Press Release

Shionogi to Present Data on Cefiderocol and Baloxavir Marboxil at IDWeek 2018

Osaka, Japan and Florham Park, N.J., September 27, 2018 – Shionogi & Co., Ltd. (hereafter "Shionogi") announced today that 14 presentations will feature the company's investigational compounds at IDWeek™ 2018, in San Francisco, October 3-7, 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 baloxavir marboxil, an investigational, first-in-class, single-dose oral medicine with a novel proposed mechanism of action that inhibits viral cap-dependent endonuclease currently under review for approval by the United States Food and Drug Administration (FDA).

Highlights of cefiderocol presentations include *in vitro* and *in vivo* activities against carbapenem-resistant Gram-negative pathogens as well as supportive epidemiological data. Baloxavir marboxil presentations include a late-breaker of positive results from the global phase III study in individuals at high risk for influenza-related complications (CAPSTONE-2)[1] and other clinical and non-clinical data.

All poster presentations will take place in Moscone Convention Center Hall S. All presentation times are represented as Pacific Daylight Time (PDT).

The 10 cefiderocol abstracts that will be presented at IDWeek 2018 are:

Thursday, October 4, 2018m 12:30 p.m.-1:45 p.m. PDT:

- **Poster #681**: Epidemiology and Outcomes of Patients with Carbapenem-resistant Bloodstream Infection in United States (U.S.) Hospitals, 2010-2015
- **Poster #696**: Mechanism of Cefiderocol High MIC Mutants Obtained in Non-clinical FoR Studies

Friday, October 5, 2018, 12:30 p.m.-1:45 p.m. PDT:

- **Poster #1191**: Prevalence and Microbiology of Carbapenem Resistance Among Six Gram-negative Pathogens in Bloodstream Infections in U.S. Hospitals, 2010-2015
- **Poster #1349**: Global Surveillance of Cefiderocol against Gram-negative Clinical Strains Collected in North America: SIDERO-WT-2015
- **Poster #1351**: *In Vitro* Activity of Cefiderocol (S-649266), a Siderophore Cephalosporin,

Against *Enterobacteriaceae* with Defined Extended-spectrum β-Lactamases and Carbapenemases
- **Poster #1366**: *In Vitro* and *In Vivo* Activity of Cefiderocol against *Stenotrophomonas maltophilia* Clinical Isolates
- **Poster #1375**: *In Vitro* Activity of Cefiderocol and Comparator Agents against Gram-negative Isolates from Cancer Patients
- **Poster #1521**: Heterogeneity of Recent Phase 3 cUTI Clinical Trials with New Antibiotics

Saturday, October 6, 2018, 12:30 p.m.-1:45 p.m. PDT:
- **Poster #2163**: Risk Factors for Carbapenem-resistant Gram-negative Bloodstream Infections (BSI) in U.S. Hospitals (2010-2015)
- **Poster #2388**: Efficacy of Humanized Cefiderocol Exposures Over 72 Hours Against a Diverse Group of Gram-negative Isolates in the Neutropenic Murine Thigh Infection Model

The four baloxavir marboxil abstracts that will be presented at IDWeek 2018 are:

Late breaker, oral presentation on Saturday, October 6, 2018 at 10:30 a.m PDT:
- **Presentation #LB16:** Phase 3 Trial of Baloxavir Marboxil in High-risk Influenza Patients (CAPSTONE-2 Study)
  Presenter: Michael G. Ison
  Location: Room S 152-154 (Session 213)

Oral presentation session on Friday, October 5, 2018 at 2:15 p.m. PDT:
- **Presentation #1645**: Exploring Clinical and Antiviral Efficacy of Baloxavir Marboxil in a Phase 3, Randomized, Double-blind, Placebo- and Active-controlled Study of Otherwise Healthy Adults/Adolescents in Seasonal Influenza: Impact on Regional Participants, Treatment Time and Influenza Type B Virus Infection (CAPSTONE-1 Study)
  Presenter: Keiko Kawaguchi
  Location: Room W 2002

Friday, October 5, 2018, 12:30 p.m.-1:45 p.m PDT:
- **Poster #1343**: Prophylactic Dosing of Baloxavir Acid Eliminates Mortality in Mice Lethal Influenza A Virus Infection Model
- **Poster #1350**: Therapeutic Effects of Baloxavir Marboxil against Influenza A Virus Infection in Ferrets

All abstracts for IDWeek 2018 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 including MDR strains. 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.[2] 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.[3] 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.[4] 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*.[5] Cefiderocol has poor *in vitro* activity against Gram-positive or anaerobic bacteria.

