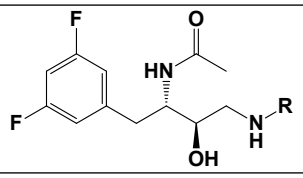
Electronic Supplementary Material (ESI) for Molecular BioSystems.

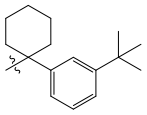
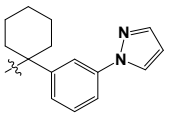
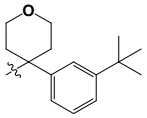
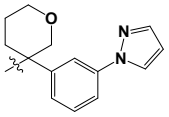
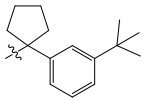
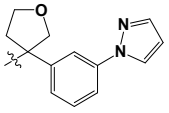
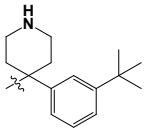
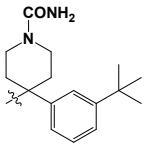
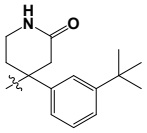
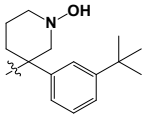
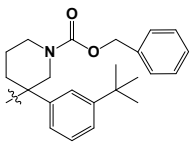
Table S1 Structure-activity relationship data related to the series of hydroxyethylamine derivatives as BACE1 inhibitors

Table S2 Observed and predicted BACE1 inhibitor activities (pIC_{50} value, M)

Table S3 The pdb files of the top structures used in docking and MD analyses

Table S1 Structure-activity relationship data related to the series of hydroxyethylamine derivatives as BACE1 inhibitors



No.	R	IC_{50} (nM)	pIC_{50}
1		47	7.33
2		59	7.23
3		61	7.21
4§		270	6.57
5		220	6.66
6		2400	5.62
7		4700	5.33
8		380	6.42
9		18	7.74
10§		400	6.4
11§		860	6.07

To be continued

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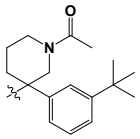
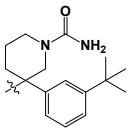
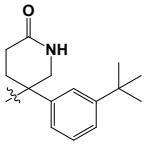
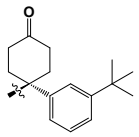
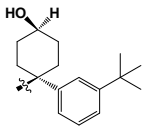
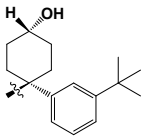
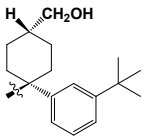
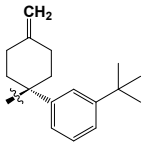
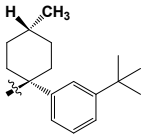
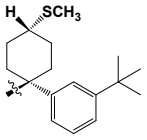
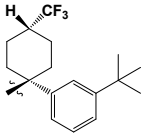
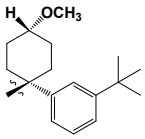
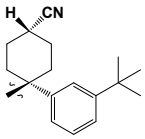
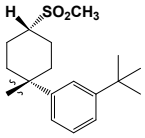
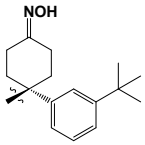
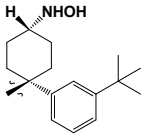
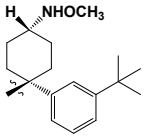
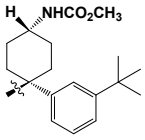
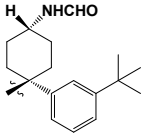
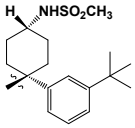
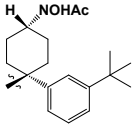
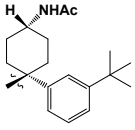
12§		1300	5.89
13		330	6.48
14		47	7.33
15		120	6.92
16§		9200	5.04
17		24	7.62
18		38	7.42
19		48	7.32
20§		49	7.31
21§		24	7.62
22		33	7.48

To be continued

No.	R	IC_{50} (nM)	pIC_{50}
23		140	6.85
24		380	6.42
25		210	6.68
26		8.8	8.06
27		19	7.72
28		100	7
29		240	6.62
30		210	6.68
31§		400	6.4
32		240	6.62
33§		350	6.46

