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SUPPLEMENTARY MATERIAL TO

Comparative *in silico*/*in vitro* analysis of pharmacokinetic profiles of BET inhibitors

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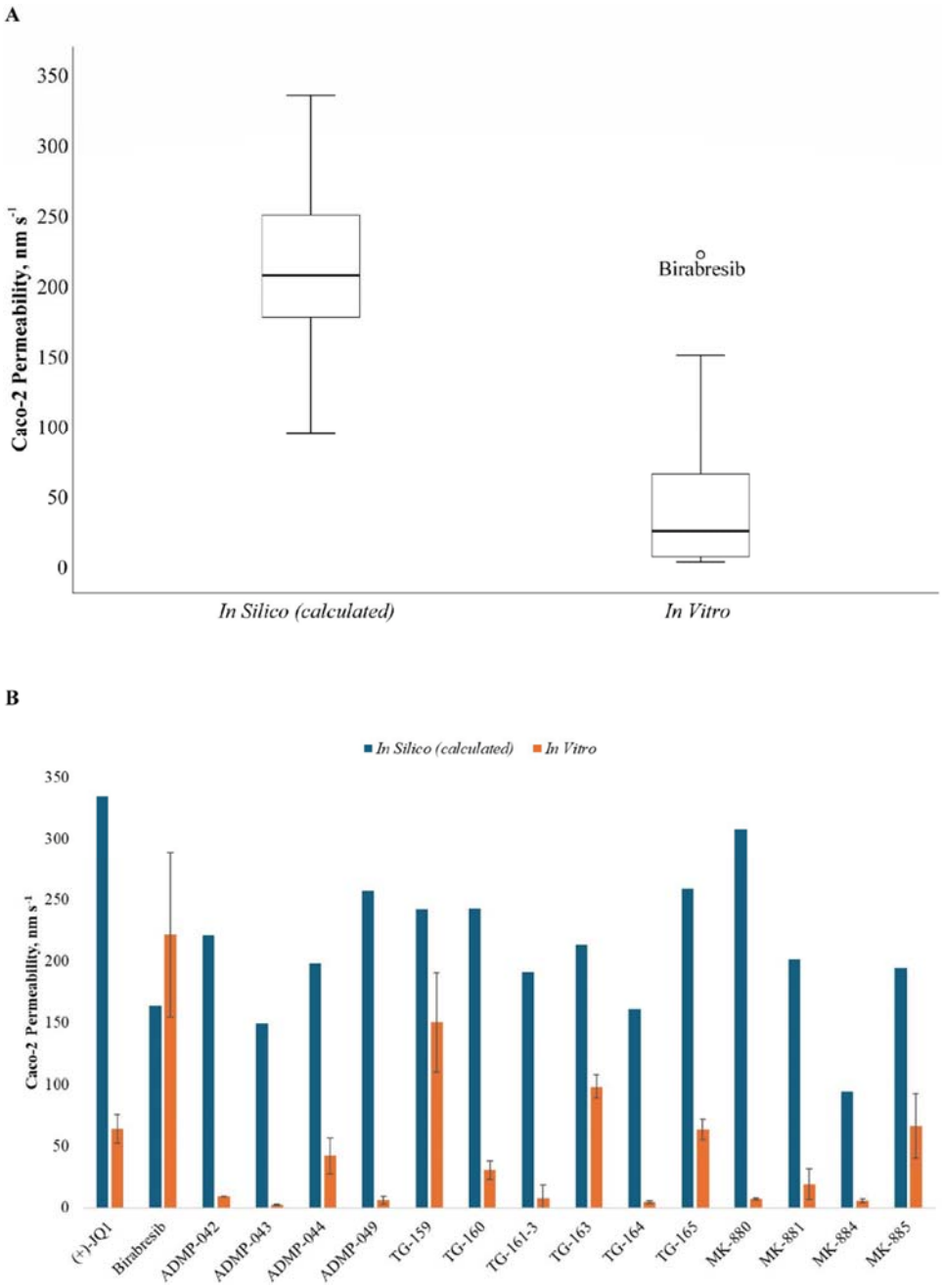

Fig. S-1. (A) Results of the Wilcoxon signed-rank test comparing *in silico* (*Caco-2 perm. calc.*) and *in vitro* (*Avg.* P_{app} *A-B*) Caco-2 permeabilities, demonstrating a statistically significant difference. (B) Bar plot with paired data emphasizing the differences between *in silico* and *in vitro* Caco-2 permeability results.

