Media Release

Roche's Vabysmo improved vision in underrepresented populations with diabetic macular edema (DME) in a first-of-its-kind study

- **The ELEVATUM study showed clinically meaningful improvement in vision and reduction in retinal fluid in people with diabetic macular edema (DME) treated with Vabysmo who identify as African American, Black, Hispanic and Latino[1]**
- **Efficacy and safety from this phase IV study were consistent with data from the Vabysmo phase III DME studies[1]**
- **These racial and ethnic groups are disproportionately affected by diabetes and at higher risk of developing DME, a leading cause of vision loss[2-3]**

Basel, 18 October 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive topline one-year results from the open-label, single-arm phase IV ELEVATUM study evaluating Vabysmo® (faricimab) for the treatment of diabetic macular edema (DME) in people from racial and ethnic groups that are often underrepresented in clinical trials.[4]

Initial data from 124 participants in the United States (US) showed that after one year of treatment with Vabysmo, administered every eight weeks, participants could read an additional 12.3 letters on average – equivalent to about two and a half lines on an eye chart. Results among major racial and ethnic groups represented in this study were similar. Hispanic and Latino participants started the study with the most severe disease and had an average vision gain of 14.1 letters from baseline at one year, equivalent to nearly three lines on an eye chart. African American and Black participants gained an average of 11.3 letters from baseline at one year. Vabysmo was well tolerated, with no new safety events identified.[1]

These data were presented in a late-breaking oral presentation at the American Academy of Ophthalmology (AAO) 2024 Annual Meeting in Chicago, Illinois, on 18 October.[1] The study is the first retina trial for historically underrepresented populations.

"Vabysmo has been shown to be an effective first-line treatment for diabetic macular edema, and for the first time, we have data specifically demonstrating its ability to improve vision in Black, African American, Hispanic and Latino patients who are disproportionately impacted by this condition," said investigator Jeremiah Brown, M.D., of Retina Consultants of Texas, who presented the data at AAO. "As a clinician who serves patients from these communities that are so often underrepresented in clinical trials, I believed it was important to take part in this groundbreaking study, and hope the findings will inform and improve the care we provide to our patients in the clinic daily."

Results were consistent with the phase III YOSEMITE and RHINE DME studies.[5] A secondary endpoint showed robust retinal drying with Vabysmo across these racial and ethnic groups,

who, on average, achieved a decrease of 206.3 microns in central subfield thickness (CST) from baseline.[1] Reducing CST indicates retinal drying, which is an important clinical measure, as swelling from excess fluid in the back of the eye is associated with distorted and blurred vision.[6]

“We established ELEVATUM to specifically evaluate Vabysmo in underrepresented populations,” said Nilesh Mehta, Roche’s Global Therapeutic Area Head for Ophthalmology. “Including diverse populations and perspectives is part of our broader Roche Diversity, Equity & Inclusion (DE&I) strategy and is essential if we want to improve scientific understanding of diabetic macular edema and ultimately improve standard of care for all people living with this condition.”

Among the 124 patients, 45% self-identified as Hispanic or Latino, and 48% as Black or African American.[1] The study was designed to facilitate enrolment and promote retention of underrepresented patients. For example, ELEVATUM was conducted at sites that treat a high proportion of these populations in urban, rural and community-based locations. In addition, eligibility criteria allowed participants with a haemoglobin A1c (HbA1c) level up to 12%.[4] An HbA1c test measures a person’s average blood sugar levels over the past three months and is used to diagnose diabetes.[7] Typically, the threshold for DME trials is an HbA1c level of 10%. However, HbA1c levels can be higher in Black, African American, Hispanic and Latino populations compared with Caucasians, meaning a lower HbA1c threshold can inadvertently lead to the exclusion of patients from various ethnic and racial groups.[8-9]

To date, Vabysmo is approved in more than 100 countries for DME and neovascular or ‘wet’ age-related macular degeneration, and in over 30 countries for macular edema following retinal vein occlusion (RVO). More than five million doses of Vabysmo have been distributed globally since its initial US approval in 2022.[10-15]

About ELEVATUM[4]

ELEVATUM (NCT05224102) is a phase IV, multicentre, open-label, single-arm study designed to evaluate Vabysmo® (faricimab) as a treatment for diabetic macular edema (DME) in patients that have been historically underrepresented in clinical trials, including people who self-identify as Black, African American, Hispanic or Latino. Trial participants have not been treated with an anti-vascular endothelial growth factor before the study. They receive treatment every four weeks with Vabysmo up to week 20, followed by treatment every eight weeks up to week 52.

