

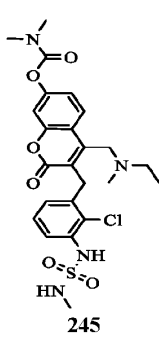
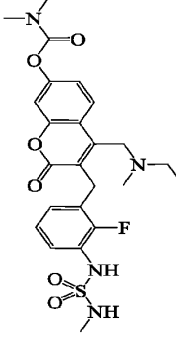
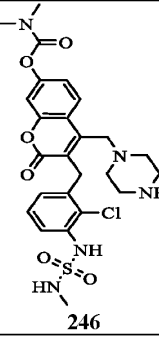
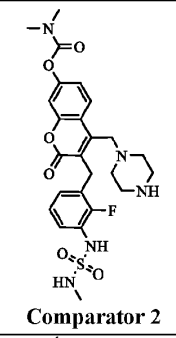
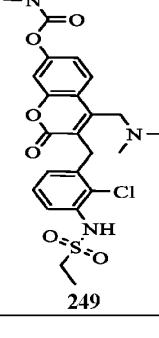
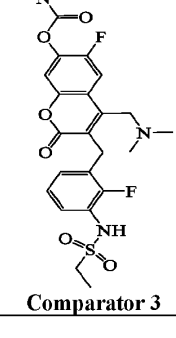
<u>Compound (A)</u>	<u>Comparator (B)</u>	<u>Ratio (A/B) of values obtained for each Compound/Comparator</u>				
		<u>Mouse</u> <u>Micr.</u> <u>half-life</u>	<u>Human</u> <u>Micr.</u> <u>Half-life</u>	<u>A549</u> <u>pERK</u> <u>(IC50,</u> <u>nM)</u>	<u>pERK:</u> <u>tERK</u> <u>@</u> <u>100nM</u> <u>(DMSO)</u>	<u>pERK:</u> <u>tERK</u> <u>@10</u> <u>microM</u> <u>(DMSO)</u>
 245	 Comparator 1	0.7	0.9	1.6	2.3	0.7
 246	 Comparator 2	>90/>90"	"69/>90"	0.5	1.0	0.6
 249	 Comparator 3	0.6	0.6	2.0	1.2	0.7

FIG. 1

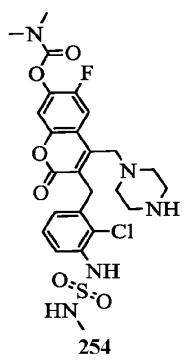
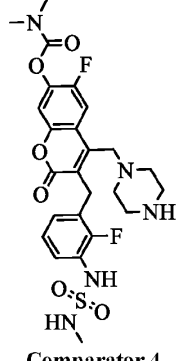
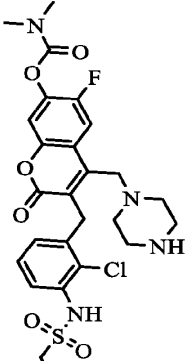
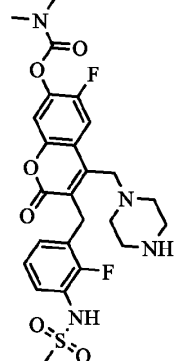
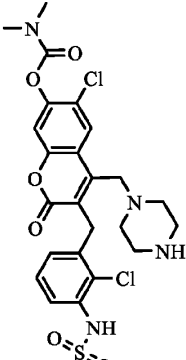
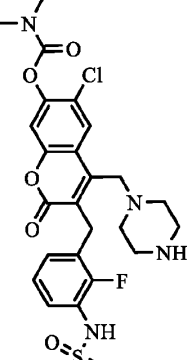
<u>Compound (A)</u>	<u>Comparator (B)</u>	<u>Ratio (A/B) of values obtained for each Compound/Comparator</u>				
		<u>Mouse</u> <u>Micr.</u> <u>half-life</u>	<u>Human</u> <u>Micr.</u> <u>Half-life</u>	<u>A549</u> <u>pERK</u> <u>(IC50,</u> <u>nM)</u>	<u>pERK:</u> <u>tERK</u> <u>@</u> <u>100nM</u> <u>(DMSO)</u>	<u>pERK:</u> <u>tERK</u> <u>@10</u> <u>microM</u> <u>(DMSO)</u>
 254	 Comparator 4	">90/>90"	">90/>90"	1.0	0.8	0.8
 255	 Comparator 5	">90/>240"	">90/145"	0.2	0.5	0.6
 256	 Comparator 6	">90/>90"	"56/>90"	0.3	0.7	0.8

FIG 1 Continued

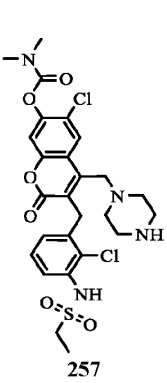
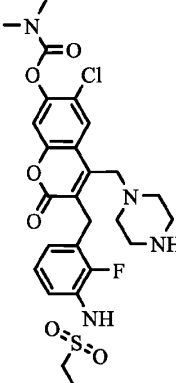
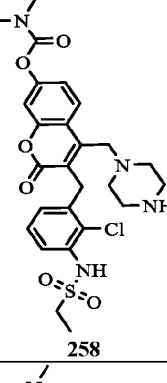
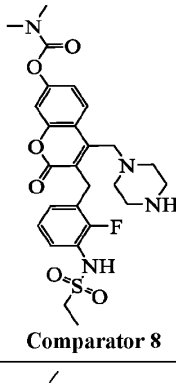
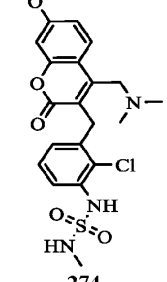
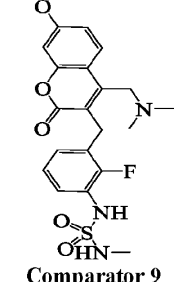
<u>Compound (A)</u>	<u>Comparator (B)</u>	<u>Ratio (A/B) of values obtained for each Compound/Comparator</u>				
		<u>Mouse</u> <u>Micr.</u> <u>half-life</u>	<u>Human</u> <u>Micr.</u> <u>Half-life</u>	<u>A549</u> <u>pERK</u> <u>(IC50,</u> <u>nM)</u>	<u>pERK:</u> <u>tERK</u> <u>@</u> <u>100nM</u> <u>(DMSO)</u>	<u>pERK:</u> <u>tERK</u> <u>@10</u> <u>microM</u> <u>(DMSO)</u>
 257	 Comparator 7	>90/>90"	>90/>90"	0.2	0.5	0.9
 258	 Comparator 8	>90/>240"	>90/139"	0.1	0.5	0.7
 274	 Comparator 9	0.8	0.7	2.0	1.6	1.0

FIG 1 Continued

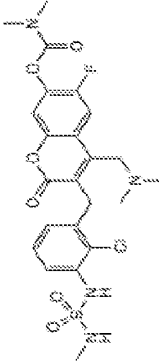
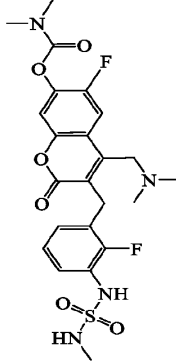
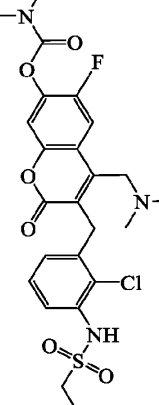
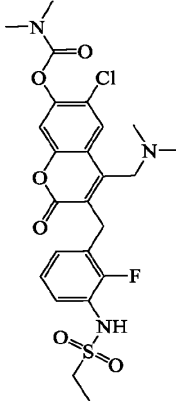
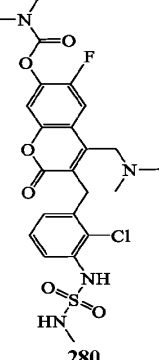
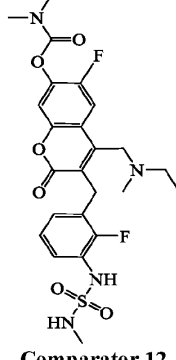
<u>Compound (A)</u>	<u>Comparator (B)</u>	<u>Ratio (A/B) of values obtained for each Compound/Comparator</u>				
		<u>Mouse</u> <u>Micr.</u> <u>half-life</u>	<u>Human</u> <u>Micr.</u> <u>Half-life</u>	<u>A549</u> <u>pERK</u> <u>(IC50,</u> <u>nM)</u>	<u>pERK:</u> <u>tERK</u> <u>@</u> <u>100nM</u> <u>(DMSO)</u>	<u>pERK:</u> <u>tERK</u> <u>@10</u> <u>microM</u> <u>(DMSO)</u>
 278	 Comparator 10	0.3	0.7	11.6	2.0	1.4
 279	 Comparator 11	0.7	1.7	18.2	3.3	1.3
 280	 Comparator 12	0.5	0.7	0.4	2.0	1.8

FIG 1 Continued

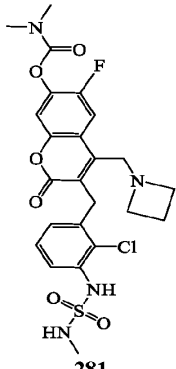
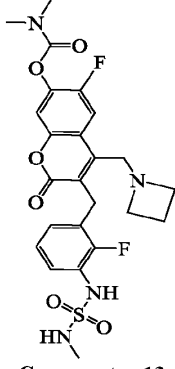
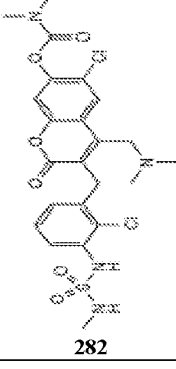
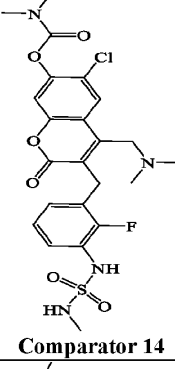
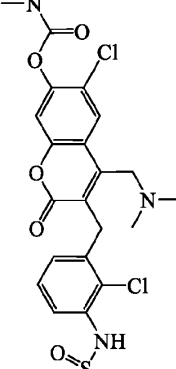
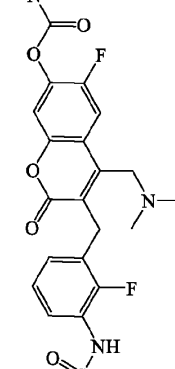
<u>Compound (A)</u>	<u>Comparator (B)</u>	<u>Ratio (A/B) of values obtained for each Compound/Comparator</u>				
		<u>Mouse</u> <u>Micr.</u> <u>half-life</u>	<u>Human</u> <u>Micr.</u> <u>Half-life</u>	<u>A549</u> <u>pERK</u> <u>(IC50,</u> <u>nM)</u>	<u>pERK:</u> <u>tERK</u> <u>@</u> <u>100nM</u> <u>(DMSO)</u>	<u>pERK:</u> <u>tERK</u> <u>@10</u> <u>microM</u> <u>(DMSO)</u>
 281	 Comparator 13	0.5	0.6	0.4	3.1	1.1
 282	 Comparator 14	0.4	0.7	0.8	1.3	1.0
 283	 Comparator 15	0.4	0.4	0.8	1.2	1.5

