Media & Investor Release

New phase III data show Roche's Vabysmo rapidly improved vision and reduced retinal fluid in people with retinal vein occlusion (RVO)

- **Vabysmo met its primary endpoint in two clinical trials, BALATON and COMINO, showing non-inferior visual acuity gains compared to aflibercept**
- **More Vabysmo patients showed an absence of blood vessel leakage in the retina compared to aflibercept in a pre-specified exploratory endpoint**
- **If approved, RVO would be the third indication for Vabysmo in addition to neovascular or 'wet' age-related macular degeneration and diabetic macular edema**

Basel, 10 February 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive new data from two global phase III studies, BALATON and COMINO, evaluating Vabysmo® (faricimab) in macular edema due to branch and central retinal vein occlusion (BRVO and CRVO) at 24 weeks.[1,2] The studies showed that treatment with Vabysmo resulted in early and sustained improvement in vision, meeting the primary endpoint of non-inferior visual acuity gains compared to treatment with aflibercept. Vabysmo also showed rapid and robust drying of retinal fluid from baseline, as measured by reduction in central subfield thickness. The safety profile of Vabysmo was consistent with previous trials. Results will be presented virtually on 11 February at Angiogenesis, Exudation and Degeneration 2023, organised by the Bascom Palmer Eye Institute in Florida, United States.[3]

"These encouraging results reinforce the potential of Vabysmo as a new treatment option for people experiencing vision loss associated with retinal vein occlusion," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "As these positive data continue to accrue, we believe Vabysmo may redefine the standard of care for multiple types of retinal conditions that can cause blindness."

Neovascular or 'wet' age-related macular degeneration (nAMD), diabetic macular edema (DME) and RVO together affect around 70 million people worldwide and are among the leading causes of vision loss.[4-8] Data from the BALATON and COMINO studies will be submitted to health authorities around the world, including the United States Food and Drug Administration and European Medicines Agency, for approval for the treatment of macular edema due to RVO. If approved, this would be the third indication for Vabysmo, which is currently approved in more than 50 countries to treat nAMD and DME.[9]

"Retinal vein occlusion can cause fluid to become trapped within and under the retina, leading to rapid and severe vision loss if left untreated," said Ramin Tadayoni, M.D., Ph.D., president-elect of EURETINA, who is presenting the data at Angiogenesis. "These promising

results show that Vabysmo effectively reduces fluid in the retina and improves vision in patients with retinal vein occlusion."

Vabysmo's efficacy and safety in nAMD and DME have been demonstrated by two-year data from four large, global studies involving more than 3,000 participants.[10-13] Vabysmo is the first bispecific antibody approved for the eye with phase III studies supporting treatment intervals of up to four months for people with these conditions.[14] It targets and inhibits two signalling pathways linked to a number of vision-threatening retinal conditions by neutralising angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A).[10,11] Globally, more than 450,000 Vabysmo doses have been distributed for treatment of these conditions to date.[9]

Study results[3]

In the BALATON and COMINO studies, patients were randomised 1:1 to receive six monthly injections of either Vabysmo® (faricimab) (6.0 mg) or aflibercept (2.0 mg) for 20 weeks, with the primary endpoint measured at week 24. Both studies met their primary endpoint, with Vabysmo showing non-inferior visual acuity gains compared to aflibercept. The average vision gains from baseline were comparable between the two treatments in both studies. In BALATON, vision gains were +16.9 eye chart letters in the Vabysmo arm and +17.5 letters in the aflibercept arm at 24 weeks. In COMINO, vision gains were +16.9 letters in the Vabysmo arm and +17.3 letters in the aflibercept arm at 24 weeks. Additionally, the percentage of patients gaining 15 or more letters was comparable across treatment arms in both studies.

Fluid in the retina in the back of the eye, which may result from blood vessel leakage, can cause swelling and blurry vision.[15] A secondary endpoint showed that Vabysmo achieved rapid and robust drying of retinal fluid from baseline, as measured by reduction in central subfield thickness (CST). In both studies, reductions in CST were comparable across treatment arms. In BALATON, CST reductions were -311.4 µm in the Vabysmo arm and -304.4 µm in the aflibercept arm. In COMINO, CST reductions were -461.6 µm in the Vabysmo arm and -448.8 µm in the aflibercept arm. Additionally, both studies showed that more Vabysmo patients had an absence of blood vessel leakage in the retina compared to aflibercept patients as seen in a pre-specified exploratory endpoint. In BALATON, one third of patients (34%) treated with Vabysmo had an absence of leakage compared to one fifth (21%) of aflibercept patients. In COMINO, the rates were 44% for Vabysmo patients versus 30% for aflibercept patients.

