

## **FDA approves Roche's Vabysmo, the first bispecific antibody for the eye, to treat two leading causes of vision loss**

- **Vabysmo (faricimab-svoa) targets and inhibits two disease pathways that drive neovascular or “wet” age-related macular degeneration (nAMD) and diabetic macular edema (DME)**
- **Vabysmo is the only injectable eye medicine approved simultaneously in the US for nAMD and DME, with flexible dosing regimens based on patient need**

Basel, 31 January 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has approved Vabysmo™ (faricimab-svoa) for the treatment of neovascular or “wet” age-related macular degeneration (nAMD) and diabetic macular edema (DME). Neovascular AMD and DME are two leading causes of vision loss worldwide.<sup>1</sup> Vabysmo 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).<sup>2</sup> Vabysmo is the first and only FDA-approved injectable eye medicine for nAMD and DME that improves and maintains vision with treatments from one to four months apart in the first year following four initial monthly doses, based on evaluation of the patient's anatomy and vision outcomes.<sup>3</sup> Standard of care for nAMD and DME typically requires eye injections every one to two months.<sup>2,4</sup>

“Vabysmo represents an important step forward for ophthalmology. It is the first bispecific antibody approved for the eye and a major advance in treating retinal conditions such as neovascular AMD and diabetic macular edema,” said Charles Wykoff, M.D., Ph.D., Director of Research at Retina Consultants of Texas in Houston and a Vabysmo phase III investigator. “With Vabysmo, we now have the opportunity to offer patients a medicine that could improve their vision, potentially lowering treatment burden with fewer injections over time.”

The approval is based on positive results across four phase III studies in nAMD and DME. The studies consistently showed that patients treated with Vabysmo given at intervals of up to four months achieved non-inferior vision gains versus aflibercept given every two months in the first year. Vabysmo was generally well tolerated in all four studies, with a favourable benefit-risk profile.<sup>2,4</sup> The most common adverse reaction (≥5%) reported in patients receiving Vabysmo was conjunctival hemorrhage (7%).<sup>3</sup> Two scientific papers and an editorial on these one-year results were recently published in *The Lancet*.<sup>2,4</sup>

Vabysmo is designed to block pathways involving Ang-2 and VEGF-A. Ang-2 and VEGF-A are thought to contribute to vision loss by destabilising blood vessels, which may cause new leaky blood vessels to form and increase inflammation. While additional research continues, inhibition of both pathways has been shown in preclinical studies to have potentially

complementary benefits, stabilising vessels, and thereby reducing vessel leakage and inflammation.<sup>2</sup>

“Vabysmo provides a new approach to treating vision-threatening retinal conditions through a mechanism of action that targets two pathways simultaneously,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “This is our second FDA approval in ophthalmology in recent months, underscoring our commitment to people living with retinal conditions.”

With Vabysmo, people with nAMD initially receive four monthly treatments. Based on anatomical and vision outcomes, they may receive subsequent treatments every two, three or four months. People with DME are initially given four monthly treatments. Subsequently, their treatment may be extended or reduced based on anatomical and vision outcomes, with a range of one to four months between doses. A second approved treatment regimen for DME involves six monthly loading doses, followed by treatment every two months. Some people with nAMD and DME may be treated monthly if needed, although additional efficacy was not demonstrated in most people given Vabysmo every month.<sup>3</sup>

Roche has ongoing long-term extension studies for Vabysmo in people with nAMD and DME. These include 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.<sup>5,6</sup> 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.<sup>7,8</sup>

Vabysmo will be available in the United States in the coming weeks. The European Medicines Agency is also currently evaluating the Vabysmo Marketing Authorisation Application for the treatment of nAMD and DME.

### **About the TENAYA and LUCERNE Studies<sup>2</sup>**

TENAYA (NCT03823287) and LUCERNE (NCT03823300) are two identical, randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of Vabysmo compared to aflibercept in 1,329 people living with neovascular or “wet” age-related macular degeneration (671 in TENAYA and 658 in LUCERNE). The studies each have two treatment arms: Vabysmo 6.0 mg administered at intervals of two, three, or four months, following four initial monthly doses, selected based on objective assessment of disease activity at weeks 20 and 24; and aflibercept 2.0 mg administered at fixed two-month intervals after three initial monthly doses. In both 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 averaged over weeks 40, 44 and 48. Secondary endpoints include: safety; the percentage of participants in the Vabysmo arm receiving treatment every two, three and four months; the percentage of participants achieving a gain, and the percentage avoiding a loss, of 15 letters or more in BCVA from baseline over time; change in central subfield thickness (CST) from baseline over time; and change in total area of choroidal neovascularisation (CNV) lesion and leakage from baseline over time.

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. In TENAYA and LUCERNE, the average vision gains from baseline at one year in the Vabysmo arms were +5.8 and +6.6 letters, respectively, compared to +5.1 and +6.6 letters in the aflibercept arms.

The studies also 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. In both studies, comparable reductions in CST and CNV size and area of leakage were observed with Vabysmo given at intervals of up to four months versus aflibercept given every two months in 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 ( $\geq 3\%$  of patients) included conjunctival haemorrhage, vitreous floaters, retinal pigment epithelial tears, increase of intraocular pressure and eye pain.<sup>3</sup> Safety results were consistent across study arms.

