Press Release

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

OSAKA, Japan, March, 31, 2020 - Shionogi & Co., Ltd. (hereafter "Shionogi") has announced that Shionogi filed a Supplemental New Drug Application (sNDA) for Xofluza® in Taiwan for the post-exposure prophylaxis of influenza virus infection in adults and children 12 years of age and older.

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 a important prophylactic treatment option for influenza. Therefore, if this indication is approved, Xofluza will help to reduce the burden of influenza in both the symptomatic and prophylactic treatment settings in Taiwan.

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 is approved and is available in Taiwan. Taiwan Shionogi & Co., Ltd., (hereafter “Taiwan Shionogi”), the Taiwan subsidiary of Shionogi, is responsible for selling Xofluza in Taiwan.[2]

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 BLOCKSTONE Study[1]

BLOCKSTONE is a Phase III, double blind, multicenter, randomised, placebo-controlled, post-exposure prophylaxis study that evaluated one dose of Xofluza compared with placebo in household members (adults and children) in Japan who were living with someone with an influenza infection confirmed by a rapid influenza diagnostic test (the 'index patient'). The study was conducted by Shionogi & Co., Ltd. during the 2018-2019 flu season in Japan.Participants enrolled in the study were household members of someone who had been diagnosed with influenza. The participants were randomised to receive one dose of Xofluza (dose according to body weight) or placebo as a preventive measure against developing influenza.

Xofluza showed a significant prophylactic effect on influenza infection after one oral dose in people exposed to an infected family member. The proportion of household members who became symptomatically ill following infection with flu was significantly lower in those treated preventively with Xofluza compared to those treated with placebo (proportion of subjects with influenza virus infection, fever and other influenza symptoms in the 10-day observation period: 1.9% versus 13.6%). Xofluza was well tolerated and no new adverse drug reactions were identified.[3]

About Xofluza (baloxavir marboxil)

Xofluza, discovered by Shionogi, has a novel mechanism of action that inhibits the 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 other 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. The U.S. Food and Drug Administration (FDA) accepted for review an NDA for a new formulation of Xofluza as single-dose, granules for oral suspension for the treatment of acute uncomplicated influenza in otherwise healthy people one year of age and older who have been symptomatic for no more than 48 hours. The FDA acceptance for review also includes Xofluza for post-exposure prophylaxis of influenza in people one year of age and older for both the oral suspension and tablet formulation. The Prescription Drug User Fee Act (PDUFA) date for an FDA decision is November 23, 2020.[6] For more information about the use in the U.S., please refer to the Xofluza® website. Roche is now conducting a phase III development program investigating Xofluza in several populations, including children under the age of one year (NCT03653364), and severely ill, hospitalized patients (NCT03684044), as well as to assess the potential to reduce transmission of influenza from an infected person to healthy people (NCT03969212). Shionogi assessed the potential of Xofluza as a post-exposure prophylaxis treatment to prevent the spread of influenza in adults and children, and submitted an sNDA based on the positive results from the phase III BLOCKSTONE study on October 16, 2019 in Japan.[7]

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 Taiwan Shionogi & Co., Ltd

Taiwan Shionogi & Co., Ltd was incorporated locally in Taiwan in 1963. It is a wholly owned

subsidiary, and also the oldest subsidiary of Shionogi & Co., Ltd, headquartered in Osaka, Japan. Taiwan Shionogi has a long history of developing drugs especially in the field of antibiotics and anti-infective agents to save the lives and wellbeing of patients. Under the corporate mission, Taiwan Shionogi continuously strives to save the lives of patients and improving their quality of life by providing better medicines. In addition to the sales expansion of its main existing antibiotic Flumarin® and Finibax®, and anti flu drug Rapiacta®, Taiwan Shionogi is making its best efforts to introduce new drugs and aiming at contributing to the medium-and-long term growth of the Shionogi Group.

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 November 25, 2019
   Shionogi Announces XOFLUZA® Tablets 20mg for the Treatment of Influenza A or B virus Acute Infection Launched in Taiwan.
3. H. Ikematsu et al. Single-dose baloxavir for the prevention of influenza among household contacts: a randomized, double-blinded, placebo controlled post-exposure prophylaxis study (BLOCKSTONE). OPTIONS X 2019; 2019 Aug 28-Sept 1; Singapore. Abstract #11718
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 March 27, 2020
FDA Accepts a New Drug Application for a New Formulation and Two Supplemental New Drug Applications for XOFLUZA® (Baloxavir Marboxil)
7. Press release on October 16, 2019
Shionogi Filed for the Supplemental New Drug Application of XOFLUZA® in Japan for the Post-Exposure Prophylaxis of Influenza Virus Infection
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.