Media & Investor Release

CHMP recommends EU approval of Roche's Vabysmo, the first bispecific antibody for the eye, for two leading causes of vision loss

- **Vabysmo (faricimab) simultaneously targets and inhibits two disease pathways that drive neovascular or "wet" age-related macular degeneration (nAMD) and diabetic macular edema (DME)**
- **The CHMP recommendation is based on results across four phase III studies: TENAYA and LUCERNE in nAMD at year one, and YOSEMITE and RHINE in DME up to two years**
- **The totality of the data across all studies in nAMD and DME available to date showed that over 60% of people treated with Vabysmo were able to extend treatment to every four months, while improving and maintaining vision**
- **If approved, Vabysmo would offer the first new mechanism of action in over a decade for people in the EU with nAMD and DME**

Basel, 22 July 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the approval of Vabysmo® (faricimab) for the treatment of neovascular or "wet" age-related macular degeneration (nAMD) and visual impairment due to diabetic macular edema (DME). Based on this recommendation, a final decision regarding the approval of Vabysmo is expected from the European Commission in the near future.

Neovascular AMD and DME are two leading causes of vision loss, together affecting over 40 million people worldwide. [1,2,3,4] The current standards of care typically require eye injections every one to two months. [5,6] Vabysmo has the potential to extend the time between eye injections to up to four months while improving and maintaining vision. [7,8,9,10] If approved, it would offer the first new mechanism of action in over a decade for people in the EU with these conditions. [11,12]

"Today's recommendation marks a significant step forward in redefining treatment for people in the EU with nAMD and DME," said Levi Garraway, M.D., PhD., Roche's Chief Medical Officer and Head of Global Product Development. "With the potential to require fewer injections over time while also improving and maintaining vision, Vabysmo could offer a less burdensome treatment schedule for patients, their caregivers, and healthcare systems."

The CHMP recommendation is based on results across four phase III studies: 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 at intervals of up to four months achieved non-inferior vision gains versus aflibercept given every two months. [7,8,9] The totality of the data

across all four studies in nAMD and DME available to date showed that over 60% of people treated with Vabysmo were able to extend treatment to every four months, while improving and maintaining vision. [7,8,9,10] Vabysmo was generally well tolerated in all four studies, with a favourable benefit-risk profile. [7,8,9]

Vabysmo is the first bispecific antibody 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). 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 and vision outcomes for longer. [7,8]

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 nAMD, and RHONE-X, an extension study of YOSEMITE and RHINE evaluating the long-term safety and tolerability of Vabysmo in DME. [13,14] Additionally, the COMINO and BALATON trials are also underway, evaluating the efficacy and safety of Vabysmo in people with macular edema following retinal vein occlusion. [15,16] Roche has also initiated the phase IV Elevatum study of Vabysmo in underrepresented patient populations with DME. [17]

Vabysmo is already approved in several countries around the world including the US, Japan and the UK for people with nAMD and DME. [18,19,20]

About the TENAYA and LUCERNE studies [7,10]

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 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 people 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.

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 participants) 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 on 14 July 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 [8,9]

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 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% (157/308) in RHINE achieved four-month dosing at the end of the first year, and an additional 21% and 20%, 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 participants) 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. [1,21] Neovascular or “wet” AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss if left untreated. [22,23] It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis. [23] 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. [1,2,24]

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. [3,25] 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. [21,26] The number of people with DME is expected to grow as the prevalence of diabetes increases. [27]

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 period of months. [28] Vabysmo® (faricimab) is the first bispecific antibody approved for the eye, which targets two disease pathways that drive retinal conditions. [8,17] Lucentis®* (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions. [6]

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 recognizing 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.