FIG 1 Continued

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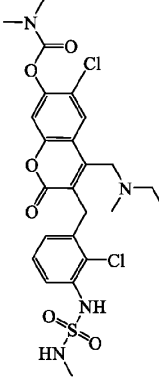
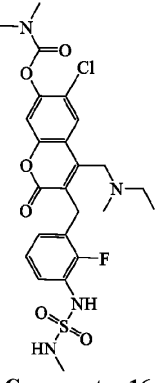
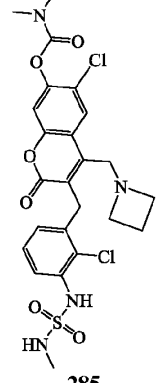
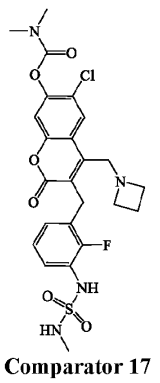
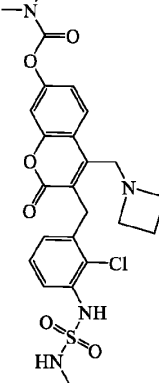
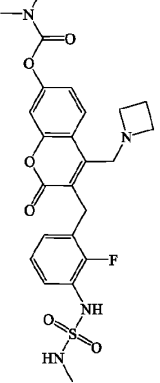
<u>Compound (A)</u>	<u>Comparator (B)</u>	<u>Ratio (A/B) of values obtained for each Compound/Comparator</u>				
		<u>Mouse</u> <u>Micr.</u> <u>half-life</u>	<u>Human</u> <u>Micr.</u> <u>Half-life</u>	<u>A549</u> <u>pERK</u> <u>(IC50,</u> <u>nM)</u>	<u>pERK:</u> <u>tERK</u> <u>@</u> <u>100nM</u> <u>(DMSO)</u>	<u>pERK:</u> <u>tERK</u> <u>@10</u> <u>microM</u> <u>(DMSO)</u>
 284	 Comparator 16	0.7	0.7	2.2	1.5	1.0
 285	 Comparator 17	0.4	0.4	1.2	1.0	1.0
 286	 Comparator 18	0.4	0.9	2.8	1.7	1.4

