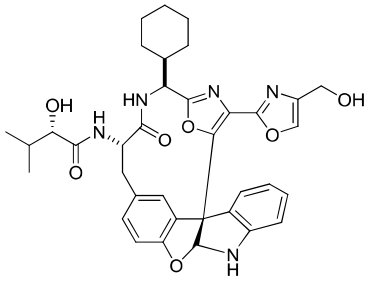
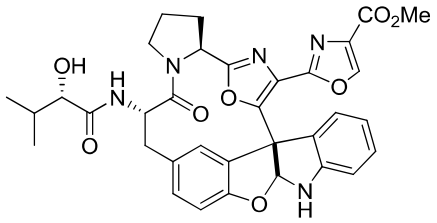
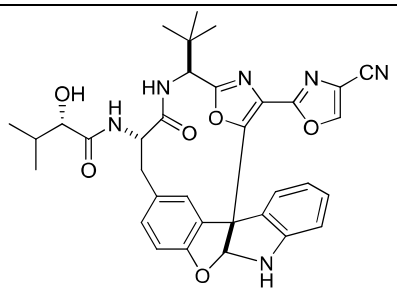
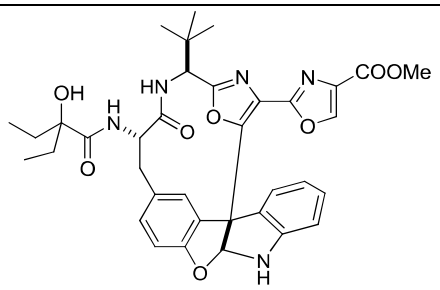
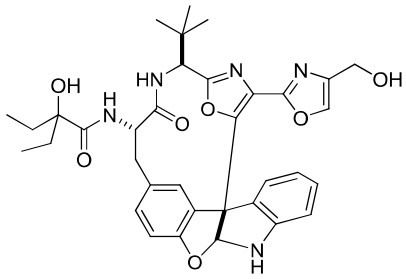
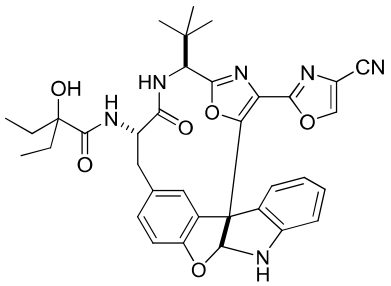
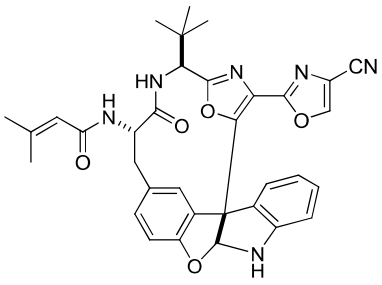
6. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

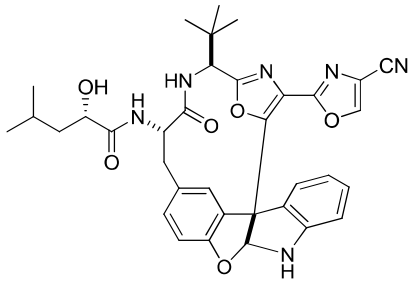
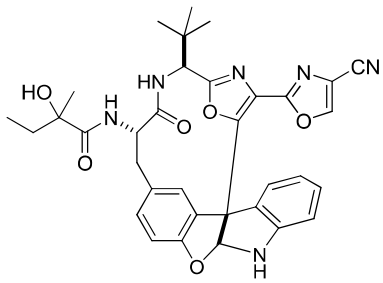
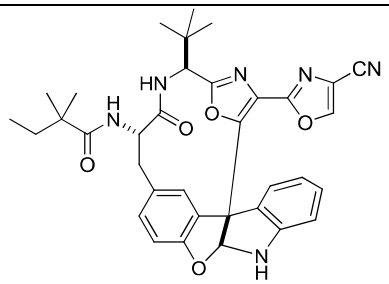
V. Oxazole, 4 oxazoyl analogs with heterocycles in position 4			
41		42	
43		44	
45		46	

