Media & Investor Release

European Commission approves Roche's Vabysmo, the first bispecific antibody for the eye, for two leading causes of vision loss

- **Phase III data that showed people with nAMD and DME treated with Vabysmo up to every four months achieved similar outcomes compared to receiving treatment every two months with aflibercept**
- **In addition, patients treated with Vabysmo received up to 33% fewer median number of injections compared to aflibercept**
- **Reducing the number of eye injections over time could offer a less burdensome treatment schedule for individuals, their caregivers and healthcare systems**
- **Vabysmo simultaneously targets and inhibits two disease pathways involving Ang-2 and VEGF-A linked to a number of vision-threatening retinal conditions**

Basel, 19 September 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission (EC) approved Vabysmo® (faricimab) for the treatment of neovascular or 'wet' age-related macular degeneration (nAMD) and visual impairment due to diabetic macular edema (DME). These retinal conditions are two of the leading causes of vision loss worldwide, affecting more than 40 million people [1,2,3,4]

"Many people with nAMD and DME struggle to keep up with the monthly eye injections and physician visits, often associated with current standards of care, and unfortunately their vision may suffer as a result of undertreatment," said Prof Ramin Tadayoni, head of the ophthalmology department, Lariboisière, Saint-Louis and Rothschild Hospitals, Paris, France, and European Society of Retina Specialists (EURETINA) president elect. "For people in Europe living with these conditions, today's approval offers the first new mechanism of action in over a decade; one which could improve and protect their vision with fewer injections over time."

Vabysmo is the only injectable eye medicine approved in Europe with phase III studies supporting treatment at intervals of up to four months for people living with nAMD and DME.[5,6,7] With the potential to require fewer eye injections over time, while also improving and maintaining vision and anatomy, Vabysmo could offer a less burdensome treatment schedule for individuals, their caregivers and healthcare systems [6,7,8,9]

"The approval of Vabysmo in Europe is the result of years of pioneering research from Roche ophthalmologists and scientists, who are deeply committed to improving outcomes for people with retinal conditions," said Levi Garraway, M.D., PhD., Roche's Chief Medical Officer and Head of Global Product Development. "We are delighted to offer people in Europe this first-of-its-kind treatment option and are working to bring Vabysmo to people with nAMD and DME as soon as possible."

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Today's approval is based on results across four phase III studies in two indications, involving 3,220 patients: TENAYA and LUCERNE in nAMD at year one, and YOSEMITE and RHINE in DME up to two years. The studies showed that people treated with Vabysmo, given at intervals of up to four months, achieved similar vision gains and anatomical improvements compared to aflibercept given every two months.[6,7,8] The totality of data across all four studies at two years showed that more than 60% of people treated with Vabysmo were able to extend treatment to every four months, while improving and maintaining vision. Additionally, up to two years, people with nAMD and DME treated with Vabysmo received 33% (10 vs. 15) and 21% (11 vs. 14) fewer median number of injections compared to aflibercept, respectively.[6,9]

Vabysmo, a bispecific antibody, is uniquely engineered to target and inhibit two disease pathways, linked to a number of vision-threatening retinal conditions, by neutralising angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A), to restore vascular stability. By independently blocking both pathways involving Ang-2 and VEGF-A, Vabysmo is designed to stabilise blood vessels and thereby reduce inflammation, leakage and abnormal vessel growth (neovascularisation) more than inhibition of VEGF-A alone.[7] This sustained blood vessel stabilisation may improve disease control, vision and anatomical outcomes for longer.[7,8]

Vabysmo is now approved in the European Union and nine other countries around the world, including the US, Japan, and the UK, for people living with nAMD and DME, and submissions to other regulatory authorities are ongoing.[5,10,11,12] Globally, more than 100,000 Vabysmo doses have been distributed for treatment of these conditions to date.[13] Roche also continues to explore areas where Vabysmo has the potential to deliver additional benefits to patients, including retinal vein occlusion.

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' age-related 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).[14,15] Additionally, the BALATON and COMINO trials are underway, evaluating the efficacy and safety of Vabysmo in people with macular edema following retinal vein occlusion.[16,17] Roche has also initiated the phase IV ELEVATUM study of Vabysmo in underrepresented patient populations with DME.[18]

About the TENAYA and LUCERNE studies[7,9]

TENAYA (NCT03823287) and LUCERNE (NCT03823300) were two identical, randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of Vabysmo® (faricimab) compared to aflibercept in 1,329 people living with neovascular or 'wet' age-related macular degeneration (671 in TENAYA and 658 in LUCERNE).