FIG 1 Continued

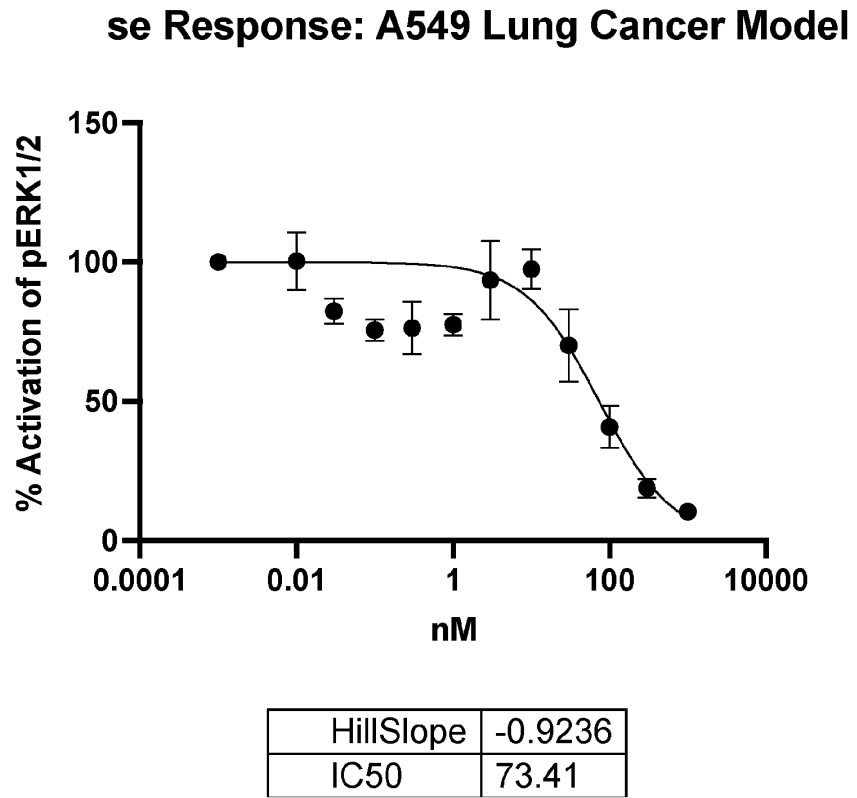


FIG 2A

Dose Response: A375 Melanoma Model

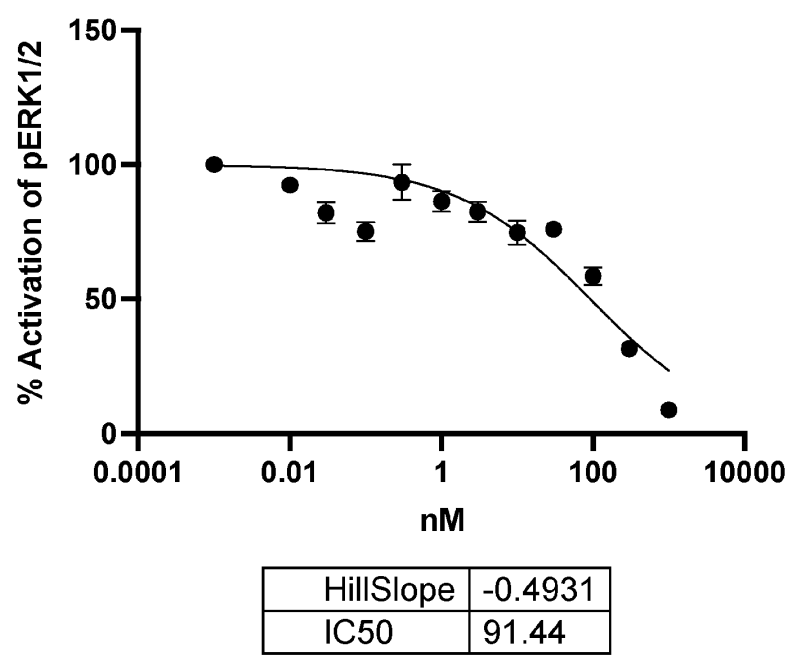


FIG. 2B

Dose Response: SK-MEL-2 Melanoma Model

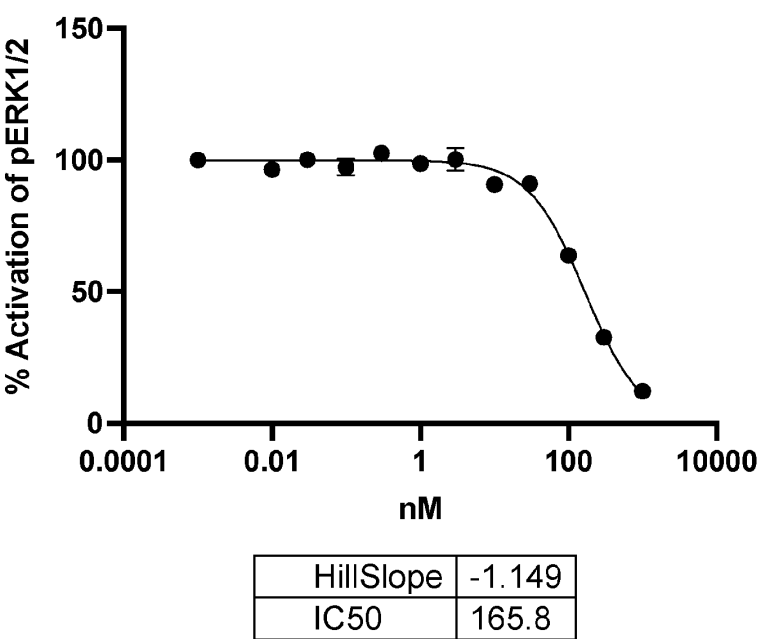


FIG. 2C

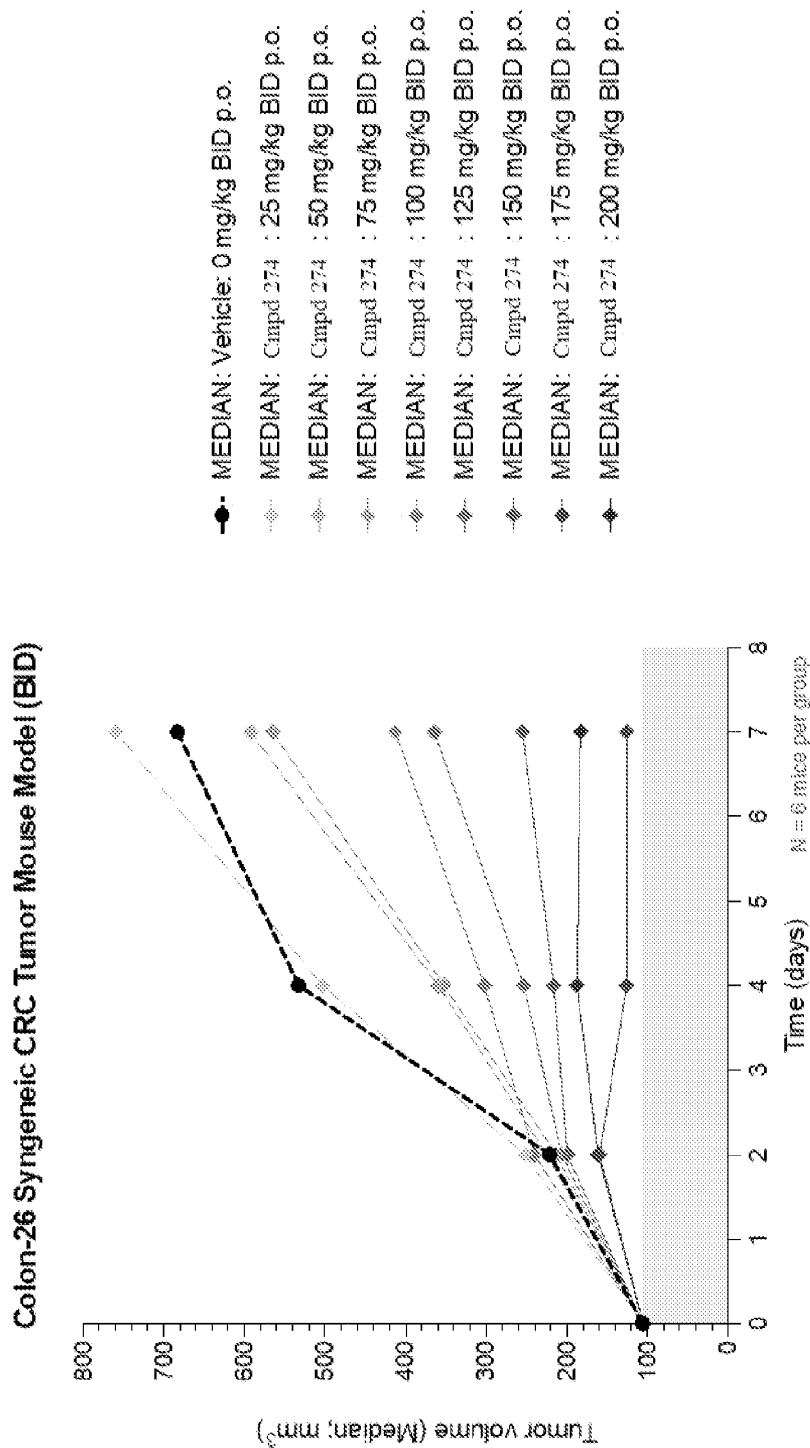


FIG. 3

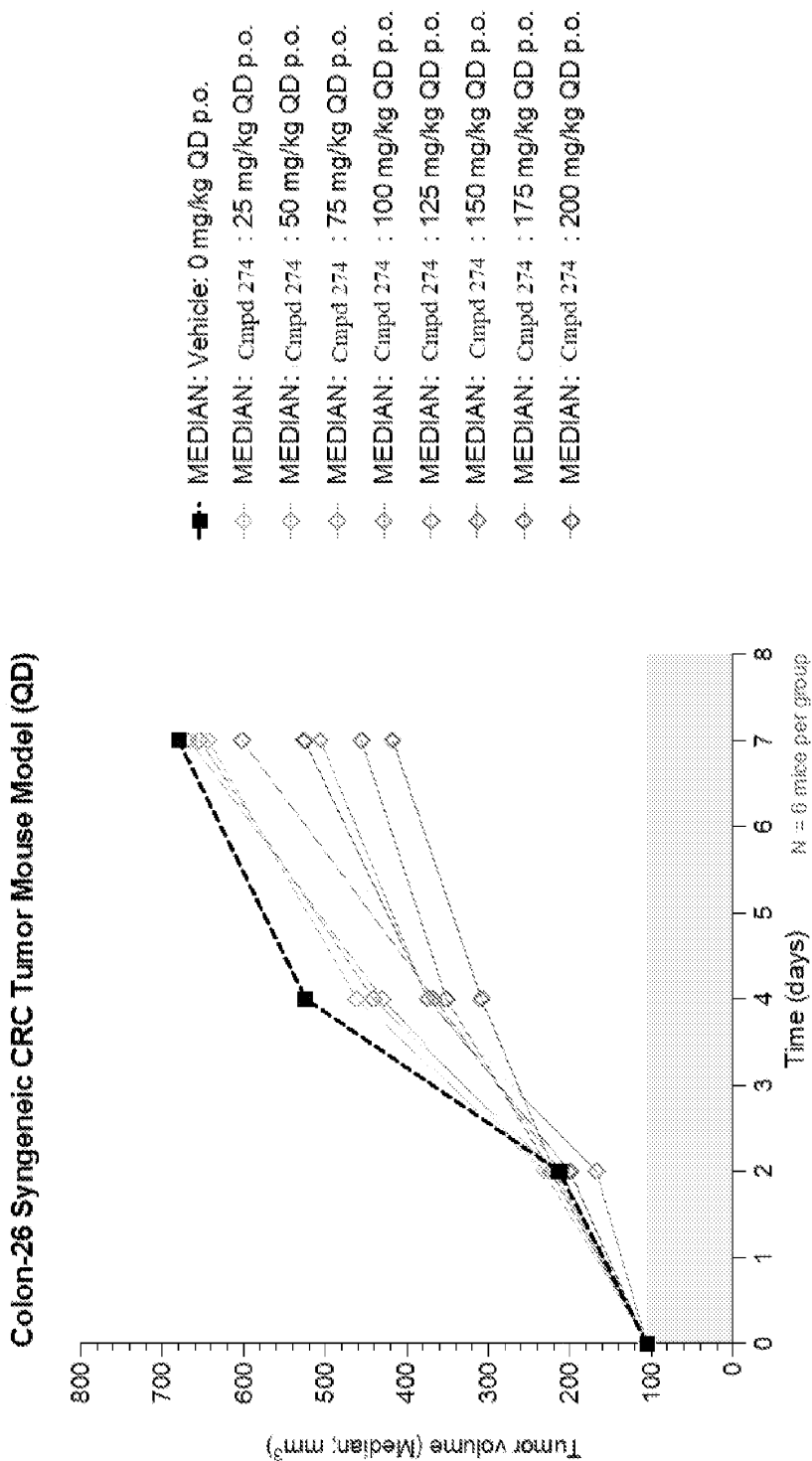


FIG. 4

Table A

No.	Structure	No.	Structure
7		9	
10		11	
12		13	
14		15	
16		17	

FIG. 5

No.	Structure	No.	Structure
18		19	
20		21	
22		23	
24		25	
26		27	

FIG 5 Continued

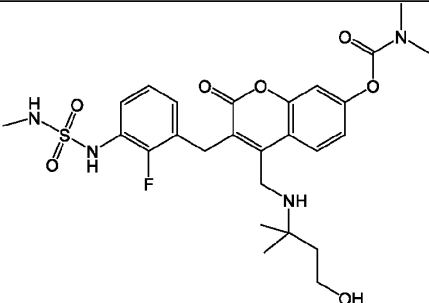
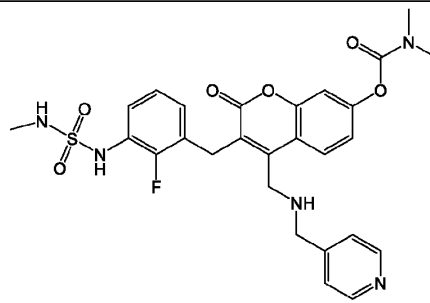
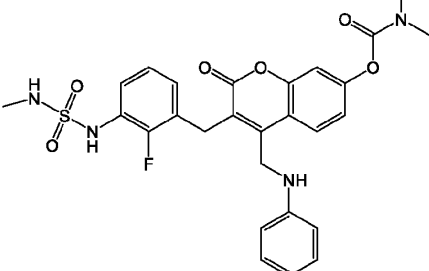
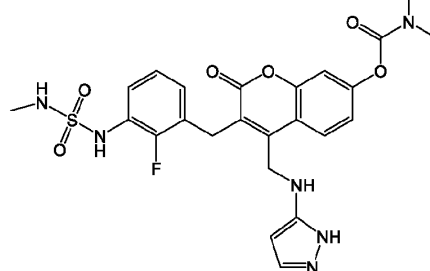
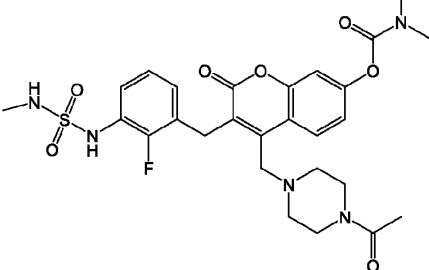
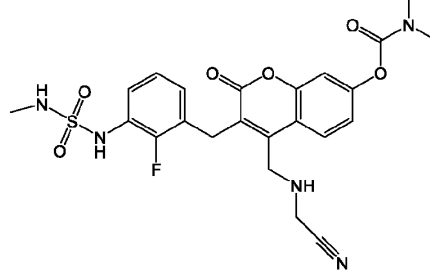
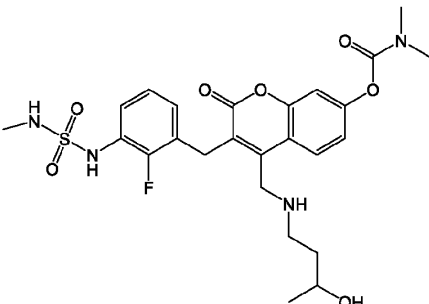
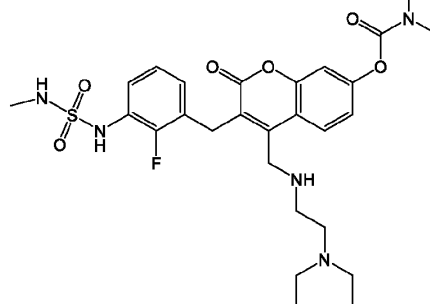
No.	Structure	No.	Structure
28		29	
30		31	
32		33	
34		35	

