Media & Investor Release

New Vabysmo data suggest greater retinal drying versus aflibercept in nAMD and DME

- **Post-hoc analyses from four phase III studies indicate Vabysmo dried retinal fluid faster with fewer injections in neovascular or 'wet' age-related macular degeneration (nAMD) and diabetic macular edema (DME)**
- **More Vabysmo patients with nAMD had absence of retinal fluid at 12 weeks in a post-hoc analysis from the phase III TENAYA and LUCERNE studies**
- **DME patients treated with Vabysmo had less blood vessel leakage in the macula at 16 weeks in a post-hoc analysis from the phase III YOSEMITE and RHINE studies**

Basel, 25 April 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that post-hoc data indicate treatment with Vabysmo® (faricimab) led to greater and faster drying of retinal fluid with fewer injections compared to aflibercept in neovascular or 'wet' age-related macular degeneration (nAMD).[1] In diabetic macular edema (DME), post-hoc data suggest Vabysmo treatment resulted in faster drying with fewer injections as well as less blood vessel leakage in the macula, the centre of the retina, compared to aflibercept.[2,3] The analyses from the phase III TENAYA and LUCERNE (nAMD) and YOSEMITE and RHINE (DME) studies were shared at the 2023 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, held from 23-27 April in New Orleans, United States.

"Reducing retinal fluid is associated with improved vision," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "These data continue to reinforce Vabysmo's ability to dry the retina and potential to make a meaningful difference for people with vision-threatening eye conditions."

Vabysmo is the first bispecific antibody for the eye and is currently approved in 60 countries to treat nAMD and DME, with more than 800,000 Vabysmo doses distributed globally.[4] Neovascular AMD and DME are two of the leading causes of vision loss worldwide, affecting more than 40 million people.[5-8] In these conditions, blood vessel leakage can cause a build-up of fluid and swelling in the back of the eye, contributing to sight loss.[9,10]

"These findings suggest that Vabysmo may provide better stability of blood vessels in the macula," said Roger Goldberg, M.D., MBA, an ophthalmologist at Bay Area Retina Associates in Walnut Creek, California, United States, and a Vabysmo phase III study investigator. "Blood vessel stability may contribute to faster drying and extended durability."

Data on retinal drying in nAMD[1]

A post-hoc analysis of pooled data from the head-to-head dosing period (weeks 0-12) of the phase III TENAYA and LUCERNE studies in nAMD showed:*

- Vabysmo reduced retinal fluid from baseline compared to aflibercept, as measured by reduction in central subfield thickness (CST).
    - At 12 weeks, CST reductions were 145 µm in the Vabysmo arm and 133 µm in the aflibercept arm.
- A larger proportion of Vabysmo patients (77%) had absence of retinal fluid at 12 weeks versus aflibercept (67%), as measured by subretinal and intraretinal fluid (SRF and IRF).
- Absence of retinal fluid, as measured by absence of SRF and IRF observed in 75% of patients in each treatment arm, occurred at eight weeks with Vabysmo versus 12 weeks with aflibercept, corresponding to a fewer number of injections for Vabysmo patients versus aflibercept.

Data on retinal drying and blood vessel leakage in DME[2,3]

A post-hoc analysis of pooled two-year data from the phase III YOSEMITE and RHINE studies in DME compared time to fluid control between Vabysmo and aflibercept, as measured by absence of DME and absence of IRF. The analysis showed:*

- Absence of DME, defined as CST <325 µm observed in 75% of patients in each treatment arm, occurred at 20 weeks with Vabysmo versus 36 weeks with aflibercept – a difference of nearly four months.
- Absence of retinal fluid, as measured by absence of IRF observed in 50% of patients in each treatment arm, occurred more than eight months earlier in Vabysmo patients versus aflibercept.
    - Absence of IRF occurred at 48 weeks with Vabysmo versus 84 weeks with aflibercept, corresponding to a fewer number of injections for Vabysmo patients versus aflibercept.

A separate post-hoc analysis of pooled data from the head-to-head dosing period (weeks 0-16) of the YOSEMITE and RHINE studies evaluated blood vessel leakage in the macula – an important marker of vascular stability. Blood vessel leakage in the macula may lead to more retinal fluid, which can cause swelling and blurry vision.[11] Results showed:*

- The macular leakage area in Vabysmo patients was more than 50% smaller compared to aflibercept at 16 weeks.
    - Vabysmo reduced the macular leakage area to 3.6 mm^2 from baseline compared to 7.6 mm^2 with aflibercept.
- Nearly twice as many patients (28.4%) had resolution of leakage versus aflibercept (15.2%) at 16 weeks.

About the TENAYA and LUCERNE studies[12,13]

TENAYA (NCT03823287) and LUCERNE (NCT03823300) are two identical, randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of Vabysmo® (faricimab) 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 as measured by optical coherence tomography and visual acuity evaluations at weeks 20 and 24; and aflibercept 2.0 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, placebo 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 the YOSEMITE and RHINE studies[14,15]

YOSEMITE (NCT03622580) and RHINE (NCT03622593) are two identical, randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of Vabysmo® (faricimab) 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 2.0 mg administered at fixed two-month intervals after five initial monthly doses. Dosing schedule for patients within the treat-and-extend arm was determined by central subfield thickness (CST) and visual acuity. In all three arms, placebo 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 at one year, averaged over weeks 48, 52 and 56. Secondary endpoints include: 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 CST from baseline over time; and percentage of patients with absence of intraretinal fluid 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.[4] Neovascular or 'wet' AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss if left untreated.[16,17] It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis.[16] 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.[5-7]

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.[7] 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.[9,11] The number of people with DME is expected to grow as the prevalence of diabetes increases.[18]

About the Vabysmo® (faricimab) clinical development programme

Roche has a robust phase III clinical development programme for Vabysmo® (faricimab). 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).[19,20] In addition, Roche is investigating the efficacy and safety of Vabysmo in people with macular edema following retinal vein occlusion in two phase III studies, BALATON and COMINO.[21,22] 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.[23-25] Roche also supports several other independent studies to further understand retinal conditions with a high unmet need.[4]

About Vabysmo® (faricimab)

Vabysmo® (faricimab) is the first bispecific antibody approved for the eye.[26,27] It targets and inhibits two signaling pathways linked to a number of vision-threatening retinal conditions by neutralising angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A).[28,29]

Ang-2 and VEGF-A contribute to vision loss by destabilising blood vessels, causing new leaky blood vessels to form and increasing inflammation.[28,29] By blocking pathways involving Ang-2 and VEGF-A, Vabysmo is designed to stabilise blood vessels.[28,29] Vabysmo is approved in 60 countries around the world, including the United States, Japan, the United Kingdom and in the European Union for people living with neovascular or 'wet' age-related macular degeneration and diabetic macular edema.[4,26,27,30,31] Review by other regulatory authorities is ongoing.[4]

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™ (Port Delivery System with ranibizumab) 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.[32] Vabysmo® (faricimab) is the first bispecific antibody approved for the eye, which targets and inhibits two signaling pathways linked to a number of vision-threatening retinal conditions by neutralising angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A).[26-29] Lucentis®** (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions.[33]

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 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.

*P-values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the P-values.

**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.

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Roche Group 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

Karsten Kleine
Phone: +41 79 461 86 83

Nina Mählitz
Phone: +41 79 327 54 74

Dr. Barbara von Schnurbein
Phone: +41 79 699 97 44

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