Supporting information for:

Identification *in silico* and experimental validation of novel phosphodiesterase 7 inhibitors with efficacy in experimental autoimmune encephalomyelitis mice

Miriam Redondo,[a] Valle Palomo,[a] José Brea,[b] Daniel I. Pérez,[a] Rocío Martín-Álvarez,[c] Concepción Pérez,[a] Nuria Paúl-Fernández,[c] Santiago Conde,[a] María Isabel Cadavid,[b] María Isabel Loza,[b] Guadalupe Mengod,[c] Ana Martínez,[a] Carmen Gil[a,*], Nuria E. Campillo[a,*]

Contents:

[a]Instituto de Química Médica (CSIC), Juan de la Cierva 3, 28006, Madrid (Spain)
[b]Instituto de Farmacia Industrial, Facultad de Farmacia, Universidad de Santiago de Compostela, Campus Universitario Sur s/n, 15782 Santiago de Compostela (Spain)
[c]Instituto de Investigaciones Biomédicas de Barcelona (CSIC-IDIBAPS-CIBERNED), Rosselló 161, 08036 Barcelona (Spain)
[d]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED)

[*] To whom correspondence should be addressed: N. E. Campillo or C. Gil, Phone: +34 91 5622900. Fax: +34 91 5644853. E-mail: nuria@suricata.iqm.csic.es or cgil@iqm.csic.es

Table S1. PDE7A inhibitors structures.

Comp.	R	SMILES code
I-1[1]	-	CC1=C(C(OCC)=O)SC(NC2=NC(NCc3ccc(OC)c(OC)c3)=C4C(N=CN4CC)=N2)=N1
I-2[2]		Cc1ccc([N+]([O-])=O)cc1S(N(C)C)(=O)=O
I-3[1]	-	CC1=C(C(OCC)=O)SC(NC2=NC(NCc3ccc(S(N)(=O)=O)cc3)=C4C(N=CN4CC)=N2)=N1
I-4[3, 4]	Me	Clc1cc(C(c2cc(c3ccc(OC)cc3)c(NS(c4ccc(C)cc4)(=O)=O)cc2)=NCC5)c5cc1
I-5[3, 4]	OCF_3	Clc1cc(C(c2cc(c3ccc(OC)cc3)c(NS(c4ccc(OC(F)(F)F)cc4)(=O)=O)cc2)=NCC5)c5cc1
I-6[5]	4-H	Clc1c(NC(NC23CCCCC3)=O)c2ccc1
I-7[6]	3-Phenyl	Clc1c(NC(NC23CCCCC3)=O)c2cc(c4ccccc4)c1
I-8[6]	1*H*-Benzo[*d*] imidazole	O=C(NC12CCCCC2)Nc3c1cc(c4cc5c(NC=N5)cc4)cc3Cl
I-9[7]	R^1=4-Cl; R^2=H	Clc1ccc(C(S/2)=NN(C)C2=N/C3CCCCC3)cc1
I-10[7]	R^2=4-Cl; R^6=3-COOH	Clc1ccc(C(S/2)=NN(C)C2=N/c3cccc(C(O)=O)c3)cc1
I-11[7]	R^1=N-(Morpholinemethyl)acetyl. R^2=H	O=C(NCN1CCOCC1)c2ccc(C(S/3)=NN(C)C3=N/C4CCCCC4)cc2
I-12[8]	R^6=3-OH (R,R); R^2 =4-$CONH_2$	O=C(N)c1ccc(C(S/2)=NN(C)C2=N/[C@@H]3C[C@H](O)CCC3)cc1
I-13[8]	R^2=3-OH(R,R); R^1 =4-SO_2Me	O[C@@H]1C[C@@H](/N=C2SC(c3ccc(S(=O)(C)=O)cc3)=NN/2C)CCC1
I-14[9]	-	O=S(c1ccc(N(C(c2cc(C)c(OC)cc2)=C3)C4=C3CC(N5CCN(C)CC5)CC4)cc1)(NC6=NC(C)=CC(C)=N6)=O
I-15[10]	-	O=C(OCC)C(S1)=C(C)N=C1NC2=NC(NCc3cc(OC)c(OC)c(OC)c3)=CC(C4CCC(N(C)C)CC4)=N2
I-16[10]	-	O=C(OCC)C(S1)=C(C)N=C1NC2=NC(C3CCC(O)CC3)=CC(C4CCC(O)CC4)=N2
I-17[10]	-	O=C1N(C2=NC(C3=CC=CS3)=NS2)N=C(c4cc(Cl)c(OC)cc4)C5CC=CCC51
I-18[11]	-	S=C(c1cccc(C)c1N2)N(c3ccccc3)C2=S
I-19[6]	CH_2CH_2OH	Clc1c(NC(NC23CCCCC3)=O)c2c(OCCO)cc1
I-20[6]	CH_2-5-CO_2-Et-furan-2-yl	Clc1c(NC(NC23CCCCC3)=O)c2c(OCC4=C(C(OCC)=O)C=CO4)cc1
I-21[6]	CH_2-1H-tetrazole-5yl	O=C1NC2=C(Cl)C=CC(OCC3=NN=NN3)=C2C4(CCCCC4)N1
I-22[6]	CH_2-5-OH-[1.2.4]oxadiazole-3-yl	O=C1NC2=C(Cl)C=CC(OCC3=NOC(O)=N3)=C2C4(CCCCC4)N1
I-23[6]	CH_2-5-CO_2H-furan-2-yl	Clc1c(NC(NC23CCCCC3)=O)c2c(OCC4=C(C(O)=O)C=CO4)cc1
I-24[6]	$CH_2CH_2CH_2$ SO_3H	Clc1c(NC(NC23CCCCC3)=O)c2c(OCCCS(=O)(O)=O)cc1
I-25[6]	CH_2CH_2-4-morpholine	O=C1NC2=C(Cl)C=CC(OCCN3CCOCC3)=C2C4(CCCCC4)N1
I-26[6]	CH_2CH_2NHMe	Clc1c(NC(NC23CCCCC3)=O)c2c(OCCNC)cc1
I-27[6]	$CH_2CH_2NMe_2$	Clc1c(NC(NC23CCCCC3)=O)c2c(OCCN(C)C)cc1
I-28[6]	$CH_2CH_2OCH_2$ CH_2NH_2	Clc1c(NC(NC23CCCCC3)=O)c2c(OCCOCCN)cc1
I-29[6]	CH_2CHOH CH_2NHMe	Clc1c(NC(NC23CCCCC3)=O)c2c(OCC(CNC)O)cc1
I-30[6]	$CH_2CHOHCH_2NMe_2$	Clc1c(NC(NC23CCCCC3)=O)c2c(OCC(CN(C)C)O)cc1
I-31[6]	$CH_2CH_2NHCH_2CO_2H$	Clc1c(NC(NC23CCCCC3)=O)c2c(OCCNCC(O)=O)cc1

Comp.	R	SMILES code
I-32[6]	4-Me	Clc1c(NC(NC23CCCCC3)=O)c2c(C)cc1
I-33[6]	4-OMe	Clc1c(NC(NC23CCCCC3)=O)c2c(OC)cc1
I-34[5]	8-F	O=C(NC12CCCCC2)Nc3c1cccc3F
I-35[5]	8-Br	O=C(NC12CCCCC2)Nc3c1cccc3Br
I-36[5]	8-CH_3	O=C(NC12CCCCC2)Nc3c1cccc3C
I-37[5]	6-Ph	O=C(NC12CCCCC1)Nc3c2cc(C4=CC=CC=C4)cc3
I-38[5]	5-Cl	O=C(NC12CCCCC1)Nc3c2c(Cl)ccc3
I-39[5]	5.6-diCl	O=C(NC12CCCCC1)Nc3c2c(Cl)c(Cl)cc3
I-40[5]	6.8-diCl	O=C(NC12CCCCC1)Nc3c2cc(Cl)cc3Cl
I-41[5]	6-Me-8-Cl	O=C(NC12CCCCC1)Nc3c2cc(C)cc3Cl
I-42[5]	6-OMe-8-Cl	O=C(NC12CCCCC1)Nc3c2cc(OC)cc3Cl
I-43[5]	4-Methylspirocyclohexyl	O=C(NC12CCC(C)CC2)Nc3c1cccc3Br
I-44[5]	p-C_6H_4-CO_2H	O=C(NC12CCCCC2)Nc3c1cc(c4ccc(C(O)=O)cc4)cc3Cl
I-45[5]	m-C_6H_4-CO_2H	O=C(NC12CCCCC2)Nc3c1cc(c4cccc(C(O)=O)c4)cc3Cl
I-46[5]	p-C_6H_4-$CONH_2$	O=C(NC12CCCCC2)Nc3c1cc(c4ccc(C(N)=O)cc4)cc3Cl
I-47[5]	p-C_6H_4-CONH-$(CH_2)_2$-NMe_2	O=C(NC12CCCCC2)Nc3c1cc(c4ccc(C(NCCN(C)C)=O)cc4)cc3Cl
I-48[5]	m-C_6H_4-CONH-$(CH_2)_2$-NMe_2	O=C(NC12CCCCC2)Nc3c1cc(c4cccc(C(NCCN(C)C)=O)c4)cc3Cl
I-49[5]	p-C_6H_4-CONH-$(CH_2)_3$-NMe_2	O=C(NC12CCCCC2)Nc3c1cc(c4ccc(C(NCCCN(C)C)=O)cc4)cc3Cl
I-50[5]	m-C_6H_4-CONH-$(CH_2)_3$-NMe_2	O=C(NC12CCCCC2)Nc3c1cc(c4cccc(C(NCCCN(C)C)=O)c4)cc3Cl
I-51[5]	p-C_6H_4-CO-N-Methylpiperazine	O=C(NC12CCCCC2)Nc3c1cc(c4ccc(C(N5CCN(C)CC5)=O)cc4)cc3Cl
I-52[5]	m-C_6H_4-CO-N-Methylpiperazine	O=C(NC12CCCCC2)Nc3c1cc(c4cccc(C(N5CCN(C)CC5)=O)c4)cc3Cl
I-53[12]	R^1=4-SO_2Me; R^2=H	CN(N=C(c1ccccc1)S/2)C2=N\c3cc(C(O)=O)c(S(=O)(C)=O)cc3
I-54[12]	R^1=3-CN; R^2= H	CN(N=C(c1ccccc1)S/2)C2=N\c3cc(C(O)=O)cc(C#N)c3
I-55[12]	R^2=H; R^1=4-CO(4-methyl-piperazin-1-yl)	CN1N=C(c2ccc(C(N3CCN(C)CC3)=O)cc2)S/C1=N/C4CCCCC4
I-56[12]	R^2=3-OH trans R^1=4-CONH(2-hydroxy-1,1dimethylethyl)	CN1N=C(c2ccc(C(NC(C)(C)CO)=O)cc2)S/C1=N/[C@H]3CCCC(O)C3
I-57[12]	R^2=3-OH trans R^1=4-NHCOMe	CN1N=C(c2ccc(NC(C)=O)cc2)S/C1=N/[C@H]3CCCC(O)C3
I-58[12]	R^2=3-OH trans R^1=4-SO_2Me	CN1N=C(c2ccc(S(C)(=O)=O)cc2)S/C1=N/[C@H]3CCCC(O)C3
I-59[12]	2- OH cis	CN1/C(SC(c2ccc(C(N)=O)cc2)=N1)=N/[C@H]3CCCCC3O
I-60[12]	4-OH trans	CN1/C(SC(c2ccc(C(N)=O)cc2)=N1)=N\C3CCC(O)CC3
I-61[12]	3-OH cis	CN1/C(SC(c2ccc(C(N)=O)cc2)=N1)=N/[C@H]3CCCC(O)C3
I-62[12]	3-OH trans	CN1/C(SC(c2ccc(C(N)=O)cc2)=N1)=N\[C@H]3CC(O)CCC3
I-63[12]	3-OH (R,R)	CN1/C(SC(c2ccc(C(N)=O)cc2)=N1)=N/[C@H]3CCC[C@@H](O)C3
I-64[7]	Bicycle[2,2,1] hept-2-yl	Clc1ccc(C(S/2)=NN(C)C2=N/C3C(C4)CCC4C3)cc1
I-65[7]	2-Hydroxy-1,1-dimethylethyl	Clc1ccc(C(S/2)=NN(C)C2=N\C(C)(C)CO)cc1
I-66[7]	Phenyl	Clc1ccc(C(S/2)=NN(C)C2=N\C3=CC=CC=C3)cc1
I-67[7]	3-OH	Clc1ccc(C(S/2)=NN(C)C2=N\c3cc(O)ccc3)cc1
I-68[7]	3-(2H-tetrazol-5-yl)	Clc1ccc(C(S/2)=NN(C)C2=N\c3cc(C4=NNN=N4)ccc3)cc1

