PRESSRELEASE

SHIONOGI

Shionogi Submits Supplemental New Drug Application for Ensitrelvir in Japan for the Treatment of COVID-19 in Pediatric Patients Aged 6 Years and Older

OSAKA, Japan, June 30, 2025 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced that it has submitted a supplemental New Drug Application (sNDA) in Japan to expand the indication of its investigational oral antiviral ensitrelvir (Generic name: ensitrelvir fumaric acid, Code No.: S-217622, hereafter "ensitrelvir") for the treatment of COVID-19, from the current approval for patients aged 12 years and older to include pediatric patients aged 6 years and older weighing 20 kg or more. Additionally, Shionogi has filed for approval of a new formulation (25mg tablet) to facilitate easier administration for pediatric patients.

The sNDA is based on the positive results from the Phase 3 study in pediatric patients aged 6 to under 12 years in Japan (jRCT：2031230140). The primary objective of this study was to evaluate the safety, tolerability, and pharmacokinetics of ensitrelvir once daily for 5 days in pediatric subjects aged 6 to 12 years. One hundred and seventeen patients were enrolled in this study. The study confirmed safety and tolerability and found the pharmacokinetics of ensitrelvir in this age group was similar to adults. Furthermore, ensitrelvir demonstrated a potent antiviral effect similar to that observed in adults.

COVID-19 remains a public health threat. However, there are no oral antiviral drugs approved for use in pediatric patients under the age of 12. There is a need for the development of safe and convenient oral antiviral treatments for this population. If this application is approved, ensitrelvir is expected to be a new treatment option available for pediatric patients aged 6 years and older weighing 20 kg or more.

Ensitrelvir was granted Fast Track designation by the FDA in 2025 for post-exposure prophylaxis of COVID-19 following contact with an individual who has COVID-19 and was granted Fast Track designation by the FDA in 2023 for the treatment of COVID-19. Shionogi initiated the rolling submission of a new drug application (NDA) with the FDA for Post-Exposure Prophylaxis of COVID-19 in 2025.

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. In 2025, based on the favorable outcomes of the SCORPIO-PEP trial, a global Phase 3 post-exposure prevention study[1], Shionogi submitted a supplemental New Drug Application for ensitrelvir in Japan for the post-exposure prophylaxis of COVID-19 in 2025. It became available in Singapore via a Special Access Route application in 2023, and it is currently under regulatory review in Taiwan. 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.

About ensitrelvir

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

Shionogi evaluated the safety and efficacy of ensitrelvir through SCORPIO-SR, a Phase 3 study conducted in Asia, during the Omicron-dominant phase of the epidemic.[3] In this study, 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.[3] Regarding safety, most adverse events were mild in severity and no deaths were seen in the study. [3] Among the most common treatment-related adverse events were temporary decreases in high-density lipoprotein and increased blood triglycerides, as observed in previous studies. [3] The data from this study were published in JAMA Network Open.

Additionally, the Phase 3 SCORPIO-HR study assessed ensitrelvir in a broad range of symptomatic, non-hospitalized participants with COVID-19, regardless of past SARS-CoV-2 infection. The study did not meet its primary endpoint of a statistically significant reduction in time to sustained resolution (symptom resolution sustained for at least 48 hours) of 15 common COVID-19 related symptoms for once-daily ensitrelvir compared to placebo.[4] No new safety concerns were identified in the study, and treatment with ensitrelvir was well tolerated, with a similar adverse event profile as placebo. [4]

Shionogi recently announced that its global, double-blind, randomized, placebo-controlled Phase 3 study (SCORPIO-PEP) assessing ensitrelvir as oral post-exposure prophylaxis met the primary endpoint of preventing symptomatic COVID-19 through day 10[1]. SCORPIO-PEP is the first and only Phase 3 study of a COVID-19 oral antiviral as a post-exposure prophylaxis to meet the primary endpoint of preventing COVID-19.*

An investigator-initiated research study with ensitrelvir is ongoing in hospitalized patients for the management of COVID-19 as part of the Strategies and Treatments for Respiratory Infections & Viral Emergencies (STRIVE) platform protocol. STRIVE was developed under the auspices of NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership.

Shionogi also recently released preliminary results from a multicenter, randomized, double-blind, placebo-controlled trial of ensitrelvir in mild to moderate COVID-19 patients aged 6 to under 12 years in Japan. The study confirmed safety and tolerability and found the pharmacokinetics of ensitrelvir in this age group similar to adults.

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 December 2024.

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2. Unoh Y, et al. Discovery of S-217622, a noncovalent oral SARS-CoV-2 3CL protease inhibitor clinical candidate for treating COVID-19. *Journal of Medicinal Chemistry*. 30 Mar 2022;65:9,6499-6512. doi:10.1021/acs.jmedchem.2c00117.
3. Yotsuyanagi H, et al. Efficacy and safety of 5-day oral Ensitrelvir for patients with mild to moderate COVID-19. *JAMA Netw Open*. 9 Feb 2024;7(2):e2354991. doi:10.1001/jamanetworkopen.2023.54991.
4. Luetkemeyer A, et al. Ensitrelvir for the Treatment of Nonhospitalized Adults with COVID-19: Results from the SCORPIO-HR, Phase 3, Randomized, Double-blind, Placebo-Controlled Trial, *Clinical Infectious Diseases*, 2025;, ciaf029, https://doi.org/10.1093/cid/ciaf029.