CEFIDEROCOL, A NOVEL INVESTIGATIONAL SIDEROPHORE CEPHALOSPORIN,
DEMONSTRATED POTENT ACTIVITY AGAINST MULTI-DRUG RESISTANT
GRAM-NEGATIVE PATHOGENS

Osaka, Japan and Florham Park, NJ (October 26, 2016) - Shionogi & Co., Ltd. (hereafter “Shionogi”) presented the results of the first global surveillance study for its in-development investigational siderophore cephalosporin, cefiderocol (S-649266), at IDWeek™ 2016 in New Orleans, Louisiana. Cefiderocol showed potent activity against Gram-negative pathogens, including carbapenem-resistant strains of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* as well as carbapenem-resistant *Enterobacteriaceae*. The results were presented using in vitro data from 8765 test strains of *P. aeruginosa*, *A. baumannii*, and *Enterobacteriaceae* isolated in 2014/2015 from patients in North America and across Europe.1

The study, conducted by International Health Management Associates, Inc, evaluated the in vitro activity of cefiderocol in comparison with various marketed Gram-negative treatments, including colistin and the newer agents ceftazidime/avibactam and ceftolozane/tazobactam. Key findings from the study included1:

- Cefiderocol showed the lowest MIC50 and MIC90 values of all compounds tested.
- The growth of 99.6% of all isolates was inhibited at 4 µg/mL of cefiderocol (MIC of ≤4 µg/mL).
- Cefiderocol was active against many of the Gram-negative pathogens that were not susceptible to other antibiotics (1290 isolates [14.7% of total studied] were non-susceptible to meropenem). Cefiderocol had MIC90 values of 1, 1, and 4 µg/mL against meropenem non-susceptible isolates of *A. baumannii*, *P. aeruginosa*, and *Enterobacteriaceae*, respectively; whereas the MIC90 values of both ceftazidime/avibactam and ceftolozane/tazobactam against these pathogens were ≥32 µg/mL.

**Multi-drug resistant pathogens—a growing worldwide threat**

The threat to public health of these MDR bacteria strains has reached a crisis point, according to the President's Council of Advisors on Science and Technology.2 The magnitude of this threat has also been confirmed by the United Nations. At the recent United Nations General Assembly high-level meeting on antimicrobial resistance, the Director-General told the member states that antimicrobial resistance is a “fundamental threat” to global health and safety.3

“There is an enormous need for new anti-infectives to battle the growing problem of drug-resistant bacteria, which has reached critical proportions,” said Dr Tsutae Den Nagata, Chief Medical Officer at Shionogi. “The study results presented at ID Week demonstrate that cefiderocol is highly active against the most problematic and serious Gram-negative carbapenem-resistant pathogens.”
Cefiderocol—an investigational antibiotic agent
Cefiderocol is a siderophore cephalosporin with a unique mechanism for penetrating efficiently into Gram-negative pathogens. Cefiderocol binds to free iron and is actively transported into bacterial cells through the outer membrane. This Trojan horse strategy allows cefiderocol to enter the space in-between the bacterial cell walls and disrupt cell wall synthesis. In addition, cefiderocol is stable against nearly all beta-lactamases, including both the serine and metallo-carbapenemases.

About the regulatory pathway of cefiderocol
Cefiderocol has been designated by the U.S. Food and Drug Administration (FDA) as a Qualified Infectious Disease Product, which allows for priority review and provides eligibility for fast-track approval status. Registrational studies are ongoing in patients with complicated urinary tract infections and in patients with carbapenem-resistant pathogens at various infection sites. Information is available at www.clinicaltrials.gov under the identifiers NCT02321800 and NCT02714595, respectively.

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 targets 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 QOL 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 US-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.

Contact:
For global inquiries: Corporate Communications, Shionogi & Co., Ltd.
Telephone: +81-6-6209-7885    Fax: +81-6-6229-9596

US Media Contact: Michele Mencer
Mobile +1-973-524-0474        Office +1-973-307-3353

References:

*Dr Echols is a paid consultant of Shionogi Inc.

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