



IDWeek 2026: New Exploratory Analyses Evaluate XOCOVA® (ensitrelvir) Following COVID-19 Exposure, Including Breakthrough Infections and Infection Present at Baseline

- A pooled analysis from the global SCORPIO clinical program showed potent antiviral activity with ensitrelvir across age, vaccination status and risk for severe disease
- New data underscores that even mild-to-moderate COVID-19 may worsen and exacerbate underlying chronic conditions, supporting the importance of prevention

OSAKA, Japan, October 21, 2026 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") will present new exploratory analyses from the global Phase 3 SCORPIO-PEP study, virology data from across the ensitrelvir phase 3 program, and new insights on the continued burden of COVID-19 at IDWeek 2026.

Ensitrelvir was approved as Xocova® in Japan in March 2026 and in the U.S. in May 2026, and as Zokovea® in the EU in September 2026, for post-exposure prophylaxis (PEP) of COVID-19 in adults and adolescents 12 years of age and older following contact with an individual who has COVID-19. These approvals were based on positive results from SCORPIO-PEP, a global, double-blind, randomized, placebo-controlled Phase 3 study.

In the primary analysis population, XOCOVA significantly reduced the risk of developing symptomatic COVID-19 by 67% in individuals following exposure to an infected individual through Day 10 compared with placebo (ensitrelvir n=1,030; placebo n=1,011).¹

In SCORPIO-PEP, 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 adverse events (regardless of causality) occurring in greater than or equal to 1% of the ensitrelvir group and at a greater frequency compared to placebo were headache, diarrhea, and cough.¹ There were no reports of altered taste (dysgeusia) attributed to ensitrelvir in the trial.^{1,2}

Exploratory SCORPIO-PEP Analyses Describe Symptom Severity and Viral Outcomes Among Participants with Breakthrough Infection or Infection Present at Baseline

In an oral presentation at IDWeek 2026, Shionogi will report new exploratory analyses from the SCORPIO-PEP study evaluating participants who had breakthrough infections or were already infected at baseline.³

Among breakthrough infection cases (based on RT-PCR positivity regardless of symptoms) in the primary analysis population, the mean maximum viral RNA levels were lower in participants receiving ensitrelvir compared to those receiving placebo (3.1 vs 4.3 mean log₁₀ copies/mL, respectively, seen in 144 and 217 breakthrough infection cases, respectively).³ In household contacts who were infected with SARS-CoV-2 at the time of enrollment (confirmed positive by baseline central RT-PCR despite testing negative on a local screening test and being asymptomatic; n=237), numerically lower mean viral RNA levels were also observed with ensitrelvir in comparison to placebo on Days 3 and 6.³

In the primary analysis population, a numerically lower proportion of participants with symptomatic breakthrough infections taking ensitrelvir developed severe symptoms, compared with those taking placebo (severe symptoms were reported in 8/28 or 28.6% of individuals receiving ensitrelvir compared with 48/89 or 53.9% of individuals receiving placebo).³ Similarly, numerically lower mean total symptom scores earlier in the study and lower mean maximum total symptom scores were observed in participants receiving ensitrelvir compared with placebo (mean maximum total scores were 6.6 vs 8.9 respectively).³

In participants receiving ensitrelvir who were infected with SARS-CoV-2 at the time of enrollment despite testing negative on a local screening test and being asymptomatic, a numerically lower proportion developed severe symptoms compared with placebo (severe symptoms were reported in 2/18 or 11.1% of individuals receiving ensitrelvir compared with 9/24 or 37.5% of individuals receiving placebo).³ Similarly, numerically lower mean total symptom scores earlier in the study and mean maximum total symptom scores were observed in those receiving ensitrelvir compared with placebo.³

“SCORPIO-PEP showed that early administration of ensitrelvir following household exposure reduced the risk of symptomatic COVID-19,” said Simon Portsmouth, MD, FRCP, Senior Vice President, Head of Clinical Development, Shionogi Inc. “This exploratory analysis provides additional insight into the antiviral activity of ensitrelvir on viral load and symptom outcomes among participants who developed COVID-19. These observations add to our understanding of the potential outcomes associated with early administration of ensitrelvir following household exposure.”

