Supporting Information

A Molecular Recipe for γ-Secretase Modulation from Computational Analysis of 60 Active Compounds

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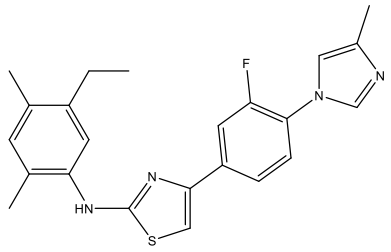
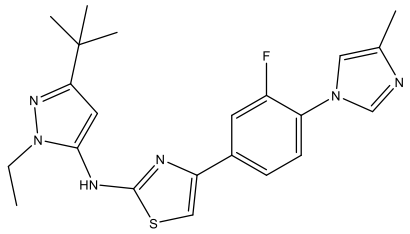
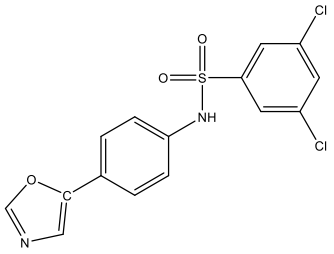
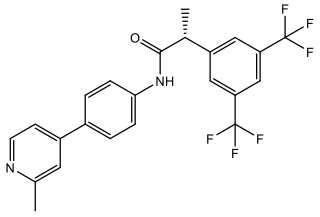
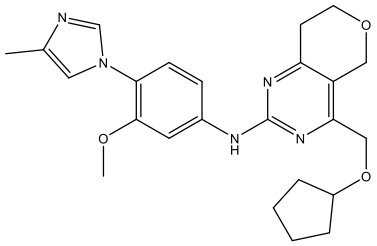
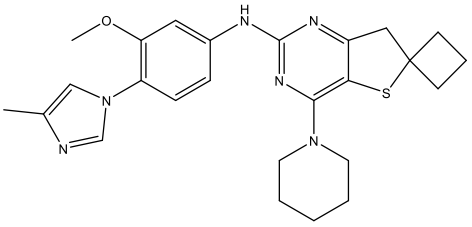
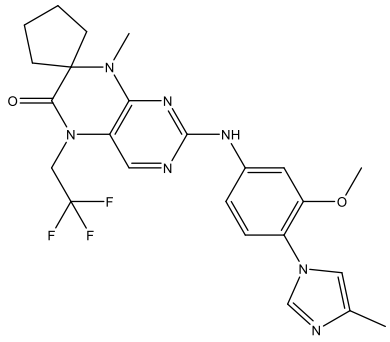
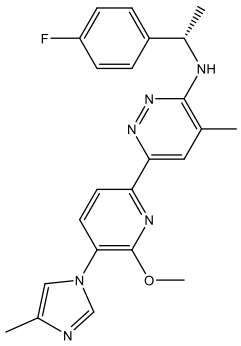
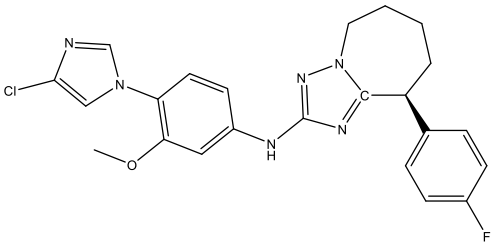
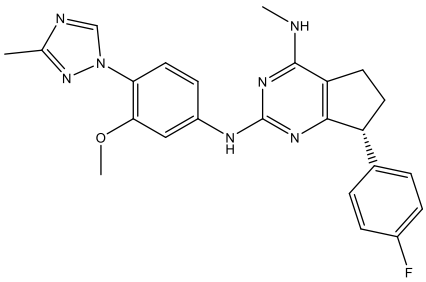
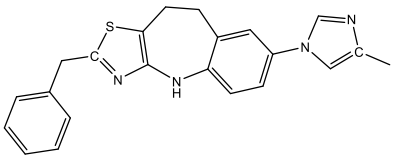
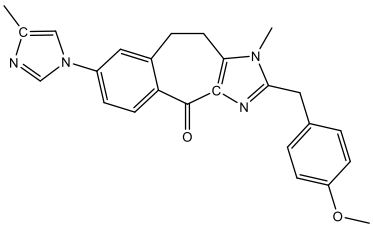
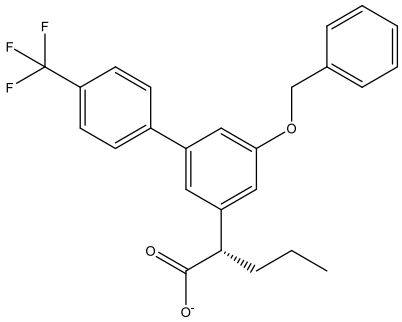
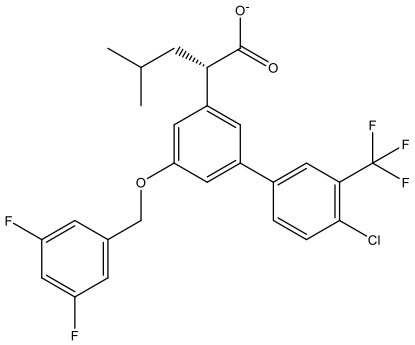
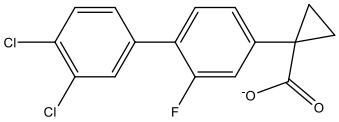
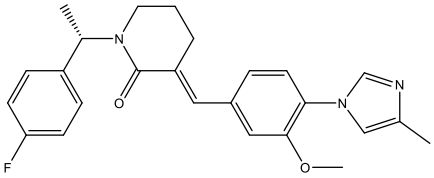
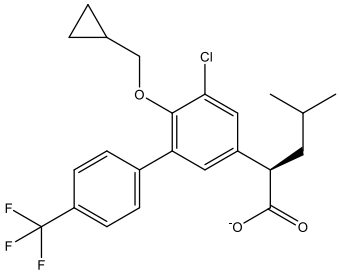
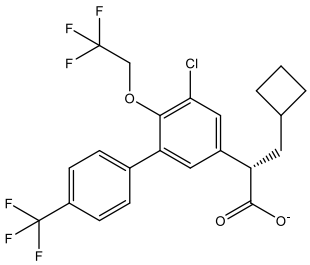
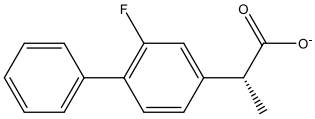
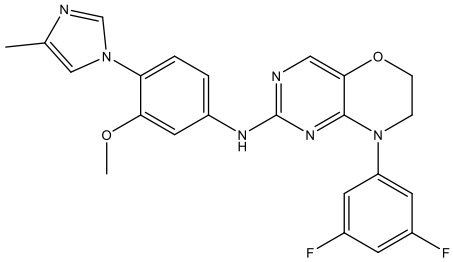
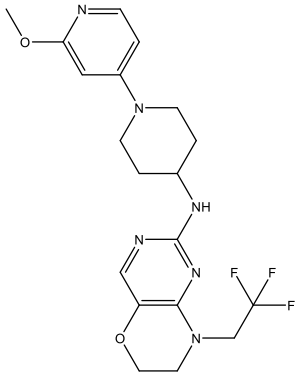
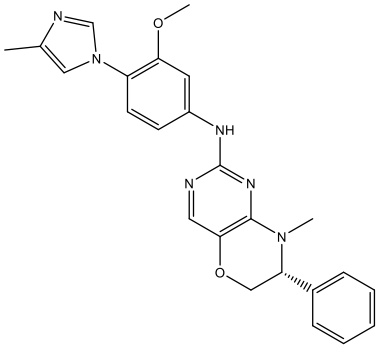
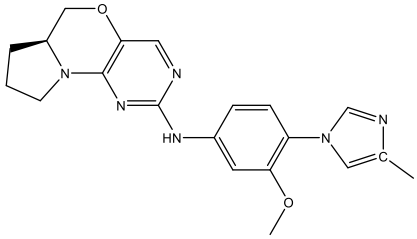
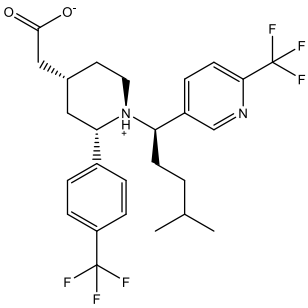
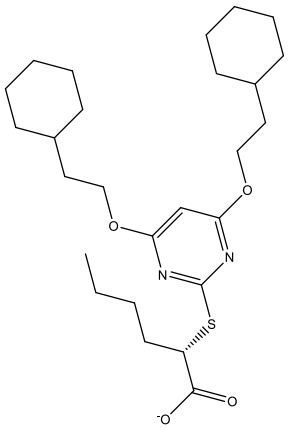
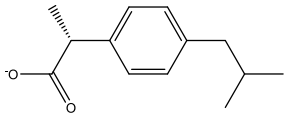
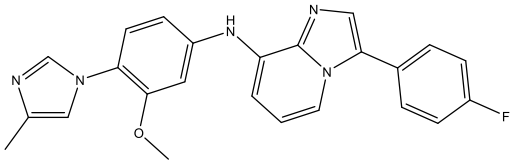
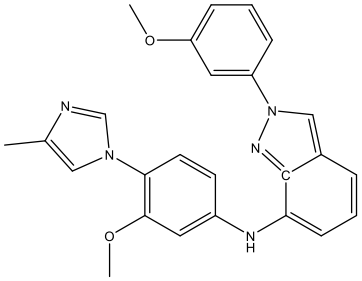
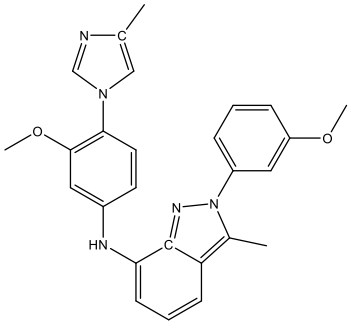
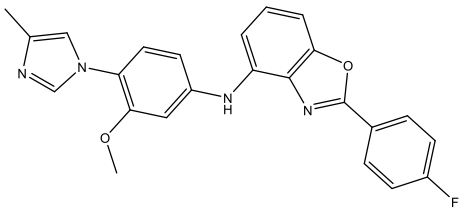
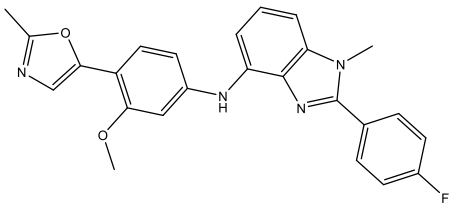
Table S1. The structure, molecular weight and Log EC_{50} value of the investigated modulators.

