Media & Investor Release

Positive phase III results show Xofluza significantly reduces the transmission of influenza viruses

- **Data from the CENTERSTONE study shows single-dose Xofluza reduces transmission of influenza from an infected person to household members**
- **This is the first time that any antiviral used in the treatment of a respiratory viral illness has demonstrated a transmission reduction benefit in a global phase III study**
- **Reducing the spread of infection in the household could help limit transmission within communities and societies, easing the burden of both seasonal and pandemic influenza on healthcare systems**

Basel, 19 September - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive topline results of the phase III CENTERSTONE study of Xofluza® (baloxavir marboxil), an antiviral, showing a reduction in the transmission of influenza viruses. The study met its primary endpoint, demonstrating that a single, oral dose of Xofluza taken by people infected with influenza significantly reduced the likelihood of others in their household contracting the virus. Xofluza was well tolerated with no new safety signals identified.

CENTERSTONE is the first global phase III study to show a transmission reduction benefit with an antiviral used in the treatment of a respiratory viral illness. This new data may add to the benefits of Xofluza, which is currently approved for treating symptoms and preventing infection following virus exposure.[1] The topline results will be presented at the 2024 OPTIONS XII for the Control of Influenza congress (29 September - 2 October, Brisbane, Australia).

“Building on Xofluza’s established efficacy in treating and preventing influenza after exposure, this new evidence of transmission reduction represents an important advance that could help improve health outcomes at an individual and community level,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “We look forward to discussing these data with regulatory authorities and public health organisations for influenza pandemic preparedness to bring these benefits to patients.”

Influenza is one of the most common yet serious infectious diseases, representing a significant burden to public health. Every year, seasonal influenza infects an estimated one billion people and causes millions of hospitalisations and up to 650,000 deaths globally.[2,3] 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 that influenza is not underestimated.[4] For the effective control of both seasonal and pandemic influenza, early diagnosis and treatment is critical.[5]

F. Hoffmann-La Roche Ltd
4070 Basel
Switzerland
Group Communications
Roche Group Media Relations
Phone +41 61 688 88 88
www.roche.com

The CENTERSTONE study has been partially supported with federal funds from the US Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under Other Transaction Agreement number: HHSO100201800036C.

About CENTERSTONE[6]

The CENTERSTONE study [NCT03969212] was a global phase III trial investigating the efficacy of single-dose Xofluza, taken within 48 hours of symptoms onset, to reduce the onward transmission of influenza within households. The study ran across 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 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. The secondary endpoint looked at the proportion of HHCs who tested positive for influenza by day five and developed influenza symptoms. The design of this randomised, placebo-controlled trial was developed with inputs from the US FDA and leading experts in influenza.

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, potentially reducing the duration of infectiousness and disease. Xofluza's mechanism of action 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.[7,8,9]

Xofluza is approved in more than 80 countries for the treatment of uncomplicated influenza types A and B.[10] In Europe, Xofluza is approved for the treatment of influenza in otherwise healthy patients and as a preventative treatment (post-exposure prophylaxis).[1] 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.[11]

Robust clinical evidence has demonstrated the benefit of Xofluza in several populations (otherwise healthy, children and post-exposure prophylaxis in individuals aged one year and above).[9,12,13,14] Xofluza was also studied in a phase III development programme in children under the age of one (NCT03653364).[15]

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 a serious infectious disease and represents a significant burden to public health. 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 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 in the treatment of both seasonal influenza and pandemic management, and we are proud to have brought this innovative medicine to patients. Roche is committed to addressing the unmet need in this area 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.

References

[1] European Medicines Agency. Summary of product characteristics, Xofluza. 2021. [Internet; cited September 2024]. Available from:https://www.ema.europa.eu/en/medicines/human/EPAR/xofluza#product-info

[2] World Health Organization (WHO). 2023. Influenza (Seasonal). [Internet; cited September 2024]. Available from: https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal).

[3] Paget J, et al. Global and national influenza-associated hospitalisation rates: Estimates for 40 countries and administrative regions. *Journal of Global Health.* 2023;13:04003. Published 2023 Jan 27. doi:10.7189/jogh.13.04003

[4] WHO. Joint Statement - influenza season epidemic kicks off early in Europe as concerns over RSV rise and COVID-19 is still a threat. [Internet; cited September 2024]. Available from: https://www.who.int/europe/news/item/01-12-2022-joint-statement---influenza-season-epidemic-kicks-off-early-in-europe-as-concerns-over-rsv-rise-and-covid-19-is-still-a-threat.

[5] Jones W, et al. Influenza Management During the COVID-19 Pandemic: A Review of Recent Innovations in Antiviral Therapy and Relevance to Primary Care Practice. *Mayo Clinic Proceedings: Innovations, Quality & Outcomes*. 2021;5(6):974-991.

[6] Clinical Trials.gov. Study to assess the efficacy of baloxavir marboxil versus placebo to reduce onward transmission of Influenza A or B in households [Internet; cited September 2024]. Available from: https://www.clinicaltrials.gov/study/NCT03969212.

[7] Hayden F, et al. Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents. *New England Journal of Medicine* 2018;379:913–923.

[8] Noshi T, et al. In vitro characterization of baloxavir acid, a first-in-class cap-dependent endonuclease inhibitor of the influenza virus polymerase PA subunit. *Antiviral Research.* 2018;160:109-117.

[9] Taniguchi K, et al. Inhibition of avian-origin influenza A(H7N9) virus by the novel cap-dependent endonuclease inhibitor baloxavir marboxil. *Scientific Reports.* 2019;9:3466**.**

[10] Roche data on file.

[11] Roche.com. Roche's Xofluza approved by the European Commission for the treatment of influenza, the first new influenza antiviral for patients in almost 20 years. [Internet; cited September 2024]. Available from: https://www.roche.com/media/releases/med-cor-2021-01-11.

[12] Baker J, et al. Baloxavir marboxil single-dose treatment in influenza-infected children: A randomized, double-blind, active controlled phase 3 safety and efficacy trial (miniSTONE-2). *The Pediatric Infectious Disease Journal*. 2020;39(8):700-705.

[13] Ikematsu H, et al. Baloxavir marboxil for Prophylaxis against Influenza in Household Contacts. *New England Journal of Medicine.* 2020;383:309-320.

[14] Ison,M et al. Early treatment with baloxavir marboxil in high-risk adolescent and adult outpatients with uncomplicated influenza (CAPSTONE-2): a randomised, placebo-controlled, phase 3 trial. *Lancet Infect Dis* 2020;20(10):1204–14.

[15] Clinicaltrials.gov. Study to assess the safety, pharmacokinetics, and efficacy of baloxavir marboxil in healthy pediatric participants from birth to < 1 year with influenza-like symptoms. [Internet; cited September 2024]. Available from: https://clinicaltrials.gov/ct2/show/NCT03653364.

Roche Global Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

Hans Trees, PhD
Phone: +41 79 407 72 58

Sileia Urech
Phone: +41 79 935 81 48

Nathalie Altermatt
Phone: +41 79 771 05 25

Lorena Corfas
Phone: +34 620 29 25 51

Simon Goldsborough
Phone: +44 797 32 72 915

Karsten Kleine
Phone: +41 79 461 86 83

Nina Mählitz
Phone: +41 79 327 54 74

Kirti Pandey
Phone: +49 172 6367262

Yvette Petillon
Phone: +41 79 961 92 50

Dr. Rebekka Schnell
Phone: +41 79 205 27 03

Roche Investor Relations

Dr. Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com