Supplementary Information

Identification of Novel Rho-Kinase-II Inhibitors with Vasodilatory Activity

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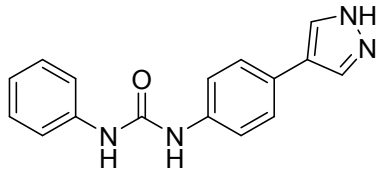
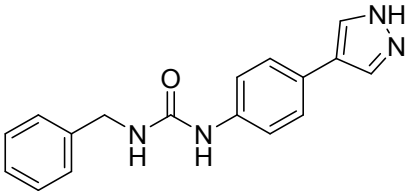
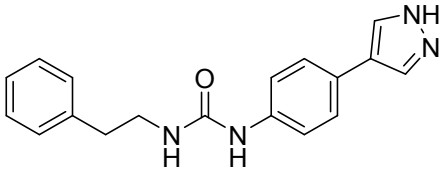
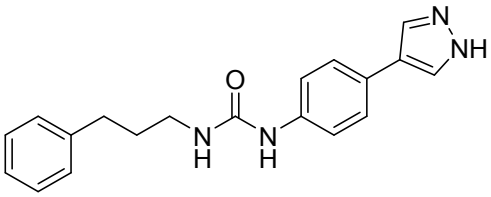
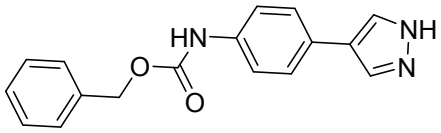
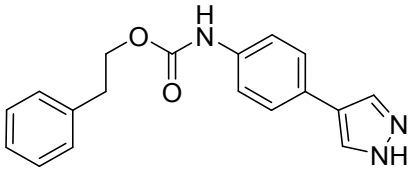
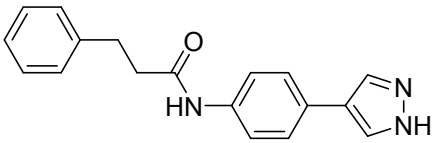
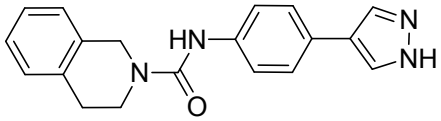
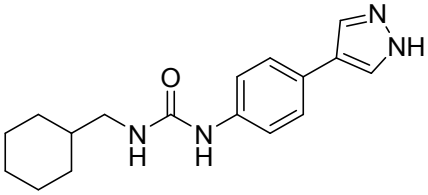