Pooled Phase 3 Study Data Analysis Shows Potent Antiviral Activity of Ensitrelvir Through Observed Reductions in Infectious Virus

In a separate poster presentation, investigators will report findings from a post-hoc pooled analysis of two Phase 3 studies designed to assess infectious-virus-based virologic outcomes across a broad range of participants with confirmed COVID-19 infection.⁵ Unlike viral RNA detection by RT-PCR, which may identify noninfectious viral remnants, infectious-virus measurements assess the presence of replication-competent virus and can provide additional insight into antiviral activity.^{4,5}

By Day 4, participants who received ensitrelvir (375 mg on Day 1, then 125 mg on Days 2-5; n=484) had numerically greater reductions in infectious virus titers than those who received placebo (n=487)

(difference in least-squares mean of 0.21 log₁₀ TCID₅₀/mL).⁵ Similar results were observed across subgroups regardless of age, vaccination status, and risk factors for severe COVID-19. Also on Day 4, a higher proportion of ensitrelvir recipients had undetectable infectious viral load compared to those receiving placebo (95.7% [463/484] vs 72.1% [351/487]).⁵

"With data pooled from two Phase 3 studies, this analysis represents the most extensive infectious virus dataset reported for a COVID-19 antiviral to date, and it helps to further characterize ensitrelvir's effect on active viral replication," said Florin Draica, MD, CMD, MBA, Senior Vice President, U.S. Medical Affairs, Shionogi Inc. "Although these results are exploratory, the observed reductions in infectious virus provide additional support of ensitrelvir's antiviral activity and warrant further evaluation of their potential implications for infectivity and transmission."

Systematic Literature Review Highlights the Continued Burden of COVID-19 and Its Impact on Underlying Chronic Conditions

Shionogi will also present a systematic literature review evaluating the impact of acute COVID-19 on individuals with underlying chronic conditions during the Omicron era or in earlier time periods. The review included 35 observational studies assessing clinical outcomes, health-related quality of life (HRQoL), and healthcare resource utilization (HCRU).⁶ Across the studies reviewed, acute COVID-19 was associated with worsening, exacerbation, or relapse of underlying chronic conditions spanning respiratory, neurologic, cardiovascular, renal, and other disease areas.⁶

More than half of studies evaluating clinical outcomes (17 out of 33) reported statistically significant worsening of underlying chronic conditions such as asthma, COPD, multiple sclerosis and CKD, following acute COVID-19.⁶ COVID-19 was also associated with worsening outcomes in five of eight studies reporting on HRQoL and increased hospitalization frequency or extended hospital length of stay in four of the six studies reporting on HCRU.⁶

"Across studies in this review, acute COVID-19 during the Omicron predominance was associated with worsening or exacerbation of underlying chronic conditions. Specifically, we found that COVID-19 infection, even mild or moderate, was associated with reduced health-related quality of life and increased healthcare resource utilization," said Alpesh N. Amin, M.D., Professor, Founding Chief and Executive Director of Hospital Medicine & Palliative Medicine, and Co-Director & Medical Director of the Institute for Precision Health at the University of California, Irvine. "These findings reinforce the continued burden of COVID-19 and underscore the importance of prevention, especially among people living with chronic conditions."

