FDA accepts application for Roche's faricimab for the treatment of neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME)

- **Across four phase III studies, approximately half of patients receiving faricimab could extend treatment time to every four months – the first time this level of durability has been achieved in phase III nAMD and DME studies**
- **If approved, faricimab would be the first and only medicine designed to target two distinct pathways that drive retinal diseases that can cause vision loss**
- **The European Medicines Agency has also validated the faricimab Marketing Authorisation Application submission in nAMD and DME**

Basel, 29 July 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has accepted the company's Biologics License Application (BLA), under Priority Review, for faricimab for the treatment of neovascular or "wet" age-related macular degeneration (nAMD) and diabetic macular edema (DME). The FDA has also accepted the company's submission for diabetic retinopathy.

Faricimab will be the first and only bispecific antibody designed for the eye, if approved. It targets two distinct pathways – via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) – that drive a number of retinal conditions that can cause vision loss.[1]

"If approved, faricimab would be the first in a new class of eye medicines targeting two key pathways that drive retinal disorders, with the potential to offer durable vision outcomes with fewer eye injections than the current standard of care," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Therefore, we hope faricimab will become a new treatment option for millions of people living with nAMD and DME."

Neovascular AMD and DME are two leading causes of vision loss among adults worldwide.[2] The BLA submission is based on positive results across four phase III studies in nAMD and DME. The studies consistently showed that faricimab, given at intervals of up to four months, offered non-inferior vision gains compared with aflibercept, given every two months. Approximately half of people eligible for extended dosing with faricimab were able to be treated every four months in the first year in the TENAYA and LUCERNE studies in nAMD and the YOSEMITE and RHINE studies in DME. Faricimab is the first injectable eye medicine to achieve this length of time between treatments in phase III studies for nAMD and DME. Furthermore, approximately three-quarters of people eligible for extended dosing with faricimab were able to be treated every three months or longer in the first year. Faricimab was generally well-tolerated in all four studies, with no new or unexpected safety signals identified.[3,4]

Roche also has long-term extension studies underway for faricimab. These include AVONELLE X, an extension study of TENAYA and LUCERNE evaluating the long-term safety and efficacy of faricimab in

nAMD, and RHONE X, an extension study of YOSEMITE and RHINE evaluating the long-term safety and efficacy of faricimab in DME.[5,6] Additionally, the COMINO and BALATON trials are also underway, evaluating the efficacy and safety of faricimab in people with macular edema secondary to two types of retinal vein occlusion (RVO): central RVO and branch RVO.[7,8]

The European Medicines Agency has also validated the faricimab Marketing Authorisation Application for the treatment of nAMD and DME.

About the TENAYA and LUCERNE Studies[3]
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 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; and 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 through week 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; and change in central subfield thickness (CST) from baseline over time.

Both studies met their primary endpoint, with faricimab consistently shown to offer non-inferior visual acuity gains to aflibercept. In TENAYA and LUCERNE, the average vision gains from baseline 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. In both studies, faricimab given at intervals of up to four months offered reductions in CST comparable to aflibercept given every two months. Faricimab was generally well-tolerated in both studies, with no new or unexpected safety signals identified.

About the YOSEMITE and RHINE Studies[4]
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 personalised treatment intervals (PTI) of up to four months; faricimab 6.0 mg administered at fixed two-month intervals; and aflibercept 2.0 mg administered at fixed two-month intervals. 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 personalised dosing arm receiving treatment 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 and change in central subfield thickness (CST) from baseline over time.

Both studies met their primary endpoint with faricimab consistently shown to offer non-inferior visual acuity gains to aflibercept. In YOSEMITE, the average vision gains from baseline were +11.6 and +10.7 eye chart letters in the faricimab PTI and two-month arms, respectively, and +10.9 letters in the aflibercept arm. In RHINE, the average vision gains from baseline were +10.8 and +11.8 letters in the faricimab PTI and two-month arms, respectively, and +10.3 letters in the aflibercept arm.

A secondary endpoint in both studies measured the proportion of people in the faricimab PTI arm that achieved dosing schedules of every three or four months at the end of the first year. Importantly, 53% (n=151/286) of faricimab PTI 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 PTI patients in YOSEMITE and 20% (n=62/308) in RHINE achieved three-month dosing. Combined, more than 70% of faricimab PTI patients were able to go three months or longer between treatments at the end of the first year. In both studies, faricimab given at intervals of up to four months demonstrated greater reductions in CST compared to aflibercept given every two months. Faricimab was generally well-tolerated in both studies, with no new or unexpected safety signals identified.

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] Neovascular or "wet" AMD (nAMD) is an advanced form of the disease that can cause rapid and severe vision loss.[10] It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis.[11] 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.[9,12,13]

About diabetic macular edema
Affecting around 21 million people globally, diabetic macular edema (DME) is a vision-threatening complication of diabetic retinopathy (DR).[14] DR occurs when damage to blood vessels and the formation of new blood vessels cause blood and/or fluid to leak into the retina – a part of the eye that sends information to the brain, enabling sight.[15] This leads to swelling, as well as blockage of blood supply to some areas of the retina.[16] 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.[15,17] The number of people with DME is expected to grow as the prevalence of diabetes increases.[18] The condition is associated with blindness when left untreated and decreased quality of life.[19] There remains a significant unmet need for more effective, longer-lasting therapies for people with DME.[2]

About faricimab
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) – that drive a number of retinal conditions.[1] Ang-2 and VEGF-A contribute to vision loss by destabilising blood vessels, causing new leaky blood vessels to form and increasing inflammation.[2] By simultaneously 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.[2]

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 two potential first-of-a-kind treatments, Port Delivery System with ranibizumab (PDS) and faricimab, which are being evaluated in a number of retinal conditions including neovascular age-related macular degeneration, diabetic macular edema and diabetic retinopathy. PDS is an investigational, permanent refillable eye implant that continuously delivers a customised formulation of ranibizumab over a period of months, potentially reducing the treatment burden associated with frequent eye injections.[20] Faricimab is the first investigational bispecific antibody designed for the eye.[1] It targets two distinct pathways – via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) – that drive a number of retinal conditions, to stabilise blood vessels, potentially improving vision outcomes for longer.[1,2] Our early stage 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 through Lucentis®* (ranibizumab injection), the first treatment approved to improve vision in people with certain retinal conditions.

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, Roche 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 twelfth consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals 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.

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