

**SHIONOGI TO PRESENT NEW DATA AT 2018 EUROPEAN CONGRESS OF CLINICAL  
MICROBIOLOGY AND INFECTIOUS DISEASES**

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**OSAKA, Japan, APRIL 18, 2018** – Shionogi & Co., Ltd. (hereafter “Shionogi”) today announced that the company will give 13 presentations on investigational agents at the upcoming European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), in Madrid, Spain, April 21-24, 2018.

Shionogi will present at this congress data on three investigational compounds including cefiderocol (S-649266), an investigational siderophore cephalosporin with a novel mechanism of cell entry in late stage development with activity against a broad range of Gram-negative pathogens including multidrug resistant (MDR) strains; baloxavir marboxil (S-033188), an oral cap-dependent endonuclease inhibitor administered as a single dose for the treatment of influenza; and for the first time, 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. Below is an overview of the oral and poster presentations at ECCMID 2018.

Presentations will include data on these Shionogi agents from company-sponsored or investigator-initiated investigational studies.

The following cefiderocol presentations will take place during a cefiderocol-focused poster session on Saturday, April 21, 2018 from 15:30-16:30, in the paper poster arena:

- **Poster #P0184:** Cefiderocol, a novel siderophore cephalosporin: *in vitro* activity against *Stenotrophomonas maltophilia* isolated globally  
**Presenter:** Masakatsu Tsuji
- **Poster #P0185:** Stability of cefiderocol against clinically-significant broad-spectrum oxacillinases  
**Presenter:** Patrice Nordmann
- **Poster #P0186:** Correlations between cefiderocol broth microdilution MICs and disk diffusion inhibitory zone diameters among target Gram-negative organisms  
**Presenter:** Masakatsu Tsuji
- **Poster #P0187:** *In vitro* activity of cefiderocol (S-649266), a siderophore cephalosporin, against carbapenem-susceptible and resistant non-fermenting Gram-negative bacteria  
**Presenter:** Robert A. Bonomo
- **Poster #P0188:** Metabolism and excretion of [14C]-cefiderocol, a siderophore cephalosporin, and drug-drug interaction potential via transporters of cefiderocol in healthy subjects  
**Presenter:** Miyazaki Shiro
- **Poster #P0189:** *In vivo* pharmacokinetic/pharmacodynamic (PK/PD) assessment of cefiderocol against *Stenotrophomonas maltophilia* in a neutropenic murine lung infection model  
**Presenter:** Miki Takemura
- **Poster #P0190:** Efficacy of humanized cefiderocol exposure against *Stenotrophomonas maltophilia* in a rat respiratory tract infection model  
**Presenter:** Miki Takemura

- **Poster #P0191:** Stability and low induction potential of cefiderocol against chromosomal AmpC beta-lactamases of *Pseudomonas aeruginosa* and *Enterobacter cloacae*  
**Presenter:** Miki Takemura

The details for the baloxavir marboxil presentations are as follows:

- **Oral presentation #O0469:** Lack of pharmacokinetic drug-drug interaction between baloxavir marboxil, a novel inhibitor of influenza virus cap-dependent endonuclease, and oseltamivir  
**Presenter:** Nao Kawaguchi  
**Date and time:** Sunday, April 22, 2018, 15:18-15:28  
**Session title and location:** Influenza - widening our armory for the next pandemic, hall B
- **Poster #P0047:** Delayed oral dosing of baloxavir marboxil exhibited significant reduction of viral titer and amelioration of virus-induced lung inflammation in mice lethally infected with influenza A virus  
**Presenter:** Keita Fukao  
**Date and time:** Saturday, April 21, 2018, 15:30-16:30  
**Session title and location:** New aspects of antiviral therapies, paper poster arena

The following COT-143 presentations will take place Tuesday, April 24, 2018 from 12:30-13:30, in the paper poster arena:

- **Poster #P2456:** Correlation between production of PcrV protein *in vitro/in vivo* of clinical isolates of *Pseudomonas aeruginosa* and their virulence in a murine infection model  
**Presenter:** Hideki Maki
- **Poster #P2457:** COT-143, a novel monoclonal antibody against the PcrV protein: *in vivo* efficacy and pharmacokinetic/pharmacodynamic assessment against *Pseudomonas aeruginosa* in murine lung infection models  
**Presenter:** Hideki Maki
- **Poster #P2458:** COT-143, a novel monoclonal antibody against the PcrV protein: binding affinity against PcrV and *in vitro* cytotoxicity inhibitory activity against *Pseudomonas aeruginosa*  
**Presenter:** Hideki Maki