The Ongoing Impact of COVID-19

COVID-19 remains highly transmissible, driven by Omicron and its subvariants, and up to 47% of people living with an infected individual may develop COVID-19.^{7,8} The U.S. Centers for Disease Control and Prevention estimates that between October 1, 2025, and September 26, 2026, there were 5.2-14.6 million

new cases in the U.S., resulting in 1.1-2.7 million outpatient visits, 170,000-270,000 hospitalizations and 17,000-48,000 deaths.⁹

Beyond acute infection, COVID-19, even mild-to-moderate, may worsen underlying chronic conditions and can have lasting health impacts. Studies have reported increased rates of new and worsening neurologic, cardiovascular, respiratory, and chronic kidney conditions in the year following COVID-19 infection.¹⁰⁻¹⁸ COVID-19 also disproportionately affects older adults with greater risk for severe illness and death in close-community settings, such as long-term care facilities.¹⁹

About SCORPIO-PEP

The global, double-blind, randomized, placebo-controlled Phase 3 study, SCORPIO-PEP, assessed the safety and efficacy of XOCOVA as post-exposure prophylaxis for COVID-19. The study was conducted from June 2023-September 2024. It 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.

More than 98% of household contacts tested positive for antibodies against SARS-CoV-2 N (nucleocapsid) or S (spike) proteins, indicating that nearly all had evidence of previous SARS-CoV-2 infection or vaccination, or both.

Study participants were randomly assigned at a 1:1 ratio to receive XOCOVA (375 mg on Day 1 and 125 mg on Days 2-5) or placebo, once daily for five days, and began treatment within 72 hours of when the household member with COVID-19 began showing symptoms.

Results from SCORPIO-PEP were published in the [New England Journal of Medicine](#). 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 XOCOVA

XOCOVA[®] (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. XOCOVA suppresses the replication of SARS-CoV-2 by selectively inhibiting the main protease.

XOCOVA is approved in the U.S., [Japan](#) and [European Union](#) for post-exposure prophylaxis of COVID-19 in adults and adolescents 12 years of age and older following contact with an individual who has COVID-19.

XOCOVA [received emergency regulatory approval](#) in Japan in November 2022 and [full approval](#) in March 2024 for the treatment of COVID-19 in adults and adolescents 12 years of age and older. XOCOVA

received [supplemental approval](#) in Japan in June 2026 for pediatric patients aged 6 to under 12 years who weigh at least 20 kg for the treatment of COVID-19.

XOCOVA is not approved for the treatment of COVID-19 in the U.S.

About Shionogi Inc.

Shionogi Inc. is a U.S. subsidiary of Shionogi & Co., Ltd., a global research-driven pharmaceutical company. Since 1878, Shionogi has been developing new treatments to improve patients' lives worldwide. Today in North America, we are focused on infectious and rare diseases, and our portfolio includes an antibiotic for serious infections caused by susceptible Gram-negative bacteria, an oral antiviral for post-exposure prophylaxis of COVID-19 and a therapy for amyotrophic lateral sclerosis (ALS). Together with our subsidiaries Qpex Biopharma Inc. and Shionogi Canada Inc., we are continuing to innovate across infectious disease, rare disease and additional high-need therapeutic areas. Learn more at [shionogi.com](https://www.shionogi.com).

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 and CNS disorders. Shionogi's research and development currently targets two therapeutic areas: infectious diseases and diseases with unmet medical needs, including rare diseases, allergy/inflammation, oncology, hearing loss, 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.

For Further Information:

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

U.S. Media: ShionogiCommunications@shionogi.com
Shionogi Europe Press Office: pressoffice@shionogi.eu