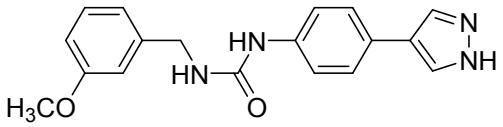
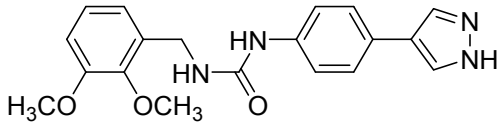
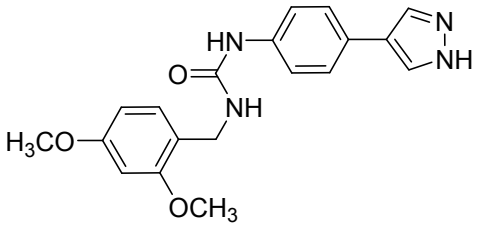
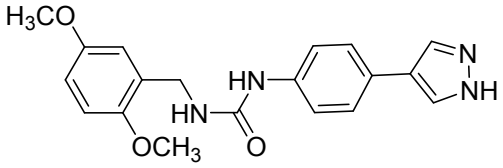
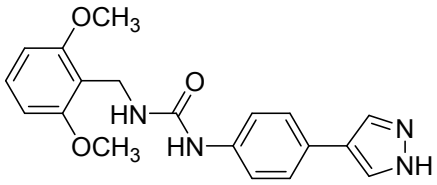
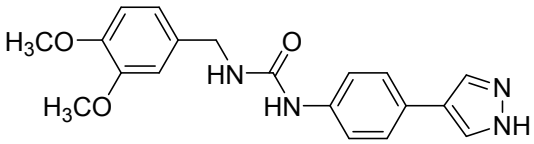
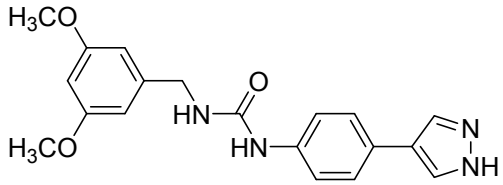
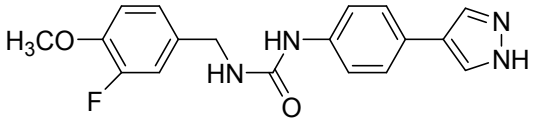
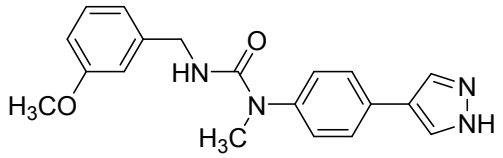
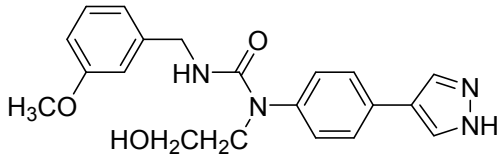
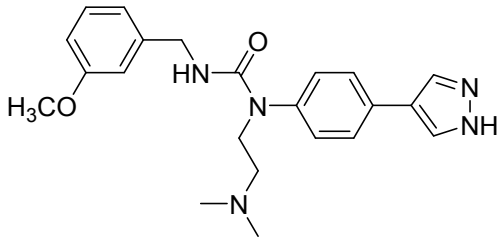
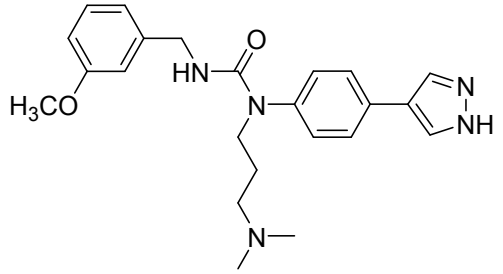
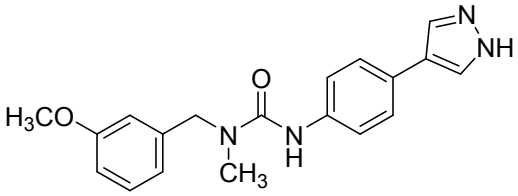
