Media & Investor Release

Roche announces the European Commission approval of Xofluza for the treatment and prevention of influenza in children aged one year and above

- **Xofluza is now approved in the EU for the treatment of uncomplicated influenza and for post-exposure prophylaxis of influenza in children aged one year and above, and in adolescents and adults**
- **Xofluza is the first influenza antiviral with a new mechanism of action in almost 20 years, stopping viral replication faster than oseltamivir**
- **Single-dose Xofluza helps reduce the societal burden of influenza by helping patients recover quickly and by preventing infection in individuals following contact with someone with the virus**

Basel, 12 January 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission (EC) has approved Xofluza® (baloxavir marboxil) in children aged one year and above for the treatment of uncomplicated influenza and for post-exposure prophylaxis of influenza. Post-exposure prophylaxis aims to prevent influenza in individuals following contact with someone infected with the influenza virus. The Commission's Decision is based on the results of the phase III miniSTONE-2 and BLOCKSTONE studies.[1,2] This approval marks the first single-dose, oral influenza medicine approved in Europe for children, and now means that Xofluza can be used to treat and prevent uncomplicated influenza in children aged one year and above, and in adolescents and adults.[3]

"We are delighted that the European Commission has approved Xofluza for children aged one year and above, as influenza can be particularly dangerous for younger children," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are hopeful that Xofluza's convenient single-dose oral regimen will help children recover quickly, as well as reduce the societal burden of influenza."

Influenza is a serious infectious disease and represents a significant threat to public health.[4-6] Rates of influenza in Europe are rising and it is expected that the virus will infect around one in four children each year.[6,7] In addition to being at higher risk of infection, children also play a significant role in the spread of influenza from one person to another.[6,8] In studies of influenza transmission in households, the risk of infection from others in the household was as high as 38%.[9] Prophylactic treatment with Xofluza, which stops viral replication faster than oseltamivir, may help to limit the spread of influenza and therefore reduce the impact and burden of influenza on society.[2,10,11]

The approval is based on the results of the phase III miniSTONE-2 and BLOCKSTONE studies.[1,2] The miniSTONE-2 study met its primary endpoint of safety and showed that Xofluza reduced

the length of time that influenza was released from the body by more than two days compared with oseltamivir (viral replication; median time of 24.2 hours versus 75.8 hours, respectively). Xofluza was well tolerated with no new safety signals identified.[1]

In the BLOCKSTONE study Xofluza showed a statistically significant prophylactic effect after a single oral dose, by reducing the risk of people developing influenza after exposure to an infected household member by 86% versus placebo (1.9% in participants treated with Xofluza and 13.6% in the placebo group).[2]

Xofluza was first approved for use in Europe in 2021 for the treatment of uncomplicated influenza and for post-exposure prophylaxis of influenza in adults and adolescents aged 12 years and above.[12] Xofluza is now approved in more than 70 countries for the treatment of influenza types A and B.[13] Roche is continuing to investigate Xofluza in phase III trials in children under the age of one (NCT03653364), as well as to assess its potential to reduce transmission of influenza from an infected person to household members (NCT03969212).[14,15]

About miniSTONE-2[1]

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 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 reduced the length of time that influenza was released from the body by more than two days compared with oseltamivir (viral replication; median time of 24.2 hours versus 75.8 hours, respectively). Xofluza was well tolerated with no new safety signals identified.

About BLOCKSTONE[2]

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 after a single oral dose, by reducing the risk of people developing influenza after exposure to an infected household member by 86% versus placebo. The proportion of households, who developed laboratory-confirmed clinical influenza was 1.9% in participants treated with Xofluza and 13.6% 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.[10,16,17] Xofluza is the first in a class of antivirals designed to inhibit the cap-dependent endonuclease protein, which is essential for viral replication.[10]

Xofluza is approved in more than 70 countries for the treatment of influenza types A and B. In Europe, Xofluza is now approved for the treatment of uncomplicated influenza and for post-exposure prophylaxis of influenza in children aged one year and above, and in adolescents and adults. Xofluza is the first innovation in mechanism of action for an influenza antiviral approved by the European Commission in almost 20 years.[18]

Robust clinical evidence has demonstrated the benefit of Xofluza in several populations (otherwise-healthy, high-risk, children and post-exposure prophylaxis in individuals aged one year and above).[1,2,10,19] Xofluza is being further studied in a phase III development programme, including in children under the age of one (NCT03653364) as well as to assess its potential to reduce transmission of influenza from an infected person to healthy people (NCT03969212).[14,15]

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 a serious infectious disease and represents a significant threat to public health. Seasonal epidemics result in three to five million cases of severe disease, millions of hospitalisations and up to 650,000 deaths globally every year.[4] 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 recognising 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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