Comp.	R	SMILES code
I-69[7]	3-$CONH_2$	Clc1ccc(C(S/2)=NN(C)C2=N\c3cc(C(N)=O)ccc3)cc1
I-70[7]	4-OH	Clc1ccc(C(S/2)=NN(C)C2=N\c3ccc(O)cc3)cc1
I-71[7]	4-F	Clc1ccc(C(S/2)=NN(C)C2=N\c3ccc(F)cc3)cc1
I-72[7]	2-OH, 5-COOH	Clc1ccc(C(S/2)=NN(C)C2=N\c3c(O)ccc(C(O)=O)c3)cc1
I-73[7]	2-OH, 3-COOH	Clc1ccc(C(S/2)=NN(C)C2=N\c3c(O)c(C(O)=O)ccc3)cc1
I-74[7]	3-COOH, 4-F	Clc1ccc(C(S/2)=NN(C)C2=N\c3cc(C(O)=O)c(F)cc3)cc1
I-75[7]	4,7-Dimethyl quinazoline	CN(N=C(C1=CC=C(C(C)=NC=N2)C2=C1)S/3)C3=N\C4CCCCC4
I-76[7]	2-Cl	CN1/C(SC(c2c(Cl)cccc2)=N1)=N/C3CCCCC3
I-77[7]	3-OH	CN1/C(SC(c2cc(O)ccc2)=N1)=N/C3CCCCC3
I-78[7]	3-Cl	CN1/C(SC(c2cc(Cl)ccc2)=N1)=N/C3CCCCC3
I-79[7]	3-SO_2NH_2	CN1/C(SC(c2cc(S(=O)(N)=O)ccc2)=N1)=N/C3CCCCC3
I-80[7]	3-$CONH_2$	CN1/C(SC(c2cc(C(N)=O)ccc2)=N1)=N/C3CCCCC3
I-81[7]	3-COOH	CN1/C(SC(c2cc(C(O)=O)ccc2)=N1)=N/C3CCCCC3
I-82[7]	4-OH	CN1/C(SC(c2ccc(O)cc2)=N1)=N/C3CCCCC3
I-83[7]	4-COOMe	CN1/C(SC(c2ccc(C(OC)=O)cc2)=N1)=N/C3CCCCC3
I-84[7]	4-Cl	CN1/C(SC(c2ccc(Cl)cc2)=N1)=N/C3CCCCC3
I-85[7]	4-COOH	CN1/C(SC(c2ccc(C(O)=O)cc2)=N1)=N/C3CCCCC3
I-86[7]	4-NH_2	CN1/C(SC(c2ccc(N)cc2)=N1)=N/C3CCCCC3
I-87[7]	3-Me, 4-$CONH_2$	CN1/C(SC(c2cc(C)c(C(N)=O)cc2)=N1)=N/C3CCCCC3
I-88[7]	3-OMe, 4-$CONH_2$	CN1/C(SC(c2cc(OC)c(C(N)=O)cc2)=N1)=N/C3CCCCC3
I-89[7]	3-SO_2NH_2.4-Cl	CN1/C(SC(c2cc(S(N)(=O)=O)c(Cl)cc2)=N1)=N/C3CCCCC3
I-90[7]	3-SO_2NHEt, 4-Cl	CN1/C(SC(c2cc(S(NCC)(=O)=O)c(Cl)cc2)=N1)=N/C3CCCCC3
I-91[7]	4-$CONHCH_2CH_3$-N-morpholinyl	CN1/C(SC(c2ccc(C(NCCN3CCOCC3)=O)cc2)=N1)=N/C4CCCCC4
I-92[7]	4-$CONHCH_2N(CH_3)_2$	CN1/C(SC(c2ccc(C(NCCN(C)C)=O)cc2)=N1)=N/C3CCCCC3

Table S2. After reduction of dimension: hidden neurons for each molecule.

Comp.	IC_{50} (μM)	A	B	C	D
I-1	0.15	0.824805	0.02059	0.027546	0.020005
I-2	0.03	0.987969	0.040606	0.031817	0.992433
I-3	0.01	0.025064	0.018587	0.871014	0.025251
I-4	0.12	0.907033	0.026002	0.009621	0.023997
I-5	0.03	0.883312	0.031732	0.028993	0.033764
I-6	0.17	0.915279	0.99687	0.986983	0.960851
I-7	0.02	0.697131	0.750226	0.995709	0.997673
I-8	0.01	0.076401	0.937887	0.000907	0.007127
I-9	1.5	0.412103	0.895437	0.903391	0.255357
I-10	0.14	0.093917	0.997256	0.89745	0.961969
I-11	0.03	0.904289	0.046262	0.027739	0.050401
I-12	0.08	0.084001	0.690593	0.116325	0.049928
I-13	0.05	0.785893	0.003162	0.064435	0.008843
I-14	0.01	0.777262	0.004367	0.006458	0.021562
I-15	0.03	0.010845	0.00676	0.006454	0.809156
I-16	0.06	0.026129	0.921301	0.023752	0.022828
I-17	0.08	0.314084	0.071012	0.068357	0.262474
I-18	1	0.994101	0.980303	0.990388	0.98975
I-19	0.05	0.358922	0.962927	0.889166	0.104338
I-20	0.01	0.869406	0.027862	0.010168	0.030562
I-21	0.01	0.415963	0.569516	0.98084	0.741146
I-22	0.01	0.415963	0.569516	0.98084	0.741146
I-23	0.02	0.929689	0.005872	0.017627	0.038603
I-24	0.02	0.674565	0.000232	0.00257	0.039804
I-25	0.04	0.001904	0.004098	0.895127	0.041666
I-26	0.93	0.97251	0.965634	0.339512	0.996595
I-27	0.16	0.922049	0.884639	0.244723	0.59938
I-28	1.62	0.205381	0.884517	0.624457	0.510516
I-29	0.21	0.977827	0.937339	0.317506	0.619464
I-30	0.40	0.014395	0.337643	0.134946	0.483521
I-31	0.04	0.002671	0.751227	0.203597	0.003908
I-32	0.10	0.036175	0.500084	0.277307	0.675212
I-33	0.01	0.11241	0.26918	0.738229	0.577431

Comp.	IC_{50} (μM)	A	B	C	D
I-34	0.39	0.205862	0.904151	0.244813	0.892184
I-35	0.06	0.863481	0.952994	0.96858	0.956333
I-36	0.79	0.324064	0.328639	0.309182	0.766063
I-37	0.98	0.576614	0.825674	0.725045	0.943223
I-38	0.84	0.977764	0.983828	0.970171	0.182014
I-39	0.60	0.942604	0.878549	0.998111	0.995413
I-40	0.12	0.947401	0.999983	0.858211	0.062039
I-41	0.16	0.813252	0.945594	0.096404	0.934502
I-42	0.16	0.741634	0.066536	0.130777	0.795944
I-43	0.21	0.741634	0.066536	0.130777	0.795944
I-44	0.01	0.069645	0.000483	0.000462	0.931533
I-45	0.03	0.935083	0.111989	9.2e-005	0.027029
I-46	0.02	0.931749	0.000223	0.000394	0.04961
I-47	0.02	0.02554	0.017693	0.021401	0.924596
I-48	0.03	0.872382	0.028165	0.022261	0.032033
I-49	0.02	0.917655	0.021888	0.015164	0.018502
I-50	0.02	0.03575	0.030505	0.793042	0.008289
I-51	0.01	0.04695	0.828941	0.014169	0.01704
I-52	0.04	0.018492	0.020606	0.015912	0.928709
I-53	0.12	0.903026	0.032933	0.001079	0.001201
I-54	0.19	0.990421	0.710036	0.114675	0.869108
I-55	0.42	0.841383	0.048273	0.064642	0.005665
I-56	0.38	0.035568	0.0494	0.035207	0.797716
I-57	0.08	0.004051	0.083507	0.002876	0.735232
I-58	0.31	0.014364	0.008668	0.15499	0.687601
I-59	0.61	0.989786	0.447801	0.992606	0.982077
I-60	0.19	0.923775	0.997781	0.916581	0.996271
I-61	1.65	0.156536	0.991634	0.982831	0.848269
I-62	0.19	0.003846	0.790941	0.101716	0.01472
I-63	0.08	0.927896	0.000554	0.009228	0.189424
I-64	1.05	0.966081	0.973558	0.941785	0.396351
I-65	1.9	0.972448	0.905577	0.803425	0.99066
I-66	2.95	0.958872	0.994647	0.99674	0.680187
I-67	1.80	0.996775	0.59624	0.996873	0.625385
I-68	0.08	0.005805	0.002796	0.836009	0.191127

Comp.	IC_{50} (μM)	A	B	C	D
I-69	1.63	0.967967	0.062628	0.99622	0.899858
I-70	1.70	0.980339	0.805035	0.998617	0.539458
I-71	2.20	0.972624	0.380912	0.994297	0.859654
I-72	1.31	0.02755	0.105842	0.065059	0.738752
I-73	0.26	0.002131	0.039907	0.708103	0.200532
I-74	0.16	0.01536	0.162492	0.006681	0.54921
I-75	0.04	0.052292	0.749734	0.9909	0.918103
I-76	1.30	0.667457	0.539127	0.536442	0.356475
I-77	0.29	0.762825	0.179308	0.144207	0.940531
I-78	0.70	0.334175	0.264264	0.5376	0.830523
I-79	0.20	0.92284	0.723142	0.738779	0.093847
I-80	0.09	0.940884	0.20657	0.159968	0.95938
I-81	0.87	0.935618	0.156566	0.318913	0.927962
I-82	0.24	0.490779	0.31032	0.969575	0.317776
I-83	0.23	0.999557	0.996463	0.981316	0.930724
I-84	1.50	0.892315	0.161231	0.777029	0.259727
I-85	0.55	0.476255	0.600632	0.846401	0.358308
I-86	0.56	0.978523	0.992109	0.987195	0.585795
I-87	0.93	0.988915	0.553073	0.963968	0.989638
I-88	0.47	0.992063	0.942551	0.989754	0.772288
I-89	0.07	0.316334	0.013032	0.112718	0.002728
I-90	0.02	0.009368	0.920609	0.004644	0.028857
I-91	0.03	0.023512	0.00926	0.913369	0.01728
I-92	0.06	0.074753	0.405584	0.050186	0.066867

Table S3. Cluster analysis of training and test set of model **1**.