References

[1] Bright Focus Foundation. Age-Related Macular Degeneration: Facts & Figures. [Internet; cited July 2022]. Available from: https://www.brightfocus.org/macular/article/age-related-macular-facts-figures.
[2] Connolly E, et al. Prevalence of age-related macular degeneration associated genetic risk factors and 4-year progression data in the Irish population. Br J Ophthalmol. 2018;102:1691–5.
[3] Yau JWY, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35:556-64.
[4] Heier JS, et al. The Angiopoietin/Tie pathway in retinal vascular diseases: a review. Retina-J Ret Vit Dis. 2021;41:1-19.
[5] Arnold et al. Two-year outcomes of "treat and extend" intravitreal therapy for neovascular age-related macular degeneration. Ophthalmology. 2015;122:1212-19.https://doi.org/10.1016/S0140-6736(22)00010-1.
[6] Peto et al. Treatment patterns and persistence rates with anti-vascular endothelial growth factor treatment for diabetic macular oedema in the UK: A real-world study. Diabetic Medicine. 2022;39:14746.
[7] Heier, et al. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomised, double-masked, phase 3, non-inferiority trials. The Lancet. 2022; https://doi.org/10.1016/S0140-6736(22)00010-1.
[8] Wykoff et al. Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with DME (YOSEMITE and RHINE): two randomised, double-masked, phase 3 trials. The Lancet. 2022; https://doi.org/10.1016/S0140-6736(22)00018-6
[9] Wells JA, et al. Faricimab in Diabetic Macular Edema: Two-Year Results From the Phase 3 YOSEMITE and RHINE Trials. Presented at: Angiogenesis, Exudation and Degeneration 2022; 2022 February 12
[10] Khanani A, et al. Faricimab in Neovascular Age-Related Macular Degeneration: Year 2 Efficacy, Safety, and Durability Results From the Phase 3 TENAYA and LUCERNE Trials. Presented at: 2022 American Society of Retina Specialists Annual Scientific Meeting; 2022 July 14.
[11] FDA. Highlights of prescribing information, Lucentis. 2006
[12] FDA. Highlights of prescribing information, Macugen. 2004
[13] Clinical Trials.gov. A study to evaluate the long-term safety and tolerability of faricimab (RO686746) in participants with neovascular age-related macular degeneration (AVONELLE-X). [Internet; cited July 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04777201
[14] Clinical Trials.gov. A study to evaluate the long-term safety and tolerability of faricimab (RO686746) in participants with diabetic macular edema (Rhone-X). [Internet; cited July 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04432831.

[15] Clinical Trials.gov A study to evaluate the efficacy and safety of faricimab in participants with macular edema secondary to central retinal or hemiretinal vein occlusion (COMINO). [Internet; cited July 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740931.
[16] Clinical Trials.gov A study to evaluate the efficacy and safety of faricimab (RO6867461) in participants with macular edema secondary to branch retinal vein occlusion (BALATON). [Internet; cited July 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740905.
[17] Clinical Trials.gov. A study to investigate faricimab treatment response in treatment-naïve, underrepresented patients with diabetic macular edema (ELEVATUM). [Internet; cited July 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT05224102.
[18] FDA. Highlights of prescribing information, Vabysmo. 2022.
[19] MHRA approves faricimab through international work-sharing initiative. [Internet; cited July 2022]. Available from: https://www.gov.uk/government/news/mhra-approves-faricimab-through-international-work-sharing-initiative.
[20] Chugai Obtains Regulatory Approval for Vabysmo, the First Bispecific Antibody in Ophthalmology, for Neovascular Age-related Macular Degeneration and Diabetic Macular Edema. [Internet; cited July 2022]. Available from: https://www.chugai-pharm.co.jp/news/cont_file_dl.php?f=220328eVabysmo_DME_nAMD_approval.pdf&src=[%0],[%1]&rep=130,909
[21] All About Vision. Macula Lutea. [Internet; cited July 2022]. Available from: https://www.allaboutvision.com/resources/macula.
[22] Pennington KL, et al. Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors. Eye and Vision. 2016;3:34.
[23] Little K, et al. Myofibroblasts in macular fibrosis secondary to neovascular age-related macular degeneration-the potential sources and molecular cues for their recruitment and activation. EBioMedicine. 2018;38:283-91.
[24] Wong WL, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health. 2014;2:106–16.
[25] Park SJ, et al. Extent of exacerbation of chronic health conditions by visual impairment in terms of health-related quality of life. JAMA Ophthalmol. 2015;133:1267-75.
[26] National Eye Institute. Facts about diabetic eye disease [Internet; cited July 2022]. Available from: https://nei.nih.gov/health/diabetic/retinopathy.
[27] Liu E, et al. Diabetic macular oedema: clinical risk factors and emerging genetic influences. Clin Exp Optom. 2017;100:569-76.
[28] FDA. Highlights of prescribing information, Susvimo. 2021

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