Media Release

Roche presents positive phase III study results for one-dose Xofluza in children with flu

- **Phase III MINISTONE-2 data are consistent with known safety profile of Xofluza (baloxavir marboxil) in children and show comparable efficacy to oseltamivir**
- **Xofluza was administered as a new one-dose oral suspension, a potentially more convenient treatment option for children**
- **Children are at high risk of developing flu, and complications lead to approximately one million children under five years old being hospitalised globally every year**

Basel, 2 September 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the phase III MINISTONE-2 study showed that one-dose Xofluza™ (baloxavir marboxil) was a well-tolerated and effective potential treatment for flu in otherwise healthy children aged one to less than 12 years old. The study met its primary endpoint, which evaluated the proportion of patients with adverse events (AEs) or severe AEs up to study day 29, demonstrating results consistent with the safety profile of Xofluza. In Xofluza-treated participants, 46.1% experienced at least one treatment-emergent AE compared to 53.4% in the oseltamivir arm. The study also showed the efficacy of Xofluza to be comparable to oseltamivir (a proven effective treatment for children with flu). In addition, consistent with data in adults and adolescents, Xofluza reduced the length of time that the flu virus continued to be released from the body by more than two days compared with oseltamivir (viral shedding; median time of 24.2 hours versus 75.8 hours, respectively). Full results of the study were presented as a late-breaking abstract during the OPTIONS X 2019 congress in Singapore on Sunday 1 September, 2019 (Abstract #11756).[1]

“Each year approximately one in three children develop flu, and their less mature immune systems mean they are slower to fight the infection and more vulnerable to complications,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We are committed to developing new, more convenient treatment options for children with flu and look forward to sharing these data with global health authorities.”

MINISTONE-2 is the first global phase III study for Xofluza in children. It showed that Xofluza was comparable to oseltamivir in relation to key secondary endpoints, including time to alleviation of influenza signs and symptoms (median 138.1 hours vs. 150.0 hours).

This is the fourth positive phase III study for Xofluza, which has now demonstrated benefit in several populations (otherwise-healthy, high-risk, children) and treatment settings (symptomatic, post-exposure prophylaxis).[1-4] Xofluza is being further studied in an ongoing phase III development programme, including children under one year, severely ill hospitalised people with flu, and to assess the potential to reduce transmission of flu from an infected person to healthy people.[5-7]

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About MINISTONE-2 (NCT03629184)[1]
MINISTONE-2 is a phase III, multicentre, randomised, double-blind study that evaluated the safety, pharmacokinetics and efficacy of one dose of Xofluza compared with oseltamivir in otherwise healthy children aged one to less than 12 years with influenza infection and displaying influenza symptoms (temperature of 38°C or over, and one or more respiratory symptom).

Participants enrolled in the study were recruited in parallel into two cohorts: patients aged five to less than 12 years and patients aged one to less than five years. Patients in both cohorts were randomly assigned to receive one dose of Xofluza (2mg/kg for patients under 20kg or 40mg for patients 20kg or over) or oseltamivir twice a day over five days (dosing according to body weight). The primary endpoint of the study was the proportion of patients with adverse events or severe adverse events up to study day 29. Secondary endpoints included pharmacokinetics, time to alleviation of influenza signs and symptoms, and duration of symptoms, including fever.

About Xofluza (baloxavir marboxil)
Xofluza is a first-in-class, one-dose oral medicine with a novel proposed 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.[8,9] Unlike other currently available antiviral treatments, Xofluza is the first in a new class of antivirals designed to inhibit the CAP-dependent endonuclease protein, which is essential for viral replication.[8]

Xofluza is currently approved in several countries, including the United States (US), for the treatment of acute, uncomplicated influenza in people 12 years of age and older. In addition, a supplemental New Drug Application (sNDA) for Xofluza as a one-dose oral treatment for people at high risk of complications from flu is under review by the FDA and a decision is expected by 4 November 2019.

Xofluza is being further studied in a phase III development programme, including children under the age of one (NCT03653364), severely ill, hospitalised patients (NCT03684044), as well as to assess the potential to reduce transmission of flu from an infected person to healthy people (NCT03969212).[5-7]

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, where rights will be retained exclusively by Shionogi & Co., Ltd.

About Roche in influenza
Influenza, or flu, is one of the most common, yet serious, infectious diseases, representing a significant threat to public health.[10] Globally, seasonal epidemics result in 3 to 5 million cases of severe disease, millions of hospitalisations and up to 650,000 deaths every year.[11-15] Children are at a particularly high risk of developing flu, with an estimated global rate of 20–30% compared with 5–10% in adults, and are more vulnerable to complications such as breathing problems, pneumonia and, in some cases, even death.[5,16] Due to these complications, approximately one million children under five years old are hospitalised globally 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 flu, there is a need for new medical options for prophylaxis and treatment. Other antiviral drugs have limitations with respect to efficacy, convenience of dosing and resistance. Roche is committed to addressing the unmet need in this area through its agreement with Shionogi & Co., Ltd. to develop and commercialise Xofluza.

About Roche in infectious disease
Infectious diseases caused by viral or bacterial pathogens are a major cause of death and morbidity worldwide, and constitute an ever-growing medical need. As such, they form a core area of research and development at Roche, with clinical development programmes focused on hepatitis B, influenza and multi-drug resistant bacterial infections. We are committed to developing medicines that aim to be transformative, personalised, and accessible.

About Roche
Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the tenth consecutive year, Roche has been recognised as the most sustainable company in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 billion. 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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