Media & Investor Release

Ad hoc announcement pursuant to Art. 53 LR

FDA approves Roche's Vabysmo for the treatment of retinal vein occlusion (RVO)

- **RVO is the third indication for Vabysmo, in addition to neovascular or 'wet' age-related macular degeneration and diabetic macular edema**
- **Approval is based on two phase III studies demonstrating early and sustained vision improvements that were non-inferior to aflibercept**
- **Vabysmo also demonstrated rapid and robust drying of retinal fluid**
- **Additional U.S. label update across indications includes information on rare post-marketing reports of retinal vasculitis and/or retinal vascular occlusion; reporting rate is in line with other broadly used intravitreal treatments**

Basel, 27 October 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the United States Food and Drug Administration (U.S. FDA) has approved Vabysmo® (faricimab) for the treatment of macular edema following retinal vein occlusion (RVO). RVO is the third indication for Vabysmo, in addition to neovascular or 'wet' age-related macular degeneration (nAMD) and diabetic macular edema (DME).[1] Together, the three retinal conditions affect around 70 million people worldwide and are among the leading causes of vision loss.[2-5]

"Vabysmo is a new treatment option for RVO that can help people preserve and improve their vision, with the added benefit of retinal drying," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "The efficacy and safety profile of Vabysmo has been well established in global clinical trials and is reinforced by a growing breadth of real-world evidence, with hundreds of thousands of people treated."

Vabysmo is the first and only bispecific antibody approved for the eye.[1,6] Today's approval in RVO is based on positive results from the global phase III BALATON and COMINO studies that demonstrated monthly treatment with Vabysmo provided early and sustained improvement in vision in people with branch and central RVO, meeting the primary endpoint of non-inferior visual acuity gains at 24 weeks compared to aflibercept. This was further supported by data showing Vabysmo achieved rapid and robust drying of retinal fluid. In BALATON and COMINO, Vabysmo was generally well tolerated and the safety profile was consistent with previous trials. The most common adverse reaction was conjunctival haemorrhage (3%). Safety results were consistent across study arms.[7-9]

Information has also been added to the Warnings and Precautions section of the U.S. label based on rare post-marketing cases of retinal vasculitis and/or retinal vascular occlusion,

typically in the presence of intraocular inflammation. The reported rate of retinal vasculitis with vascular occlusion is 0.06 per 10,000 injections, in line with real-world reported frequencies of other broadly used intravitreal treatments for people living with nAMD, DME and RVO.[10-12]

To date, Vabysmo is approved in more than 80 countries around the world for people living with nAMD and DME, with approximately 2 million doses distributed globally.[12]

About retinal vein occlusion (RVO)

RVO is the second most common cause of vision loss due to retinal vascular conditions. It affects an estimated 28 million adults globally, mainly those aged 60 or older, and can lead to severe and sudden vision loss.[2,13] The level of angiopoietin-2 (Ang-2) is elevated in RVO and it is thought that increased Ang-2 expression drives disease progression.[14,15] 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.[13,16,17] Currently, macular edema due to RVO is typically treated with repeated intravitreal injections of anti-vascular endothelial growth factor therapies.[16] 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.[2,17]

About the BALATON and COMINO studies[8,9]

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 were randomised 1:1 to receive monthly injections for six months of either Vabysmo (6.0 mg) or aflibercept (2.0 mg). From weeks 24 to 72, all patients received Vabysmo (6.0 mg) up to every four months, using a treat-and-extend dosing regimen.

The BALATON study was conducted in 553 people with branch retinal vein occlusion. The COMINO study was conducted in 729 people with central retinal or hemiretinal vein occlusion. The primary endpoint of each study was the change in best-corrected visual acuity from baseline at 24 weeks. Secondary endpoints (weeks 0-24) included change in central subfield thickness and drying of retinal fluid, from baseline over time up to week 24. Secondary endpoints (weeks 24-72) were treatment durability at 68 weeks and continuation of weeks 0-24 endpoints.

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).[18,19] 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.[20-22] Roche also supports several other independent studies to further understand retinal conditions with a high unmet need.[12]

About Vabysmo® (faricimab)

Vabysmo is the first bispecific antibody approved for the eye.[1,6] 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. By blocking pathways involving Ang-2 and VEGF-A, Vabysmo is designed to stabilise blood vessels.[23,24] Vabysmo is approved in more than 80 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, and in the United States for people living with macular edema following retinal vein occlusion. Review by other regulatory authorities is ongoing.[1,6,12,25,26]

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.[1,6,23,24] 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 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.

References

[1] U.S. Food and Drug Administration (FDA). Highlights of prescribing information, Vabysmo. 2023. [Internet; cited October 2023]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761235s000lbl.pdf.
[2] Song P, et al. Global epidemiology of retinal vein occlusion: a systematic review and meta-analysis of prevalence, incidence, and risk factors. J Glob Health. 2019;9:010427. Song P, et al. Global epidemiology of retinal vein occlusion: a systematic review and meta-analysis of prevalence, incidence, and risk factors. J Glob Health. 2019;9:010427.
[3] Yau JWY, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35:556–64.
[4] 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;102:1691–95.
[5] Bright Focus Foundation. Age-Related Macular Degeneration: Facts & Figures [Internet; cited October 2023]. Available from: https://www.brightfocus.org/macular/article/age-related-macular-facts-figures.