FIG 5 Continued

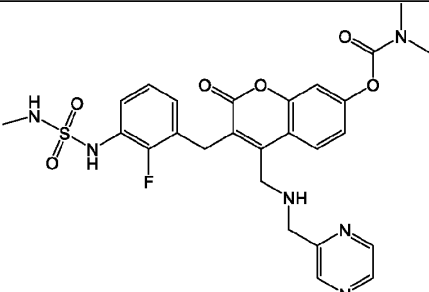
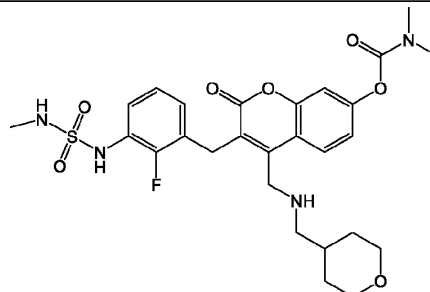
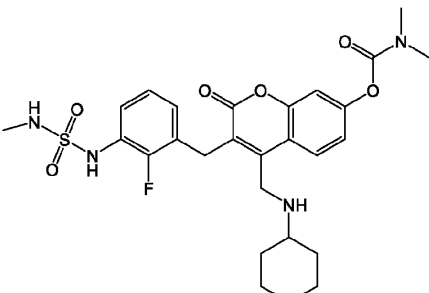
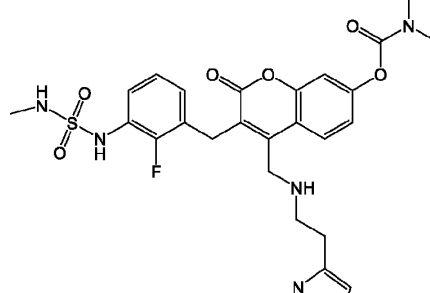
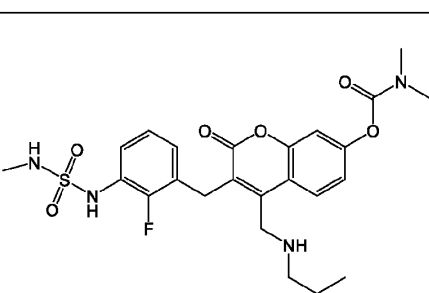
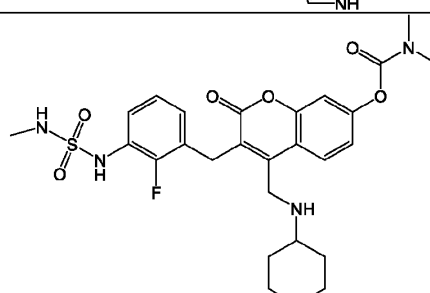
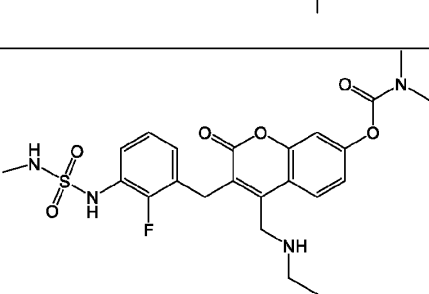
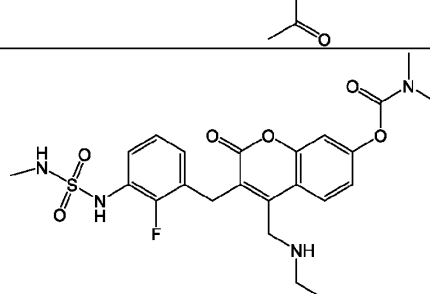
No.	Structure	No.	Structure
36		37	
38		39	
40		41	
42		43	

FIG 5 Continued

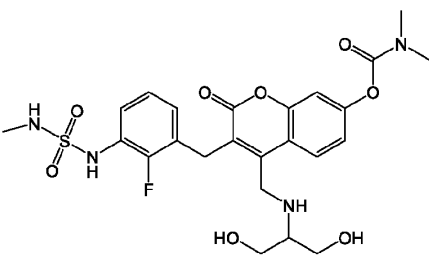
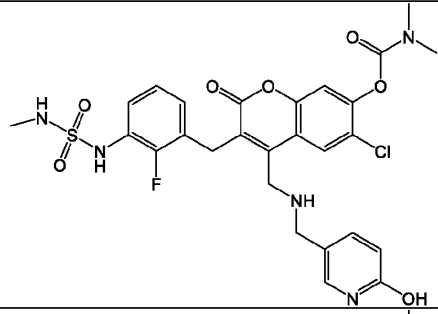
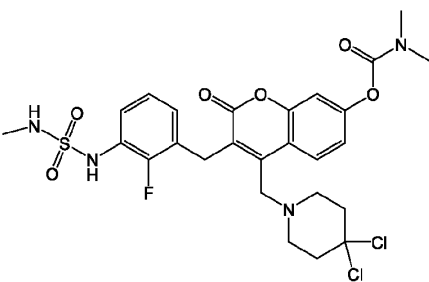
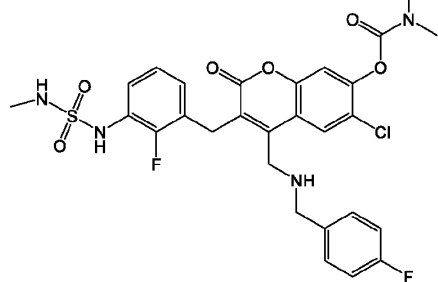
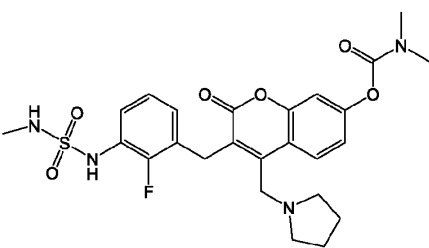
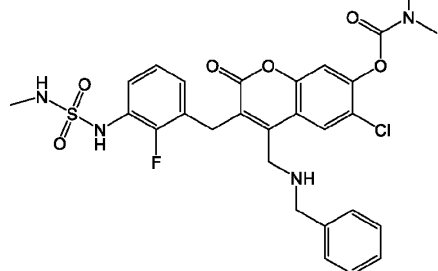
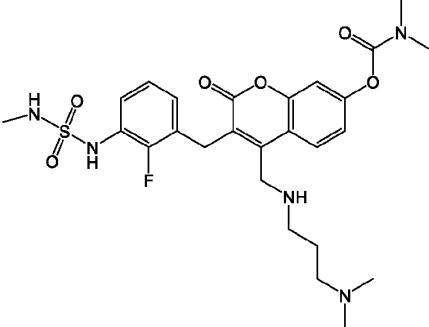
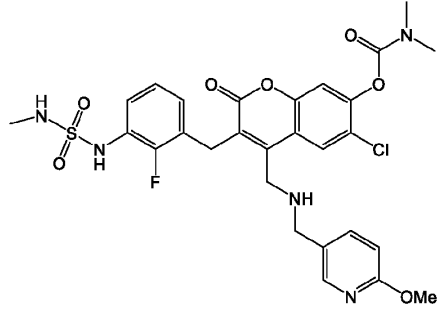
No.	Structure	No.	Structure
44		45	
46		47	
48		49	
50		51	

FIG 5 Continued

No.	Structure	No.	Structure
52		53	
54		55	
56		57	
58		59	

FIG 5 Continued

No.	Structure	No.	Structure
60		61	
62		63	
64		65	
66		67	

FIG 5 Continued

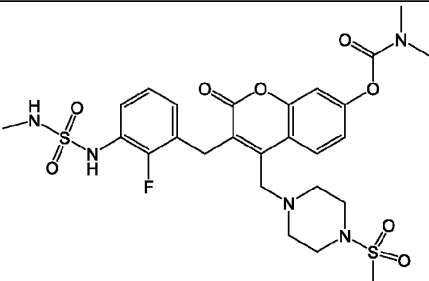
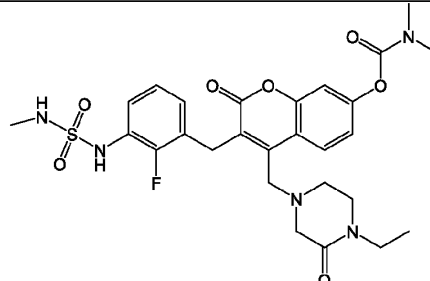
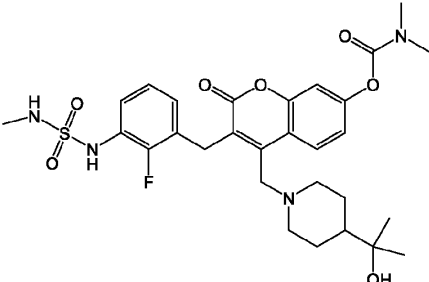
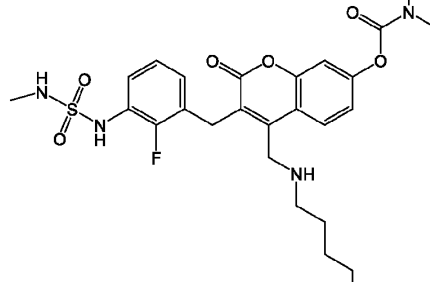
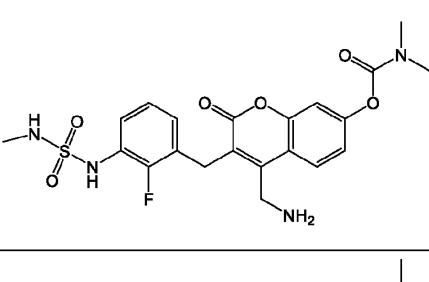
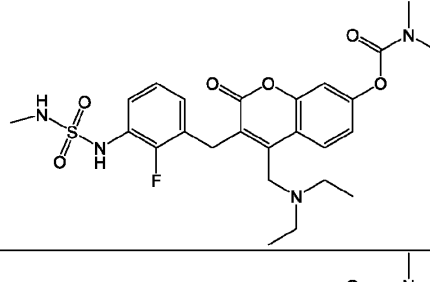
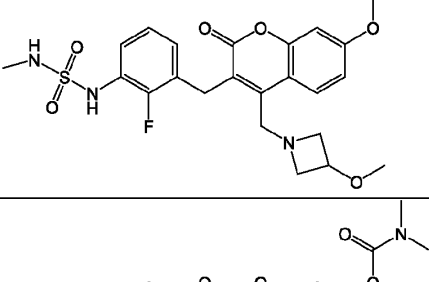
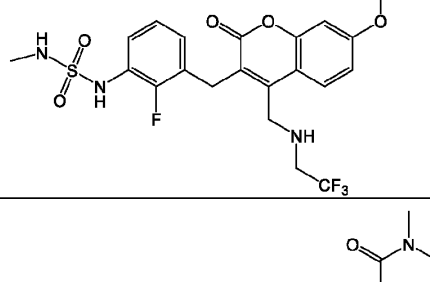
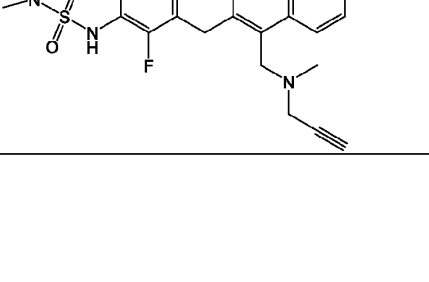
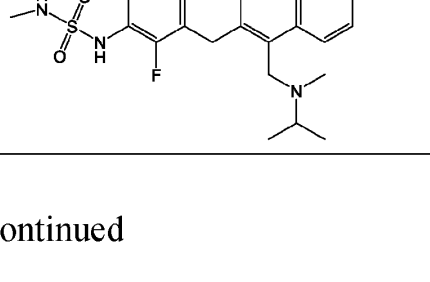
No.	Structure	No.	Structure
68		69	
70		71	
72		73	
74		75	
76		77	

