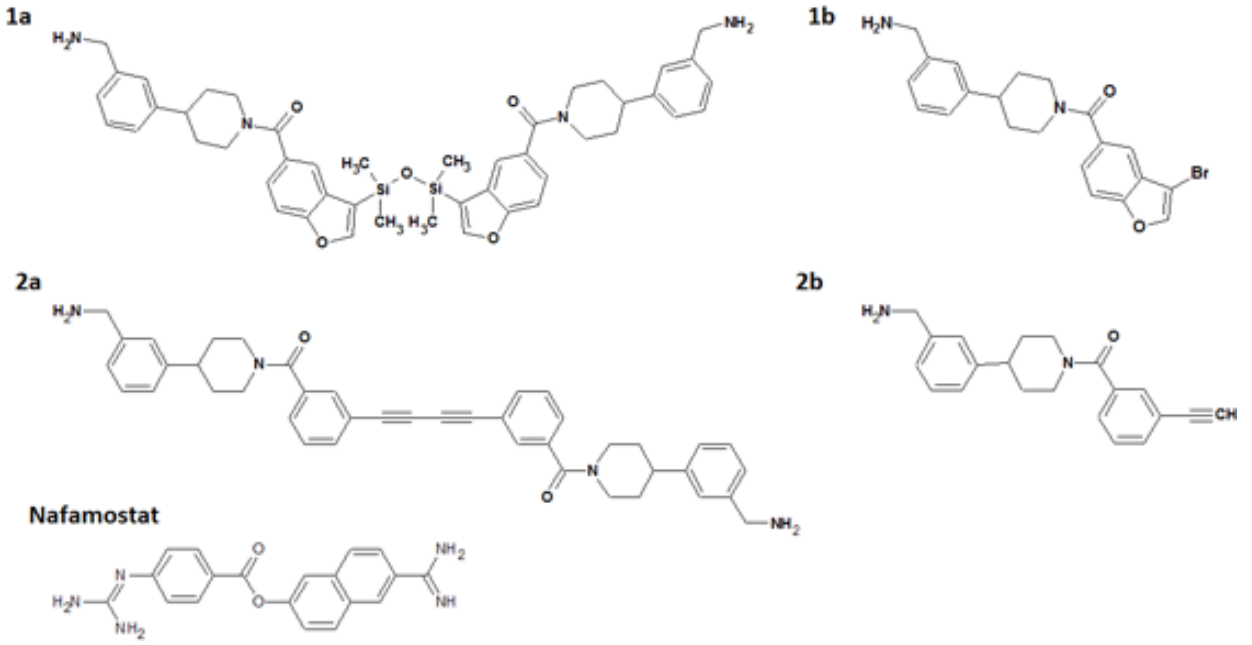
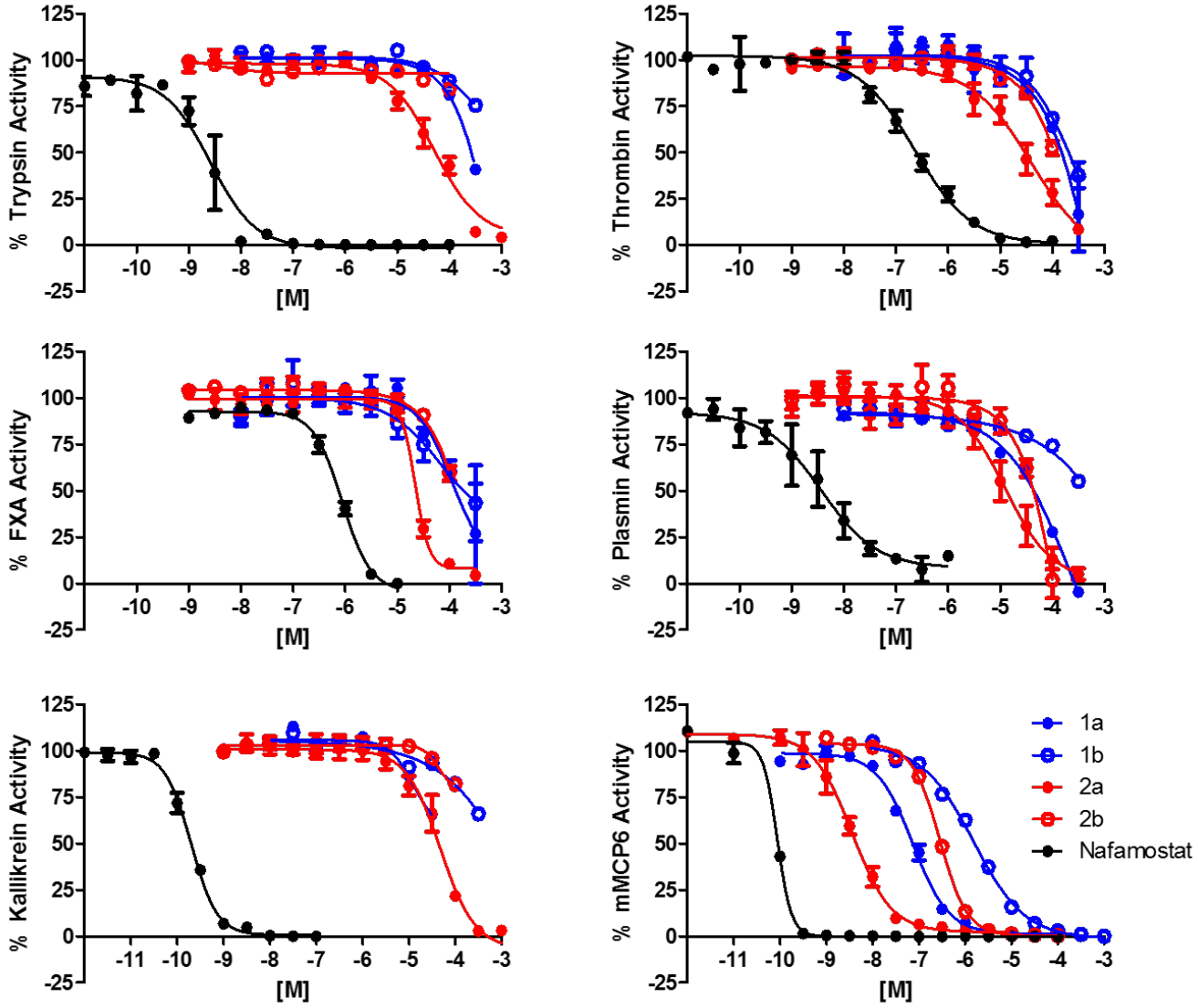