[6] MHRA approves faricimab through international work-sharing initiative [Internet; cited October 2023]. Available from: https://www.gov.uk/government/news/mhra-approves-faricimab-through-international-work-sharing-initiative.
[7] Tadayoni R, et al. Faricimab in RVO: Results from the BALATON and COMINO phase 3 studies. Presented at: Angiogenesis, Exudation and Degeneration 2023, 10-11 February 2023; Florida, United States.
[8] Clinical Trials.gov. A study to evaluate the efficacy and safety of faricimab in participants with macular edema secondary to branch retinal vein occlusion (BALATON) [Internet; cited October 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740905.
[9] 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 October 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740931.
[10] Ma P, et al. Ocular adverse events associated with anti-VEGF therapy: A pharmacovigilance study of the FDA adverse event reporting system (FAERS). Frontiers in Pharmacology. 2022;13:1017889.
[11] Food and Drug Administration. FDA AEs reporting system (FAERS) public dashboard. [Internet; cited October 2023]. Available from: https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard.
[12] Roche data on file.
[13] Moorfields Eye Hospital, United Kingdom National Health Service Foundation Trust. RVO [Internet; cited October 2023]. Available from: https://www.moorfields.nhs.uk/condition/retinal-vein-occlusion.
[14] Joussen et al. Angiopoietin/Tie2 signalling and its role in retinal and choroidal vascular diseases: a review of preclinical data. Eye. 2021;35:1305-1316.
[15] Regula JT, et al. Targeting key angiogenic pathways with a bispecific CrossMab optimized for neovascular eye diseases. EMBO Molecular Medicine. 2016;8:1265–88.
[16] Schmidt-Erfurth U, et al. Guidelines for the Management of Retinal Vein Occlusion by the European Society of Retina Specialists (EURETINA). Ophthalmologica. 2019;242:123-162.
[17] Campochiaro P. Molecular pathogenesis of retinal and choroidal vascular diseases. Prog Retin Eye Res. 2015;49:67-81.
[18] Clinical Trials.gov. A study to evaluate the long-term safety and tolerability of Vabysmo in participants with nAMD (AVONELLE-X) [Internet; cited October 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT04777201.
[19] Clinical Trials.gov. A study to evaluate the long-term safety and tolerability of Vabysmo in participants with DME (Rhone-X) [Internet; cited October 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT04432831.
[20] Clinical Trials.gov. A study to investigate faricimab treatment response in treatment-naïve, underrepresented patients with DME (ELEVATUM). [Internet; cited October 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT05224102.
[21] APVRS. Design and Rationale of the SALWEEN Trial: A Phase 3b/4 Study of Faricimab, a Dual Angiopoietin-2 and Vascular Endothelial Growth Factor-A Inhibitor, in Patients With Polypoidal Choroidal Vasculopathy. [Internet; cited October 2023]. Available from: https://2022.apvrs.org/abstract/?code=200351.
[22] Clinical Trials.gov. A Real-World Study to Gain Clinical Insights Into Roche Ophthalmology Products (VOYAGER). [Internet; cited October 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT05476926.
[23] Heier JS, 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; 399:729-740.
[24] Wykoff C, 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; 399:741-755.
[25] Chugai obtains regulatory approval for Vabysmo, the first bispecific antibody in ophthalmology, for neovascular age-related macular degeneration and diabetic macular edema [Internet; cited October 2023]. Available from: https://www.chugai-pharm.co.jp/english/news/detail/20220328160002_909.html.

[26] European Medicines Agency. Summary of Product Characteristics, Vabysmo, 2022 [Internet; cited April 2023]. Available from: https://www.ema.europa.eu/en/documents/product-information/vabysmo-epar-product-information_en.pdf.
[27] U.S. FDA. Highlights of prescribing information, Susvimo. 2006 [Internet; cited October 2023]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761197s000lbl.pdf.
[28] U.S. FDA. Highlights of prescribing information, Lucentis. 2006 [Internet; cited October 2023]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125156s114lbl.pdf.

Roche Global Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

Hans Trees, PhD
Phone: +41 79 407 72 58

Nathalie Altermatt
Phone: +41 79 771 05 25

Simon Goldsborough
Phone: +44 797 32 72 915

Karsten Kleine
Phone: +41 79 461 86 83

Nina Mählitz
Phone: +41 79 327 54 74

Kirti Pandey
Phone: +49 172 6367262

Rebekka Schnell
Phone: +41 79 205 27 03

Sileia Urech
Phone: +41 79 935 81 48

Roche Investor Relations

Dr. Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com