PRESSRELEASE

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IDWeek 2025: Shionogi Presents Real-World and Surveillance Data Reinforcing Role of Cefiderocol Across Range of Patient Populations and Difficult-to-Treat Infections

- Latest analysis of U.S. real-world evidence demonstrates improved clinical outcomes when cefiderocol is used as earlier treatment

- Additional presentations demonstrate cefiderocol's activity against difficult-to-treat pathogens, including those that are non-susceptible to other antibiotics

OSAKA, Japan, October 20, 2025 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") presents new data at IDWeek 2025, demonstrating broad activity of Fetroja®/Fetcroja® (cefiderocol) across infection types and adult patient populations. Results from the PROVE (Retros**p**ective Cefide**ro**col Chart Re**vie**w) study showed the effectiveness of earlier appropriate cefiderocol use in real-world settings, while data from the SENTRY Antimicrobial Surveillance Program further demonstrated the susceptibility of a broad range of clinically significant Gram-negative (GN) pathogens to cefiderocol.[1,2,3,4,5]

Cefiderocol is an innovative siderophore cephalosporin for the treatment of seriously ill adult patients with complicated urinary tract infections (cUTIs) and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by certain GN bacterial infections.[6] See Fetroja U.S. full indications and important safety information below in the About Cefiderocol section.

PROVE is a five-year, international, retrospective, observational medical chart review study, conducted between November 2020 and July 2024 in >1000 patients in the U.S. and EU.[1,2,7,8] The study is designed to evaluate the effectiveness and safety of real-world cefiderocol use in adult patients with serious infections caused by GN pathogens, the majority of which were resistant to carbapenem antibiotics.[7]

The analysis of the U.S. cohort of the PROVE study assessed clinical cure rate (defined as resolution or improvement of signs or symptoms with no subsequent signs of relapse or mortality) in mostly seriously ill patients treated with cefiderocol.[2] In the study, 57.3% of patients were in the intensive care unit and 47.6% were receiving organ support (such as mechanical ventilation or use of vasopressor medication) at cefiderocol initiation.[2] The overall clinical cure rate for infections across different infection sites was 70.1%.[2] Clinical cure rate was 73.7% among patients who received cefiderocol before the causative bacteria had been identified (empiric treatment), while the clinical cure rate was lower (54.3%) when cefiderocol was used as salvage therapy.[2]

"Real-world studies like PROVE build on the insights of controlled clinical trials by showing how therapies perform in real-life clinical settings against the difficult-to-treat infections patients currently face in the U.S.," said Cornelius (Neil) Clancy, MD, Professor of Medicine, University of Pittsburgh. "These results demonstrate that cefiderocol effectively treated seriously ill patients with a range of GN pathogens across multiple infection sites, particularly when used earlier in the treatment course – even before

identifying the causative bacteria when appropriate risk factors exist. This finding can help guide clinical decision-making for these patients and meaningfully improve care."

The analysis included 508 patients in the U.S. with serious infections caused by GN bacteria who received cefiderocol for the first time and for at least 72 hours (median of 10 days).[2] Respiratory tract infections were the most common infections (53.5%), followed by skin and skin structure infections (14.6%) and bloodstream infections (9.3%).[2] Cefiderocol was effective across a range of serious infections caused by GN pathogens; the most frequent monomicrobial infections observed were from *Pseudomonas aeruginosa* (29.9%), *Acinetobacter baumannii* (21.7%), Enterobacterales (11.4%), and *Stenotrophomonas maltophilia* (4.9%).[2] Cefiderocol was also effective across polymicrobial infections, which represented 29.9% of infections in this analysis.[2]

Additional analyses from the PROVE global cohort demonstrate cefiderocol effectiveness against serious and difficult-to-treat infections[3,4]

Cefiderocol effectiveness against bloodstream infections (BSIs) was examined:
BSIs are the leading cause of mortality from infection.[9] In a separate analysis from the real-world PROVE study examining 1,075 patients worldwide, BSIs were reported in 226 patients.[4,8] In this analysis, 5.3% of patients were in the intensive care unit and 46.0% were receiving organ support.[4] Patients were infected with a range of pathogens, including *Pseudomonas aeruginosa,* Enterobacterales, *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia,* which are typically associated with poor clinical outcomes.[4] Results showed that cefiderocol treatment led to a 63.7% overall clinical cure rate in patients with BSIs.[4] Clinical cure rates were higher when cefiderocol was used as empiric treatment (72%), defined as treatment before the causative bacteria had been identified, and were lower when cefiderocol was used as salvage therapy.[4] Please see U.S. indications and Important Safety Information for cefiderocol below.