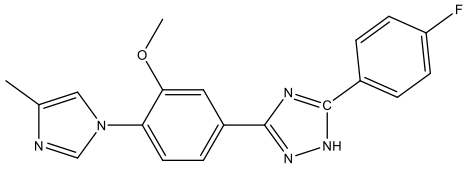
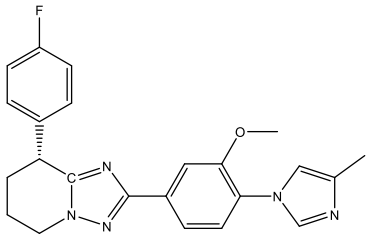
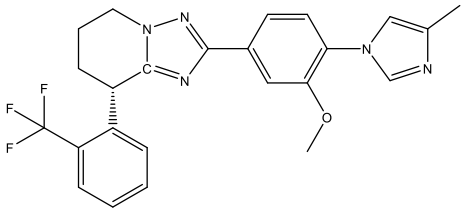
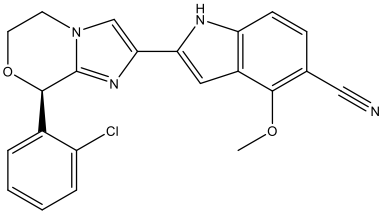
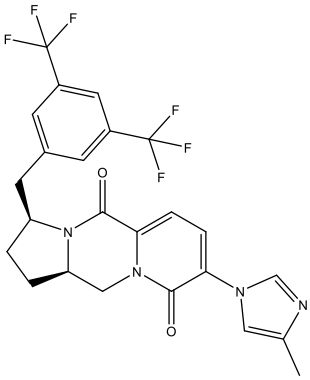
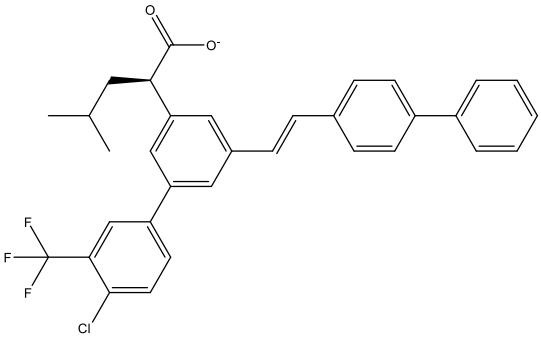
Compound	Structure	Molecular weight	Log EC_{50}
Compound 1		406.52	1.46
Compound 2		424.54	1.80
Compound 3		369.22	3.19
Compound 4		452.40	2.41
Compound 5		435.53	1.34
Compound 6		462.62	1.95

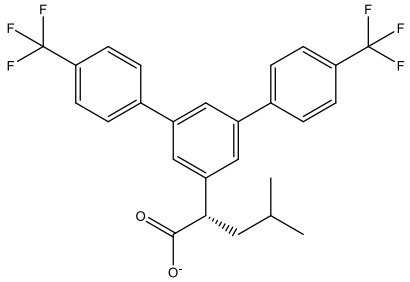
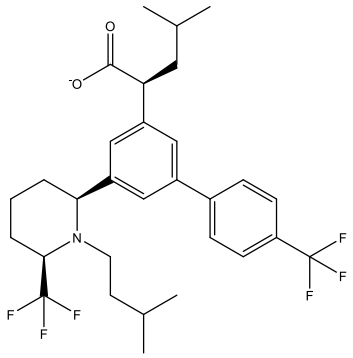
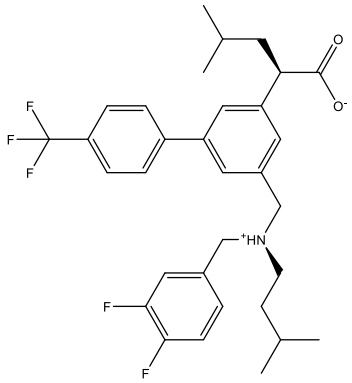
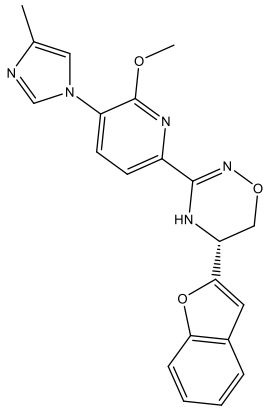
Compound 7		501.51	1.34
Compound 8		418.48	0.85
Compound 9		452.92	0.78
Compound 10		445.50	0.85
Compound 11		372.49	1.46
Compound 12		412.49	3.04

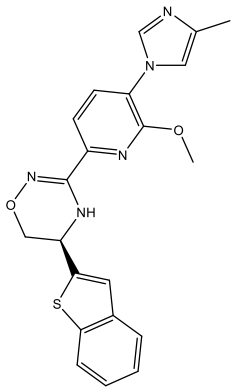
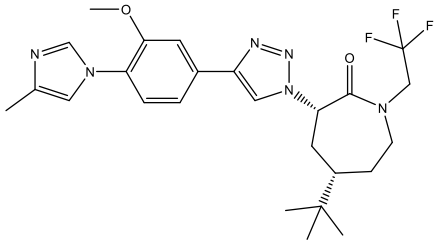
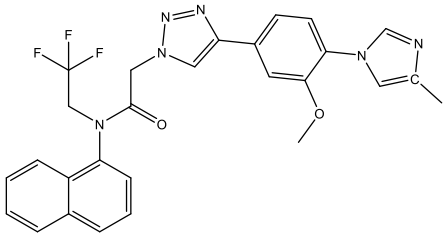
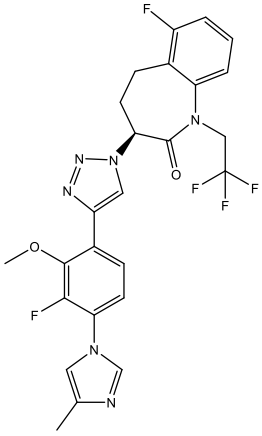
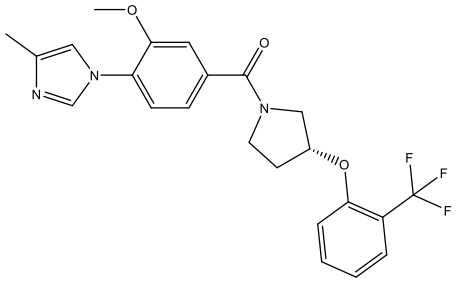
Compound 13		427.44	3.40
Compound 14		511.89	2.28
Compound 15		324.15	4.60
Compound 16		419.50	1.92
Compound 17		439.88	1.84
Compound 18		479.82	1.83
Compound 19		243.26	5.40

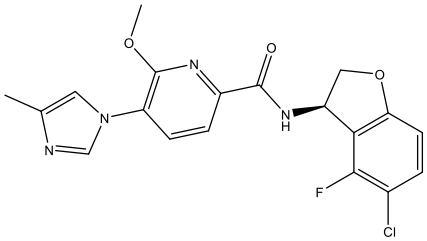
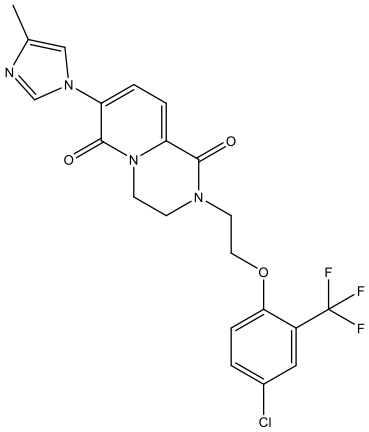
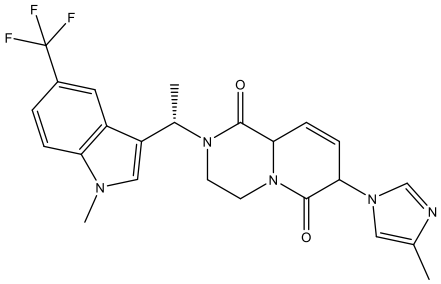
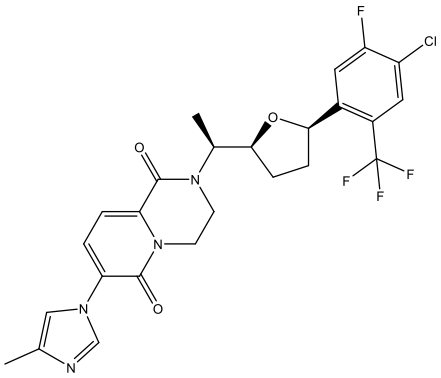
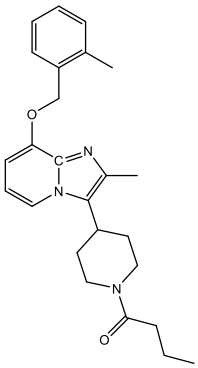
Compound 20		450.45	1.15
Compound 21		424.43	2.02
Compound 22		428.50	1.20
Compound 23		378.44	1.85
Compound 24		516.53	2.90

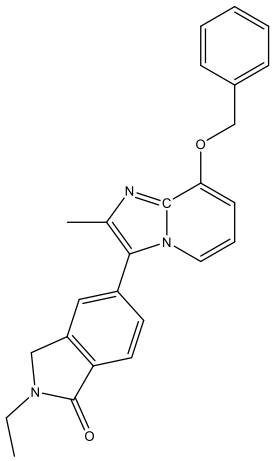
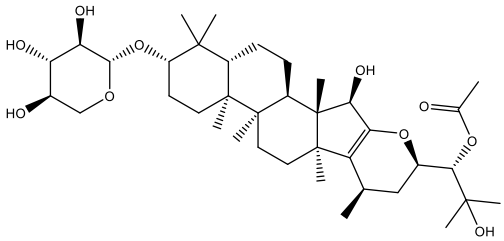
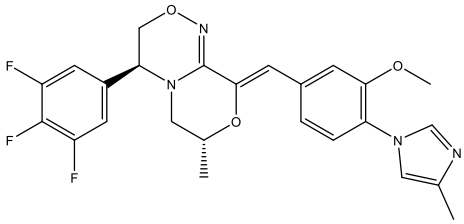
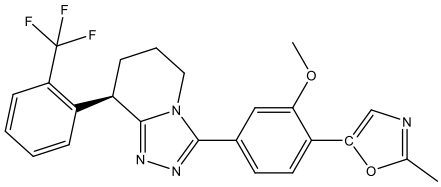
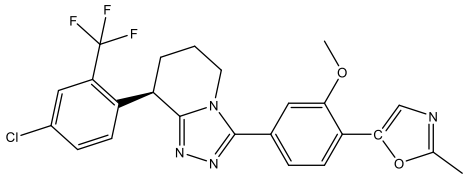
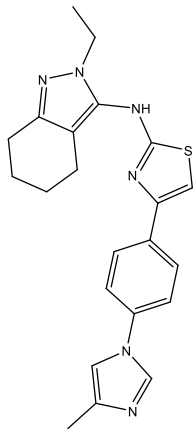
Compound 25		477.68	3.71
Compound 26		205.28	5.30
Compound 27		413.46	2.91
Compound 28		425.49	2.12
Compound 29		439.52	1.26
Compound 30		414.44	3.72
Compound 31		428.47	0.95

