Media & Investor Release

New two-year data for Roche's Vabysmo and Susvimo reinforce potential to maintain vision with fewer treatments for people with two leading causes of vision loss

- **In the YOSEMITE and RHINE studies in diabetic macular edema, at least 60% of eligible Vabysmo patients could extend treatment to every four months at two years, compared to 50% at year one**
- **Almost 80% of eligible Vabysmo patients could extend treatment to every three months or longer in both studies**
- **In the Archway study in neovascular age-related macular degeneration, 95% of Susvimo patients maintained a six-month treatment schedule at two years**

Basel, 11 February 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that new two-year data from its phase III studies of Vabysmo™ (faricimab) and Susvimo™ (previously called Port Delivery System with ranibizumab) will be presented at Angiogenesis, Exudation and Degeneration 2022 on 12 February. These longer-term results from the Vabysmo YOSEMITE and RHINE studies in diabetic macular edema (DME) and the Susvimo Archway study in neovascular or "wet" age-related macular degeneration (nAMD) further reinforce the potential to allow for longer time between treatments and fewer eye injections for people with these conditions, while still achieving and maintaining vision gains seen with previous standard-of-care injections. Neovascular AMD and DME are two leading causes of vision loss, together affecting around 40 million people worldwide, which require treatment with eye injections as often as once a month.[1-4]

"Results from these three studies reinforce the potential of Vabysmo and Susvimo to redefine standards of care and reduce treatment burden for people living with diabetic macular edema and neovascular AMD," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "These two first-of-their-kind treatments are the culmination of over a decade of pioneering research, aiming to better address the needs of people with retinal conditions."

In the YOSEMITE and RHINE studies, at least 60% of people eligible for extended dosing with Vabysmo could be treated every four months at two years – a 10 percentage point increase since the primary analyses at one year – while achieving non-inferior vision gains versus aflibercept given every two months. Furthermore, nearly 80% of people eligible for extended dosing with Vabysmo could be treated every three months or longer. In the Archway study, Susvimo allowed 95% of people to go six months between treatments at two years – the fourth complete refill-exchange interval – while maintaining vision outcomes that were non-inferior to monthly ranibizumab injections. Across all three studies, with longer follow-up, Vabysmo and Susvimo continued to be generally well-tolerated, with favourable benefit-risk profiles. Safety will continue to be monitored closely in the post-market setting.

Vabysmo™ (faricimab-svoa) is the first bispecific antibody for the eye approved by the U.S. Food and Drug Administration (FDA), and the only injectable eye medicine approved for treatments from one to four months apart in the first year following four initial monthly doses, based on evaluation of the patient's anatomy and vision outcomes.[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). 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. While additional research continues, inhibition of both pathways has been shown in preclinical studies to have potentially complementary benefits, stabilising vessels and thereby reducing vessel leakage and inflammation more than inhibition of VEGF-A alone.[4]

Susvimo is the first nAMD treatment in 15 years to provide an alternative to standard-of-care eye injections. By continuously delivering medicine into the eye through a refillable implant, Susvimo™ (ranibizumab injection) 100 mg/mL for intravitreal use via ocular implant is the only FDA-approved treatment that may help people with nAMD maintain their vision with as few as two treatments per year.[6]

Vabysmo: YOSEMITE and RHINE Two-Year Results

In the YOSEMITE and RHINE studies, DME patients received Vabysmo, given either every two months or up to every four months using a treat and extend approach, or aflibercept given every two months. Two-year results showed Vabysmo patients maintained the vision improvements achieved in the first year and vision gains continued to be non-inferior to those achieved by aflibercept patients. In YOSEMITE, the average vision gains from baseline at two years were +10.7 eye chart letters in both the Vabysmo treat and extend and two-month arms, and +11.4 letters in the aflibercept arm. In RHINE, the average vision gains from baseline at two years were +10.1 and +10.9 letters in the Vabysmo treat and extend and two-month arms, respectively, and +9.4 letters in the aflibercept arm.

Importantly, 60% (n=162/270) of Vabysmo treat and extend patients in YOSEMITE and 64.5% (n=185/287) in RHINE achieved four-month dosing at two years. This is an increase over one-year results, which showed 52.8% (n=151/286) of Vabysmo treat and extend patients in YOSEMITE and 51% (n=157/308) in RHINE achieved four-month dosing. An additional 18.1% (n=49/270) of Vabysmo treat and extend patients in YOSEMITE and 13.6% (n=39/287) in RHINE achieved three-month dosing. Combined, almost 80% of Vabysmo treat and extend patients were able to go three months or longer between treatments at the end of the second year. Across study arms, Vabysmo showed consistent two-step or better improvement in diabetic retinopathy according to the Early Treatment Diabetic Retinopathy Study – Diabetic Retinopathy Severity Score (ETDRS-DRSS). At two years, 42.8% of Vabysmo treat and extend patients in YOSEMITE and 44.3% in RHINE achieved a two-step or better improvement from baseline. In the two-month Vabysmo arms, 51.4% and 53.5% of patients in YOSEMITE and RHINE, respectively, achieved a two-step or better improvement in diabetic retinopathy

severity. Vabysmo given at intervals of up to four months continued to demonstrate greater reductions in central subfield thickness (CST) compared to aflibercept given every two months in both studies. Safety results were consistent across study arms, with no reported cases of retinal vasculitis or retinal occlusive events.