Cefiderocol was effective in treating bacteria not susceptible to beta-lactam–beta-lactamase inhibitor (BL-BLI) combinations:
Additional real-world data from PROVE showed that cefiderocol is effective against bacteria that are both susceptible (clinical cure rate: 70.5%) and non-susceptible (clinical cure rate: 70.2%) to newer BL-BLI combinations.[3] Non-susceptible bacteria were defined as resistant or intermediate to at least one BL–BLI tested.[3] In a real-world setting, BL-BLI non-susceptible infections showed a low rate of cross-resistance to cefiderocol, with 90.6% remaining susceptible, a finding further supported by SENTRY Antimicrobial Surveillance Program data presented at IDWeek.[3,5]

SENTRY Antimicrobial Surveillance Program further demonstrates cefiderocol activity against a broad range of clinically relevant Gram-negative pathogens and show susceptibility remains high five years after cefiderocol commercialization[1,5,8,10]

The SENTRY Antimicrobial Surveillance Program monitors pathogen prevalence and antimicrobial susceptibility patterns worldwide.[10,11] Surveillance programs like SENTRY track how bacterial resistance evolves over time and across regions, offering critical early warning of emerging strains and helping guide clinical treatment decisions.[10,11,12]

Cefiderocol was active against bacteria not susceptible to BL-BLI combinations:

*In vitro** data from the SENTRY Antimicrobial Surveillance Program further support that cefiderocol is highly active against bacteria not susceptible to BL-BLI combinations.[5]

"Bacterial isolates collected from SENTRY were examined to determine their susceptibility to multiple antibiotics, including BL-BLI combinations and cefiderocol. This analysis identified isolates that were resistant to BL-BLI combinations, a serious threat to public health, but remained susceptible to cefiderocol," said Marianna Castanheira, PhD, FIDSA, FAAM, Chief Scientific Officer, Element Materials Technology. "These results show that pathogens which showed cross resistance to multiple BL-BLI combinations remained susceptible to cefiderocol. It is encouraging to see that cefiderocol remained active against these bacteria of serious concern."

Cefiderocol was active against metallo-beta-lactamase (MBL)-carrying A. baumannii:
*In vitro** data from SENTRY also showed cefiderocol as one of the few agents tested which demonstrated activity against MBL-carrying *A. baumannii,* a class of bacteria that has become highly resistant to multiple antibiotics, and for which treatment options are limited.[1]

Microbial susceptibility to cefiderocol remained high after 5 years:
*In vitro** data from SENTRY from 2020 to 2024 demonstrated consistent high susceptibility for cefiderocol against GN bacteria, including carbapenem non-susceptible bacteria, since the EU and U.S. approval of cefiderocol, with the high activity of cefiderocol maintained over the five-year period. [10]

**In vitro activity does not necessarily correlate with clinical efficacy.*

About Shionogi in Infectious Disease
Since 1953, Shionogi has been a leader in infectious disease discovery and commercialization. Our R&D story extends beyond antibiotics to include novel medications for HIV and influenza. Today, our global pipeline includes investigational agents developed to address global health challenges including antimicrobial resistance, COVID-19, influenza, rare fungal diseases and respiratory syncytial virus.

As part of our commitment to addressing unmet medical needs, Shionogi is partnering with several non-governmental organizations to increase equitable access to our medications worldwide. Shionogi has a landmark license and technology transfer agreement for cefiderocol with Global Antibiotic Research and Development Partnership (GARDP) and a collaboration agreement with the Clinton Health Access Initiative (CHAI) to transform the landscape of access to antibiotics in many low-income countries, most lower-middle and upper-middle income countries, and select high income countries.

About Shionogi & Co. Ltd.
Shionogi & Co., Ltd. is a 146-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.

