**ABSTRACT**

Background: Integration of Phase 1 pharmacokinetics (PK) and non-clinical data provides for the potential to optimize antimicrobial dosing regimens for Phase 2/3 studies. A murine-thigh infection residual error model, CL (14.5 L/h), Vc (9.43 L), and t1/2 (0.5 h) were estimated. A subset of the

**RESULTS:**

- Phase 1 data were obtained from a double-blind, dose escalation study conducted in healthy subjects.
- Blood samples were collected at time points ranging from 0.5 to 24 h after the first dose of 500 mg TID dosing regimen.
- Blood concentrations were measured using liquid chromatography-mass spectrometry.
- PK parameter estimates and a covariance matrix were estimated using the population PK model.
- The predicted concentrations were compared with the observed concentrations.
- The goodness-of-fit of the final model was assessed using the log-likelihood ratio test.

**DISCUSSION & CONCLUSIONS:**

- PK-PD target attainment was achieved at doses of 1000 mg q12h and 2000 mg q24h.
- The results indicate that doripenem has a high therapeutic index and is well tolerated.
- The study provides a foundation for further clinical development of doripenem.