In both studies, Vabysmo's safety profile was consistent with previous trials. The most common adverse reaction was conjunctival haemorrhage (3%). Safety results were consistent across study arms.

The studies are ongoing, and data from weeks 24 to 72 will assess the potential of Vabysmo to extend dosing intervals up to every four months.

About the BALATON and COMINO studies[1,2]

BALATON (NCT04740905) and COMINO (NCT04740931) are two randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of Vabysmo® (faricimab) compared to aflibercept. For the first 20 weeks, patients are randomised 1:1 to receive six monthly injections of either Vabysmo (6.0 mg) or aflibercept (2.0 mg). From weeks 24-72, all patients receive Vabysmo (6.0 mg) up to every four months – according to a personalised treatment interval dosing regimen – using a treat-and-extend approach.

The BALATON study is being conducted in 553 people with branch retinal vein occlusion. The COMINO study is being conducted in 729 people with central retinal or hemiretinal vein occlusion.

The primary endpoint of each study is the change in best-corrected visual acuity from baseline at 24 weeks. Secondary endpoints include change in central subfield thickness and drying of retinal fluid from baseline over time up to 24 weeks.

About retinal vein occlusion (RVO)

RVO is the second most common cause of vision loss due to retinal vascular diseases.[4] It affects an estimated 28 million adults globally, mainly those aged 60 or older, and can lead to severe and sudden vision loss.[4,16] RVO typically results in sudden, painless vision loss in the affected eye because the vein blockage restricts normal blood flow in the affected retina, resulting in ischaemia, bleeding, fluid leakage and retinal swelling called macular edema.[16-18] Currently, macular edema due to RVO is typically treated with repeated intravitreal injections of anti-vascular endothelial growth factor therapies.[18] There are two main types of RVO: branch retinal vein occlusion, which affects more than 23 million people globally and occurs when one of the four smaller 'branches' of the main central retinal vein becomes blocked; and central retinal vein occlusion, which is less common, affecting more than four million people worldwide, and occurs when the eye's central retinal vein becomes blocked.[4,18]

About the Vabysmo® (faricimab) clinical development programme

Roche has a robust phase III clinical development programme for Vabysmo. The programme includes AVONELLE-X, an extension study of TENAYA and LUCERNE evaluating the long-term safety and tolerability of Vabysmo in neovascular or 'wet' macular degeneration (nAMD), and Rhone-X, an extension study of YOSEMITE and RHINE evaluating the long-term safety and tolerability of Vabysmo in diabetic macular edema (DME).[19,20] Roche has also initiated several phase IV studies, including the Elevatum study of Vabysmo in underrepresented patient populations with DME, the SALWEEN study of Vabysmo in a subpopulation of nAMD highly prevalent in Asia, as well as the VOYAGER study, a global real-world data collection platform.[21-23] Roche also supports several other independent studies to further understand retinal conditions with a high unmet need.

About Vabysmo® (faricimab)

Vabysmo is the first bispecific antibody approved for the eye.[24,25] It targets and inhibits two signalling pathways linked to a number of vision-threatening retinal conditions by neutralising angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A). Ang-2 and VEGF-A contribute to vision loss by destabilising blood vessels, causing new leaky blood vessels to form and increasing inflammation.[10,11] By blocking pathways involving Ang-2 and VEGF-A, Vabysmo is designed to stabilise blood vessels.[10,11] Vabysmo is approved in more than 50 countries around the world, including the United States, Japan, the United Kingdom and the European Union for people living with neovascular or 'wet' age-related macular degeneration and diabetic macular edema. Review by other regulatory authorities is ongoing.[9,14,24-26]

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, which is led by science and informed by insights from people with eye diseases. Our 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. Susvimo™ (previously called Port Delivery System with ranibizumab) 100 mg/mL for intravitreal use via ocular implant is the first United States Food and Drug Administration-approved refillable eye implant for neovascular or 'wet' age-related macular degeneration that continuously delivers a customised formulation of ranibizumab over a period of months.[27] Vabysmo® (faricimab) is the first bispecific antibody approved for the eye, which targets and inhibits two signalling pathways linked to a number of vision-threatening retinal conditions by neutralising angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A).[10,11,24,25] Lucentis® (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions.[28]

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.

In recognising our endeavor to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

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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