

## 基于机器学习方法的丙型肝炎病毒聚合酶 NS5B 非核苷抑制剂的定量构效关系研究

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## Quantitative Structure-Activity Relationship Study of the Non-Nucleoside Inhibitors of HCV NS5B Polymerase by Machine Learning Methods

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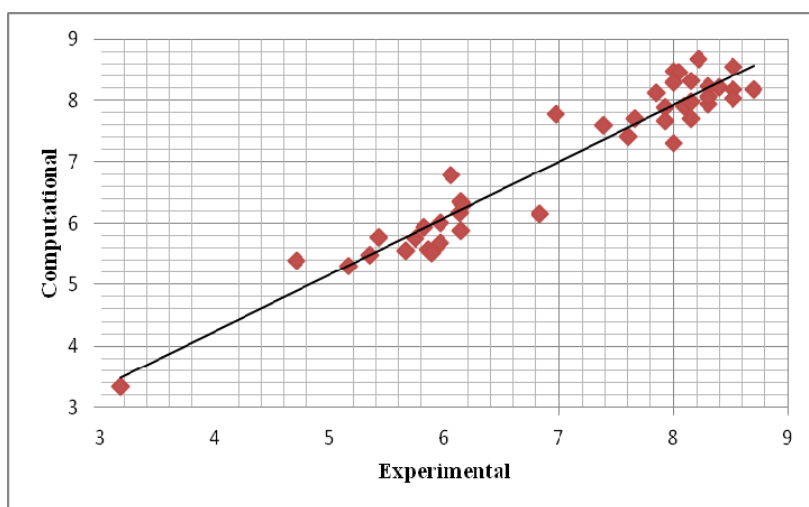
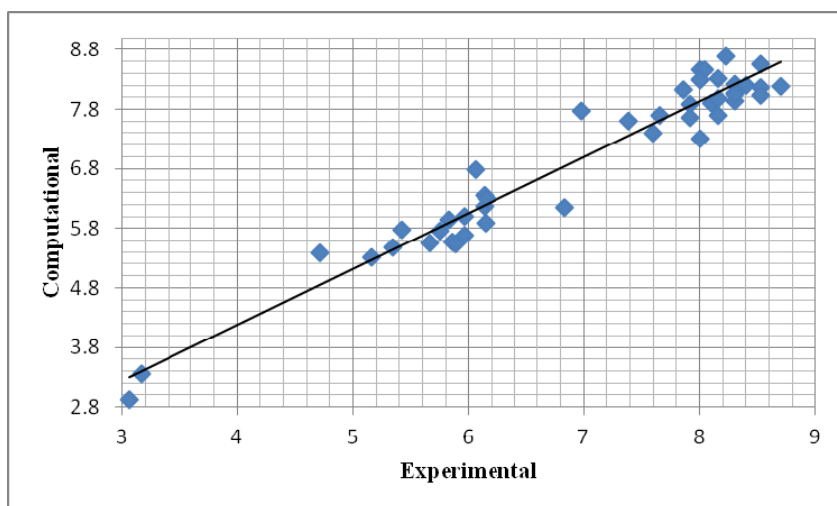
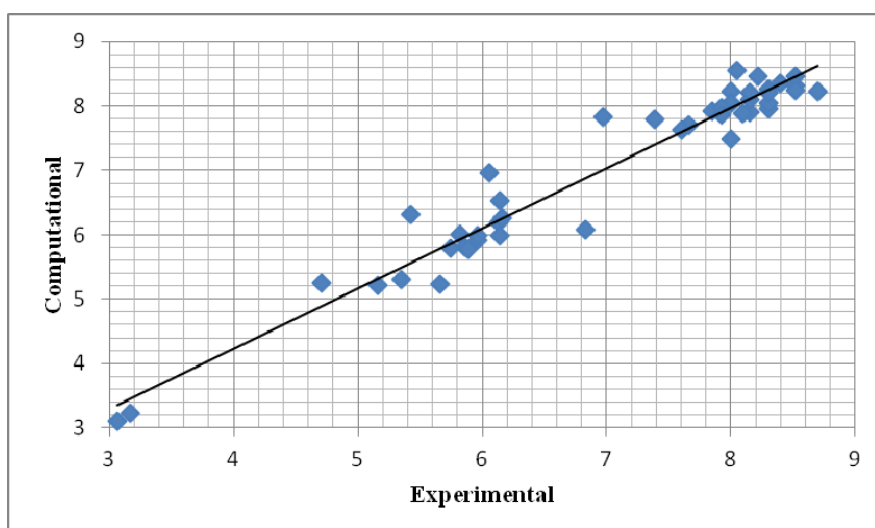


图 S1 实验与预测  $pIC_{50}$  数值对比图(使用线性逐步回归分析选择的描述符建立的多元线性回归模型, 训练集为蓝色, 测试集为红色)

Fig.S1 The experimental vs. computational  $\log(10^9/IC_{50})$  (The MLR Model with the LSRA selected descriptors, Training set in blue, test set in red)



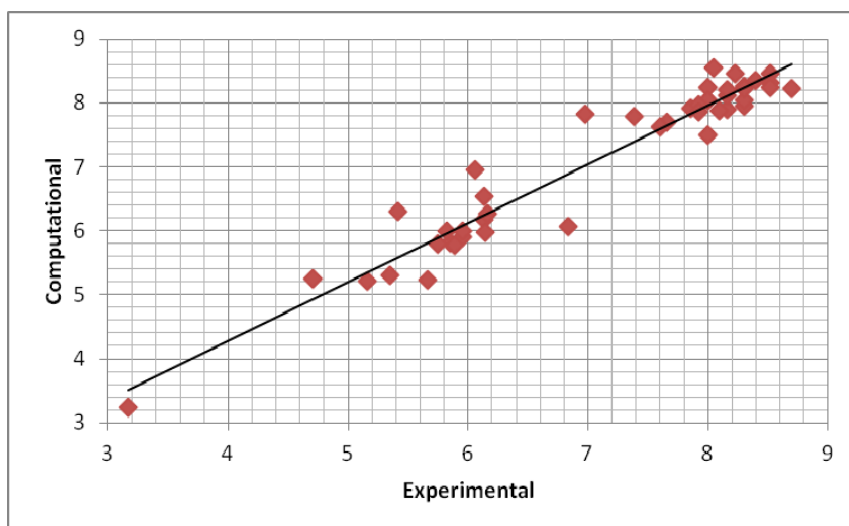
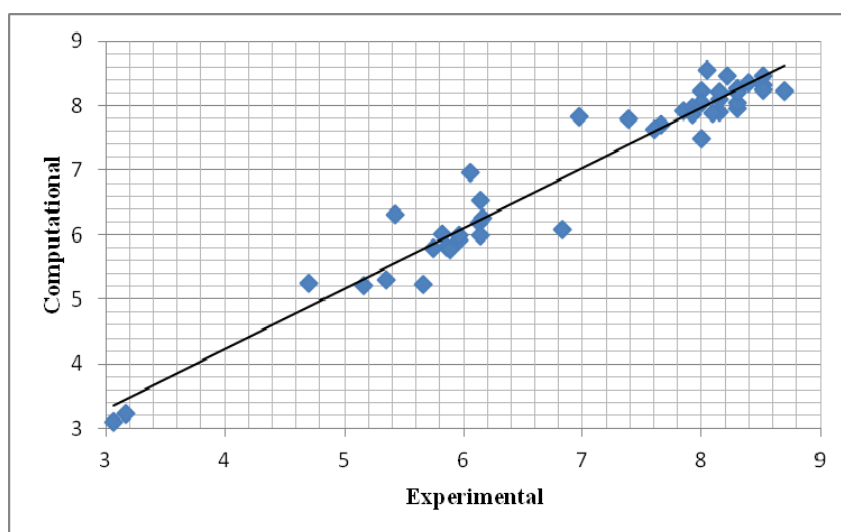


图 S2 实验与预测  $pIC_{50}$  数值对比图(使用线性逐步回归分析选择的描述符建立的偏最小二乘回归模型, 训练集为蓝色, 测试集为红色)

Fig.S2 The experimental vs. computational  $\log(10^9/IC_{50})$  (The PLS Model with the LSRA selected descriptors, Training set in blue, test set in red)



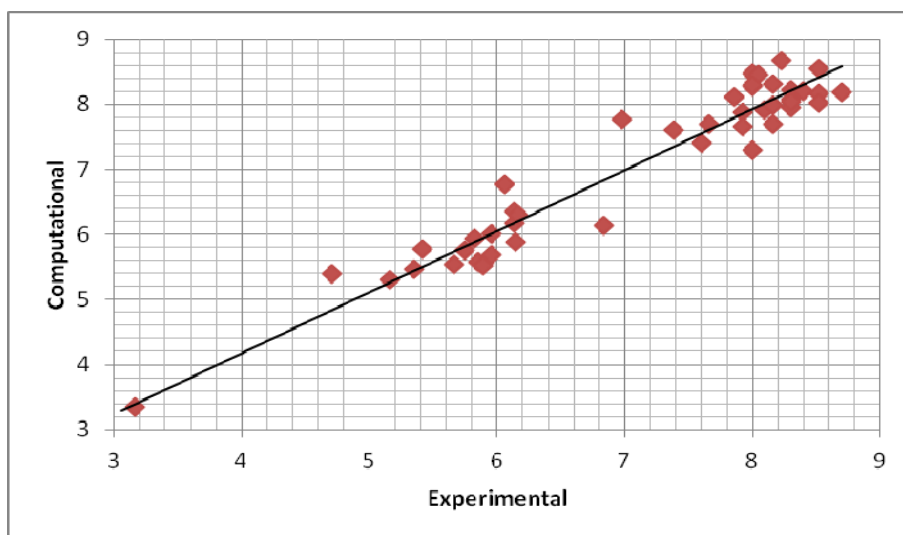


图 S3 实验与预测  $pIC_{50}$  数值对比图(使用线性逐步回归分析选择的描述符建立的支持向量回归模型, 训练集为蓝色, 测试集为红色)

Fig.S3 The experimental vs. computational  $\log(10^9/IC_{50})$  (The SVM Model with the LSRA selected descriptors, Training set in blue, test set in red)

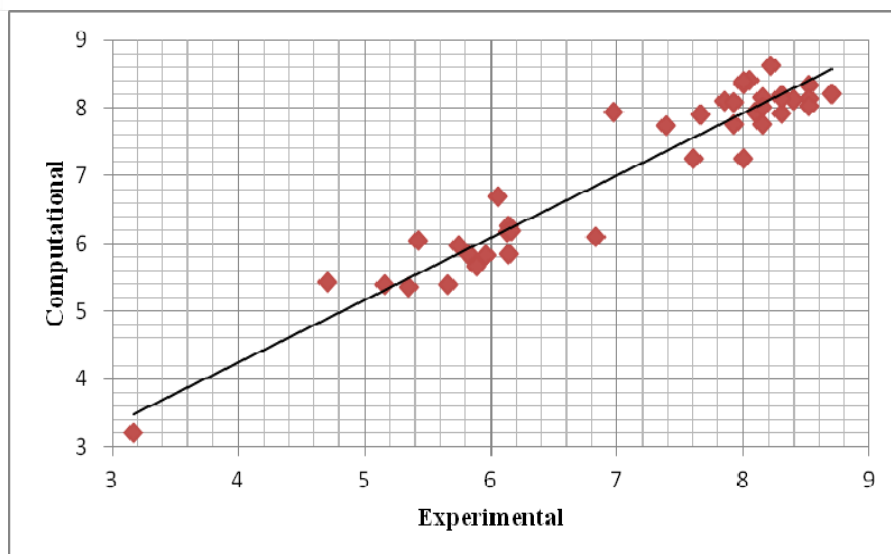
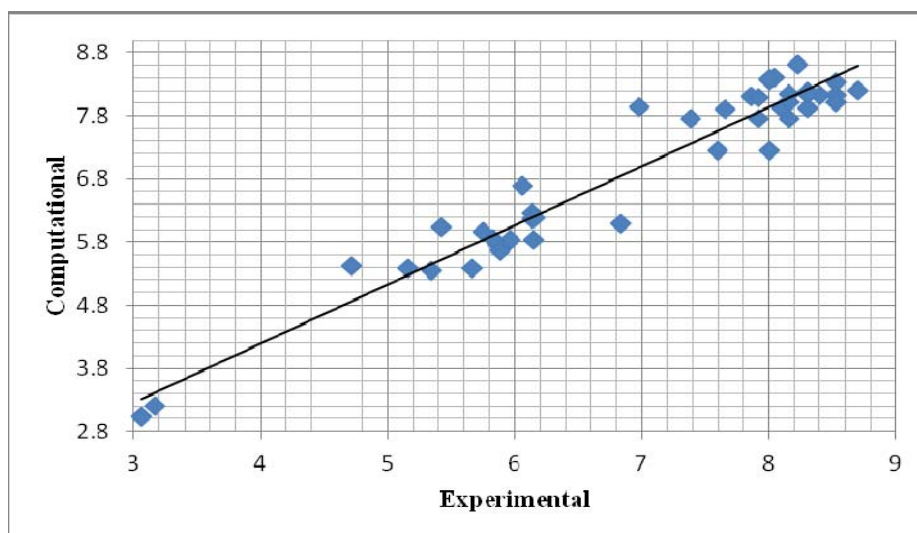


图 S4 实验与预测  $pIC_{50}$  数值对比图(使用遗传算法组合偏最小二乘选择的描述符建立的多元线性回归模型, 训练集为蓝色, 测试集为红色)

Fig.S4 The experimental vs. computational  $\log(10^9/IC_{50})$  (The MLR Model with the GA-PLS selected descriptors, Training set in blue, test set in red)

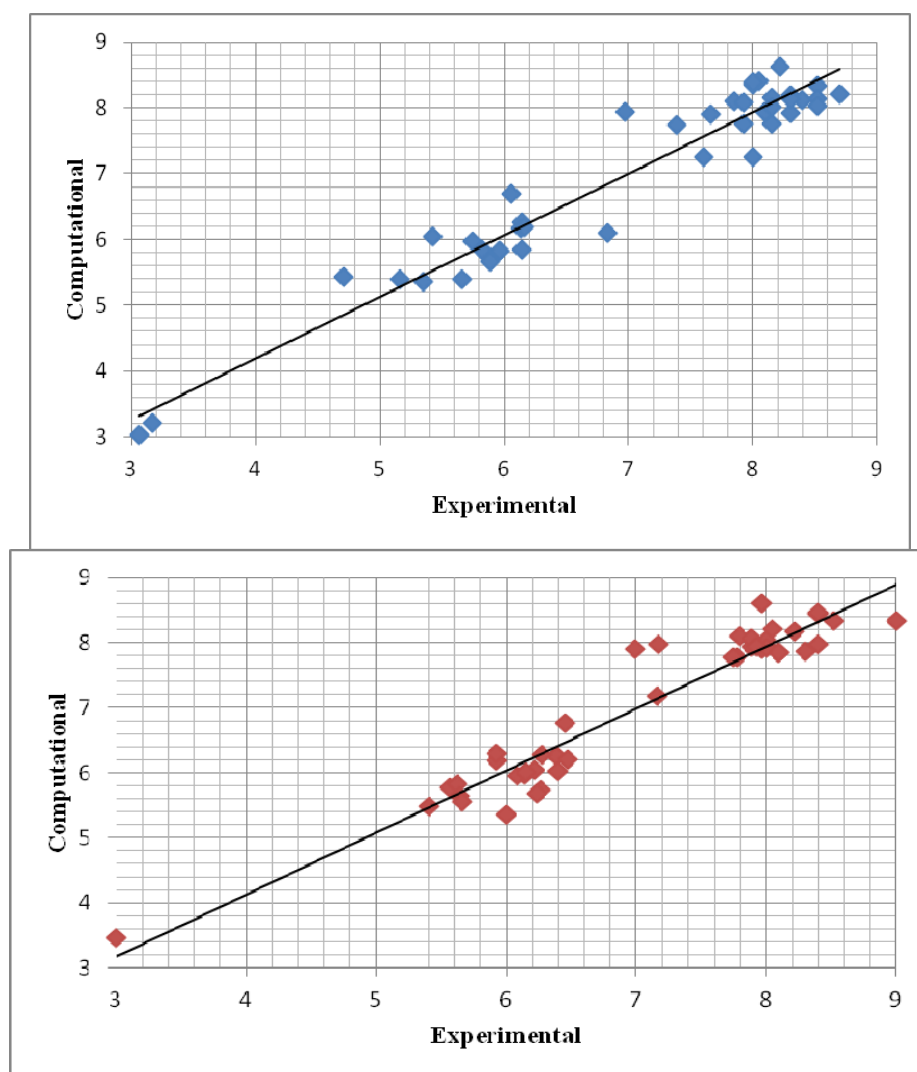


图 S5 实验与预测  $pIC_{50}$  数值对比图(使用遗传算法组合偏最小二乘选择的描述符建立的偏最小二乘回归模型, 训练集为蓝色, 测试集为红色)

Fig.S5 The experimental vs. computational  $\log(10^9/IC_{50})$  (The PLS Model with the GA-PLS selected descriptors, Training set in blue, test set in red)