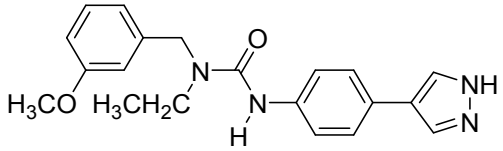
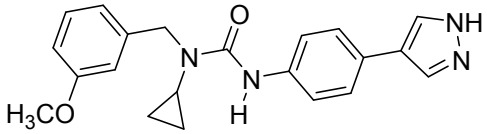
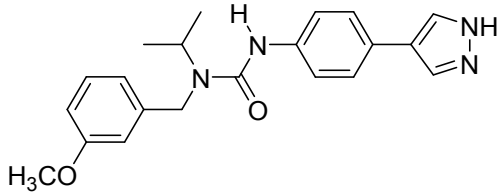
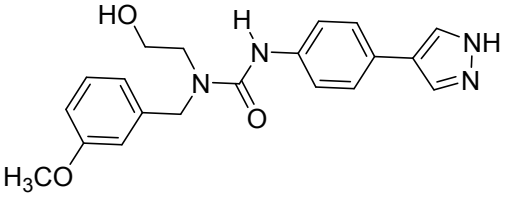
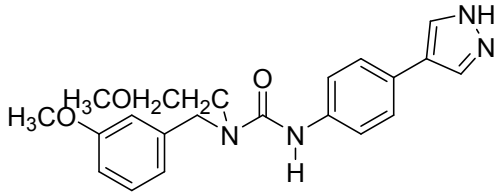
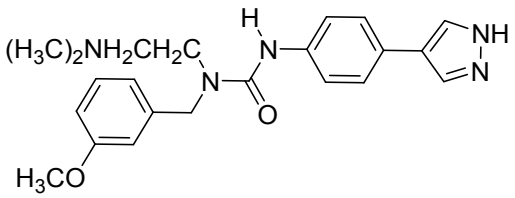
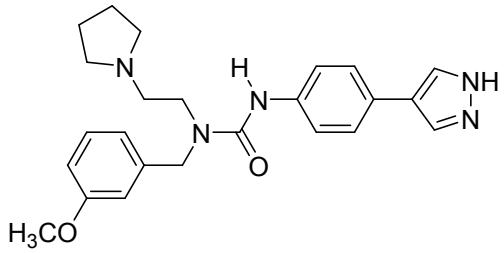
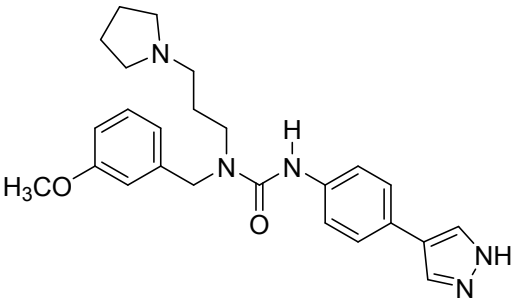
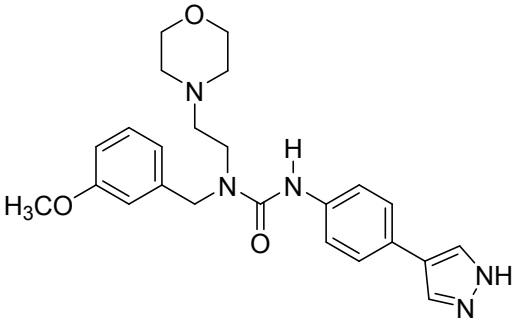
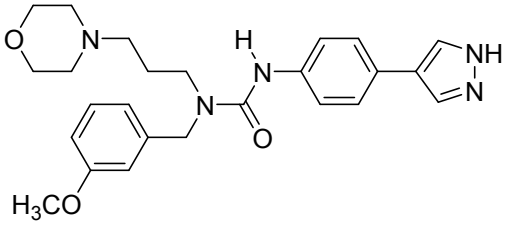
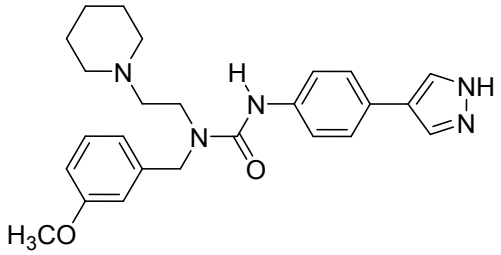
1	5a		304
2	5b		18
3	5c		88
4	5d		1017
5	5e		7
6	5f		55
7	5g		24
8	5h		280
9	5i		751

