SHIONOGI TO HIGHLIGHT RESEARCH ON CEFIDEROCOL (S-649266), A SIDEROPHORE CEPHALOSPORIN, AND S-033188, A CAP-DEPENDENT ENDONUCLEASE INHIBITOR FOR TREATMENT OF INFLUENZA, AT IDWEEK 2017

OSAKA, Japan and FLORHAM PARK, NJ, SEPTEMBER 27, 2017 – Shionogi & Co., Ltd. (hereafter "Shionogi") today announced it will share the latest data on 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 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 for the treatment of influenza at IDWeek™ 2017, in San Diego, October 4 – 8, 2017.

Highlights of cefiderocol presentations include clinical trial results, as well as supportive *in vitro* data. S-033188 presentations will showcase both clinical and non-clinical data.

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

Cefiderocol		
Session Title	**Presentation**	**Poster Number & Presentation Information**
Symposium: New Antibiotics: What's in the Pipeline	Cefiderocol	Presentation number: 859 Thursday, October 5, 2017 2:18 p.m. Room 20ABCD
HAI: MDRO-GNR/Emerging Resistant Bacterial Pathogens	National Prevalence and Regional Variation of Carbapenem-Resistant Gram-Negative Bacteria in the Ambulatory and Acute Care Settings in the United States in 2016	Poster number: 371 Thursday, October 5, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
	Burden of Carbapenem-Resistant Gram-Negative Infections in US Hospitals	Poster number: 374 Thursday, October 5, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD

Expanded Spectrum - New Antimicrobial Susceptibility Testing	*In Vitro* Activity of Cefiderocol against Globally Collected Carbapenem-Resistant Gram-Negative Bacteria Isolated from Urinary Tract Source: SIDERO-CR-2014/2016	Poster number: 1199 Friday, October 6, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
	In Vitro Activity of Cefiderocol against Gram-Negative Clinical Isolates Collected from Urinary Tract Source: SIDERO-WT-2014/SIDERO-WT-2015	Poster number: 1229 Friday, October 6, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
Preclinical Study with New Antibiotics and Antifungals	*In Vivo* Efficacy of Cefiderocol against Carbapenem-Resistant Gram-Negative Bacilli in Murine Urinary Tract Infection Models	Poster number: 1512 Friday, October 6, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
	In Vivo Efficacy of Humanized Exposures of Cefiderocol Compared with Cefepime (FEP) and Meropenem (MEM) against Gram-Negative Bacteria in a Murine Thigh Model	Poster number: 1520 Friday, October 6, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
	Good Correlation of Cefiderocol Between *In Vivo* Efficacy Murine Thigh/Lung Infection Models and MIC Determined in Iron-Depleted Conditions	Poster number: 1524 Friday, October 6, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
Clinical Study with New Antibiotics and Antifungals	Population Pharmacokinetic and Pharmacokinetic/Pharmacodynamic Analyses of Cefiderocol in Subjects without Infection and Patients with Complicated Urinary Tract Infection and Acute Uncomplicated Pyelonephritis	Poster number: 1831 Saturday, October 7, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
	Clinical Response of 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)	Poster number: 1869 Saturday, October 7, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD

S-033188		
Session Title	**Poster Number & Presentation**	**Poster Number & Presentation Information**
Expanded Spectrum - New Antimicrobial Susceptibility Testing	Synergistic Antiviral Activity of S-033188/S-033447, a Novel Inhibitor of Influenza Virus Cap-Dependent Endonuclease, in Combination with Neuraminidase Inhibitors *In Vitro*	Poster number: 1214 Friday, October 6, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
Preclinical Study with New Antibiotics and Antifungals	Delayed Dosing Of S-033188, a Novel Inhibitor of Influenza Virus Cap-Dependent Endonuclease, Exhibited Significant Reduction of Viral Titer and Mortality in Mice Infected with Influenza A Virus	Poster number: 1514 Friday, October 6, 2017 12:30 p.m. – 2:00 p.m. Poster Hall CD
Late Breaker Oral Abstracts	Cap-Dependent Endonuclease Inhibitor S-033188 for the Treatment of Influenza: Results from a Phase 3, Randomized, Double-Blind, Placebo- and Active-Controlled Study in Otherwise Healthy Adolescents and Adults with Seasonal Influenza	Saturday, October 7, 2017 10:40 a.m. Room: 02

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.[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 *A. baumannii, P. aeruginosa*, Enterobacteriaceae, and *S. maltophilia*.[4] Cefiderocol has poor *in vitro* activity against Gram-positive or anaerobic bacteria.

About S-033188—an investigational product
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 deliver higher potency antiviral effects than existing marketed anti-influenza products. Development and commercialization are in collaboration with F. Hoffmann-La Roche Ltd.

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 epidemics are estimated to result in 3 to 5 million cases of severe illness, and about 250,000 to 500,000 deaths.[5] 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 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/. 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. For more information on Shionogi Ltd., the UK-based subsidiary of Shionogi & Co. Ltd., headquartered in London, England, please visit 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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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. n 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. http://www.who.int/mediacentre/factsheets/fs211/en/ WHO website, Influenza (Seasonal), Fact sheet N°211, March 2014