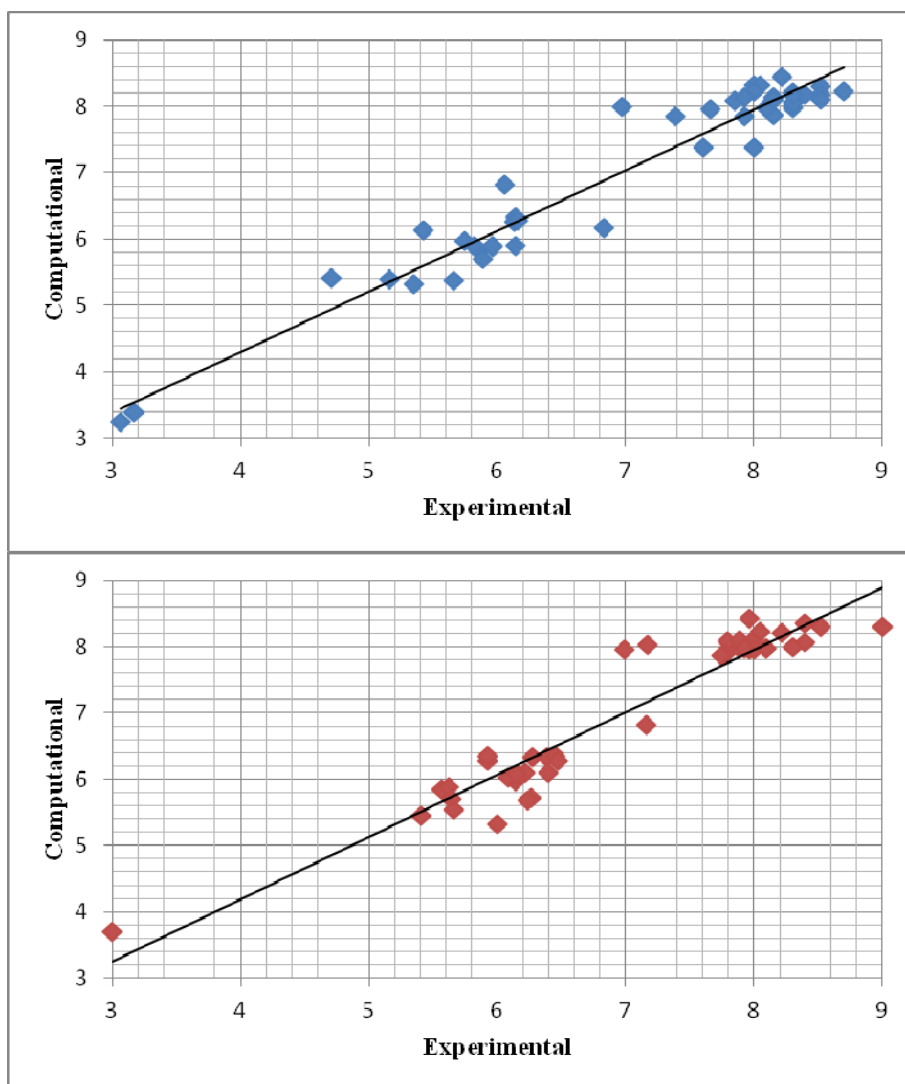
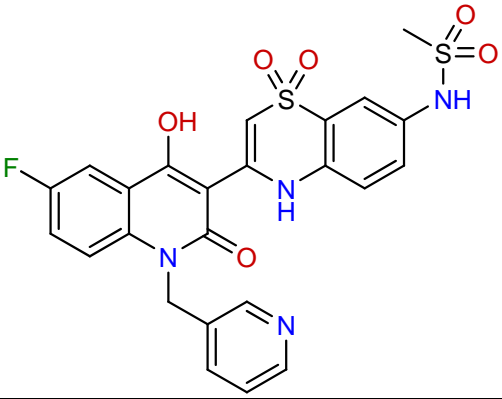
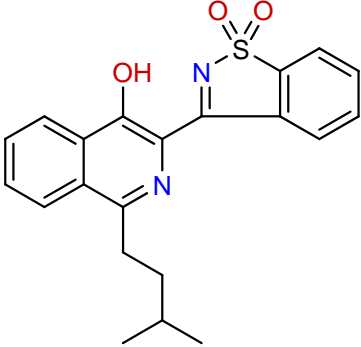
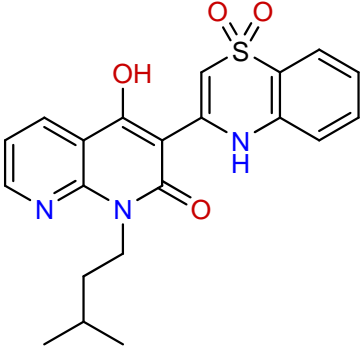
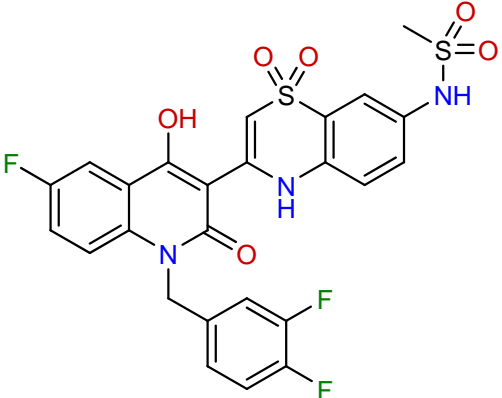


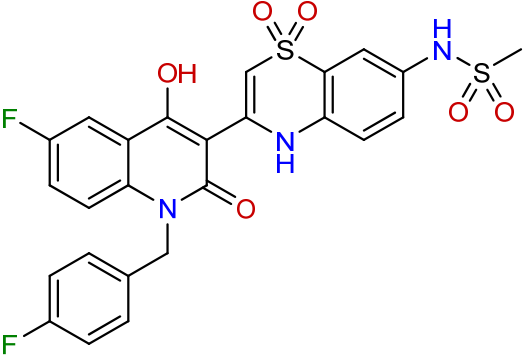
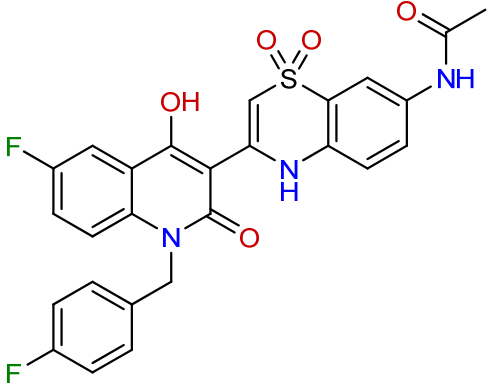
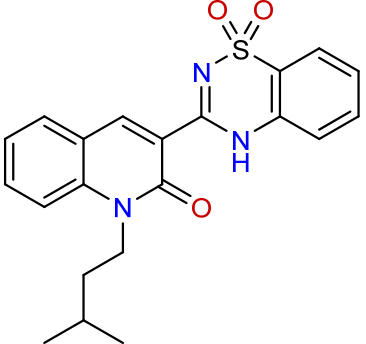
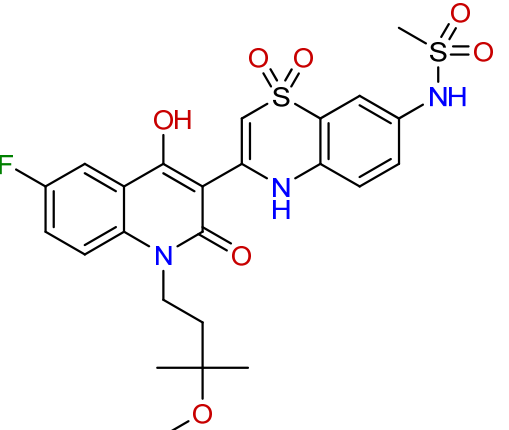
图 S6 实验与预测  $pIC_{50}$  数值对比图(使用遗传算法组合偏最小二乘选择的描述符建立的支持向量机回归模型, 训练集为蓝色, 测试集为红色)

Fig.S6 The experimental vs. computational  $\log(10^9/IC_{50})$  (The SVM Model with the GA-PLS selected descriptors, Training set in blue, test set in red)

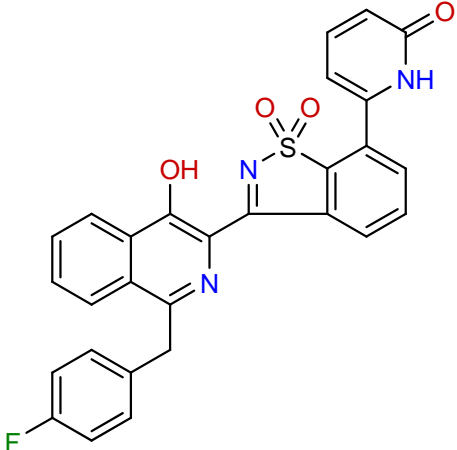
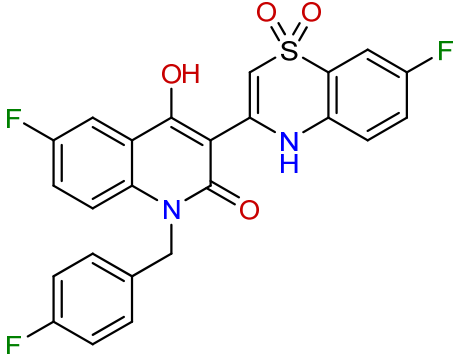
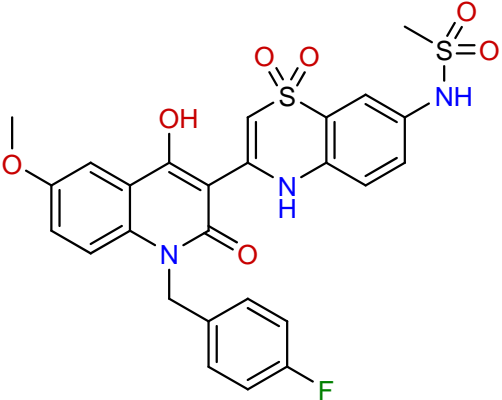
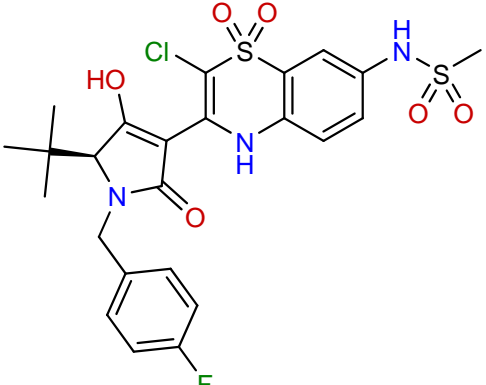
表 S1 选用 LSRA 描述符子集建立的机器学习模型对抑制剂活性的预测结果

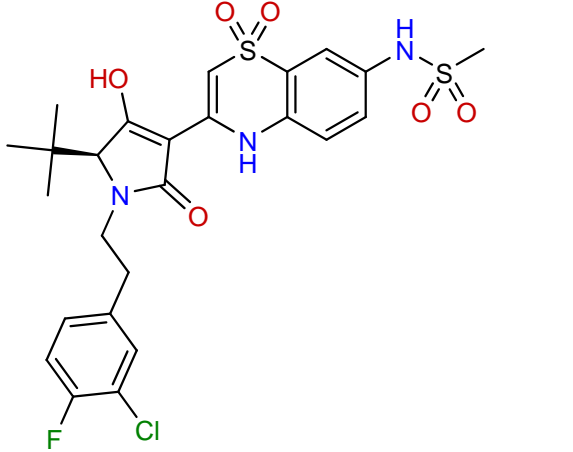
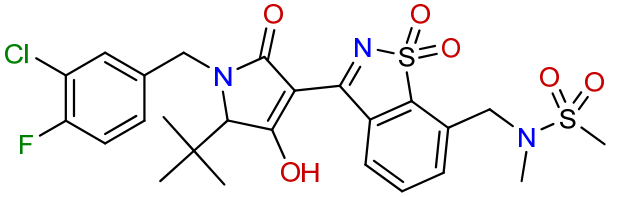
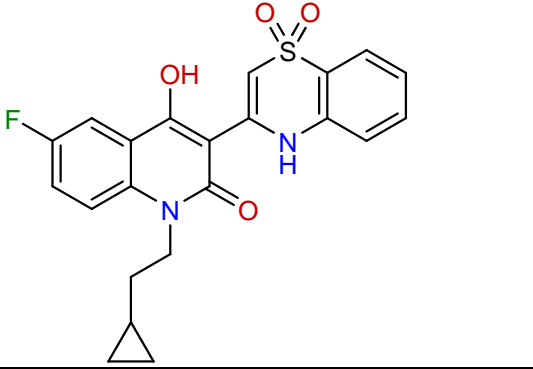
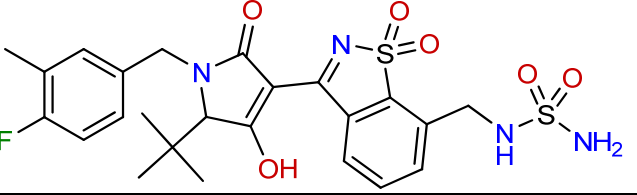
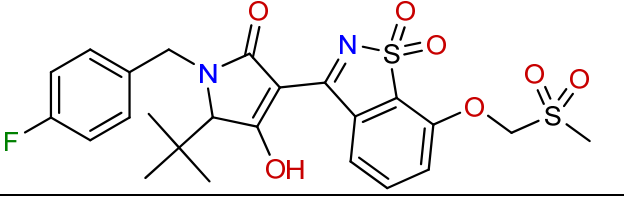
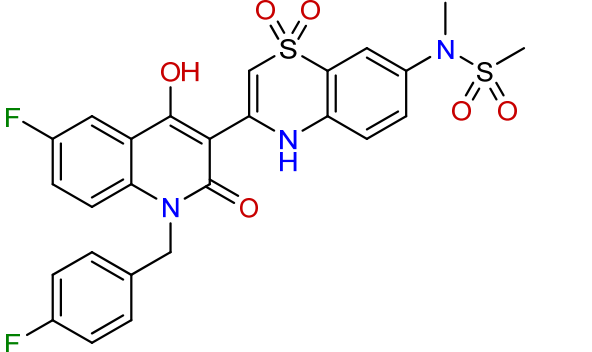
**Table S1 The molecular structures of compounds and its actual and calculated HCV NS5B polymerase inhibitory activities with LSRA selected descriptors**

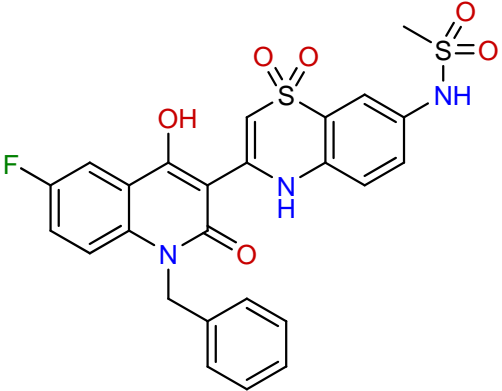
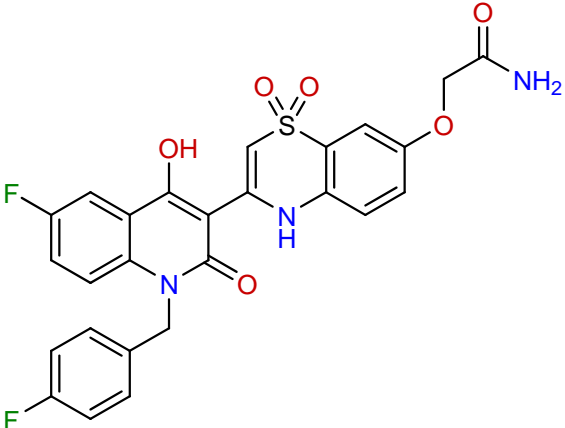
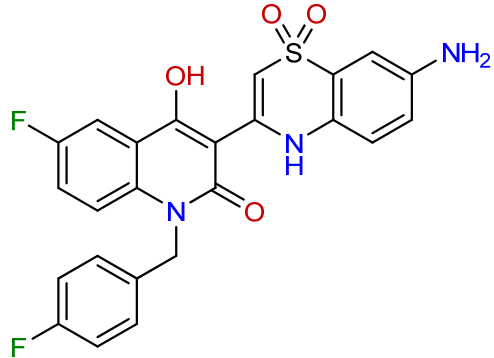
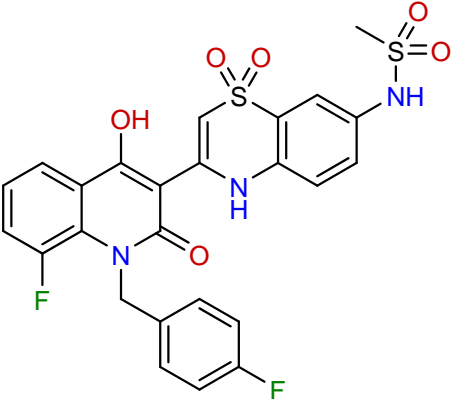
Structure	Actual activity ( $\log(10^9/IC_{50})$ )	Calculated activity <sup>a</sup> (MLR)	Calculated Activity <sup>b</sup> (PLS)	Calculated activity <sup>c</sup> (SVM)
	7.6580	7.7022	7.7791	7.70438
	5.3470	5.4759	5.4281	5.30053
	5.8540	5.5711	5.8512	5.80746
	7.8540	8.1219	7.9914	7.9223

