Media & Investor Release

The Lancet publishes studies showing Roche's faricimab improved and maintained vision in two leading causes of vision loss, extending time between treatments up to four months

- **Two papers in The Lancet highlight one-year results from Roche's phase III trials evaluating faricimab in neovascular or "wet" age-related macular (nAMD) and diabetic macular edema (DME)**
- **Across four studies, about half of eligible faricimab patients were able to go four months between treatments, and approximately three-quarters could be treated every three months or longer**
- **Reductions in central subfield thickness (CST) and resolution of intraretinal fluid consistently favoured faricimab over aflibercept in DME, and meaningful and comparable CST reductions were seen in nAMD in the first year**

Basel, 24 January 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that The Lancet has published two papers highlighting one-year results from four pivotal phase III studies of faricimab, an investigational bispecific antibody, in neovascular or "wet" age-related macular degeneration (nAMD) and diabetic macular edema (DME). [1,2] All four studies – which enrolled more than 3,000 people in total – met their primary endpoints, showing that people treated with faricimab up to every four months achieved non-inferior vision gains compared to aflibercept given every two months. Notably, about half of eligible faricimab patients were able to go four months between treatments in the first year, and approximately three-quarters could go three months or longer in the TENAYA and LUCERNE nAMD studies and the YOSEMITE and RHINE DME studies. [1,2] The current standard of care for these potentially blinding conditions requires eye injections as often as once a month [3,4].

"These data published in The Lancet reinforce the potential of faricimab as an important treatment option that may help improve and maintain vision while extending the time between treatments up to four months," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We remain deeply committed to developing new medicines such as faricimab that may help preserve sight in many people living with serious retinal conditions."

If approved, faricimab would be the first bispecific antibody for the eye, targeting and inhibiting two distinct pathways linked to a number of vision-threatening retinal conditions by neutralising angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A). [5] Inhibition of both pathways has been shown to have potentially complementary benefits, stabilising vessels and thereby reducing vessel leakage and inflammation more than

inhibition of the VEGF-A pathway alone. [6]

Key Findings [1,2]
In the TENAYA and LUCERNE studies in nAMD, the average vision gains from baseline at one-year in the faricimab arms were +5.8 and +6.6 letters, respectively, compared to +5.1 and +6.6 letters in the aflibercept arms. The studies also measured the proportion of people in the faricimab arm that were treated on dosing schedules of every three or four months during the first year. Importantly, 46% (n=144/315) of patients in TENAYA and 45% (n=142/316) in LUCERNE were able to be treated every four months in the first year. An additional 34% (n=107/315) of patients in TENAYA and 33% (n=104/316) in LUCERNE were able to be treated every three months. Combined, nearly 80% of faricimab-treated patients were able to go three months or longer between treatments during the first year. Consistent with vision outcomes, faricimab treatment resulted in a meaningful and comparable reduction in central subfield thickness (CST) and comparable decreases in choroidal neovascularisation lesion size and area. Faricimab was generally well-tolerated in both studies, with a favourable benefit-risk profile. Ocular adverse events (AEs) were comparable across treatment arms and consistent with those expected with intravitreal anti-VEGF injections in patients with nAMD.

In the YOSEMITE and RHINE studies in DME, the average vision gains from baseline at one-year were +11.6 and +10.8 eye chart letters in the faricimab treat-and-extend arms, +10.7 and +11.8 letters in the two-month arms and +10.9 and +10.3 letters in the aflibercept arms, respectively. A secondary endpoint in both studies measured the proportion of people in the faricimab treat-and-extend arms that achieved dosing schedules of every three or four months at the end of the first year. Importantly, 53% (n=151/286) of faricimab treat-and-extend patients in YOSEMITE and 51% (n=157/308) in RHINE achieved four-month dosing at one-year. An additional 21% (n=60/286) of faricimab treat-and-extend patients in YOSEMITE and 20% (n=62/308) in RHINE achieved three-month dosing. Combined, more than 70% of faricimab treat-and-extend patients were able to go three months or longer between treatments at the end of the first year. Reductions in CST and resolution of intraretinal fluid through the first year consistently favoured faricimab over aflibercept. Faricimab was generally well-tolerated in both studies, with a favourable benefit-risk profile. Ocular AEs were comparable across treatment arms and consistent with those expected with intravitreal anti-VEGF injections in patients with DME.

Faricimab is currently under review by the U.S. Food and Drug Administration for the treatment of nAMD and DME. The European Medicines Agency is also currently evaluating the faricimab Marketing Authorisation Application for the treatment of nAMD and DME. Additionally, the COMINO and BALATON trials are underway, evaluating the efficacy and safety of faricimab in people with macular edema following retinal vein occlusion. [7,8]

Two-year results for faricimab in DME will be presented at the Angiogenesis, Exudation, and

Degeneration 2022 meeting, on Saturday 12 February.

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 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: faricimab 6.0 mg administered at fixed intervals of every two, three, or four months, selected based on objective assessment of disease activity at weeks 20 and 24; aflibercept 2.0 mg administered at fixed two-month intervals. 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 faricimab 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; change in central subfield thickness from baseline over time; and change in total area of choroidal neovascularization lesion and leakage from baseline over time.

