Seven manufacturers sign sublicence agreements with the Medicines Patent Pool to produce generic versions of Shionogi's COVID-19 oral antiviral ensitrelvir to increase access in low- and middle-income countries.

Tokyo, 26 June 2023 — Japanese pharmaceutical company Shionogi & Co., Ltd and the Medicines Patent Pool (MPP), a United Nations-backed international public health organisation, have today announced that MPP has signed seven sublicence agreements for Shionogi's ensitrelvir fumaric acid, a COVID antiviral currently approved in Japan and being evaluated in clinical trials outside of Japan. The announcement was made on the sidelines of a business briefing in Tokyo co-convened by MPP and global health partnership Unitaid. The sublicence agreements were signed with three generic manufacturing companies from China: Zhejiang Charioteer Pharmaceutical Co., Ltd., Zhejiang Lepu Pharmaceutical Co.,Ltd., and Fosun International Limited.; two from India: Hetero and Laurus Labs Limited; and with Ukrainian company Joint Stock Company Lekhim and Vietnamese company Stellapharm J.V. Co., Ltd.

Ensitrelvir is an oral antiviral that suppresses the replication of SARS-CoV-2 by selectively inhibiting the viral 3CL protease. Known 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 November 2022. In April 2023, ensitrelvir was granted Fast Track designation by the U.S. Food and Drug Administration.

The head licence agreement between MPP and Shionogi was signed in October 2022, a first for MPP with a Japanese pharmaceutical company. Under the terms of the licence agreement, the seven selected generic manufacturers will be able to manufacture and supply ensitrelvir in 117 low- and middle-income countries (LMICs), pending regulatory authorisation or approval in those countries.

Isao Teshirogi, Representative Director, President and CEO of Shionogi said: "Shionogi is excited that these seven manufacturers across four countries have signed sublicences agreements with MPP, showing their commitment to making generic versions of ensitrelvir for LMICs. What has been important for Shionogi is to work upstream with MPP, as we believe that the public health-oriented licensing agreement we signed with MPP has the potential to increase affordable COVID-19 treatment options for people

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living in LMICs. We consistently strive to supply the best possible medicines to protect the health and wellbeing of the patients we serve. It is another great example of what partnerships can achieve to advance global health."

Charles Gore, Executive Director of MPP, said: "We look forward to working closely with all seven generic manufacturing partners on developing generic versions of ensitrelvir and making it available soonest. Even though COVID-19 is no longer classified as a Public Health Emergency of International Concern, we see numbers ebb and flow across continents as we learn to live with the disease. So having quality effective treatments readily available in LMICs is still so important. I warmly welcome Lekhim JSC from Ukraine, and Zhejiang Charioteer and Lepu Pharma from China, as these are the first sublicence agreements that they have signed with MPP."

Tenu Avafia, Deputy Executive Director of Unitaid, said: " Unitaid's vision is for new health technologies to be as quickly available and widely accessible in low-and middle-income countries as possible. This includes embedding access considerations into efforts to prevent, prepare for, and respond to pandemics, present and future. We commend Shionogi for reflecting G7 priorities to account for equity, efficiency, and affordability in the development of its treatment and for its early engagement with MPP on voluntary licensing. The signing of these seven sublicence agreements is an important milestone."

Nombeko Mpongo, Community Liaison Administrator, Desmond Tutu HIV Centre, South Africa, said: "Through my work, I support two sisters who lost their parents to COVID-19 at the height of the pandemic. In our communities, such loss goes beyond the terrible grief as the young adolescents have been left to fend for themselves at a vulnerable age, curbing their future opportunities as they struggle to survive without the guidance of their parents. Access to treatment is so much more than a question of life and death, it is about the well-being of entire communities, so I welcome this announcement that will enable equitable access to COVID-19 treatments in my country and other LMICs."

Access the sublicence agreements

The press release is also available in French, Spanish and Japanese

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. 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 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 the Medicines Patent Pool

The Medicines Patent Pool (MPP) is a United Nations-backed public health organisation working to increase access to and facilitate the development of life-saving medicines for low- and middle-income countries. Through its innovative business model, MPP partners with civil society, governments, international organisations, industry, patient groups, and other stakeholders to prioritise and license needed medicines and pool intellectual property to encourage generic manufacture and the development of new formulations. To date, MPP has signed agreements with 18 patent holders for 13 HIV antiretrovirals, one HIV technology platform, three hepatitis C direct-acting antivirals, a tuberculosis treatment, a cancer treatment, four long-acting technologies, three oral antiviral treatments for COVID-19 and 12 COVID-19 technologies. MPP was founded by Unitaid, which continues to be MPP's main funder. MPP's work on access to essential medicines is also funded by the Swiss Agency for Development and Cooperation (SDC). MPP's activities in COVID-19 are undertaken with the financial support of the Japanese Government, the French Ministry for Europe and Foreign Affairs, the German Agency for International Cooperation and SDC. More information at https://medicinespatentpool.org/ and follow us on Twitter, LinkedIn and YouTube.

About SHIONOGI

Shionogi & Co., Ltd. is a leading global research-driven pharmaceutical company based in Japan dedicated to bringing benefits to patients based on its corporate philosophy of "supplying the best possible medicine to protect the health and well-being of the

patients we serve." The company has discovered and developed novel medicines for HIV, influenza and antimicrobial resistance and currently markets products in several therapeutic areas including anti-infectives with the first siderophore cephalosporin. We are working to solve healthcare social issues by identifying disease areas with great social needs as core areas for research and development, with a focus on infectious diseases. For more information on Shionogi & Co., Ltd., visit https://www.shionogi.com/global/en/.

Shionogi Inc. is a U.S. subsidiary of Shionogi & Co., Ltd. based in New Jersey. For more information on Shionogi Inc., please visit https://www.shionogi.com/us/en/.

Shionogi B.V. is the European headquarters of Shionogi & Co., Ltd. For more information on Shionogi B.V., please visit https://www.shionogi.com/eu/en/ .

Other partners

Ping An

Ping An Insurance (Group) Company of China, Ltd. is collaborating with Shionogi to develop ensitrelvir in Asia through their joint venture companies and both companies are committed to support access to medicines for patients living in low- and middle-income countries (LMICs). To help make ensitrelvir affordable and available to more people in Asia, Ping An Insurance (Group) Company of China, Ltd. supports the Shionogi collaboration with MPP.

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

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