10	5j		2
11	5k		253
12	5l		331
13	5m		570
14	5n		924
15	5o		425
16	5p		281
17	5q		357
18	8a		87
19	8b		611

20	8c		2984
21	8e		3324
22	12a		1
23	12b		1
24	12c		1
25	12d		3
26	12e		1
27	12f		17

28	12h		1
29	12i		3
30	12j		5
31	12k		13
32	12l		4
33	12m		5

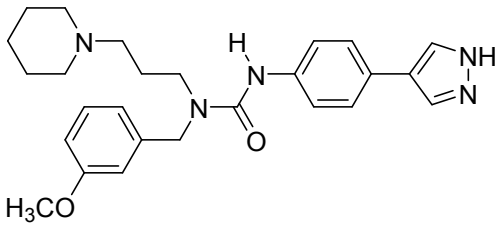
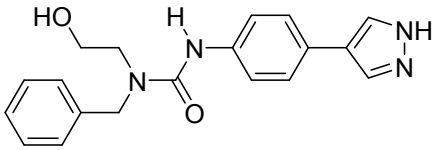
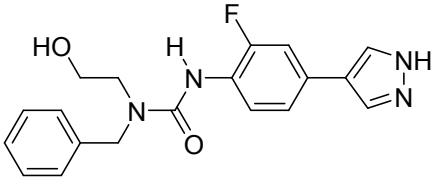
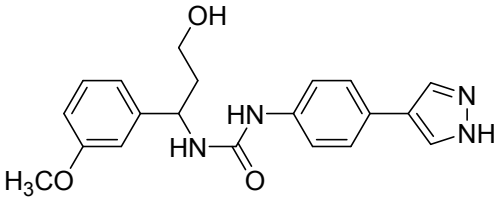
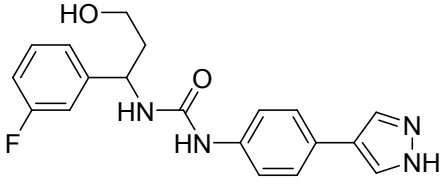
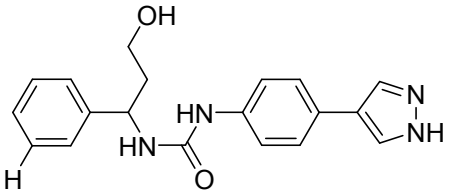
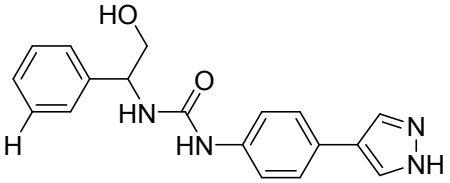
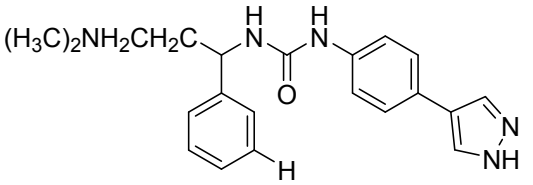
34	12n		4
35	12o		12
36	12p		14
37	14a		2
38	14b		2
39	14c		1
40	14d		2
41	14e		2

Table S2. Statistical results of the best 10 pharmacophore hypothesis generations

Hypo	RMSD	Correlation	Weight	Configuration	Feature
1	0.98	0.90	2.56	14.93	2HBA 1HY 1HBD
2	1.43	0.79	1.74	14.93	2HBD 1HY 1HBA
3	1.34	0.83	6.69	14.93	2HBA 1HY 1HBD
4	1.48	0.76	1.56	14.93	1HBA 1HBD 1HY 1RA
5	1.53	0.75	1.92	14.93	1HBA 1HBD 1HY 1RA
6	1.55	0.74	1.17	14.93	1HBA 2HBD 1HY
7	1.57	0.73	1.27	14.93	1HBA 1HBD 1HY 1RA
8	1.57	0.73	1.12	14.93	1HBA 1HBD 1HY 1RA
9	1.60	0.72	1.15	14.93	2HBA 1HY 1HBD
10	1.62	0.71	1.14	14.93	1HBA 1HBD 1HY 1RA

Table S3. Results of various parameters calculated during Güner-Henry scoring

S. No.	Parameter	ROCK-II inhibitors
1	Total molecules in database (D)	440
2	Total number of actives in database (A)	360
3	Total hits (Ht)	318
4	Active hits (Ha)	298
5	%Yield of actives[(Ha/Ht)×100]	94
6	Enrichment factor (E) [(Ha×D)/(Ht×A)	0.77
7	False positives (Ht-Ha)	20
8	Goodness of hit score	0.68

Table S4. List of selected hits from NCI database

S. No.	Name of hits	Estimated Value (nm)	Fit Value
1	NSC 2888	4.67	8.29
2	NSC 4231	4.68	8.31
3	NSC 2488	12.31	7.87

4	NSC 3597	15.37	7.77
5	NSC 2101	19.11	7.67
6	NSC 3837	19.15	7.66
7	NSC 3596	20.02	7.65

Table S5. Experimental and predicted activity values of training set and test set compounds

Compound name	Experimental activities	Predicted activities
1	304	160.49
2	18	79.16
5	7	55.98
7	24	59.15
8	280	101.70
10	2	6.85
11	253	110.02
12	331	72.70
13	570	92.29
15	425	81
16	281	35.72
19	611	382.26
20	2984	2797.13
21	3324	5993.95
25	3	7.38
26	1	5.10
27	17	8.49
28	1	0.54
29	3	2.59
31	13	18.56
32	4	7.48
33	5	5.17
34	4	3.68
36	14	34.61
37	2	6.85
39	1	1.46
40	2	5.10
5c*	88	59.21
5d*	1017	70.92
5f*	55	59.77
5i*	751	65.64
5n*	924	122.16
5q*	357	63.36
12a*	1	14.71
12o*	12	37.63
14a*	2	6.58
14b*	2	2.77