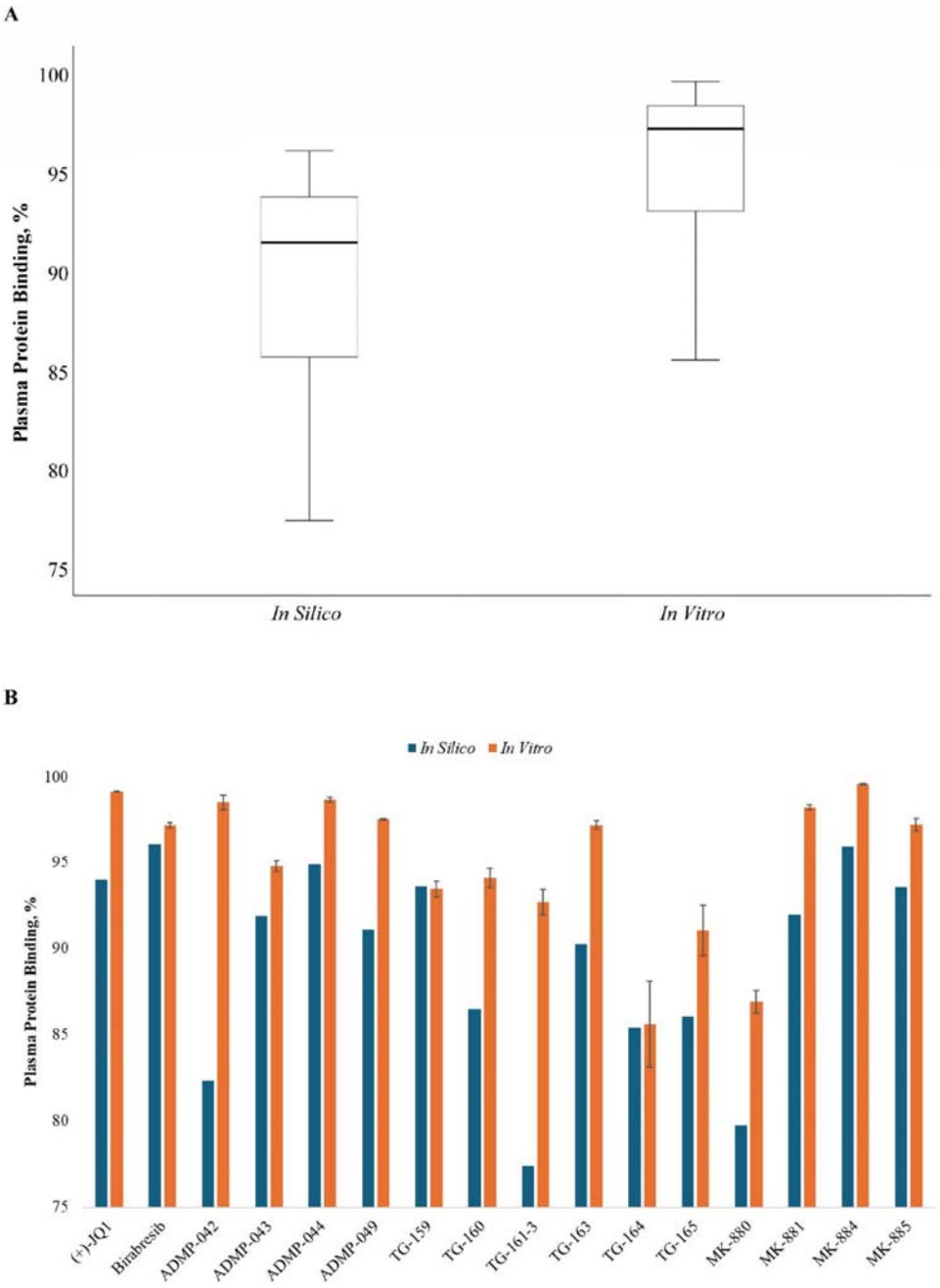

Fig. S-2. (A) Results of the Wilcoxon signed-rank test indicating a statistically significant difference between *in silico*-predicted and *in vitro*-assessed plasma protein binding values. (B) Bar plot with paired data comparing *in silico* and *in vitro* plasma protein binding values, illustrating the relation between the two data sets.

