

IMS-P23 S-649266, a Novel Siderophore Cephalosporin Antibiotic: Its Potent Activity against Multidrug-Resistant Gram-Negative Bacteria

○Akinobu ITO¹, Toru NISHIKAWA¹, Shuhei MATSUMOTO¹, Tsukasa HORIYAMA¹, Naoki KOHIRA¹, Hidenori YOSHIKAWA¹, Rio NAKAMURA¹, Masakatsu TSUJI¹, Yoshinori YAMANO¹

¹Discovery Research Laboratory for Core Therapeutic Areas, Shionogi & Co., Ltd.

Spread of multidrug-resistant (MDR) Gram-negative bacteria presents major clinical challenges. S-649266 ('266) is a novel catechol-substituted siderophore cephalosporin antibiotic with potent antibacterial activity against Gram-negative bacteria including MDR pathogens. '266 has a unique mechanism of entry into bacterial cells in which the compound is transported into bacterial cells via iron transporters under iron deficient conditions, and has high stability to carbapenem-hydrolyzing beta-lactamases such as KPC, VIM, IMP and NDM. Due to these unique characteristics, '266 showed potent *in vitro* activity against Gram-negative bacteria including MDR strains such as carbapenem resistant Enterobacteriaceae, MDR *Pseudomonas aeruginosa*, and MDR *Acinetobacter baumannii*, and *in vivo* efficacy against these MDR pathogens in rat lung infection model where exposure profile of free concentration of '266 in human plasma was recreated. These results showed the potential of '266 for the treatment of the infection caused by MDR pathogens, which will meet unmet medical needs.