

Roche announces FDA approval of Xofluza (baloxavir marboxil) for people at high risk of developing influenza-related complications

- **Single-dose Xofluza is the first and only antiviral medicine indicated specifically for patients at high risk of developing serious complications from influenza (flu)**
- **The Centers for Disease Control and Prevention (CDC) defines people at high risk of serious flu complications as those who have conditions such as asthma, chronic lung disease, diabetes, heart disease or morbid obesity, or adults 65 years of age or older^[1]**

Basel, 18 October 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved a supplemental New Drug Application (sNDA) for Xofluza™ (baloxavir marboxil) for the treatment of acute, uncomplicated influenza, or flu, in people 12 years of age and older who have been symptomatic for no more than 48 hours and who are at high risk of developing flu-related complications. Xofluza is a first-in-class, one-dose oral medicine with a novel proposed mechanism of action that inhibits polymerase acidic endonuclease, an enzyme essential for viral replication.^[2,3]

“With flu season rapidly approaching, we can now offer Xofluza as the first and only FDA-approved treatment option indicated specifically for those at high risk of flu complications,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “People with chronic conditions such as asthma, heart disease and diabetes are at higher risk of developing serious complications from flu, so it is critical that these patients speak with their healthcare providers about possible treatment at the first signs and symptoms of the disease.”

Flu has the potential to cause a variety of complications, ranging from sinus or ear infections to more serious complications such as pneumonia.^[4] This expanded indication for Xofluza was approved based on results from the phase III CAPSTONE-2 study of a single dose of 40mg or 80mg of Xofluza compared to oseltamivir (75mg twice daily for five days), or placebo in people 12 years of age or older who met CDC criteria for being at high risk of complications from flu.^[1,5] Xofluza significantly reduced the time to improvement of flu symptoms compared to placebo, including in people infected with the flu type B virus. Adverse events reported in at least 1% of adult and adolescent subjects treated with Xofluza included diarrhoea (3%), bronchitis (3%), nausea (2%), sinusitis (2%) and headache (1%).^[5]

Xofluza is currently approved in several countries for the treatment of influenza types A and B. In October 2018, Xofluza was first approved by the FDA for the treatment of acute, uncomplicated flu in otherwise healthy people 12 years of age and older who have been symptomatic for no more than 48 hours, representing the first new antiviral to treat influenza in the United States in 20 years.^[3]

About CAPSTONE-2^[5]

CAPSTONE-2 is a phase III, multicentre, randomised, double-blind study that evaluated a single dose of Xofluza compared with placebo and oseltamivir in people 12 years of age or older who are at a high risk of complications from flu. The Centers for Disease Control and Prevention (CDC) defines people at high risk of serious flu complications as those who have conditions such as asthma, chronic lung disease, diabetes, heart disease or morbid obesity, or adults 65 years of age or older.^[1] The study was conducted globally by Shionogi & Co., Ltd.

Participants enrolled in the study were randomly assigned to receive a single dose of 40mg or 80mg of Xofluza, placebo or 75mg of oseltamivir twice a day for five days. The primary objective of the study was to evaluate the efficacy of a single dose of Xofluza compared with placebo by measuring the time to improvement of influenza symptoms. Key findings from the study, which were first presented in October 2018 at IDWeek, found that:

- Xofluza significantly reduced the time to improvement of influenza symptoms versus placebo in people at high risk of complications from influenza (median time 73 hours versus 102 hours; $p < 0.001$).
- Similar efficacy results were seen between Xofluza and oseltamivir in relation to duration of symptoms (median time 73 hours versus 81 hours).
- In subjects infected with type B virus, the median time to improvement of influenza symptoms was shorter in the Xofluza group compared to the placebo group (75 hours versus 101 hours respectively).
- Adverse events reported in at least 1% of adult and adolescent subjects treated with Xofluza included diarrhoea (3%), bronchitis (3%), nausea (2%), sinusitis (2%) and headache (1%). Xofluza was well-tolerated and no new safety signals were identified.

About XofluzaTM (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.^[6,7] 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.^[2,3]

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).^[2,5,8,9] Xofluza is being further studied in a phase III development programme, including children under the age of one (NCT03653364), and 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).^[10-12]

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, or flu, is one of the most common, yet serious, infectious diseases, representing a significant threat to public health.^[13] Globally, seasonal epidemics result in 3 to 5 million cases of severe disease, millions of hospitalisations and up to 650,000 deaths every year.^[14-16] 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.^[17,18] 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 eleventh consecutive year, Roche has been recognised as one of the most sustainable companies 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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