The primary endpoint is change from baseline in best corrected visual acuity at week 56. Secondary endpoints include safety and change in central subfield thickness from baseline over time.

About Diabetic Macular Edema

Affecting around 29 million people globally, diabetic macular edema (DME) is a vision-threatening retinal condition associated with blindness and decreased quality of life when left untreated.[16-17] 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.[18-19] The number of people with DME is expected to grow as the prevalence of diabetes increases.[20]

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).[21-22] The POYANG study is evaluating Vabysmo in adult treatment-naive patients with choroidal neovascularisation secondary to pathologic myopia.[23] Roche has initiated several phase IV studies, including the ELEVATUM study of Vabysmo in underrepresented patient populations with DME and the SALWEEN study of Vabysmo in a subpopulation of nAMD highly prevalent in Asia.[4, 24] Roche has also initiated the VOYAGER study, a global real-world data collection platform, and supports several other independent studies to further understand retinal conditions with a high unmet need.[25]

About Vabysmo® (faricimab)

Vabysmo is the first bispecific antibody approved for the eye.[11, 26] 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.[5, 26] Vabysmo is approved in more than 100 countries around the world, including the United States (US), Japan, the United Kingdom and the European Union (EU) for people living with neovascular or 'wet' age-related macular degeneration and diabetic macular edema, and in more than 30 countries, including the US, EU and Japan, for people living with macular edema following retinal vein occlusion. Review by other health authorities is ongoing.[10-15]

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 innovative treatments across different modalities, such as antibodies, and gene and cell therapies targeting multiple vision-threatening conditions, including retinal vascular and diabetic eye diseases, geographic atrophy, and autoimmune conditions, such as thyroid eye disease and uveitic macular edema.

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 (US) Food and Drug Administration-approved refillable eye implant for neovascular or 'wet' age-related macular degeneration (nAMD) that continuously delivers a customised formulation of ranibizumab over a period of months.[27, 28] 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 by neutralising angiopoietin-2 and vascular endothelial growth factor-A.[5, 11, 12, 26] Vabysmo is approved around the world for people living with nAMD, diabetic macular edema and macular edema following retinal vein occlusion.[10-15] Lucentis® (ranibizumab injection)* was the first treatment approved to improve vision in people with certain retinal conditions.[29]

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.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

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.

All trademarks used or mentioned in this release are protected by law.

