Media Release

Phase III CAPSTONE-2 study showed that baloxavir marboxil reduced symptoms in people at high risk of complications from the flu

- **Baloxavir marboxil – an investigational oral, single-dose antiviral – is the first flu medicine with a novel proposed mechanism of action in nearly 20 years and to demonstrate significant efficacy in high-risk patients**
- **Influenza, or "flu," represents a serious threat to public health – globally, annual epidemics result in 3 to 5 million cases of severe disease, millions of hospitalisations and up to 650,000 deaths worldwide** [1], [2], [3], [4], [5]

Basel, 17 July 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the phase III CAPSTONE-2 study assessing the safety and efficacy of baloxavir marboxil in people at high risk of complications from the flu met the study's primary objective, and showed superior efficacy in the primary endpoint of time to improvement of influenza symptoms versus placebo The Centers for Disease Control and Prevention (CDC) defines people at high risk for serious flu complications to include adults 65 years of age or older, or those who have conditions such as asthma, chronic lung disease, diabetes, or heart disease – for these people, flu can lead to hospitalisation or even death.[6] Baloxavir marboxil also demonstrated superior efficacy compared to placebo and oseltamivir for important secondary endpoints, including reducing the time that the virus continued to be 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. Full results from the CAPSTONE-2 study will be presented at upcoming medical meetings. Baloxavir marboxil was discovered and developed by Shionogi & Co., Ltd., and is sold in Japan under the trade name Xofluza®.

"Baloxavir marboxil is the first antiviral to show a clinically meaningful benefit in people who are most susceptible to complications from the flu, including older people and those living with certain medical conditions," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "We plan to submit the results of this second positive phase III study for baloxavir marboxil to healthcare authorities, and look forward to discussing next steps since there are no current antiviral medicines approved to specifically treat this high-risk population."

Baloxavir marboxil has already demonstrated a clinically significant benefit over placebo in otherwise healthy people in the phase III CAPSTONE-1 study. The U.S. Food and Drug Administration (FDA) recently accepted a New Drug Application (NDA) and granted Priority Review to baloxavir marboxil as a single-dose, oral treatment for acute, uncomplicated influenza in people 12 years and older based on the CAPSTONE-1 study and the phase II study, and is expected to make a decision on approval by 24 December 2018. If approved, baloxavir marboxil would be the first single-dose oral antiviral, and the first medicine with a novel proposed mechanism of action to treat the flu in nearly 20 years.

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About CAPSTONE-2
CAPSTONE-2 is a phase III, multicentre, randomised, double-blind study that evaluated a single dose of baloxavir marboxil compared with placebo and oseltamivir in people 12 years or older who are at a high risk of complications from the flu. The Centers for Disease Control and Prevention (CDC) defines people at high risk for serious flu complications to include adults 65 years of age or older, or those who have conditions such as asthma, chronic lung disease, diabetes, or heart disease.[6] The study was conducted globally by Shionogi & Co., Ltd.

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 objective of the study evaluated the efficacy of a single dose of baloxavir marboxil compared with placebo by measuring the time to improvement of influenza symptoms. Important secondary endpoints were time to resolution of fever, time to cessation of viral shedding and the proportion of participants positive for influenza virus titre, or virus levels in the body, by time point, and incidences of influenza-related complications.

About baloxavir marboxil
Baloxavir marboxil is a first-in-class, single-dose investigational oral medicine with a novel proposed mechanism of action designed to target the influenza ("flu") A and B viruses, including oseltamivir-resistant strains and avian strains (e.g. H7N9, H5N1). [7], [8], [9] Unlike other currently available antiviral treatments, baloxavir marboxil is the first in a new class of antivirals designed to inhibit the cap-dependent endonuclease protein within the flu virus, which is essential for viral replication. [10], [11]

Baloxavir marboxil will also be studied in a phase III development programme including paediatric and severely ill hospitalised patients with influenza.

Baloxavir marboxil was discovered by Shionogi & Co., Ltd. and is being developed globally by the Roche Group (which includes Genentech in the U.S.) and Shionogi & Co., Ltd. Under the terms of this agreement, Roche holds worldwide rights to baloxavir marboxil excluding Japan and Taiwan, which will be retained exclusively by Shionogi & Co., Ltd. Baloxavir marboxil was approved in February 2018 by the Japanese Ministry of Health, Labour and Welfare for the treatment of influenza types A and B in adult and paediatric patients, and is being commercialised in Japan and marketed under the brand name Xofluza®.

About Roche in influenza
Influenza, or flu, is one of the most common, yet serious, infectious diseases. Globally, annual epidemics result in 3 to 5 million cases of severe disease, millions of hospitalisations and up to 650,000 deaths worldwide. [1], [2], [3], [4], [5] For patients at a higher risk of flu complications, like pneumonia and bronchitis, the flu can lead to hospitalisation or death, or can make long-term health problems worse. [6] 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 the flu, there is a need for new medical options for prophylaxis and treatment.

Current treatments – including vaccines and antiviral medicines – have limitations as flu viruses are constantly changing and new antiviral medicines are necessary. Roche is committed to addressing the unmet need in this area through its agreement with Shionogi & Co., Ltd. to develop and commercialise baloxavir marboxil.

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. 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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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