	Training			***Test***		
	Experimental					
Predicted	*Inactive*	*Moderate*	*Active*	*Inactive*	*Moderate*	*Active*
Active	9 %	8 %	75 %	5 %	27 %	60 %
Moderate	31 %	55 %	-	55 %	46 %	-
Inactive	60 %	37 %	-	40 %	26 %	-

Table S4. Statistical parameters of training and test set model **1**.

	Training set	**Test set**
FC	100 %	45 %
FAR	0 %	27 %
POD	98 %	96 %

(FC) Fraction correct. (FAR) False alarm rate.
(POD) Probability of detection.

Table S5. Training set of **NNE3** model.

	Quantitative analysis		Qualitative analysis	
Comp.	**Log IC_{50}**	**Theoretical**	**Experimental**	**Theoretical**
I-25	-1.4202	-1.7242	1	1
I-73	-0.585	-1.1484	0	1
I-31	-1.3768	-0.9403	1	0
I-62	-0.7212	-0.9746	0	0
I-57	-1.0706	-0.802	1	0
I-68	-1.0969	-1.3853	1	1
I-90	-1.6576	-1.3782	1	1
I-15	-1.5229	-1.2288	1	1
I-58	-0.5086	-0.249	0	0
I-30	-0.3979	-0.4022	0	0
I-74	-0.7959	-0.5412	0	0
I-52	-1.3566	-1.3995	1	1
I-91	-1.5229	-1.8016	1	1
I-3	-2	-1.7836	1	1
I-47	-1.6778	-1.3457	1	1
I-16	-1.2219	-1.4873	1	1
I-72	0.1173	-0.32	-1	0
I-56	-0.4202	-0.7523	0	0
I-50	-1.7213	-1.7777	1	1
I-32	-1	-0.4568	1	0
I-51	-1.8539	-1.4563	1	1
I-75	-1.5686	-1.1323	1	1
I-44	-1.8861	-1.5321	1	1
I-92	-1.2007	-0.6968	1	0

	Quantitative analysis		Qualitative analysis	
Comp.	**Log IC_{50}**	**Theoretical**	**Experimental**	**Theoretical**
I-12	-1.0555	-0.8912	1	0
I-10	-0.8539	-0.5548	0	0
I-33	-1.8539	-1.611	1	1
I-61	0.2175	-0.2591	-1	0
I-28	0.2095	-0.1251	-1	0
I-34	-0.4089	-0.6351	0	0
I-17	-1.1024	-0.8584	1	0
I-89	-1.1612	-1.2677	1	1
I-36	-0.1024	-0.0163	0	0
I-78	-0.1549	-0.1698	0	0
I-19	-1.2596	-0.7644	1	0
I-83	-0.6383	-0.378	0	0
I-9	0.1761	-0.0659	-1	0
I-21	-2.3979	-2.0685	1	1
I-22	-2.4559	-2.0685	1	1
I-85	-0.2596	-0.3773	0	0
I-49	-1.6198	-1.2667	1	1
I-27	-0.8041	-0.6087	0	0
I-79	-0.699	-0.4791	0	0
I-60	-0.7212	-0.3459	0	0
I-63	-1.0555	-1.4179	1	1
I-23	-1.7959	-1.333	1	1
I-46	-1.699	-1.4888	1	1
I-45	-1.6021	-1.0669	1	1
I-81	-0.0605	-0.1542	0	0

	Quantitative analysis		Qualitative analysis	
Comp.	**Log IC_{50}**	**Theoretical**	**Experimental**	**Theoretical**
I-39	-0.2218	-0.5704	0	0
I-40	-0.9208	-0.7238	0	0
I-66	0.4698	-0.0622	-1	0
I-64	0.0212	0.2194	-1	-1
I-69	0.2122	0.3445	-1	-1
I-65	0.2788	-0.195	-1	0
I-26	-0.0146	-0.2573	0	0
I-71	0.3424	0.1197	-1	-1
I-38	-0.0757	-0.116	0	0
I-29	-0.6716	-0.5493	0	0
I-86	-0.2518	0.1696	0	-1
I-70	0.2304	0.1321	-1	-1
I-2	-1.585	-1.5274	1	1
I-87	-0.0315	-0.1727	0	0
I-59	-0.2147	-0.0458	0	0
I-54	-0.7212	-0.5611	0	0
I-88	-0.3279	-0.2797	0	0
I-18	0	-0.3835	0	0
I-67	0.2553	-0.085	-1	0

Figure S1. Workflow of the virtual screening procedure.

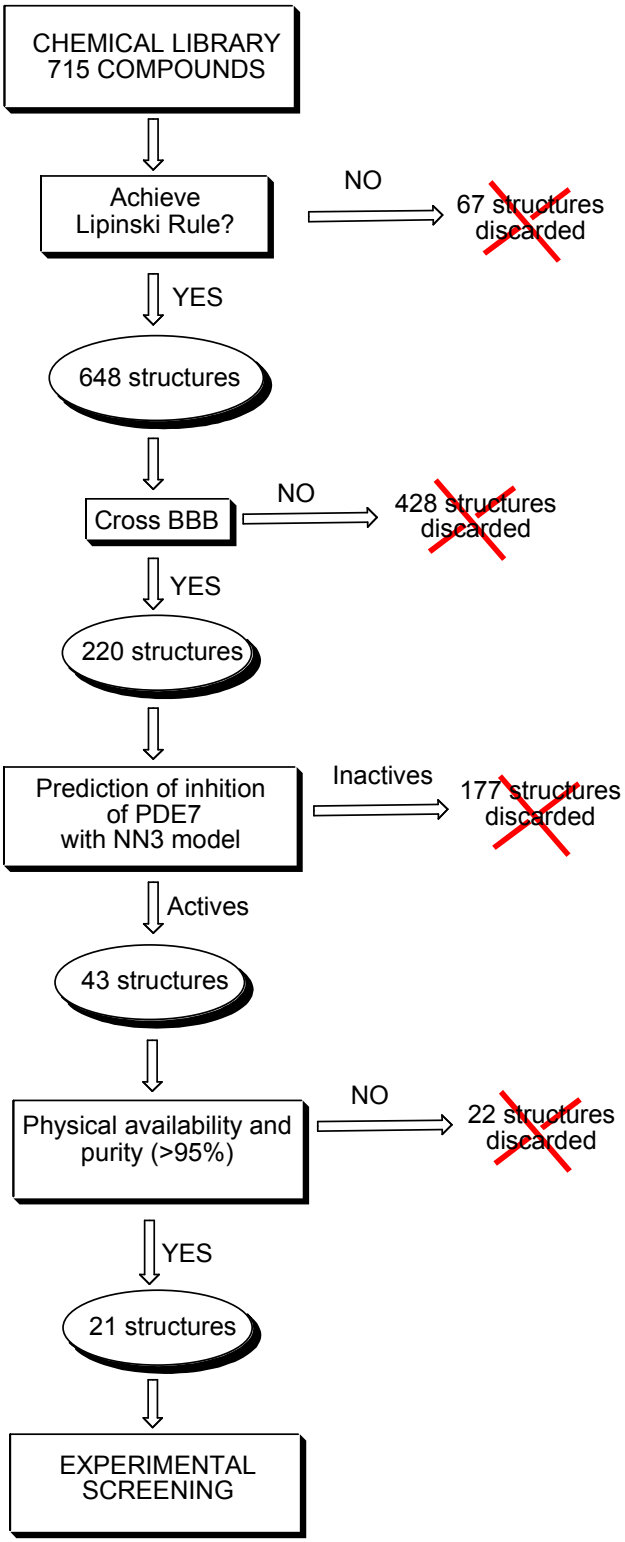

Tabla S6. SMILE code and physicochemical property filters for each molecule of the virtual screening

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
1	AM003	C1CCc2c(C1)c(c(s2)N)C#N	2.06	178.26	2	2	0	0	0.06
2	AM019	N1=C(C=C(N(CCc2ccccc2)S1(=O)=O)c1ccccc1)c1ccccc1	4.73	388.49	4	0	0	5	0.73
3	AM032	n1cnc2c(c1SC(=O)Cc1ccccc1)ncn2C(=O)Cc1ccccc1	3.98	388.45	6	0	0	6	-0.02
4	CG056	c1(cc(c(c(c1)C(=O)OC)N)Cl)Cl	2.98	220.06	3	2	0	2	-0.02
5	AM047	C1CCc2c(C1)c(nn2c1sc2c(n1)cccc2)C	4.04	269.37	3	0	0	1	1.04
6	AM048	C1CCC2=C(C1)[C@H](N(N2)c1sc2c(n1)cccc2)C	4.53	271.39	3	1	0	1	1.53
7	AM048	C1CCC2=C(C1)[C@@H](N(N2)c1sc2c(n1)cccc2)C	4.53	271.39	3	1	0	1	1.53
8	AM049	[C@H]1(C=CNN1c1sc2c(n1)cccc2)C	2.73	217.30	3	1	0	1	-0.27
9	AM052	N1=NC2=C([C@H]1C)CCC2	1.61	122.17	2	0	0	0	-0.39
10	AM053	C1(=NN=C(C1O)c1ccccc1)c1ccccc1	2.57	236.27	3	1	0	2	-0.43
11	AM054	N1=NC2=C([C@H]1C)CCC2	1.61	122.17	2	0	0	0	-0.39
12	AM054	N1=NC2=C([C@@H]1C)CCC2	1.61	122.17	2	0	0	0	-0.39
13	AM056	N1=NC2=C([C@H]1C)CCC2	1.61	122.17	2	0	0	0	-0.39
14	AM056	N1=NC2=C([C@@H]1C)CCC2	1.61	122.17	2	0	0	0	-0.39
15	AM057	N1=NC2=C([C@H]1C)CCC2	1.61	122.17	2	0	0	0	-0.39
16	AM080	c1ccc(c(c1)O)/C=N/c1ccccc1	3.41	197.24	2	1	0	2	1.41
17	AC004	c1cnc(cc1)NC(=S)NCc1ccccc1	2.49	243.34	3	2	0	5	-0.52
18	AC010	c1ccc(cc1)NC(=S)NCC	1.73	180.28	2	2	0	4	-0.28
19	AC012	c1ccc2c(c1)o/c(=N\CC)[nH]2	2.26	162.19	3	1	0	1	0.26
20	AC014	c1cnc(cc1)/N=c1\scc(n1C)C	2.86	205.29	3	0	0	1	-0.14
21	AC016	c1cnc(cc1)/N=c1\n(c(ns1)c1ccccc1)C	4.22	268.35	4	0	0	2	0.22
22	AC023	c1ccc2c(c1)sc(n2)NCC	2.73	178.26	2	1	0	2	0.73
23	AC027	c1(ccc(cn1)Cl)NC(=O)NCc1ccccc1	2.79	225.42	4	2	0	3	-0.21