47		48	

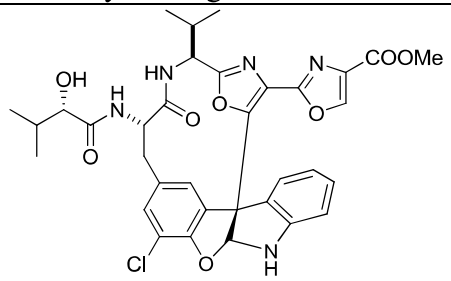
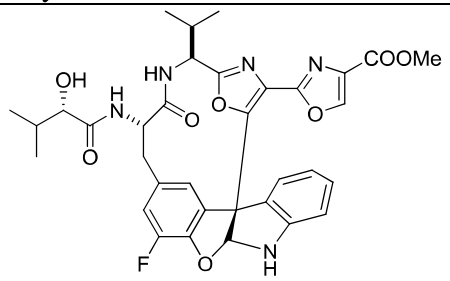
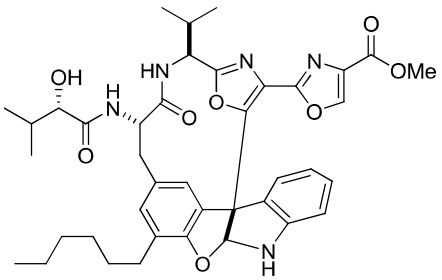
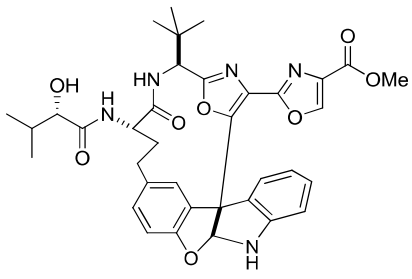
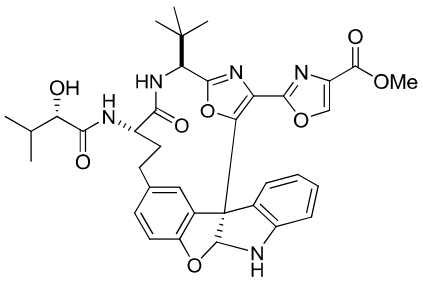
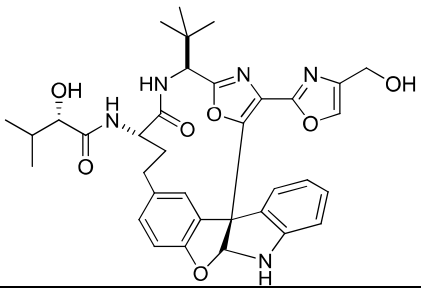
7. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

VI. Oxazole, 4 oxazoyl analogs with substituents replacing isopropyl group			
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51		52	
53		54	
55		56	