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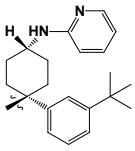
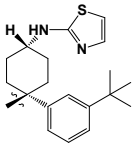
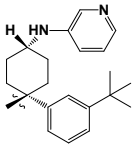
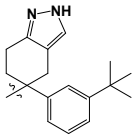
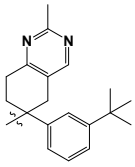
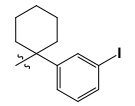
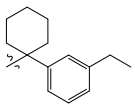
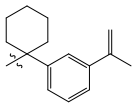
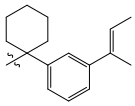
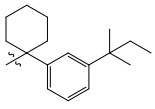
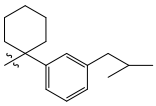
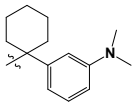
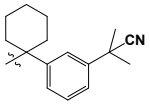
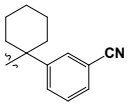
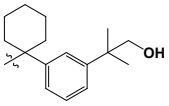
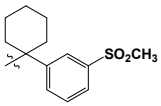
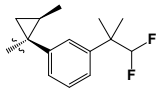
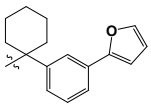
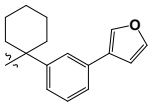
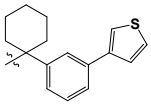
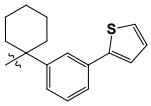
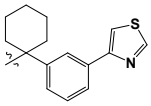
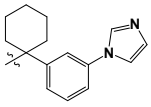
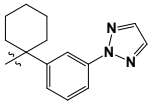
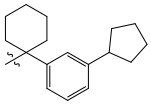
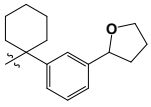
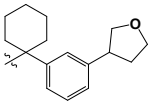
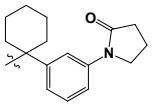
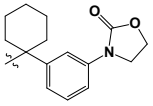
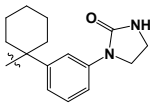
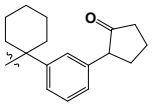
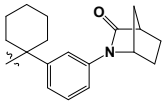
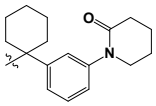
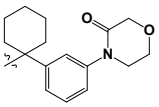
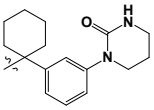
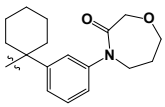
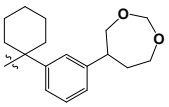
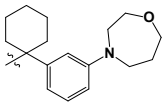
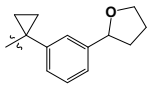
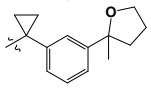
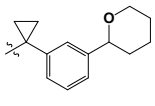
No.	R	IC_{50} (nM)	pIC_{50}
34§		73	7.14
35		85	7.07
36		500	6.3
37		12	7.92
38		14	7.85
39§		460	6.34
40§		690	6.16
41		100	7
42		380	6.42
43§		130	6.89
44		810	6.09
45		410	6.39

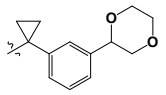
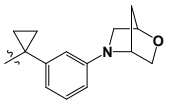
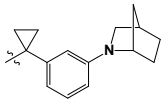
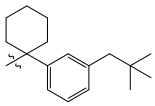
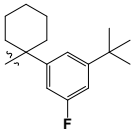
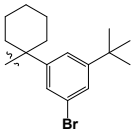
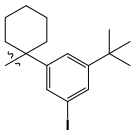
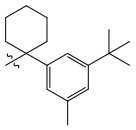
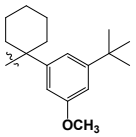
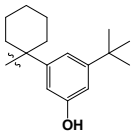
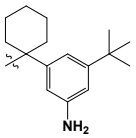
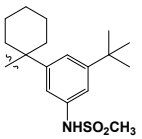
To be continued

No.	R	IC_{50} (nM)	pIC_{50}
46		166	6.78
47§		6200	5.21
48		260	6.59
49		720	6.14
50§		1700	5.77
51		1100	5.96
52		120	6.92
53§		44	7.36
54		370	6.43
55§		110	6.96
56		1600	5.8
57		7700	5.11
58		940	6.03
59§		180	6.74

