PRESSRELEASE

SHIONOGI

Initiation of a Phase 3 Clinical Trial in Japanese Pediatric Patients of Ensitrelvir for COVID-19

OSAKA, Japan, June 29, 2023 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced the first patient has been enrolled in its Phase 3 study in Japanese pediatric patients. The study will evaluate the pharmacokinetics, safety and tolerability of the novel COVID-19 oral antiviral ensitrelvir (Generic name: ensitrelvir fumaric acid, Code No.: S-217622, hereafter "ensitrelvir") once daily for 5 days in pediatric subjects aged 6 to 12 years with mild to moderate COVID-19. This randomized, double-blind, placebo-controlled Japanese pediatric study will recruit approximately 120 patients. (jRCT:2031230140)

Ensitrelvir is an investigational oral antiviral that suppresses the replication of SARS-CoV-2 by selectively inhibiting the viral 3CL protease. Marketed as Xocova® in Japan, ensitrelvir received emergency regulatory approval from the Ministry of Health, Labour and Welfare (MHLW) for the treatment of SARS-CoV-2 infection in individuals 12 years of age and older in November 2022. It remains an investigational drug outside Japan. In April 2023, ensitrelvir was granted Fast Track designation by the U.S. Food and Drug Administration.

COVID-19 is a significant public health priority. It is expected to remain a continually transmitted respiratory disease that individuals and public health systems will need to manage.[1] It is also anticipated that new variants of SARS-CoV-2 will emerge, but it is not known how these variants could affect viral transmission, severity of COVID-19, or effectiveness of current therapies.[2]

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 continues its extensive global development program for ensitrelvir [3-8], and will continue to focus on 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 the future prevalence of the disease.

About ensitrelvir

Ensitrelvir (marketed as in Japan as Xocova®), an oral antiviral drug for COVID-19 in individuals 12 years of age and older 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. 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 reduced risk of development of long COVID and further evaluations in this regard are still ongoing.

Recently, the U.S. Food and Drug Administration (FDA) granted Fast Track designation to ensitrelvir for COVID-19. 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 remains 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 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, 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. Additionally, Shionogi conducted SCORPIO-SR in patients with mild-to-moderate COVID-19 irrespective of risk factors for COVID-19 progression.

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 in low- and middle-income countries (LMICs), and by strengthening its manufacturing and global supply chain.

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:
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