Media & Investor Release

Roche announces U.S. FDA approval of Xofluza to treat influenza in children aged five years and older

- **Xofluza is the first and only single-dose oral medicine for the treatment of influenza to be approved in the US for children as young as five years of age**
- **The FDA also approved Xofluza to prevent influenza in children aged five years and older following contact with an infected person**

Basel, 12 August 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the United States (U.S.) Food and Drug Administration (FDA) has approved a supplemental New Drug Application (sNDA) for Xofluza® (baloxavir marboxil) for the treatment of acute uncomplicated influenza in otherwise healthy children aged five to less than 12 years of age who have been symptomatic for no more than 48 hours. This marks the first single-dose oral influenza medicine approved in the US for children in this age group. Additionally, the FDA approved Xofluza for the prevention (post-exposure prophylaxis) of influenza in children aged five to less than 12 years of age following contact with someone with influenza.

“Despite the ongoing COVID-19 pandemic, influenza continues to be a threat to public health, and effective influenza antivirals remain critical to alleviating the burden on healthcare systems,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “Xofluza has proven to be an important tool in fighting and preventing influenza in adults as well as adolescents, and we are pleased to now offer households and younger children our single-dose oral treatment.”

According to the U.S. Centers for Disease Control and Prevention, influenza can be a serious illness for young children.[1] During the ongoing COVID-19 pandemic there have been significantly fewer influenza cases, likely due in large part to social distancing and mask wearing.[2] However, in the US 2018-2019 influenza season, there were more than 6 million illnesses, thousands of hospitalisations and over 100 deaths among children aged five to 17 caused by influenza.[3]

“Historically, school-aged children have played a significant role in the community transmission of influenza. The annual influenza vaccine continues to be the most important first step to prevent illness in children, though there can still be breakthrough cases where antiviral treatment is needed,” said Dr. Pedro Piedra, miniSTONE-2 Study Investigator and Professor of Molecular Virology, Microbiology and Pediatrics at Baylor College of Medicine. “Today’s FDA approval provides children with a single-dose antiviral option, Xofluza, to treat influenza."

The FDA approval is based on results from two phase III studies: miniSTONE-2, which evaluated the use of Xofluza in children, and BLOCKSTONE, which evaluated Xofluza as a

preventive treatment for household members, in both adults and children. The results from these studies were published in The Pediatric Infectious Disease Journal and The New England Journal of Medicine respectively.[4,5]

Xofluza is already FDA-approved to treat influenza in people 12 years of age and older who have had influenza symptoms for no more than 48 hours and who are otherwise healthy or at high risk of developing influenza-related complications. Xofluza is also approved to prevent influenza in people 12 years of age and older following contact with someone with influenza (known as post-exposure prophylaxis). Xofluza is available as a one-dose, single-tablet.[6]

About miniSTONE-2[4]

miniSTONE-2 was a phase III, multicentre, randomised, double-blind study that evaluated the safety, pharmacokinetics and efficacy of a single-dose of Xofluza® (baloxavir marboxil) compared with oseltamivir in otherwise healthy children aged one to less than 12 years with influenza infection and displaying influenza symptoms for no more than 48 hours (temperature of 38°C or over, and one or more respiratory symptoms).

Participants enrolled in the study were recruited in parallel into two cohorts: children aged five to less than 12 years and children aged one to less than five years. Participants in both cohorts were randomly assigned to receive a single-dose of Xofluza or oseltamivir twice a day over five days (dosing according to body weight).

Time to alleviation of influenza signs and symptoms were comparable between Xofluza and oseltamivir. The median time to alleviation of signs and symptoms in influenza-infected participants was 138 hours (95% CI: 117, 163) and 150 hours (95% CI: 115, 166) for those who received Xofluza or oseltamivir, respectively. Xofluza was well tolerated with no new safety signals identified.

About BLOCKSTONE[5]

BLOCKSTONE was a phase III, double-blind, multicentre, randomised, placebo-controlled, post-exposure prophylaxis study that evaluated single-dose Xofluza® (baloxavir marboxil) compared with placebo in household members (adults and children) who were living with someone with influenza confirmed by a rapid influenza diagnostic test (the 'index patient').

Participants enrolled in the study were household members of someone who had been diagnosed with influenza. The participants were randomised to receive a single-dose of Xofluza (dose according to body weight) or placebo as a preventive measure against developing influenza.

Xofluza showed a statistically significant prophylactic effect on influenza after a single oral dose, by reducing the risk of individuals aged 12 years and above from developing influenza after exposure to an infected household member by 90% versus placebo. The proportion of household members aged 12 years and above who developed laboratory-confirmed clinical

influenza was 1.3% in participants treated with Xofluza and 13.2% in the placebo-treated group.

Xofluza was well tolerated in this study and no new safety signals were identified. The study was conducted in Japan by Shionogi & Co., Ltd.

About Xofluza® (baloxavir marboxil)

Xofluza is a first-in-class, single-dose oral medicine with an innovative mechanism of action that has demonstrated efficacy in a wide range of influenza viruses, including in vitro activity against oseltamivir-resistant strains and avian strains (H7N9, H5N1) in non-clinical studies. [7-9] Xofluza is the first in a class of antivirals designed to inhibit the cap-dependent endonuclease protein, which is essential for viral replication.[7]

Xofluza is approved in more than 70 countries for the treatment of influenza types A and B. In the United States (US), Xofluza is approved for the treatment of acute, uncomplicated influenza in patients aged 12 years and above who are otherwise-healthy or at high-risk of developing serious complications from influenza, and who have been symptomatic for no more than 48 hours. Xofluza is also approved for post-exposure prophylaxis of influenza in individuals 12 years of age and older. Xofluza was the first new antiviral to be approved by the FDA in 20 years, and is the first innovation in mechanism of action for an influenza antiviral approved by the European Commission in almost 20 years.[6,10]

Robust clinical evidence has demonstrated the benefit of Xofluza in several populations (otherwise-healthy, high-risk and post-exposure prophylaxis in individuals aged 12 years and above).[5,7,11] Xofluza is being further studied in a phase III development programme, including children under the age of one (NCT03653364) as well as to assess the potential to reduce transmission of influenza from an infected person to healthy people (NCT03969212). [12,13]

Xofluza was discovered by Shionogi & Co., Ltd. and is being further developed and commercialised globally in collaboration with the Roche Group (which includes Genentech in the US) and Shionogi & Co., Ltd. Under the terms of this agreement, Roche holds worldwide rights to Xofluza excluding Japan and Taiwan, which will be retained exclusively by Shionogi & Co., Ltd.

About Roche in Influenza

Influenza is one of the most common, yet serious, infectious diseases, representing a significant threat to public health. Globally, seasonal epidemics result in three to five million cases of severe disease, millions of hospitalisations and up to 650,000 deaths every year. [14] Roche has a long heritage in developing medicines that contribute to public health. We are committed to bringing innovation in the field of infectious diseases, including influenza. Tamiflu® (oseltamivir) has made a significant difference both to the treatment of seasonal influenza as well as in the management of recent pandemics, and we are proud to have brought this innovative medicine to patients. Although vaccines are an important first line of

defence in preventing influenza, there is a need for new medical options for prevention (prophylaxis) and treatment. Roche is committed to addressing the unmet need in this area through its agreement with Shionogi & Co., Ltd. to develop and commercialise Xofluza® (baloxavir marboxil).

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognizing our endeavor to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

For more information, please visit www.roche.com.

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