PRESSRELEASE

SHIONOGI

Shionogi and Osaka University Establish a New Joint Research Lab on Post-COVID-19 Condition (Long COVID)

Conducting clinical research aimed at establishing methods to prevent Long COVID

OSAKA, Japan, March 1, 2024 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced that Shionogi and Osaka University (Location: Suita, Osaka, President: Shojiro Nishio) have established a joint research laboratory (research lab's name: Joint Research Laboratory for Long COVID) at the Graduate School of Medicine Faculty of Medicine, Osaka University, aiming to establish prevention methods for post-COVID-19 condition (Long COVID).

Many people infected with COVID-19 experience post-infection symptoms such as fatigue, shortness of breath, hair loss, and decreased concentration, commonly known as "Long COVID," which has become a significant global issue[1,2,3,4]. However, treatments and prevention methods for Long COVID have not yet been established. In the phase 2/3 clinical trial (SCORPIO-SR) of the COVID-19 therapeutic drug, ensitrelvir fumaric acid (marketed in Japan as Xocova®, hereafter "ensitrelvir"), it has shown the possibility to reduce the risk of persistent and new late-onset symptoms associated with Long COVID[5,6,7]. However, further accumulation of data is necessary to establish treatments and preventive methods.

Therefore, in order to promote collaborative research between Shionogi and Osaka University, where Shionogi offers potential therapeutic drugs that can address social issues, and Osaka University provides specialized expertise and healthcare infrastructure, we have established a new joint research chair as a base for fostering swift research advancement through industry-academia collaboration.
Furthermore, in this joint research laboratory, we will conduct clinical research to evaluate the efficacy and safety of ensitrevir for Long COVID. This clinical research is a randomized, double-blind, placebo-controlled study that evaluates the suppression of Long COVID and safety of ensitrelvir once-daily, 5 days oral treatment in 2,000 patients with SARS-CoV-2 infection（jRCTs051230184）.

Shionogi is committed to the principle "Protecting people worldwide from the threat of infectious diseases" as our key focus, and is working on the realization of total care for infectious diseases. Shionogi is continuing to progress its extensive global development program for ensitrelvir, and will continue research and development for COVID-19 so as to be prepared for the swift provision of therapeutic drugs and vaccines as necessary depending on the situation, such as the emergence of new variants or increases in the future prevalence of, or threat from, the disease.

About overview of joint research laboratory and research
In this laboratory, research will be led by Professor Kenji Kutsuna of the Infection Control Department at the Graduate School of Medicine Faculty of Medicine, Osaka University

1. Laboratory name: Post-COVID-19 condition treatment joint research laboratory
2. Location: Graduate School of Medicine Faculty of Medicine, Osaka University
3. Period: March 1, 2024 to February 28, 2027
4. Principal Investigator: Kenji Kutsuna (Professor, the Infection Control Department at the Graduate School of Medicine Faculty of Medicine, Osaka University)
5. Research details: To verify the efficacy and safety of ensitrelvir once-daily, 5 days oral treatment in 2,000 patients with mild SARS-CoV-2 infection
6. Research site: Osaka University Hospital (only 1 site)
7. Number of subjects: 2,000 cases
8. Research method: Decentralized Clinical Trial (DCT) method that do not require a visit to Research site
9. Number of partner medical sites: 150 (planned)

About ensitrelvir
Ensitrelvir (known in Japan as Xocova®), an oral antiviral drug for COVID-19 currently approved under the emergency regulatory approval system in Japan, 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. Ensitrelvir suppresses the replication of SARS-CoV-2 by selectively inhibiting the 3CL protease. Ensitrelvir is the first antiviral agent to show both clinical symptomatic efficacy 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, in the results of the Phase 3 part of the Phase 2/3 study conducted during the Omicron-dominant phase of the epidemic[8]. With regard to safety, 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. Initial exploratory analyses from the Phase 2/3 study also indicated a potential for reduced risk of development of Long COVID and further evaluations in this regard are still ongoing.

The U.S. Food and Drug Administration (FDA) granted Fast Track designation to ensitrelvir for COVID-19[9]. FDA Fast Track designation is designed to facilitate the development and expedite the review of potential new therapies that treat serious conditions and fulfill an unmet medical need. Ensitrelvir was approved in Singapore in November 2023 based on the Special Access Route application[10]. Ensitrelvir remains 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 the ensitrelvir Clinical Development Program
As SARS-CoV-2 continuously evolves, Shionogi is studying its investigational oral antiviral, ensitrelvir, across a range of patient populations and disease severity to evaluate how ensitrelvir may address the current needs. Shionogi has a comprehensive, global clinical development program underway for ensitrelvir that includes four Phase 3 trials, including SCORPIO-HR[11], a trial for non-hospitalized, symptomatic COVID-19 patients who have tested positive for COVID-19. SCORPIO-HR is also evaluating the potential effect of ensitrelvir on the symptoms of Long COVID. An investigator-initiated research study is also ongoing in hospitalized patients for the management of COVID-19 as part of the new Strategies and Treatments for Respiratory Infections & Viral

Emergencies (STRIVE) platform protocol[12]. SCORPIO-PEP is evaluating the safety and efficacy in the prevention of symptomatic SARS-CoV-2 infection when exposed to household contacts who are symptomatic and tested positive for SARS-CoV-2[13]. Lastly, Shionogi is studying the safety and efficacy of ensitrelvir in Japan for children between the ages of 6 to 11 years old[14].

About Shionogi in Infectious Disease

Shionogi is committed to "Protect people worldwide from the threat of infectious diseases" with research and development of therapeutics, whilst also working towards total care through awareness building, epidemiologic monitoring, prevention, diagnosis, and addressing exacerbations, as well as treating infections directly. As SARS-CoV-2 continues to have a major impact on people's lives and to represent a global threat, Shionogi will seek to contribute to re-establishing the safety and security of society by developing new products and services to address this pandemic. Shionogi is committed to equitable access worldwide, including by working with the Medicines Patent Pool to provide access to low- and middle-income countries (LMICs), and by strengthening its manufacturing and global supply chain[15,16].

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, Contact:

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

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