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
24	CG106	C1CCc2c(C1)c(c(s2)N)C(=O)OCC	2.52	225.31	3	2	0	3	-0.48
25	CG108	c1ccc2c(c1)c(c(s2)C(=O)OC)N	2.39	207.25	3	2	0	2	-0.61
26	AC033	c1cnc2c(c1)[nH]/c(=N\CC)s2	2.76	179.25	3	1	0	1	-0.24
27	AC044	c1nc(ccc1)NC(=S)SC	1.83	184.29	2	1	0	3	-0.17
28	AC052	c1ccc2c(c1)N[C@@H](S2)[NH3]	1.54	153.23	2	4	0	0	-0.46
29	AC061	c1ccc2c(c1)sc(n2)N	1.98	150.21	2	2	0	0	-0.02
30	AC068	C1CC(CCC1)/N=c1/n(c(=O)n(s1)C(C)C)CC	4.04	269.41	4	0	0	3	0.04
31	AC092	c1cnc(cc1)/N=c1/n(c(ns1)c1ccccc1)CC	4.60	282.37					0.60
32	AC093	c1cnc(cc1)/N=c1/n(c(ns1)CC)Cc1ccccc1	4.36	296.40	4	0	0	4	0.36
33	AC098	c1ccc(nc1)/N=c1/n(c(=O)n(s1)C1CCCCC1)CC	4.10	304.42	5	0	0	3	0.10
34	AC105	c1ccc(cc1)/N=c1/n(c(=O)n(s1)C(C)C)CC	3.83	263.37	4	0	0	3	-0.17
35	CG008	N1=C(c2c(N(Cc3ccccc3)S1(=O)=O)cccc2)OCc1ccc(cc1)Cl	4.75	412.90	5	0	0	5	-0.25
36	CG013	c12c(cccc1)N(Cc1ccc(cc1)Cl)S(=O)(=O)N(C2=O)Cc1ccc(cc1)Cl	4.79	447.34	5	0	0	4	-0.21
37	CG015	c12c(cccc1)N(Cc1ccccc1Cl)S(=O)(=O)N(C2=O)Cc1c(cccc1)Cl	4.70	447.34	5	0	0	4	-0.30
38	CG019	N1(C(=O)c2c(N(Cc3ccccc3Cl)S1(=O)=O)cccc2)Cc1ccccc1	4.07	412.90	5	0	0	4	0.07
39	CG026	N1(C(=O)c2c(N(Cc3cc(ccc3)Cl)S1(=O)=O)cccc2)Cc1cc(ccc1)Cl	4.75	447.34	5	0	0	4	0.75
40	CG035	N1(C(=O)c2c(N(Cc3ccc(cc3)OC)S1(=O)=O)cccc2)Cc1ccc(cc1)OC	3.55	438.51	7	0	0	6	-0.45
41	CG036	N1(C(=O)c2c(N(Cc3ccc(cc3)C(F)(F)F)S1(=O)=O)cccc2)Cc1ccccc1	4.33	446.45	5	0	0	5	0.33
42	CG059	N1(C(=O)c2c(N(Cc3cc(c(cc3)Cl)Cl)S1(=O)=O)ccs2)Cc1ccccc1	4.60	453.37	5	0	0	4	-0.40
43	CG060	n1(c(=S)n(c2c(c1=O)cccc2)Cc1ccc(cc1)Cl)Cc1ccccc1	4.97	392.91	3	0	0	4	1.97
44	CG062	n1(c(=S)n(c2c(c1=O)cccc2)Cc1ccc(cc1)C(F)(F)F)Cc1ccccc1	5.19	426.46	3	0	1	5	2.19
45	CG067	N1(C(=O)c2c(N(Cc3cccc4c3cccc4)S1(=O)=O)cccc2)Cc1ccccc1	4.60	428.51	5	0	0	4	-0.40
46	CG069	n1(c(=O)n(c2c(c1=O)cccc2)Cc1ccc(cc1)Cl)Cc1ccccc1	4.63	376.84	4	0	0	4	0.63
47	CG072	n1(c(=S)[nH]c2c(c1=O)cccc2)Cc1ccccc1	2.63	268.34	3	1	0	2	-0.37
48	CG073	N1(C(=O)c2c(N(Cc3ccc(c(c3)Cl)Cl)S1(=O)=O)cccc2)CC(C)C	4.45	413.33	5	0	0	4	-0.55
49	CG074	N1=C(c2c(N(Cc3ccc(c(c3)Cl)Cl)S1(=O)=O)cccc2)OCC(C)C	4.89	413.33	5	0	0	5	-0.12

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
50	CG086	N1(C(=O)c2c(N(CC(=O)c3ccc(cc3)Cl)S1(=O)=O)cccc2)Cc1ccccc1	3.87	440.91	6	0	0	5	-0.14
51	CG088	N1=C(c2c(N(Cc3ccc(cc3)Cl)S1(=O)=O)cccc2)OCC	3.53	350.83	5	0	0	4	-0.47
52	CG090	N1=C(c2c(N(Cc3ccc(c(c3)Cl)Cl)S1(=O)=O)cccc2)OCC	4.14	385.27	5	0	0	4	0.14
53	CG093	N1(C(=O)c2c(N(Cc3ccc(cc3)Cl)S1(=O)=O)cccc2)CCC	3.60	364.85	5	0	0	4	-0.40
54	CG099	c1(ccc(cc1)CCOCCl)OC	2.75	200.67	2	0	0	5	0.75
55	CG101	c1ccc(cc1)CCOCCl	2.69	170.64	1	0	0	4	1.69
56	AE009	c1(sc(cc1C(=O)OCC)c1ccccc1)N	3.26	247.32	3	2	0	4	0.26
57	AE010	C1CCCc2c(C1)cn[nH]2	2.00	136.20	2	1	0	0	0.00
58	AE084	c1(sc(c(c1)N)C(=O)OC)c1ccccc1	3.00	233.29	3	2	0	3	0.00
59	EF016	c1ccc(cc1)NC(=S)NC1CC[NH](CC1)Cc1ccccc1	3.01	326.49	3	3	0	6	0.00
60	EF017	C1C(CC[NH](C1)Cc1ccccc1)CCNC(=S)Nc1ccccc1	3.84	354.54	3	3	0	8	0.84
61	EF019	c1ccc2c(c1)sc(n2)NC1CC[NH](CC1)Cc1ccccc1	4.01	324.47	3	2	0	4	1.01
62	AM094	C1CCC2=C(C1)C(=NON2)C	2.13	152.20	3	1	0	0	-0.88
63	AM096	c1(c(cc2c(c1)ncn2C)C)C	2.30	160.22	2	0	0	0	0.30
64	AM0101	c1(c(c(c(o1)c1ccccc1)c1ccccc1)C#N)N	3.89	260.30	3	2	0	2	1.89
65	AM106	N1=C(C=C(NO1)c1ccccc1)c1ccccc1	4.07	236.27	3	1	0	2	1.07
66	TC2.30	c1(ccc2c(c1)c(=O)n(c(=S)[nH]2)c1ccccc1)Br	3.10	333.21	3	1	0	1	0.10
67	TC2.41	c1ccc2c(c1)c(=O)n(c(n2)SC)c1c(c(c(cc1)F)F)F	3.80	322.31	3	0	0	2	0.80
68	TC2.42	c1c2c(sc1)c(=O)n(c(n2)SC)c1ccccc1	3.00	274.37	3	0	0	2	0.00
69	TC2.43	c1ccc2c(c1)c(=O)n(c(n2)SC)c1c(cccc1F)F	3.90	304.32	3	0	0	2	0.90
70	TC2.44	c1ccc2c(c1)sc1c2nc(n(c1=O)c1c(cccc1F)F)SC	4.97	360.41	3	0	0	2	1.97
71	TC2.45	c1ccc2c(c1)c(=S)n(c(=S)[nH]2)c1c(c(c(cc1)F)F)F	3.21	324.35	2	1	0	1	1.21
72	TC2.47	c1cc2c(s1)c(=O)n(c(n2)SC)c1c(cccc1F)F	3.66	310.35	3	0	0	2	0.66
73	TC2.51	c1ccc2c(c1)c(=S)n(c(n2)SC)c1c(c(c(cc1)F)F)F	4.15	338.38	2	0	0	2	2.15
74	TC3.1	c1ccc2c(c1)c(=S)n(c(n2)SC)c1c(cccc1F)F	4.24	320.39	2	0	0	2	2.24
75	TC3.9	c1ccc2c(c1)c(=S)n(c(n2)SC)c1ccccc1	3.59	284.41	2	0	0	2	1.59
76	TC3.13	c1ccc2c(c1)c(=S)n(c(n2)SC)c1c(cccc1)Br	4.56	363.31	2	0	0	2	2.56