Antimicrobial Resistance

AMR is a major health burden that urgently needs to be addressed.[11] Globally, in 2021, there were 1.14 million deaths attributable to bacterial AMR.[13] Infections caused by carbapenem-resistant Gram-negative bacteria are often associated with a high mortality rate.[14] If no action is taken, drug-resistant pathogens could cause more than 39 million deaths over the next 25 years.[13]

About Shionogi in AMR
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 R&D in anti-infectives.

About Cefiderocol
In the U.S., cefiderocol is commercially 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 and complicated urinary tract infections caused by certain susceptible Gram-negative microorganisms.[6] 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.[15] In Japan, cefiderocol is commercially available under the brand name Fetroja® and received manufacturing and marketing approval from the Ministry of Health, Labour and Welfare for various infections caused by strains resistant to carbapenem antibiotics among sensitive strains of *Escherichia coli, Citrobacter species, Klebsiella pneumoniae, Enterobacter species, Serratia marcescens, Proteus species, Morganella morganii, Pseudomonas aeruginosa, Burkholderia species, Stenotrophomonas maltophilia,* and *Acinetobacter species*.

U.S. INDICATIONS
Fetroja® (cefiderocol) is indicated in patients 18 years of age or older for the treatment of complicated urinary tract infections (cUTIs), including pyelonephritis caused by the following susceptible Gram-negative microorganisms: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa,* and *Enterobacter cloacae* complex.

Fetroja is indicated in patients 18 years of age or older for the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by the following susceptible Gram-negative microorganisms: *Acinetobacter baumannii* complex*, Escherichia coli, Enterobacter cloacae* complex*, Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Serratia marcescens*.

USAGE
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Fetroja and other antibacterial drugs, Fetroja should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
Fetroja is contraindicated in patients with a known history of severe hypersensitivity to cefiderocol or other beta-lactam antibacterial drugs, or any other component of Fetroja.

WARNINGS AND PRECAUTIONS
Increase in All-Cause Mortality in Patients with Carbapenem-Resistant Gram-Negative Bacterial Infections

An increase in 28-day all-cause mortality was observed in Fetroja-treated nosocomial pneumonia, bloodstream infections, or sepsis patients compared to those treated with best available therapy (BAT) in a clinical study (NCT02714595). Most BAT regimens contained colistin. All-cause mortality remained higher in patients treated with Fetroja than in patients treated with BAT through Day 49.

Generally, deaths were in patients with infections caused by Gram-negative organisms, including non-fermenters such as *Acinetobacter baumannii* complex, *Stenotrophomonas maltophilia*, and *Pseudomonas aeruginosa*, and were the result of worsening or complications of infection, or underlying comorbidities. The cause of the increase in mortality has not been established. Closely monitor the clinical response to therapy in patients with cUTI and HABP/VABP.

Hypersensitivity Reactions
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions and serious skin reactions have been reported in patients receiving beta-lactam antibacterial drugs. Hypersensitivity was observed with Fetroja. Before Fetroja is instituted, inquire about previous hypersensitivity to cephalosporins, penicillins, or other beta-lactam drugs. If an allergic reaction occurs, discontinue Fetroja.

***Clostridioides difficile*-associated Diarrhea (CDAD)**
CDAD has been reported with nearly all systemic antibacterial agents, including Fetroja. Careful medical history is necessary because CDAD has been reported to occur more than 2 months after the administration of antibacterial agents. If CDAD is suspected or confirmed, antibacterial drugs not directed against *C. difficile* may need to be discontinued.

Seizures and Other Central Nervous System (CNS) Adverse Reactions
Cephalosporins, including Fetroja, have been implicated in triggering CNS adverse reactions such as seizures. Encephalopathy, coma, asterixis, and neuromuscular excitability have been reported with cephalosporins, particularly in patients with a history of epilepsy and/or when recommended dosages of cephalosporins were exceeded due to renal impairment. Adjust Fetroja dosing based on creatinine clearance. If focal tremors or seizures occur, evaluate patients to determine whether Fetroja should be discontinued.