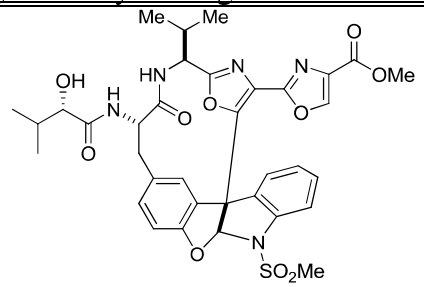
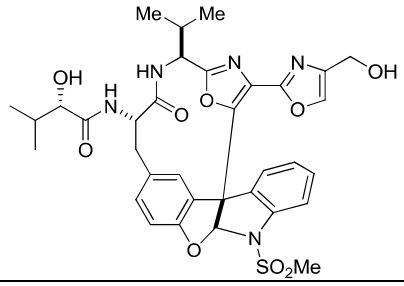
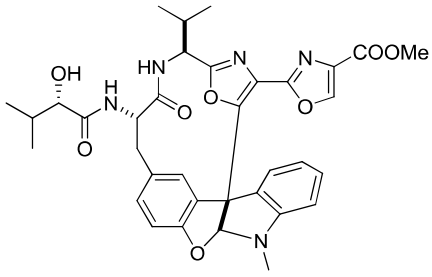
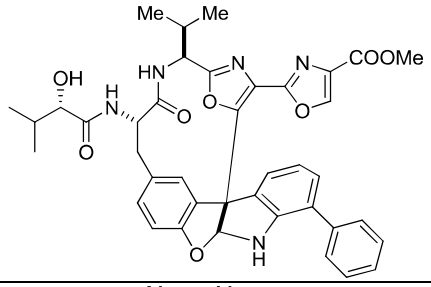
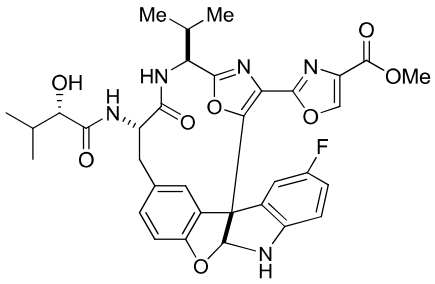
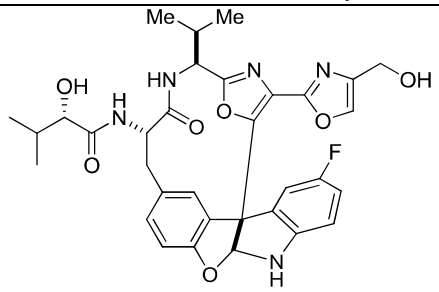
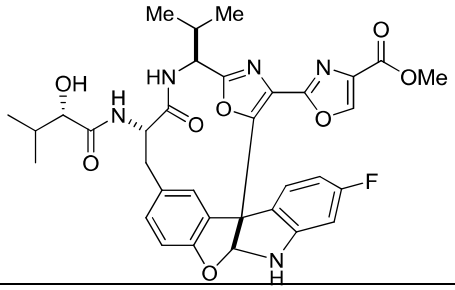
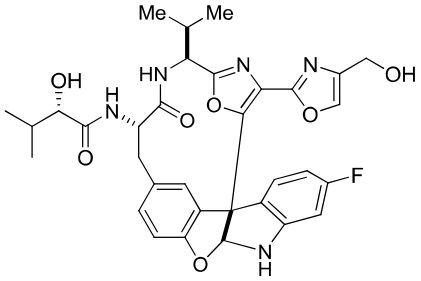
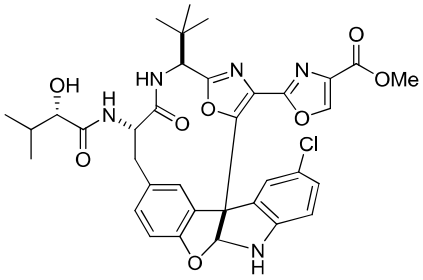
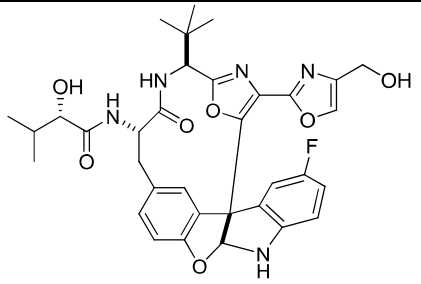
57		58	
59		60	
61		62	
63		64	
65		66	

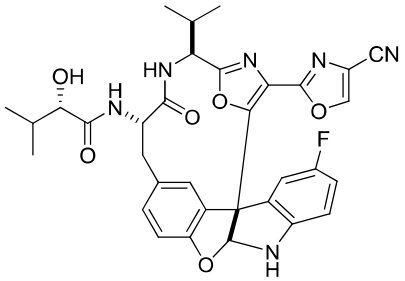
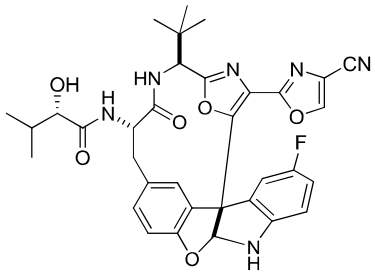
67		68	
69			

8. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

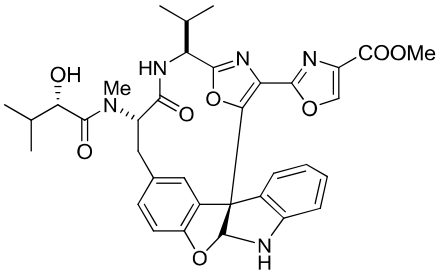
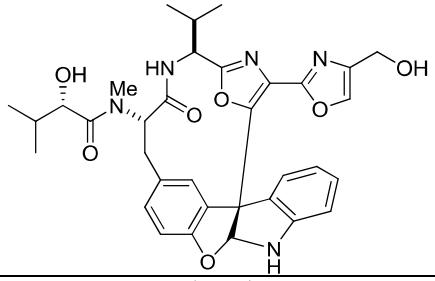
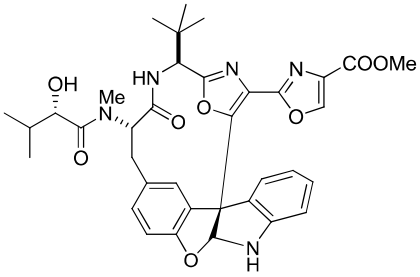
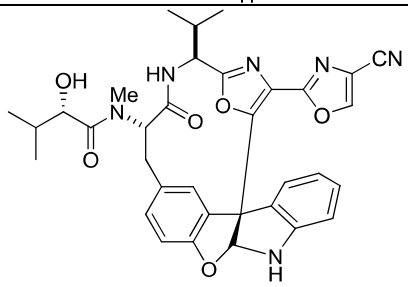
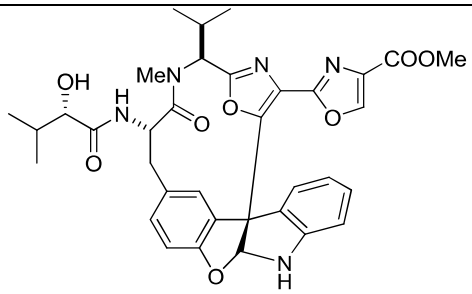
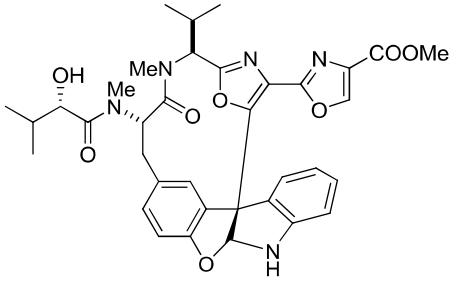
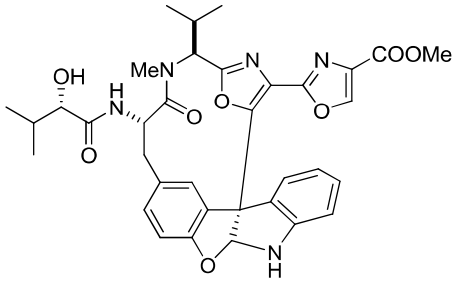
VII. Oxazole, 4 oxazoyl analogs with variations in tyrosine moiety			
70		71	
72		73	
74		75	

9. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

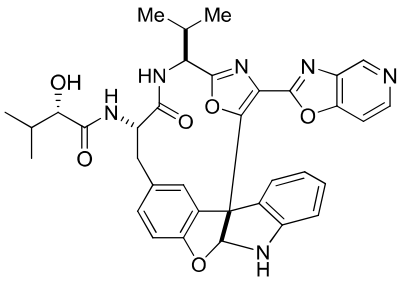
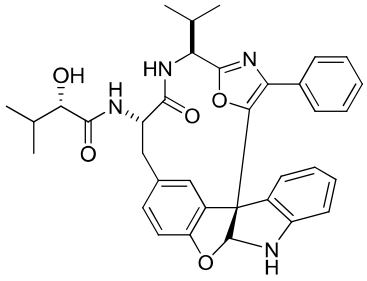
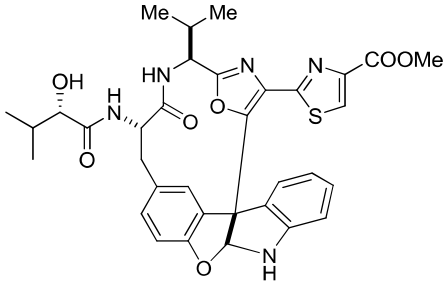
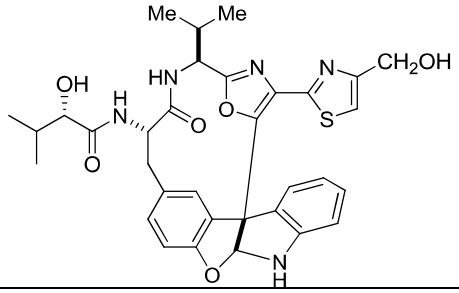
VIII. Oxazole, 4 oxazoyl analogs with variations in indoline moiety			
76		77	
78		79	
80		81	
82		83	
84		85	