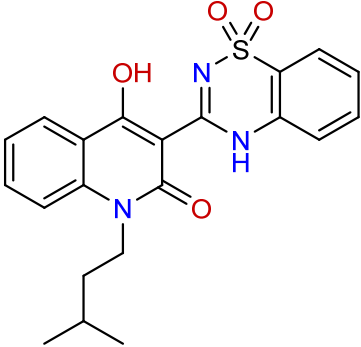
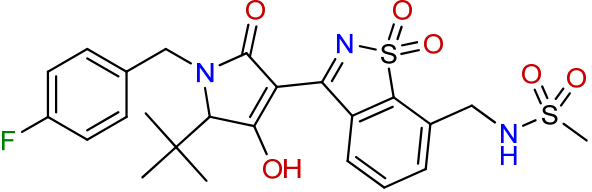
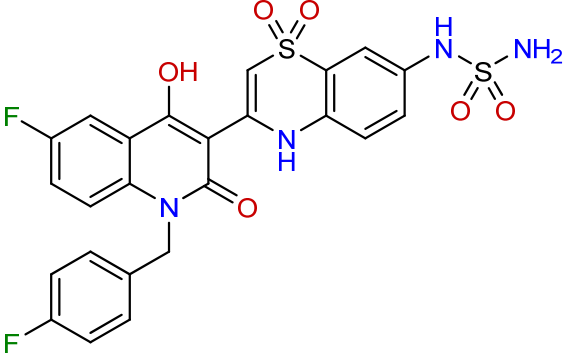
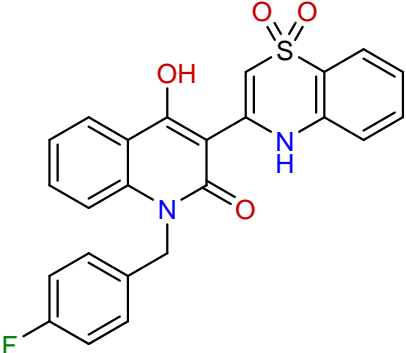
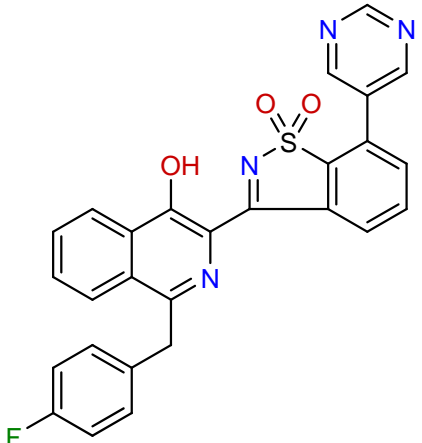
	8.3010	7.9430	7.7603	7.95313
	6.0610	6.7768	6.9102	6.95793
	3.1660	3.3451	3.2421	3.23069
	8.0000	8.4705	8.5682	8.04658

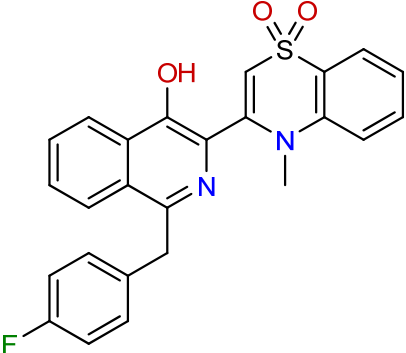
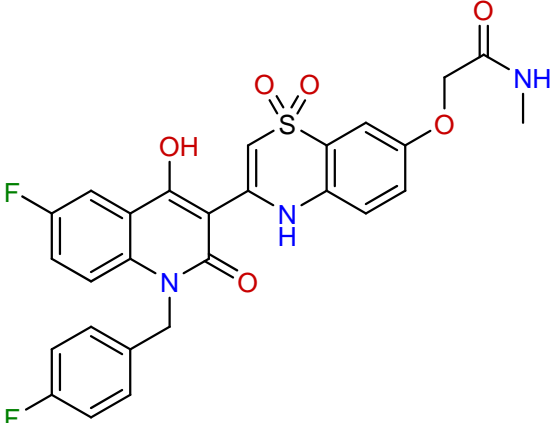
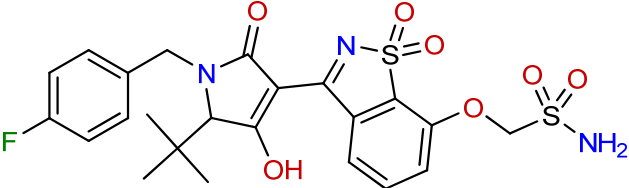
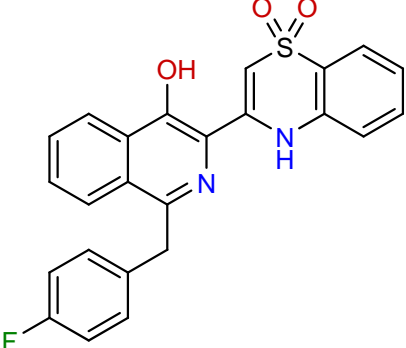
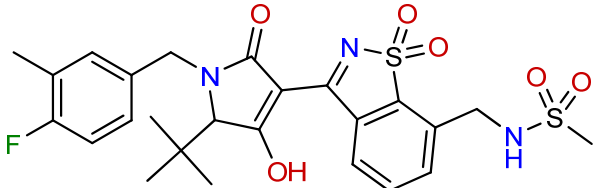


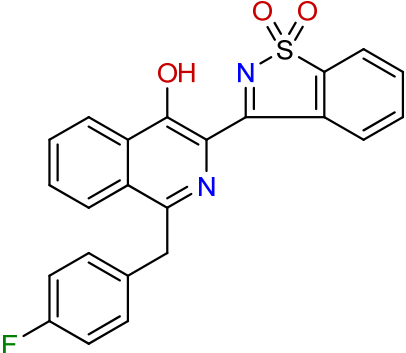
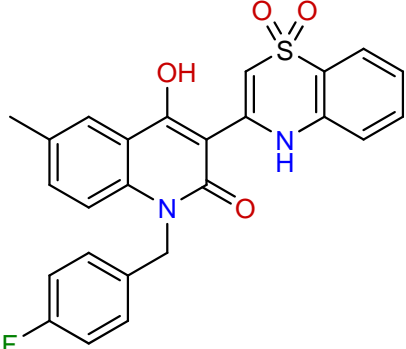
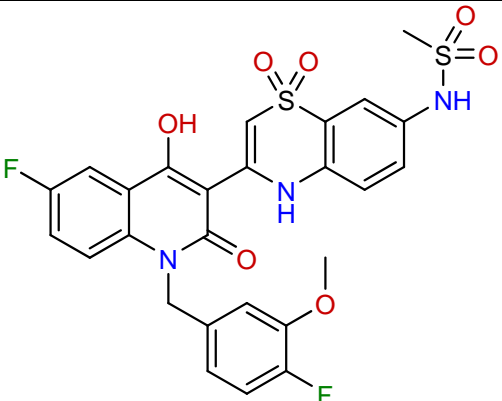
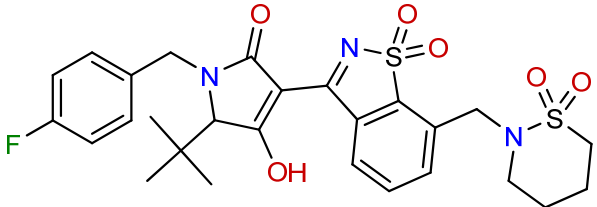
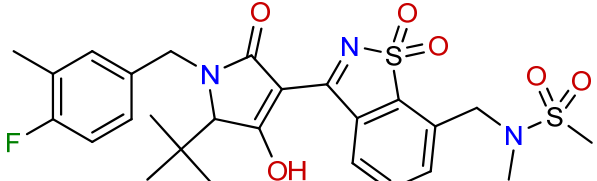
	6.1370	6.3572	6.3919	6.53784
	6.8300	6.1450	6.1434	6.0734
	8.3010	8.0714	7.9642	8.04676
	8.6990	8.1782	8.1488	8.21821

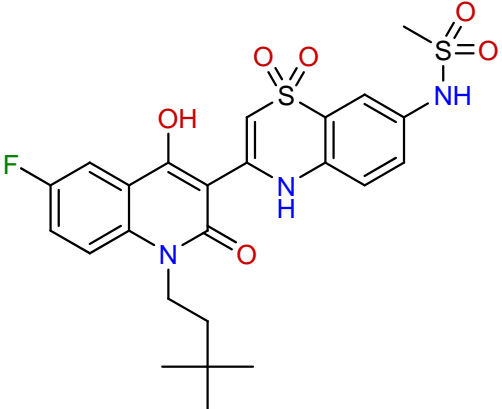
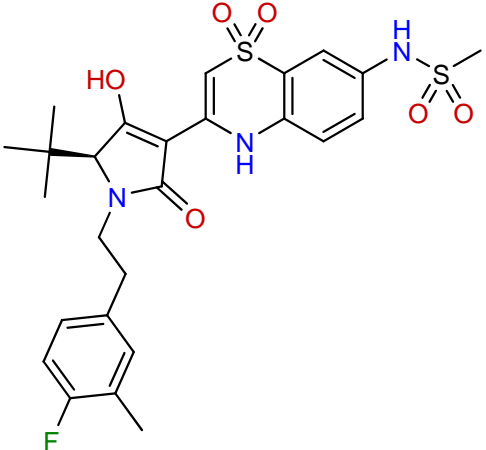
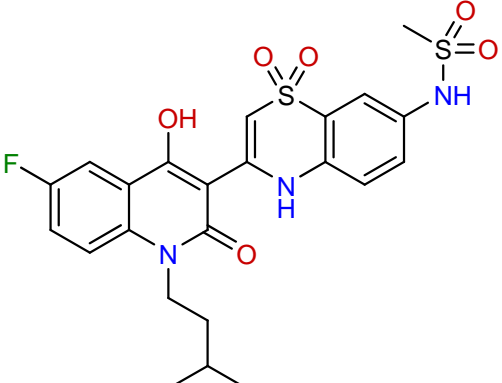
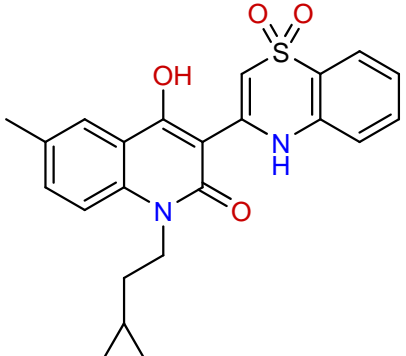
	8.3010	8.2223	8.1835	8.25545
	8.0000	8.2854	8.3458	8.23343
	5.9590	5.6818	5.7730	5.90883
	8.5230	8.5551	8.4726	8.4619
	8.0460	8.4647	8.6072	8.54461
	6.9750	7.7735	7.6193	7.83153

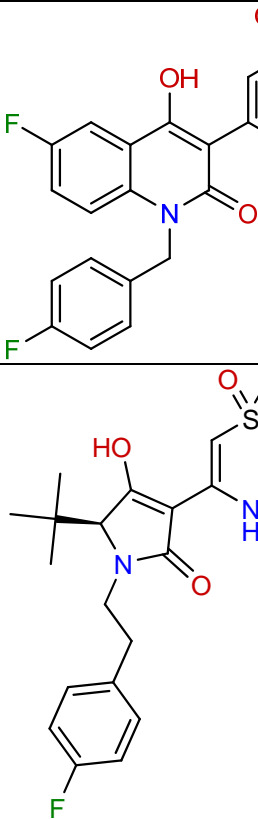
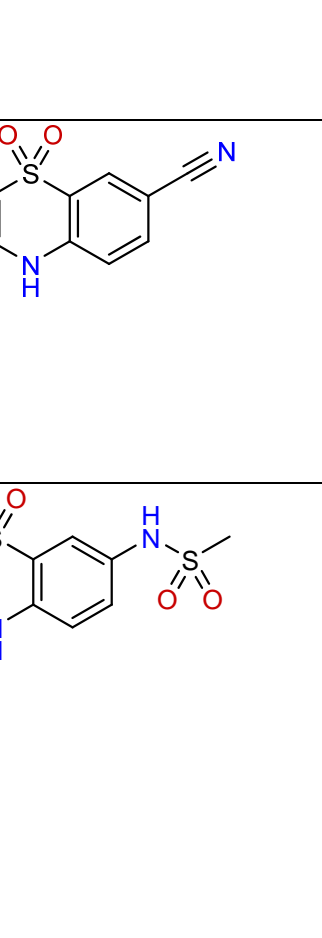
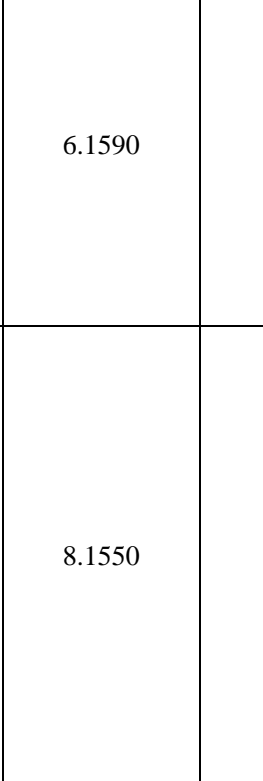
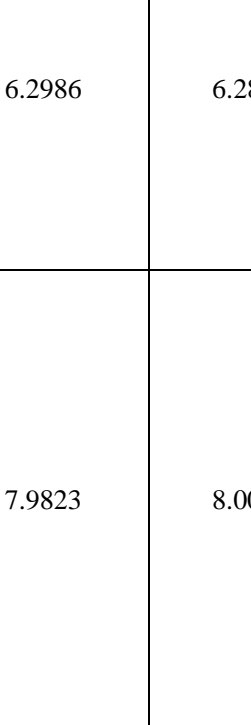
	8.1550	7.7017	7.5550	7.89836
	8.0000	7.3022	7.6836	7.48994
	6.1340	6.1743	6.2745	6.18075
	8.0970	7.9073	7.8765	7.87742

	5.9590	6.0066	5.9509	5.99738
	8.5230	8.1697	8.2130	8.32178
	8.1550	8.3081	8.1032	8.10899
	6.1430	5.8807	5.8673	5.98199
	5.7450	5.7620	6.0737	5.78681

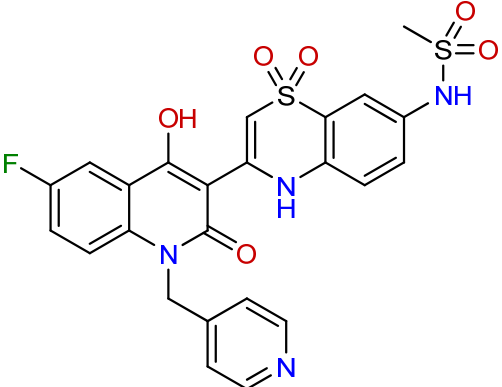
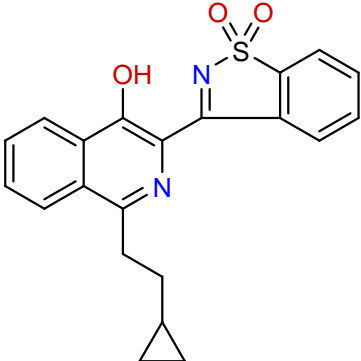
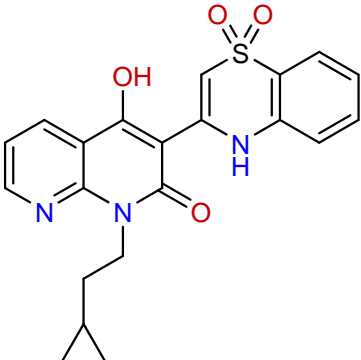
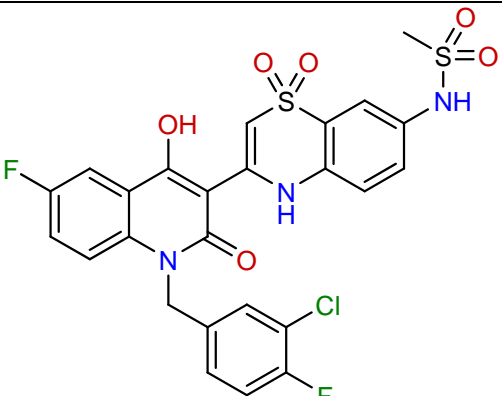
	4.7100	5.3889	5.2994	5.24684
	7.6020	7.4062	7.6346	7.62846
	8.2220	8.6835	8.9527	8.46541
	5.1610	5.3040	5.3260	5.20845
	8.3980	8.2025	8.1493	8.35153