FIG 5 Continued

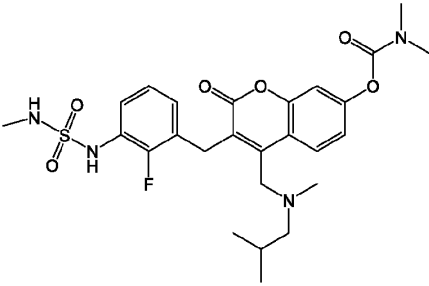
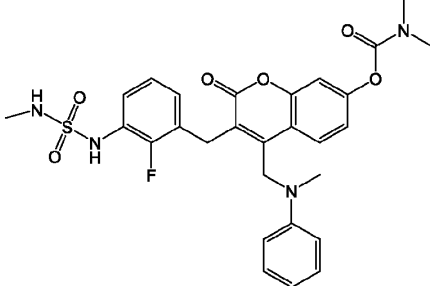
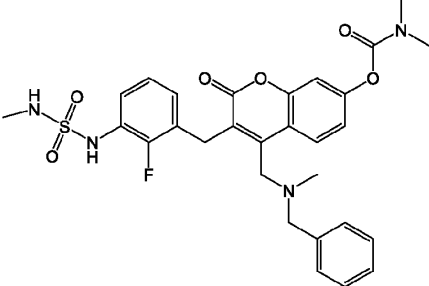
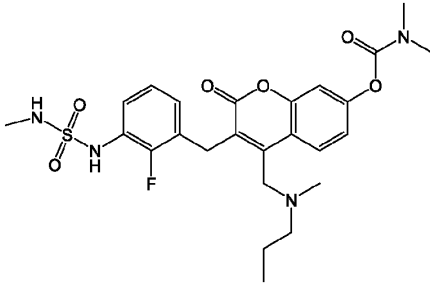
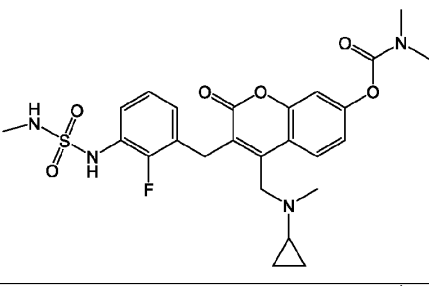
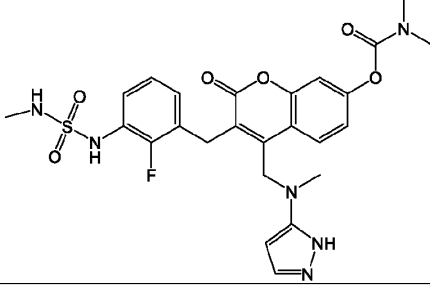
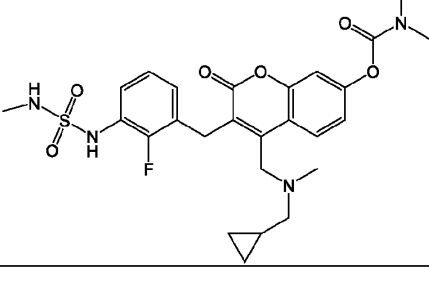
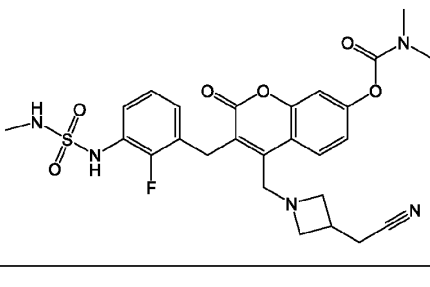
No.	Structure	No.	Structure
78		79	
80		81	
82		83	
84		85	

FIG 5 Continued

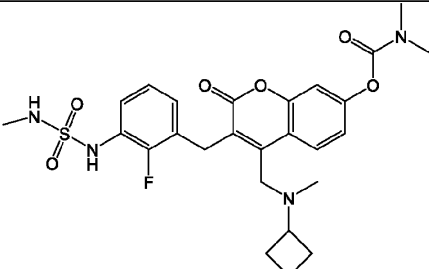
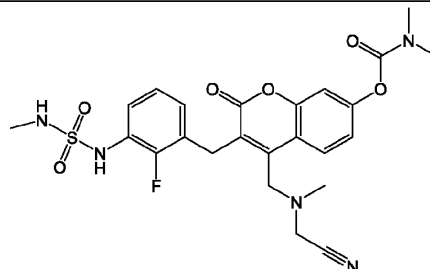
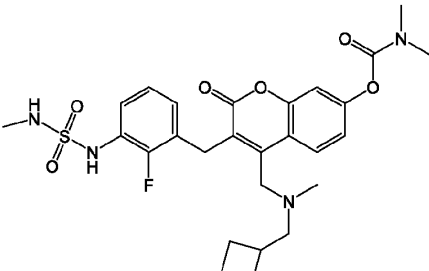
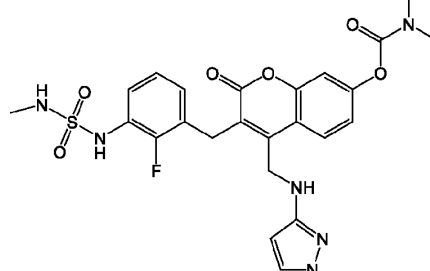
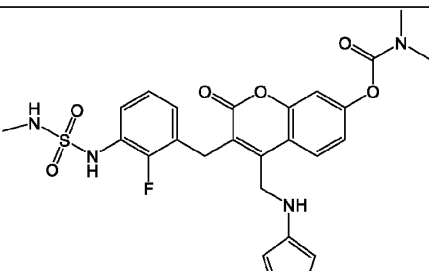
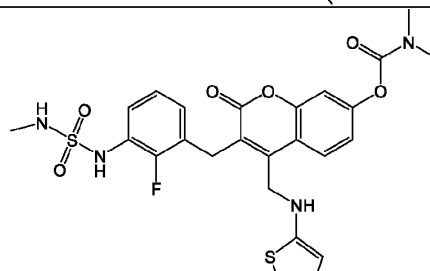
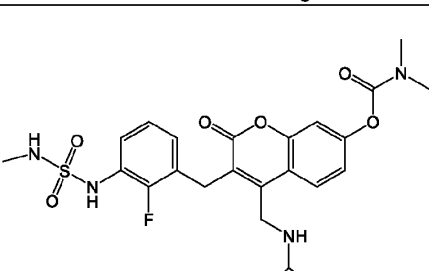
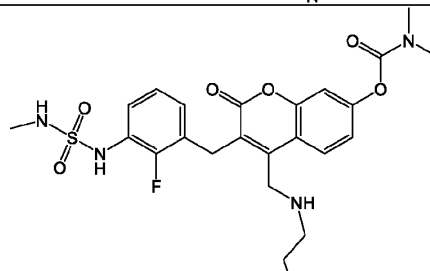
No.	Structure	No.	Structure
86		87	
88		89	
90		91	
92		93	