Compound 32		349.37	3.11
Compound 33		403.46	2.34
Compound 34		453.47	1.38
Compound 35		404.85	1.32
Compound 36		510.44	1.70
Compound 37		548.02	2.18

Compound 38		479.44	1.95
Compound 39		556.61	2.04
Compound 40		561.64	1.81
Compound 41		389.42	1.54

Compound 42		405.48	0.90
Compound 43		504.56	1.95
Compound 44		520.52	0.95
Compound 45		532.48	1.11
Compound 46		445.44	2.51

Compound 47		402.81	2.28
Compound 48		466.85	2.00
Compound 49		469.47	0.78
Compound 50		538.93	0.90
Compound 51		405.54	2.84

Compound 52		397.48	2.59
Compound 53		678.90	2.00
Compound 54		484.48	1.04
Compound 55		454.45	2.58
Compound 56		488.90	1.78
Compound 57		404.54	2.54

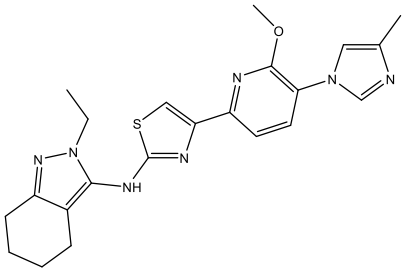
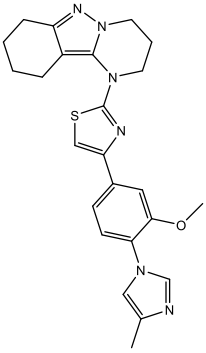
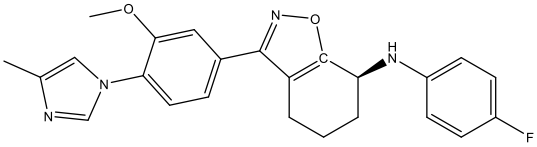
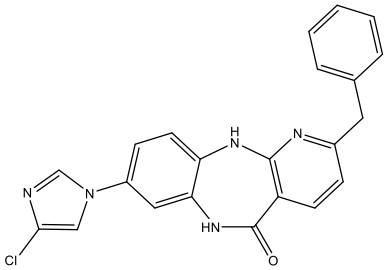
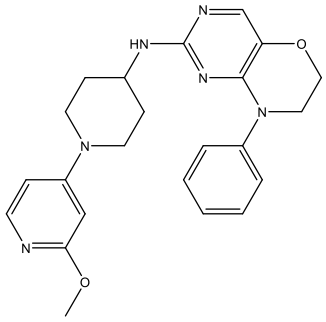
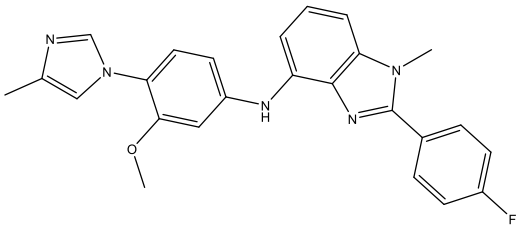
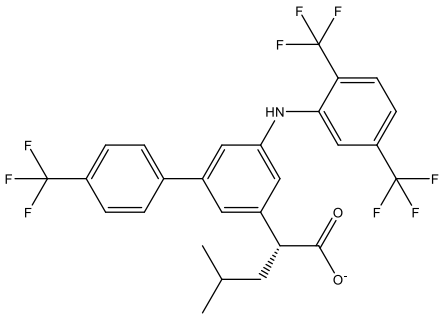
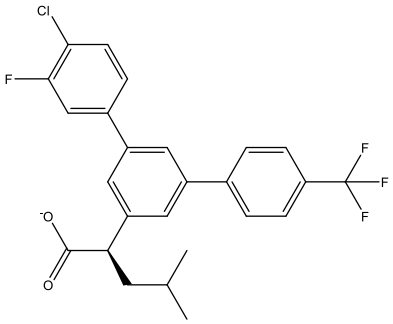
Compound 58		435.55	1.48
Compound 59		446.57	0.78
Compound 60		418.47	1.59

Table S2. The structure, molecular weight and Log EC_{50} value of 10 modulators used for external validation of the prediction model.

Compound	Structure	Molecular weight	Log EC_{50}
Compound 1		401.85	2.28
Compound 2		418.50	1.40
Compound 3		427.48	1.23
Compound 4		562.46	2.00
Compound 5		463.88	2.40

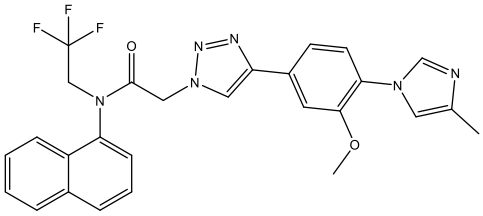
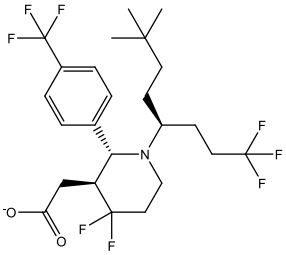
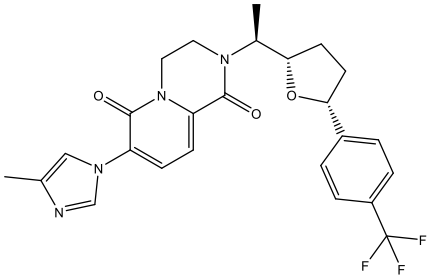
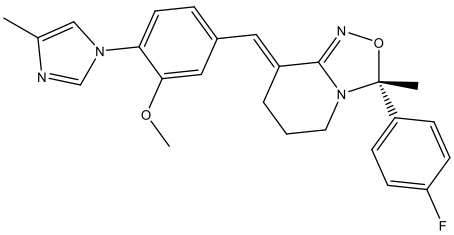
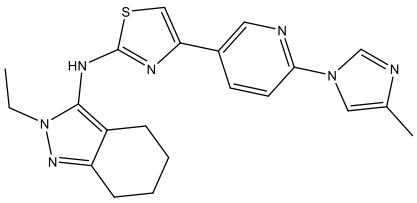
Compound 6		520.52	1.95
Compound 7		516.50	2.78
Compound 8		486.50	1.15
Compound 9		432.50	1.76
Compound 10		405.52	3.11

Table S3. The evaluation metrics (R^2, adjusted R^2 and root mean square error for the training dataset, testing dataset and the whole dataset) of the best method among ten used algorithms for establishing the QSAR models for predicting Log EC_{50} values of the modulators using different descriptors as selected through different variable selection methods.

Model	Method	adj.R^2 training	RMSE training	R^2 training	adj.R^2 test	RMSE test	R^2 test	adj.R^2 Both	RMSE Both	R^2 Both	Descriptors
Model 1	nnet	0.56	0.69	0.54	0.35	0.77	0.46	0.54	0.68	0.57	4
Model 2	nnet	0.57	0.68	0.53	0.36	0.76	0.47	0.55	0.67	0.58	4
Model 3	glmStepAIC	0.48	0.75	0.51	0.33	0.78	0.45	0.49	0.71	0.53	4
Model 4	nnet	0.56	0.67	0.52	0.34	0.77	0.46	0.54	0.68	0.57	4
Model 5	nnet	0.56	0.67	0.55	0.33	0.79	0.45	0.54	0.68	0.57	4
Model 6	nnet	0.54	0.69	0.54	0.37	0.76	0.48	0.55	0.68	0.58	4
Model 7	glmStepAIC	0.47	0.73	0.53	0.35	0.77	0.47	0.50	0.71	0.53	4
Model 8	nnet	0.57	0.68	0.53	0.34	0.78	0.45	0.55	0.68	0.58	4
Model 9	nnet	0.55	0.66	0.53	0.35	0.77	0.46	0.54	0.68	0.57	4
Model 10	nnet	0.53	0.68	0.53	0.36	0.77	0.47	0.54	0.69	0.57	4
Model 11	nnet	0.56	0.69	0.54	0.32	0.80	0.44	0.52	0.69	0.56	4
Model 12	nnet	0.54	0.73	0.52	0.32	0.94	0.44	0.50	0.78	0.54	4
Model 13	nnet	0.51	0.75	0.50	0.24	0.94	0.37	0.45	0.79	0.49	4
Model 14	nnet	0.57	0.69	0.52	0.34	0.80	0.45	0.54	0.69	0.57	4
Model 15	nnet	0.57	0.67	0.52	0.33	0.78	0.44	0.53	0.68	0.57	4
Model 16	nnet	0.52	0.72	0.52	0.27	0.88	0.40	0.48	0.75	0.51	4
Model 17	nnet	0.53	0.69	0.54	0.33	0.80	0.44	0.52	0.70	0.55	4
Model 18	nnet	0.54	0.67	0.53	0.32	0.80	0.44	0.53	0.69	0.56	4
Model 19	nnet	0.50	0.71	0.52	0.30	0.83	0.42	0.49	0.73	0.52	4
Model 20	nnet	0.55	0.68	0.53	0.33	0.78	0.45	0.53	0.68	0.57	4
Model 21	nnet	0.49	0.74	0.52	0.30	0.81	0.42	0.49	0.72	0.52	4
Model 22	nnet	0.52	0.74	0.51	0.26	0.83	0.39	0.48	0.72	0.51	4
Model 23	glmStepAIC	0.43	0.80	0.48	0.30	0.82	0.42	0.45	0.75	0.49	4
Model 24	rf	0.91	0.74	0.53	0.27	0.83	0.40	0.67	0.60	0.69	4
Model 25	nnet	0.48	0.72	0.53	0.30	0.81	0.42	0.49	0.72	0.52	4
Model 26	lm	0.45	0.77	0.50	0.30	0.81	0.42	0.46	0.73	0.50	4
Model 27	nnet	0.54	0.69	0.53	0.33	0.79	0.45	0.53	0.69	0.56	4
Model 28	nnet	0.52	0.72	0.52	0.31	0.81	0.43	0.51	0.71	0.54	4
Model 29	nnet	0.54	0.68	0.53	0.33	0.79	0.44	0.53	0.69	0.56	4