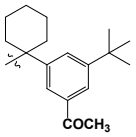
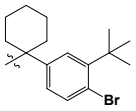
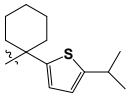
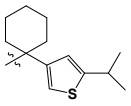
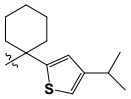
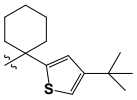
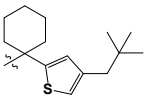
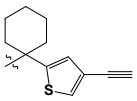
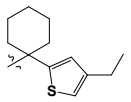
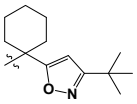
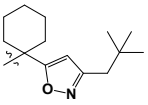
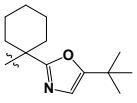
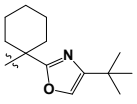
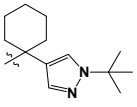
To be continued

No.	R	IC_{50} (nM)	pIC_{50}
60§		88	7.06
61§		820	6.09
62		1300	5.89
63		1400	5.85
64		800	6.1
65		340	6.47
66		250	6.6
67		1300	5.89
68		1000	6
69		750	6.12
70§		560	6.25
71		700	6.15
72		580	6.24
73§		580	6.24
74		1700	5.77

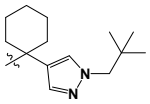
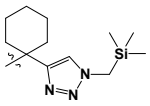
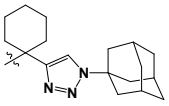
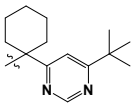
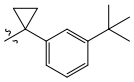
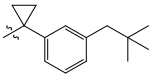
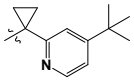
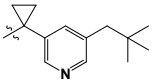
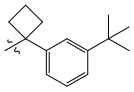
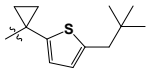
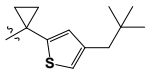
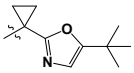
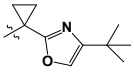
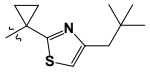
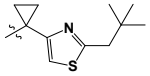
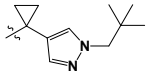
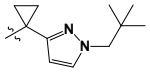
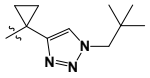
To be continued

No.	R	IC_{50} (nM)	pIC_{50}
75		4000	5.4
76		2400	5.62
77§		1900	5.72
78		2100	5.68
79		46	7.34
80		174	6.76
81		223	6.65
82		180	6.74
83		77	7.11
84§		170	6.77
85		318	6.5
86		93	7.03

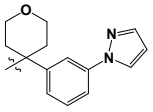
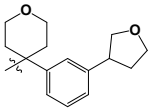
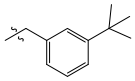
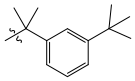
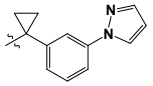
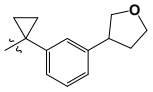
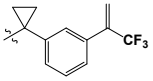
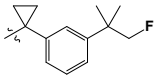
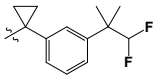
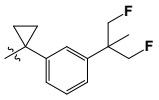
To be continued

No.	R	IC_{50} (nM)	pIC_{50}
87		160	6.8
88§		6900	5.16
89		4010	5.4
90		320	6.49
91		352	6.45
92		104	6.98
93		131	6.88
94§		4316	5.36
95		1740	5.76
96§		4457	5.35
97		139	6.86
98		1580	5.8
99		137800	3.86
100		1840	5.74

To be continued

No.	R	IC_{50} (nM)	pIC_{50}
101		210	6.68
102		154	6.81
103		392	6.41
104§		2430	5.61
105§		140	6.85
106		341	6.47
107		640	6.19
108		780	6.11
109		610	6.21
110		1620	5.79
111		470	6.33
112		4900	5.31
113		42880	4.37
114		9360	5.03
115		3050	5.52
116		346	6.46
117		870	6.06
118		450	6.35

To be continued

No.	R	IC_{50} (nM)	pIC_{50}
119		110	6.96
120		290	6.54
121		1300	5.89
122§		200	6.7
123§		980	6.01
124§		760	6.12
125		1300	5.89
126		290	6.54
127		230	6.64
128		390	6.41

§ Test set

Table S2 Observed and predicted BACE1 inhibitor activities (pIC_{50} value, M)

