PRESSRELEASE

SHIONOGI

Xocova® (Ensitrelvir Fumaric Acid) Tablets 125mg Approved in Japan for the Treatment of SARS-CoV-2 Infection, under the Emergency Regulatory Approval System

OSAKA, Japan, November 22, 2022 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced that Xocova® (Generic name: ensitrelvir fumaric acid, Code No.: S-217622), a novel anti-SARS-CoV-2 drug for COVID-19, obtained emergency regulatory approval from the Ministry of Health, Labour and Welfare (MHLW) in Japan for the indication of SARS-CoV-2 infection. This approval was granted under the emergency regulatory approval system provided for in Article 14-2-2 of the Pharmaceuticals and Medical Devices Act. In addition, a contract with the MHLW for the Japanese government to purchase 1 million courses of Xocova® is now effective in accordance with the basic agreement for domestic supply of Xocova® signed by Shionogi and the MHLW in March 2022 [1].

Xocova® is an oral antiviral agent administered once daily for five days that suppresses the replication of SARS-CoV-2 by selectively inhibiting the viral 3CL protease. Shionogi filed for manufacturing and sales approval in Japan on February 25, 2022 based on the results obtained through the Phase 2b part of a Phase 2/3 clinical trial [2, 3, 4], requesting review under the “conditional approval system”. On May 27, Shionogi refiled the application requesting review under the "emergency regulatory approval system", newly established after revision of the Pharmaceutical and Medical Device Act. Review by the Pharmaceuticals and Medical Devices Agency (PMDA) has been proceeding, and the emergency approval of Xocova® was deliberated in the Pharmaceutical Affairs and Food Sanitation Council meeting held today, including the newly submitted topline results of the Phase 3 part demonstrating achievement of the primary endpoint [5]. Xocova® is the first drug approved under the new emergency approval system. “We are proud to reach this landmark step which marks the start of our real contribution to people’s recovery from SARS-CoV-2 infection. Shionogi will continue to work intensively to deliver this new option for the treatment of SARS-CoV-2 infected patients not only in Japan but also throughout the world, including in low- and middle-income countries (LMICs).,” said Isao Teshirogi, Ph.D.

Given the continuing spread and urgency of the ongoing COVID-19 pandemic, Shionogi has been working closely with the MHLW and cooperating institutions regarding management of the distribution of Xocova® to allow prompt supply to medical institutions in Japan. Starting tomorrow, Shionogi will begin shipping to pharmaceutical wholesalers and accepting orders from registered medical institutions and pharmacies that can prescribe and prepare Xocova® based on the notice from the MHLW. Since Xocova® has received emergency approval, Shionogi will continue to diligently collect clinical safety information and to provide that information to medical institutions in a timely manner.

This emergency approval was granted on the anticipated efficacy of Xocova® and the acceptability of its safety profile based on the results obtained through the Phase 2 part (497 cases including the Phase 2a and Phase 2b parts combined) and the Phase 3 part (1,821 cases) of the Phase 2/3 study. Xocova® 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, during the Omicron-dominant phase of the epidemic. Shionogi will work

toward obtaining a standard approval for Xocova® and will discuss with the MHLW the transition to general distribution in Japan. We will continue to pursue global registration, including working with the Medicines Patent Pool to provide access to LMICs, and to expand and strengthen our manufacturing and global supply chain, in parallel with accumulating additional evidence on efficacy and safety.

Shionogi is committed to "Protect people worldwide from the threat of infectious diseases" as our key focus. We are not only pursuing the research and development of therapeutics, but are also working towards total care for infectious diseases, through awareness building, epidemiologic monitoring, prevention, diagnosis, and addressing exacerbations, as well as treating the infection itself. As SARS-CoV-2 continues to have a major impact on people's lives and to represent a global threat, we will seek to contribute to re-establishing the safety and security of society by developing new products and services to address this pandemic, and will keep all stakeholders informed regarding the progress of our efforts.

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About Xocova®

Xocova® (ensitrelvir fumaric acid), an 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. Xocova® suppresses the replication of SARS-CoV-2 by selectively inhibiting 3CL protease. Currently, the Phase 2b/3 part of the Phase 2/3 study targeting SARS-CoV-2 infected persons with asymptomatic/mild symptoms only is being conducted in Asia, mainly in Japan. With regard to safety, ensitrelvir was well tolerated, and there were no treatment-related serious adverse events or deaths in the study. The most common treatment-related adverse events were transient decreases in high-density lipoprotein and increases blood triglycerides, as observed in previous studies. A global Phase 3 trial (SCORPIO-HR study[6]) in non-hospitalized SARS-CoV-2 infected patients is ongoing. In addition, a global Phase 3 trial (STRIVE study[7]) for hospitalized SARS-CoV-2 infected patients is scheduled to initiate soon. An onset prevention study for household members living with SARS-CoV-2 infected individuals and a pediatric study for children under the age of 12 are also in preparation.

To that end, we 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:
SHIONOGI Website Inquiry Form : https://www.shionogi.com/global/en/contact.html

Reference

1. Press release on March 25,2022
   Notice Regarding the Signing of a Basic Agreement with the Ministry of Health, Labor and Welfare for Domestic Supply of S-217622, a Therapeutic Drug for COVID-19
2. Press release on February 7,2022
   Shionogi Presents Phase 2/3 Clinical Trial Results (Phase 2a Part) for the COVID-19 Therapeutic Drug S-217622
3. Press realease on February 25,2022
   Shionogi Files for Approval of S-217622, a Therapeutic Drug for COVID-19, in Japan
4. Press release on April 24,2022
   New Data for Shionogi's COVID-19 Once-Daily Oral Antiviral S-217622 Show Rapid Virus Clearance
5. Press release on September 28, 2022
   Shionogi Announces Achievement of the Primary Endpoint for Ensitrelvir Fumaric Acid (S-217622) in the Phase 3 part of the Phase 2/3 Clinical Trial in Asia
6. ClinicalTrials.gov：NCT05305547
7. ClinicalTrials.gov：NCT05605093

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