FDA accepts application for Roche's Port Delivery System with ranibizumab (PDS) for treatment of neovascular or "wet" age-related macular degeneration (nAMD)

- **If approved, PDS would be the first and only eye implant with continuous drug delivery that offers people living with nAMD an alternative to frequent eye injections**
- **A pivotal study showed PDS extends time between treatments up to six months for more than 98% of patients and provides vision outcomes equivalent to monthly ranibizumab injections**
- **The European Medicines Agency has also validated the PDS Marketing Authorisation Application in nAMD**

Basel, 24 June 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 Port Delivery System with ranibizumab (PDS) for the treatment of neovascular or "wet" age-related macular degeneration (nAMD). Neovascular AMD is a leading cause of blindness for people aged 60 and over and impacts approximately 20 million people worldwide.[1,2,3] If approved, PDS would be a first-of-its-kind therapeutic approach, offering people living with nAMD an alternative to frequent eye injections of anti-vascular endothelial growth factor (VEGF), the current standard of care.[4] The FDA is expected to make a decision on approval by 23 October 2021.

"Anti-VEGF therapy brings significant benefit to people with nAMD, but optimal results require frequent trips to the doctor's office for eye injections. This burden leaves many people under-treated and susceptible to vision loss," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "If approved, PDS would transform nAMD treatment by providing up to six months of uninterrupted therapy that could potentially improve vision outcomes compared to what is currently achieved in the clinic."

PDS is a permanent refillable eye implant, approximately the size of a grain of rice, designed to continuously deliver a customised formulation of ranibizumab over a period of months, potentially reducing the treatment burden associated with frequent eye injections.[4,5]

The BLA submission is based on positive results from the phase III Archway study primary analysis, which showed that of those nAMD patients being treated with PDS, more than 98% were able to go six months without needing additional treatment prior to the refill-exchange. In addition, these patients achieved vision outcomes equivalent to patients receiving monthly ranibizumab eye injections. In the study, PDS was generally well-tolerated, with a favourable benefit-risk profile. The safety profile of PDS in the clinical trial setting is well understood and will continue to be closely monitored. If approved, PDS would be the first and only nAMD therapy indicated to allow six months between treatments.[4,6]

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Roche has a robust phase III clinical development programme underway for PDS, including the Portal, Pagoda and Pavilion studies. Portal is an extension study evaluating the long-term safety and efficacy of PDS in nAMD.[7] Pagoda is evaluating PDS for the treatment of diabetic macular edema (DME),[8] while Pavilion is a study of PDS in diabetic retinopathy without DME.[9] Both the Pagoda and Pavilion trials are actively recruiting participants.[8,9]

The PDS Marketing Authorisation Application has also been validated by the European Medicines Agency and is currently under review.

About the Archway Study[4,6,10]

Archway (NCT03677934) is a randomised, multicentre, open-label phase III study evaluating the efficacy and safety of Port Delivery System with ranibizumab (PDS), refilled every six months at fixed intervals, compared to monthly intravitreal injections of ranibizumab 0.5 mg in 418 people living with neovascular age-related macular degeneration (nAMD). 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 is the 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 the average of Week 36 and Week 40. Secondary endpoints include safety, overall change in BCVA from baseline and change from baseline in center point thickness over time.

According to pre-specified study criteria, PDS was shown to be non-inferior and equivalent to monthly ranibizumab injections. On average, patients had received five prior ranibizumab injections before their first Archway visit. In the PDS arm of the study, patients gained an average of 0.2 eye chart letters in visual acuity from baseline compared with 0.5 eye chart letters for the monthly ranibizumab arm. During the first treatment interval, before the first scheduled refill, 1.6% of PDS patients assessed (n=4/246) received supplemental treatment, and 98.4% of patients (n=242/246) did not receive supplemental treatment.

In addition, PDS controlled retinal thickness as effectively as monthly ranibizumab, with patients in both arms achieving a mean change in center point thickness within 10 µm from baseline at Week 36. In the study, PDS was generally well-tolerated, with a favourable benefit-risk profile. The safety profile of PDS in the clinical trial setting is well understood and will continue to be closely monitored.

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] 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.[1,2,3]

About Port Delivery System with ranibizumab (PDS)
PDS is a permanent refillable eye implant, approximately the size of a grain of rice, which is designed to continuously release a customised formulation of ranibizumab into the eye over time.[4] Ranibizumab is a vascular endothelial growth factor (VEGF) inhibitor designed to bind to and inhibit VEGF-A, a protein that is believed to play a critical role in the formation of new blood vessels and the leakiness of the vessels.[13] PDS contains a customised formulation of ranibizumab not approved by regulatory authorities. It is different from the ranibizumab intravitreal injection, a medicine marketed as Lucentis® (ranibizumab injection), which is approved to treat neovascular age-related macular degeneration (nAMD) and other retinal diseases.[14]

By maintaining therapeutic drug concentration levels of ranibizumab with two refills per year, PDS may offer greater outcomes certainty in terms of vision gains and maintaining those gains for people living with retinal diseases, including nAMD.[6] Additionally, by decreasing the need for frequent injections and physician visits, PDS may reduce the burden of treatment associated with standard anti-VEGF treatments.[4,5]

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. 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, to stabilise blood vessels, potentially improving vision outcomes for longer. 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.

*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. In May 2019, Roche acquired exclusive rights from Novartis to develop, manufacture, and commercialise ranibizumab in the PDS platform ex-US.

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