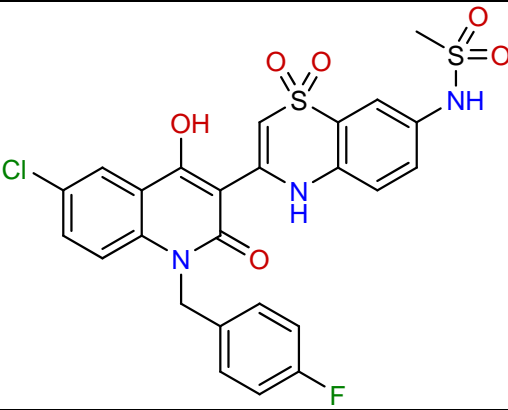
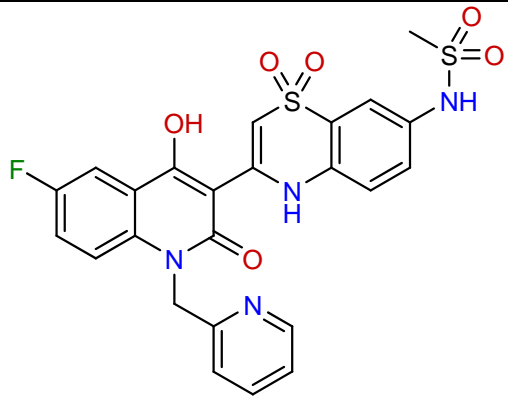
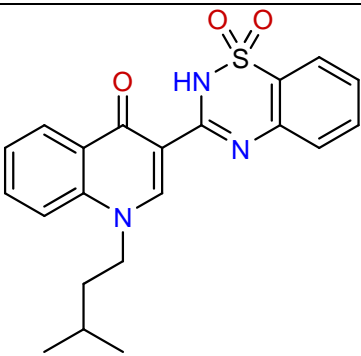
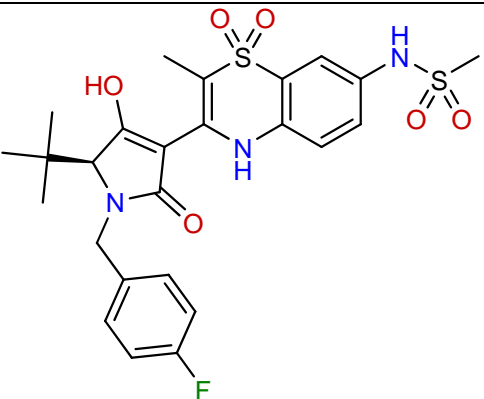
	5.6580	5.5492	5.3470	5.23552
	5.8240	5.9426	5.8249	5.99914
	8.0000	8.2988	8.3202	8.04641
	7.9210	7.8768	7.7255	7.96753
	8.3010	8.0475	8.0118	8.21603

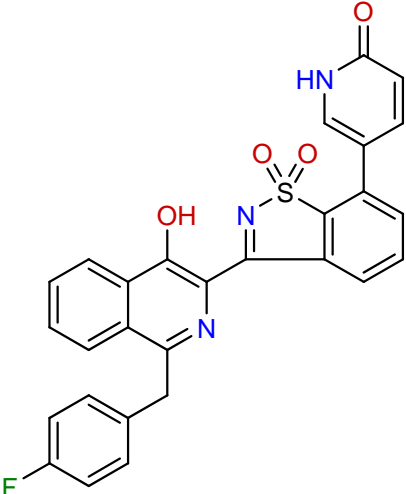
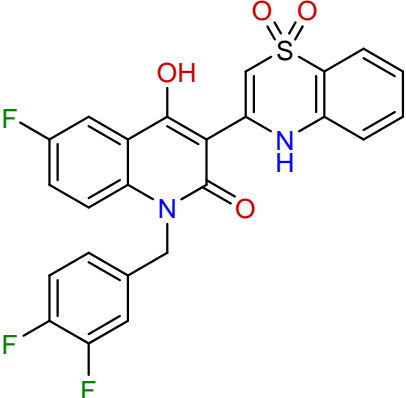
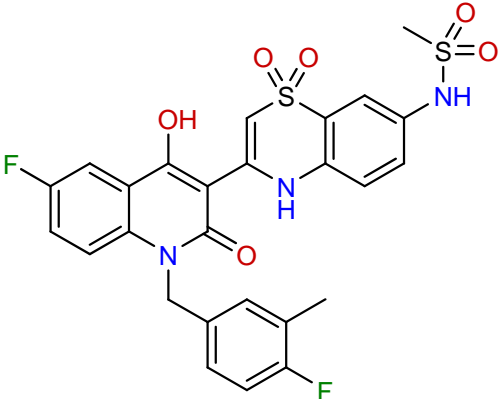
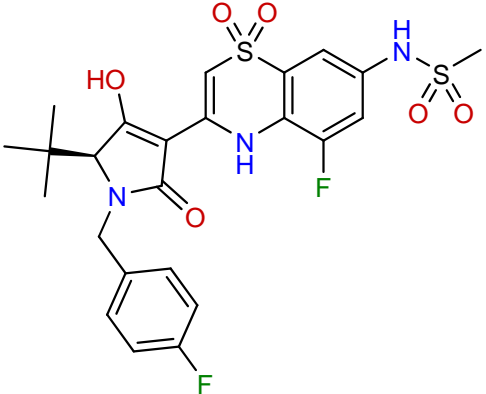
	7.9210	7.6668	7.5626	7.86223
	8.5230	8.0273	7.9625	8.24101
	7.3870	7.5992	7.5917	7.79642
	5.8860	5.5276	5.5109	5.77535

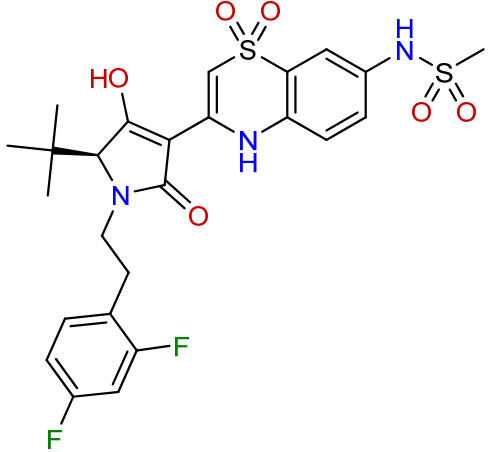
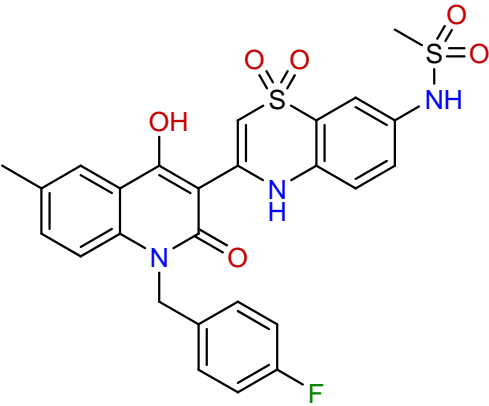
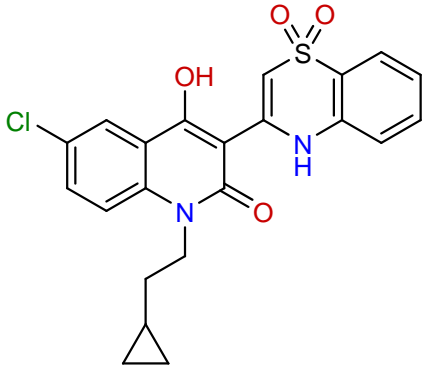
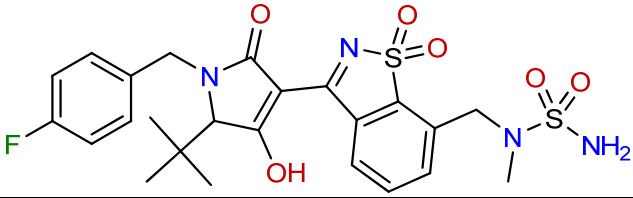
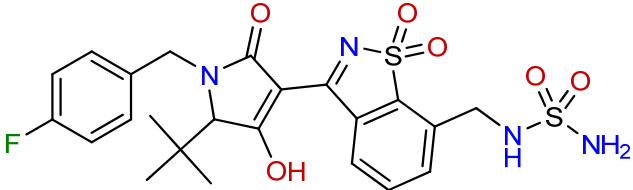
	6.1590	6.2986	6.2800	6.25803
	8.1550	7.9823	8.0046	8.20206
	5.4200	5.7693	5.9645	6.30609
	3.0610	2.9308	2.9964	3.10778

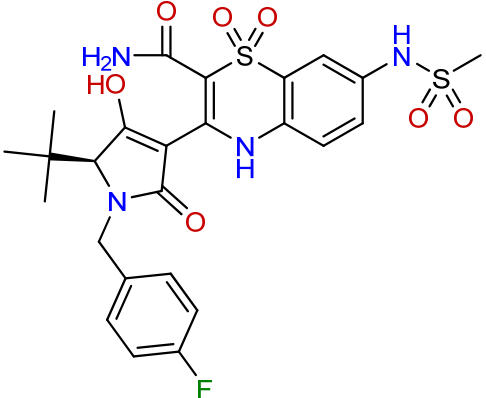
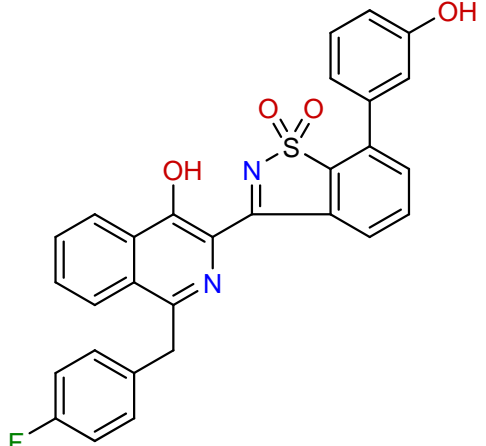
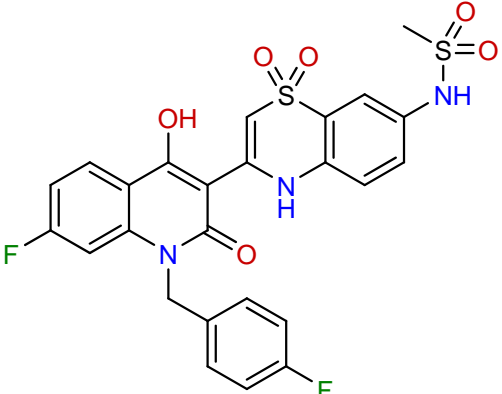
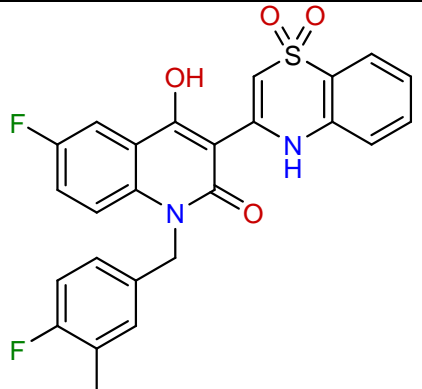


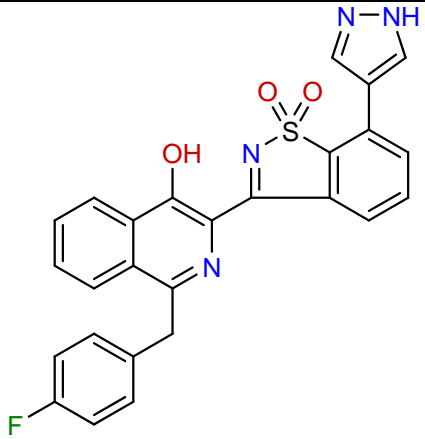
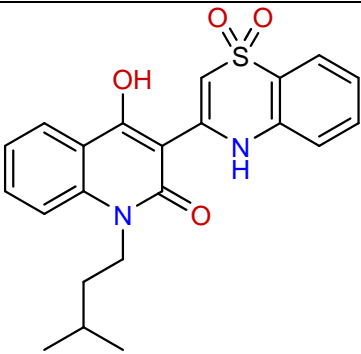
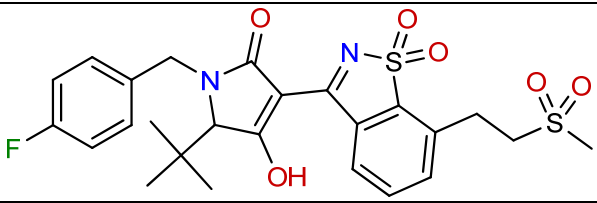
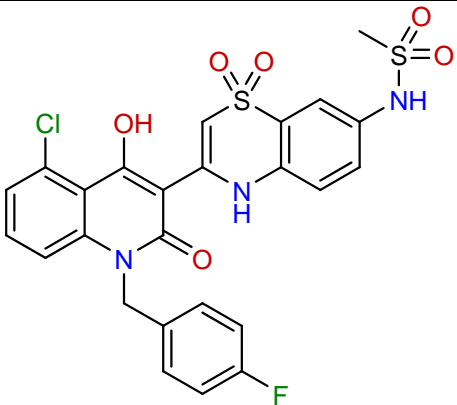
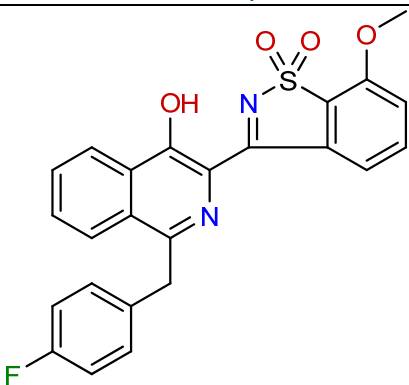
	7.9590 <sup>d</sup>	7.7023	7.7741	7.70662
	6.0000 <sup>d</sup>	5.3828	5.3053	5.28991
	5.5690 <sup>d</sup>	5.4823	5.7337	5.78478
	7.7960 <sup>d</sup>	8.1834	7.9403	7.99413

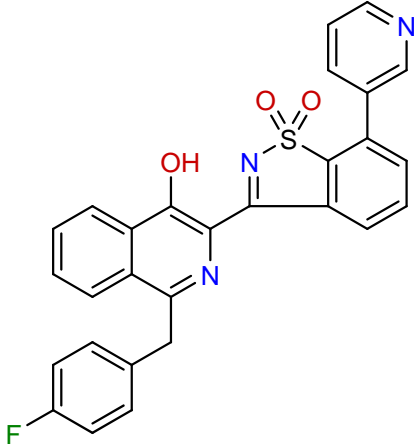
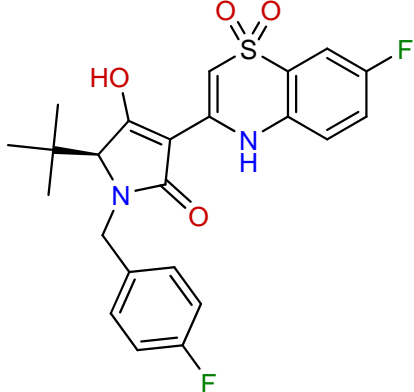
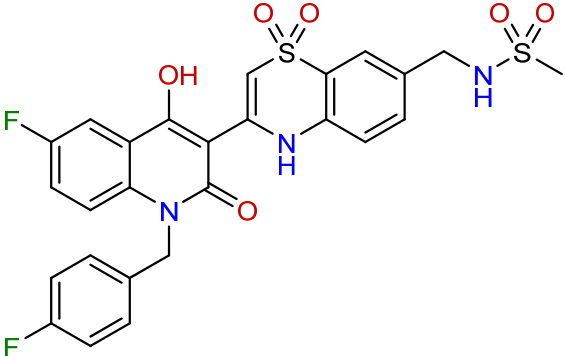
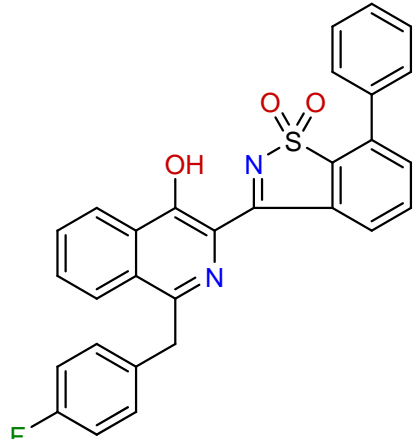
	8.0000 <sup>d</sup>	8.0143	7.7631	8.03723
	6.9870 <sup>d</sup>	7.6750	7.7798	7.67369
	3.0000 <sup>d</sup>	3.5662	3.5470	3.50181
	8.0000 <sup>d</sup>	7.9101	7.9486	8.15456