Development of Drug-Resistant Bacteria
Prescribing Fetroja in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

ADVERSE REACTIONS
The most common adverse reactions occurring in ≥2% of patients receiving Fetroja in the cUTI trial were: diarrhea (4%), infusion site reactions (4%), constipation (3%), rash (3%), candidiasis (2%), cough (2%), elevations in liver tests (2%), headache (2%), hypokalemia (2%), nausea (2%), and vomiting (2%). The most common adverse reactions occurring in ≥4% of patients receiving Fetroja in the HABP/VABP trial were: elevations in liver tests (16%), hypokalemia (11%), diarrhea (9%), hypomagnesemia (5%), and atrial fibrillation (5%).

Please click here for Full U.S. Prescribing Information for Fetroja® (cefiderocol).

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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REFERENCES:

[1] DeJonge, et al. Activity of Cefiderocol and Comparator Agents Against Metallo-β-Lactamase Carrying *Acinetobacter baumanni-calcoaceticus* Complex Isolates Collected in the SENTRY Antimicrobial Surveillance Program. Poster presented at IDWeek 2025. Poster #P-1300.

[2] Clancy C, et al. Earlier Cefiderocol Use Was Associated with Better Outcomes for Challenging Gram-Negative Bacterial Infections: US Results From the Global Observational PROVE Study. Poster presented at IDWeek 2025. Poster #P-1353.

[3] Shields, R.K., et al. Outcomes of Patients Treated With Cefiderocol For Infections Caused by β-Lactam–β-Lactamase Inhibitor Non-Susceptible Bacteria: Subgroup Analysis of the PROVE Study. Poster presented at IDWeek 2025. Poster #P-1354.

[4] Drwiega E, et al. Clinical Outcomes of Cefiderocol for Treatment of Bloodstream Infections Caused by Gram-Negative Bacteria: Subgroup Analysis of the PROVE Study. Poster presented at IDWeek 2025. Poster #P-1352.

[5] DeJonge et al. β-Lactam–β-Lactamase Inhibitor Combinations Show a High Degree of Cross-Resistance in Gram-Negative Bacteria, but Not to Cefiderocol. Oral presentation at ID Week 2025. Oral #627.

[6] Fetroja® Prescribing information. Available at: https://www.shionogi.com/content/dam/shionogi/si/products/pdf/fetroja.pdf. Accessed September 22, 2025.

[7] Clancy CJ, Cornely OA, Marcella SW, et al. Effectiveness and safety of cefiderocol in clinical practice for treatment of patients with Gram-negative bacterial infections: US interim results of the PROVE study. *Infection and Drug Resistance*. 2024 Dec 31:4427-43. DOI: 10.2147/IDR.S475462

[8] Clancy, N. Real-World Effectiveness and Safety of Cefiderocol in the Treatment of Patients with Serious Gram-negative Bacterial Infections: Results of the PROVE Chart Review Study. Poster 1475 presented at IDWeek 2024. October 16-19, 2024. Los Angeles, CA.

[9] Verway M, et al. Prevalence and mortality associated with bloodstream organisms: a population-wide retrospective cohort study. *J Clin Microbiol*. 2022 Apr;60(4):e02429-21. DOI: 10.1128/jcm.02429-21

[10] Yoshinori Y, et al. Analyzing Trends of Cefiderocol Susceptibility Across Five Years of the SENTRY Surveillance Program. Poster presented at IDWeek 2025. Poster #P-1220.

[11] Shortridge D, Streit JM, Mendes R, et al. In vitro activity of cefiderocol against US and European Gram-negative clinical isolates collected in 2020 as part of the SENTRY antimicrobial surveillance program. *Microbiology spectrum*. 2022 Apr 27;10(2):e02712-21. DOI: 10.1128/spectrum.02712-21

[12] SENTRY Antimicrobial Surveillance Program. Available at: https://www.jmilabs.com/sentry-surveillance-program/. Accessed October 8, 2025.

[13] Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022; 399: 629–55.

[14] GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050. Lancet. 2024 Sep 28;404(10459):1199-1226. doi: 10.1016/S0140-6736(24)01867-1. Epub 2024 Sep 16. PMID: 39299261.

[15] Perez F, et al. 'Carbapenem-Resistant Enterobacteriaceae: A Menace to our Most Vulnerable Patients'. Cleve Clin J Med. Apr 2013; 80(4): 225–33.