PRESSRELEASE

SHIONOGI

New England Journal of Medicine Publishes Shionogi Study Demonstrating Ensitrelvir Prevents COVID-19 Following Exposure

*SCORPIO-PEP is the first and only Phase 3 study of an oral antiviral to meet the primary endpoint of preventing symptomatic COVID-19 following exposure to an infected individual**

Ensitrelvir is an investigational oral antiviral that could offer a new approach to preventing COVID-19 by blocking viral replication during the critical window between exposure and COVID-19 symptom onset

Ensitrelvir is under review by FDA for post-exposure prophylaxis (PEP) of COVID-19, with a Prescription Drug User Fee Act (PDUFA) action date of June 16, 2026

OSAKA, Japan, May 13, 2026 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, PhD; hereinafter "Shionogi") announced that results from its global, double-blind, randomized, placebo-controlled Phase 3 study, SCORPIO-PEP, were published in the *New England Journal of Medicine*. A five-day course of ensitrelvir significantly reduced the risk of symptomatic COVID-19 by 67% in individuals following exposure to an infected individual through Day 10 compared to placebo.[1]

Among participants in the primary analysis population (n=2,041) who received ensitrelvir, 2.9% developed symptomatic COVID-19, compared to 9.0% of those who received placebo through Day 10 (risk ratio: 0.33; 95% confidence interval [CI]: 0.22-0.49; p<0.0001).[1,2] In a prespecified subgroup analysis of participants with one or more risk factors for severe disease, a 76% reduction in relative risk for symptomatic COVID-19 was observed with ensitrelvir through day 10, compared to placebo.[1] In this subgroup, 2.4% of participants who received ensitrelvir (9/382) developed symptomatic COVID-19 compared to 9.9% who received placebo (37/374) (risk ratio: 0.24; 95% CI: 0.12-0.49).[1]

"Ensitrelvir works to inhibit viral replication, helping protect people who have been exposed to COVID-19 from becoming sick. In this study, people taking ensitrelvir within 72 hours after household exposure were three times less likely to develop COVID-19 compared with those given placebo," said Frederick Hayden, MD, professor emeritus of clinical virology and professor emeritus of medicine, University of Virginia School of Medicine. "These first, clearly positive results with an oral antiviral underscore ensitrelvir's potential to protect a range of individuals from COVID-19, including those at higher risk of severe disease and potentially in other settings."

In the SCORPIO-PEP study, ensitrelvir was generally well tolerated, with similar rates of adverse events across groups (15.1% in the ensitrelvir group (n=1,190) and 15.5% in the placebo group (n=1,187)).[1] The most common treatment-emergent adverse events (greater than or equal to 1%) were headache, diarrhea, nasopharyngitis, cough, fatigue and influenza.[3] There were no reports of altered taste (dysgeusia) attributed to ensitrelvir in the trial.[1]

Future SARS-CoV-2 transmission and impact are unpredictable, with the potential for surges and

emergence of new variants, such as the heavily mutated Omicron subvariant BA.3.2, nicknamed "Cicada" now circulating in at least 25 U.S. states.[4,5,6,7] COVID-19 can become severe, and even if mild or moderate, it can exacerbate or worsen chronic conditions or lead to the onset of new ones, including long COVID.[8,9,10,11,12]

Following exposure to COVID-19, an effective way to avoid its potentially serious and long-term complications is to block viral replication, which helps prevent the development of the disease.[13,14,15,16] There are currently no approved therapies to help prevent COVID-19 following exposure.[17,18] Other COVID-19 antivirals approved for treatment are taken after illness has developed and the immune cascade has begun.[19]

"Ensitrelvir offers a potential new approach to help prevent COVID-19 after exposure. By preventing COVID-19, people can avoid not only potentially serious consequences of acute disease, but also the risk of exacerbating pre-existing conditions or acquiring new conditions, such as long COVID. Ensitrelvir cuts the chances of developing COVID-19 by two-thirds, which is substantial, particularly in households where the risk of spread is high," said Aeron Hurt, PhD, vice president, global medical science, Shionogi. "Shionogi's deep expertise in antivirals has changed the way we treat and prevent other viral infections, including influenza and HIV, and there is an opportunity to do the same with COVID-19. Ensitrelvir has the potential to be the first oral antiviral to help prevent COVID-19 after exposure."

About SCORPIO-PEP

The global, double-blind, randomized, placebo-controlled Phase 3 study, SCORPIO-PEP, assessed the safety and efficacy of ensitrelvir as post-exposure prophylaxis. The study included 2,387 study participants aged 12 years and older with a negative local screening test for SARS-CoV-2 infection and no symptoms at the time of enrollment, who were exposed to a person living in their household with symptomatic COVID-19. The primary analysis included 2,041 household contact participants with a central laboratory-confirmed negative SARS-CoV-2 test.

The trial was conducted from June 2023–September 2024. More than 98% of household contacts tested positive for SARS-CoV-2 N and/or S antibodies, indicating that nearly all had evidence previous SARS-CoV-2 infection or vaccination, or both.

Study participants were randomly assigned at a 1:1 ratio to receive ensitrelvir (375 mg on day 1 and 125 mg on days 2-5) or placebo, once daily, and began treatment within 72 hours of when the household member with COVID-19 (index patient) began showing symptoms. Participants then continued ensitrelvir (125 mg) or placebo for five days. SCORPIO-PEP is 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.

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, which is essential for the replication of the virus. Ensitrelvir suppresses the replication of SARS-CoV-2 by selectively inhibiting the main protease.

Ensitrelvir is under review by the U.S. FDA for post-exposure prophylaxis (PEP) of COVID-19, with a Prescription Drug User Fee Act (PDUFA) action date of June 16, 2026.

Ensitrelvir, known as XOCOVA® in Japan, 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. Results from this study were published in *JAMA Network Open*.

In 2025, Shionogi submitted a supplemental New Drug Application for COVID-19 treatment in pediatric patients aged 6 to under 12 years in Japan. In March 2026, XOCOVA received approval in Japan for the prevention of COVID-19 following exposure. Ensitrelvir is currently under regulatory review in Taiwan for post-exposure prophylaxis of COVID-19.

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

About Shionogi & Co., Ltd.

Shionogi & Co., Ltd. is a 148-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 and cardiovascular diseases. Shionogi's research and development currently targets two therapeutic areas: infectious diseases and diseases with unmet medical needs in pain/CNS, including Alzheimer's disease, oncology, rare diseases, and sleep apnea. 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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**Literature search conducted March 2026.*

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