#### **About the YOSEMITE and RHINE Studies<sup>4</sup>**

YOSEMITE (NCT03622580) and RHINE (NCT03622593) are two identical, randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of Vabysmo compared to aflibercept in 1,891 people with diabetic macular edema (940 in YOSEMITE and 951 in RHINE). The studies each have three treatment arms: Vabysmo 6.0 mg administered up to every four months after four initial monthly doses using a treat-and-extend approach; Vabysmo 6.0 mg administered at two-month intervals after six initial monthly doses; and aflibercept administered at fixed two-month intervals after five initial monthly doses. 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 BCVA score from baseline at one year, averaged over weeks 48, 52 and 56. Secondary endpoints included: safety; the percentage of participants in the treat-and-extend arm receiving Vabysmo every one, two, three and four months 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, and the percentage avoiding a loss, of 15 letters or more in BCVA from baseline over time; change in central subfield thickness (CST) from baseline over time; and percentage of patients with absence of intraretinal fluid over time.

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. In YOSEMITE, the average vision gains from baseline at one year were +11.6 and +10.7 eye chart letters in the Vabysmo treat-and-extend and two-month arms, respectively, and +10.9 letters in the aflibercept arm. In RHINE, the average vision gains from baseline at one year were +10.8 and +11.8 letters in the Vabysmo treat-and-extend and two-month arms, respectively, and +10.3 letters in the aflibercept arm.

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 at the end of the first year. In both studies, greater reductions in CST and intraretinal fluid were observed with Vabysmo given at intervals of up to four months versus aflibercept given every two months in the first year. Vabysmo was generally well-tolerated in both studies, with a favourable benefit-risk profile. In YOSEMITE and RHINE, the most common adverse reactions ( $\geq 3\%$  of patients) included conjunctival haemorrhage, vitreous floaters and increase of intraocular pressure.<sup>3</sup> 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.<sup>9,10</sup> Neovascular or “wet” AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss if left untreated.<sup>11,12</sup> It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis.<sup>12</sup> 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.<sup>9,13,14</sup>

### **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.<sup>15,16</sup> DME occurs when damaged blood vessels in the retina leak into and cause swelling in the macula – the central area of the retina responsible for the sharp vision needed for reading and driving.<sup>10,17</sup> The number of people with DME is expected to grow as the prevalence of diabetes increases.<sup>18</sup> There remains a significant unmet need for more effective, longer-lasting therapies for people with DME.<sup>4</sup>

### **About Vabysmo™ (faricimab-svoa)<sup>2</sup>**

Vabysmo (faricimab-svoa) 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 FDA-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.<sup>19</sup> Vabysmo™ (faricimab-svoa), the first FDA-approved bispecific antibody for the eye, which targets two disease pathways that drive retinal conditions.<sup>3</sup> Lucentis®\* (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions.<sup>20</sup>

### **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, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

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. In recent years, the company has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

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 thirteenth consecutive year, Roche has been recognised as one of the most sustainable companies in the pharmaceutical industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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](http://www.roche.com).

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## References

- [1] Heier JS, et al. The Angiopoietin/Tie pathway in retinal vascular diseases: a review. *Retina-J Ret Vit Dis.* 2021;41:1-19.
- [2] 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](https://doi.org/10.1016/S0140-6736(22)00010-1).
- [3] FDA. Highlights of prescribing information, Vabysmo. 2022.
- [4] 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](https://doi.org/10.1016/S0140-6736(22)00018-6).
- [5] ClinicalTrials.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 January 2022]. Available from: <https://clinicaltrials.gov/ct2/show/NCT04777201>.
- [6] ClinicalTrials.gov. A study to evaluate the long-term safety and tolerability of faricimab (RO686746) in participants with diabetic macular edema (Rhone-X). [Internet; cited January 2022]. Available from: <https://clinicaltrials.gov/ct2/show/NCT04432831>.
- [7] ClinicalTrials.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 January 2022]. Available from: <https://clinicaltrials.gov/ct2/show/NCT04740931>.
- [8] ClinicalTrials.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 January 2022]. Available from: <https://clinicaltrials.gov/ct2/show/NCT04740905>.
- [9] Bright Focus Foundation. Age-Related Macular Degeneration: Facts & Figures. [Internet; cited January 2022]. Available from: <https://www.brightfocus.org/macular/article/age-related-macular-facts-figures>.
- [10] All About Vision. Macula Lutea. [Internet; cited January 2022]. Available from: <https://www.allaboutvision.com/resources/macula>.
- [11] 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.
- [12] 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.

- [13] 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.
- [14] 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.
- [15] Yau JWY, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35:556-64.
- [16] 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.
- [17] National Eye Institute. Facts about diabetic eye disease [Internet; cited January 2022]. Available from: <https://nei.nih.gov/health/diabetic/retinopathy>.
- [18] Liu E, et al. Diabetic macular oedema: clinical risk factors and emerging genetic influences. *Clin Exp Optom*. 2017;100:569-76.
- [19] FDA. Highlights of prescribing information, Susvimo. 2021
- [20] FDA. Highlights of prescribing information, Lucentis. 2006

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