86		87	

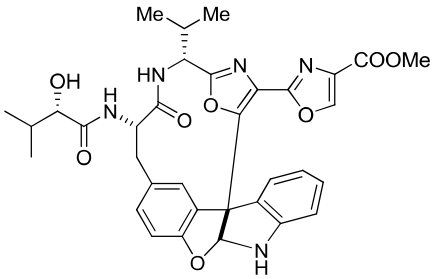
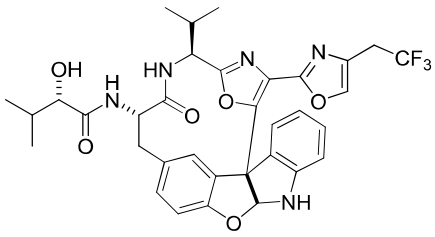
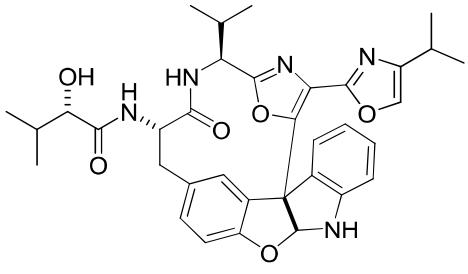
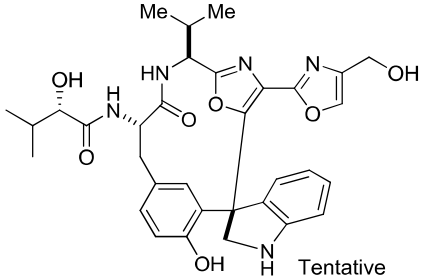
10. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

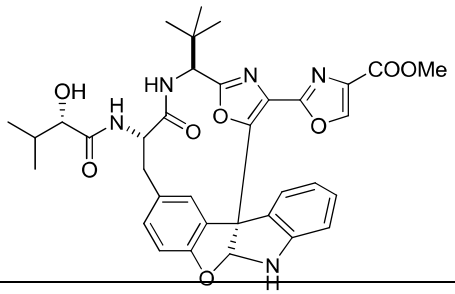
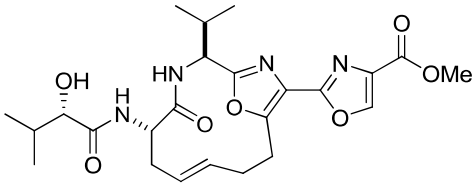
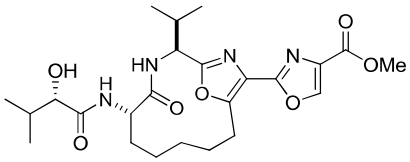
IX. Oxazole, 4 oxazoyl analogs with N-Methyl group in side chain and/or macrocyclic moiety			
88		89	
90		91	
92		93	
94			

11. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

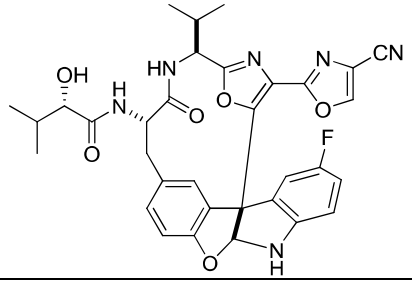
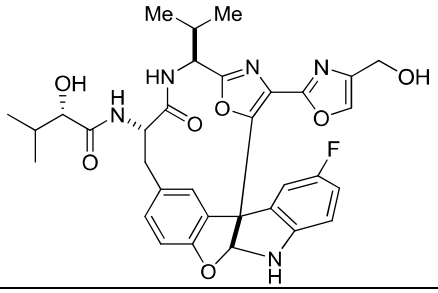
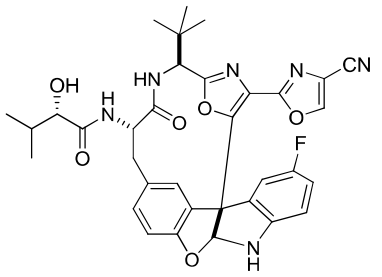
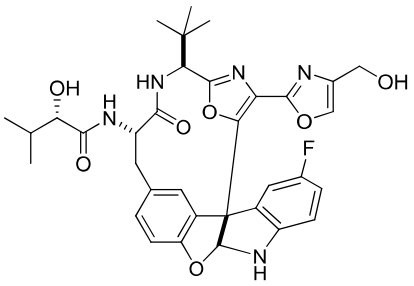
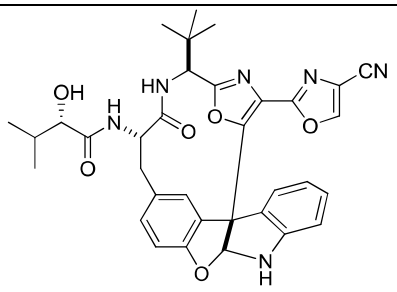
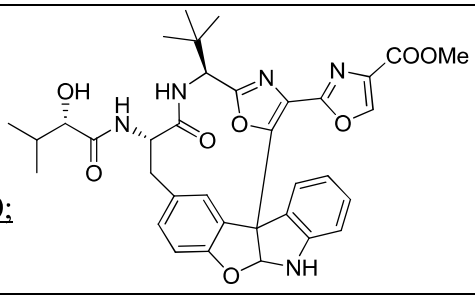
X. Oxazole, 4-aryl (non-oxazole) analogs			
95		96	
97		98	

