PRESSRELEASE

SHIONOGI

FDA Accepts Shionogi's Ensitrelvir NDA for Review as the First Oral Therapy for the Prevention of COVID-19 Following Exposure

*Application is based on results from SCORPIO-PEP, the first and only Phase 3 study of an oral antiviral to meet the primary endpoint of preventing COVID-19 following exposure to an infected individual**

OSAKA, Japan, September 3, 2025 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced the U.S. Food and Drug Administration (FDA) has accepted for review a New Drug Application (NDA) from Shionogi Inc., a New Jersey-based subsidiary of Shionogi, for ensitrelvir (Generic name: ensitrelvir fumaric acid, Code No.: S-217622), an investigational oral antiviral for the prevention of COVID-19 following exposure to an infected individual. The FDA has set an action date of June 16, 2026 under the Prescription Drug User Fee Act (PDUFA).

The NDA is supported by results from the global, double-blind, randomized, placebo-controlled Phase 3 study, SCORPIO-PEP, which studied ensitrelvir as post-exposure prophylaxis (PEP). If approved, ensitrelvir would be the first and only oral therapy for the prevention of COVID-19 following exposure to an infected individual.[1,2]

SARS-CoV-2 remains highly transmissible and up to half of people living with an infected individual may develop COVID-19.[3,4] The virus is constantly evolving, with novel symptoms reported.[5,6] COVID-19 continues to impact daily life and may lead to absences from school and work, may cause long COVID, and in some cases, may progress to severe disease.[7-12] Even patients with mild COVID-19 may experience worsening of preexisting chronic conditions.[13-17]

Following exposure to COVID-19, the best way to avoid its potentially serious and long-term complications is to stop viral replication, which prevents the development of the disease.[1,2] There are currently no approved antiviral therapies proven to prevent COVID-19 following exposure.[1,2,18] COVID-19 vaccines are received before exposure, and they do not stop viral replication.[19,20] Other COVID-19 antivirals are taken following exposure and diagnosis, after viral replication has occurred and disease is already established.[21]

"Shionogi has a long history of innovation in infectious disease treatment and prevention. Our dedication to this field has led to significant breakthroughs in the development of novel antimicrobials and antivirals for HIV/AIDS, influenza and COVID-19. If approved, ensitrelvir will be the first and only oral therapy to help protect people in the U.S. from COVID-19 following exposure," said Nathan McCutcheon, MBA, President and CEO, Shionogi Inc.

About ensitrelvir

Ensitrelvir is a SARS-CoV-2 main protease inhibitor created through joint research between Hokkaido University and Shionogi. SARS-CoV-2 has an enzyme called the main protease (3-CL), which is essential for the replication of the virus. Ensitrelvir suppresses the replication of SARS-CoV-2 by selectively inhibiting the main protease.

Ensitrelvir, known as Xocova® in countries where it is approved, received emergency regulatory approval in Japan in November 2022 and full approval in March 2024 for the treatment of COVID-19 based on results from SCORPIO-SR, a Phase 3 study conducted in Asia, during the Omicron-dominant phase of the pandemic.

In SCORPIO-SR, ensitrelvir showed both clinical symptomatic efficacy (symptom resolution sustained for at least 24 hours) for five typical Omicron-related symptoms (primary endpoint) and antiviral efficacy (key secondary endpoint) in a predominantly vaccinated population of patients with mild-to-moderate SARS-CoV-2 infection, regardless of risk factors. Most adverse events were mild in severity and no deaths were seen in the study. Among the most common treatment-related adverse events were temporary decreases in high-density lipoprotein and increased blood triglycerides, as observed in previous studies. Results from this study were published in JAMA Network Open.

In 2025, Shionogi submitted two new drug applications in Japan for post-exposure prophylaxis of COVID-19 and for COVID-19 treatment in pediatric patients aged six to under 12 years. The pediatric submission is based on a multicenter, randomized, double-blind, placebo-controlled trial of ensitrelvir in mild-to-moderate COVID-19 patients aged 6 to 12 years in Japan. The study confirmed safety and tolerability and found the pharmacokinetics of ensitrelvir in this age group to be similar to that in adults.

Ensitrelvir became available in Singapore for the treatment of COVID-19 via a Special Access Route application in 2023, and it is currently under regulatory review in Taiwan for the treatment of COVID-19. Ensitrelvir is also under regulatory review with the European Medicines Agency for COVID-19 post-exposure prophylaxis and treatment.[22]

Ensitrelvir is an investigational drug outside of Japan and Singapore. In addition, the brand name Xocova® has not been approved for use outside of Japan and Singapore and pertains only to the approved drug in Japan and Singapore.

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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* Literature search conducted May 2025.

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