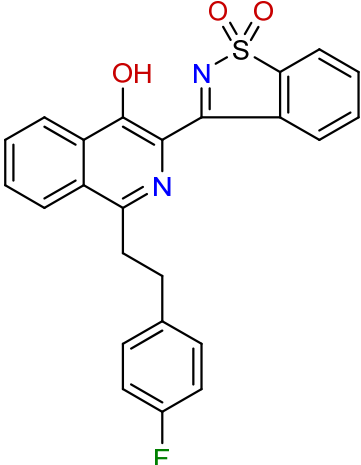
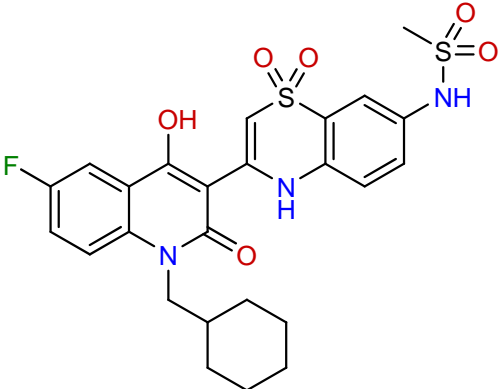
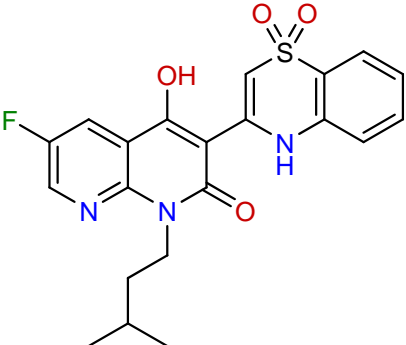
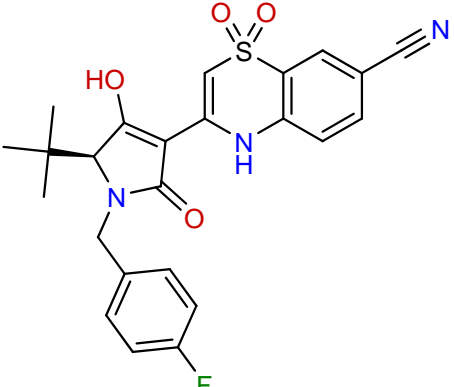
	6.3870 <sup>d</sup>	6.4865	6.3740	6.57326
	5.9210 <sup>d</sup>	6.2754	6.2952	6.23989
	7.8860 <sup>d</sup>	8.0614	7.8163	8.02931
	8.0460 <sup>d</sup>	8.1396	8.3098	8.14373

	7.8860 <sup>d</sup>	8.0073	8.0002	8.03582
	7.7700 <sup>d</sup>	7.7677	7.5303	7.96263
	5.6200 <sup>d</sup>	5.7599	5.7304	5.93064
	9.0000 <sup>d</sup>	8.3928	8.4004	8.35496
	8.5230 <sup>d</sup>	8.5240	8.5344	8.42245

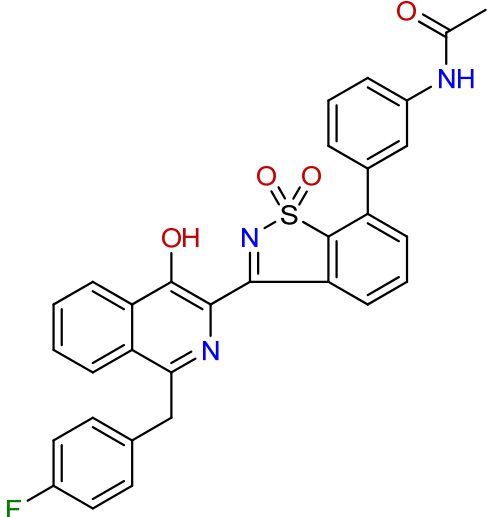
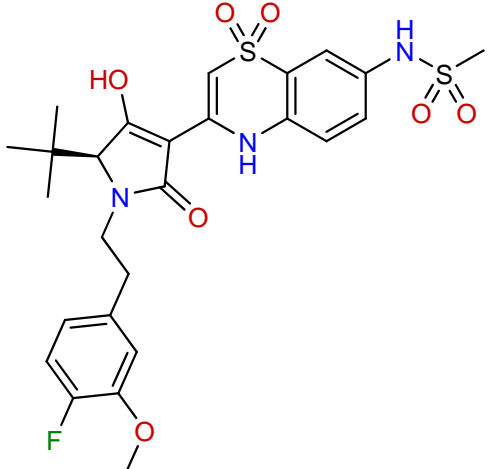
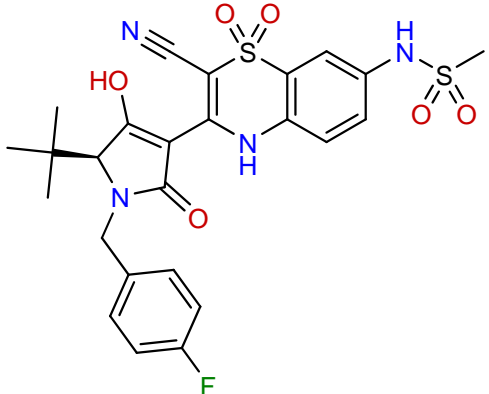
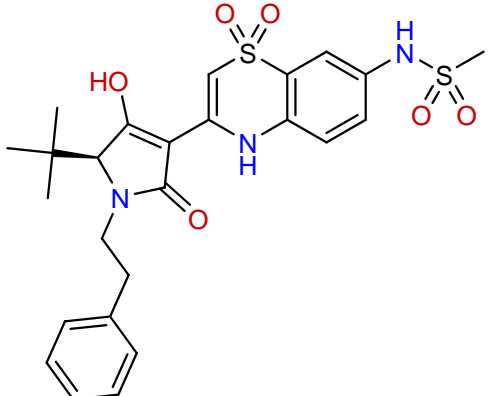
	7.9590 <sup>d</sup>	8.5267	8.6704	8.2359
	6.4560 <sup>d</sup>	6.2293	6.1333	6.37448
	8.0000 <sup>d</sup>	7.9966	7.8436	7.93941
	6.3980 <sup>d</sup>	6.1719	6.0321	6.15552

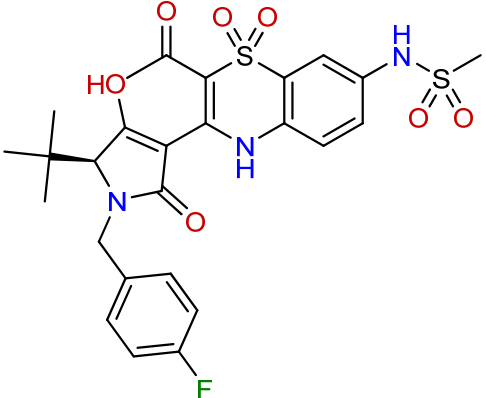
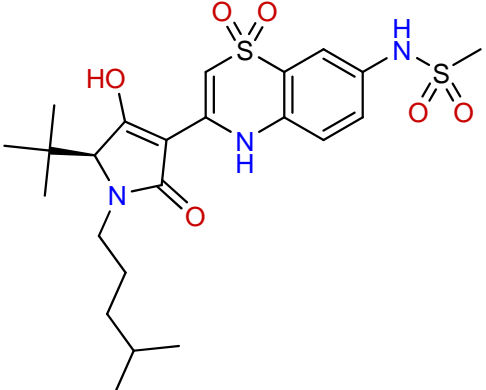
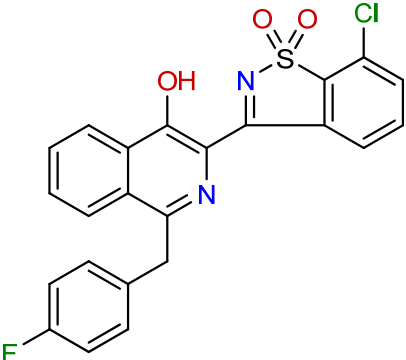
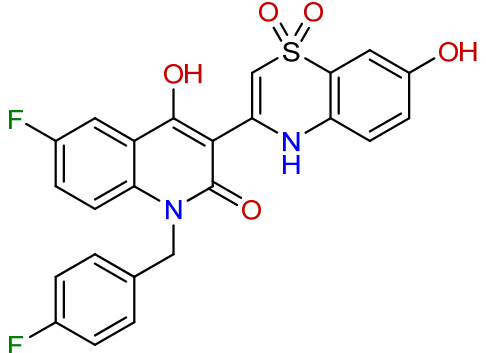
	6.1430 <sup>d</sup>	5.8880	6.0841	5.83493
	5.6380 <sup>d</sup>	5.5491	5.6768	5.78548
	8.3980 <sup>d</sup>	7.9823	7.9435	8.26345
	7.9210 <sup>d</sup>	7.9551	7.7148	7.9774
	6.2150 <sup>d</sup>	5.9702	6.2450	6.25515

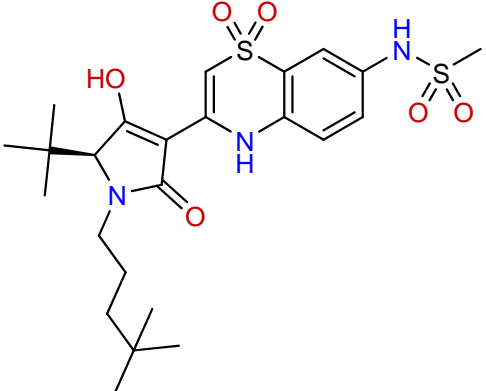
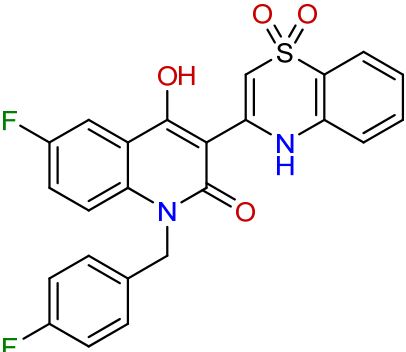
	6.2600 <sup>d</sup>	5.6561	5.7043	5.59333
	6.4710 <sup>d</sup>	6.1684	6.4654	6.36583
	7.1670 <sup>d</sup>	7.9469	7.7895	8.00165
	5.4090 <sup>d</sup>	5.6081	5.2704	5.32562

	5.6580 <sup>d</sup>	5.7898	5.5921	5.49657
	7.7450 <sup>d</sup>	7.5892	7.4189	7.82692
	6.0810 <sup>d</sup>	5.7202	6.0727	5.89906
	5.9210 <sup>d</sup>	6.3131	6.5973	6.53446



	6.2760 <sup>d</sup>	6.3826	6.3433	6.56164
	8.3980 <sup>d</sup>	8.3335	8.5072	8.30763
	8.2220 <sup>d</sup>	8.1033	8.1674	8.14673
	8.0970 <sup>d</sup>	7.7336	7.7920	8.11641

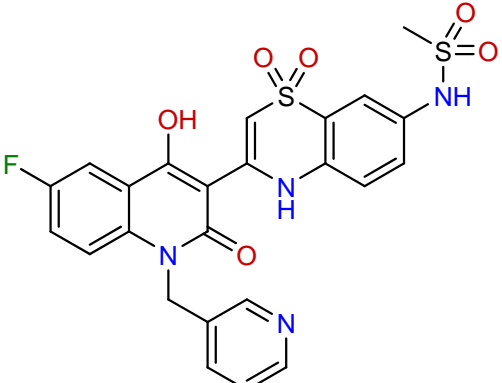
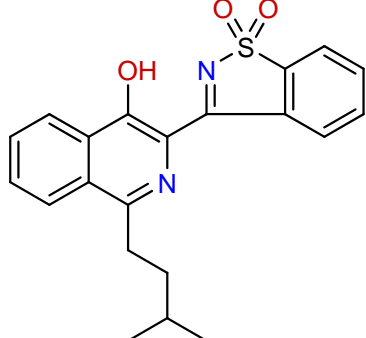
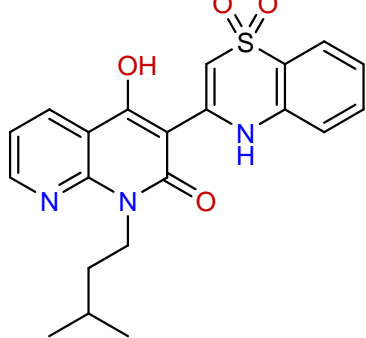
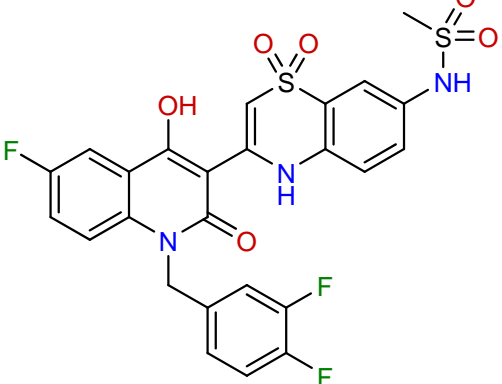
	8.3980 <sup>d</sup>	8.3042	8.4641	8.28773
	8.3010 <sup>d</sup>	7.6646	7.9031	8.04976
	6.2370 <sup>d</sup>	5.8323	5.7143	5.57263
	7.1610 <sup>d</sup>	6.5758	6.7039	6.81786

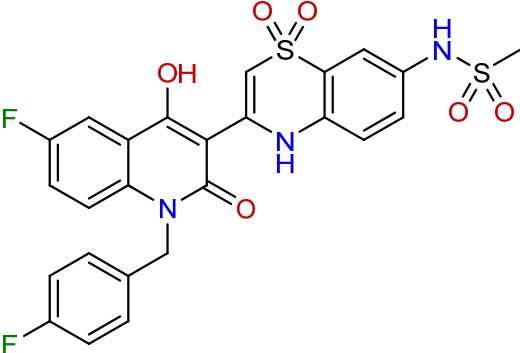
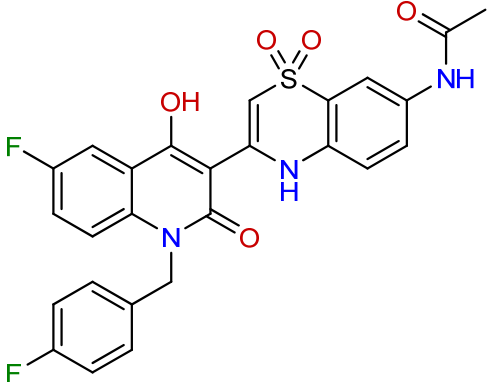
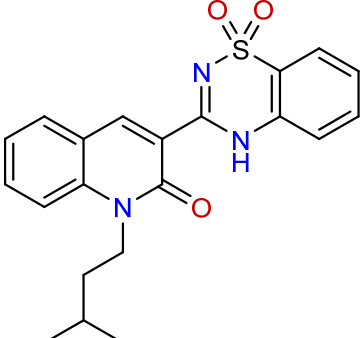
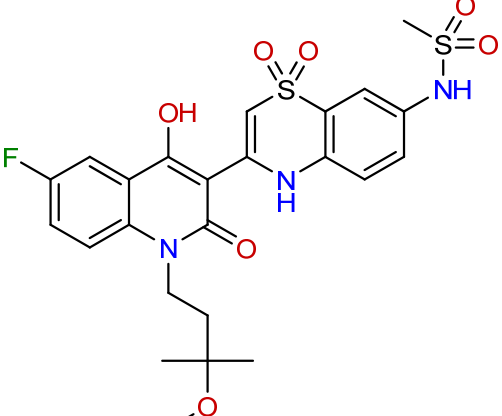
	8.0970 <sup>d</sup>	7.7062	7.8299	8.09136
	6.1550 <sup>d</sup>	6.1128	6.0687	6.12209

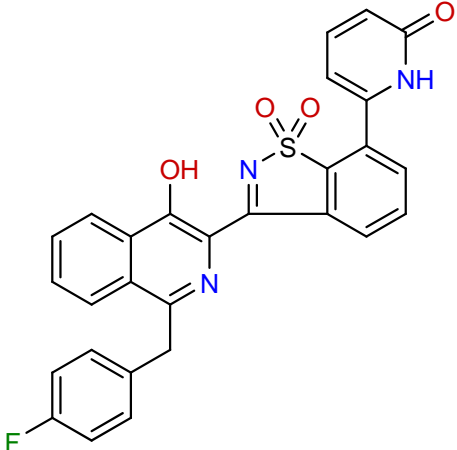
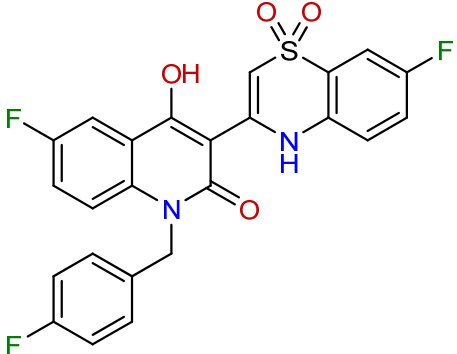
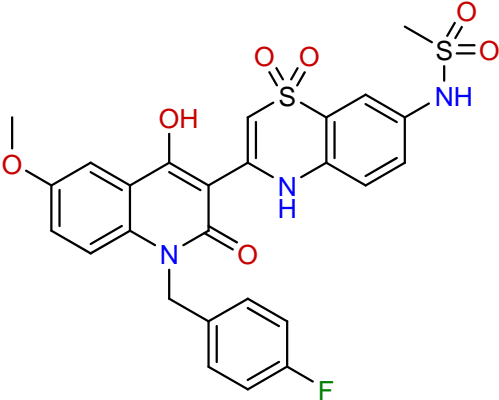
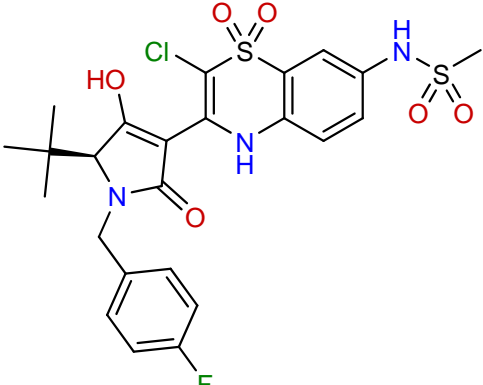
<sup>a</sup> Predicted  $\log(10^9/IC_{50})$  by Multiple Linear Regression. <sup>b</sup> Predicted  $\log(10^9/IC_{50})$  by Partial Least Square. <sup>c</sup> Predicted  $-\log(IC_{50})$  by Support Vector Machine. <sup>d</sup> Compounds in the testing set.