No.	Observed activity	CoMFA		CoMSIA	
		Predicted	Residue	Predicted	Residue
1	7.33	6.671	0.659	6.638	0.692
2	7.23	7.121	0.109	7.081	0.149
3	7.21	6.945	0.265	6.981	0.229
4	6.57	6.649	-0.079	6.541	0.029
5	6.66	6.497	0.163	6.474	0.186
6	5.62	5.308	0.312	5.517	0.103
7	5.33	5.822	-0.492	5.251	0.079
8	6.42	6.695	-0.275	6.788	-0.368
9	7.74	7.059	0.681	7.668	0.072
10	6.4	6.64	-0.24	6.208	0.192
11	6.07	6.348	-0.278	6.456	-0.386
12	5.89	6.409	-0.519	6.05	-0.16
13	6.48	6.955	-0.475	6.659	-0.179
14	7.33	6.975	0.355	6.852	0.478
15	6.92	6.677	0.243	7.012	-0.092
16	5.04	6.326	-1.286	5.06	-0.02
17	7.62	7.135	0.485	7.315	0.305
18	7.42	7.274	0.146	7.452	-0.032
19	7.32	6.647	0.673	7.264	0.056
20	7.31	6.245	1.065	7.275	0.035
21	7.62	5.512	2.108	7.285	0.335
22	7.48	7.116	0.364	7.11	0.37
23	6.85	7.036	-0.186	7.124	-0.274
24	6.42	7.153	-0.733	6.823	-0.403
25	6.68	6.894	-0.214	6.655	0.025
26	8.06	7.305	0.755	8.182	-0.122
27	7.72	7.27	0.45	7.854	-0.134
28	7	6.844	0.156	7.081	-0.081
29	6.62	6.985	-0.365	6.513	0.107
30	6.68	7.107	-0.427	6.903	-0.223
31	6.4	6.822	-0.422	6.299	0.101
32	6.62	6.751	-0.131	6.324	0.296

To be continued

No.	Observed activity	CoMFA		CoMSIA	
		Predicted	Residue	Predicted	Residue
33	6.46	6.67	-0.21	6.282	0.178
34	7.14	5.834	1.306	6.693	0.447
35	7.07	7.128	-0.058	6.989	0.081
36	6.3	6.766	-0.466	5.915	0.385
37	7.92	7.482	0.438	7.896	0.024
38	7.85	6.865	0.985	7.852	-0.002
39	6.34	6.238	0.102	6.297	0.043
40	6.16	6.129	0.031	6.481	-0.321
41	7	6.25	0.75	6.482	0.518
42	6.42	6.147	0.273	6.454	-0.034
43	6.89	6.675	0.215	6.623	0.267
44	6.09	6.12	-0.03	6.437	-0.347
45	6.39	6.037	0.353	6.471	-0.081
46	6.78	6.789	-0.009	6.579	0.201
47	5.21	6.025	-0.815	5.311	-0.101
48	6.59	6.577	0.013	6.796	-0.206
49	6.14	6.58	-0.44	6.063	0.077
50	5.77	5.95	-0.18	5.517	0.253
51	5.96	6.406	-0.446	6.423	-0.463
52	6.92	6.287	0.633	6.475	0.445
53	7.36	6.433	0.927	7.215	0.145
54	6.43	6.406	0.024	6.406	0.024
55	6.96	6.178	0.782	6.734	0.226
56	5.8	6.292	-0.492	6.033	-0.233
57	5.11	5.152	-0.042	5.23	-0.12
58	6.03	6.245	-0.215	6.513	-0.483
59	6.74	6.203	0.537	6.476	0.264
60	7.06	6.023	1.037	7.062	-0.002
61	6.09	6.197	-0.107	5.996	0.094
62	5.89	6.019	-0.129	5.926	-0.036
63	5.85	5.743	0.107	5.893	-0.043
64	6.1	5.986	0.114	6.171	-0.071