Model 30	nnet	0.56	0.70	0.53	0.34	0.78	0.46	0.55	0.68	0.58	4
Model 31	nnet	0.47	0.75	0.50	0.24	0.85	0.37	0.45	0.74	0.48	4
Model 32	svmRadial	0.72	0.74	0.53	0.24	0.86	0.37	0.56	0.66	0.59	4
Model 33	nnet	0.53	0.73	0.49	0.29	0.90	0.42	0.48	0.76	0.52	4
Model 34	svmRFE	0.53	0.78	0.57	0.27	0.88	0.37	0.47	0.79	0.50	3.4
Model 35	rf	0.92	0.75	0.52	0.24	0.85	0.37	0.66	0.61	0.68	4
Model 36	nnet	0.53	0.71	0.51	0.31	0.85	0.43	0.50	0.73	0.54	4
Model 37	nnet	0.49	0.74	0.51	0.25	0.84	0.38	0.47	0.73	0.51	4
Model 38	nnet	0.53	0.70	0.51	0.28	0.82	0.41	0.50	0.71	0.54	4
Model 39	nnet	0.51	0.71	0.52	0.31	0.83	0.43	0.49	0.72	0.53	4
Model 40	nnet	0.53	0.70	0.51	0.31	0.81	0.43	0.52	0.70	0.55	4
Model 41	nnet	0.51	0.73	0.52	0.28	0.82	0.41	0.49	0.72	0.52	4
Model 42	nnet	0.53	0.72	0.52	0.28	0.83	0.40	0.50	0.71	0.53	4
Model 43	nnet	0.53	0.74	0.50	0.30	0.85	0.42	0.50	0.74	0.53	4
Model 44	nnet	0.55	0.69	0.51	0.30	0.85	0.43	0.51	0.72	0.55	4
Model 45	nnet	0.51	0.71	0.52	0.29	0.82	0.41	0.49	0.72	0.53	4
Model 46	nnet	0.51	0.71	0.53	0.32	0.80	0.44	0.51	0.70	0.55	4
Model 47	nnet	0.54	0.68	0.53	0.32	0.80	0.44	0.52	0.70	0.56	4
Model 48	nnet	0.51	0.72	0.52	0.30	0.82	0.43	0.50	0.72	0.53	4
Model 49	nnet	0.53	0.68	0.53	0.32	0.80	0.44	0.52	0.70	0.55	4
Model 50	nnet	0.53	0.70	0.51	0.33	0.79	0.45	0.52	0.70	0.56	4
Model 51	rfRFE	0.90	0.74	0.51	0.23	0.88	0.33	0.63	0.64	0.65	2.8
Model 52	nnet	0.53	0.72	0.51	0.26	0.86	0.39	0.48	0.73	0.52	4
Model 53	nnet	0.51	0.74	0.49	0.26	0.92	0.39	0.46	0.77	0.49	4
Model 54	svmRadial	0.73	0.76	0.49	0.22	0.88	0.35	0.55	0.68	0.58	4
Model 55	nnet	0.55	0.69	0.51	0.27	0.88	0.40	0.49	0.73	0.53	4
Model 56	svmRadial	0.73	0.78	0.49	0.20	0.88	0.34	0.55	0.67	0.58	4
Model 57	svmRadial	0.72	0.74	0.53	0.26	0.85	0.39	0.57	0.66	0.60	4
Model 58	nnet	0.53	0.69	0.52	0.27	0.83	0.39	0.49	0.71	0.53	4
Model 59	nnet	0.50	0.71	0.52	0.29	0.84	0.41	0.48	0.73	0.52	4
Model 60	nnet	0.53	0.70	0.51	0.30	0.81	0.42	0.51	0.70	0.55	4
Model 61	nnet	0.46	0.74	0.52	0.24	0.85	0.37	0.44	0.75	0.48	4
Model 62	nnet	0.48	0.74	0.51	0.25	0.84	0.38	0.46	0.74	0.50	4
Model 63	nnet	0.53	0.70	0.51	0.24	0.84	0.37	0.48	0.72	0.52	4
Model 64	nnet	0.48	0.75	0.49	0.20	0.88	0.34	0.43	0.76	0.47	4
Model 65	nnet	0.55	0.70	0.50	0.22	0.90	0.35	0.47	0.74	0.51	4
Model 66	nnet	0.53	0.71	0.49	0.23	0.87	0.36	0.47	0.73	0.50	4

Model 67	nnet	0.37	0.78	0.52	0.20	0.89	0.34	0.37	0.80	0.41	4
Model 68	svmRFE	0.51	0.79	0.52	0.17	0.92	0.30	0.43	0.80	0.47	3.8
Model 69	nnet	0.52	0.71	0.52	0.28	0.83	0.40	0.49	0.72	0.53	4
Model 70	nnet	0.54	0.70	0.52	0.22	0.90	0.36	0.46	0.74	0.50	4
Model 71	nnet	0.46	0.77	0.49	0.14	0.90	0.29	0.39	0.77	0.44	4
Model 72	nnet	0.58	0.70	0.52	0.23	0.97	0.37	0.46	0.77	0.50	4
Model 73	rfRFE	0.88	0.79	0.49	0.08	0.95	0.23	0.57	0.69	0.60	3.6
Model 74	nnet	0.53	0.72	0.49	0.18	0.89	0.32	0.45	0.74	0.49	4
Model 75	svmRadial	0.76	0.75	0.53	0.22	0.89	0.35	0.57	0.66	0.60	4
Model 76	nnet	0.53	0.70	0.54	0.34	0.78	0.45	0.52	0.70	0.55	4
Model 77	nnet	0.53	0.71	0.52	0.34	0.78	0.45	0.52	0.70	0.55	4
Model 78	glmStepAIC	0.46	0.76	0.52	0.36	0.76	0.47	0.50	0.71	0.53	4
Model 79	nnet	0.55	0.68	0.53	0.35	0.79	0.46	0.54	0.69	0.57	4
Model 80	glmStepAIC	0.46	0.73	0.54	0.35	0.79	0.46	0.48	0.72	0.52	4
Model 81	lm	0.48	0.74	0.53	0.34	0.78	0.45	0.50	0.71	0.53	4
Model 82	glmStepAIC	0.46	0.73	0.54	0.37	0.76	0.48	0.50	0.71	0.53	4
Model 83	nnet	0.53	0.70	0.54	0.37	0.76	0.48	0.54	0.69	0.57	4
Model 84	nnet	0.55	0.66	0.54	0.36	0.77	0.47	0.54	0.68	0.57	4
Model 85	glmStepAIC	0.47	0.75	0.53	0.35	0.77	0.46	0.50	0.71	0.53	4
Model 86	nnet	0.53	0.71	0.53	0.32	0.79	0.44	0.51	0.70	0.54	4
Model 87	nnet	0.53	0.70	0.52	0.31	0.84	0.43	0.50	0.73	0.53	4
Model 88	nnet	0.54	0.72	0.51	0.32	0.80	0.44	0.51	0.70	0.54	4
Model 89	nnet	0.53	0.72	0.52	0.30	0.81	0.42	0.50	0.71	0.53	4
Model 90	nnet	0.56	0.69	0.52	0.31	0.81	0.43	0.52	0.70	0.55	4
Model 91	nnet	0.52	0.71	0.51	0.31	0.81	0.43	0.50	0.71	0.53	4
Model 92	nnet	0.51	0.70	0.53	0.34	0.79	0.45	0.51	0.70	0.55	4
Model 93	nnet	0.55	0.68	0.52	0.31	0.81	0.43	0.52	0.70	0.55	4
Model 94	nnet	0.50	0.71	0.52	0.33	0.81	0.44	0.50	0.72	0.54	4
Model 95	nnet	0.55	0.68	0.53	0.35	0.79	0.47	0.54	0.69	0.57	4
Model 96	nnet	0.43	0.76	0.51	0.37	0.77	0.48	0.46	0.73	0.50	4
Model 97	pls	0.33	0.77	0.52	0.38	0.80	0.48	0.41	0.77	0.45	4
Model 98	pls	0.33	0.77	0.52	0.38	0.80	0.48	0.41	0.77	0.45	4
Model 99	rfRFE	0.85	0.78	0.50	0.34	0.80	0.45	0.66	0.61	0.68	3.8
Model 100	rf	0.87	0.76	0.49	0.38	0.77	0.49	0.69	0.58	0.71	4
Model 101	nnet	0.42	0.76	0.52	0.34	0.78	0.45	0.45	0.74	0.49	4
Model 102	rf	0.89	0.78	0.48	0.33	0.80	0.45	0.69	0.59	0.71	4
Model 103	rf	0.90	0.74	0.52	0.39	0.77	0.49	0.71	0.57	0.73	4

Model 104	nnet	0.41	0.76	0.52	0.33	0.78	0.45	0.44	0.74	0.48	4
Model 105	nnet	0.41	0.76	0.52	0.33	0.78	0.45	0.44	0.74	0.48	4
Model 106	rfRFE	0.89	0.71	0.58	0.46	0.75	0.54	0.73	0.56	0.74	3
Model 107	rf	0.89	0.75	0.51	0.39	0.77	0.50	0.71	0.57	0.73	4
Model 108	nnet	0.43	0.75	0.51	0.43	0.74	0.53	0.50	0.71	0.53	4
Model 109	nnet	0.42	0.76	0.50	0.42	0.74	0.52	0.49	0.72	0.52	4
Model 110	nnet	0.39	0.79	0.50	0.36	0.78	0.47	0.44	0.75	0.48	4
Model 111	rf	0.89	0.74	0.52	0.42	0.75	0.52	0.72	0.56	0.74	4
Model 112	nnet	0.42	0.76	0.50	0.42	0.74	0.52	0.49	0.72	0.52	4
Model 113	nnet	0.42	0.76	0.50	0.41	0.75	0.52	0.48	0.72	0.52	4
Model 114	rf	0.90	0.73	0.52	0.45	0.73	0.55	0.73	0.54	0.75	4
Model 115	rfRFE	0.85	0.76	0.52	0.36	0.78	0.47	0.68	0.60	0.70	4
Model 116	rf	0.90	0.75	0.51	0.40	0.76	0.51	0.71	0.56	0.73	4
Model 117	nnet	0.42	0.76	0.50	0.40	0.76	0.50	0.48	0.73	0.51	4
Model 118	nnet	0.46	0.75	0.51	0.35	0.78	0.46	0.47	0.73	0.51	4
Model 119	nnet	0.44	0.77	0.50	0.35	0.78	0.46	0.46	0.73	0.50	4
Model 120	rf	0.88	0.77	0.49	0.35	0.78	0.46	0.68	0.58	0.70	4
Model 121	rf	0.91	0.67	0.58	0.35	0.81	0.46	0.70	0.57	0.72	4
Model 122	rfRFE	0.91	0.66	0.62	0.51	0.72	0.59	0.76	0.54	0.78	4
Model 123	nnet	0.49	0.74	0.53	0.43	0.73	0.53	0.53	0.69	0.56	4
Model 124	rfRFE	0.92	0.68	0.58	0.42	0.78	0.52	0.74	0.57	0.76	3.8
Model 125	nnet	0.46	0.76	0.53	0.41	0.75	0.51	0.51	0.71	0.54	4
Model 126	rfRFE	0.92	0.65	0.60	0.45	0.76	0.54	0.74	0.55	0.76	3.8
Model 127	nnet	0.51	0.72	0.52	0.40	0.75	0.51	0.54	0.69	0.57	4
Model 128	nnet	0.46	0.75	0.50	0.38	0.77	0.49	0.51	0.71	0.54	4
Model 129	rfRFE	0.90	0.69	0.54	0.47	0.74	0.56	0.75	0.55	0.77	4
Model 130	rf	0.92	0.70	0.55	0.38	0.78	0.49	0.73	0.56	0.74	4
Model 131	rfRFE	0.91	0.67	0.58	0.45	0.76	0.54	0.74	0.56	0.75	3.6
Model 132	nnet	0.52	0.72	0.53	0.42	0.77	0.52	0.54	0.70	0.57	4
Model 133	rf	0.91	0.69	0.56	0.38	0.79	0.49	0.72	0.57	0.74	4
Model 134	nnet	0.53	0.73	0.51	0.36	0.77	0.47	0.53	0.69	0.56	4
Model 135	svmRadial	0.72	0.77	0.53	0.34	0.81	0.46	0.59	0.64	0.62	4
Model 136	nnet	0.55	0.72	0.54	0.36	0.77	0.47	0.53	0.69	0.56	4
Model 137	svmRadial	0.74	0.74	0.55	0.37	0.79	0.48	0.61	0.63	0.64	4
Model 138	nnet	0.52	0.74	0.52	0.38	0.76	0.49	0.53	0.69	0.56	4
Model 139	nnet	0.52	0.73	0.52	0.39	0.77	0.49	0.53	0.69	0.56	4
Model 140	rfRFE	0.92	0.67	0.60	0.41	0.80	0.49	0.72	0.58	0.74	3.4