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
77	TC3.14	c1cc(c2c(c1)c(=O)n(c(=S)[nH]2)c1c(cccc1)Br)C	3.69	347.24	3	1	0	1	0.69
78	TC3.16	c1cc(c2c(c1)c(=O)n(c(=S)[nH]2)c1c(cccc1F)F)C	3.37	304.32	3	1	0	1	0.37
79	TC3.17	c1cc(c2c(c1)c(=O)n(c(=S)[nH]2)c1c(c(c(cc1)F)F)F)C	3.27	322.31	3	1	0	1	0.27
80	TC3.22	c1cc(c2c(c1)c(=O)n(c(n2)SC)c1c(cccc1)Br)C	4.62	361.26	3	0	0	2	1.62
81	TC3.23	c1cc(c2c(c1)c(=O)n(c(n2)SC)c1c(cccc1F)F)C	4.30	318.35	3	0	0	2	1.30
82	TC3.24	c1cc(c2c(c1)c(=O)n(c(n2)SC)c1c(c(c(cc1)F)F)F)C	4.20	336.34	3	0	0	2	1.20
83	TC3.28	c1(ccc2c(c1)c(=O)n(c(=S)[nH]2)c1c(cccc1)Br)Br	4.07	412.11	3	1	0	1	1.07
84	TC3.29	c1(ccc2c(c1)c(=O)n(c(=S)[nH]2)c1c(cccc1F)F)Br	3.75	369.19	3	1	0	1	0.75
85	TC3.30	c1(ccc2c(c1)c(=O)n(c(=S)[nH]2)c1c(c(c(cc1)F)F)F)Br	3.66	387.18	3	1	0	1	0.66
86	TC3.32	c1(ccc2c(c1)c(=O)n(c(n2)SC)c1c(c(c(cc1)F)F)F)Br	4.59	401.21	3	0	0	2	1.59
87	TC3.36	c1(ccc2c(c1)c(=O)n(c(n2)SC)c1c(cccc1F)F)Br	4.68	383.22	3	0	0	2	1.68
88	TC3.47	c1(ccc2c(c1)c(=O)n(c(n2)SC)c1ccccc1)Br	4.03	347.24	3	0	0	2	1.03
89	S016	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1ccc(cc1)C(F)(F)F	3.21	322.31	3	1	0	2	0.21
90	S015	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1ccc(cc1)C	2.76	268.34	3	1	0	1	-0.24
91	S022	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1ccc(cc1)Cl	2.99	288.76	3	1	0	1	-0.01
92	S023	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1ccc(cc1)F	2.48	272.30	3	1	0	1	-0.52
93	S025	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1cc(c(c(c1)F)F)F	3.08	308.28	3	1	0	1	0.08
94	S026	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1ccc(cc1)Br	3.12	333.21	3	1	0	1	0.12
95	S027	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1cc(ccc1)Br	3.31	333.21	3	1	0	1	0.31
96	S028	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1c(cccc1)Br	3.29	333.21	3	1	0	1	0.29
97	S029	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1c(cc(cc1)Br)F	3.43	351.20	3	1	0	1	0.43
98	S033	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)c1cccc2c1cccc2	3.68	304.37	3	1	0	1	0.68
99	S035	c1ccc2c(c1)c(=O)n(c(=S)[nH]2)CCc1ccccc1	2.84	282.37	3	1	0	3	-0.16
100	S037	c1ccc2c(c1)c(=O)n(c(n2)SC)c1ccccc1	3.25	268.34	3	0	0	2	0.25
101	S038	c1ccc2c(c1)c(=O)n(c(n2)SC)c1c(cccc1)Br	4.22	347.24	3	0	0	2	2.22
102	S041	c1cc2c(s1)c(=O)n(c(=S)[nH]2)c1c(cc(cc1)Br)F	3.19	357.23	3	1	0	1	0.19
103	S043	c1cc2c(s1)c(=O)n(c(=S)[nH]2)c1c(c(c(cc1)F)F)F	2.63	314.31	3	1	0	1	-0.37

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
104	S045	c12c(c3c(s1)c(=O)n(c(=S)[nH]3)c1ccccc1)cccc2	3.38	310.40	3	1	0	1	0.38
105	S047	c12c(c3c(s1)c(=O)n(c(=S)[nH]3)c1c(cc(cc1)Br)F)cccc2	4.49	407.29	3	1	0	1	1.49
106	S048	c12c(c3c(s1)c(=O)n(c(=S)[nH]3)c1c(cccc1F)F)cccc2	4.03	346.38	3	1	0	1	1.03
107	S049	c12c(c3c(s1)c(=O)n(c(=S)[nH]3)c1c(c(c(cc1)F)F)F)cccc2	3.94	364.37	3	1	0	1	0.94
108	**VP0.1**	C1[C@H](Cc2c(C1)c(c(s2)NC(=O)CCCCl)C(=O)OCCC)C	4.34	357.90	4	1	0	8	0.34
109	SC003	C1CCc2c(C1)c(cs2)OC[C@H](CNC(C)C)O	2.57	269.41	3	2	0	6	-0.43
110	SC004a	c1(c(c(cs1)Cl)Cl)[C@@H]([C@@H](C)N)Cl	2.82	244.57	1	2	0	2	1.82
111	SC004b	c1(c(c(cs1)Cl)Cl)[C@@H]([C@H](C)N)Cl	2.82	244.57	1	2	0	2	1.82
112	SC004c	c1(c(c(cs1)Cl)Cl)[C@H]([C@@H](C)N)Cl	2.82	244.57	1	2	0	2	1.82
113	SC004d	c1(c(c(cs1)Cl)Cl)[C@H]([C@H](C)N)Cl	2.82	244.57	1	2	0	2	1.82
114	SC005	c1(nn(c(n1)CCCl)c1ccccc1)c1ccccc1	3.74	283.76	3	0	0	4	0.74
115	SC006	c1(ccc2c(c1)c1c(n2NC(=O)c2ccccc2)cccc1)Cl	4.98	320.78	3	1	0	2	1.98
116	SC007a	c1c(sc(c1Cl)[C@@H]([C@H](C)CN)Cl)Cl	3.36	258.60	1	2	0	3	1.36
117	SC007b	c1c(sc(c1Cl)[C@@H]([C@@H](C)CN)Cl)Cl	3.36	258.60	1	2	0	3	2.36
118	SC007c	c1c(sc(c1Cl)[C@H]([C@H](C)CN)Cl)Cl	3.36	258.60	1	2	0	3	2.36
119	SC007d	c1c(sc(c1Cl)[C@H]([C@@H](C)CN)Cl)Cl	3.36	258.60	1	2	0	3	2.36
120	SC008	c1cccc(c1)N(C(=O)C)NC(=O)c1ccccc1	2.19	254.29	4	1	0	3	-0.81
121	SC009	c1cccc(c1)N(NC(=O)c1ccccc1)C	2.83	226.28	3	1	0	3	-0.17
122	SC013	c1ccc2c(c1)n([nH]c(nc2=O)c1ccccc1)c1ccccc1	4.24	313.36	4	1	0	2	0.24
123	SC013	c1ccc2c(c1)n(nc([nH]c2=O)c1ccccc1)c1ccccc1	4.24	313.36	4	1	0	2	0.24
124	SC015a	c1(c(ccs1)Br)[C@@H](CNC(C)(C)C)O	2.73	278.22	2	2	0	4	0.73
125	SC015b	c1(c(ccs1)Br)[C@H](CNC(C)(C)C)O	2.73	278.22	2	2	0	4	0.73
126	SC016	c12c(ccc(c1)Cl)Sc1c(N2CCNN2CCN(CC2)C)cccc1	4.41	374.94	4	1	0	4	0.41
127	SC018	c1ccc2c(c1)c1c(n2N=O)cccc1	3.33	196.21	3	0	0	1	0.33
128	SC019	c1ccc2c(c1)c1c(n2N)c(ccc1)Cl	3.55	216.67	2	2	0	0	1.55
129	SC109a	Cl[C@@H]1CCCN1CC(=O)O	3.55	216.67	2	2	0	0	0.55
130	SC109b	Cl[C@H]1CCCN1CC(=O)O	3.55	216.67	2	2	0	0	0.55

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
131	SC023	n1(c(nc(n1)c1ccccc1)SC)c1ccccc1	3.77	267.36	3	0	0	3	0.77
132	SC024	c1(NNC(=O)c2ccccc2)ccccc1	2.59	212.25	3	2	0	3	-0.41
133	SC025	c1(N(NC(=O)c2ccccc2)c2ccccc2)ccccc1	4.53	288.35	3	1	0	4	1.53
134	SC027a	c1csc(c1Cl)C[C@@H](CCl)CN	2.40	224.16	1	2	0	4	1.40
135	SC027b	c1csc(c1Cl)C[C@H](CCl)CN	2.40	224.16	1	2	0	4	1.40
136	SC030	c12c(cccc1)Sc1c(N2CCNN2CCN(CC2)C)cccc1	3.76	340.50	4	1	0	4	-0.24
137	SC031	c12c(cccc1)Sc1c(N2CCNN(C)C)cccc1	3.87	285.42	3	1	0	4	0.87
138	SC034	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCCC1)ccc(c2)Cl	4.75	373.91	4	1	0	3	0.75
139	SC035	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCC1)cc(cc2)Cl	4.25	359.88	4	1	0	3	0.25
140	SC036	c12c(N(c3c(S1)cccc3)NC(=O)CCN(C)C)ccc(c2)Cl	4.11	347.87	4	1	0	4	0.11
141	SC037	c12c(N(c3c(S1)cccc3)NC(=O)CN(CC)CC)cc(cc2)Cl	4.60	361.90	4	1	0	5	0.60
142	SC038	c12c(N(c3c(S1)cccc3)NC(=O)C)cccc2	3.20	256.33	3	1	0	1	0.20
143	SC039	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCC1)cccc2	3.59	325.44	4	1	0	3	0.59
144	SC040	c12c(N(c3c(S1)cccc3)NC(=O)C)cc(cc2)Cl	3.85	290.78	3	1	0	1	0.85
145	SC041	c12c(N(c3c(S1)cccc3)NC(=O)CN(C)C)cc(cc2)Cl	3.84	333.84	4	1	0	3	-0.16
146	SC042	c12c(N(c3c(S1)cccc3)CC=O)cc(cc2)Cl	4.55	275.76	2	0	0	2	2.55
147	SC043	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCCC1)cc(cc2)Cl	4.75	373.91	4	1	0	3	0.75
148	SC044	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCCC1)ccccc2	4.10	339.46	4	1	0	3	0.10
149	SC045	c12c(N(c3c(S1)cccc3)NC(=O)CN(C)C)ccc(c2)Cl	3.84	333.84	4	1	0	3	-0.16
150	**VP1.16**	O=C(OCC)C/N=C1SN(C2=CC=CC=C2)C(C3=CC=CC=C3)=N\1.Br	4.94	339.42	5	0	0	6	-0.06
151	SC046	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCC1)ccc(c2)Cl	4.25	359.88	4	1	0	3	0.25
152	SC047	c12c(N(c3c(S1)cccc3)CCNN1CCCCC1)ccccc2	4.78	325.48	3	1	0	4	1.78
153	SC048	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCCC1)c(ccc2)Cl	4.73	373.91	4	1	0	3	0.73
154	SC049	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCC1)cc(cc2)Cl	4.25	359.88	4	1	0	3	0.25
155	SC050	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCCC1)c(ccc2)Cl	4.73	373.91	4	1	0	3	0.73
156	SC051	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCC1)ccc(c2)Cl	4.25	359.88	4	1	0	3	0.25
157	SC052	c12c(N(c3c(S1)cccc3)N)cccc2	3.46	214.29	2	2	0	0	1.46

