Press Release

Shionogi Filed for the Supplemental New Drug Application of XOFLUZA® in Japan for the Post-Exposure Prophylaxis of Influenza Virus Infection

OSAKA, Japan, October, 16, 2019 - Shionogi & Co., Ltd. (hereafter "Shionogi") has announced that Shionogi filed a Supplemental New Drug Application (sNDA) for XOFLUZA® in Japan for the post-exposure prophylaxis of influenza virus infection on October 16, 2019.

The sNDA is based on data from the phase III BLOCKSTONE study; this study assessed XOFLUZA in the post-exposure prophylaxis of influenza virus infection in subjects who were household members of influenza-infected patients.[1] "The results from BLOCKSTONE show the potential of XOFLUZA as an important prophylactic treatment option for influenza," said Dr. Tsutae Den Nagata, Chief Medical Officer at Shionogi. "Therefore, if this indication is approved, we believe that XOFLUZA will help to reduce the burden of influenza in both the symptomatic and prophylactic treatment settings."

Shionogi and Roche Group (hereafter "Roche") are in a license and collaboration agreement to further develop and commercialize XOFLUZA. Under the terms of this agreement, Roche holds worldwide rights to XOFLUZA excluding Japan and Taiwan where the rights are retained exclusively by Shionogi. XOFLUZA® was approved in Japan on February 23, 2018 and is available for the treatment of influenza types A and B in adults and pediatric patients.[2] In the U.S., XOFLUZA™ was first approved by the FDA for the treatment of acute, uncomplicated influenza in otherwise healthy people 12 years of age and older on October 25, 2018.[3]

Shionogi's research and development efforts target infectious diseases as one of its priority areas, and Shionogi has defined "protecting people from the threat of infectious diseases" as one of its core social missions. Shionogi strives constantly to bring forth innovative drugs for the treatment of infectious diseases, to protect the health of the many patients we serve. Shionogi will continue to work diligently to collect and analyze data on the efficacy and safety of XOFLUZA and provide information for proper use.

About XOFLUZA

XOFLUZA, discovered by Shionogi, has a novel mechanism of action that inhibits cap-dependent endonuclease in the polymerase acidic (PA) protein (in the United States Prescribing Information, this enzyme is stated as polymerase acidic endonuclease), an enzyme essential for viral replication. The regimen for XOFLUZA is a single oral dose to treat uncomplicated influenza, which is different from all currently available antiviral treatments. In non-clinical studies, XOFLUZA demonstrated an antiviral effect against a wide range of influenza viruses including oseltamivir-resistant strains and avian strains (H7N9, H5N1).[4, 5] XOFLUZA is currently approved in several countries including Japan and the U.S. XOFLUZA was approved in Taiwan on August 28, 2019, for the treatment of acute influenza types A and B in patients aged 12 years and older.[6] In addition, The U.S. Food and Drug Administration (FDA) has accepted a supplemental New Drug Application for XOFLUZA™ for the treatment of influenza in individuals at high-risk for influenza-related complications 12 years and older. The Prescription Drug User Fee Act (PDUFA) date for an FDA decision on this additional indication is November 4, 2019.[7] For more information about the use of XOFLUZA in the U.S., please refer to the XOFLUZA website. Roche is now conducting a phase III development program including children under the age of one year, and severely ill, hospitalized patients, as well as to assess the potential to reduce transmission of influenza from an infected person to healthy people.

About BLOCKSTONE Study

The BLOCKSTONE study was a phase III, multicenter, randomized, double-blind study that evaluated a single oral dose of XOFLUZA compared with placebo for the post-exposure prophylaxis of influenza virus infection in subjects who are household members of influenza-infected patients. The study was conducted by Shionogi in Japan. Participants enrolled in the study were randomly assigned to receive either a single dose of XOFLUZA (the dose was set according to age and body weight*) or placebo. The primary endpoint of the study was the proportion of subjects who were infected with influenza virus and presented with fever and at least one respiratory symptom during the 10 days after taking XOFLUZA or placebo.

*Dosage of XOFLUZA in the BLOCKSTONE study:

1.12 years of age or older

Body weight	Dosage
80 kg or more	80 mg
Less than 80 kg	40 mg

2.Under 12 years of age

Body weight	Dosage
40 kg or more	40 mg
Less than 40 kg and 20 kg or more	20 mg
Less than 20 kg and 10 kg or more	10 mg (granule)
10 kg or less	1 mg/kg (granule)

About Influenza

Seasonal and pandemic influenza remain a major public health concern, and novel influenza drugs that will offer significant improvement over current therapies are urgently needed. Globally, seasonal epidemics result in 3 to 5 million cases of severe disease, millions of hospitalizations and up to 650,000 deaths every year.[8, 9, 10, 11, 12]

About Shionogi

Shionogi & Co., Ltd. is a Japanese major research-driven pharmaceutical company dedicated to bringing benefits to patients based on its corporate philosophy of "supplying the best possible medicine to protect the health and wellbeing of the patients we serve." The company currently markets products in several therapeutic areas including anti-infectives, pain, cardiovascular diseases and gastroenterology. Our pipeline is focused on infectious disease, pain, CNS and oncology. For more information on Shionogi & Co., Ltd., visit www.shionogi.co.jp/en.

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 outcomes 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, unavailability 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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References

1. Press release on September 2, 2019
   Shionogi Announces Positive Post-Exposure Prophylaxis Results for XOFLUZA® in Phase III Study (BLOCKSTONE) of Influenza Virus Infection in Household Members
2. Press release on March 14, 2018
   XOFLUZA™ (Baloxavir Marboxil) Tablets 10mg/20mg for the Treatment of Influenza Types A and B launched in Japan
3. Press release on October 25, 2018
   Shionogi Announces FDA Approval of XOFLUZA™ (Baloxavir Marboxil)- for the Treatment of Acute, Uncomplicated Influenza –
4. T. Noshi et al. In vitro Characterization of Baloxavir Acid, a First-in-Class Cap-dependent Endonuclease Inhibitor of the Influenza Virus Polymerase PA Subunit. Antiviral Research 2018;160:109-117
5. K. Taniguchi et al. Inhibition of avian-origin influenza A(H7N9) virus by the novel cap-dependent endonuclease inhibitor baloxavir marboxil. Scientific Reports volume 9, Article number: 3466 (2019)
6. Press release on August 29, 2019
   Shionogi Announces XOFLUZA® Tablets 20mg for The Treatment of Influenza Types A and B in Patients 12 years of Age and older Approved in Taiwan
7. Press release on March 6, 2019
   FDA Accepts XOFLUZATM (Baloxavir Marboxil) Supplemental New Drug Application for the Treatment of Influenza in Individuals at High Risk for Influenza-Related Complications
8. http://www.who.int/mediacentre/news/releases/2017/seasonal-flu/en/ World Health Organization website, Up to 650 000 people die of respiratory diseases linked to seasonal flu each year, Accessed December 14, 2017.
9. http://www.who.int/mediacentre/factsheets/fs211/en World Health Organization website, Influenza (Seasonal), Accessed January 31, 2018.
10. Baxter D. Evaluating the case for trivalent or quadrivalent influenza vaccines. Hum Vaccin Immunother. 2016; 12(10):2712-2717.
11. https://www.cdc.gov/flu/about/disease/2015-16.htm CDC website, Estimated Influenza Illnesses, Medical Visits, Hospitalizations, and Deaths Averted by Vaccination in the United State. Accessed April 19, 2017.
12. Nair H, et al. Global burden of respiratory infections due to seasonal influenza in young children:

a systematic review and meta-analysis. Lancet. 2011 Dec 3;378(9807):1917-30.