Objectives: To select safe and efficacious doses of ceftolozane/tazobactam for Phase 2 studies in pediatric patients (birth to <18 yr) with complicated urinary tract infection (cUTI) and complicated intra-abdominal infection (cIAI), using population pharmacokinetic (PK) modeling.

Methods: Population PK models to characterize ceftolozane/tazobactam PK were developed using NONMEM (ver.7) with ceftolozane data from 421 adult and 31 pediatric subjects, and tazobactam data from 288 adult and 30 pediatric subjects. The models were used to estimate PK exposure and the probability of achieving PK/pharmacodynamics (PD) targets at various doses in pediatric patients, using published pediatric weight distributions and estimated glomerular filtration rate (eGFR) based on age.

Results: Two-compartment linear models with first-order elimination best described the PK of ceftolozane and tazobactam. Allometric scaling on clearance (CL), central volume of distribution (Vc), intercompartmental clearance (Q, for tazobactam only), and peripheral volume of distribution (Vp) were included to characterize the pediatric PK. Presence of infection was a covariate on CL for tazobactam, and eGFR was a covariate on CL for ceftolozane and tazobactam. Other covariates tested (age, sex, and race) were not significant in the model. Based on simulations in pediatric patients, doses of 1.5 g [1 g/0.5 g] (12 to <18 yr) and 20/10 mg/kg (birth to <12 yr) administered via a 1-hour intravenous (IV) infusion provided exposures comparable to adult exposures at the approved 1.5 g clinical dose and a ≥90% probability of achieving the PK/PD targets (percent of time above a 4 μg/mL minimum inhibitory concentration for ceftolozane and above a 1 μg/mL threshold concentration for tazobactam).

Conclusions: The population PK models well-characterized ceftolozane/tazobactam PK for pediatric patients and support the evaluation of 1.5 g (12 to <18 yr) and 20/10 mg/kg (birth to <12 yr) administered as a 1-hour IV infusion to pediatric cUTI and cIAI patients in Phase 2 studies.