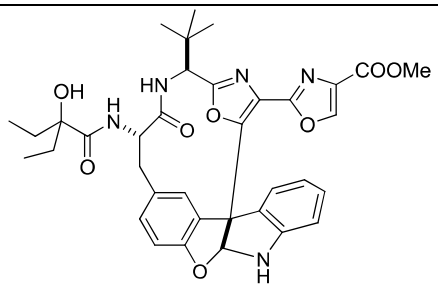
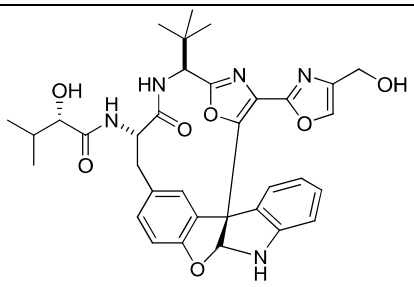
12. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

XI. Oxazole, 4 oxazoyl analogs			
99		100	
101		102	 Tentative

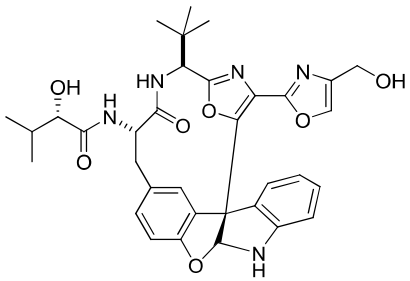
103		104	
105			

13. A compound of claim 1 and of the following table, or a pharmaceutically acceptable salt thereof:

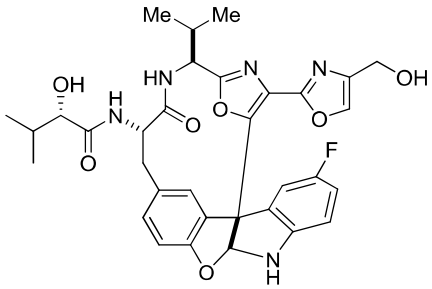
86;		81;	
87;		85;	
62;		50;	

63; 	57. 

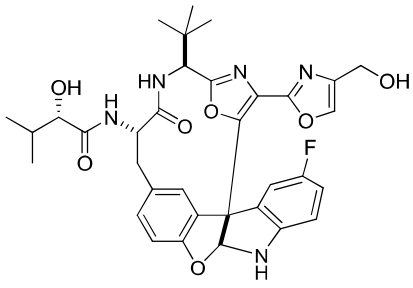
14. A compound of claim 1 having the following formula, or a pharmaceutically acceptable salt thereof:

57. 

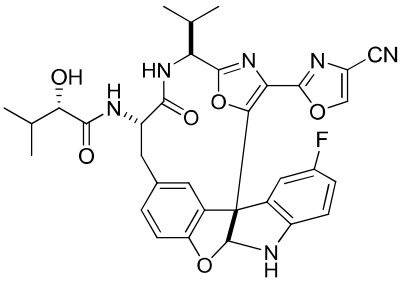
15. A compound of claim 1 having the following formula, or a pharmaceutically acceptable salt thereof:

81. 

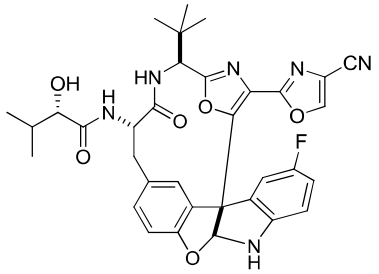
16. A compound of claim 1 having the following formula, or a pharmaceutically acceptable salt thereof:

85. 

17. A compound of claim 1 having the following formula, or a pharmaceutically acceptable salt thereof:

86. 

18. A compound of claim 1 having the following formula, or a pharmaceutically acceptable salt thereof:

87. 

19. A pharmaceutical composition comprising (a) the compound of claim 1 in unit dosage form with at least one pharmaceutically acceptable excipient, or (b) the compound of claim 1 and a different chemotherapeutic drug.