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
158	SC054	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCCC1)ccc(c2)Cl	4.75	373.91	4	1	0	3	0.75
159	SC055	c12c(N(c3c(S1)cccc3)NC(=O)CN1CCCCC1)cc(cc2)Cl	4.75	373.91	4	1	0	3	0.75
160	SC056	c12c(N(c3c(S1)cccc3)NC(=O)CN(C)C)ccc(c2)Cl	3.84	333.84	4	1	0	3	-0.16
161	SC057	c12c(N(c3c(S1)cccc3)NC(=O)C)ccc(c2)Cl	3.85	290.78	3	1	0	1	0.85
162	SC059	S1c2c(N=Nc3c1cccc3)ccc(c2)Cl	4.43	246.72	2	0	0	0	2.43
163	SC070	c1(ccc(c(c1)Sc1c(cccc1)[N](=O)O)N)Cl	3.90	280.74	4	2	0	3	-0.10
164	SC074	c1cc(cc(c1)Sc1c(cccc1)NNC(=O)CN1CCCCC1)Cl	4.39	375.93	4	2	0	6	0.39
165	SC083a	c1(c(cc(s1)Cl)C[C@H](N)C)Cl	2.51	210.13	1	2	0	2	1.51
166	SC083b	c1(c(cc(s1)Cl)C[C@@H](N)C)Cl	2.51	210.13	1	2	0	2	1.51
167	SC084	c1(cc(c(s1)Br)Br)I	4.47	367.83	0	0	0	0	4.47
168	SC086	c1(c(c(c(s1)Br)Br)Cl)Br	4.81	355.28	0	0	0	0	4.81
169	SC089a	c1(cccs1)C[C@@H](C)N	1.22	141.24	1	2	0	2	0.22
170	SC089b	c1(cccs1)C[C@H](C)N	1.22	141.24	1	2	0	2	0.22
171	SC090a	c1(c(cc(s1)Cl)Cl)C[C@@H](C)N	2.63	210.13	1	2	0	2	1.63
172	SC090b	c1(c(cc(s1)Cl)Cl)C[C@H](C)N	2.63	210.13	1	2	0	2	1.63
173	SC091a	c1(cc(cs1)Cl)C[C@@H](C)N	1.83	175.68	1	2	0	2	0.83
174	SC091b	c1(cc(cs1)Cl)C[C@H](C)N	1.83	175.68	1	2	0	2	0.83
175	SC093a	c1(c(ccs1)Cl)C[C@H](CCl)N	2.09	210.13	1	2	0	3	1.09
176	SC093b	c1(c(ccs1)Cl)C[C@@H](CCl)N	2.09	210.13	1	2	0	3	1.09
177	SC094a	c1(cc(c(s1)Cl)Cl)C[C@H](CCl)N	2.89	244.57	1	2	0	3	1.89
178	SC094b	c1(cc(c(s1)Cl)Cl)C[C@@H](CCl)N	2.89	244.57	1	2	0	3	1.89
179	SC096	c1(c(c(cs1)Cl)Cl)C[C@H](CCl)N	2.70	244.57	1	2	0	3	1.70
180	SC103	c1(ccc(cc1)Cl)/C(=C/[N](=O)O)C	2.66	197.62	3	0	0	2	-0.34
181	SC113	c1c(cc(c(c1)Sc1c(cccc1)[N](=O)O)N)Cl	3.90	280.74	4	2	0	3	-0.10
182	SC114	c1ccc(c(c1)Sc1c(cccc1)[N](=O)O)Br	4.58	310.17	3	0	0	3	1.58
183	SC115	c1(c(c(c(s1)Cl)Cl)O)C(=O)OC	2.79	227.07	3	1	0	2	-0.22
184	SC116	c1cccc(c1)Nc1ccccc1	3.93	169.23	1	1	0	2	2.93

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
185	SC118	c1ccc(c(c1)Sc1c(cccc1)NNC(=O)C)Br	3.60	337.24	3	2	0	4	0.60
186	SC119	s1c2c([n]([n](c3c1cccc3)C(=O)C)C(=O)C)cccc2	4.45	298.37	4	0	0	0	0.45
187	SC120	c1c(sc(c1O)C(=O)OC)c1ccccc1	3.30	234.28	3	1	0	3	0.30
188	CO1101	c12c(cccc1)nc(n2Cc1sccc1)c1sccc1	4.89	296.42	8	5	0	0	2.89
189	CO1102	c12c(cccc1)[nH]c([nH]2)c1cccs1	3.34	201.27	9	4	0	2	1.34
190	CO1103	c12c(cccc1)nc([nH]2)c1ccc(s1)C	3.55	214.29	2	1	0	1	1.55
191	CO1104	c12c(cccc1)[nH]c(n2)c1ccccc1	3.55	194.24	7	4	0	0	1.55
192	CO1105	c12c(cccc1)[nH]c(n2)c1cscc1	3.31	200.27	7	4	0	1	1.31
193	CO1106	c12c(cccc1)nc(n2Cc1cscc1)c1cscc1	4.38	296.42	7	4	0	1	2.38
194	CO2103	c12c(cccc1)nc(c(n2)c1sccc1)c1sccc1	4.65	294.40	2	0	0	2	2.65
195	CO2106	c12c(cccc1)nc(c(n2)c1occc1)c1occc1	3.36	262.27	4	0	0	2	1.36
196	CO2107	[C@H]12[C@@H](CCCC1)N=C(C(=N2)c1ccccc1)c1ccccc1	4.62	288.39	2	0	0	2	2.62
197	CO2109	c12c(CCCC1)nc(c(n2)c1ccccc1)c1ccccc1	4.82	286.38	2	0	0	2	2.82
198	CO2110	[C@@H]12[C@H](CCCC1)N=C(C(=N2)c1ccccc1)c1ccccc1	4.62	288.39	2	0	0	2	2.62
199	CO2301	n1c(c(nc2c1nccc2)c1ccccc1)c1ccccc1	4.18	283.33	3	0	0	2	1.18
200	CO2302	n1c(c(nc2c1cncc2)c1ccccc1)c1ccccc1	3.98	283.33	3	0	0	2	0.98
201	CO4002	c1(ccn([n]1C)Cl)C	1.69	237.06	2	0	0	1	0.69
202	SC122	c12c(sc(c1O)C(=O)OCC)CCC2	2.41	212.27	3	1	0	3	-0.59
203	SC126	c1(csc(c1O)C(=O)OC)c1ccccc1	3.10	234.28	3	1	0	3	0.10
204	SC132	c1c(sc(c1O)C(=O)OCC)c1ccccc1	3.67	248.30	3	1	0	4	0.67
205	SC130	c1c(sc(c1O)C(=O)OC)c1ccccc1	3.30	234.28	3	1	0	3	0.30
206	SC127	c1(csc(c1O)C(=O)OC)c1ccccc1	3.10	234.28	3	1	0	3	0.10
207	SC133	c1(c(scc1OC[C@@H](CNC(C)(C)C)O)Cl)C	3.09	277.82	3	2	0	6	0.09
208	SC134	s1ccc2c1c(c(s2)C(=O)OC)OC[C@H]1CO1	2.55	270.33	4	0	0	5	-0.45
209	SC138	c1(cc(sc1C(=O)OC)c1ccccc1)O	3.30	234.28	3	1	0	3	0.30
210	SC139	c1(csc(c1O)C(=O)OC)Sc1ccccc1	3.27	266.34	3	1	0	4	0.27
211	SC140	c1csc2c1sc(c2O)C(=O)OC	2.44	214.27	3	1	0	2	-0.56

	CODE	SMILE	LogP	MW	nON	nOHNH	nviolations	nrotb	LogBB
212	SC141	c1(c(sc(c1O)C(=O)CC)Sc1ccccc1)C	4.58	278.40	2	1	0	4	2.58
213	SC142	c1(c(sc(c1O)C(=O)OC)Cl)Cl	2.79	227.07	3	1	0	2	-0.22
214	SC143	c1(c(sc(c1O)C(=O)OC)Cl)c1ccccc1	3.90	268.72	3	1	0	3	0.90
215	SC145	c1(c(sc(c1OC)C(=O)OC)OC)c1ccccc1	3.56	278.33	4	0	0	5	-0.44
216	SC154	c1(c(sc(c1OC)C(=O)OC)C)Cl	2.48	220.68	3	0	0	3	-0.52
217	SC155	c1(c(scc1OC[C@@H](CNC(C)(C)C)O)Cl)C	3.09	277.82	3	2	0	6	0.09
218	SC156	s1cc(OC[C@@H](CNC(C)(C)C)O)c2c1ccs2	2.98	285.43	3	2	0	6	-0.02
219	SC159	c1(c(sc(c1O)C(=O)OC)Cl)C	2.56	206.65	3	1	0	2	-0.44
220	SV047	C1CN=C(NC1)SCl	1.66	256.11	2	1	0	2	-0.34

Tabla S7. Hidden neurons (input parameter) and activity prediction for each molecule of the virtual screening

		CODES INPUT				OUTPUT
	CODE	**P1**	**P2**	**P3**	**P4**	**NNE3A**
1	AM003	0.646981	0.50407	0.993123	0.433044	Moderate
2	AM019	0.075575	0.030073	0.056933	0.579541	Moderate
3	AM032	0.039968	0.02834	0.080709	0.646056	Moderate
4	CG056	0.360127	0.761412	0.786028	0.277918	Inactive
5	AM047	0.954122	0.231238	0.096872	0.722267	Active
6	AM048	0.069716	0.449017	0.477391	0.889873	Moderate
7	AM048	0.069716	0.449017	0.477391	0.889873	Moderate
8	AM049	0.992739	0.901818	0.968266	0.187912	Inactive
9	AM052	0.973953	0.951481	0.840147	0.990882	Inactive
10	AM053	0.181515	0.201039	0.220135	0.687929	Inactive
11	AM054	0.973953	0.951481	0.840147	0.990882	Inactive
12	AM054	0.973953	0.951481	0.840147	0.990882	Inactive
13	AM056	0.973953	0.951481	0.840147	0.990882	Inactive
14	AM056	0.973953	0.951481	0.840147	0.990882	Inactive
15	AM057	0.973953	0.951481	0.840147	0.990882	Inactive
16	AM080	0.29542	0.312935	0.357	0.962855	Inactive
17	AC004	0.98703	0.855442	0.994864	0.879907	Moderate
18	AC010	0.957765	0.954347	0.92282	0.955923	Moderate
19	AC012	0.968477	0.972872	0.960112	0.800413	Moderate
20	AC014	0.864613	0.988576	0.948761	0.969593	Moderate
21	AC016	0.015888	0.495793	0.602327	0.564297	Moderate
22	AC023	0.959196	0.923104	0.784099	0.968428	Inactive
23	AC027	0.987427	0.941515	0.860259	0.982507	Inactive
24	CG106	0.22051	0.482973	0.265691	0.963187	Inactive
25	CG108	0.850859	0.796238	0.949868	0.956023	Moderate
26	AC033	0.976578	0.979627	0.974184	0.767305	Inactive
27	AC044	0.795491	0.618753	0.528143	0.930132	Inactive
28	AC052	0.812415	0.970408	0.975954	0.959967	Moderate
29	AC061	0.384145	0.317166	0.996089	0.618574	Active
30	AC068	0.720327	0.061557	0.613571	0.47946	Inactive
31	AC092	0.625804	0.830321	0.17809	0.32794	Moderate
32	AC093	0.071158	0.685921	0.939931	0.434535	Moderate
33	AC098	0.129303	0.051769	0.90818	0.982267	Moderate
34	AC105	0.154034	0.448104	0.845114	0.574054	Active
35	CG008	0.042355	0.046759	0.733485	0.036279	Active
36	CG013	0.018732	0.034463	0.896256	0.014484	Active
37	CG015	0.028916	0.887116	0.036391	0.028687	Active
38	CG019	0.019219	0.015416	0.044378	0.823456	Moderate
39	CG026	0.931867	0.020498	0.009128	0.031542	Active
40	CG035	0.020549	0.020641	0.772693	0.031912	Active

