Media & Investor Release

Roche's Vabysmo maintained vision improvements with extended treatment intervals up to four months for people with retinal vein occlusion (RVO) in phase III studies

- **Vabysmo showed robust and sustained retinal drying up to 72 weeks and a safety profile consistent with previous studies**
- **Regulatory applications for Vabysmo in RVO are under review by health authorities around the world; if approved, RVO would be the third indication in addition to nAMD and DME**
- **Vabysmo is the first and only treatment that targets and inhibits two signalling pathways linked to a number of vision-threatening retinal conditions**

Basel, 10 October 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive topline long-term results from the global phase III BALATON and COMINO studies, evaluating extended treatment intervals with Vabysmo® (faricimab) in macular edema due to branch and central retinal vein occlusion (BRVO and CRVO).[1,2]

From weeks 24 to 72, all people in both studies received Vabysmo using a treat-and-extend dosing regimen, which allows tailoring of their treatment interval according to the individual patient's response to treatment. Data showed that people treated with Vabysmo extended their treatment intervals up to every four months while maintaining the vision gains achieved in the first 24 weeks of the studies. Vabysmo continued to show robust and sustained drying of retinal fluid from baseline up to week 72, as measured by reduction in central subfield thickness. This is the first time that vision and anatomical improvements have been maintained for more than a year using a personalised treat-and-extend dosing regimen in global phase III studies for both BRVO and CRVO. In both studies, Vabysmo was generally well-tolerated and the safety profile was consistent with previous studies.

"These are the first retinal vein occlusion (RVO) studies to show vision maintenance and anatomical improvements up to 72 weeks in both central and branch RVO," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "These data further support Vabysmo's potential as a new treatment for RVO, allowing people to preserve their vision while spending less time managing their condition."

RVO impacts 28 million people globally and, if approved, would be the third indication for Vabysmo in addition to neovascular or 'wet' age-related macular degeneration (nAMD) and diabetic macular edema (DME).[3-7] Together, the three conditions affect around 70 million people worldwide and are among the leading causes of vision loss.[3,8-11]

Detailed results from weeks 24 to 72 of the phase III BALATON and COMINO studies will be presented at an upcoming medical meeting.

Data from the first 24 weeks of the phase III BALATON and COMINO studies, presented at Angiogenesis, Exudation and Degeneration 2023, demonstrated early and sustained vision improvement with Vabysmo, with both studies meeting their primary endpoints of non-inferior vision gains compared to aflibercept. A secondary endpoint showed that Vabysmo achieved rapid and robust drying of retinal fluid from baseline to week 24, as measured by reduction in central subfield thickness.[12]

Data up to 24 weeks have been submitted to global health authorities, including the United States Food and Drug Administration (U.S. FDA) and European Medicines Agency. A decision from the U.S. FDA is expected in late 2023.

Vabysmo is uniquely engineered to target and inhibit two signalling pathways, which are 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.[13,14] The level of Ang-2 is elevated in RVO and it is thought that increased Ang-2 expression drives disease progression.[11,15]

To date, Vabysmo is approved in more than 80 countries around the world for people living with nAMD and DME, including the United States, Japan, the United Kingdom and the European Union, with public reimbursement in over 25 markets and more than 1.5 million doses distributed globally.[16]

About retinal vein occlusion (RVO)

RVO is the second most common cause of vision loss due to retinal vascular diseases. It affects an estimated 28 million adults globally, mainly those aged 60 or older, and can lead to severe and sudden vision loss.[3,17] The level of angiopoietin-2 (Ang-2) is elevated in RVO and it is thought that increased Ang-2 expression drives disease progression.[11,15] 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.[17-19] 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 (BRVO), 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 (CRVO), which is less common, affecting more than four million people worldwide, and occurs when the eye’s central retinal vein becomes blocked.[3,19]

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 were randomised 1:1 to receive six-monthly injections 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).[20,21] 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.[22-24] Roche also supports several other independent studies to further understand retinal conditions with a high unmet need.[16]

About Vabysmo® (faricimab)

Vabysmo is the first bispecific antibody approved for the eye.[4,6] 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.[13,14] 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. Review by other regulatory authorities is ongoing.[4-6,16]

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.[25] 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.[4,6,13,14] Lucentis® (ranibizumab injection)^ is the first treatment approved to improve vision in people with certain retinal conditions.[26]

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] 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.
[2] 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.
[3] 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.
[4] U.S. Food and Drug Administration (FDA). Highlights of prescribing information, Vabysmo. 2022. [Internet; cited October 2023]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761235s000lbl.pdf.
[5] 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.
[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] European Medicines Agency. Summary of Product Characteristics, Vabysmo, 2022.
[8] Yau JWY, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35:556–64.
[9] 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.
[10] 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.
[11] 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.
[12] 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.
[13] 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.
[14] 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.
[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] Roche data on file.
[17] 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.
[18] 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.
[19] Campochiaro P. Molecular pathogenesis of retinal and choroidal vascular diseases. Prog Retin Eye Res. 2015;49:67-81.
[20] 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.
[21] 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.
[22] 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.
[23] 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.
[24] 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.
[25] 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.
[26] 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

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