Media & Investor Release

New two-year data confirm Roche's Vabysmo improves vision with fewer treatments for people with neovascular age-related macular degeneration

- **In the TENAYA and LUCERNE studies, more than 60% of Vabysmo patients could be treated every four months at two years. This represents an increase from 45% at year one**
- **Patients treated with Vabysmo received a median number of 10 injections over the two years versus 15 injections for those treated with aflibercept, potentially decreasing the number of injections**
- **No new safety signals were identified and Vabysmo continued to be well tolerated, with a favourable benefit-risk profile**

Basel, 14 July 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new two-year data from the TENAYA and LUCERNE studies that reinforce the long-term efficacy, safety and durability of Vabysmo® (faricimab) in neovascular or "wet" age-related macular degeneration (nAMD), a leading cause of vision loss. [1,2] Neovascular AMD affects nearly 20 million people globally and can require treatment with eye injections every one to two months. [2,3,4] The two-year data were presented at the 2022 American Society of Retina Specialists Annual Scientific Meeting on 14 July. [1]

"These longer-term results reinforce confidence in Vabysmo and support its continued use in people with neovascular AMD," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. "With the potential to require fewer injections over time, Vabysmo continues to represent an important step forward for people with vision-threatening retinal conditions, and these data exemplify our commitment to redefining standards of care and reducing treatment burden."

In the TENAYA and LUCERNE studies, at two years:[1]

- More than 60% of people receiving Vabysmo could be treated every four months – an increase of over 15 percentage points since the primary analysis at one year – while achieving comparable vision gains versus aflibercept given every two months.
- Nearly 80% of people receiving Vabysmo could be treated every three months or longer.
- Patients treated with Vabysmo received a median number of 10 injections over the two years versus 15 injections for those patients treated with aflibercept, potentially decreasing the number of injections.

- Comparable reductions in central subfield thickness (CST) were observed with Vabysmo given at intervals of up to four months versus aflibercept given every two months.
- No new safety signals were identified and Vabysmo continued to be well tolerated, with a favourable benefit-risk profile.

The primary analyses at one year formed the basis of the recent nAMD approvals in the US, Japan, the UK and several other countries around the world. Vabysmo is also approved in these countries for diabetic macular edema (DME). Vabysmo is currently under review by the European Medicines Agency for these conditions, and submissions to other regulatory authorities around the world are ongoing.

Vabysmo is the first bispecific antibody for the eye and the only injectable eye medicine approved in a number of countries for treatments up to four months apart. [4,5] Vabysmo is designed to block 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). [4] While research is underway to better understand the role of the Ang-2 pathway in retinal disease, 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. [4]

Detailed Two-Year Results [1]

In the TENAYA and LUCERNE studies, nAMD patients received Vabysmo given at intervals of two, three or four months or aflibercept given every two months. In the second year, the dosing schedule for Vabysmo patients could be adjusted based on their response to treatment.

At two years, vision improvements were comparable across both treatment arms. In TENAYA, the average vision gains from baseline at two years were +3.7 eye chart letters in the Vabysmo arm and +3.3 letters in the aflibercept arm. In LUCERNE, the average vision gains from baseline at two years were +5.0 letters in the Vabysmo arm and +5.2 letters in the aflibercept arm.

Furthermore, 59% (n=160/271) of Vabysmo patients in TENAYA and 67% (n=192/287) in LUCERNE achieved four-month dosing at two years. This is an increase over one-year results, which showed 46% (n=144/315) of Vabysmo patients in TENAYA and 45% (n=142/316) in LUCERNE achieved four-month dosing. An additional 15% (n=41/271) of Vabysmo patients in TENAYA and 14% (n=41/287) in LUCERNE achieved three-month dosing at two years. Combined, more than 78% of Vabysmo patients were able to go three months or longer between treatments at the end of the second year.

In both studies, comparable reductions in CST were observed with Vabysmo given at intervals of up to four months versus aflibercept given every two months. Safety results were consistent across study arms, with no reported cases of retinal vasculitis or intraocular inflammation (IOI) associated with retinal vein or retinal artery occlusion.

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. [6,7] 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. [8,9] Roche has also initiated the phase IV Elevatum study of Vabysmo in underrepresented patient populations with DME. [10]

About the TENAYA and LUCERNE studies [1]

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 nAMD (671 in TENAYA and 658 in LUCERNE). The studies each have two treatment arms: Vabysmo 6 mg administered at intervals of two, three, or four months, following four initial monthly doses, selected based on objective assessment of disease activity as measured by optical coherence tomography and visual acuity evaluations at weeks 20 and 24; and aflibercept 2 mg administered at fixed two-month intervals after three initial monthly doses. At week 60, patients randomised to the Vabysmo arm were treated using a treat-and-extend approach up to week 108. Dosing schedule for Vabysmo patients during the treat-and-extend phase was adjusted based on treatment response as determined by central subfield thickness (CST) and visual acuity. 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; and change in CST from baseline over time.

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. [2,11] Neovascular or “wet” AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss if left

untreated. [12,13] It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis. [13] 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. [2,3,14]

About Vabysmo® (faricimab) [4]

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. [15] Vabysmo® (faricimab) is the first bispecific antibody approved for the eye, which targets two disease pathways that drive retinal conditions. [5] Lucentis®* (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions. [16]

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.

*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] 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.
[2] Bright Focus Foundation. Age-Related Macular Degeneration: Facts & Figures. [Internet; cited June 2022]. Available from: https://www.brightfocus.org/macular/article/age-related-macular-facts-figures.
[3] 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.
[4] 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.
[5] FDA. Highlights of prescribing information, Vabysmo. 2022.
[6] 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 June 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04777201.
[7] 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 June 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04432831.
[8] 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 June 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740931.
[9] 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 June 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740905.
[10] Clinical Trials.gov. A study to investigate faricimab treatment response in treatment-naïve, underrepresented patients with diabetic macular edema (ELAVATUM). [Internet; cited June 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT05224102.
[11] All About Vision. Macula Lutea. [Internet; cited July 2022]. Available from: https://www.allaboutvision.com/resources/macula.

[12] 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.
[13] 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.
[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] FDA. Highlights of prescribing information, Susvimo. 2021.
[16] FDA. Highlights of prescribing information, Lucentis. 2006.

Roche Group Media Relations

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

Hans Trees, PhD
Phone: +41 61 687 41 47

Karsten Kleine
Phone: +41 61 682 28 31

Nina Mählitz
Phone: +41 79 327 54 74

Nathalie Meetz
Phone: +41 79 771 05 25

Dr. Barbara von Schnurbein
Phone: +41 61 687 89 67

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