	CODES INPUT					OUTPUT
	CODE	P1	P2	P3	P4	NNE3A
41	CG036	0.034542	0.042274	0.676817	0.020171	Active
42	CG059	0.92735	0.027111	0.04786	0.013748	Active
43	CG060	0.740186	0.008658	0.004119	0.080253	Active
44	CG062	0.01724	0.027607	0.83982	0.0232	Active
45	CG067	0.081005	0.846374	0.013299	0.022367	Active
46	CG069	0.018708	0.779637	0.037718	0.026537	Active
47	CG072	0.11462	0.740787	0.069565	0.752178	Moderate
48	CG073	0.017942	0.804116	0.008505	0.058193	Moderate
49	CG074	0.036371	0.004972	0.827688	0.08324	Active
50	CG086	0.856686	0.029058	0.027358	0.021996	Active
51	CG088	0.999013	0.907471	0.994804	0.815858	Moderate
52	CG090	0.874682	0.228732	0.002806	0.001513	Moderate
53	CG093	0.054696	0.052219	0.597347	0.053933	Active
54	CG099	0.92136	0.929339	0.228564	0.026661	Active
55	CG101	0.776965	0.951308	0.956743	0.932058	Moderate
56	AE009	0.948169	0.786233	0.985223	0.012486	Moderate
57	AE010	0.951684	0.523389	0.484239	0.873251	Inactive
58	AE084	0.979397	0.96467	0.854025	0.016546	Moderate
59	EF016	0.647869	0.976075	0.985607	0.735824	Moderate
60	EF017	0.252488	0.016913	0.0174	0.036694	Active
61	EF019	0.993096	0.831279	0.949672	0.551415	Inactive
62	AM094	0.698238	0.783135	0.587045	0.982615	Moderate
63	AM096	0.994103	0.968392	0.987458	0.756826	Inactive
64	AM0101	0.387532	0.2381	0.466592	0.514519	Moderate
65	AM106	0.983981	0.055363	0.982152	0.011205	Moderate
66	TC2.30	0.252344	0.784158	0.162189	0.638304	Moderate
67	TC2.41	0.940325	0.732683	0.98625	0.986903	Moderate
68	TC2.42	0.994182	0.976292	0.967515	0.121537	Moderate
69	TC2.43	0.94305	0.976532	0.667627	0.972141	Moderate
70	TC2.44	0.97079	0.084121	0.824111	0.772783	Moderate
71	TC2.45	0.943329	0.992825	0.805749	0.95616	Moderate
72	TC2.47	0.958718	0.989111	0.757928	0.99801	Moderate
73	TC2.51	0.988615	0.918291	0.826508	0.849174	Inactive
74	TC3.1	0.632092	0.899358	0.742268	0.995395	Moderate
75	TC3.9	0.945494	0.955056	0.9949	0.999908	Moderate
76	TC3.13	0.998352	0.993675	0.9649	0.998837	Moderate
77	TC3.14	0.899312	0.955049	0.999132	0.144836	Moderate
78	TC3.16	0.815661	0.989187	0.99608	0.725864	Moderate
79	TC3.17	0.96266	0.640989	0.973966	0.996762	Moderate
80	TC3.22	0.933247	0.990717	0.655515	0.694386	Moderate
81	TC3.23	0.958243	0.724496	0.824042	0.700614	Inactive
82	TC3.24	0.999257	0.927163	0.989845	0.930332	Moderate
83	TC3.28	0.912148	0.860432	0.872921	0.956881	Moderate
84	TC3.29	0.892964	0.993092	0.920857	0.960428	Moderate

	CODES INPUT					OUTPUT
	CODE	**P1**	**P2**	**P3**	**P4**	**NNE3A**
85	TC3.30	0.997316	0.584151	0.616186	0.991131	Inactive
86	TC3.32	0.957181	0.847148	0.576076	0.996173	Moderate
87	TC3.36	0.718472	0.489575	0.998227	0.988654	Moderate
88	TC3.47	0.792155	0.86635	0.965556	0.977626	Moderate
89	S016	0.995007	0.995483	0.983526	0.819976	Moderate
90	S015	0.091647	0.141366	0.670239	0.935058	Inactive
91	S022	0.82943	0.401508	0.34919	0.20511	Moderate
92	S023	0.81734	0.849885	0.891995	0.906192	Moderate
93	S025	0.9934	0.966413	0.981011	0.64557	Inactive
94	S026	0.920309	0.226057	0.815886	0.304833	Inactive
95	S027	0.895419	0.961495	0.956591	0.966145	Moderate
96	S028	0.131616	0.818974	0.06542	0.668761	Moderate
97	S029	0.50798	0.988891	0.99259	0.77189	Moderate
98	S033	0.942765	0.915024	0.26918	0.126082	Active
99	S035	0.812543	0.54843	0.937858	0.418083	Inactive
100	S037	0.131658	0.841031	0.352617	0.385105	Moderate
101	S038	0.7339	0.962824	0.636369	0.994711	Moderate
102	S041	0.996458	0.992694	0.769943	0.863159	Moderate
103	S043	0.487171	0.884561	0.98331	0.964499	Active
104	S045	0.916335	0.970672	0.989132	0.96047	Moderate
105	S047	0.983357	0.838205	0.994765	0.782272	Moderate
106	S048	0.990416	0.922879	0.997135	0.960594	Moderate
107	S049	0.926405	0.774995	0.798642	0.129012	Inactive
108	**VP0.1**	0.703623	0.027812	0.004	0.107048	Active
109	SC003	0.994097	0.968727	0.90412	0.775071	Inactive
110	SC004a	0.983341	0.820646	0.736874	0.910604	Inactive
111	SC004b	0.983341	0.820646	0.736874	0.910604	Moderate
112	SC004c	0.983341	0.820646	0.736874	0.910604	Moderate
113	SC004d	0.983341	0.820646	0.736874	0.910604	Moderate
114	SC005	0.865749	0.185696	0.097944	0.779632	Active
115	SC006	0.750098	0.567481	0.831145	0.154949	Inactive
116	SC007a	0.385744	0.992295	0.038351	0.011149	Active
117	SC007b	0.923743	0.983726	0.882052	0.965654	Moderate
118	SC007c	0.018269	0.000221	0.517114	0.007859	Active
119	SC007d	0.018269	0.000221	0.517114	0.007859	Active
120	SC008	0.865749	0.185696	0.097944	0.779632	Active
121	SC009	0.750098	0.567481	0.831145	0.154949	Inactive
122	SC013	0.385744	0.992295	0.038351	0.011149	Active
123	SC013	0.385744	0.992295	0.038351	0.011149	Moderate
124	SC015a	0.923743	0.983726	0.882052	0.965654	Moderate
125	SC015b	0.923743	0.983726	0.882052	0.965654	Moderate
126	SC016	0.018269	0.000221	0.517114	0.007859	Active
127	SC018	0.942095	0.968073	0.944532	0.859359	Moderate
128	SC019	0.843217	0.914222	0.987228	0.945192	Moderate

	CODES INPUT					OUTPUT
	CODE	**P1**	**P2**	**P3**	**P4**	**NNE3A**
129	SC109a	0.975144	0.959479	0.960841	0.980686	Moderate
130	SC109b	0.975144	0.959479	0.960841	0.980686	Moderate
131	SC023	0.621918	0.697046	0.972368	0.737418	Active
132	SC024	0.98822	0.852607	0.135973	0.062941	Active
133	SC025	0.629357	0.964304	0.874849	0.187881	Inactive
134	SC027a	0.916217	0.432778	0.131367	0.473901	Moderate
135	SC027b	0.916217	0.432778	0.131367	0.473901	Moderate
136	SC030	0.053888	0.02107	0.455218	0.009373	Active
137	SC031	0.902784	0.891084	0.736955	0.532509	Inactive
138	SC034	0.475867	0.005765	0.003716	0.019339	Active
139	SC035	0.602799	0.035635	0.051793	0.129587	Moderate
140	SC036	0.995584	0.984071	0.988153	0.993025	Moderate
141	SC037	0.136507	0.101676	0.749694	0.021657	Active
142	SC038	0.996162	0.984482	0.964425	0.96959	Moderate
143	SC039	0.967461	0.951828	0.911369	0.760654	Inactive
144	SC040	0.648571	0.833029	0.09525	0.903295	Moderate
145	SC041	0.826721	0.86411	0.992027	0.865264	Moderate
146	SC042	0.994695	0.920104	0.959523	0.982524	Moderate
147	SC043	0.152471	0.00729	0.546227	0.000841	Active
148	SC044	0.839709	0.649083	0.354361	0.933078	Inactive
149	SC045	0.960413	0.521084	0.898102	0.998129	Inactive
150	**VP1.16**	0.009814	0.798164	0.145732	0.003521	Active
151	SC046	0.11147	0.056888	0.058049	0.659519	Moderate
152	SC047	0.778927	0.892843	0.881091	0.99175	Moderate
153	SC048	0.05953	0.60935	0.029967	0.032362	Moderate
154	SC049	0.602799	0.035635	0.051793	0.129587	Moderate
155	SC050	0.05953	0.60935	0.029967	0.032362	Moderate
156	SC051	0.11147	0.056888	0.058049	0.659519	Moderate
157	SC052	0.386625	0.953441	0.288397	0.947091	Moderate
158	SC054	0.475867	0.005765	0.003716	0.019339	Active
159	SC055	0.152471	0.00729	0.546227	0.000841	Active
160	SC056	0.960413	0.521084	0.898102	0.998129	Inactive
161	SC057	0.562126	0.349673	0.087205	0.820645	Inactive
162	SC059	0.897659	0.409392	0.994277	0.984534	Inactive
163	SC070	0.993678	0.998652	0.99696	0.983607	Moderate
164	SC074	0.705914	0.004215	0.17499	0.003067	Moderate
165	SC083a	0.163234	0.791742	0.128304	0.946791	Moderate
166	SC083b	0.589843	0.63512	0.977338	0.931913	Active
167	SC084	0.475595	0.994351	0.600943	0.73035	Moderate
168	SC086	0.475595	0.994351	0.600943	0.73035	Moderate
169	SC089a	0.976649	0.969413	0.966917	0.867704	Moderate
170	SC089b	0.976649	0.969413	0.966917	0.867704	Moderate
171	SC090a	0.103711	0.93235	0.235906	0.596884	Moderate
172	SC090b	0.103711	0.93235	0.235906	0.596884	Moderate

