

**Shionogi to Present New Data on Cefiderocol (S-649266), a Siderophore Cephalosporin, and S-033188 a Cap-Dependent Endonuclease Inhibitor for Treatment of Influenza, at the 27th European Congress of Clinical Microbiology and Infectious Diseases**

**Osaka, Japan, April 14, 2017** - Shionogi & Co., Ltd. today announced it will be presenting new data on cefiderocol (S-649266), an investigational siderophore cephalosporin in late stage development with activity against a broad range of Gram-negative pathogens, including those highly resistant to currently available agents such as colistin and carbapenem-resistant strains of *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and Enterobacteriaceae (CRE) and *Stenotrophomonas maltophilia*, and S-033188, an investigational cap-dependent endonuclease inhibitor targeting influenza at this year's European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), held in Vienna, Austria, April 22 – 25, 2017.

Highlights of cefiderocol presentations include first time clinical trial efficacy results, as well as supportive *in vitro* data, and S-033188 presentations will showcase both clinical and non-clinical data (e.g., non-clinical efficacy against avian influenza virus A/H5N1).

Below is an overview of the oral and poster presentations featuring cefiderocol and S-033188 at ECCMID 2017:

<b>Cefiderocol</b>		
<b>Session Title</b>	<b>Presentation</b>	<b>Abstract Number &amp; Presentation Information</b>
Late-breaker: Recent clinical trials	Cefiderocol Compared with Imipenem/Cilastatin in the Treatment of Adults with Complicated Urinary Tract Infections with or without Pyelonephritis or Acute Uncomplicated Pyelonephritis: Results from a Multicenter, Double-blind, Randomized Study (APEKS*-cUTI)	Abstract #7582 Oral Presentation Saturday, April 22, 2017 17:09-17:20 PM Presenter: Simon Portsmouth
Advances in Japanese Chemotherapy	Mode of action of cefiderocol, a novel siderophore cephalosporin, active against highly resistant Gram-negative bacteria including carbapenem-resistant strains of Enterobacteriaceae and non-fermenting	Abstract #3177 Oral Presentation Monday, April 24, 2017 14:54-15:04 PM Presenter: Yoshinori Yamano

\* *Acinetobacter*, *Pseudomonas*, *Escherichia*, *Klebsiella* and *Stenotrophomonas*

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	bacteria	
Cefiderocol	<i>In vitro</i> activity of cefiderocol against globally collected carbapenem-resistant Gram-negative bacteria including isolates resistant to ceftazidime/avibactam, ceftolozane/tazobactam and colistin: SIDERO-CR-2014/2016 study	Poster #1316 Poster Presentation Monday, April 24, 2017 12:30-13:30 PM Presenter: Yoshinori Yamano
	Surveillance of cefiderocol <i>in vitro</i> activity against Gram-negative clinical isolates collected in Europe: SIDERO-WT-2014	Poster #1314 Poster Presentation Monday, April 24, 2017 12:30-13:30 PM Presenter: Masakatsu Tsuji
	The <i>in vitro</i> activity of cefiderocol, a siderophore cephalosporin, against a global collection of <i>Stenotrophomonas maltophilia</i>	Poster #1313 Poster Presentation Monday, April 24, 2017 12:30-13:30 PM Presenter: Masakatsu Tsuji
<b>S-033188</b>		
<b>Session Title</b>	<b>Presentation</b>	<b>Abstract Number &amp; Presentation Information</b>
Advances in Japanese chemotherapy	Pharmacokinetic/pharmacodynamic analysis of S-033188, an influenza Cap-dependent endonuclease inhibitor, from a phase 2, randomized, double-blind, placebo-controlled study in otherwise healthy adults with seasonal influenza	Abstract #1033 Oral Presentation Monday, April 24, 2017 15:18-15:28 PM Presenter: Takeki Uehara
Novel and improved therapeutical approaches to viral infections	One day oral dosing of S-033188, a novel inhibitor of influenza virus Cap-dependent endonuclease, exhibited significant reduction of viral titer and prolonged survival in mice infected with influenza B virus	Poster #1971 Poster Presentation Tuesday, April 25, 2017 12:30-13:30 PM Presenter: Takao Shishido