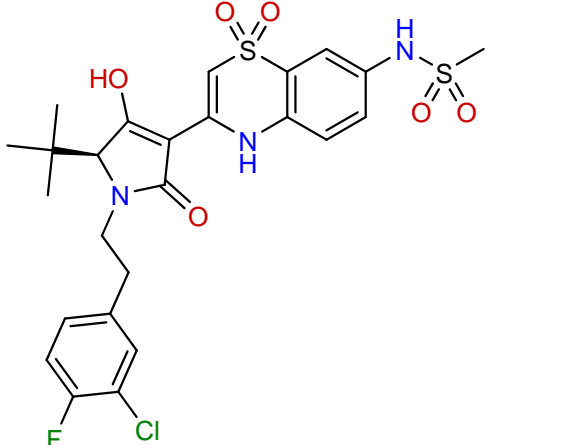
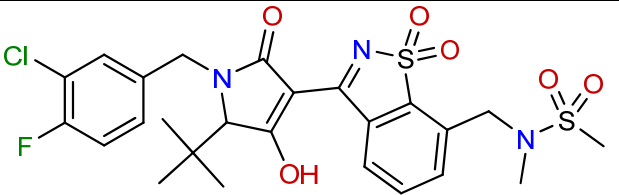
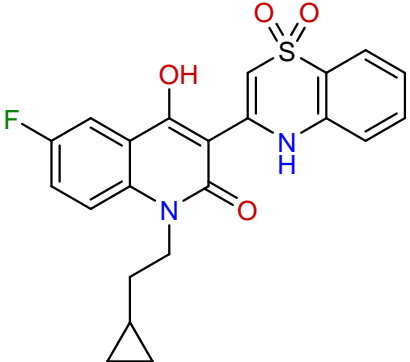
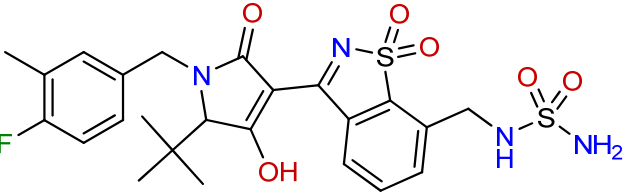
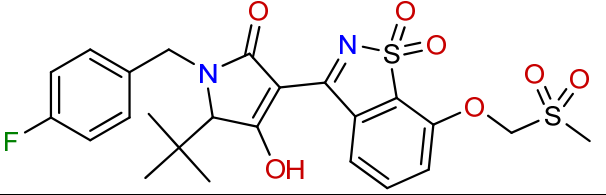
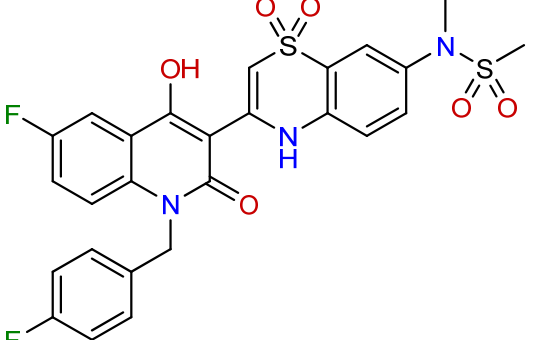
表 S2 选用 GA-PLS 描述符子集建立的机器学习模型对抑制剂活性的预测结果

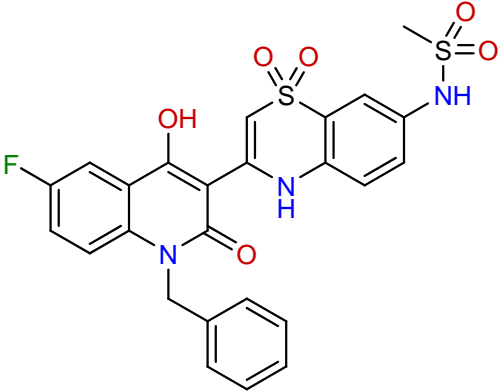
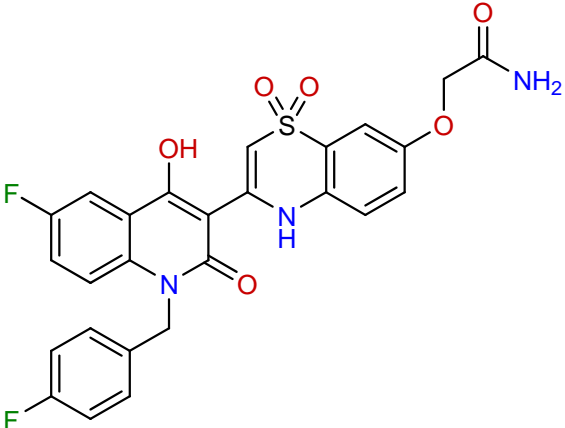
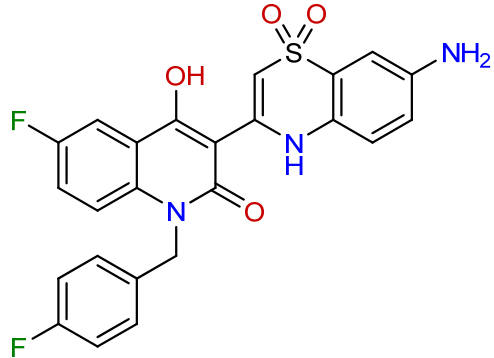
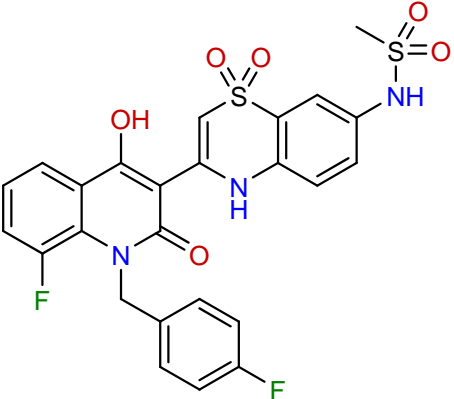
**Table S2 The molecular structures of compounds and its actual and calculated HCV NS5B polymerase inhibitory activities with GA-PLS selected descriptors**

Structure	Actual activity ( $\log(10^9/IC_{50})$ )	Calculated activity <sup>a</sup> (MLR)	Calculated Activity <sup>b</sup> (PLS)	Calculated activity <sup>c</sup> (SVM)
	7.6580	7.8743	7.9098	7.95188
	5.3470	5.3728	5.3492	5.32284
	5.8540	5.7573	5.7700	5.83432
	7.8540	8.1044	8.1071	8.07864

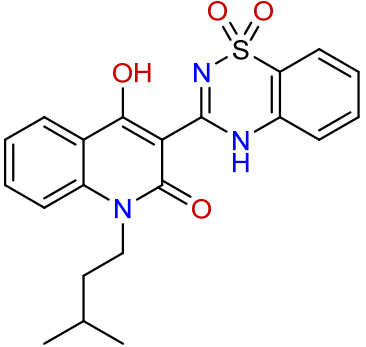
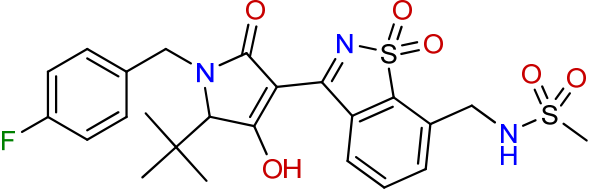
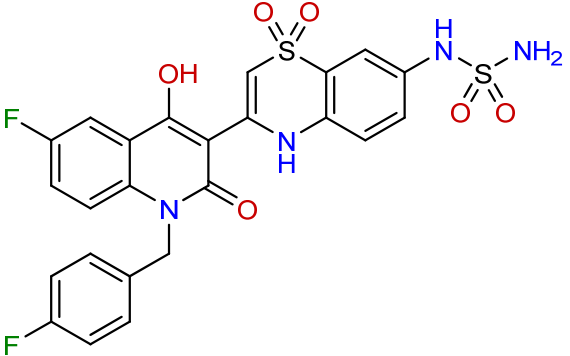
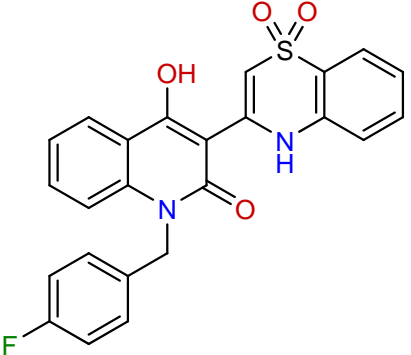
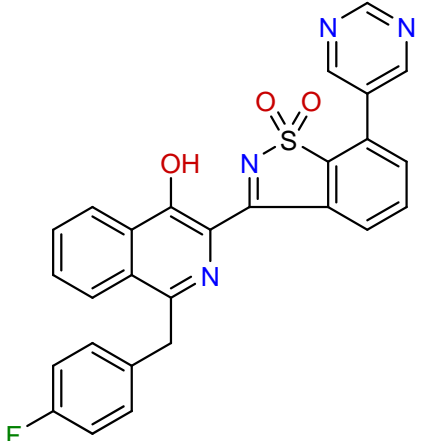
	8.3010	7.8917	7.9285	7.97115
	6.0610	6.7663	6.6908	6.8189
	3.1660	3.2476	3.2045	3.39128
	8.0000	8.2579	8.3596	8.22528

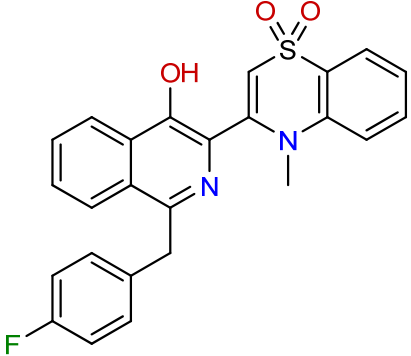
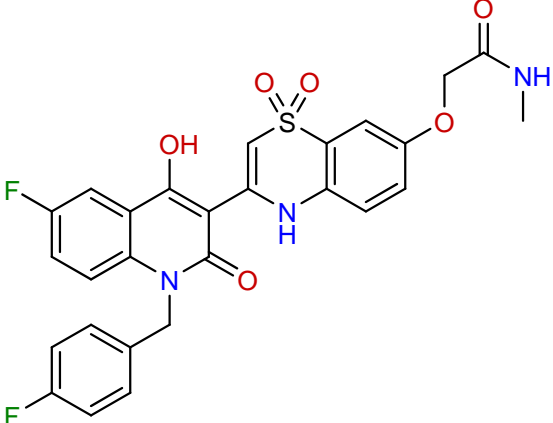
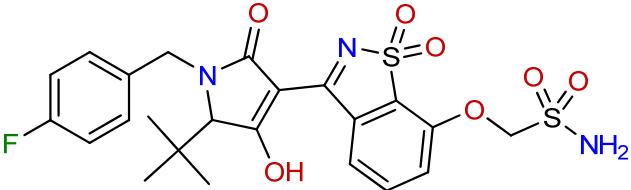
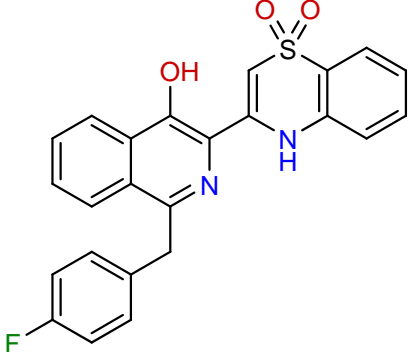
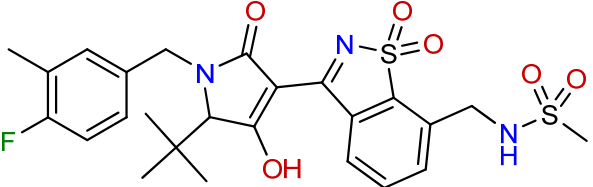
	6.1370	6.3560	6.2635	6.32661
	6.8300	6.0919	6.0993	6.17818
	8.3010	8.0797	8.1520	8.04664
	8.6990	8.2243	8.2056	8.22366

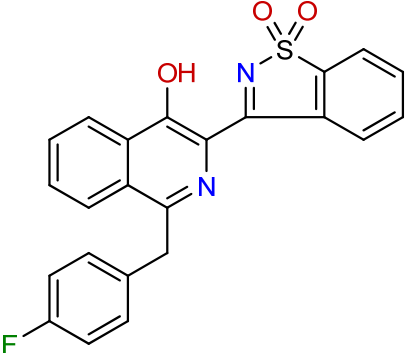
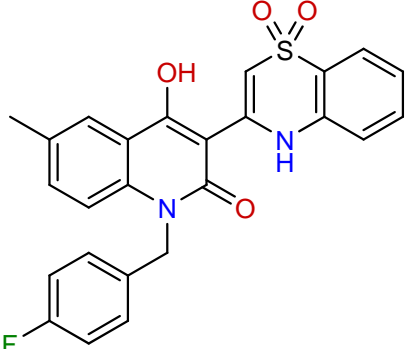
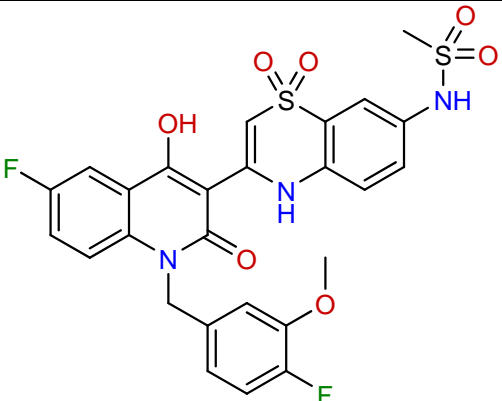
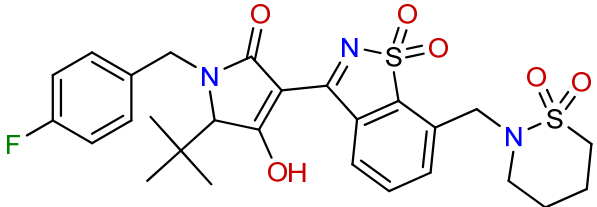
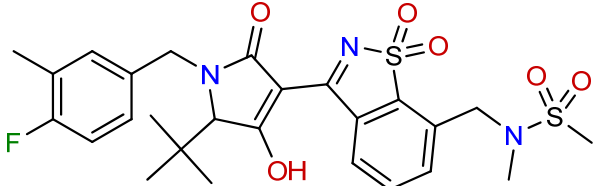
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	8.0000	8.4261	8.3691	8.31075
	5.9590	5.8100	5.8289	5.88778
	8.5230	8.3944	8.3360	8.2978
	8.0460	8.4157	8.3994	8.32326
	6.9750	7.9066	7.9464	7.98873

