Predicted CL
(microsomes with cofactors)

	Predicted CL, L/h/kg		
Species	**GS-PI1**	**DRV**	**ATV**
Rat	0.10	2.8	3.7
Dog	0.45	1.2	1.4
Human	**0.05**	**1.20**	**1.07**

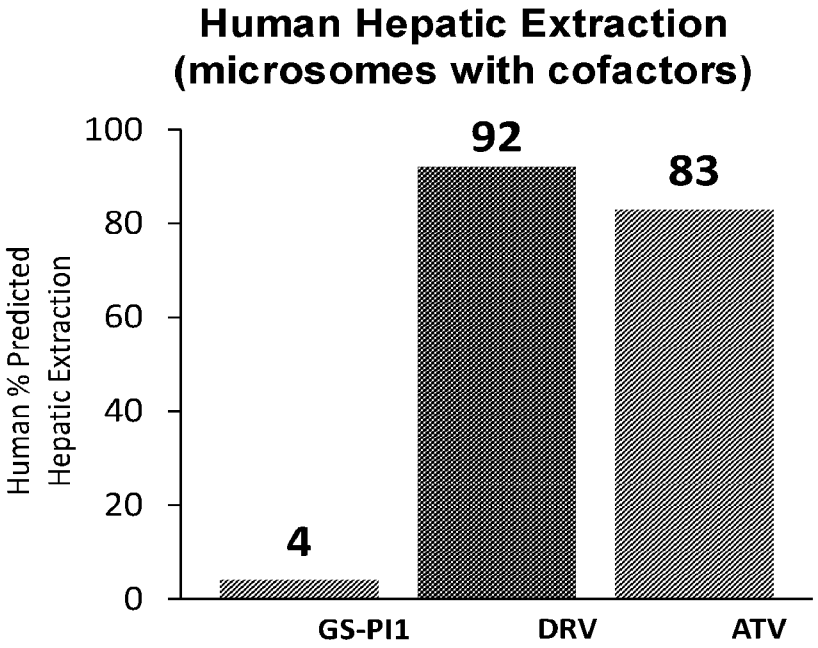
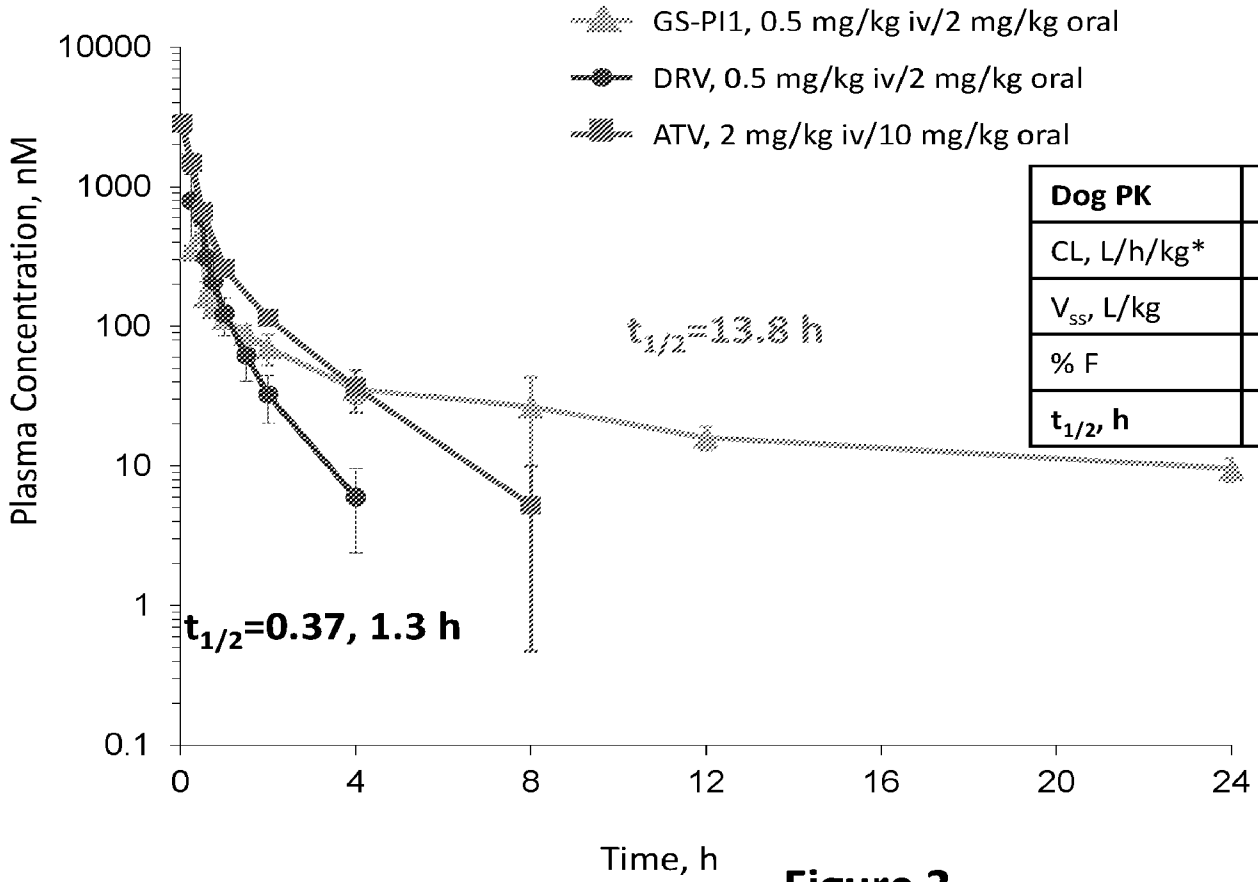