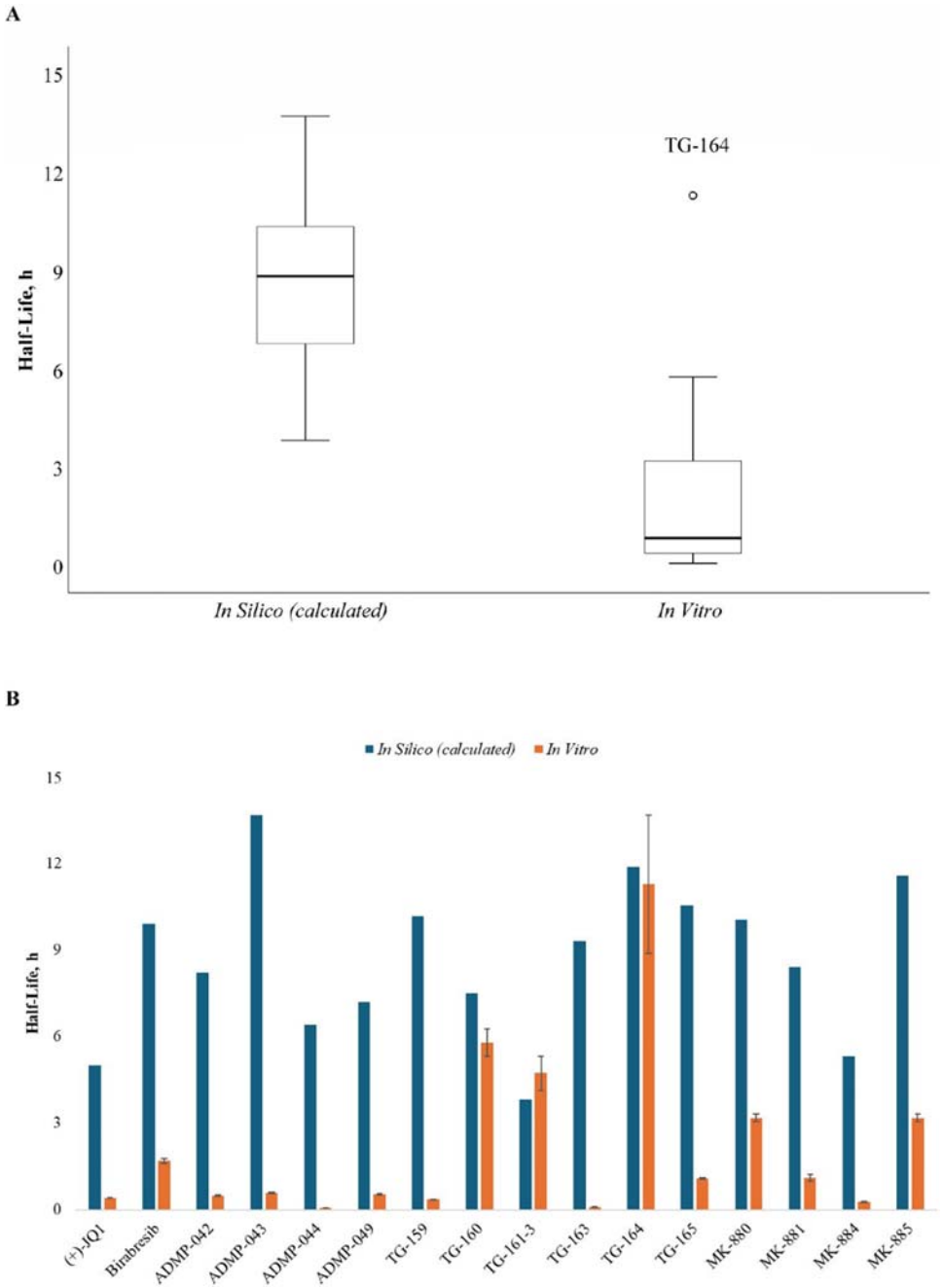

Fig. S-3. (A) Results of the Wilcoxon signed-rank test indicating a statistically significant difference between calculated and *in vitro*-assessed half-lives. (B) Bar plot with paired data emphasizing the differences between calculated and *in vitro*-assessed half-lives.

TABLE S-I. Statistical Correlations Between *In Silico*- and *In Vitro*-Obtained Results

In Silico-Obtained Results		*In Vitro*-Obtained Results							
		ABSORPTION					DISTRIB.	METABOLISM & EXCRETION	
		Avg. P	*R*	*Avg. P_{app} A-B*	*Avg. P_{app} B-A*	*ER*	*PPB*	CL_{int}	$t_{1/2}$
ABSORPTION	*prob. HIA*	ρ = -0.581 p = 0.042	ρ = -0.618 p = 0.011	ρ = -0.304 p = 0.252	ρ = -0.067 p = 0.805	**ρ = 0.122** **p = 0.652**	**ρ = -0.094** **p = 0.729**	ρ = 0.076 p = 0.779	ρ = -0.076 p = 0.779
	F(20% HIA)	ρ = -0.108 p = 0.713	ρ = -0.376 p = 0.152	ρ = -0.063 p = 0.818	ρ = 0.094 p = 0.729	**ρ = 0.188** **p = 0.486**	**ρ = -0.094** **p = 0.729**	ρ = 0.031 p = 0.908	ρ = -0.031 p = 0.908
	F(30%)	ρ = -0.436 p = 0.119	ρ = -0.216 p = 0.421	ρ = -0.338 p = 0.200	ρ = -0.190 p = 0.480	ρ = 0.169 p = 0.531	ρ = 0.398 p = 0.127	ρ = 0.155 p = 0.566	ρ = -0.155 p = 0.566
	Caco-2 perm.	ρ = 0.053 p = 0.658	ρ = -0.194 p = 0.471	ρ = 0.303 p = 0.254	ρ = 0.491 p = 0.053	ρ = 0.279 p = 0.295	ρ = -0.091 p = 0.737	ρ = 0.091 p = 0.737	ρ = -0.091 p = 0.737
