Supplemental Material

Table 3 Pharmacokinetic of JPC-3210 following oral and intravenous administration to male CD1 mice

Characterization of the Preclinical Pharmacology of the New 2-aminomethylphenol, JPC-3210 for Malaria Treatment and Prevention

Geoffrey W. Birrell, Gavin D. Heffernan, Guy A. Schiehser, John Anderson, Arba L. Ager, Pablo Morales, Donna MacKenzie, Karin van Breda, Marina Chavchich, Laura R. Jacobus, G. Dennis Shanks, David P. Jacobus and Michael D. Edstein

JPC-3210 Pharmacokinetic Parameters	**IV (2 mg/kg)**	**Oral (16 mg/kg)**
Tmax (hours)	0.083	2
Cmax (ng/mL)	847	1180
t1/2 elimination (168-672 hours)	139	169
AUC0-last (ng*h/mL)	16100	111000
AUC0-inf (ng*h/mL)	17300	116000
Percent AUC Extrapolated	7.5	4.5
Clearance (mL/h/kg)[1]	116	119*
Volume of distribution (mL/kg)[2]	23200	29000*
Bioavailability (AUC0-last)	NA	86.2
Bioavailability (AUC0-inf)	NA	83.8

NA: Not Applicable
[1]Mouse Renal Plasma Flow ~1980 mL/h/kg
[2]Mouse Blood Volume ~80 mL/kg
*Calculated using bioavailability of 86.2%
WinNonlin, version 6.3 (Pharsight Corp., Mountain View, California)

For the preparation of JPC-3210 the following procedures were performed:

a. The oral dose of JPC-3210 (16 mg/kg) was diluted with the vehicle (99.4% distilled sterile water/0.1% Tween 80 / 0.5% hydroxyethylcellulose) and wet milled with a Dounce glass grinder until a uniform white suspension was achieved at the appropriate concentration of 1.6 mg/ml.

b. For the preparation of the intravenous dose of JPC-3210 (2 mg/kg) the compound was dissolved in ethanol to obtain a stock solution of 10 mg/ml and then diluted using a 5% Tween 80 in phosphate buffered saline solution to obtain a 0.20 mg/ml concentration (light yellow solution).