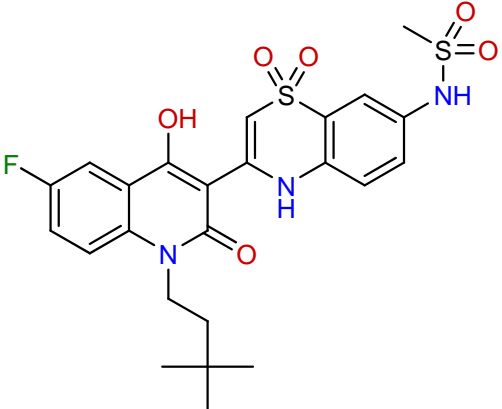
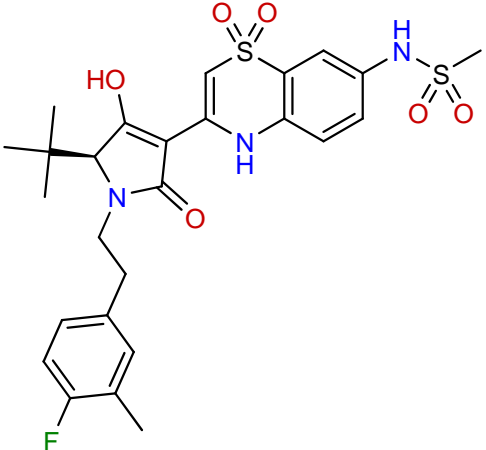
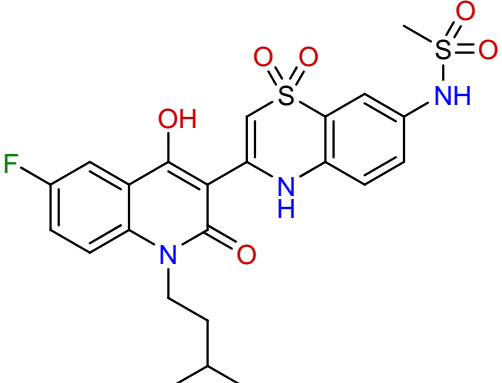
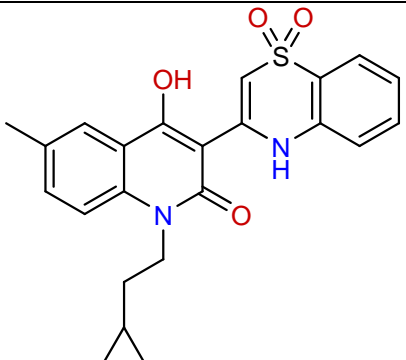
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	6.1340	6.1990	6.1745	6.25855
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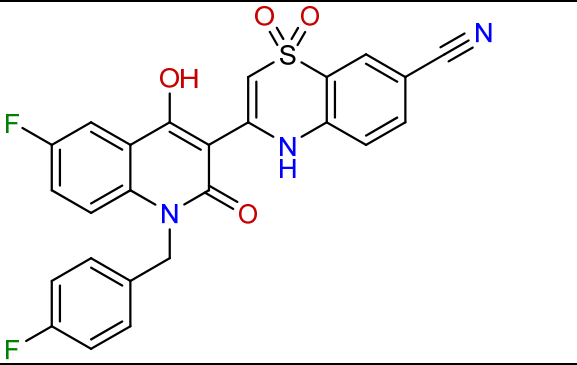
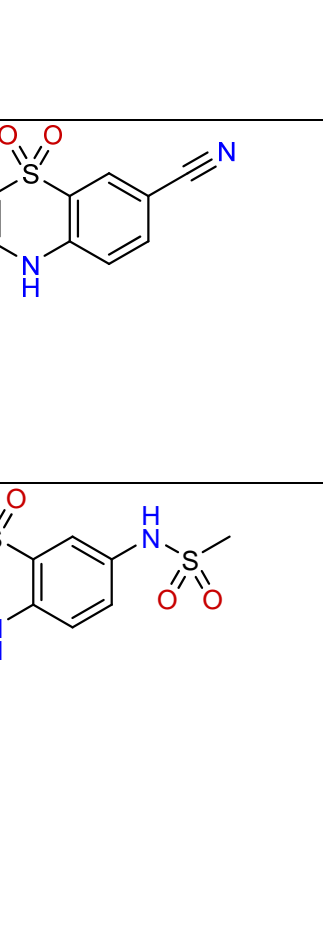
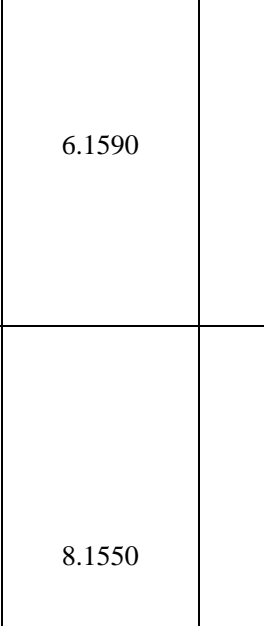
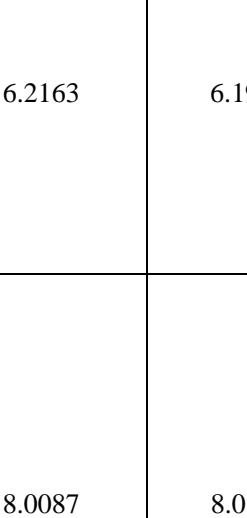


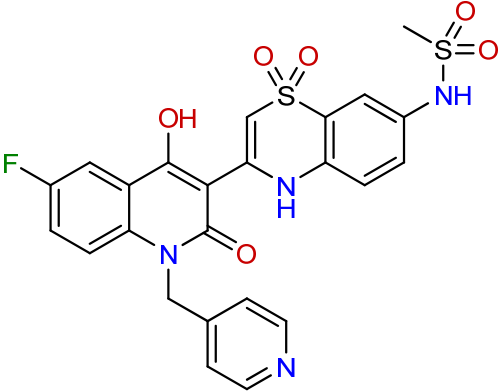
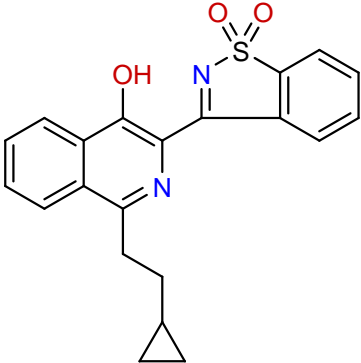
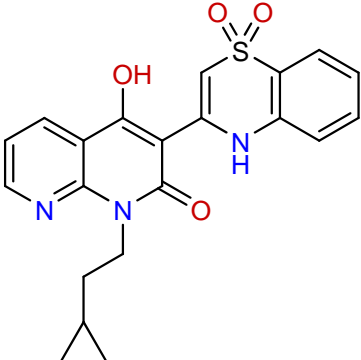
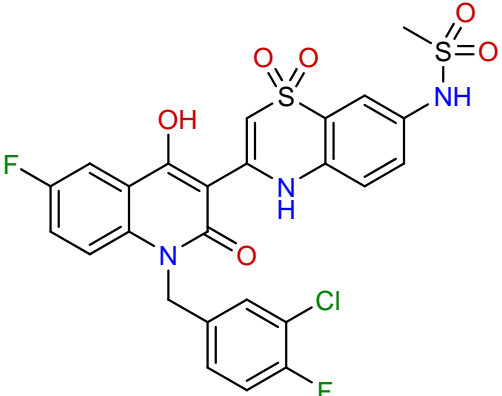
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	8.5230	8.1427	8.1291	8.17498
	8.1550	8.1806	8.1528	8.13157
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	5.7450	6.0567	5.9702	5.97013

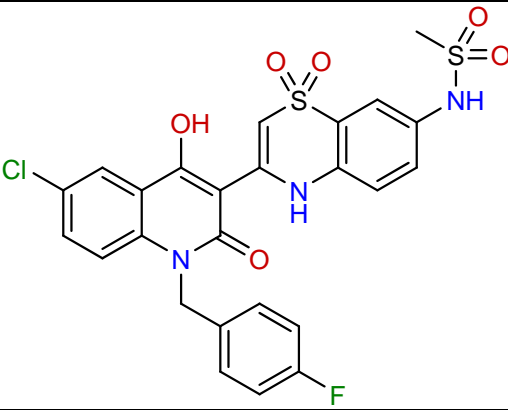
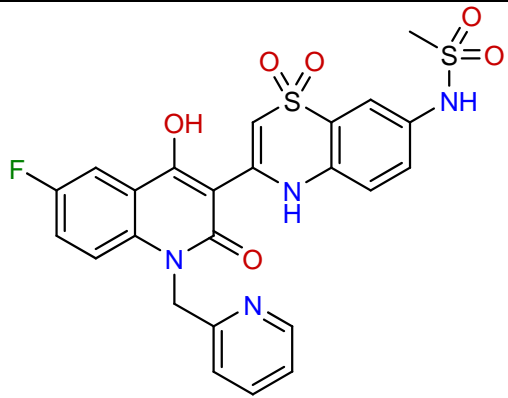
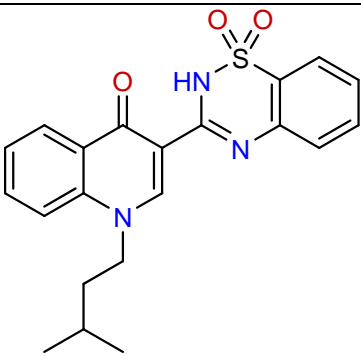
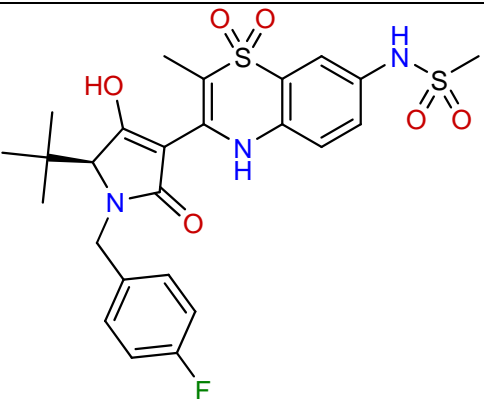
	4.7100	5.3903	5.4245	5.4111
	7.6020	7.4082	7.2511	7.37688
	8.2220	8.6964	8.6175	8.44411
	5.1610	5.3778	5.3908	5.3862
	8.3980	8.1266	8.1272	8.17265

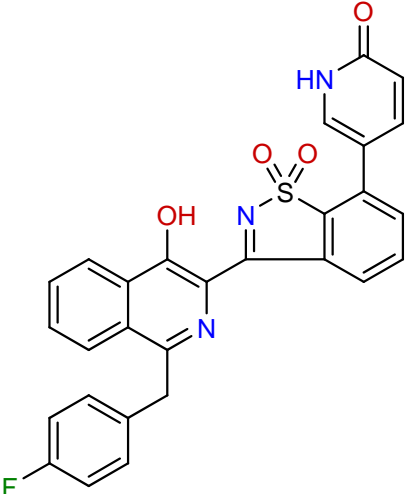
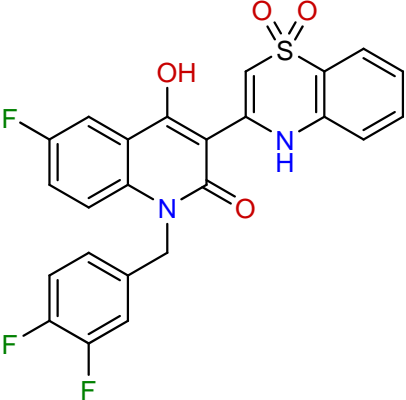
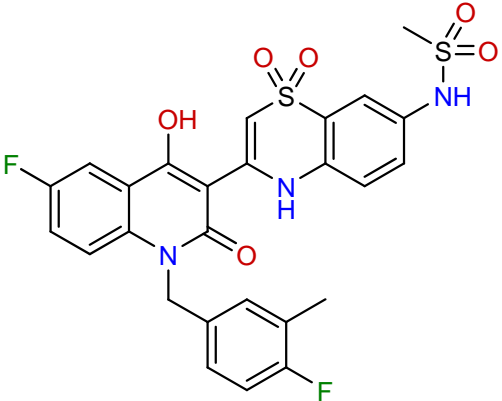
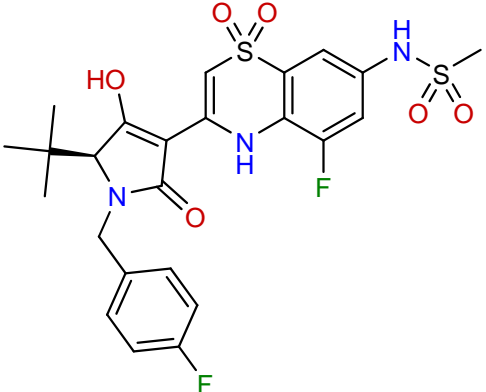
	5.6580	5.3670	5.3871	5.38175
	5.8240	5.8101	5.8532	5.90513
	8.0000	8.3926	8.3935	8.22537
	7.9210	8.0459	8.0796	8.14158
	8.3010	8.1305	8.1387	8.17791

	7.9210	7.6919	7.7520	7.85424
	8.5230	8.0105	8.0205	8.10607
	7.3870	7.6983	7.7473	7.85248
	5.8860	5.6009	5.6606	5.69918

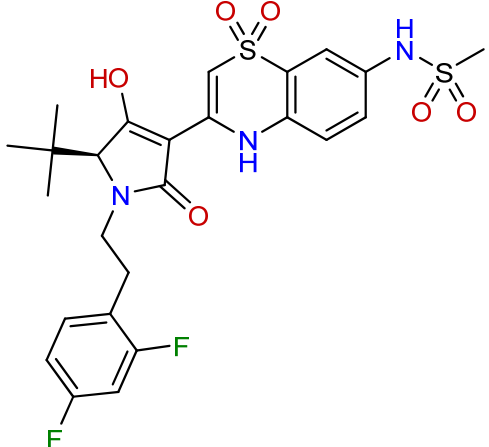
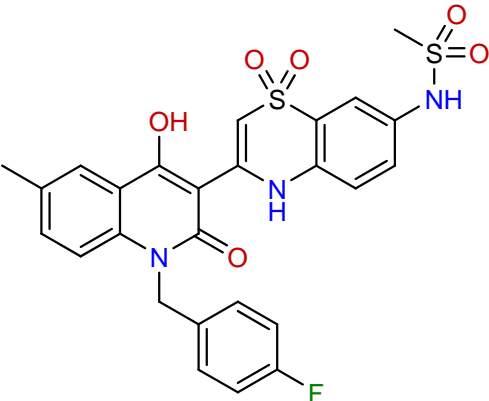
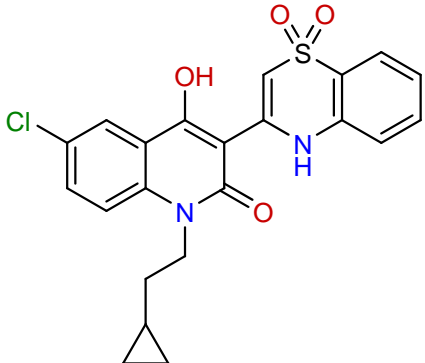
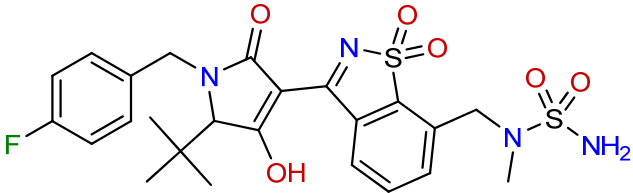
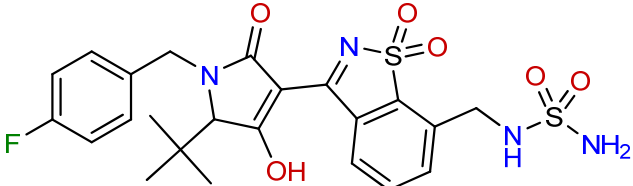
	6.1590	6.2163	6.1950	6.27748
	8.1550	8.0087	8.0113	8.1008
	5.4200	5.9866	6.0441	6.13207
	3.0610	2.9953	3.0326	3.24172

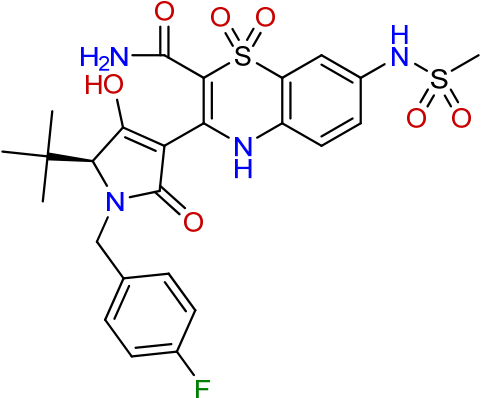
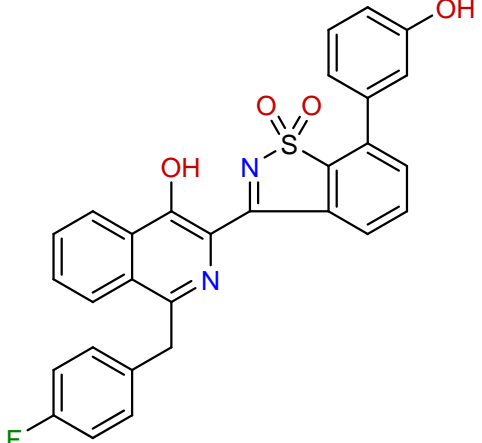
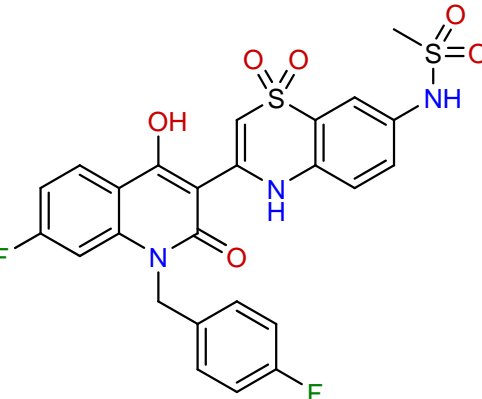
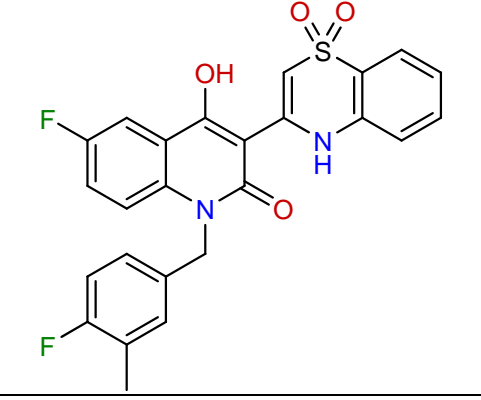
	7.9590 <sup>d</sup>	7.8738	7.9094	7.95143
	6.0000 <sup>d</sup>	5.3724	5.3489	5.3226
	5.5690 <sup>d</sup>	5.7612	5.7727	5.8371
	7.7960 <sup>d</sup>	8.1041	8.1069	8.07842

