Press Release

Shionogi Announces Positive Top-Line Results for Baloxavir Marboxil Phase III Study (CAPSTONE-2) in Individuals at High Risk for Influenza-Related Complications

OSAKA, Japan, July 17, 2018 - Shionogi & Co., Ltd. (hereafter "Shionogi") has announced that the global phase III study (CAPSTONE-2) assessing baloxavir marboxil in individuals at high risk for influenza-related complications met the study's primary objective and showed superior efficacy in the primary endopoint of time to improvement of influenza symptoms compared with placebo. Baloxavir marboxil also demonstrated superior efficacy compared with placebo and compared with oseltamivir in key secondary endpoints, including reducing the time that the virus was released (viral shedding), and reducing viral levels in the body. Furthermore, baloxavir marboxil significantly reduced the incidence of influenza-related complications compared to placebo. Baloxavir marboxil was well tolerated and no safety signals were identified. The results from the CAPSTONE-2 study will be presented at upcoming medical meetings.

Baloxavir marboxil has a novel mechanism of action that inhibits cap-dependent endonuclease, an essential enzyme for viral replication. Baloxavir marboxil has already demonstrated a clinically significant benefit over both placebo and oseltamivir in the global phase III study in otherwise healthy patients (CAPSTONE-1).[1, 2] Baloxavir marboxil was approved in Japan on February 23, 2018 and is available under the brand name XOFLUZA® for the treatment of influenza Types A and B in adults and pediatric patients.[3] Shionogi submitted the New Drug Application (NDA) for baloxavir marboxil in U.S. on April 24, 2018 for the treatment of acute uncomplicated influenza in patients 12 years of age and older and the U.S. Food and Drug Administration (FDA) recently accepted the NDA and granted Priority Review. The Prescription Drug User Fee Act (PDUFA) date for an FDA decision is December 24, 2018.[4] Shionogi submitted a NDA for baloxavir marboxil in Taiwan on June 29, 2018, for the treatment of influenza in patients 12 years of age and older.[5]

The data from the CAPSTONE-2 study demonstrate that baloxavir marboxil provides a clinically meaningful benefit for patients who are most susceptible to influenza-related complications. There are no medicines which have demonstrated clear benefit specifically in high-risk populations in clinical studies. "Following the successful Phase III study reported previously in otherwise healthy patients, this study showed a positive result in high risk patients, including those with asthma or chronic lung disease, endocrine disorders, heart disease, metabolic disorders and morbid obesity or those who are 65 years of age or older, who tend to develop complications with influenza. We believe that baloxavir marboxil has the potential to offer an improved treatment for influenza for a wider patient population." said Dr. Tsutae Den Nagata, Chief Medical Officer.

Press Release

Shionogi's research and development efforts target infectious diseases as one of its priority areas, and Shionogi has positioned “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.

About Baloxavir Marboxil

Baloxavir marboxil, discovered and developed by Shionogi, has a novel mechanism of action that inhibits cap-dependent endonuclease, an essential enzyme for viral replication. The regimen for baloxavir marboxil is a single-oral dose to treat influenza, which is different from currently available antiviral treatments. In non-clinical studies, baloxavir marboxil demonstrated an antiviral effect against a wide range of influenza viruses including oseltamivir-resistant strains and avian strains (H7N9, H5N1).[6, 7, 8]

Shionogi and F. Hoffmann-La Roche Ltd. (hereafter "Roche") are in a license and collaboration agreement to further develop and commercialize baloxavir marboxil globally. Under the terms of this agreement, Roche holds worldwide rights to baloxavir marboxil excluding Japan and Taiwan where the rights are retained exclusively by Shionogi.

About CAPSTONE-2 Study

The CAPSTONE-2 study is a phase III, multicentre, randomised, double-blind study that evaluated a single oral dose of baloxavir marboxil compared with placebo and oseltamivir in patients 12 years or older who are at a high risk for influenza-related complications. The study was conducted globally by Shionogi. Participants enrolled in the study were randomly assigned to receive a single dose of 40 mg or 80 mg of baloxavir marboxil (according to body weight), placebo or 75 mg of oseltamivir twice a day for 5 days. The primary endpoint of the study was the time to improvement of influenza symptoms. Important secondary endpoints were time to resolution of fever, time to cessation of viral shedding and virus levels in the body, by time point, and incidences of influenza-related complications.

About Influenza

Seasonal, epidemic and pandemic influenza remain a major public health concern, and novel influenza drugs that will offer significant improvement over current therapy are urgently needed. Globally, annual epidemics result in 3 to 5 million cases of severe disease, millions of hospitalizations and up to 650,000 deaths worldwide.[9, 10, 11, 12, 13] The Centers for Disease Control and Prevention (CDC) describes high-risk categories including children under 2 years of age, adults of 65 years of age and older, pregnant women, and people of any age with certain medical conditions, including asthma and chronic lung disease, heart desease, blood disorders, endocrine disorders, metabolic diseases, extreme obesity and weakened immune systems.[14]

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 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, 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 13, 2017
   S-033188 Phase 3 CAPSTONE-1 Study Results for Treatment of Influenza Presented at the European Scientific Working Group on Influenza Conference
2. Press release on October 5, 2017
   SHIONOGI TO PRESENT S-033188 PHASE 3 CAPSTONE-1 STUDY RESULTS FOR TREATMENT OF INFLUENZA AT IDWEEK 2017
3. Press release on March 14, 2018
   XOFLUZA (Baloxavir Marboxil) Tablets 10mg/20mg for the Treatment of Influenza Types A and B launched in Japan
4. Press release on June 26, 2018
   FDA Accepts Baloxavir Marboxil New Drug Application and Grants Priority Review for the Treatment of Influenza
5. Press release on July 2, 2018
   Shionogi Filed for the New Drug Application of Baloxavir Marboxil in Taiwan for the Treatment of Influenza

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