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	Pharmacokinetic and pharmacodynamic analysis of S-033188/S-033447, a novel inhibitor of influenza virus Cap-dependent endonuclease, in mice infected with influenza A virus	Poster #1973 Poster Presentation Tuesday, April 25, 2017 12:30-13:30 PM Presenter: Takeshi Noshi
	Inhibitory effect of S-033188/S-033447, a novel inhibitor of influenza virus Cap-dependent endonuclease, against highly pathogenic avian influenza virus A/H5N1	Poster #1974 Poster Presentation Tuesday, April 25, 2017 12:30-13:30 PM Presenter: Keiichi Taniguchi

### **Cefiderocol—an investigational antibiotic agent<sup>1</sup>**

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>2</sup> This Trojan Horse strategy 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>3</sup> In addition, cefiderocol is stable against all known classes of beta-lactamases, including both the metallo- and serine-carbapenemases.<sup>4</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*, *Pseudomonas aeruginosa*, and Enterobacteriaceae and *Stenotrophomonas maltophilia*.<sup>5</sup>

### **About the regulatory pathway of cefiderocol**

Cefiderocol is currently in clinical development and recently completed a US registrational study in patients with cUTI (APEKS\*-cUTI). An additional Phase 3 trial in patients with carbapenem-resistant pathogens at various infection sites (CREDIBLE-CR) is ongoing. In 2017 Shionogi will initiate a Phase 3 HAP/VAP/HCAP† (APEKS\*-NP‡) clinical trial. The Company plans to submit a new drug application to the U.S. FDA in 2017 and to the EMA in 2018. Information is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) under the identifiers NCT02321800, NCT02714595 and NCT03032380, respectively.

### **About Influenza**

Epidemic and pandemic influenza remain a major public health concern, and novel influenza drugs that will offer significant improvement over current therapy are urgently needed. Worldwide, annual influenza

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epidemics are estimated to result in 3 to 5 million cases of severe illness, and about 250,000 to 500,000 deaths.<sup>6</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 S-033188**

S-033188 is a cap-dependent endonuclease inhibitor with a novel mechanism of action being studied for the treatment of influenza. S-033188 is an investigational product being developed for one-time dosing, and has the potential to be more effective than existing marketed anti-influenza products. Development and commercialization are in collaboration with F. Hoffmann-La Roche Ltd.

### **About Shionogi**

Shionogi & Co., Ltd. is a 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 well-being of the patients we serve.” Shionogi’s research and development currently target two therapeutic areas: infectious diseases, and pain/CNS disorders. For over 50 years, Shionogi has developed and commercialized innovative oral and parenteral anti-infectives. In addition, Shionogi is engaged in new research areas, such as obesity/geriatric metabolic disease and oncology/immunology. Contributing to the health and quality of life of patients around the world through development in these therapeutic areas is Shionogi's primary goal. For more details, please visit [www.shionogi.co.jp/en/](http://www.shionogi.co.jp/en/). For more information on Shionogi Inc., the U.S.-based subsidiary of Shionogi & Co., Ltd., headquartered in Florham Park, NJ, USA, please visit [www.shionogi.com](http://www.shionogi.com). For more information on Shionogi Ltd., the UK-based subsidiary of Shionogi & Co. Ltd., headquartered in London, England, please visit [www.shionogi.eu](http://www.shionogi.eu).

### ***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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Carbapenem Non-Susceptible Isolates: The SIDERO-WT-2014 Study. *Antimicrobial Agents Chemotherapy*  
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6. <http://www.who.int/mediacentre/factsheets/fs211/en/> WHO website, Influenza (Seasonal), Fact sheet N°211, March 2014

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