Cefiderocol is currently in clinical development. Two Phase III 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). The company plans to submit a New Drug Application (NDA) to the United States FDA later in the year followed by a marketing authorization application to the European Medicines Agency and other countries. Information is available at www.clinicaltrials.gov under the identifiers NCT02714595 and NCT03032380, respectively.

About Baloxavir Marboxil – An Investigational Antiviral Drug for the Treatment of Influenza

Baloxavir marboxil, discovered and developed by Shionogi, has a novel mechanism of action that inhibits cap-dependent endonuclease, an essential enzyme for viral replication. Different from all currently available antiviral treatments, baloxavir marboxil is a single-oral dose to treat uncomplicated influenza.. In non-clinical studies, baloxavir marboxil demonstrated an antiviral effect against a wide range of influenza viruses including oseltamivir-resistant strains and avian strains (H7N9, H5N1).[6,7,8] Baloxavir marboxil was approved and is now available in Japan under the brand name XOFLUZA® for the treatment of influenza Types A and B in adults and pediatric patients. Shionogi submitted a NDA for baloxavir marboxil in the U.S. on April 24, 2018 for the treatment of acute uncomplicated influenza in patients 12 years of age and older in collaboration with F. Hoffmann-La Roche Ltd. (hereafter “Roche”). The FDA accepted the NDA and granted Priority Review based on a phase II study in Japan and a global phase III study (CAPSTONE-1) in otherwise healthy patients.[9] The Prescription Drug User Fee Act (PDUFA) date for the FDA decision is December 24, 2018.[10] Shionogi submitted a NDA for baloxavir marboxil in Taiwan on June 29, 2018, for the treatment of influenza in patients 12 years of age and older.[11]

Shionogi and the Roche Group, which includes Genentech in the U.S., are in a license and collaboration agreement to further develop and commercialize baloxavir marboxil, with a submission

for approval planned in the U.S. and in other regions, globally. Under the terms of this agreement, the Roche Group holds worldwide rights to baloxavir marboxil excluding Japan and Taiwan where the rights are retained exclusively by Shionogi. Roche will further investigate baloxavir marboxil in a global Phase III development program including pediatric and severely ill hospitalized populations with influenza. Shionogi will conduct a post-exposure Phase III prophylaxis study in Japan in the 2018/2019 flu season.

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 information on Shionogi & Co., Ltd., please visit www.shionogi.co.jp/en. For more information on Shionogi Inc., please visit www.shionogi.com.

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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   Shionogi Announces Positive Top-Line Results for Baloxavir Marboxil Phase III Study (CAPSTONE-2) in Individuals at High Risk for Influenza-Related Complications
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6. T. Noshi et al. S-033447/S-033188, a Novel Small Molecule Inhibitor of Cap-dependent Endonuclease of Influenza A and B Virus: In Vitro Antiviral Activity against Laboratory Strains of Influenza A and B Virus in Madin-Darby Canine Kidney Cells. Poster presentation at OPTIONS IX, August 2016.
7. K.Taniguchi et al. Inhibitory Effect of S-033188, a novel inhibitor of influenza virus cap-dependent endonuclease, against avian influenza A/H7N9 virus in vitro and in vivo. Poster presentation at ESWI, September 2017.
8. K.Taniguchi et al. 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 presentation at ECCMID, April 2017.

9. Frederick G. Hayden et al. Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents. N Engl J Med 2018 Sep 6;
379:913-923. https://www.nejm.org/doi/full/10.1056/NEJMoa1716197?query=featured_home
10. Press release on June 26, 2018
FDA Accepts Baloxavir Marboxil New Drug Application and Grants Priority Review for the Treatment of Influenza
11. Press release on July 2, 2018
Shionogi Filed for the New Drug Application of Baloxavir Marboxil in Taiwan for the Treatment of Influenza