14d*	2	0.50

*Test set Compounds

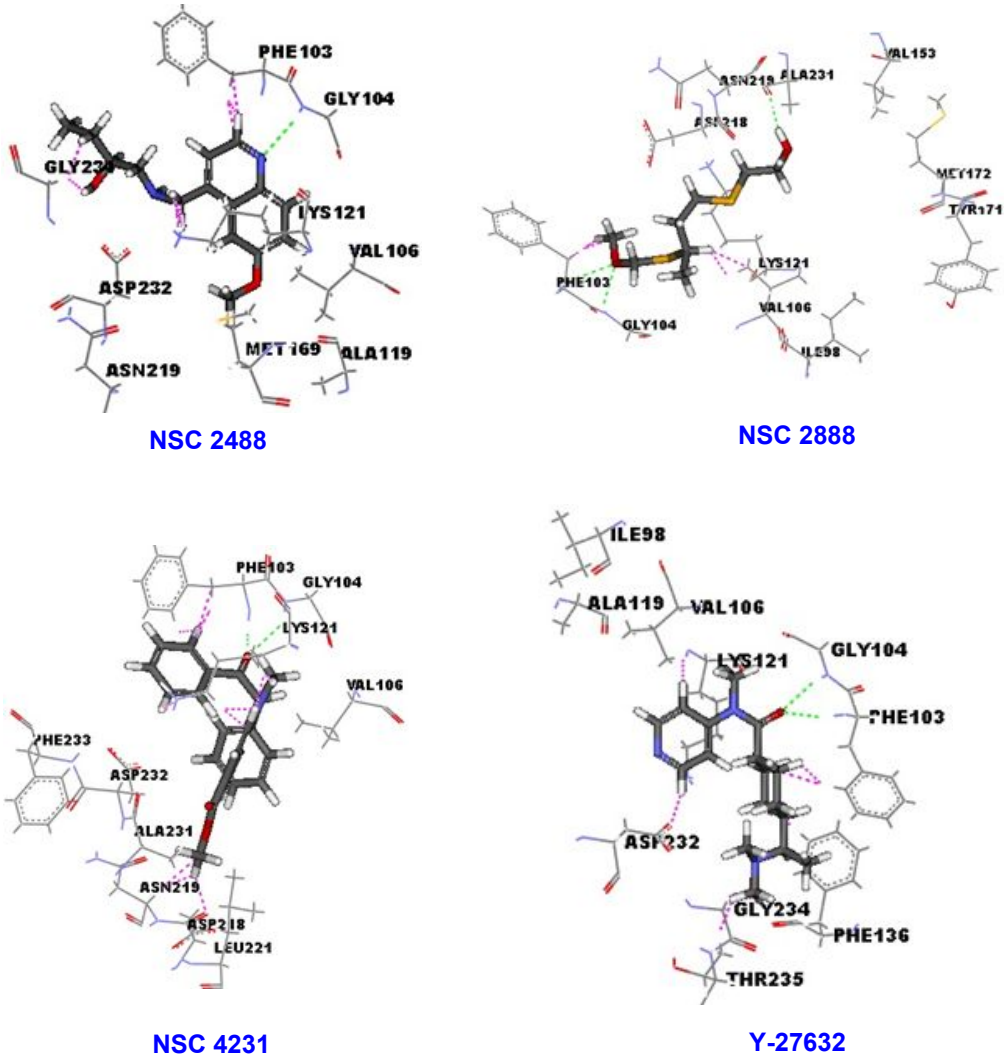


Figure S1. Docked conformations of NCI hits and the standard drug on the active site of Rho-kinase. Green dotted lines characterize hydrogen binding interaction. Pink dotted lines represent Van der Waals interaction and some of the amino acids around the structure created hydrophobic environment.