References

[1] Emanuelli A. ELEVATUM, the First Industry Sponsored Trial Focused on Underrepresented Patients in Retina in the US. Presented at: American Academy of Ophthalmology (AAO) Annual Meeting; 2024, October 18; Chicago, IL, USA.
[2] Coney J, Scott A. Racial disparities in the screening and treatment of diabetic retinopathy. Journal of the National Medical Association. 2022;114 (2):171-181.
[3] Lee R, et al. Epidemiology of diabetic retinopathy, DME and related vision loss. Eye and Vision. 2015; 2, 17.
[4] Clinical Trials.gov. A Study to Investigate Faricimab Treatment Response in Treatment-Naive, Underrepresented Patients With Diabetic Macular Edema (ELEVATUM) [Internet; cited October 2024]. Available from: https://www.clinicaltrials.gov/study/NCT05224102.
[5] 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 III trials. The Lancet. 2022; 399:741-755.
[6] US National Institutes of Health - National Eye Institute. Macular edema. 2023. [Internet; cited October 2024]. Available from: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema.
[7] Eyth E, Naik R. Hemoglobin A1C. 2023. [Internet; cited October 2024]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549816/.
[8] Cavagnolli G, et al. Effect of ethnicity on HbA1c levels in individuals without diabetes: Systematic review and meta-analysis. PloS one. 2017;12 (2).
[9] Borkar DS, et al. Understanding the impact of HbA1c thresholds on DME clinical trial eligibility by race. Presented at: AAO 2023; November 3-6, 2023; San Francisco, CA, USA. Poster PO492.
[10] European Medicines Agency. Summary of product characteristics, Vabysmo. 2022. [Internet; cited October 2024]. Available from: https://www.ema.europa.eu/en/documents/product-information/vabysmo-epar-product-information_en.pdf.
[11] US FDA. Highlights of prescribing information, Vabysmo. 2023 [Internet; cited October 2024]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761235s003lbl.pdf.
[12] Medicines and Healthcare products Regulatory Agency approves faricimab through international work-sharing initiative. [Internet; cited October 2024]. Available from: https://www.gov.uk/government/news/mhra-approves-faricimab-through-international-work-sharing-initiative.
[13] Chugai obtains regulatory approval for Vabysmo, the only bispecific antibody in the ophthalmology field, for additional indication of macular edema associated with RVO. [Internet; cited October 2024]. Available from: https://www.chugai-pharm.co.jp/english/news/detail/20240326160000_1054.html.
[14] Chugai obtains regulatory approval for Vabysmo, the first bispecific antibody in ophthalmology, for nAMD and DME. [Internet; cited October 2024]. Available from: https://www.chugai-pharm.co.jp/english/news/detail/20220328160002_909.html.
[15] Roche data on file.
[16] Im JHB, et al. Prevalence of DME based on optical coherence tomography in people with diabetes: a systematic review and meta-analysis. Survey of Ophthalmology. 2022 Jul-Aug;67(4):1244-1251.
[17] The Lancet. Diabetes: A defining disease of the 21st century. Lancet. 2023 24;401 (10394):2087.
[18] All About Vision. Macula lutea. [Internet; cited October 2024]. Available from: https://www.allaboutvision.com/resources/macula.
[19] National Eye Institute. Diabetic Retinopathy. [Internet; cited October 2024]. Available from: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy.
[20] Liu E, et al. DME: Clinical risk factors and emerging genetic influences. Clinical and Experimental Optometry. 2017;100:569–76.
[21] Clinical Trials.gov. A study to evaluate the long-term safety and tolerability of Vabysmo in participants with nAMD (AVONELLE-X). [Internet; cited October 2024]. Available from:

https://clinicaltrials.gov/ct2/show/NCT04777201.
[22] Clinical Trials.gov. Clinical Trials.gov. A study to evaluate the long-term safety and tolerability of Vabysmo in participants with diabetic macular edema (DME) (RHONE-X). [Internet; cited October 2024]. Available from: https://clinicaltrials.gov/ct2/show/NCT04432831.
[23] Clinical Trials.gov. A study to evaluate the efficacy and safety of faricimab in patients with choroidal neovascularization secondary to pathologic myopia (POYANG). [Internet; cited October 2024]. Available from: https://www.clinicaltrials.gov/study/NCT06176352.
[24] APVRS. Design and rationale of the SALWEEN trial: A phase IIIb/IV study of faricimab, a dual angiopoietin-2 and vascular endothelial growth factor-a inhibitor, in patients with polypoidal choroidal vasculopathy. [Internet; cited October 2024]. Available from: https://2022.apvrs.org/abstract/?code=200351.
[25] Clinical Trials.gov. A real-world study to gain clinical insights into Roche ophthalmology products (VOYAGER). [Internet; cited October 2024]. Available from: https://clinicaltrials.gov/ct2/show/NCT05476926.
[26] Heier JS, et al. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for nAMD (TENAYA and LUCERNE): two randomised, double-masked, phase III, non-inferiority trials. The Lancet. 2022; 399:729-40.
[27] US FDA. Highlights of prescribing information, Susvimo. 2021. [Internet; cited October 2024]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761197s000lbl.pdf.
[28] Holekamp N, et al. Archway randomised phase III trial of the Port Delivery System with ranibizumab for neovascular age-related macular degeneration (nAMD). Ophthalmology. 2021.
[29] US FDA. Highlights of prescribing information, Lucentis. 2014. [Internet; cited October 2024]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125156s0069s0076lbl.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

Sileia Urech
Phone: +41 79 935 81 48

Nathalie Altermatt
Phone: +41 79 771 05 25

Lorena Corfas
Phone: +41 79 568 24 95

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

Yvette Petillon
Phone: +41 79 961 92 50

Dr. Rebekka Schnell
Phone: +41 79 205 27 03