SHIONOGI ANNOUNCES POSITIVE TOP-LINE RESULTS FOR CEFIDEROCOL PIVOTAL cUTI CLINICAL TRIAL

Osaka, Japan and Florham Park, NJ, US (January 12, 2017) - Shionogi & Co., Ltd. (hereafter "Shionogi") has announced that cefiderocol (S-649266), a novel siderophore cephalosporin in late-stage development, met the FDA pre-specified primary endpoint for non-inferiority vs imipenem/cilastatin (IPM/CS) in patients with serious complicated urinary tract infection (cUTI) with Gram-negative bacteria. Cefiderocol was superior to IPM/CS at test of cure (TOC).

The study APEKs-cUTI* enrolled 452 patients with cUTI. The median duration of treatment was nine days for both cefiderocol and IPM/CS for all populations. Cefiderocol met the FDA primary efficacy endpoint of composite of clinical cure and microbiologic eradication at test of cure (TOC) in 72.6 percent of patients (n=252) which was superior to IPM/CS at 54.6 percent (n=119), a weighted difference of 18.58 percent (95 percent CI: 8.23, 28.92).

"We are very excited about the results of this trial. Unlike most studies, this cUTI study was designed to include patients that are more difficult to treat. The data clearly demonstrate that cefiderocol will be an important option for serious Gram-negative infections," said Dr. Tsutae Den Nagata, Chief Medical Officer.

Cefiderocol was well tolerated in the study, with 40 percent of patients experiencing an adverse event in the cefiderocol arm vs 50 percent of patients in the IPM/CS arm. Serious adverse events (SAEs) occurred in 14 patients (4.7 percent) who received cefiderocol and 12 patients (8.1 percent) who received IPM/CS. Shionogi plans to submit an NDA for cefiderocol to the FDA in 2017. The data from the APEKs-cUTI* clinical study are planned to be presented in early 2017.

APEKs-cUTI* Clinical Trial[1]

APEKs-cUTI* was an international multicenter, double-blind, randomized, non-inferiority trial designed to evaluate the efficacy, safety, and tolerability of cefiderocol vs IPM/CS in hospitalized adult patients with cUTI, with or without pyelonephritis, at TOC (approximately 7 days following the end of treatment). The study permitted enrollment of immunocompromised patients, including renal transplant, and limited acute uncomplicated pyelonephritis to less than 30 percent. Switch to oral therapy was not permitted. Patients with Gram-negative pathogens were randomized on a 2:1 basis to receive cefiderocol (2 grams) administered intravenously every 8 hours, or high-dose IPM/CS (1/1 gram) administered intravenously every 8 hours, for 7 to 14 days in hospital. Of the 452 patients randomized, 448 were treated and 371 met the definition of the micro-ITT population and were assessed for efficacy. All treated subjects were assessed for safety.

Cefiderocol—an investigational antibiotic agent[2]

Cefiderocol is a siderophore cephalosporin with a unique mechanism for efficiently penetrating the outer cell membrane into 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.[3] This Trojan Horse strategy allows cefiderocol to achieve higher concentrations in the periplasmic space where it can then bind to receptors to inhibit cell wall synthesis in the bacterial cells.[4] In addition, cefiderocol is stable against all known classes of beta-lactamases, including both the metallo- and serine carbapenemases.[5] Data from the first global surveillance study for cefiderocol demonstrated potent in vitro activity against a wide spectrum of Gram-negative pathogens including carbapenem-resistant Acinetobacter baumannii, Pseudomonas aeruginosa, Stenotrophomonas maltophilia, and Enterobacteriaceae (CRE).

About the regulatory pathway of cefiderocol[6,7]

Cefiderocol has been designated by the (FDA) as a Qualified Infectious Disease Product (QIDP), which allows for priority review and provides eligibility for fast-track approval status. A registrational study in patients with cUTI (APEKs-cUTI*) has been completed while an additional trial in patients with carbapenem-resistant pathogens at various infection sites (CREDIBLE-CR) is ongoing. Information is available at www.clinicaltrials.gov under the identifiers NCT02321800 and NCT02714595, respectively.

* *Acinetobacter, Pseudomonas*, *Escherichia coli*, and *Klebsiella* complicated urinary tract infections

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. A 138 year old company, Shionogi has developed and commercialized innovative oral and parenteral anti-infectives for over 50 years. 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 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 European-based subsidiary of Shionogi & Co., Ltd., headquartered in London, England, please visit www.shionogi.eu.

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 outcomes 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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