FIG 5 Continued

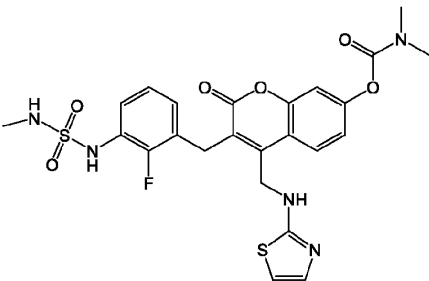
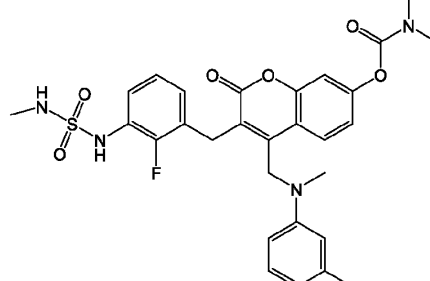
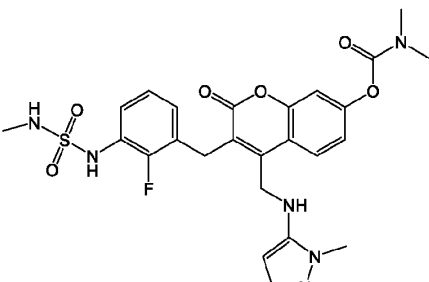
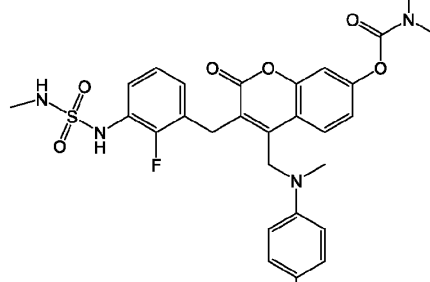
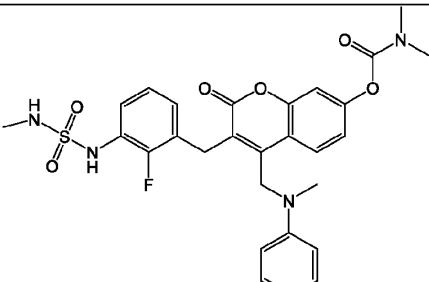
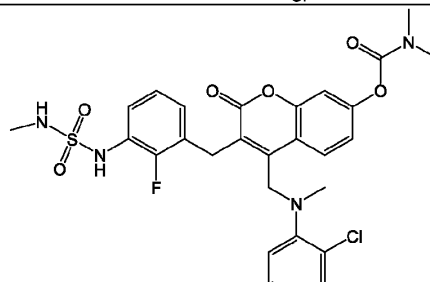
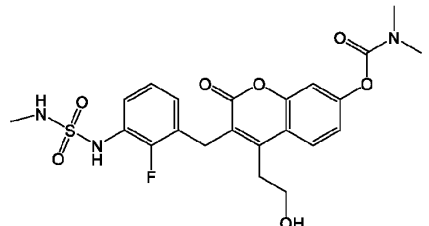
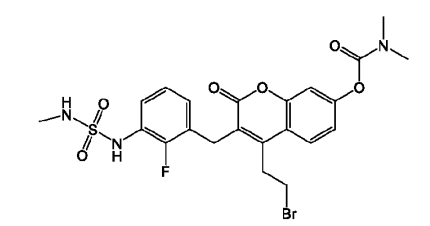
No.	Structure	No.	Structure
94		95	
96		97	
98		99	
100		101	

FIG 5 Continued

No.	Structure	No.	Structure
102		103	
104		105	
106		107	
108		109	
110		111	

FIG 5 Continued

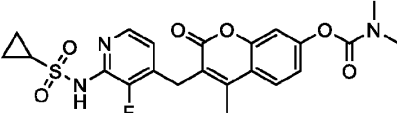
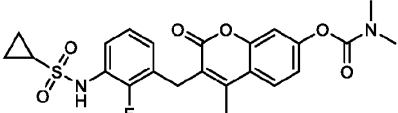
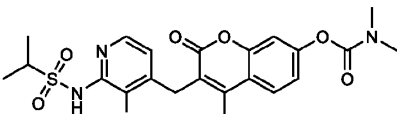
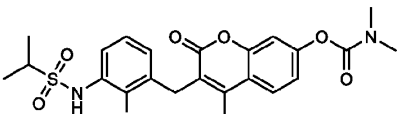
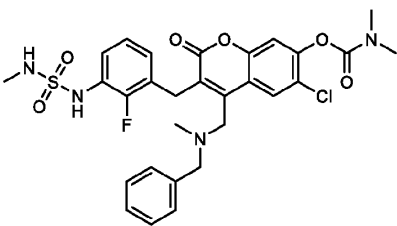
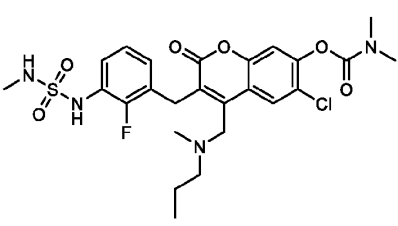
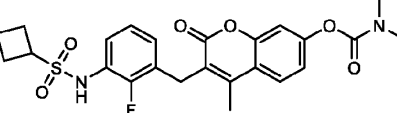
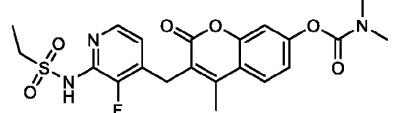
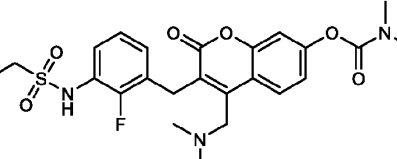
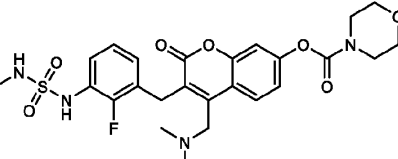
No.	Structure	No.	Structure
112		113	
114		115	
116		117	
118		119	
120		121	

FIG 5 Continued

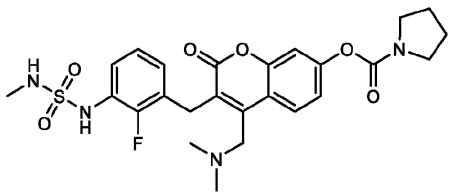
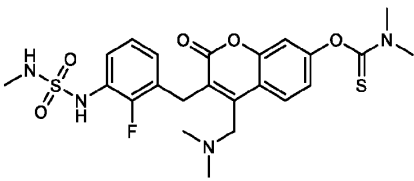
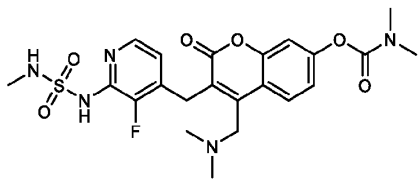
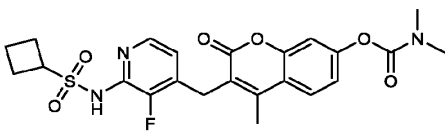
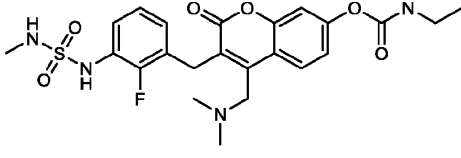
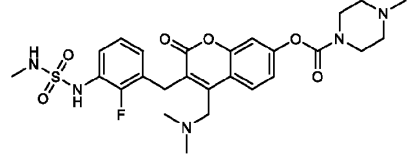
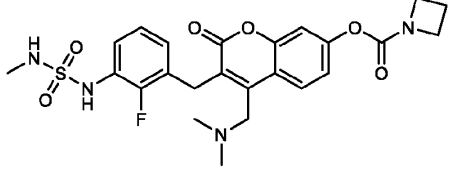
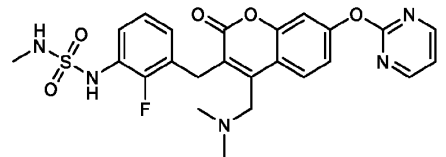
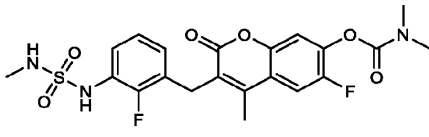
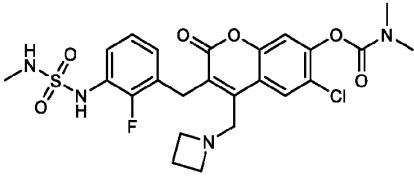
No.	Structure	No.	Structure
122		123	
124		125	
126		127	
128		129	
130		131	

FIG 5 Continued

No.	Structure	No.	Structure
132		133	
134		135	
136		137	
138		139	
140		141	

FIG 5 Continued

No.	Structure	No.	Structure
142		143	
144		145	
146		147	
148		149	
150		151	

FIG 5 Continued

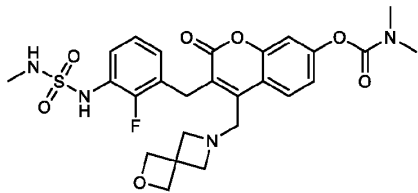
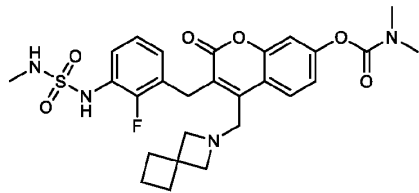
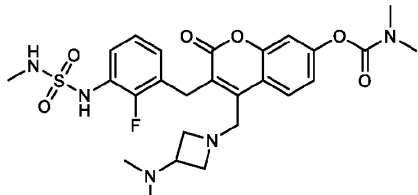
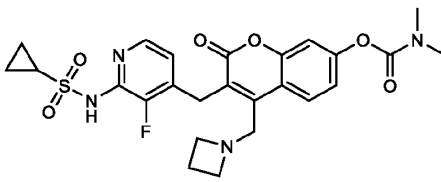
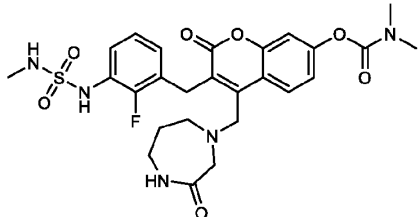
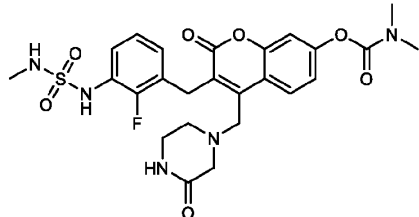
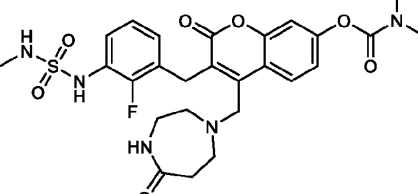
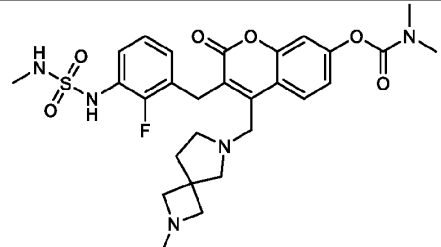
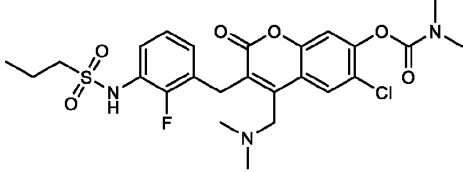
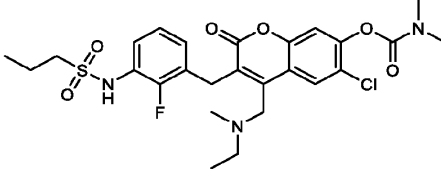
No.	Structure	No.	Structure
152		153	
154		155	
156		157	
158		159	
160		161	