	MDCK perm.	ρ = 0.053 p = 0.658	ρ = -0.194 p = 0.471	ρ = 0.303 p = 0.254	ρ = 0.491 p = 0.053	ρ = 0.279 p = 0.295	ρ = -0.091 p = 0.737	ρ = 0.091 p = 0.737	ρ = -0.091 p = 0.737
	P-gp sub.	ρ = 0.004 p = 0.988	ρ = -0.132 p = 0.625	ρ = 0.082 p = 0.762	ρ = 0.359 p = 0.172	ρ = 0.491 p = 0.053	ρ = -0.215 p = 0.425	ρ = -0.350 p = 0.184	ρ = 0.350 p = 0.184
	P-gp inh.	ρ = -0.550 p = 0.042	ρ = -0.379 p = 0.147	ρ = -0.462 p = 0.072	ρ = -0.206 p = 0.444	ρ = 0.412 p = 0.113	ρ = -0.308 p = 0.249	ρ = -0.468 p = 0.068	ρ = 0.468 p = 0.068
DISTRIBUTION	*BBB pen*	ρ = 0.338 p = 0.237	ρ = 0.317 p = 0.232	ρ = 0.139 p = 0.609	ρ = -0.168 p = 0.533	ρ = -0.558 p = 0.025	ρ = 0.327 p = 0.217	ρ = 0.436 p = 0.092	ρ = -0.436 p = 0.092
	PPB	ρ = 0.632 p = 0.015	ρ = 0.284 p = 0.286	ρ = 0.293 p = 0.271	ρ = 0.012 p = 0.965	ρ = -0.259 p = 0.332	ρ = 0.172 p = 0.523	ρ = 0.362 p = 0.168	ρ = -0.362 p = 0.168
	V_d	ρ = 0.790 p < 0.001	ρ = 0.703 p = 0.002	ρ = 0.403 p = 0.122	ρ = 0.068 p = 0.803	ρ = -0.376 p = 0.151	ρ = 0.656 p = 0.006	ρ = 0.494 p = 0.052	ρ = -0.494 p = 0.052
	F_u	ρ = -0.257 p = 0.374	ρ = -0.300 p = 0.259	ρ = -0.126 p = 0.641	ρ = 0.312 p = 0.240	ρ = 0.685 p = 0.003	ρ = 0.082 p = 0.762	ρ = 0.244 p = 0.362	ρ = -0.244 p = 0.362
METABOLISM &	*CL*	ρ = -0.739 p = 0.003	ρ = -0.665 p = 0.005	ρ = -0.371 p = 0.158	ρ = 0.032 p = 0.905	ρ = 0.456 p = 0.076	ρ = -0.491 p = 0.053	ρ = -0.312 p = 0.240	ρ = 0.312 p = 0.240