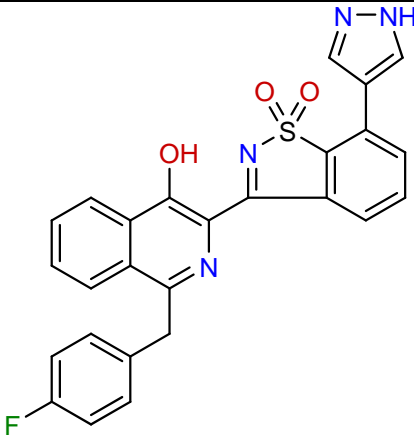
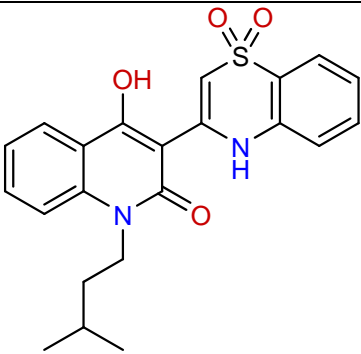
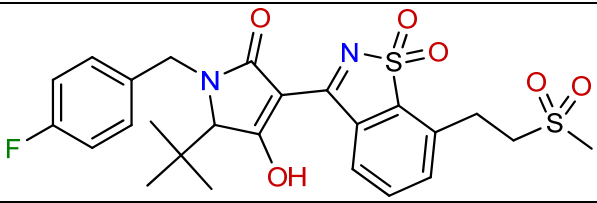
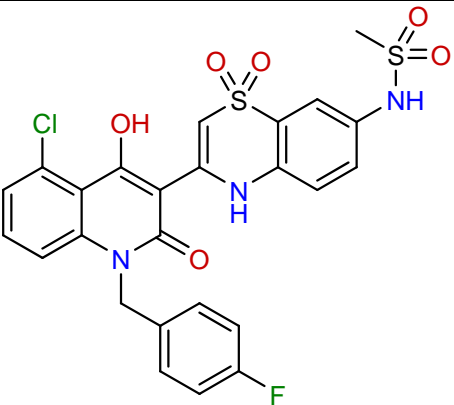
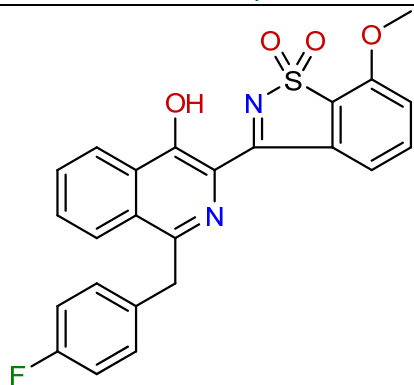
	8.0000 <sup>d</sup>	7.9253	7.9526	7.99856
	6.9870 <sup>d</sup>	7.8712	7.9077	7.94936
	3.0000 <sup>d</sup>	4.0459	3.4699	3.68881
	8.0000 <sup>d</sup>	8.0152	8.0374	8.11579

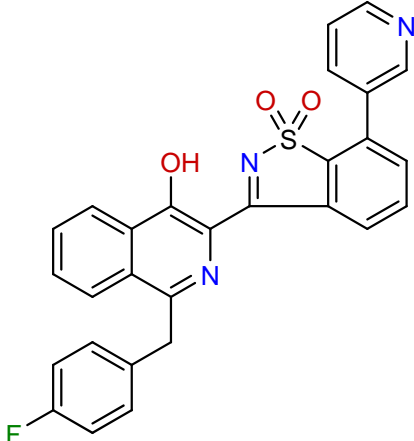
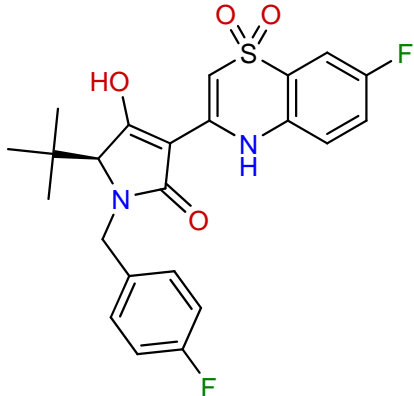
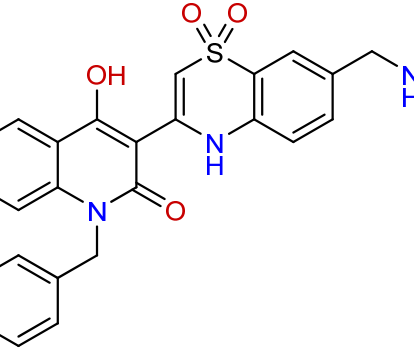
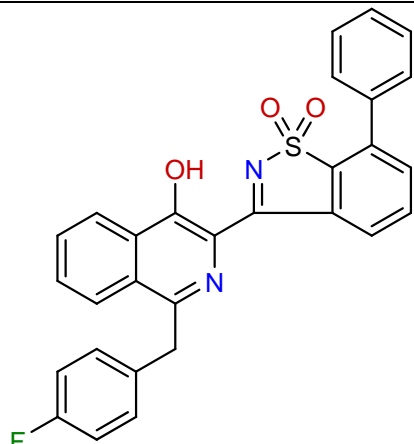
	6.3870 <sup>d</sup>	6.3549	6.2618	6.32531
	5.9210 <sup>d</sup>	6.2150	6.1879	6.272
	7.8860 <sup>d</sup>	7.8935	7.9340	7.97579
	8.0460 <sup>d</sup>	8.2355	8.2039	8.22444

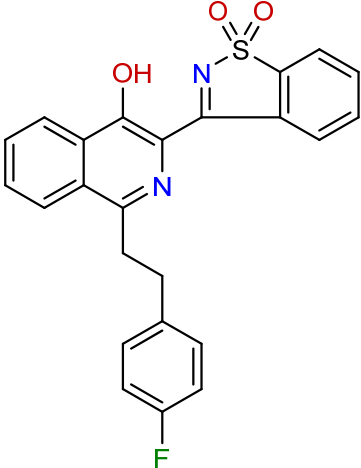
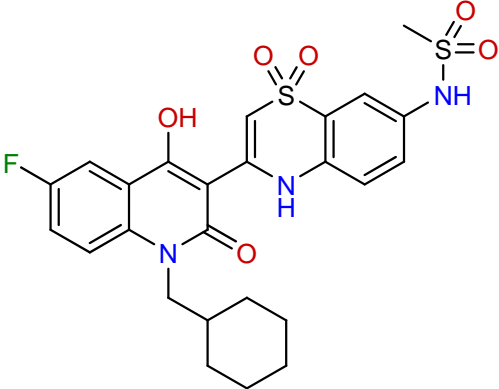
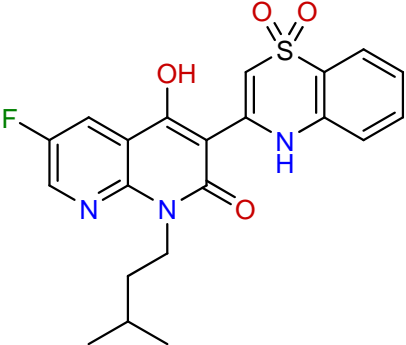
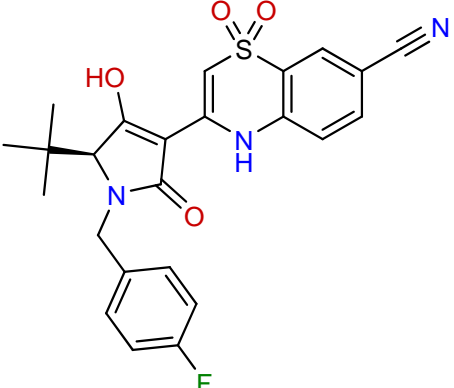


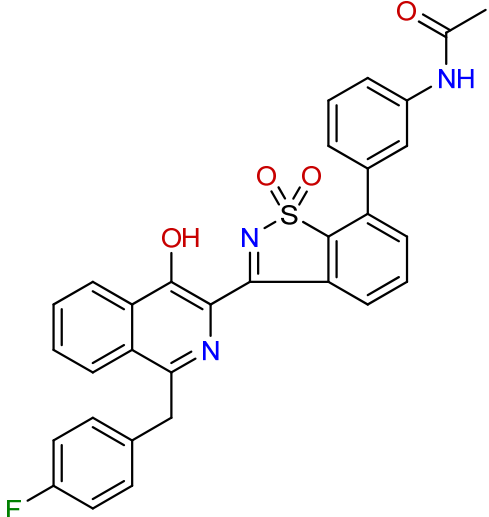
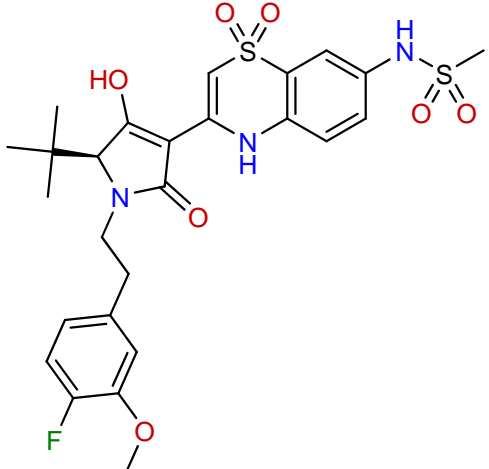
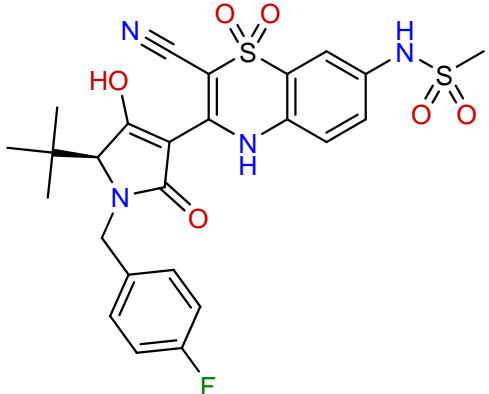
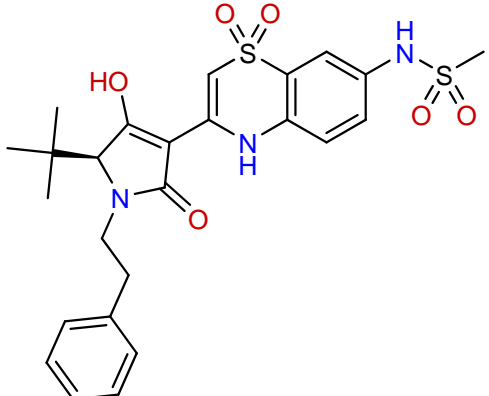
	7.8860 <sup>d</sup>	8.0390	8.0606	8.10439
	7.7700 <sup>d</sup>	7.7051	7.7764	7.87646
	5.6200 <sup>d</sup>	5.8105	5.8292	5.88812
	9.0000 <sup>d</sup>	8.3921	8.3334	8.29671
	8.5230 <sup>d</sup>	8.4092	8.3370	8.29898

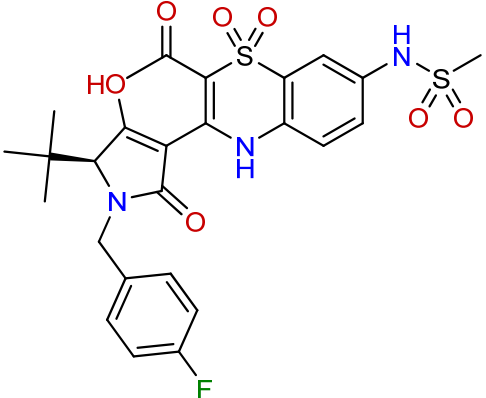
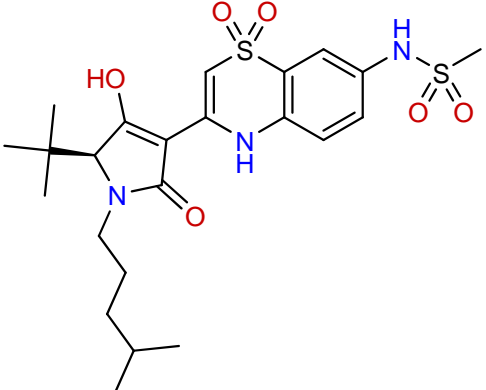
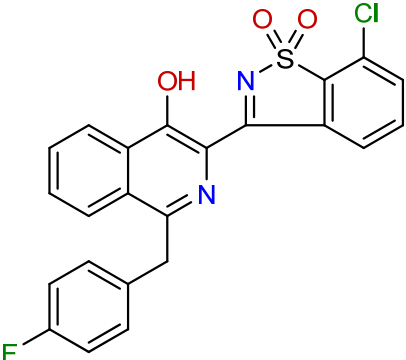
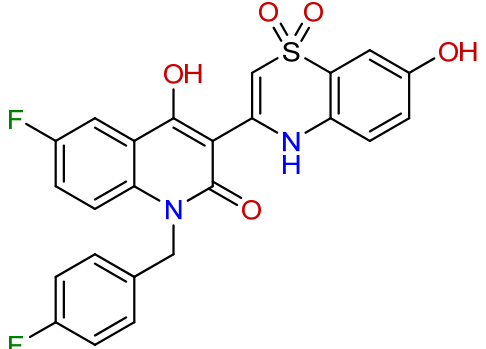
	7.9590 <sup>d</sup>	8.6228	8.6098	8.41831
	6.4560 <sup>d</sup>	4.9903	6.7661	6.34099
	8.0000 <sup>d</sup>	7.8841	7.9135	7.95763
	6.3980 <sup>d</sup>	6.0133	6.0250	6.09379

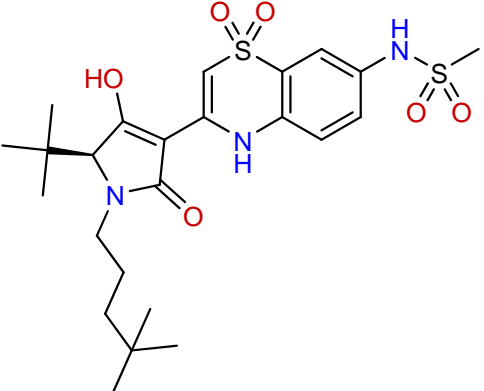
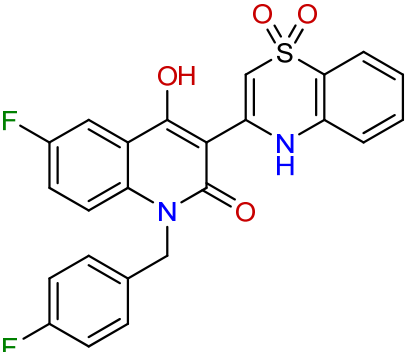
	6.1430 <sup>d</sup>	6.0692	5.9723	5.97364
	5.6380 <sup>d</sup>	5.6162	5.6498	5.69472
	8.3980 <sup>d</sup>	7.9608	7.9815	8.06708
	7.9210 <sup>d</sup>	7.8902	7.9372	7.97721
	6.2150 <sup>d</sup>	6.1174	6.0390	6.0952

	6.2600 <sup>d</sup>	5.7604	5.7391	5.72648
	6.4710 <sup>d</sup>	6.2319	6.1982	6.26916
	7.1670 <sup>d</sup>	7.9536	7.9761	8.02313
	5.4090 <sup>d</sup>	5.4209	5.4769	5.45191

	5.6580 <sup>d</sup>	5.5932	5.5510	5.53355
	7.7450 <sup>d</sup>	7.7008	7.7684	7.86921
	6.0810 <sup>d</sup>	5.9481	5.9469	6.02256
	5.9210 <sup>d</sup>	6.3524	6.2910	6.35466

	6.2760 <sup>d</sup>	6.3620	6.2820	6.33978
	8.3980 <sup>d</sup>	8.4670	8.4457	8.34399
	8.2220 <sup>d</sup>	8.1665	8.1794	8.20094
	8.0970 <sup>d</sup>	7.8047	7.8403	7.97745

	8.3980 <sup>d</sup>	8.4470	8.4694	8.35321
	8.3010 <sup>d</sup>	7.8604	7.8626	7.99844
	6.2370 <sup>d</sup>	5.7368	5.6832	5.68466
	7.1610 <sup>d</sup>	5.4338	7.1728	6.81275

	8.0970 <sup>d</sup>	7.8189	7.8420	7.98077
	6.1550 <sup>d</sup>	6.0066	6.0123	6.08313

<sup>a</sup> Predicted  $\log(10^9/IC_{50})$  by Multiple Linear Regression. <sup>b</sup> Predicted  $\log(10^9/IC_{50})$  by Partial Least Square. <sup>c</sup> Predicted  $-\log(IC_{50})$  by Support Vector Machine. <sup>d</sup> Compounds in the testing set.

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