FIG 5 Continued

No.	Structure	No.	Structure
162		163	
164		165	
166		167	
168		169	
170		171	

FIG 5 Continued

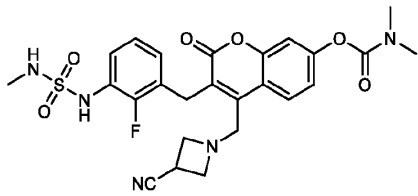
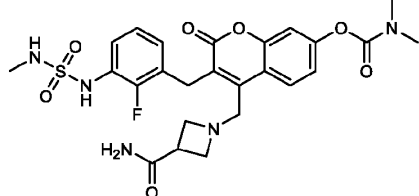
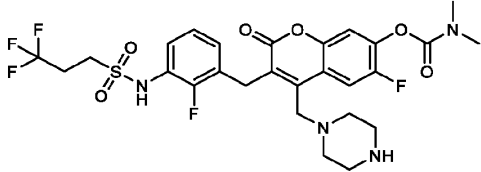
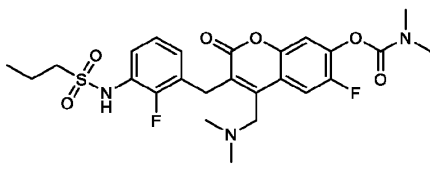
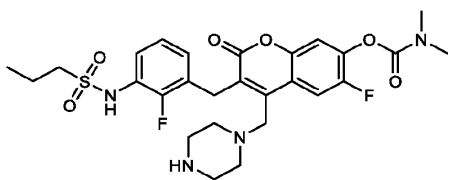
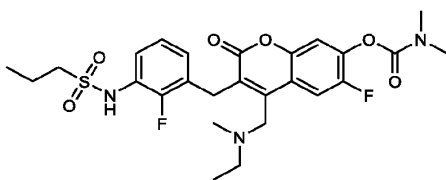
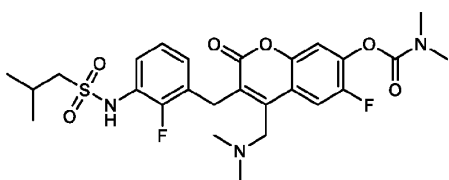
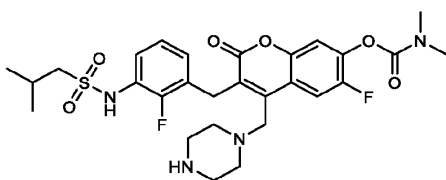
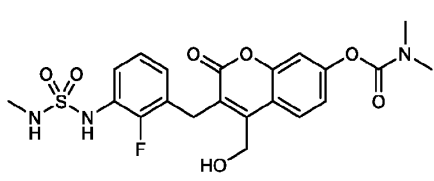
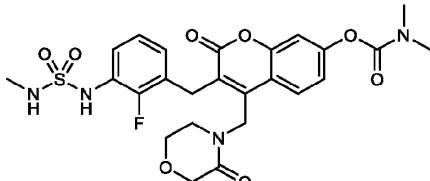
No.	Structure	No.	Structure
172		173	
174		175	
176		177	
178		179	
180		181	

FIG 5 Continued

No.	Structure	No.	Structure
182		183	
184		185	
186		187	
188		189	
190		191	

FIG 5 Continued

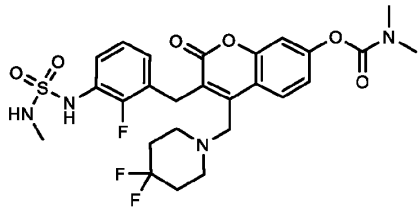
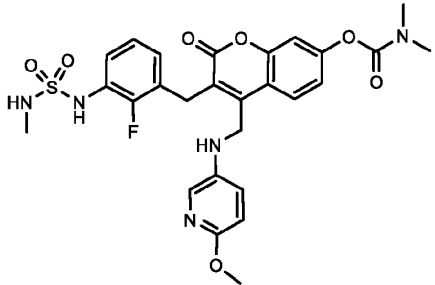
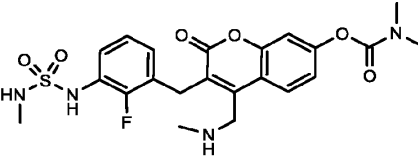
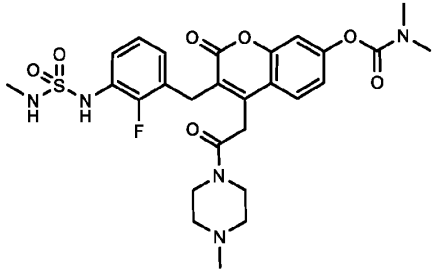
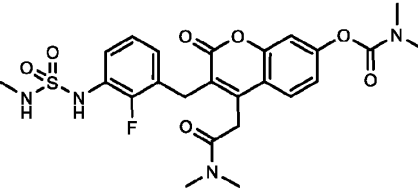
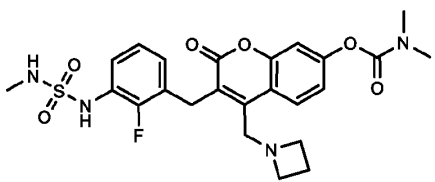
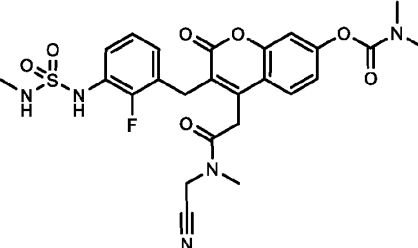
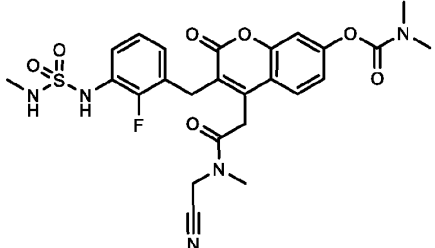
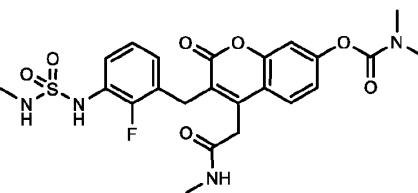
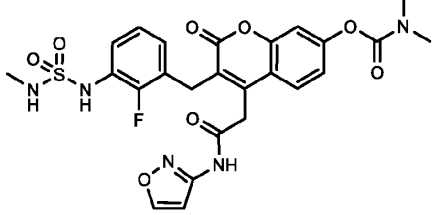
No.	Structure	No.	Structure
192		193	
194		195	
196		197	
198		199	
200		201	

FIG 5 Continued

No.	Structure	No.	Structure
202		203	
204		205	
206		207	
208		209	
210		211	

FIG 5 Continued

No.	Structure	No.	Structure
212		213	
214		215	
216		217	
218		219	
220		221	

FIG 5 Continued

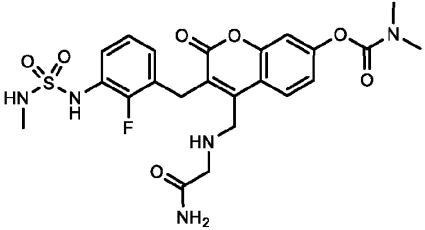
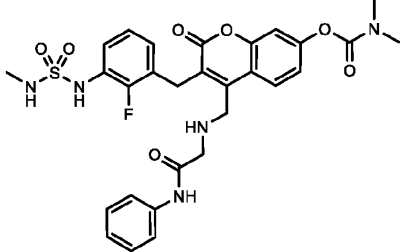
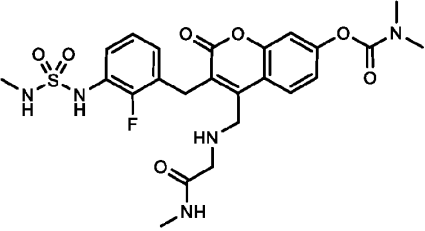
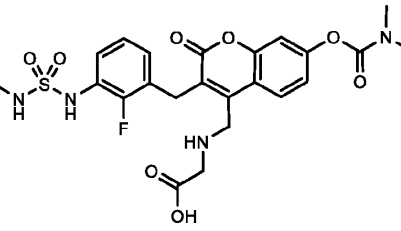
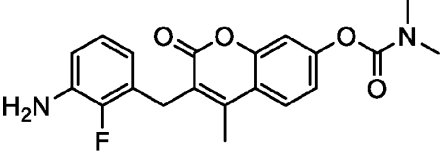
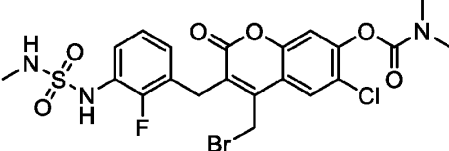
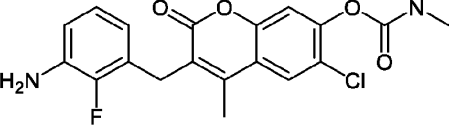
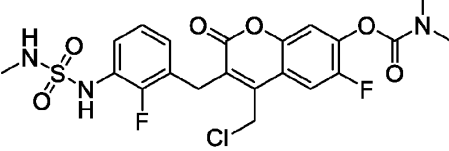
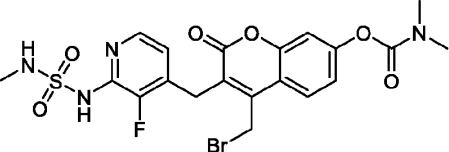
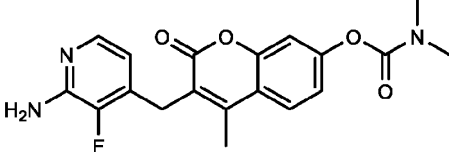
No.	Structure	No.	Structure
222		223	
224		225	
226		227	
228		229	
230		231	

