

**Table S3. Final Covariate Model Parameter Estimates**

Parameter	Descriptor	Estimate	Bootstrap 95%	
			95% CI	CI
$\theta_1$	CL/F, L·h <sup>-1</sup>	9.4	8.9 to 9.9	9.0 to 9.9
$\theta_2$	V <sub>1</sub> /F, L	554.0	440 to 668	463 to 667
$\theta_3$	k <sub>tr</sub> , h <sup>-1</sup>	1.0	0.9 to 1.2	0.9 to 1.2
$\theta_4$	Proportional error	0.3	0.3 to 0.4	0.3 to 0.4
$\theta_5$	Additive error	0, fixed	NC	NC
$\theta_6$	Proportional error single- observation	0.5	0.5 to 0.6	0.5 to 0.6
$\theta_7$	F <sub>1</sub> , phase 1	1.9	1.6 to 2.3	1.7 to 2.3
$\theta_8$	CL <sub>cov,females</sub>	-0.2	-0.3 to -0.1	-0.3 to -0.1
$\theta_9$	CL <sub>cov,study 14295</sub>	-0.5	-0.6 to -0.5	-0.6 to -0.4
$\omega_{1,1}^2$	IIV, CL	0.2	0.2 to 0.3	0.2 to 0.3
$\omega_{2,2}^2$	IIV, V <sub>1</sub>	0.4	0.2 to 0.7	0.3 to 0.6
$\sigma_{1,1}^2$	Residual error	1, fixed	NC	NC

$\theta$ =parameter estimate for population average;  $\omega$ =random effects parameter estimate;  $\sigma$ =residual error model parameter estimate; CL=clearance; CL/F=apparent oral clearance; F<sub>1</sub>=relative bioavailability; IIV=interindividual variability; k<sub>tr</sub>=transit rate constant; NC=not calculated; V<sub>1</sub>=volume of distribution; V<sub>1</sub>/F=apparent volume of distribution.