PRESSRELEASE

SHIONOGI

Shionogi Advances Ensitrelvir Fumaric Acid COVID-19 Antiviral Clinical Program

OSAKA, Japan, February 15, 2023 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced progress on its comprehensive clinical development program for the novel COVID-19 oral antiviral ensitrelvir (Generic name: ensitrelvir fumaric acid, Code No.: S-217622, hereafter "ensitrelvir"). The program includes several Phase 3 clinical studies evaluating ensitrelvir's safety and effectiveness across a wide range of COVID-19 patient populations.

Ensitrelvir, known as Xocova® in Japan, recently received emergency regulatory approval from the Ministry of Health, Labour and Welfare (MHLW) for SARS-CoV-2 infection based on the results obtained through the Phase 3 part of the Phase 2/3 study in non-hospitalized patients conducted in Asia. It remains an investigational drug in the rest of the world.

The World Health Organization (WHO) has stated that the COVID-19 pandemic continues to be a public health emergency of international concern.[1] It is also expected that new variants of SARS-CoV-2 will emerge, but it is not known how these could affect transmission, severity of COVID-19 or effectiveness of current therapies.[2]

As the pandemic continues to evolve, and the needs of the public, patients with COVID-19, and treatment evolve along with it, Shionogi is investigating ensitrelvir across a range of patient populations, including:

- **STRIVE** (ClinicalTrials.gov Identifier: NCT05605093): Today, the U.S. National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), announced the first patient was enrolled in a global multi-site clinical trial evaluating ensitrelvir in patients who are hospitalized for the management of COVID-19 as part of the new Strategies and Treatments for Respiratory Infections & Viral Emergencies (STRIVE) platform protocol.[3] STRIVE was developed under the auspices of NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership. Ensitrelvir is the first drug to be evaluated in the STRIVE program, a new agile research approach set up to rapidly assess interventions during epidemics adversely affecting public health. It will evaluate the safety and efficacy of a five-day course of ensitrelvir, given in addition to standard of care, for hospitalized patients with COVID-19, when compared to placebo. The study will recruit 1,500 patients across sites worldwide and is expected to be complete in early 2024.
- **SCORPIO-HR** (ClinicalTrials.gov Identifier: NCT05305547): The global Phase 3 trial (SCORPIO-HR study) in non-hospitalized symptomatic SARS-CoV-2 infected patients is ongoing and includes outpatient adults who have tested positive for COVID-19, including patients regardless of risk factors or vaccination status. This NIH-supported study, also part of ACTIV, is being conducted by the AIDS Clinical Trials Group (ACTG), the largest global HIV research network which expanded its focus to include evaluating outpatient treatments for COVID-19. This study will recruit approximately 1,500 patients in Europe, South America, North America, Africa, and Asia and is expected to be complete in

the second half of 2023. For information on eligibility for this study, please visit www.treatcovidearlystudy.com.

- **SCORPIO-PEP:** Shionogi plans to initiate a post-exposure prevention global Phase 3 trial, SCORPIO-PEP. This trial will evaluate the safety and efficacy of ensitrelvir in the prevention of symptomatic SARS-CoV-2 infection from household contacts of people who tested positive for COVID-19, when compared to placebo. It will recruit more than 1,800 participants in Europe, South America, North America, Africa, and Asia, starting in early 2023.
- **Pediatric Trial:** Shionogi plans to initiate a Phase 3 pediatric study evaluating the safety and effectiveness of ensitrelvir for children ages 6-12 in Japan, starting in early 2023.

"With the sustained prevalence of COVID-19, there is a need for more treatment options that have the potential to benefit a broad range of patients," said Isao Teshirogi, Ph.D. "The scope and reach of our ensitrelvir clinical program reflect our goal to supply effective medicines to protect the health and well-being of the patients we serve. We are grateful to our respected partners and patients participating worldwide to advance this program."

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 working with the Medicines Patent Pool to provide access to low- and middle-income countries (LMICs), and strengthening its manufacturing and global supply chain.

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 patients with mild to moderate SARS-CoV-2 infection, regardless of risk factors or vaccination status, in the Phase 3 part of the Phase 2/3 study conducted during the Omicron-dominant phase of the epidemic. With regard to safety, ensitrelvir was well tolerated, and there were no serious treatment related adverse events or deaths 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.

Note that ensitrelvir is 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.

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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