References

1. Hayden FG, Shinkai M, et al. Ensitrelvir for COVID-19 postexposure prophylaxis in household contacts. *N Engl J Med*. 2026;394(19):1905-1915. doi:[10.1056/NEJMoa2509306](https://doi.org/10.1056/NEJMoa2509306).
2. Hayden FG, Shinkai M, Clark TW, et al. Ensitrelvir for COVID-19 postexposure prophylaxis in household contacts. Supplementary Appendix. *N Engl J Med*. 2026;394(19). Available from: https://www.nejm.org/doi/suppl/10.1056/NEJMoa2509306/suppl_file/nejmoa2509306_appendix.pdf.
3. Fukushi A, Nobori H, Sakaguchi H, et al. Early Pre-Symptomatic Treatment with Ensitrelvir Among PCR-Positive, SARS-CoV-2-Exposed and Infected Household Contacts: SCORPIO-PEP Subpopulation Analysis. Presented at: IDWeek 2026; Washington, D.C., United States.
4. Binnicker MJ. Can Testing Predict SARS-CoV-2 Infectivity? The Potential for Certain Methods To Be Surrogates for Replication-Competent Virus. *Journal of Clinical Microbiology*. 2021;59(11):e00469-21. doi:10.1128/JCM.00469-21.
5. Hurt AC, Sakaguchi H, Nobori H, et al. Reduction of Infectious SARS-CoV-2 and Viral RNA with Ensitrelvir: A Pooled Analysis of SCORPIO-SR and SCORPIO-HR Trials [poster presentation]. Presented at: IDWeek 2026; Washington, D.C., United States.
6. Draica F, Verdi D, Fedele M, et al. Impact of Acute COVID-19 on Underlying Chronic Conditions: Systematic Literature Review [poster presentation]. Presented at: IDWeek 2026; Washington, D.C., United States.
7. Baker JM, Nakayama JY, O'Hegarty M, et al. Household transmission of SARS-CoV-2 in five US jurisdictions: comparison of Delta and Omicron variants. *PLoS One*. 2025;20(1):e0313680. doi:10.1371/journal.pone.0313680.
8. Madewell ZJ, Yang Y, Longini IM Jr, Halloran ME, Dean NE. Household secondary attack rates of SARS-CoV-2 by variant and vaccination status: an updated systematic review and meta-analysis. *JAMA Netw Open*. 2022;5(4):e229317. doi:10.1001/jamanetworkopen.2022.9317.
9. Centers for Disease Control and Prevention [Internet]. Preliminary 2025-2026 COVID-19 burden estimates. Available from: <https://www.cdc.gov/covid/php/surveillance/burden-estimates.html>.
10. Xie Y, Xu E, et al. Long-term cardiovascular outcomes of COVID-19. *Nat Med*. 2022;28(3):583-590. doi:10.1038/s41591-022-01689-3.
11. Sax PE, Draica F, et al. New onset conditions, exacerbations and worsening of underlying conditions following COVID-19 infection [poster presentation]. Presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 2026; Denver, CO, United States.
12. Graham EL, Clark JR, et al. Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized COVID-19 "long haulers." *Ann Clin Transl Neurol*. 2021;8(5):1073-1085. doi:10.1002/acn3.51350.
13. Xie Y, Xu E, Bowe B, et al. Risks of mental health outcomes in people with COVID-19: a cohort study. *BMJ*. 2022;376:e068993. doi:10.1136/bmj-2021-068993.
14. Srivastava S, Garg I. Post-COVID-19 infection: long-term effects on liver and kidneys. *World J MetaAnal*. 2021;9(3):220-233. doi:10.13105/wjma.v9.i3.220.
15. Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network—United States, March-June 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(30):993-998. doi:10.15585/mmwr.mm6930e1.
16. Kwok WC, Chau CH, et al. Outcomes among patients with chronic obstructive pulmonary disease after recovery from COVID-19 infection of different severity. *Sci Rep*. 2024;14(1):13881. doi:10.1038/s41598-024-64670-9.
17. Conway SE, Healy BC, Zurawski J, et al. COVID-19 severity is associated with worsened neurological outcomes in multiple sclerosis and related disorders. *Mult Scler Relat Disord*. 2022;63:103946. doi:10.1016/j.msard.2022.103946.
18. Chen IW, Chang LC, Ho CH, et al. Association between COVID-19 and the development of chronic kidney disease in patients without initial acute kidney injury. *Sci Rep*. 2025;15(1):10924. doi:10.1038/s41598-025-96032-4.

19. Gravenstein S, Cooke CE, Verdi D, et al. Current impact of COVID-19 in long-term care facilities in the United States: a systematic literature review. *Sr Care Pharm.* 2026;41(5):167-186. doi:10.4140/TCP.n.2026.167.