Figure S1: β-tryptase inhibitors used in the current study.



	IC50 [M]															
	TRYPSIN			THROMBIN			FXA			PLASMIN			KALLIKREIN			TRYPTASE
	IC_{50}	SEM	fold difference	IC_{50}	SEM	fold difference	IC_{50}	SEM	fold difference	IC_{50}	SEM	fold difference	IC_{50}	SEM	fold difference	IC_{50}
1a	2.74E-03	0.55	636935.26	>100uM		619003.26	1.13E-04	0.38	26315.79	2.41E-04	0.39	56194.69	1.28E-05	0.26	2971.59	**4.294E-09**
1b	3.14E-04	0.29	705.12	2.71E-04	0.97	607.72	6.82E-05	0.70	153.10	>100uM			>100uM			**4.456E-07**
2a	5.10E-05	0.10	20539.89	3.97E-05	0.34	15995.17	2.21E-05	0.04	8887.99	1.24E-05	0.19	4979.85	4.83E-05	0.11	19452.05	**2.482E-09**
2b	3.39E-09	0.84	0.01	>100uM		14992.68	>100uM			3.04E-04	2.66	889.54	4.17E-05	0.51	122.12	**3.413E-07**
naf	2.62E-09	0.13	5.67	2.30E-07	0.06	498.16	8.77E-07	0.04	1899.67	3.69E-09	0.20	8.00	2.01E-10	0.03	0.43	**4.615E-10**

Figure S2: Selectivity of β-tryptase inhibitors over closely related proteases and the murine homolog, mMCP6. Apparent IC50s for compounds 1a, 1b, 2a, 2b and nafamostat with select serine proteases assayed at 1nM. Fold-selectivity for tryptase is indicated.

	1a
PDB ID	4MPW
Cell dimensions *a*=*b*, *c* (Å)	78.462, 165.620
Resolution (Å)[†]	30-1.95 (2.02-1.95)
R_{sym}[‡]	0.088 (0.439)
Average I/σI	21.4 (3.5)
Completeness (%)	100 (100)
Redundancy	5.4 (5.5)
Resolution (Å)	1.95
No. reflections[§]	40961
R_{factor} , R_{free}	0.164 (0.206)
Protein atoms	3828
Water molecules	421
Compound atoms	57
rmsd bond lengths (Å)	0.018
rmsd bond angles (°)	2.03

Table S1: X-ray data collection and refinement statistics. [†]The highest resolution shells are shown in parentheses. [‡]$R_{sym} = \Sigma |I_i - \langle I \rangle| / \Sigma I_i$ where I_i is the intensity of a measurement and $\langle I \rangle$ is the average intensity for that reflection. [§]Of these reflections, 5% are used for the R_{free} calculation.

Component	Fold IC_{50} Shift at 1nM Tryptase
3% BSA	0.55
5% BSA	0.49
1mg/ml αGP1	1.67
8mM Glucose	0.94
100μM Sorbitol	1.15
10mM L-Glutathione	1.06
10% Human Plasma	1.57
20% Human Plasma	2.56
10% Mouse Plasma	3.52
20% Mouse Plasma	7.76

Table S2: Compound 1a IC50 shifts in the presence of plasma components. Dose response curves and resultant IC50s were compared for shifts in potency against Bovine serum albumin (BSA), α1-glycoprotein (αGP1), glucose, sorbitol, L-glutathione and human and mouse plasma. To inhibit proteolytic activity of enzymes present in plasma, protease inhibitors demonstrating no inhibitory actions against tryptase, were added to the assay buffer. Ratios of the IC50s between no additives and additives are presented.