Figure 1

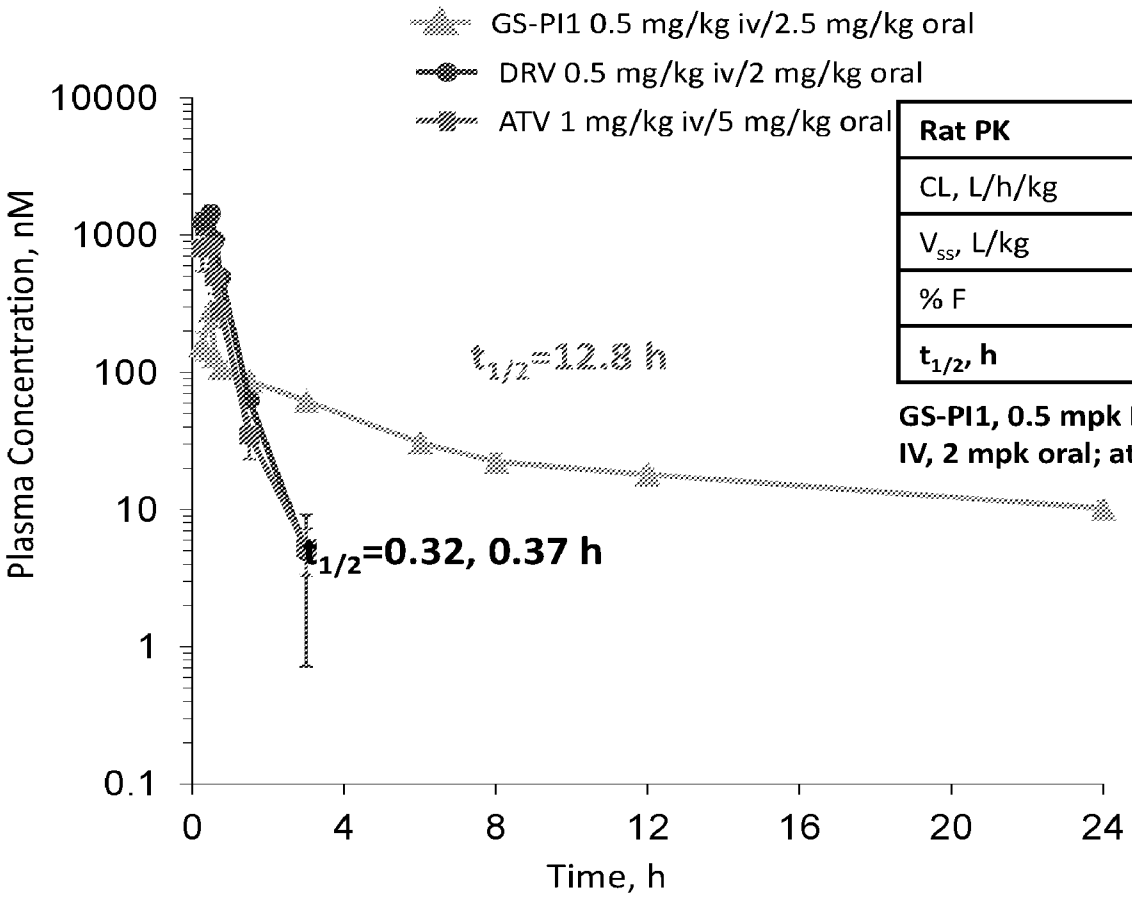
Intravenous Pharmacokinetics of GS-PI1, DRV, and ATV