	CODES INPUT					OUTPUT
	CODE	P1	P2	P3	P4	NNE3A
173	SC091a	0.993096	0.939206	0.986876	0.879903	Moderate
174	SC091b	0.993096	0.939206	0.986876	0.879903	Moderate
175	SC093a	0.892427	0.442443	0.756128	0.18351	Inactive
176	SC093b	0.892427	0.442443	0.756128	0.18351	Inactive
177	SC094a	0.207088	0.638318	0.07177	0.939913	Moderate
178	SC094b	0.207088	0.638318	0.07177	0.939913	Moderate
179	SC096	0.565474	0.437244	0.072731	0.94398	Moderate
180	SC103	0.462694	0.701835	0.135976	0.931421	Inactive
181	SC113	0.201281	0.764014	0.737779	0.49553	Moderate
182	SC114	0.988207	0.971045	0.945724	0.159186	Inactive
183	SC115	0.953313	0.909668	0.956284	0.942964	Moderate
184	SC116	0.901485	0.588961	0.701257	0.553794	Inactive
185	SC118	0.809545	0.130194	0.243296	0.455275	Moderate
186	SC119	0.006865	0.21455	0.570236	0.03064	Active
187	SC120	0.194914	0.481644	0.925033	0.270904	Moderate
188	CO1101	0.960446	0.879399	0.907751	0.978067	Moderate
189	CO1102	0.989246	0.983634	0.93894	0.811026	Inactive
190	CO1103	0.990117	0.936669	0.854229	0.989988	Inactive
191	CO1104	0.837912	0.945261	0.972918	0.959639	Moderate
192	CO1105	0.953594	0.939595	0.871896	0.964808	Moderate
193	CO1106	0.992762	0.964211	0.942656	0.996925	Moderate
194	CO2103	0.110622	0.258619	0.698966	0.824974	Moderate
195	CO2106	0.148093	0.732172	0.224327	0.741617	Moderate
196	CO2107	0.052539	0.984946	0.001294	0.003892	Active
197	CO2109	0.234712	0.181612	0.116858	0.872373	Inactive
198	CO2110	0.950512	0.061935	0.001056	0.000506	Active
199	CO2301	0.020459	0.892987	0.039398	0.824574	Moderate
200	CO2302	0.965779	0.932472	0.976835	0.953736	Moderate
201	CO4002	0.965779	0.932472	0.976835	0.953736	Moderate
202	SC122	0.941895	0.887017	0.925845	0.952871	Moderate
203	SC126	0.270483	0.951403	0.895671	0.07501	Active
204	SC132	0.712161	0.082149	0.432934	0.946884	Inactive
205	SC130	0.194914	0.481644	0.925033	0.270904	Moderate
206	SC127	0.270483	0.951403	0.895671	0.07501	Moderate
207	SC133	0.111566	0.882579	0.630823	0.230165	Inactive
208	SC134	0.999757	0.654171	0.841588	0.998497	Inactive
209	SC138	0.859402	0.175321	0.278504	0.959012	Inactive
210	SC139	0.988597	0.179453	0.120231	0.828116	Active
211	SC140	0.912975	0.980572	0.97316	0.850134	Moderate
212	SC141	0.131606	0.082863	0.656117	0.718082	Moderate
213	SC142	0.110833	0.820911	0.415595	0.980798	Moderate
214	SC143	0.160825	0.074056	0.95419	0.888182	Moderate
215	SC145	0.036413	0.039982	0.672389	0.901072	Inactive
216	SC154	0.45842	0.972553	0.143912	0.89637	Moderate

		CODES INPUT				OUTPUT
	CODE	**P1**	**P2**	**P3**	**P4**	**NNE3A**
217	SC155	0.111566	0.882579	0.630823	0.230165	Inactive
218	SC156	0.788695	0.990721	0.997533	0.804252	Moderate
219	SC159	0.955765	0.972385	0.804334	0.987875	Inactive
220	SV047	0.989768	0.848763	0.941183	0.964177	Moderate
221	**Rolipram**	0.641492	0.694212	0.560717	0.276594	Inactive
222	**MR1.51**	0.065314	0.045325	0.792774	0.024013	Active

Table S8. Experimental results of the compounds from virtual screening

	CODE	% inhibition of PDE7A @10 μM	Purity by HPLC
1	AC105	18.43	>99%
2	AM047	60.00	97.96%
3	CG015	24.83	96.32%
4	CG062	2.89	>99%
5	CG060	7.36	>99%
6	CG067	12.51	>99%
7	CG069	17.96	>99%
8	CG074	10.12	>99%
9	CG093	22.52	95.24%
10	EF17A	23.82	>99%
11	VP0.1[a]	72.40	>99%
12	SC005	18.42	>99%
13	SC007a	3.73	98.85%
14	SC008	10.09	>99%
15	S033	2.10	95.73%
16	SC034	7.22	96.25%
17	SC055	1.68	99.00%
18	SC083	8.30	98.43%
19	SC119	51.07	>99%
20	SC126	7.06	>99%
21	VP1.16	82.00	N. D.[b]

[a] ^{1}H-NMR (400MHz, acetone-d_6): δ 11.23 (s, 1H), 4.25 (t, J = 6.5 Hz, 2H), 3.73 (t, J = 6.6 Hz, 2H), 3.01 – 2.92 (m, 1H), 2.76 – 2.62 (m, 4H), 2.30 – 2.12 (m, 2H), 1.95 – 1.83 (m, 2H), 1.82 – 1.71 (m, 2H), 1.43 – 1.25 (m, 2H), 1.06 (d, J = 6.5 Hz, 3H), 1.02 (t, J = 7.4 Hz, 3H).
^{13}C-NMR (100MHz, acetone-d_6): δ 168.89, 166.25, 147.68, 130.44, 126.01, 111.25, 66.16, 44.31, 33.28, 32.20, 31.19, 28.20, 26.28, 22.04, 20.96, 10.34.

[b] The purity of compound VP 1.16 was determined by elemental analysis and its structural characterizacion is reported in *J. Med. Chem.* **2012**, *55*, 1645-1661

References

1. Pitts, W. J., Vaccaro, W., Huynh, T., Leftheris, K., Roberge, J. Y., Barbosa, J., Guo, J., Brown, B., Watson, A., Donaldson, K., Starling, G. C., Kiener, P. A., Poss, M. A., Dodd, J. H., and Barrish, J. C. (2004) Identification of purine inhibitors of phosphodiesterase 7 (PDE7). *Bioorg. Med. Chem. Lett. 14*, 2955-2958.

2. Smith, S. J., Cieslinski, L. B., Newton, R., Donnelly, L. E., Fenwick, P. S., Nicholson, A. G., Barnes, P. J., Barnette, M. S., and Giembycz, M. A. (2004) Discovery of BRL 50481 [3-(N,N-dimethylsulfonamido)-4-methyl-nitrobenzene], a selective inhibitor of phosphodiesterase 7: in vitro studies in human monocytes, lung macrophages, and CD8+ T-lymphocytes. *Mol. Pharmacol. 66*, 1679-1689.

3. Grundler, G., Gutterer, B., Hatzelmann, A., Stadlwieser, J., Sterk, G., and Weinbrenner, S. (2002) (Dihydro)isoquinoline derivatives as phosphodiesterase inhibitors. BYK Gulden Lomberg Chemische Fabrik. BMBH WO0240450.

4. Grundler, G., Gutterer, B., Hatzelmann, A., Stadlwieser, J., Sterk, G., and Weinbrenner, S. (2002) Dihydroisoquinolines as novel phosphodiesterase inhibitors. BKY Gulden Lomberg Chemische Fabrik. GMBH WO0240449.

5. Lorthiois, E., Bernardelli, P., Vergne, F., Oliveira, C., Mafroud, A. K., Proust, E., Heuze, L., Moreau, F., Idrissi, M., Tertre, A., Bertin, B., Coupe, M., Wrigglesworth, R., Descours, A., Soulard, P., and Berna, P. (2004) Spiroquinazolinones as novel, potent, and selective PDE7 inhibitors. Part 1. *Bioorg. Med. Chem. Lett. 14*, 4623-4626.

6. Bernardelli, P., Vergne, F., Mendes, C., and Ducrot, P. (2004) New Spirocondensed quinazolinones and their use as phosphodiesterase inhibitors. Warner-lambert, WO2004/026818.

7. Vergne, F., Bernardelli, P., Lorthiois, E., Pham, N., Proust, E., Oliveira, C., Mafroud, A. K., Royer, F., Wrigglesworth, R., Schellhaas, J., Barvian, M., Moreau, F., Idrissi, M., Tertre, A., Bertin, B., Coupe, M., Berna, P., and Soulard, P. (2004) Discovery of thiadiazoles as a novel structural class of potent and selective PDE7 inhibitors. Part 1: design, synthesis and structure-activity relationship studies. *Bioorg. Med. Chem. Lett. 14*, 4607-4613.

8. Jones, N. A., Leport, M., Holand, T., Vos, T., Morgan, M., Fink, M., Pruniaux, M. P., Berthelier, C., O'Connor, B. J., Bertrand, C., and Page, C. P. (2007) Phosphodiesterase (PDE) 7 in inflammatory cells from patients with asthma and COPD. *Pulm. Pharmacol. Ther. 20*, 60-68.

9. Yamamoto, S., Sugahara, S., Ikeda, K., and Shimizu, Y. (2006) Pharmacological profile of a novel phosphodiesterase 7A and -4 dual inhibitor, YM-393059, on acute and chronic inflammation models. *Eur. J. Pharmacol. 550*, 166-172.

10. Pitts, W. J., Watson, A. J., and Dodd, J. H. (2002) Dual inhibitors of PDE7 and PDE4. Bristol-Myers Squibb Company. WO02088080.

11. Castaño, T., Wang, H., Campillo, N. E., Ballester, S., Gonzalez-Garcia, C., Hernandez, J., Perez, C., Cuenca, J., Perez-Castillo, A., Martinez, A., Huertas, O., Gelpi, J. L., Luque, F. J., Ke, H., and Gil, C. (2009) Synthesis, structural analysis, and biological evaluation of thioxoquinazoline derivatives as phosphodiesterase 7 inhibitors. *ChemMedChem 4*, 866-876.

12. Vergne, F., Bernardelli, P., Lorthiois, E., Pham, N., Proust, E., Oliveira, C., Mafroud, A. K., Ducrot, P., Wrigglesworth, R., Berlioz-Seux, F., Coleon, F., Chevalier, E., Moreau, F., Idrissi, M., Tertre, A., Descours, A., Berna, P., and Li, M. (2004) Discovery of thiadiazoles as a novel structural class of potent and selective PDE7

inhibitors. Part 2: metabolism-directed optimization studies towards orally bioavailable derivatives. *Bioorg. Med. Chem. Lett. 14*, 4615-4621.