Model 141	rf	0.94	0.66	0.58	0.45	0.76	0.54	0.75	0.54	0.76	4
Model 142	nnet	0.52	0.71	0.53	0.42	0.76	0.52	0.55	0.69	0.58	4
Model 143	rfRFE	0.93	0.66	0.56	0.45	0.77	0.54	0.75	0.56	0.76	3.8
Model 144	rfRFE	0.91	0.68	0.56	0.45	0.76	0.54	0.74	0.56	0.76	3.8
Model 145	nnet	0.60	0.69	0.54	0.30	0.81	0.42	0.52	0.69	0.56	4
Model 146	rfRFE	0.93	0.66	0.64	0.48	0.76	0.56	0.76	0.55	0.77	3.4
Model 147	rfRFE	0.90	0.69	0.57	0.38	0.79	0.49	0.71	0.58	0.73	4
Model 148	nnet	0.60	0.68	0.56	0.35	0.78	0.46	0.55	0.67	0.58	4
Model 149	rf	0.92	0.67	0.57	0.34	0.81	0.45	0.70	0.57	0.72	4
Model 150	nnet	0.59	0.70	0.55	0.32	0.80	0.44	0.53	0.69	0.56	4
Model 151	rfRFE	0.86	0.73	0.55	0.21	0.88	0.35	0.61	0.65	0.64	4
Model 152	rfRFE	0.91	0.70	0.52	0.34	0.82	0.45	0.70	0.60	0.72	4
Model 153	rfRFE	0.90	0.66	0.59	0.46	0.76	0.54	0.74	0.56	0.75	3.4
Model 154	rfRFE	0.92	0.69	0.57	0.39	0.79	0.50	0.72	0.58	0.74	4
Model 155	nnet	0.55	0.72	0.53	0.40	0.76	0.51	0.55	0.68	0.58	4
Model 156	rfRFE	0.92	0.68	0.56	0.39	0.80	0.49	0.72	0.58	0.74	4
Model 157	nnet	0.55	0.73	0.53	0.32	0.80	0.44	0.51	0.70	0.54	4
Model 158	rfRFE	0.92	0.65	0.63	0.47	0.75	0.56	0.76	0.55	0.77	3.8
Model 159	lm	0.49	0.74	0.51	0.34	0.78	0.46	0.50	0.70	0.54	4
Model 160	lm	0.47	0.75	0.50	0.35	0.78	0.46	0.49	0.71	0.53	4
Model 161	rfRFE	0.91	0.67	0.58	0.44	0.77	0.52	0.73	0.56	0.75	3.6
Model 162	lm	0.50	0.73	0.52	0.40	0.74	0.51	0.53	0.69	0.56	4
Model 163	rf	0.91	0.71	0.54	0.35	0.81	0.46	0.70	0.58	0.72	4
Model 164	lm	0.49	0.75	0.51	0.37	0.76	0.48	0.51	0.70	0.54	4
Model 165	rfRFE	0.92	0.67	0.61	0.42	0.79	0.52	0.73	0.57	0.75	4
Model 166	rfRFE	0.92	0.66	0.59	0.43	0.77	0.52	0.74	0.56	0.76	3.8
Model 167	nnet	0.56	0.71	0.52	0.30	0.81	0.42	0.51	0.70	0.54	4
Model 168	rfRFE	0.91	0.69	0.61	0.38	0.78	0.48	0.71	0.58	0.73	3.8
Model 169	nnet	0.53	0.71	0.55	0.35	0.76	0.46	0.52	0.69	0.55	4
Model 170	rf	0.92	0.69	0.57	0.32	0.80	0.44	0.70	0.57	0.72	4
Model 171	nnet	0.52	0.72	0.54	0.33	0.78	0.44	0.50	0.70	0.54	4
Model 172	rfRFE	0.92	0.65	0.63	0.52	0.73	0.60	0.77	0.53	0.78	3.8
Model 173	rfRFE	0.90	0.69	0.56	0.34	0.82	0.44	0.70	0.60	0.72	3.8
Model 174	nnet	0.45	0.77	0.53	0.38	0.77	0.49	0.49	0.72	0.52	4
Model 175	rf	0.93	0.69	0.57	0.40	0.77	0.51	0.73	0.55	0.75	4
Model 176	nnet	0.53	0.68	0.53	0.44	0.72	0.53	0.56	0.67	0.59	4
Model 177	nnet	0.54	0.67	0.55	0.45	0.71	0.55	0.57	0.66	0.60	4

Model 178	nnet	0.55	0.66	0.55	0.44	0.72	0.54	0.57	0.66	0.60	4
Model 179	nnet	0.56	0.67	0.53	0.40	0.74	0.51	0.56	0.66	0.59	4
Model 180	nnet	0.56	0.65	0.56	0.46	0.70	0.56	0.59	0.65	0.62	4
Model 181	nnet	0.55	0.67	0.53	0.41	0.74	0.51	0.56	0.67	0.59	4
Model 182	nnet	0.55	0.66	0.55	0.46	0.71	0.56	0.58	0.66	0.61	4
Model 183	nnet	0.56	0.65	0.55	0.40	0.73	0.51	0.57	0.66	0.60	4
Model 184	nnet	0.53	0.69	0.52	0.38	0.77	0.49	0.54	0.69	0.57	4
Model 185	nnet	0.56	0.66	0.56	0.45	0.71	0.55	0.58	0.65	0.61	4
Model 186	nnet	0.53	0.69	0.52	0.38	0.78	0.48	0.53	0.69	0.56	4
Model 187	nnet	0.54	0.67	0.55	0.45	0.72	0.55	0.57	0.66	0.60	4
Model 188	nnet	0.55	0.67	0.54	0.42	0.73	0.52	0.56	0.67	0.59	4
Model 189	nnet	0.53	0.68	0.52	0.41	0.74	0.51	0.55	0.67	0.58	4
Model 190	nnet	0.54	0.67	0.56	0.45	0.72	0.55	0.56	0.67	0.59	4
Model 191	nnet	0.56	0.66	0.56	0.45	0.70	0.55	0.58	0.65	0.61	4
Model 192	nnet	0.54	0.68	0.52	0.40	0.75	0.50	0.55	0.68	0.58	4
Model 193	nnet	0.54	0.67	0.56	0.42	0.76	0.52	0.54	0.69	0.57	4
Model 194	nnet	0.55	0.67	0.55	0.45	0.72	0.55	0.57	0.66	0.60	4
Model 195	nnet	0.55	0.66	0.55	0.43	0.73	0.53	0.57	0.66	0.60	4
Model 196	nnet	0.52	0.68	0.54	0.39	0.75	0.49	0.54	0.68	0.57	4
Model 197	nnet	0.52	0.68	0.54	0.39	0.76	0.50	0.54	0.68	0.57	4
Model 198	nnet	0.56	0.66	0.54	0.37	0.76	0.48	0.55	0.67	0.58	4
Model 199	nnet	0.56	0.66	0.54	0.36	0.77	0.47	0.55	0.68	0.58	4
Model 200	nnet	0.54	0.67	0.53	0.43	0.72	0.53	0.56	0.67	0.59	4
Model 201	nnet	0.50	0.71	0.52	0.34	0.78	0.45	0.51	0.70	0.55	4
Model 202	nnet	0.49	0.71	0.52	0.36	0.78	0.47	0.52	0.71	0.55	4
Model 203	nnet	0.51	0.69	0.53	0.33	0.79	0.44	0.51	0.70	0.55	4
Model 204	nnet	0.51	0.69	0.53	0.35	0.78	0.46	0.52	0.70	0.55	4
Model 205	nnet	0.56	0.66	0.56	0.47	0.70	0.56	0.59	0.65	0.61	4
Model 206	nnet	0.54	0.68	0.53	0.44	0.71	0.54	0.57	0.66	0.60	4
Model 207	nnet	0.55	0.66	0.56	0.46	0.71	0.56	0.58	0.65	0.61	4
Model 208	nnet	0.55	0.66	0.55	0.44	0.72	0.54	0.57	0.66	0.60	4
Model 209	nnet	0.55	0.68	0.55	0.34	0.77	0.45	0.52	0.69	0.56	4
Model 210	nnet	0.55	0.68	0.55	0.34	0.77	0.45	0.52	0.69	0.56	4
Model 211	nnet	0.53	0.67	0.53	0.43	0.73	0.53	0.56	0.67	0.59	4
Model 212	nnet	0.55	0.66	0.56	0.46	0.70	0.56	0.58	0.65	0.61	4

Table S4. The coefficients for the obtained neural network model shown in **Figure S6**.