	$t_{1/2}$ prob.	ρ = -0.359 p = 0.208	ρ = -0.224 p = 0.405	ρ = -0.276 p = 0.300	ρ = -0.197 p = 0.464	ρ = 0.035 p = 0.897	ρ = 0.365 p = 0.165	ρ = 0.271 p = 0.311	ρ = -0.271 p = 0.311
	$t_{1/2}$ calc.	ρ = -0.915 p < 0.001	ρ = -0.803 p < 0.001	ρ = -0.488 p = 0.055	ρ = -0.068 p = 0.803	ρ = 0.365 p = 0.165	ρ = -0.638 p = 0.008	ρ = -0.432 p = 0.094	ρ = 0.432 p = 0.094
		ρ = 0.029 p = 0.923	ρ = -0.176 p = 0.513	ρ = 0.006 p = 0.983	ρ = 0.159 p = 0.557	ρ = 0.268 p = 0.316	ρ = -0.571 p = 0.021	ρ = -0.303 p = 0.254	ρ = 0.303 p = 0.254

Cells in green, yellow, and red denote strong ($\rho \geq 0.700$ and $\rho \leq -0.700$), moderate ($0.400 \leq \rho < 0.700$ and $-0.400 \geq \rho > -0.700$), or weak correlation ($-0.400 < \rho < 0.400$), respectively, for $p < 0.050$.

TABLE S-II. Predicted Degrees of Ionization and log*D* Values

Compound	Degree of Ionization (pH = 7,4)	log*D* (pH = 7,4)
(+)-JQ1	99.90% non-ionized	3.64
Birabresib	99.06% non-ionized	4.03
ADMP-042	95.09% non-ionized	2.01
ADMP-043	96.25% non-ionized	1.76
ADMP-044	99.88% non-ionized	3.93
ADMP-049	99.93% non-ionized	1.72
TG-159	99.96% non-ionized	2.59
TG-160	99.96% non-ionized	2.08
TG-161-3	87.96% non-ionized	1.68
TG-163	99.87% non-ionized	2.77
TG-164	99.92% ionized	-1.94
TG-165	99.92% non-ionized	1.73
MK-880	99.91% non-ionized	1.41
MK-881	99.65% non-ionized	3.57
MK-884	99.86% non-ionized	4.28
MK-885	99.13% non-ionized	2.23