Both studies met their primary endpoint, with Vabysmo given at intervals of up to every four months consistently shown to offer visual acuity gains and anatomical improvements that were non-inferior to aflibercept given every two months. A secondary endpoint in both studies measured the proportion of people in the Vabysmo arm that were treated on dosing schedules of every three or four months during the first year. Importantly, 46% (n=144/315) of those receiving Vabysmo in TENAYA and 45% (n=142/316) in LUCERNE were able to be treated every four months in the first year, and an additional 34% (n=107/315) and 33% (n=104/316), respectively, were able to be treated every three months. Combined, nearly 80% of people receiving Vabysmo were able to go three months or longer between treatments during the first year.

At two years, vision improvements were comparable across both treatment arms. In TENAYA, the average vision gains from baseline at two years were +3.7 eye chart letters in the Vabysmo arm and +3.3 letters in the aflibercept arm. In LUCERNE, the average vision gains from baseline at two years were +5.0 letters in the Vabysmo arm and +5.2 letters in the aflibercept arm. Furthermore, 59% (n=160/271) of Vabysmo patients in TENAYA and 67% (n=192/287) in LUCERNE achieved four-month dosing at two years. This is an increase over one-year results, which showed 46% (n=144/315) of Vabysmo patients in TENAYA and 45% (n=142/316) in LUCERNE achieved four-month dosing. An additional 15% (n=41/271) of Vabysmo patients in TENAYA and 14% (n=41/287) in LUCERNE achieved three-month dosing at two years. Combined, approximately 80% of Vabysmo patients were able to go three months or longer between treatments at the end of the second year.

Vabysmo was generally well tolerated in both studies, with a favourable benefit-risk profile. In TENAYA and LUCERNE, the most common adverse reactions (≥3% of people) included cataract, conjunctival haemorrhage, vitreous floaters, retinal pigment epithelial tears, increase of intraocular pressure and eye pain. Safety results were consistent across study arms.

Two-year data from TENAYA and LUCERNE were presented at the 2022 American Society of Retina Specialists Annual Scientific Meeting. These data will be submitted to the European Medicines Agency in due course.

About the YOSEMITE and RHINE studies[6,8]

YOSEMITE (NCT03622580) and RHINE (NCT03622593) were two identical, randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of Vabysmo® (faricimab) compared to aflibercept in 1,891 people with visual impairment due to diabetic macular edema (940 in YOSEMITE and 951 in RHINE).

Both studies met their primary endpoint, with Vabysmo given at intervals of up to every four months consistently shown to offer visual acuity gains and anatomical improvements that were non-inferior to aflibercept given every two months. A secondary endpoint in both studies measured the proportion of people in the Vabysmo treat-and-extend arm that achieved dosing schedules of every three or four months. Importantly, 53% (n=151/286) of those in the Vabysmo treat-and-extend arm in YOSEMITE and 51% (n=157/308) in RHINE achieved four-month dosing at the end of the first year, and an additional 21% (n=60/286) and 20% (n=63/308), respectively, achieved three-month dosing. At two years, the number of people in the Vabysmo treat-and-extend arm achieving four-month dosing increased to 60% (n=162/270) in YOSEMITE and 64% (n=185/287) in RHINE. An additional 18% (n=49/270) of people in YOSEMITE and 14% (n=39/287) in RHINE achieved three-month dosing. Combined, almost 80% of people in the Vabysmo treat-and-extend arm were able to go three months or longer between treatments at the end of the second year.

Vabysmo was generally well tolerated in both studies, with a favourable benefit-risk profile. In YOSEMITE and RHINE, the most common adverse reactions (≥3% of people) included cataract, conjunctival haemorrhage, vitreous floaters, increase of intraocular pressure and eye pain. Safety results were consistent across study arms.

About neovascular age-related macular degeneration

Age-related macular degeneration (AMD) is a condition that affects the part of the eye that provides sharp, central vision needed for activities like reading.[1,19] Neovascular or 'wet' AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss if left untreated.[20,21] It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis.[21] Worldwide, around 20 million people are living with nAMD – the leading cause of vision loss in people over the age of 60 – and the condition will affect even more people around the world as the global population ages.[1,2,22]

About diabetic macular edema

Affecting around 21 million people globally, diabetic macular edema (DME) is a vision-threatening retinal condition associated with blindness and decreased quality of life when left untreated.[3,23] DME occurs when 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.[19,24] The number of people with DME is expected to grow as the prevalence of diabetes increases.[25]

About Vabysmo® (faricimab)[8]

Vabysmo is the first bispecific antibody approved for the eye. It targets and inhibits two disease 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. By blocking pathways involving Ang-2 and VEGF-A, Vabysmo is designed to stabilise blood vessels.

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™ (ranibizumab injection) 100 mg/mL for intravitreal use via ocular implant is the first U.S. 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 certain period of months.[26] Vabysmo® (faricimab) is the first bispecific antibody approved for the eye, which targets two disease pathways that drive retinal conditions.[8,10] Lucentis®* (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions.[27]

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 endeavour 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.

*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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