B2 -> O	H1 -> O	H2 -> O	H3 -> O	H4 -> O	H5 -> O
0.31	0.66	0.66	2.68	0.67	2.69
B1 -> H1	I1 -> H1	I2 -> H1	I3 -> H1	I4 -> H1	
0.06	-0.37	-0.31	-0.29	0.14	
B1 -> H2	I1 -> H2	I2 -> H2	I3 -> H2	I4 -> H2	
0.06	-0.37	-0.31	-0.3	0.14	
B1 -> H3	I1 -> H3	I2 -> H3	I3 -> H3	I4 -> H3	
0.36	-1.3	-1.68	-1.11	1.11	
B1 -> H4	I1 -> H4	I2 -> H4	I3 -> H4	I4 -> H4	
0.06	-0.37	-0.32	-0.3	0.15	
B1 -> H5	I1 -> H5	I2 -> H5	I3 -> H5	I4 -> H5	
0.36	-1.3	1.68	-1.12	1.12	

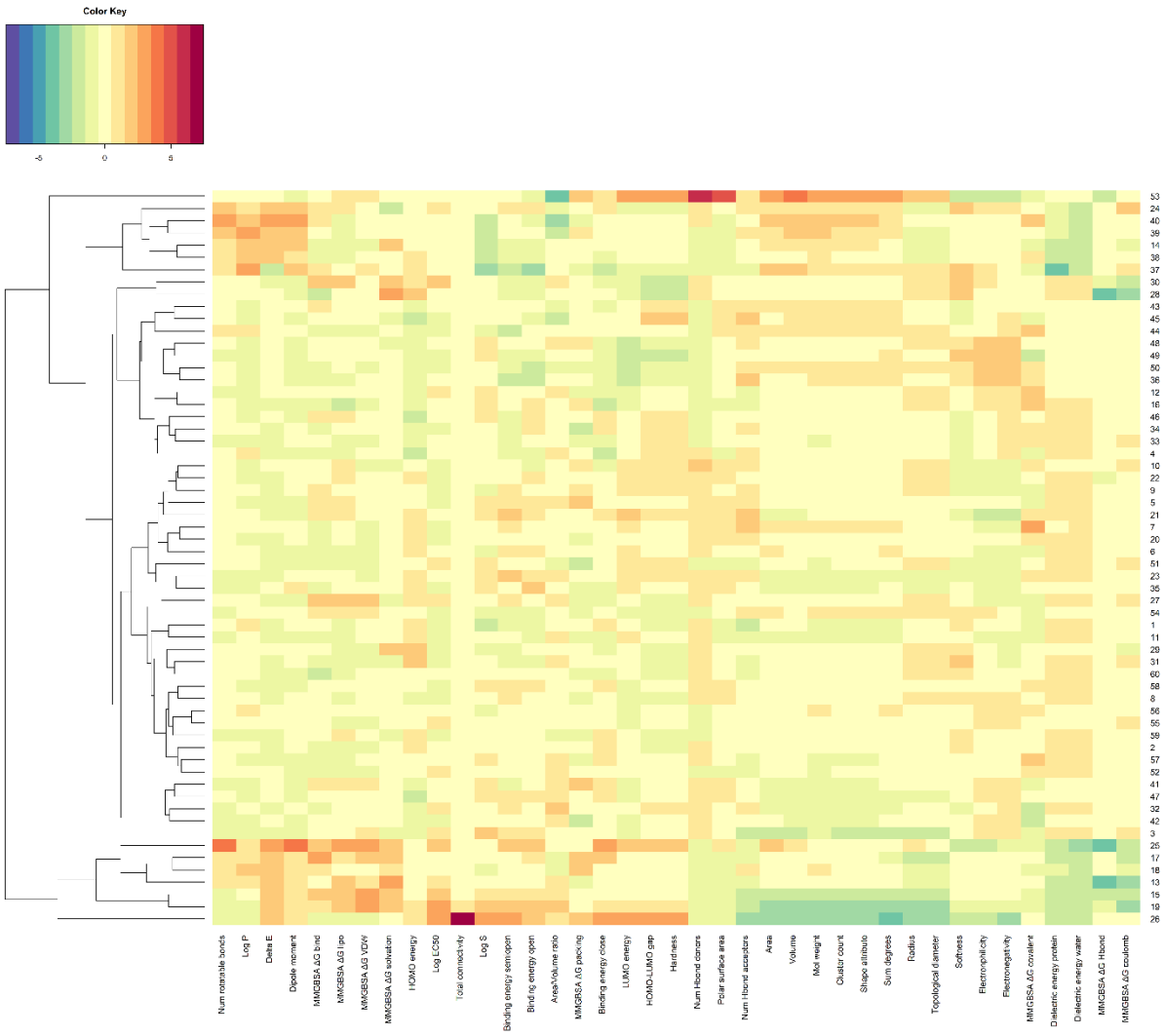


Figure S1. Heatmap and cluster analysis for the investigated γ-secretase modulators according to their chemical properties obtained from different computational calculations.

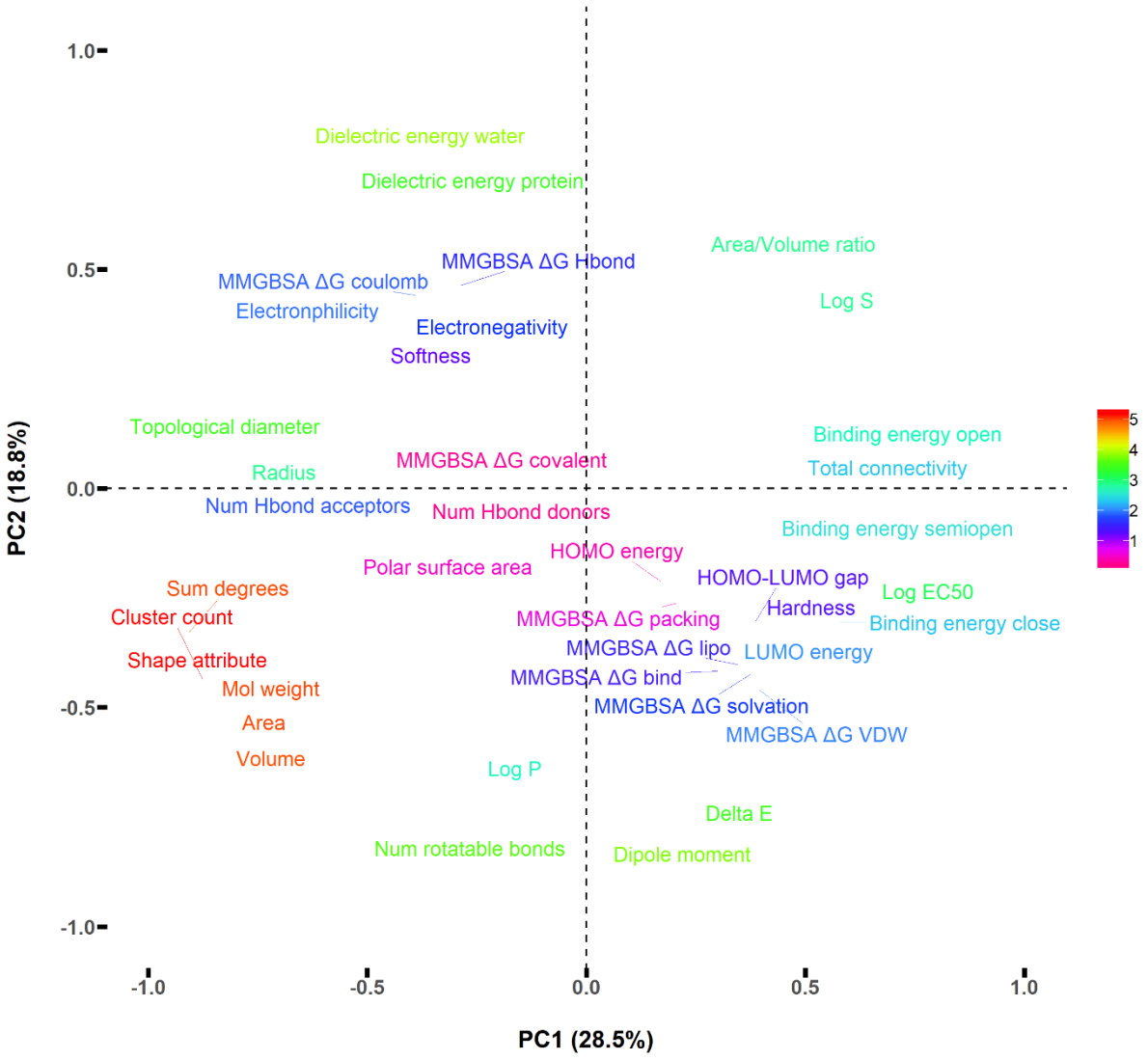


Figure S2. Loading plot of the principal component analysis (showing principal component 1 (PC 1) versus principal component 2 (PC 2). The color of the descriptor shown in the figure was colored based on the importance to the analysis.

