

## **CHMP recommends EU approval of Roche's Xofluza® (baloxavir marboxil) for the treatment of influenza**

- **One-dose, oral Xofluza has been recommended for approval for the treatment of uncomplicated influenza in patients aged 12 years and above**
- **Xofluza has also been recommended for approval as a preventive treatment (post-exposure prophylaxis) of influenza in individuals aged 12 years and above**
- **If approved, Xofluza would be the first innovation in mode of action for an influenza antiviral approved by the European Commission in almost 20 years**

Basel, 13 November 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of Xofluza® (baloxavir marboxil) for the treatment of uncomplicated influenza in patients aged 12 years and above. In addition, Xofluza has been recommended for approval as a preventive treatment (post-exposure prophylaxis) of influenza in individuals aged 12 years and above. The CHMP recommendation is based on the results of the phase III CAPSTONE-1, CAPSTONE-2 and BLOCKSTONE studies.<sup>1,2,3</sup> A final decision regarding the approval is expected from the European Commission in the near future.

“Today's CHMP recommendation brings patients with influenza one step closer to potentially benefiting from Xofluza's oral one-dose regimen, setting adults and adolescents on the path to feeling better sooner compared to placebo,” said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. “We believe that access to effective antivirals for influenza, and particularly their use in the prophylactic setting, could help reduce the strain of the COVID-19 pandemic on healthcare systems in Europe.”

Influenza is one of the most common, yet serious, infectious diseases, representing a significant threat to public health. Globally, seasonal epidemics result in three to five million cases of severe disease, millions of hospitalisations and up to 650,000 deaths every year.<sup>4,5,6</sup> The WHO estimates that up to 72,000 people in the European region die prematurely due to causes associated with influenza each year.<sup>7</sup> Antivirals, like Xofluza, are designed to target and treat the influenza virus.<sup>8,9,10</sup>

### **About CAPSTONE-1<sup>1</sup>**

CAPSTONE-1 was a phase III multicentre, randomised, double-blind, placebo-controlled study that evaluated the efficacy and safety of Xofluza® (baloxavir marboxil) in 1,436 individuals aged 12 and above in the US and Japan. The primary endpoint of the study was time to alleviation of symptoms. The study found the following results:

- Xofluza met its primary endpoint compared to placebo:
  - Significantly reduced the duration of influenza symptoms by more than one day (median time 53.7 hours versus 80.2 hours;  $p < 0.001$ ).

- Similar efficacy results were seen between Xofluza and oseltamivir in relation to time to alleviation of symptoms (median time 53.5 hours versus 53.8 hours).

The most common adverse events reported were diarrhoea (3.0%), bronchitis (2.6%), nausea (1.3%) and sinusitis (1.1%), and all of these adverse events occurred at a lower frequency than placebo. The study was conducted in the US and Japan by Shionogi & Co., Ltd.

### **About CAPSTONE-2<sup>2</sup>**

CAPSTONE-2 was a phase III, multicentre, randomised, double-blind study that evaluated the efficacy and safety of one-dose of Xofluza® (baloxavir marboxil) compared with placebo and oseltamivir in individuals aged 12 years and above who were at high-risk of complications from influenza. The Centers for Disease Control and Prevention (CDC) defines people at high-risk for serious influenza complications to include adults 65 years of age or older, or those who have conditions such as asthma, chronic lung disease, morbid obesity, or heart disease. The study was conducted globally by Shionogi & Co., Ltd.

A total of 2,184 participants enrolled in the study and were randomly assigned to receive one, oral dose of 40mg or 80mg of Xofluza (according to body weight), placebo or 75mg of oseltamivir twice daily for five days. The predominant influenza virus in this study were the A/H3 subtype (46.9 to 48.8%) and influenza B subtype (38.3 to 43.5%). The most common risk factors were asthma or chronic lung disease (39.2%), age ≥65 years (27.4%), endocrine disorders (32.8%), metabolic disorders (13.5%), heart disease (12.7%), and morbid obesity (10.6%).

The primary objective of the study evaluated the efficacy of one-dose of Xofluza compared with placebo by measuring the time to improvement of influenza symptoms. CAPSTONE-2 was the first prospective, controlled phase III clinical trial to demonstrate a significant and clinically meaningful benefit from an antiviral medicine in people at high-risk of serious influenza complications (median time to improvement in symptoms 73.2 hours for Xofluza, 102.3 hours for placebo,  $p < 0.0001$ ).

### **About BLOCKSTONE<sup>3</sup>**

BLOCKSTONE was a phase III, double-blind, multicentre, randomised, placebo-controlled, post-exposure prophylaxis study that evaluated one-dose of 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'). The study was conducted by Shionogi & Co., Ltd. in Japan during the 2018-2019 influenza season.

Those diagnosed with influenza were required to have onset of symptoms for less than 48 hours and participants were required to have lived with those diagnosed for more than 48 hours. The participants were randomised to receive one-dose of Xofluza (dose according to body weight) or placebo as a preventive measure against developing influenza.

Xofluza showed a statistically significant prophylactic effect on influenza after one oral dose in people exposed to an infected household contact. The proportion of household members aged 12 years and above who developed influenza was 1.3% in participants treated with Xofluza and 13.2% in the placebo-treated group. Xofluza was well tolerated in this study and no new safety signals were identified.

### **About Xofluza® (baloxavir marboxil)**

Xofluza is a first-in-class, one-dose oral medicine with an innovative 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.<sup>11,12,13</sup> Xofluza is the first in a class of antivirals designed to inhibit the cap-dependent endonuclease protein, which is essential for viral replication.<sup>1,14</sup>

Xofluza is available in the US and in several other countries for the treatment of influenza types A and B. In the US, Xofluza is approved for the treatment of acute, uncomplicated influenza in patients aged 12 years and above who are otherwise-healthy or at high-risk of developing serious complications from influenza, and who have been symptomatic for no more than 48 hours. Xofluza was the first new antiviral to be approved by the FDA in 20 years.

Robust clinical evidence has demonstrated the benefit of Xofluza in several populations (otherwise-healthy, high-risk and post-exposure prophylaxis in individuals aged 12 years and above). Xofluza is being further studied in a phase III development programme, including children under the age of one (NCT03653364) as well as to assess the potential to reduce transmission of influenza from an infected person to healthy people (NCT03969212).<sup>1,2,3,15</sup>

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 one of the most common, yet serious, infectious diseases, representing a significant threat to public health. Globally, seasonal epidemics result in three to five million cases of severe disease, millions of hospitalisations and up to 650,000 deaths every year.<sup>4,5,6</sup> 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.

## 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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](http://www.roche.com).

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