Media Release

New England Journal of Medicine publishes phase III data showing single-dose Xofluza significantly reduces influenza virus transmission

- **Detailed results from the CENTERSTONE trial show treatment with Xofluza reduced the odds of transmission, or spread of the influenza virus, from an infected person to household members by 32%[1]**
- **CENTERSTONE is the first global phase III trial that demonstrates the benefit of an antiviral in reducing the spread of a respiratory virus[1]**
- **Reducing the spread of infection within households could help limit transmission within institutions and communities, potentially easing the burden of both seasonal and pandemic influenza on healthcare systems[2,3]**

Basel, 25 April 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the *New England Journal of Medicine* (NEJM) has published a detailed analysis of the phase III CENTERSTONE trial of Xofluza® (baloxavir marboxil).[1] The trial met its primary endpoint, showing a single, oral dose of Xofluza taken by people infected with influenza reduced the odds of untreated household members contracting the virus by 32%.[1] For the key secondary endpoint of influenza virus transmission resulting in symptoms, Xofluza showed a clinically meaningful reduction although statistical significance was not reached. Xofluza was well tolerated, with no new safety signals identified.[1]

“This trial is the first to demonstrate an antiviral effect that reduces transmission of influenza viruses within a household. This result may potentially have broad-reaching implications for public health,” said Levi Garraway, MD, PhD, Roche’s Chief Medical Officer and Head of Global Product Development. “This publication reminds us of the ongoing societal need for solutions that can help ease the burden of influenza on society.”

Results from the CENTERSTONE trial have been submitted to health authorities, including the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

Influenza poses a significant health and economic burden, particularly for those at high risk of influenza-related complications.[2,3] Every year, seasonal influenza infects an estimated one billion people worldwide and causes millions of hospitalisations, with up to 650,000 deaths globally.[2,3] Approximately one-third of all influenza virus transmission occurs within households.[4] As many as 75% of working adults experience approximately two days of absenteeism due to influenza, whether they or someone within their household is sick, with most reporting that they go to work despite exhibiting symptoms.[5] In the event of a pandemic, influenza would likely have a significant impact on the overall functioning of healthcare systems.[6,7] With the co-circulation and burden of multiple respiratory viruses (including

COVID-19) infecting individuals within and outside of the winter season, it is more important than ever to have effective options to treat and prevent the spread of influenza.[6,7]

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About CENTERSTONE[8]

The CENTERSTONE trial [NCT03969212] was a global phase III trial investigating the efficacy of single-dose Xofluza, taken within 48 hours of symptom onset, to reduce the onward transmission of influenza within households. The trial was conducted in 272 sites across the globe, with over 4,000 participants, and involved otherwise healthy patients from five to 64 years who had been diagnosed with influenza via a polymerase chain reaction (PCR) or rapid influenza diagnostic test, known as index patients (IPs), and those within their household (known as household contacts, HHCs). The design of this randomised, placebo-controlled trial was developed with input from the US FDA and leading experts in influenza.

The primary endpoint was the proportion of HHCs who tested positive for influenza within five days after the IP had been treated with either Xofluza or placebo (1:1 randomisation within 48 hours of symptoms onset). There was a 32% reduction in the odds of transmission (adjusted odds ratio [aOR] = 0.68 [95.38% CI: 0.50–0.93]; adjusted incidence of transmission:13.4% with placebo vs 9.5% with baloxavir; p=0.013) with Xofluza versus placebo.[1]

For the key secondary endpoint of symptomatic transmission of influenza virus by day five, Xofluza showed a clinically meaningful reduction, although statistical significance was not reached. There was a 25% reduction in the odds of transmission resulting in symptoms (aOR = 0.75 [95.38% CI: 0.50–1.12]; p=0.155). Numerical reductions were observed for additional endpoints, including transmission at the household level and transmission up to day nine.[1]

About Xofluza® (baloxavir marboxil)

Xofluza is a first-in-class, single-dose oral medicine with an innovative mechanism of action designed to block viral replication by inhibiting the cap-dependent endonuclease protein, reducing the duration of infectiousness and disease. Xofluza has demonstrated effectiveness against a wide range of influenza viruses, including in vitro and in vivo activity against oseltamivir-resistant strains and avian strains (H7N9, H5N1) in non-clinical studies. [9,10,11]

Xofluza is approved in more than 75 countries for the treatment of uncomplicated influenza types A and B.[12] In several countries, Xofluza is approved for the treatment of influenza in otherwise healthy patients and as a preventative treatment (post-exposure prophylaxis). Xofluza represents the first innovation in mechanism of action for an influenza antiviral approved in almost 20 years for treatment in children, adolescents, and adults.[14]

Robust clinical evidence has demonstrated the clinical benefit of single-dose Xofluza in the treatment of influenza in several populations (otherwise healthy and high-risk individuals and, children) and as post-exposure prophylaxis in the EU for children aged one and older, and in the US and China aged five and older.[11, 13, 15,16,17] Xofluza was also studied in a phase III trial in children under the age of one year (NCT03653364).[18]

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). 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 a serious infectious disease and represents a significant burden to public health through annual epidemics and periodic pandemics.[2,3] Seasonal epidemics result in an estimated one billion cases, millions of hospitalisations, and up to 650,000 deaths globally every year.[2,3]

Roche has a long history of developing transformative medicines and diagnostics that contribute to public health. Roche's Tamiflu® (oseltamivir) has significantly improved the treatment of seasonal influenza and pandemic management. The Roche Diagnostics portfolio includes a range of tests and solutions that help differentiate influenza from other respiratory viruses, including the cobas® Respiratory flex test, the cobas liat system, and the recently acquired LumiraDx point of care platform.

Roche is committed to addressing the unmet need in influenza through its agreement with Shionogi & Co., Ltd. to develop and commercialise Xofluza® (baloxavir marboxil).

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

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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