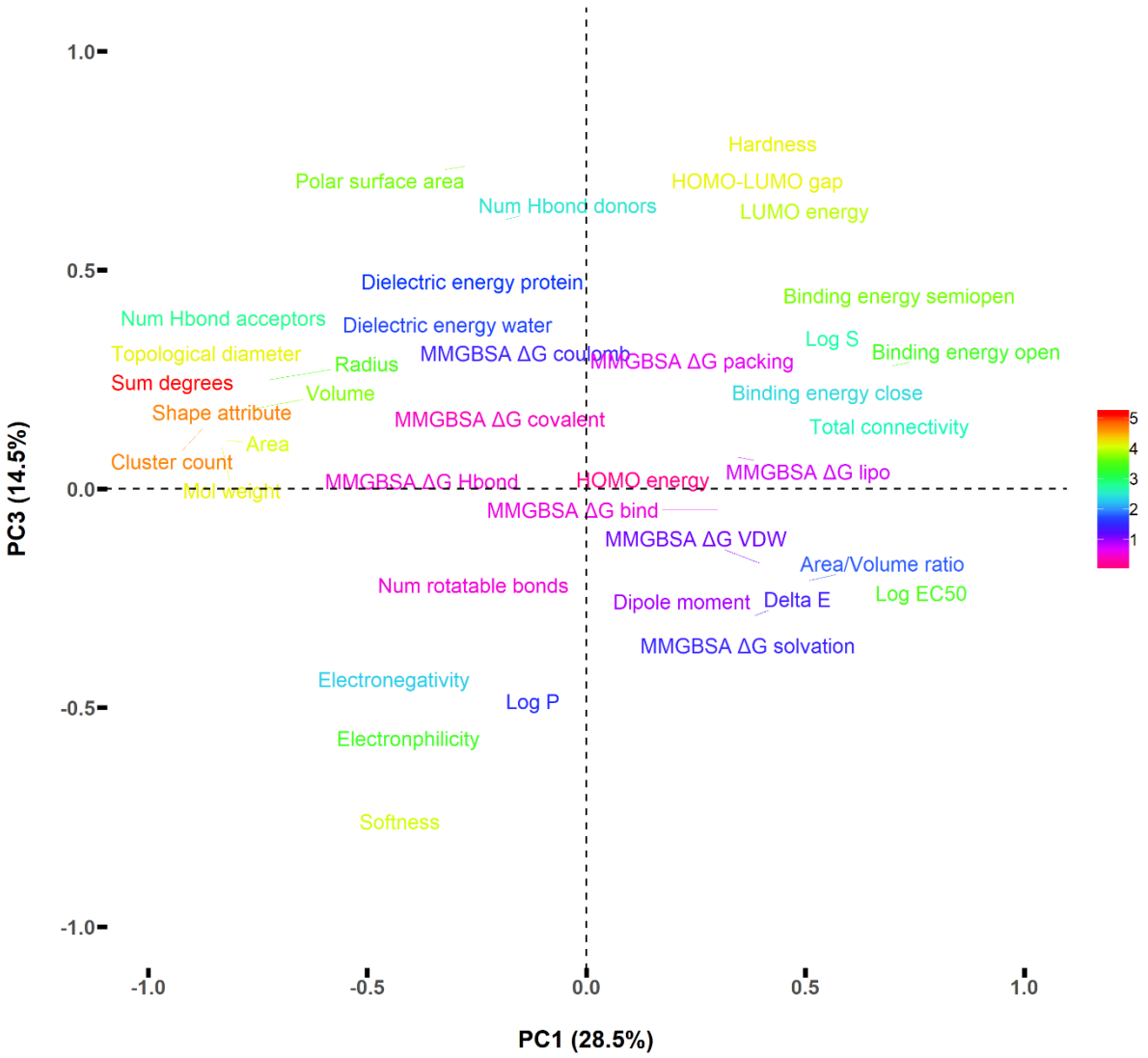


Figure S3. Loading plot of the principal component analysis showing principal component 1 (PC 1) versus principal component 3 (PC 3). The color of the descriptor shown in the figure was colored based on the importance to the analysis.

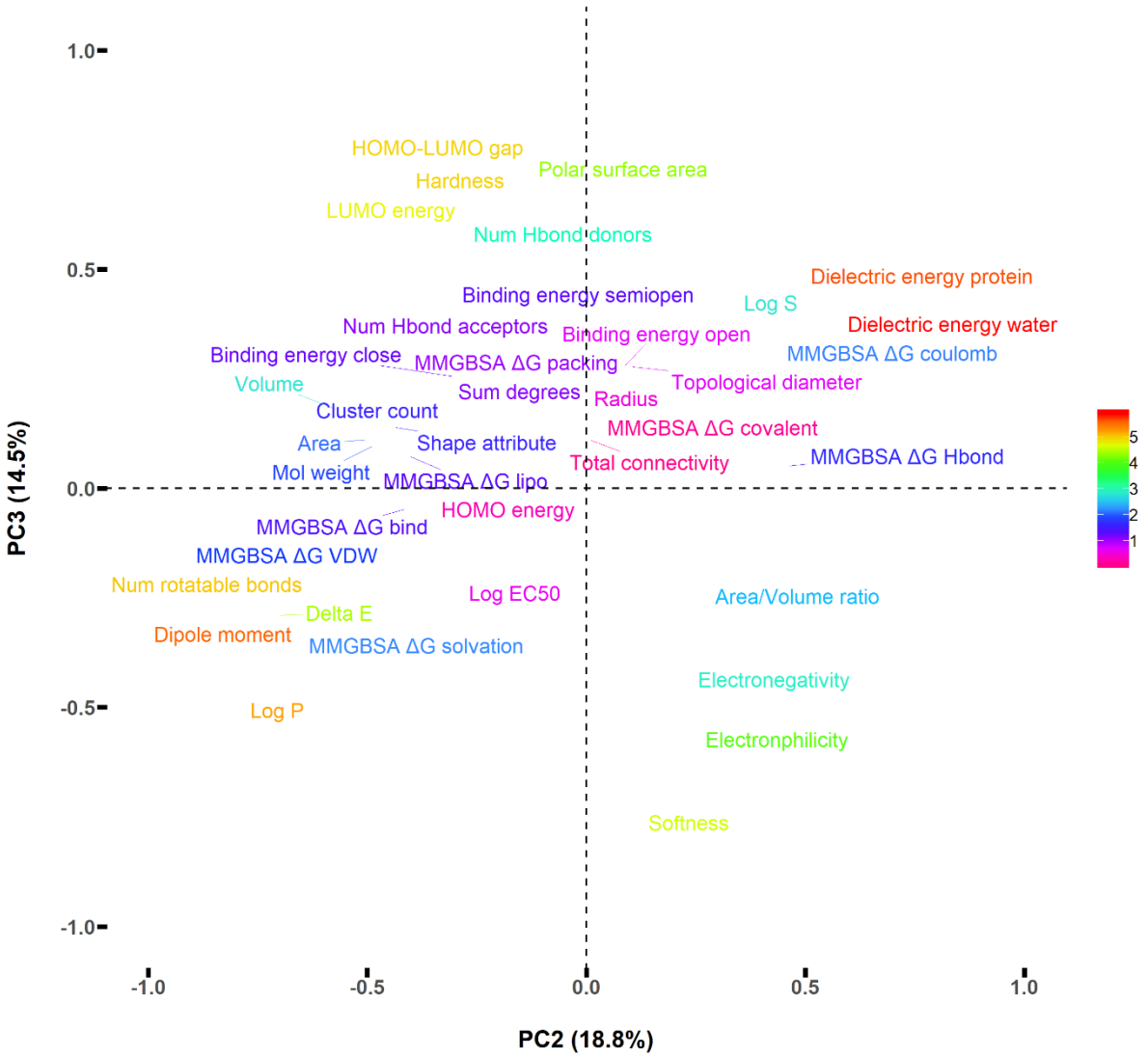


Figure S4. Loading plot of the principal component analysis showing principal component 2 (PC 2) versus principal component 3 (PC 3). The color of the descriptor shown in the figure was colored based on the importance to the analysis.

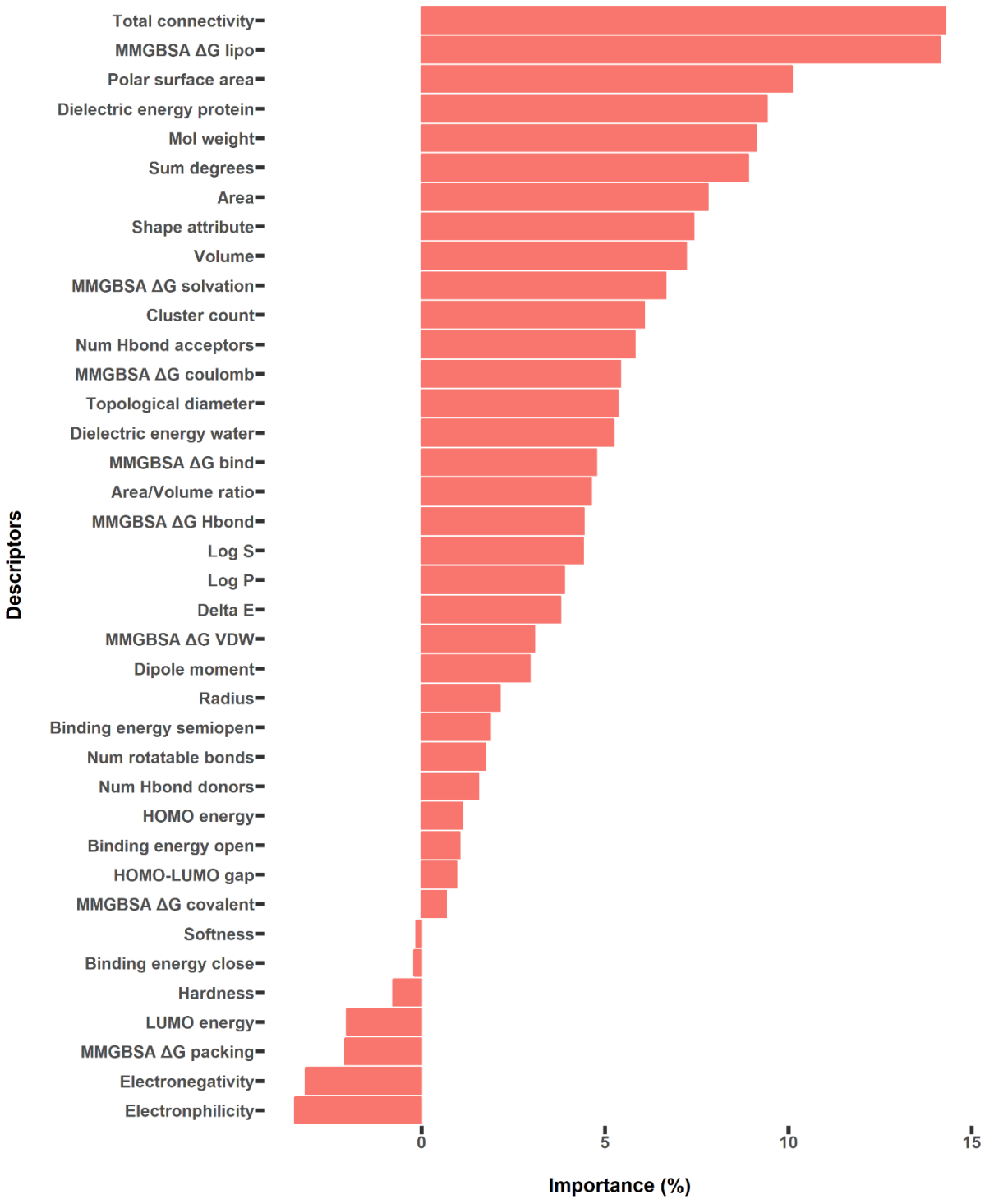


Figure S5. The variable importance of the used descriptors for the Log EC_{50} values using the random forest algorithm.

