PRESSRELEASE

SHIONOGI

ECCMID 2023: Shionogi to Present Data Showing COVID-19 Symptom Recurrence is Not Associated with Ensitrelvir Treatment

Additional Data to be Presented Showing Significantly Faster Time to Negative Viral Titer (Culture) Compared to Placebo

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OSAKA, Japan, April 5, 2023 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced that two late-breaking poster presentations featuring new results from the Phase 3 and Phase 2b/3 parts of the pivotal SCORPIO-SR trial (Phase 2/3 study) conducted in Japan, South Korea, and Vietnam (hereafter, the "study") on novel COVID-19 oral antiviral ensitrelvir (Generic name: ensitrelvir fumaric acid, Code No.: S-217622, hereafter "ensitrelvir") will be published as posters at the 33rd European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) in Copenhagen, Denmark 15 - 18 April 2023.

Ensitrelvir, known as Xocova® 125 mg tablet in Japan, received emergency regulatory approval from the Ministry of Health, Labour and Welfare (MHLW) for the treatment of SARS-CoV-2 infection. It remains an investigational drug outside Japan. Recently, ensitrelvir was granted Fast Track designation by the U.S. Food and Drug Administration (FDA), which is designed to expedite review of potential new therapies for serious conditions with an unmet medical need.

The first late-breaking poster presentation included a post-hoc analysis of the Phase 3 part showing that viral rebound and symptom recurrence were infrequently seen up to 21 days after treatment with ensitrelvir. Viral RNA rebound by PCR testing was observed in 7.8% in the ensitrelvir 125 mg group (n=590) and 4.7% in the placebo group (n=574). Symptom recurrence was rare and was not associated with viral RNA rebound. Although RNA rebound was observed in a small number of patients, there was only one (1/310) low level viral titer positive in follow up, suggesting no concerns for infectivity or transmission.

A second late-breaking poster presentation included new results from the study (Phase 2b/3 part) of patients who tested positive for SARS-CoV-2 but were either asymptomatic or had only mild symptoms at the time of randomization. These results were based on 572 patients who were followed up for ten days after randomization. Ensitrelvir 125 mg showed a significant reduction from baseline viral RNA on Day 4, a reduction of 1.12 $\log_{10}$ copies/mL versus placebo ($p<0.0001$). The time to first negative SARS-CoV-2 culture was significantly shorter with ensitrelvir 125 mg compared to placebo (a median time of 38.3 hours versus 66.7 hours, $p<0.0001$, respectively). Although these results were exploratory, the reduction in viral RNA and faster time to a negative viral culture may be predicted to reduce the period of infectivity which may have implications for reducing the risk of transmission.

In a subset of 70 asymptomatic patients, ensitrelvir 125 mg (n=23) showed a numerical reduction in the proportion of patients developing symptoms. In the 502 patients presenting with mild symptoms, treated with

ensitrelvir 125 mg (n=171), a numerical reduction in the proportion reporting a worsening of symptoms compared with placebo was observed. Ensitrelvir was well tolerated, and no new safety concerns were identified.

"COVID-19 continues to affect many individuals around the world," said Prof. Yohei Doi, Department of Infectious Diseases, Fujita Health University School of Medicine, Tokyo, Japan "Whilst there are certain treatments available, there is still a need for treatments that can resolve symptoms, reduce the incidence of rebound and transmission. This will be important so that people can be confident COVID-19 will not disrupt their lives."

A separate Phase 3 study of ensitrelvir (SCORPIO-HR) is underway across Asia, Africa, North America and Europe in non-hospitalized adults who have tested positive for SARS-CoV-2 and includes those both with and without risk factors for severe disease and regardless of vaccination status. Shionogi also plans to initiate a post-exposure prevention global Phase 3 study, SCORPIO-PEP.

"We are encouraged by these new data regarding the potential reduction of transmission among asymptomatic patients and patients with mild COVID-19 symptoms," said Isao Teshirogi, Ph.D. "We are continuing to evaluate ensitrelvir in multiple patient populations through our robust global clinical program and look forward to continued scientific exchange on this important compound."

The full abstracts and oral presentations are available on the ECCMID website.

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 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 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. Currently, the Phase 2b/3 part of the Phase 2/3 study targeting SARS-CoV-2 infected persons who were asymptomatic or only had mild symptoms is being conducted in Asia, mainly in Japan.

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 and has not been approved 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 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.

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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