

## Regarding the Filing for Approval of Cefiderocol in Japan

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**OSAKA, Japan, March 24, 2021** - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced that Shionogi has filed for approval to manufacture and sell cefiderocol, the novel siderophore cephalosporin antibacterial drug, in Japan today.

Cefiderocol has completed three global trials (a Phase 2 trial [APEKS-cUTI] in patients with complicated urinary tract infections, a Phase 3 trial in patients with carbapenem-resistant gram-negative bacterial infections [CREDIBLE-CR], and a Phase 3 trial in patients with nosocomial pneumonia [APEKS-NP]) and has been approved by the U.S. Food and Drug Administration (FDA) and the European Commission (EC)<sup>1-3</sup>. Based on the results of these clinical trials, Shionogi has filed for approval to manufacture and sell cefiderocol in Japan.

The increasing number of carbapenem antibiotic-resistant Gram-negative bacterial infections, including Enterobacterales, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*, has become a major medical issue<sup>4-7</sup>. Infectious diseases caused by these bacteria are difficult to treat with existing antibacterial drugs and increase mortality<sup>8</sup>. The development of new antibiotics to fight Gram-negative bacteria that are resistant to carbapenem antibiotics has been designated as a top priority by WHO and CDC<sup>4,9</sup>. In addition, the Japan Agency for Medical Research and Development (AMED) Public and Private Partnerships for Infectious Diseases R&D has published a pathogens list targeted for drug discovery and is calling for the further promotion of research and development<sup>10</sup>.

Shionogi is committed to "Protect people worldwide from the threat of infectious diseases" as our key focus. We are not only pursuing the research and development of therapeutics, but are also working towards total care for infectious diseases. Shionogi is committed to overcoming the global AMR problem and to rapidly providing infectious disease drugs required to protect the health of patients around the world.

### **About cefiderocol**

Cefiderocol is a novel siderophore cephalosporin antibacterial drug which effectively penetrates the outer cell membrane of Gram-negative pathogens. Cefiderocol is unaffected by the three major mechanisms associated with bacterial resistance to carbapenem: inactivation by beta-lactamase, reduction of membrane permeability by mutation of porin channel, and overexpression of efflux pumps. Cefiderocol is actively transported into bacteria via the bacterial iron transporter due to its unique structure (siderophore) that binds to iron<sup>11</sup>. As a result, cefiderocol is efficiently incorporated into the bacterial periplasm and inhibits cell wall synthesis<sup>12</sup>.

### **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*

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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.

## For Further Information, Contact:

SHIONOGI Website Inquiry Form : <https://www.shionogi.com/global/en/contact.html>

## References

1. [Press release on November 15, 2019](#)  
FETROJA® (cefiderocol) Approved by the FDA for Treatment of Complicated Urinary Tract Infections (cUTI) in Adult Patients with Limited or No Alternative Treatment Options
2. [Press release on September 29, 2020](#)  
Shionogi Announces FDA Approval of FETROJA® (cefiderocol) for the Treatment of Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia
3. [Press release on April 28, 2020](#)  
Shionogi Receives European Commission Marketing Authorisation for FETCROJA® (cefiderocol) for the Treatment of Infections Due to Aerobic Gram-negative Bacteria in Adults with Limited Treatment Options
4. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. February 27, 2017. Retrieved from <https://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/>.
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7. Brooke JS. *Stenotrophomonas maltophilia*: an emerging global opportunistic pathogen. *Clin Microbiol Rev* 2012; 25:2–41.
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9. Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States 2019, Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019. Retrieved from <https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf>
10. AMED) Public and Private Partnerships for Infectious Diseases R&D, pathogen list [https://id3catalyst.jp/apid/list\\_e.html](https://id3catalyst.jp/apid/list_e.html)

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12. Tillotson GS. Trojan Horse Antibiotics—A Novel Way to Circumvent Gram-Negative Bacterial Resistance? *Infectious Diseases: Research and Treatment*. 2016; 9:45-52 doi:10.4137/IDRT.S31567.

Regarding more information about our commitment to AMR, please check [here](#).