Roche's faricimab meets primary endpoint and shows strong durability across two global phase III studies for diabetic macular edema, a leading cause of blindness

- **Faricimab given every eight weeks and at personalised dosing intervals of up to 16 weeks demonstrated non-inferior visual acuity gains compared to aflibercept given every eight weeks in both studies**
- **More than half of participants in the faricimab personalised dosing arms had extended time between treatments to 16 weeks at year one – the first time this level of durability has been achieved in a phase III diabetic macular edema study**
- **Faricimab is the first investigational bispecific antibody designed for the eye and targets two distinct pathways – via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) – that drive a number of retinal conditions**
- **Faricimab was generally well-tolerated, with no new safety signals identified**

Basel, 21 December 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive topline results from two identically designed global phase III studies, YOSEMITE and RHINE, evaluating its investigational bispecific antibody, faricimab, in people living with diabetic macular edema (DME). Both studies met their primary endpoint and showed that faricimab given every eight weeks and at personalised dosing intervals of up to 16 weeks demonstrated non-inferior visual acuity gains compared to aflibercept given every eight weeks. Faricimab was generally well-tolerated, with no new safety signals identified. The studies each have three treatment arms, with participants randomised to receive either faricimab or aflibercept at fixed eight-week intervals, or faricimab at personalised intervals of up to 16 weeks, following a loading phase.

In a secondary endpoint, across both studies, more than half of participants in the faricimab personalised dosing arms achieved an extended time between treatments of 16 weeks at year one. This is the first time any investigational medicine has achieved this level of durability in a phase III study of people with DME.

Worldwide, an estimated 21 million people are living with DME, a leading cause of vision loss among working-age adults.[1] Whilst anti-vascular endothelial growth factor (VEGF) monotherapy injections have significantly reduced vision loss from DME, the treatment burden associated with frequent eye injections and physician visits can lead to under-treatment and, potentially, less than optimal vision outcomes.[2,3] It has been almost a decade since a medicine with a new mechanism of action has been approved to treat DME.[4] Faricimab is the first investigational bispecific antibody designed for the eye.[5] It targets two distinct pathways – via angiopoietin-2 (Ang-2) and VEGF-A – that drive a number of retinal conditions, including DME.[6]

"These positive results show that faricimab has the potential to offer lasting vision improvements for people with diabetic macular edema, while also reducing the treatment burden associated with frequent eye injections," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We look forward to discussions with global regulatory authorities, with the aim of bringing this potential new treatment option to people with this condition as soon as possible."

In addition to the YOSEMITE and RHINE studies, the phase III Rhone-X study is investigating the long-term safety and tolerability of faricimab for the treatment of DME.[7] Faricimab is also being studied in the phase III TENAYA and LUCERNE studies as a potential treatment for neovascular or "wet" age-related macular degeneration (nAMD), an advanced form of AMD, which can cause rapid, severe and irreversible vision loss.[8,9,10,11] Detailed results from the YOSEMITE and RHINE studies will be presented in February at Angiogenesis, Exudation, and Degeneration 2021, a medical symposium presented by Bascom Palmer Eye Institute of the University of Miami Miller School of Medicine, and submitted for approval for the treatment of DME around the world.

About the YOSEMITE and RHINE studies [5,12,13]

YOSEMITE (NCT03622580) and RHINE (NCT03622593) are two identical, randomised, multicentre, double-masked, global phase III studies, evaluating the efficacy and safety of faricimab compared to aflibercept in 1,891 people living with diabetic macular edema (940 in YOSEMITE and 951 in RHINE). The studies each have three treatment arms: faricimab 6.0 mg administered at personalised dosing intervals of up to 16 weeks; faricimab 6.0 mg administered at fixed eight-week intervals; aflibercept 2.0 mg administered at fixed eight-week intervals. In all three arms, sham injections were administered at study visits when treatment injections were not scheduled, to maintain the masking of investigators and participants.

The primary endpoint of the studies is the average change in best-corrected visual acuity (BCVA) score (the best distance vision a person can achieve – including with correction such as glasses – when reading letters on an eye chart) from baseline at one year. Secondary endpoints include: safety; the percentage of participants in the personalised dosing arm receiving treatment every four, eight, 12 and 16 weeks, at week 52; the percentage of participants achieving a two-step or greater improvement from baseline in diabetic retinopathy severity at week 52; the percentage of participants achieving a gain of at least 15 letters in BCVA from baseline over time; the percentage of participants avoiding a loss of at least 15 letters in BCVA from baseline over time; and change in central subfield thickness from baseline over time.

About diabetic macular edema

Affecting around 21 million people globally, diabetic macular edema (DME) is a vision-threatening complication of diabetic retinopathy (DR).[1] DR occurs when damage to blood vessels and the formation of new blood vessels causes blood and/or fluid to leak into the retina – a part of the eye that sends information to the brain, enabling sight.[14] This leads to swelling, as well as blockage of blood supply to some areas of the retina.[15] DME occurs when the damaged blood vessels leak into and cause swelling in the macula – the central area of the retina responsible for the sharp vision needed for reading and driving.[14,16] The number of people with DME is expected to grow as the prevalence of diabetes increases.[17] The condition is associated with blindness when left untreated and decreased quality of life.[14,18] There remains a significant unmet need for more effective, longer-lasting therapies for people with DME.[3]

About faricimab

Faricimab is the first investigational bispecific antibody designed for the eye.[5] It targets two distinct pathways – via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) – that drive a number of retinal conditions.[6] Ang-2 and VEGF-A contribute to vision loss by destabilising blood vessels, causing new leaky blood vessels to form and increasing inflammation.[3] By independently blocking both pathways,

faricimab is designed to stabilise blood vessels, potentially resulting in better vision outcomes, for longer, for people living with retinal conditions.[3]

About Roche in Ophthalmology
Roche is focused on saving people's eyesight from the leading causes of vision loss through pioneering therapies. Through our innovation in the scientific discovery of new potential drug targets, personalised healthcare, molecular engineering, biomarkers and continuous drug delivery, we strive to design the right therapies for the right patients.

We have the broadest retina pipeline in Ophthalmology, covering early and late stage products, which is led by science and informed by insights from people with eye diseases. Our late stage pipeline includes two potential first-of-a-kind treatments, Port Delivery System with ranibizumab (PDS) and faricimab, which are being evaluated in a number of retinal conditions including neovascular age-related macular degeneration, diabetic macular edema and diabetic retinopathy. PDS is a permanent refillable eye implant that continuously delivers a customised formulation of ranibizumab over a period of months, potentially reducing the treatment burden associated with frequent eye injections.[19,20] Faricimab is the first investigational bispecific antibody designed for the eye.[5] It targets two distinct pathways – via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) – that drive a number of retinal conditions, to stabilise blood vessels, potentially resulting in better vision, for longer.[3,6] Our early stage pipeline includes gene therapies and treatments for geographic atrophy and other vision-threatening diseases, including rare and inherited conditions.

Applying our extensive experience, we have already brought breakthrough ophthalmic treatments to people living with vision loss through Lucentis®* (ranibizumab injection), the first treatment approved to improve vision in people with certain retinal conditions.

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 twelfth 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.

*Lucentis® (ranibizumab injection) was developed by Genentech, a member of the Roche Group. Genentech retains commercial rights in the United States and Novartis has exclusive commercial rights for the rest of the world.

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