About the YOSEMITE and RHINE studies [2]

YOSEMITE (NCT03622580) and RHINE (NCT03622593) are two identical, randomised, multicentre, double-masked, global phase III studies evaluating the efficacy and safety of 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: faricimab 6.0 mg administered at intervals of up to every four months using a treat and extend approach, after four initial monthly doses; faricimab 6.0 mg administered at fixed two-month intervals after six initial monthly doses; and aflibercept administered at fixed two-month intervals after five initial monthly doses. 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 from baseline at one-year. Secondary endpoints include: safety; the percentage of participants in the treat and extend arm receiving faricimab 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 central subfield thickness 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. [9,10] Neovascular or "wet" AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss. [11,12] It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis. [12] 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. [9,13,14]

About diabetic macular edema

Affecting around 21 million people globally, diabetic macular edema (DME) is a vision-threatening complication of diabetic retinopathy (DR). [15] 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. [10,16] The number of people with DME is expected to grow as the prevalence of diabetes increases. [17] The condition is associated with blindness when left untreated and decreased quality of life. [18] There remains a significant unmet need for more effective, longer-lasting therapies for people with DME. [6]

About faricimab [5]

Faricimab is the first investigational bispecific antibody designed for the eye. It targets two distinct 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, faricimab is designed to stabilise blood vessels, potentially improving vision outcomes for longer for people living with retinal conditions.

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, covering early- and late-stage products, which is led by science and informed by insights from people with eye diseases. Our late-stage pipeline includes faricimab, a potential first-of-a-kind treatment being evaluated in a number of retinal conditions including neovascular or "wet" age-related macular

degeneration (nAMD), diabetic macular edema and diabetic retinopathy. Faricimab is the first investigational bispecific antibody designed for the eye. It targets two distinct pathways – via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) – linked to a number of vision threatening retinal conditions, to stabilise blood vessels, potentially improving vision outcomes for longer. [5] 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 two breakthrough ophthalmic treatments to people living with vision loss. SusvimoTM (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 nAMD that continuously delivers a customised formulation of ranibizumab over a period of months. Lucentis®* (ranibizumab injection) is the first treatment approved to improve vision in people with certain retinal conditions. [3,19]

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. In recent years, the company has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the thirteenth consecutive year, Roche has been recognised as one of the most sustainable companies in the pharmaceutical industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 billion. 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.

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

References

[1] 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.
[2] Wykoff 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; https://doi.org/10.1016/S0140-6736(22)00018-6.
[3] FDA. Highlights of prescribing information, Lucentis. 2012 [Internet; cited January 2022]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125156s0069s0076lbl.pdf.
[4] FDA. Highlights of prescribing information, Eylea. 2011 [Internet; cited January 2022]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/125387lbl.pdf.
[5] Sharma, et al. Faricimab phase 3 DME trial significance of personalized treatment intervals (PTI) regime for future DME trials. Eye. 2021; https://doi.org/10.1038/s41433-021-01831-4.
[6] Heier JS, et al. The Angiopoietin/Tie pathway in retinal vascular diseases: a review. Retina-J Ret Vit Dis. 2021;41:1-19.
[7] ClinicalTrials.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 January 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740931.
[8] ClinicalTrials.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 January 2022]. Available from: https://clinicaltrials.gov/ct2/show/NCT04740905.
[9] Bright Focus Foundation. Age-Related Macular Degeneration: Facts & Figures. [Internet; cited January 2022]. Available from: https://www.brightfocus.org/macular/article/age-related-macular-facts-figures.
[10] All About Vision. Macula Lutea. [Internet; cited January 2022]. Available from: https://www.allaboutvision.com/resources/macula.
[11] 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.
[12] 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.
[13] 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.
[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] Yau JWY, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35:556-64.
[16] National Eye Institute. Facts about diabetic eye disease [Internet; cited January 2022]. Available from: https://nei.nih.gov/health/diabetic/retinopathy.
[17] Liu E, et al. Diabetic macular oedema: clinical risk factors and emerging genetic influences. Clin Exp Optom. 2017;100:569-76.
[18] Park SJ, et al. Extent of exacerbation of chronic health conditions by visual impairment in terms of health-related quality of life. JAMA Ophthalmol. 2015;133:1267-75.
[19] FDA. Highlights of prescribing information, Susvimo. 2021 [Internet; cited January 2022]. Available from: https://www.gene.com/download/pdf/susvimo_prescribing.pdf

Roche Group Media Relations

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

Dr. Nicolas Dunant
Phone: +41 61 687 05 17

Sileia Urech
Phone: +41 79 935 81 48

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

Karsten Kleine
Phone: +41 61 682 28 31

Nina Mählitz
Phone: +41 79 327 54 74

Nathalie Meetz
Phone: +41 61 687 43 05

Roche Investor Relations

Dr. Karl Mahler
Phone: +41 61 68-78503
e-mail: karl.mahler@roche.com

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. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com