One-year results from the YOSEMITE and RHINE studies and the TENAYA and LUCERNE studies in nAMD were recently published in *The Lancet*.[4,7]

Susvimo: Archway Two-Year Results

Neovascular AMD patients in Archway received either Susvimo refilled every six months or monthly ranibizumab 0.5 mg eye injections. Two-year results showed vision was maintained by Susvimo patients and continued to be non-inferior to that achieved with monthly ranibizumab injections. Susvimo patients averaged -1.1 eye chart letters in visual acuity from baseline at two years, while monthly ranibizumab patients averaged -0.5 letters from baseline. In addition, 95% of Susvimo patients were able to go six months without needing additional treatment in the second, third and fourth refill-exchange intervals. In Archway, Susvimo was generally well-tolerated, with a favourable benefit-risk profile. The most common adverse events of special interest (≥5%) were cataract, conjunctival bleb and vitreous haemorrhage. The safety profile of Susvimo in the clinical trial setting is well understood and will continue to be monitored closely.

In addition to Archway results, two-year interim data from the ongoing phase III Portal study will be presented at the Angiogenesis meeting. Portal is an extension study evaluating the long-term safety and efficacy of Susvimo in nAMD.

Vabysmo is approved by the FDA for the treatment of nAMD and DME.[5] Susvimo is approved by the FDA for the treatment of people with nAMD who have previously responded to at least two anti-VEGF injections.[6] Vabysmo is currently under review by the European Medicines Agency for the treatment of nAMD and DME and Susvimo is under review for the treatment of nAMD. Submissions to other regulatory authorities around the world are ongoing.

Roche has a robust phase III clinical development programme for Vabysmo and Susvimo. 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.[8,9] 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.[10,11]

For Susvimo, the clinical development programme includes the Portal, Pagoda, Pavilion and Velodrome studies.[12-15] Portal is an extension study evaluating the long-term safety and efficacy of Susvimo in nAMD.[12] Pagoda is evaluating Susvimo for the treatment of DME, while

Pavilion is a study of Susvimo in diabetic retinopathy without DME.[13,14] Velodrome is evaluating Susvimo refilled every nine months in nAMD.[15]

About the YOSEMITE and RHINE studies[7]

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 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, 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 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 the Archway study[16]

Archway (NCT03677934) was a randomised, multicentre, open-label phase III study evaluating the efficacy and safety of Susvimo™ (previously called Port Delivery System with ranibizumab), refilled every six months at fixed intervals, compared to monthly intravitreal injections of ranibizumab 0.5 mg in 415 people living with neovascular or “wet” age-related macular degeneration. Patients enrolled in Archway were responders to prior treatment with anti-vascular endothelial growth factor (VEGF) therapy. In both study arms, patients were treated with at least three anti-VEGF injections within the six months prior to their Archway screening visit. The primary endpoint of the study was the change in best-corrected visual acuity (BCVA) score from baseline at the average of Week 36 and Week 40. Secondary endpoints include safety, overall change in vision (BCVA) from baseline and change from baseline in centre point thickness 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.[1] Neovascular or "wet" AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss.[17,18] It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis.[18] 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.[1,2,19]

About diabetic macular edema

Affecting around 21 million people globally, diabetic macular edema (DME) is a vision-threatening condition associated with blindness and decreased quality of life when left untreated.[3,20] DME occurs when the 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.[21,22] The number of people with DME is expected to grow as the prevalence of diabetes increases.[23] There remains a significant unmet need for more effective, longer-lasting therapies for people with DME.[7]

About Vabysmo™ (faricimab)

Vabysmo™ (faricimab) is the first bispecific antibody designed 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 both pathways involving Ang-2 and VEGF-A, Vabysmo is designed to stabilise blood vessels.[4]

About Susvimo™ (previously called Port Delivery System with ranibizumab)

Susvimo™ (previously called Port Delivery System with ranibizumab) is a refillable eye implant surgically inserted into the eye during a one-time, outpatient procedure. Susvimo continuously delivers a customised formulation of ranibizumab over time. Susvimo is indicated for intravitreal use via the Susvimo eye implant only. Ranibizumab is a vascular endothelial growth factor (VEGF) inhibitor designed to bind to and inhibit VEGF-A, a protein that has been shown to play a critical role in the formation of new blood vessels and the leakiness of the vessels.[6]

Susvimo is different from the ranibizumab intravitreal injection, a medicine marketed as Lucentis®* (ranibizumab injection), which is approved to treat nAMD and other retinal diseases. Lucentis* was first approved for nAMD by the FDA in 2006.[24]

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 (FDA)-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.[6] Vabysmo™ (faricimab-svoa) is the first FDA-approved bispecific antibody for the eye, which targets two distinct pathways that drive retinal conditions.[5] Lucentis®* (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions.[24]

About Roche

Founded in1896 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.

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