Press Release

Shionogi Announces Upcoming Presentations at American Society for Microbiology Microbe Meeting

OSAKA, Japan, JUNE 6, 2018 - Shionogi & Co., Ltd. (hereafter "Shionogi") announced today that eight scientific posters will feature the company's investigational compounds at the American Society for Microbiology (ASM) Microbe meeting in Atlanta, June 7-11, 2018.

Shionogi will present data on cefiderocol (S-649266), a late stage investigational siderophore cephalosporin with a novel mechanism of cell entry that has activity against a broad range of Gram-negative pathogens including multidrug resistant (MDR) strains; and COT-143, an investigational humanized monoclonal antibody demonstrating anti-virulence activity targeting the PcrV protein, an essential component of the *Pseudomonas aeruginosa* type III secretion system.

All poster presentations will take place in the Exhibit and Poster Hall, Building B, Halls B2-B5.

The following five poster presentations will share cefiderocol findings:

- **Poster #619**: Frequency of Resistance Acquisition and Resistance Mechanisms to Cefiderocol
  Presenter: Naoki Kohira
  Date and time: June 9, 2018, 11 a.m.-1 p.m.

- **Poster #620**: Cefiderocol Minimum Inhibitory Concentrations (MICs) against Ceftazidime-Avibactam Susceptible and Resistant Carbapenem-Resistant *Enterobacteriaceae* (CRE)
  Presenter: Ryan Shields
  Date and time: June 9, 2018, 11 a.m.-1 p.m.

- **Poster #621**: *In vitro* Activity of Siderophore Cephalosporin Cefiderocol against YRIN(K) PBP3 Insertion-Carrying *Escherichia coli*
  Presenter: Takafumi Sato
  Date and time: June 9, 2018, 11 a.m.-1 p.m.

- **Poster #622**: Cefiderocol (S-649266) Activity against Globally Isolated Meropenem Non-Susceptible Gram-Negative Bacteria Containing Serine- and Metallo-Carbapenemase Genes
  Presenter: Masakatsu Tsuji
  Date and time: June 9, 2018, 11 a.m.-1 p.m.

- **Poster #623**: Resistance Acquisition Studies of Cefiderocol by Serial Passage and *in vitro* Pharmacodynamic Model Under Human Simulated Exposure
  Presenter: Naoki Kohira
  Date and time: June 9, 2018, 11 a.m.-1 p.m.

The following poster presentations will share COT-143 findings:

- **Poster #627**: Correlation between *in vitro*/*in vivo* Production of *Pseudomonas aeruginosa* PcrV Protein Isolated from Ventilator-associated Pneumonia Patients and Their Virulence in Murine Lung Infection Models
  Presenter: Hideki Maki
  Date and time: June 8, 2018, 11 a.m.-1 p.m.

- **Poster #636**: COT-143, a Novel Monoclonal Antibody against the PcrV Protein: *In vivo* Efficacy in Combination with Antimicrobials or G-CSF against *Pseudomonas aeruginosa* in Murine Lung Infection Models
  Presenter: Hideki Maki
  Date and time: June 10, 2018, 0:45 p.m.-2:45 p.m.

The following poster presentation will share Gram-negative pathogens information from patients diagnosed with hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP):

- **Poster #406**: Non-Fermenters as Predominant Source of Carbapenem-Resistance in HAP/VAP Patients in US Hospitals between 2010 and 2015
  Presenter: Bin Cai
  Date and time: June 8, 2018, 11 a.m.-1 p.m.

All abstracts for ASM Microbe are available online here.

About cefiderocol—an investigational antibiotic agent

Cefiderocol is a siderophore cephalosporin with a novel mechanism for penetrating the outer cell membrane of Gram-negative pathogens. Cefiderocol binds to ferric iron and is actively transported into bacterial cells through the outer membrane via the bacterial iron transporters, which function to incorporate this essential nutrient for bacterial.[1] This mechanism allows cefiderocol to achieve higher concentrations in the periplasmic space where it can then bind to receptors and inhibit cell wall synthesis in the bacterial cells.[2] In addition, cefiderocol can also enter cells by passive diffusion through porin channels and is stable against all known classes of beta-lactamases, including both the metallo- and serine-carbapenemases.[3] Data from global surveillance studies for cefiderocol demonstrated potent in vitro activity against a wide spectrum of Gram-negative pathogens including carbapenem-resistant *Acinetobacter baumannii*, *P. aeruginosa*, Enterobacteriaceae, and *S.*

maltophilia.[4] Cefiderocol has poor *in vitro* activity against Gram-positive or anaerobic bacteria.

Cefiderocol is currently in clinical development. Two Phase 3 studies are ongoing and enrolling patients with carbapenem-resistant pathogens at various infection sites (CREDIBLE-CR) and a HAP/VAP/HCAP clinical trial (APEKS-NP). Information is available at www.clinicaltrials.gov under the identifiers NCT02714595 and NCT03032380, respectively.

About COT-143—an investigational compound

COT-143 is a humanized monoclonal antibody that binds to the PcrV protein of *P. aeruginosa.* The PcrV protein is an essential component of the type III secretion system responsible for releasing harmful toxins and is related to the pathogenicity of *P. aeruginosa.* By using a variety of nonclinical *in vitro* and *in vivo* models, COT-143 has demonstrated the potential to reduce tissue and cellular damage by the toxins released by this system, leading to the treatment of infection caused by *P. aeruginosa.*

It is estimated that 51,000 healthcare-associated *P. aeruginosa* infections occur in the US each year and the rates of antibiotic resistance are increasing worldwide.[5,6] As resistance rises there are limited options to treat or prevent *P. aeruginosa* infections. COT-143 is in early-stage development.

About Shionogi

Shionogi & Co., Ltd. is a Japanese major research-driven pharmaceutical company dedicated to bringing benefits to patients based on its corporate philosophy of "supplying the best possible medicine to protect the health and wellbeing of the patients we serve." Shionogi Inc., the U.S. based subsidiary of Shionogi & Co., Ltd., continues this focus on the development and commercialization of high quality medicines that protect the health and well-being of the patients we serve. The company currently markets products in several therapeutic areas including anti-infectives, pain, cardiovascular diseases and gastroenterology. Our pipeline is focused on infectious disease, pain, CNS and oncology. For more details on Shionogi Inc., visit www.shionogi.com. For more information on Shionogi & Co., Ltd., visit www.shionogi.co.jp/en.

Forward-Looking Statements

This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing

risks, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.

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References

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5. Healthcare-associated Infections. Centers for Disease Control and Prevention. https://www.cdc.gov/hai/organisms/pseudomonas.html. Published March 9, 2018. Accessed April 16, 2018.

6. Hirsch EB, Tam VH. Impact of multidrug-resistant Pseudomonas aeruginosa infection on patient outcomes. Expert review of pharmacoeconomics & outcomes research. 2010;10(4):441-451. doi:10.1586/erp.10.49.