Dog PK	GS-PI1	DRV	ATV
CL, L/h/kg*	0.47	2.7	1.0
V_{ss}, L/kg	6.3	0.87	0.90
% F	18	38	48
$t_{1/2}$, h	**13.8**	**0.37**	**1.3**

Figure 2

Intravenous Pharmacokinetics of GS-PI1, DRV, and ATV



Rat PK	GS-PI1	DRV	ATV
CL, L/h/kg	0.48	2.2	2.7
V_{ss}, L/kg	6.7	0.73	0.87
% F	29	24	38
$t_{1/2}$, h	**12.8**	**0.32**	**0.37**

GS-PI1, 0.5 mpk IV, 2.5 mpk oral; darunavir, 0.5 mpk IV, 2 mpk oral; atazanavir, 1 mpk IV, 5 mpk oral

Figure 3

Fold Change vs Wild Type for Clinically Relevant RAMs

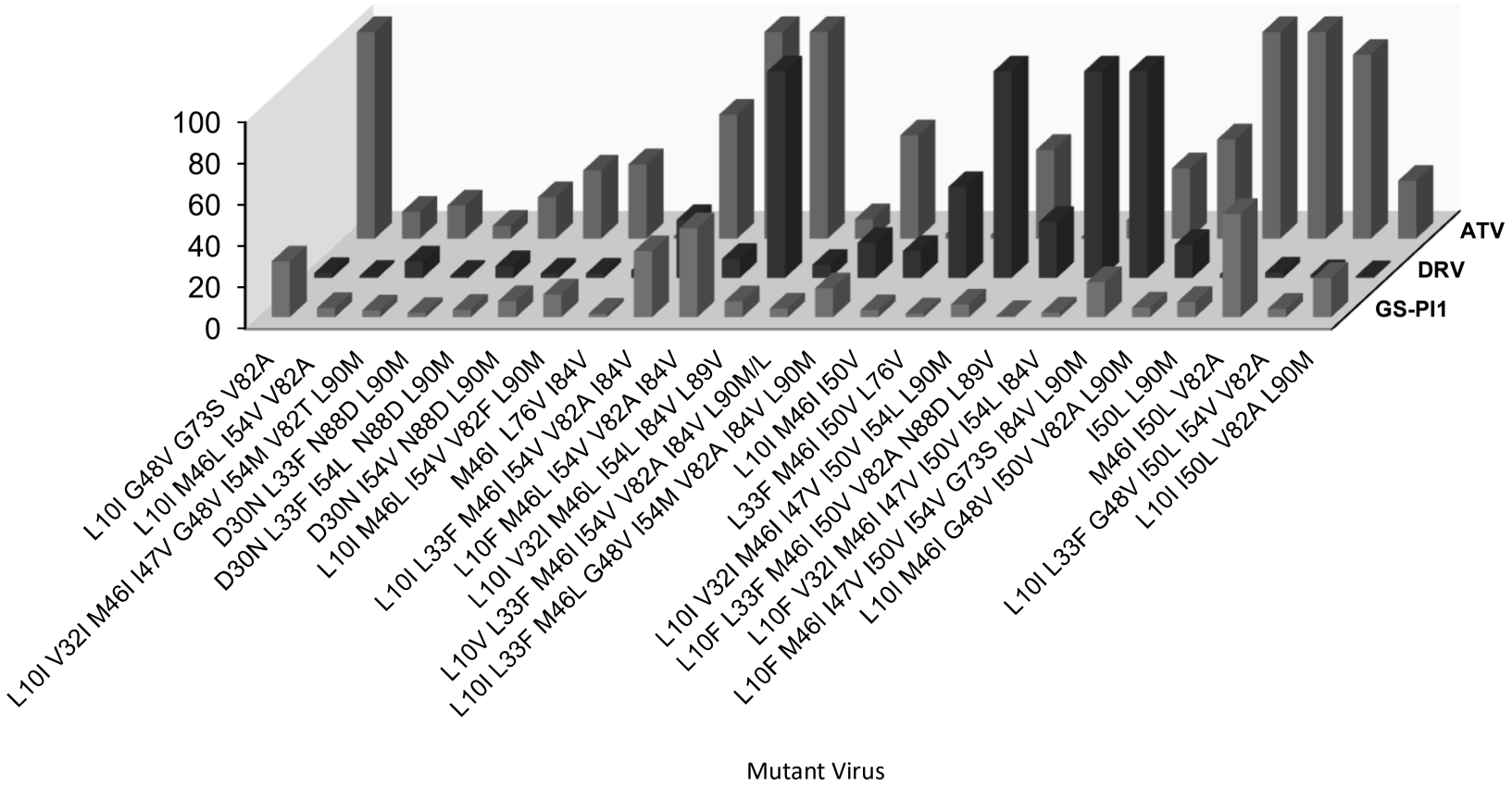
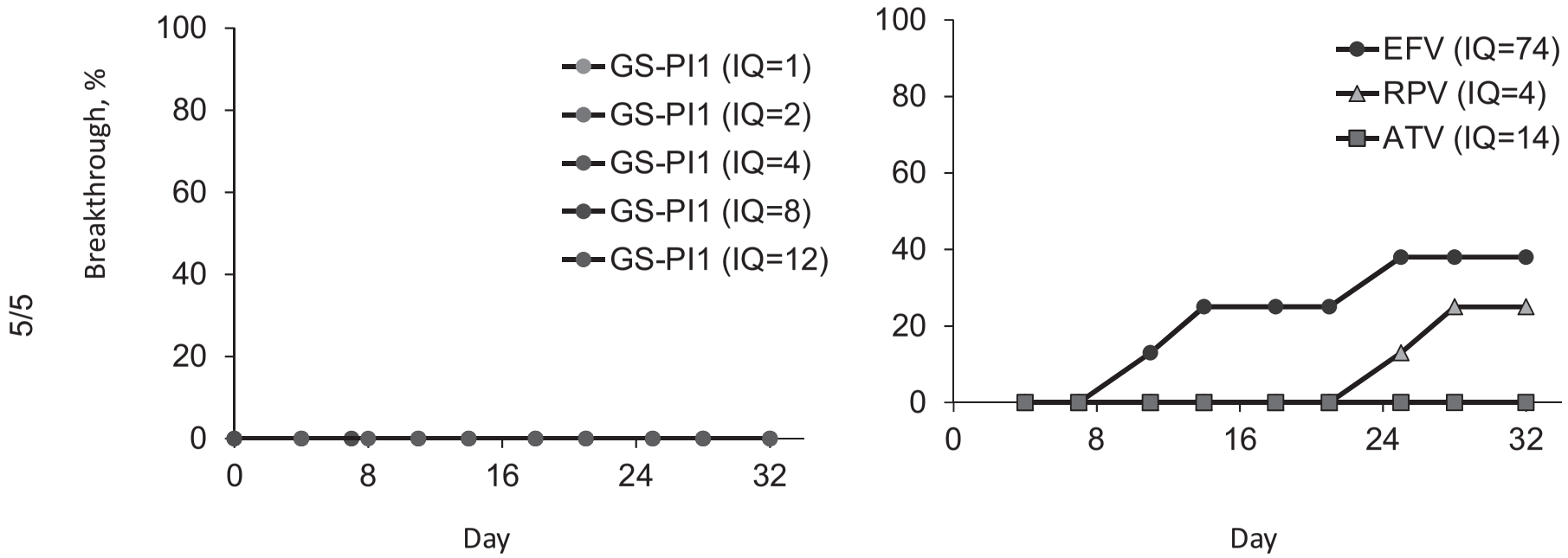


Figure 4

Resistance Breakthrough Assay



- GS-PI1 does not breakthrough at IQ of 1
- EFV and RPV breakthrough at their clinical IQ; ATV does not

Figure 5