To be continued

No.	Observed activity	CoMFA		CoMSIA	
		Predicted	Residue	Predicted	Residue
65	6.47	6.281	0.189	6.684	-0.214
66	6.6	5.954	0.646	6.463	0.137
67	5.89	6.026	-0.136	5.753	0.137
68	6	5.886	0.114	5.729	0.271
69	6.12	6.006	0.114	6.189	-0.069
70	6.25	6.053	0.197	5.914	0.336
71	6.15	5.983	0.167	6.416	-0.266
72	6.24	5.955	0.285	5.933	0.307
73	6.24	5.98	0.26	6.214	0.026
74	5.77	5.861	-0.091	5.821	-0.051
75	5.4	5.826	-0.426	5.381	0.019
76	5.62	5.786	-0.166	5.718	-0.098
77	5.72	5.944	-0.224	5.594	0.126
78	5.68	6.224	-0.544	6.414	-0.734
79	7.34	6.533	0.807	6.654	0.686
80	6.76	6.583	0.177	6.655	0.105
81	6.65	6.579	0.071	6.702	-0.052
82	6.74	6.69	0.05	6.744	-0.004
83	7.11	6.715	0.395	6.697	0.413
84	6.77	6.538	0.232	6.551	0.219
85	6.5	6.654	-0.154	6.703	-0.203
86	7.03	7.159	-0.129	6.895	0.135
87	6.8	6.63	0.17	6.926	-0.126
88	5.16	6.182	-1.022	5.218	-0.058
89	5.4	6.026	-0.626	6.121	-0.721
90	6.49	6.422	0.068	6.499	-0.009
91	6.45	6.375	0.075	6.459	-0.009
92	6.98	6.718	0.262	6.309	0.671
93	6.88	6.386	0.494	6.508	0.372
94	5.36	6.201	-0.841	5.722	-0.362
95	5.76	6.45	-0.69	6.292	-0.532
96	5.35	6.133	-0.783	5.32	0.03

To be continued

No.	Observed activity	CoMFA		CoMSIA	
		Predicted	Residue	Predicted	Residue
97	6.86	5.897	0.963	6.83	0.03
98	5.8	6.203	-0.403	5.704	0.096
99	3.86	6.806	-2.946	4.132	-0.272
100	5.74	5.657	0.083	5.727	0.013
101	6.68	6.556	0.124	6.586	0.094
102	6.81	6.611	0.199	6.665	0.145
103	6.41	6.053	0.357	6.537	-0.127
104	5.61	6.126	-0.516	5.456	0.154
105	6.85	6.174	0.676	6.552	0.298
106	6.47	5.931	0.539	6.367	0.103
107	6.19	5.832	0.358	5.939	0.251
108	6.11	6.005	0.105	6.346	-0.236
109	6.21	6.477	-0.267	6.488	-0.278
110	5.79	5.629	0.161	5.804	-0.014
111	6.33	5.822	0.508	6.439	-0.109
112	5.31	6.106	-0.796	5.662	-0.352
113	4.37	5.967	-1.597	4.487	-0.117
114	5.03	5.636	-0.606	4.529	0.501
115	5.52	5.836	-0.316	5.753	-0.233
116	6.46	6.764	-0.304	6.485	-0.025
117	6.06	5.884	0.176	5.837	0.223
118	6.35	6.582	-0.232	6.183	0.167
119	6.96	7.575	-0.615	7.183	-0.223
120	6.54	6.681	-0.141	6.462	0.078
121	5.89	6.557	-0.667	6.146	-0.256
122	6.7	5.953	0.747	6.744	-0.044
123	6.01	6.896	-0.886	5.934	0.076
124	6.12	5.842	0.278	6.215	-0.095
125	5.89	6.176	-0.286	6.406	-0.516
126	6.54	6.359	0.181	6.511	0.029
127	6.64	6.456	0.184	6.518	0.122
128	6.41	6.149	0.261	6.523	-0.113

Table S3 The pdb files of the top structures used in docking and MD analyses

The top structures	Description	Pdb file
X-ray structure	PDB code: 3IVH	 3ivh.pdb
Obtained from the re-docking study	Fig. 7A Superimposed binding conformations of co-crystallized and re-docked compound C1.	 3IVH+redocked ligand
	Fig. 7B Superimposition of the predicted and re-docked conformations of compound C1	 redocked_predicted ligand
	Fig. 7C Superimposition of the predicted compound 26 and re-docked compound C1 poses	 redocked ligand_26
Obtained from the docking analysis	Fig. 8C The binding interactions of compound 26 with amino acids of BACE1.	 M026_docking
	Fig. 10B The binding modes of compound 25 with amino acids of BACE1	 025-docking
	Fig. 10C The binding modes of compounds 123 with amino acids of BACE1	 123-docking
	Fig. 10D The binding modes of compounds 96 with amino acids of BACE1	 96-docking
Obtained from the MD simulation	Fig. 9A The projection of the superimposed backbone atoms of the average structure of the last 1 ns of the MD simulation and the initial structure	 MD_Docking
	Fig. 9C The binding interactions between the ligand and the protein of MD simulation	 Md_26