

# Pharmacokinetic-Pharmacodynamic (PK-PD) Target Attainment (TA) Analysis Supporting CEM-101 Phase 2 Dose Selection

## Abstract A1-692

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### Background:

CEM-101 is a novel flouroketolide with activity against typical and atypical bacterial respiratory pathogens. A PK-PD TA analysis was conducted to evaluate CEM-101 dosing regimens for Phase 2 studies for the treatment of patients with community-acquired bacterial pneumonia (CABP).

### Methods:

Monte Carlo simulation (n=1,000) using Phase 1 PK and non-clinical PK-PD data were utilized to determine the probability of PK-PD TA by MIC for different CEM-101 dosing regimens. Parameter estimates and the variance-covariance matrix from a population PK model, developed using data from 91 healthy subjects in 3 Phase 1 studies, was used to simulate plasma and ELF profiles. Resultant ELF  $AUC_{0-24}$  values were divided by fixed MIC values (0.125 to 1 mg/L). Using ELF  $AUC_{0-24}:MIC$  targets associated with net bacterial stasis and a  $1\text{-log}_{10}$  CFU change from baseline in neutropenic murine-pneumonia infection models evaluating CEM-101 against *S. pneumoniae* of 1.3 and 15.1, respectively, probabilities of PK-PD TA by MIC were computed for each CEM-101 dosing regimen evaluated

### Results:

Probabilities of PK-PD TA by MIC based on Day 1 ELF  $AUC_{0-24}$  for each dosing regimen evaluated are presented (see table).

### Conclusions:

High probabilities of PK-PD TA based on the ELF  $AUC_{0-24}:MIC$  target associated with net bacterial stasis were demonstrated for all dosing regimens evaluated. A high of probability of PK-PD TA at a MIC of 1 mg/L (0.91) based on the PK-PD target associated with a  $1\text{-log}_{10}$  CFU decline was observed for the CEM-101 800 mg on Day 1 followed by 400 mg Q24h regimen. These results will be utilized to support dose decisions for a Phase 2 study in patients with CABP.