FIG 5 Continued

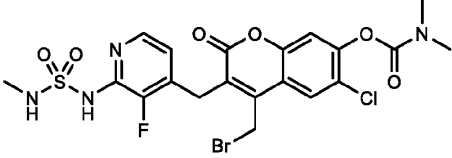
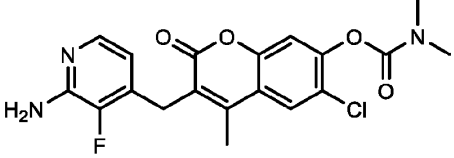
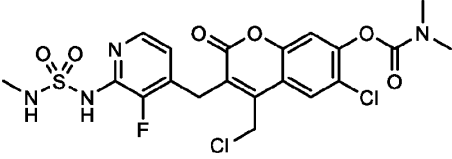
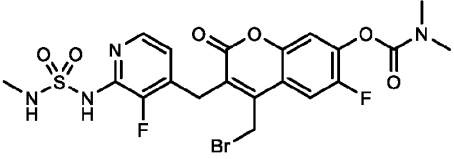
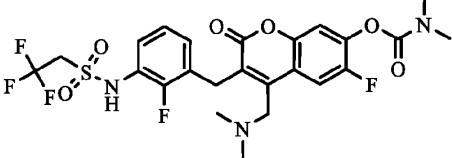
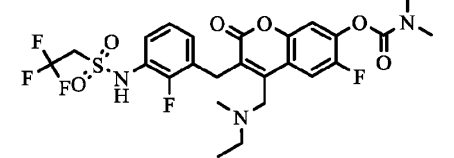
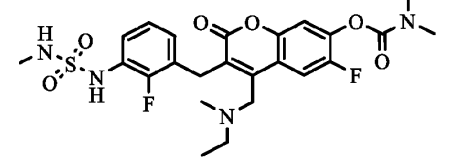
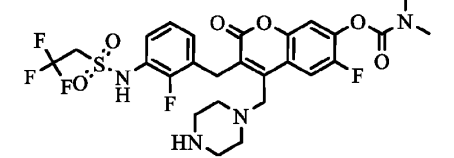
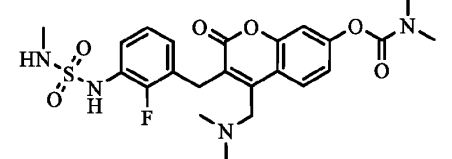
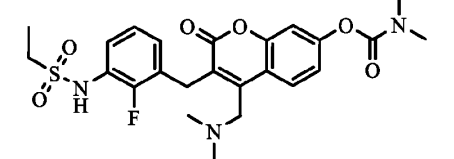
No.	Structure	No.	Structure
232		233	
234		235	
236		237	
238		239	
240		241	

FIG 5 Continued

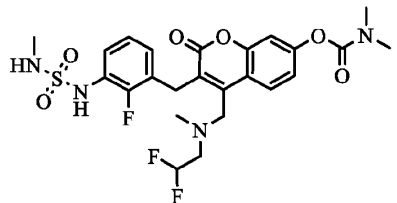
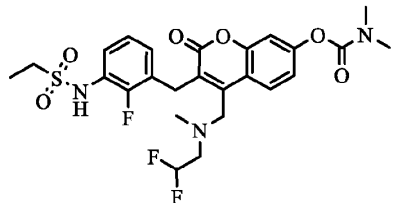
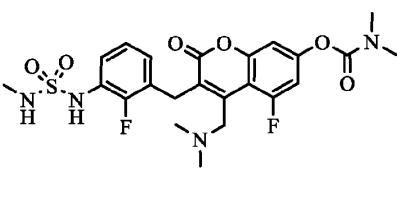
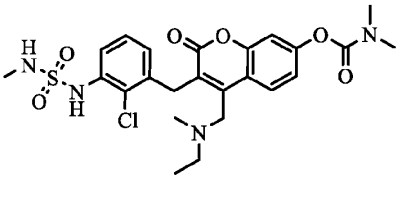
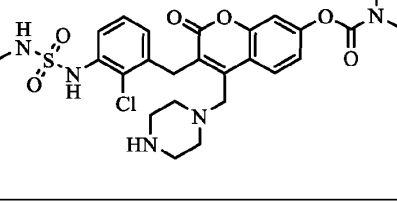
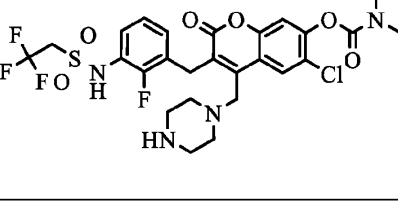
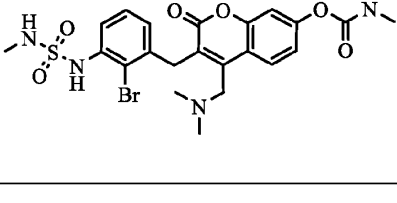
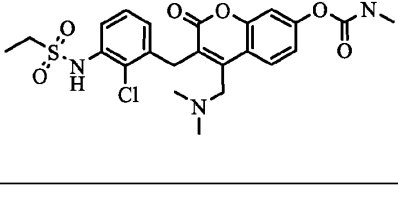
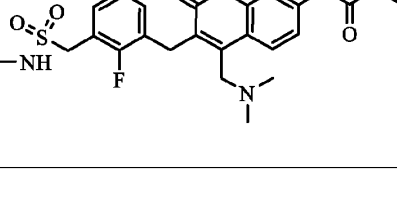
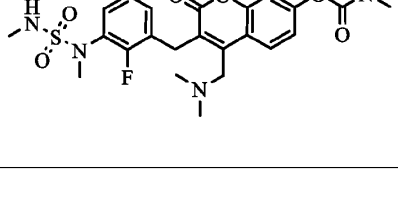
No.	Structure	No.	Structure
242		243	
244		245	
246		247	
248		249	
250		251	

FIG 5 Continued

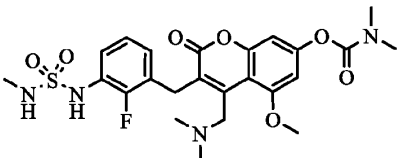
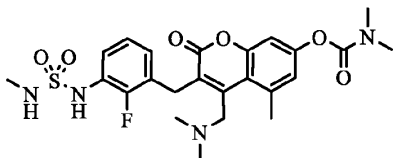
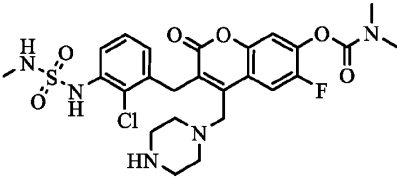
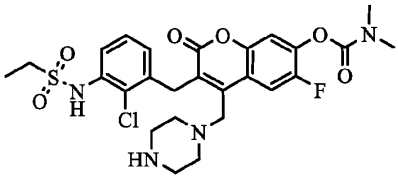
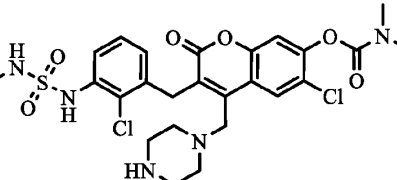
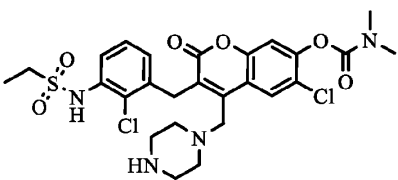
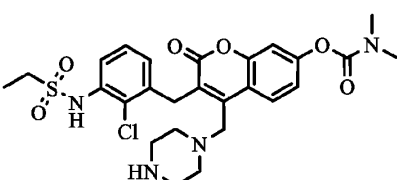
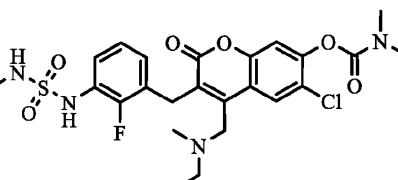
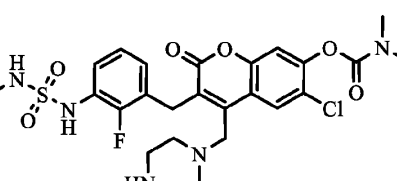
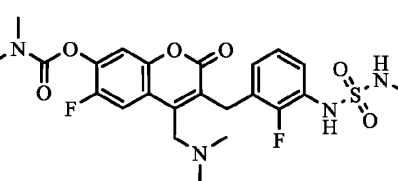
No.	Structure	No.	Structure
252		253	
254		255	
256		257	
258		259	
260		261	

FIG 5 Continued

No.	Structure	No.	Structure
262		263	
264		265	
266		267	
268		269	
270		271	

FIG 5 Continued

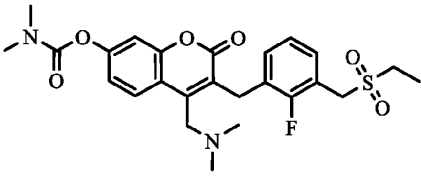
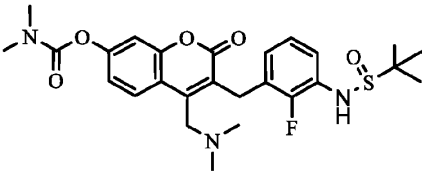
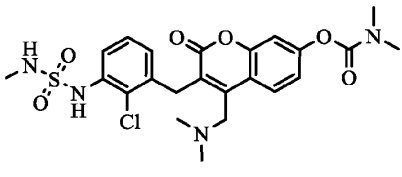
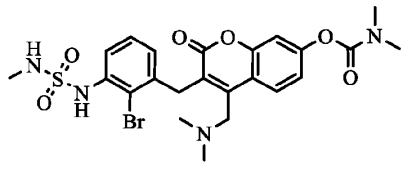
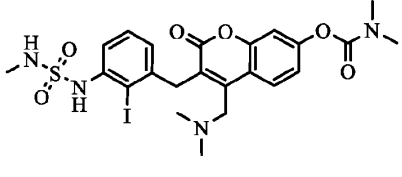
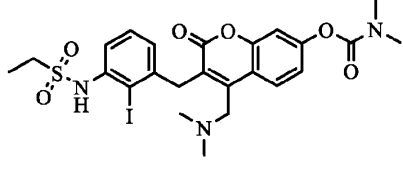
No.	Structure	No.	Structure
272		273	
274		275	
276		277	

FIG 5 Continued