### **About cefiderocol—an investigational antibiotic agent**

Cefiderocol is a siderophore cephalosporin with a novel mechanism for efficiently 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 bacteria.<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup> 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*.<sup>4</sup> 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 HAP/VAP/HCAP (APEKS-NP) and with carbapenem-resistant pathogens at various



infection sites (CREDIBLE-CR). Information is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) under the identifiers NCT02714595 and NCT03032380, respectively.

#### **About baloxavir marboxil—an investigational antiviral product**

Baloxavir marboxil is an oral cap-dependent endonuclease inhibitor with a new mechanism of action being studied for the treatment of influenza. Nonclinical studies with baloxavir marboxil demonstrated its anti-viral spectrum against seasonal influenza A and B strains and neuraminidase inhibitor-resistant flu strains and avian flu strains (e.g. A/H7N9) of which potential outbreak is one of several global public health concerns. An additional global Phase 3 study (CAPSTONE-2) in individuals at high risk for influenza-related complications is ongoing.

Shionogi submitted a New Drug Application (NDA) to the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in late 2017 and baloxavir marboxil is now commercially available in Japan. Further development and commercialization of baloxavir marboxil is in collaboration with F. Hoffmann-La Roche Ltd (hereafter “Roche”). Under the terms of this agreement, Roche holds worldwide rights to baloxavir marboxil excluding Japan and Taiwan, which will be retained exclusively by Shionogi. Discussions with other health authorities worldwide are currently ongoing and Shionogi and Roche are committed to bringing this important medicine to patients as quickly as possible.

Epidemic and pandemic influenza remain a major public health concern, and influenza drugs that will offer significant improvement over the current therapy are urgently needed. Worldwide, annual influenza epidemics are estimated to result in 3 to 5 million cases of severe illness, and about 250,000 to 500,000 deaths.<sup>5</sup> In general, those at highest risk of influenza-associated complications include children under 2 years of age, adults over 65 years of age, pregnant women, and people of any age with certain medical conditions, including chronic heart, lung, metabolic diseases (such as diabetes) and weakened immune systems.

#### **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 a reduction in tissue and cellular damage by the toxins released by the type III secretion system, which, if supported by clinical trials, could lead to a new treatment option for infections caused by *P. aeruginosa*, including MDR strains.

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.<sup>6,7</sup> 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](http://www.shionogi.com). For more information on Shionogi & Co., Ltd., visit [www.shionogi.co.jp/en](http://www.shionogi.co.jp/en).

#### **Forward Looking Statement**

*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**

1. Ito A, Nishikawa T., Masumoto S, et al. Siderophore Cephalosporin Cefiderocol Utilizes Ferric Iron Transporter Systems for Antibacterial Activity against *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother.* 2016;60(12):7396-7401.
2. Tillotson GS. Trojan Horse Antibiotics—A Novel Way to Circumvent Gram-Negative Bacterial Resistance? *Infectious Diseases: Research and Treatment.* 2016;9:45-52  
doi:10.4137/IDRT.S31567.
3. Ito-Horiyama T, Ishii Y, Ito A, et al. Stability of Novel Siderophore Cephalosporin S-649266 against Clinically Relevant Carbapenemases. *Antimicrob Agents Chemother.* 2016;60(7):4384-4386.
4. M Hackel, M Tsuji, Y Yamano, et al. In Vitro Activity of the Siderophore Cephalosporin, Cefiderocol, Against a Recent Collection of Clinically Relevant Gram-Negative Bacilli from North America and Europe, Including Carbapenem Non-Susceptible Isolates: The SIDERO-WT-2014 Study. *Antimicrobial Agents Chemotherapy.* 2017;61(9), posted online.

5. Influenza (Seasonal). World Health Organization.  
<http://www.who.int/mediacentre/factsheets/fs211/en/>. Published March 13, 2018. Accessed April 16, 2018.
6. 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.
7. 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.