Media Release

Positive phase III results show Xofluza reduces risk of developing flu after contact with an infected person by 86%

- **BLOCKSTONE study reaches primary endpoint of fewer people testing positive for flu, with fever and at least one respiratory symptom, when treated with Xofluza versus placebo**
- **Xofluza may represent an important and convenient treatment for both reducing the burden of seasonal flu and limiting the impact of a pandemic**

Basel, 2 September 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the phase III BLOCKSTONE study showed preventive treatment with Xofluza™ (baloxavir marboxil) after exposure to an infected household member significantly reduced the risk of people developing flu by 86% versus placebo. The results show just 1.9% of Xofluza-treated household members had flu compared with 13.6% in the placebo-treated group ($p<0.0001$). This benefit with Xofluza remained statistically significant versus placebo regardless of influenza A subtype (H1N1: 1.1% vs 10.6%, $p=0.0023$; H3: 2.8% vs. 17.5%, $p<0.0001$). It was also observed in household contacts who are at high risk of flu-associated complications (2.2% vs 15.4%, $p=0.0435$), and children under 12 years of age (4.2% vs 15.5%, $p=0.0339$), who are more vulnerable to developing flu. Xofluza had a comparable safety profile to placebo, with an overall incidence of adverse events being 22.2% for Xofluza and 20.5% for placebo. No serious adverse events were reported for Xofluza. 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 #11718).[1]

"As the influenza virus can rapidly infect those around us, limiting the spread of infection within households potentially avoids a significant impact on the wider community – a critical step in the global fight against flu," said Sandra Horning, M.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are encouraged by the BLOCKSTONE study, the first to show that Xofluza is an effective preventive treatment following exposure to flu and we look forward to sharing these data with health authorities."

The BLOCKSTONE study also demonstrated that even when fewer criteria for flu were applied (proportion of participants with flu, with fever OR one or more respiratory symptom), there was still a significant 76% reduction in the risk of household members developing flu with Xofluza versus placebo (5.3% vs 22.4% respectively, $p<0.0001$).[1]

Xofluza is the first and only one-dose oral medicine approved to treat flu in otherwise-healthy patients, and the first new flu medicine with a novel proposed mechanism of action approved by the FDA in nearly 20 years. Robust clinical evidence has demonstrated the benefit of Xofluza in several populations (otherwise-healthy, high-risk, children) and treatment settings (symptomatic flu, post-exposure prophylaxis).[1-4]

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About BLOCKSTONE[1]
BLOCKSTONE is a phase III, randomised, post-exposure prophylaxis study that evaluated a single dose of Xofluza compared with placebo as a preventive treatment for household members (adults and children) who are 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 a single dose of Xofluza (dose according to body weight) or placebo as a preventive measure against developing influenza. The primary endpoint of the study was to evaluate the proportion of participants who tested positive for the influenza virus and had fever, and one or more respiratory symptoms between day one and ten. Secondary endpoints were clinical efficacy, pharmacokinetics and, safety and tolerability.

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.[5,6] 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.[5]

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).[7-9]

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. Globally, seasonal epidemics result in 3 to 5 million cases of severe disease, millions of hospitalisations and up to 650,000 deaths every year.[10-14] Central to the threat of flu is the ability of the virus to spread quickly and efficiently from person to person. Limiting the spread of infection is critical in the fight against flu.[15]

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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