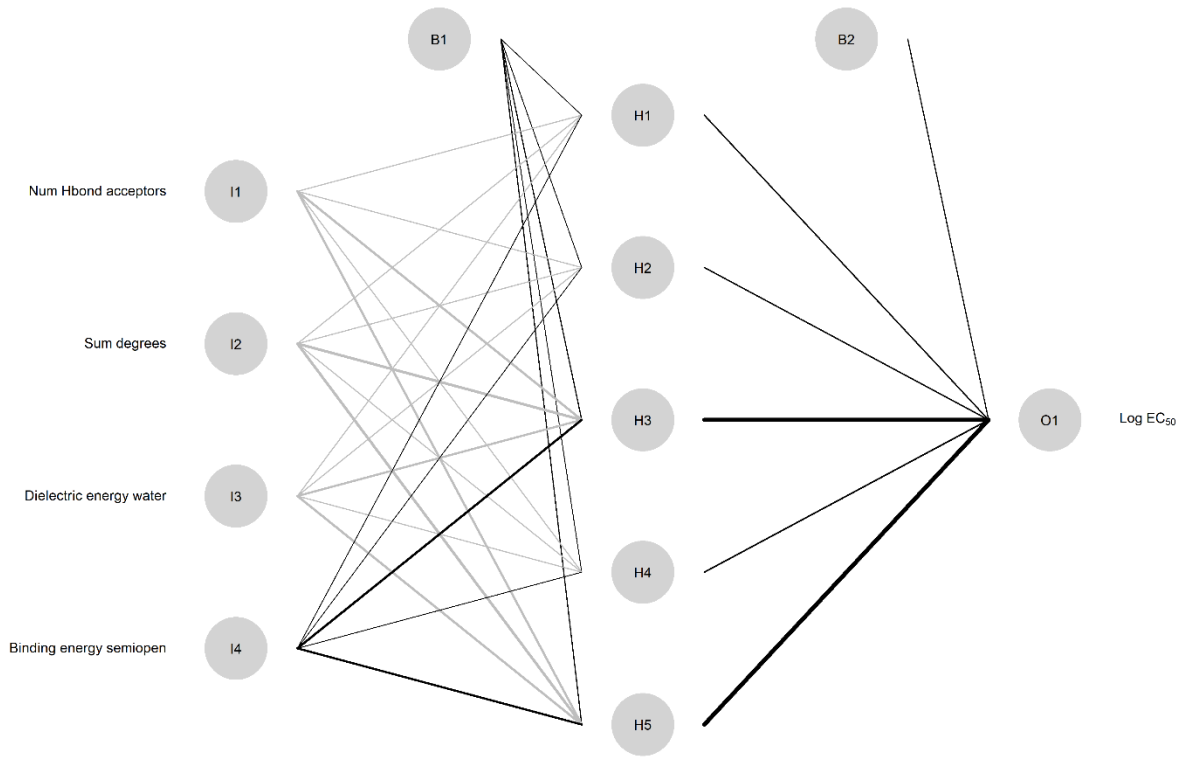


Figure S6. The obtained neural network model with 4 input layer neurons, 5 hidden layer neurons and 1 out layer neurons. B1 and B2 represent the bias upon modeling. The bold lines represent coefficients that are positive.

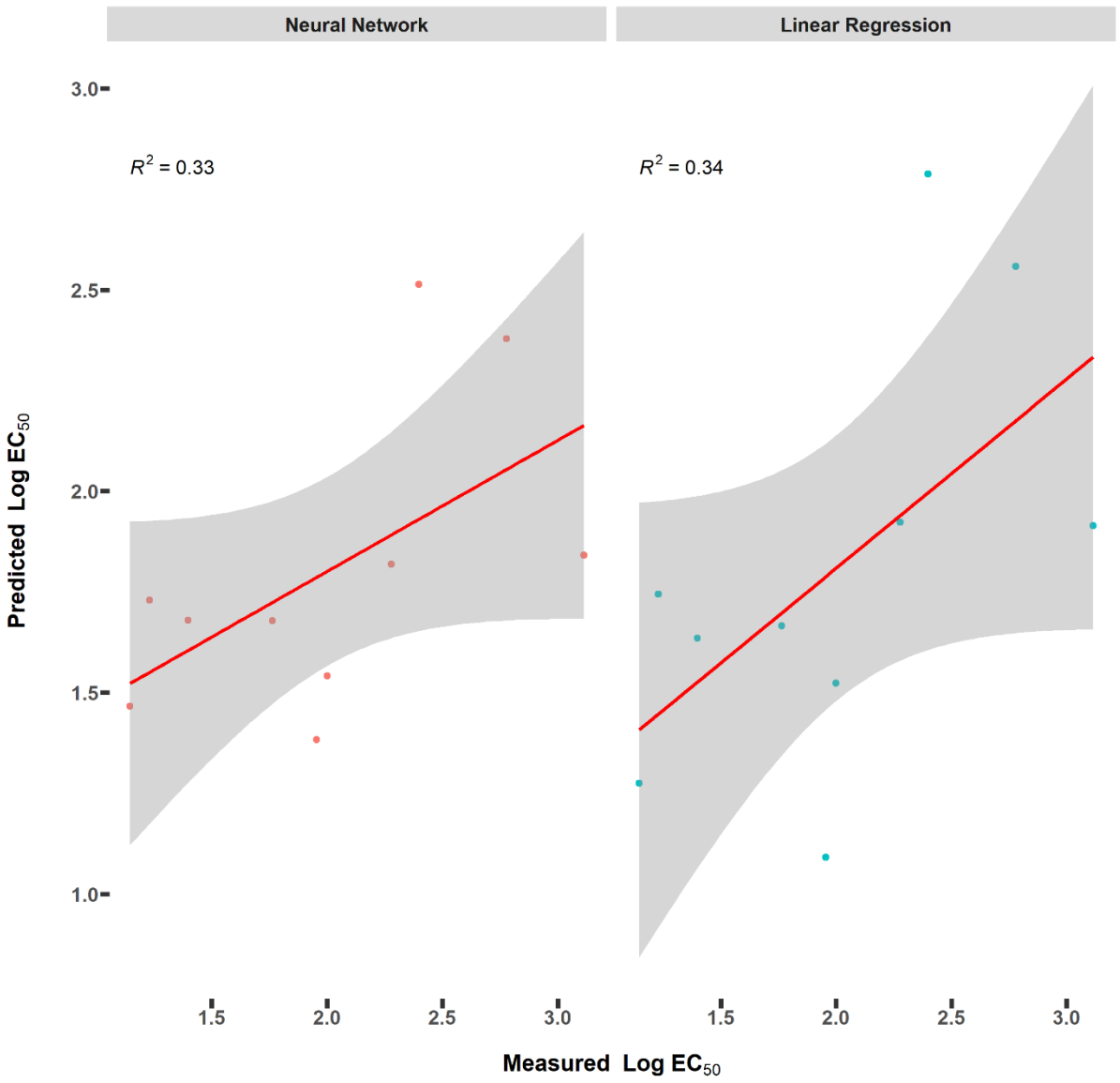


Figure S7. Linear relationship between the measured and predicted Log EC_{50} values for the external modulators based on the neural network model (left panel) and multiple linear regression model (right panel).

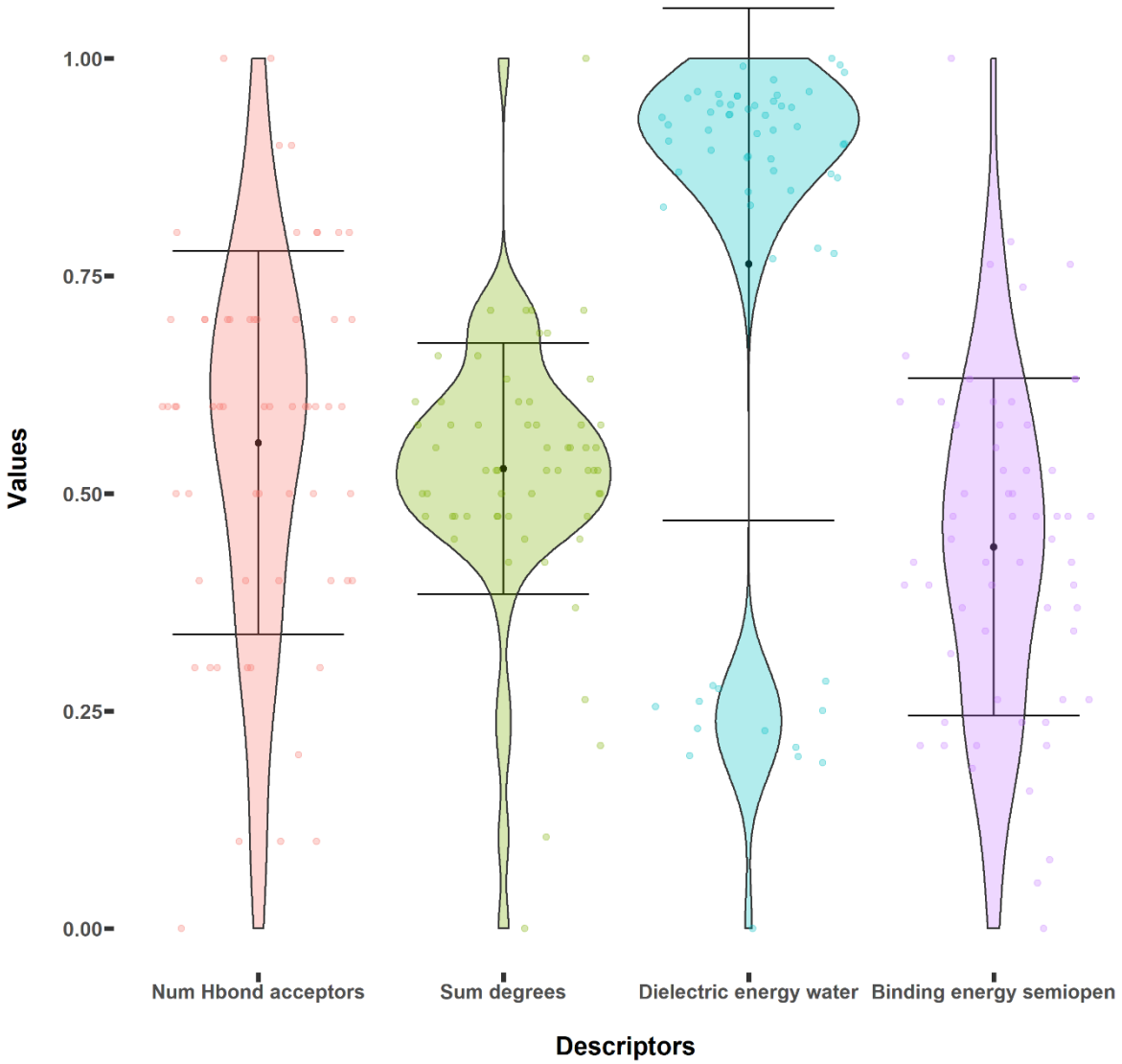


Figure S8. The value distribution of the four descriptors used for building the final QSAR model. The values were scaled by standardization.