PRESSRELEASE

SHIONOGI

ECCMID 2023: Shionogi Announces Real-World Evidence Demonstrating the Efficacy of Fetcroja® (cefiderocol) Against Some of the Most Difficult-to-Treat Gram-Negative Bacterial Pathogens

A retrospective chart review interim analysis demonstrated that cefiderocol achieved clinical cure in 65% and 60% of patients with *Pseudomonas aeruginosa* and *Acinetobacter baumannii* respectively, the majority of whom were severely ill with comorbidities.

OSAKA, Japan, APRIL 17, 2023 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announces key data for Fetcroja® (cefiderocol), an innovative siderophore cephalosporin, to be presented at the 33rd European Congress of Clinical Microbiology & Infectious Diseases (ECCMID), April 15-18, 2023, including new real-world evidence demonstrating its efficacy against some of the most difficult-to-treat Gram-negative bacterial infections.

In Europe, cefiderocol is commercially available under the brand name Fetcroja® for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options.[1] In the US, cefiderocol is available under the brand name Fetroja® and is indicated in patients 18 years of age or older for the treatment of hospital-acquired bacterial pneumonia, ventilator-associated bacterial pneumonia (HABP/VABP) and complicated urinary tract infections (cUTIs) caused by certain susceptible Gram-negative microorganisms.[2]

Interim results are emerging from PROVE (Retrospective Cefiderocol Chart Review), an ongoing international, retrospective study of the real-world use of cefiderocol for Gram-negative infections across EU and US sites.[3,4] The study includes 194 patients with *Pseudomonas aeruginosa* infections treated with cefiderocol (123 from the US and 71 from the EU). These were generally seriously ill patients, many requiring mechanical ventilation and/or vasopressor support. The interim results show that cefiderocol achieved clinical cure in 65% of these patients, and 81% of patients were alive within 30 days of starting cefiderocol treatment. The patients principally had respiratory tract and bloodstream infections. Cefiderocol was initiated for a documented pathogen in the majority of cases (77%) and as monotherapy in 57% of patients.

Also in the study were 98 patients with *Acinetobacter baumannii* infections (71 from US and 27 from the EU). The patients had respiratory infection and bacteraemia as the most common infections. High levels of organ support were required in these patients, with 45% receiving mechanical ventilation and 30% requiring vasopressor support. Cefiderocol achieved clinical cure in 60% of patients, and 76% of patients were alive within 30-days of starting treatment. Cefiderocol was targeted as first treatment or as salvage therapy in 93% of patients, and as monotherapy in 41% of patients.

"These interim results from PROVE build on a growing body of real-world evidence across Europe and the US demonstrating the efficacy of cefiderocol in treating patients with life-threatening infections, such as Acinetobacter baumannii and Pseudomonas aeruginosa, the majority of whom are very sick with multiple comorbidities," commented Prof. Dr. Dominic Wichmann, Consultant in department of Intensive Care Medicine, University of Hamburg-Eppendorf. *"These are pathogens that fall into the World Health Organization's critical priority list, for which effective treatments are urgently needed."*

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Antimicrobial resistance (AMR)
Antimicrobial resistance (AMR) is a major health burden which urgently needs to be addressed. Globally, in 2019, there were 1.27 million deaths attributable to bacterial AMR.[5] Infections caused by carbapenem-resistant Gram-negative bacteria are often associated with a high mortality rate.[6] If no action is taken, antimicrobial resistance is predicted to kill 10 million people every year by 2050, at a cumulative cost to global economic output of 100 trillion USD.[7]

About FETCROJA® (Cefiderocol)
Cefiderocol is a siderophore cephalosporin antibiotic with an innovative mechanism for penetrating the outer cell membrane of Gram-negative pathogens by acting as a siderophore. In addition to entering cells by passive diffusion through porin channels, 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.[8] These mechanisms allow cefiderocol to achieve higher concentrations in the periplasmic space where it can bind to penicillin-binding proteins and inhibit cell wall synthesis in the bacterial cells.[9] Cefiderocol has also demonstrated *in vitro* activity against certain bacteria that contain very problematic resistant enzymes such as ESBLs, AmpC, serine- and metallo-carbapenemases.[10,11] Data from multinational surveillance studies for cefiderocol demonstrated potent *in vitro* activity against a wide spectrum of Gram-negative pathogens including carbapenem-resistant *A. baumannii, P. aeruginosa*, Enterobacterales, and *S. maltophilia*.[12] The clinical significance of the *in vitro* data is unknown. Cefiderocol has no clinically relevant activity against Gram-positive or anaerobic bacteria.

FETCROJA® (Cefiderocol) INDICATION
In Europe, cefiderocol is commercially available under the brand name Fetcroja® for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options.

Shionogi's commitment to fighting antimicrobial resistance
Shionogi has a strong heritage in the field of anti-infectives and has been developing antimicrobial therapies for more than 60 years. Shionogi is proud to be one of the few large pharmaceutical companies that continues to focus on research and development in anti-infectives. The company invests the highest proportion of its pharmaceutical revenues in relevant anti-infectives R&D compared to other large pharmaceutical companies.[13]

For more information, please refer to: https://www.shionogi.com/global/en/sustainability/amr.html

About Shionogi
Shionogi & Co., Ltd. is a 145-year-old global, research-driven pharmaceutical company headquartered in Osaka, Japan, that is 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." The company currently markets products in several therapeutic areas including anti-infectives, pain, CNS disorders, cardiovascular diseases and gastroenterology. Shionogi's research and development currently target two therapeutic areas: infectious diseases, and pain/CNS disorders.

For more information on Shionogi & Co., Ltd., please visit https://www.shionogi.com/global/en/

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, lack of availability 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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