

New STAIRWAY study data shows potential for extended durability with Roche's faricimab in neovascular age-related macular degeneration (nAMD)

- **Faricimab – the first bispecific antibody designed for the eye – dosed every four months demonstrated sustained vision outcomes compared to monthly ranibizumab for people with nAMD ^[1]**
- **Further phase II data for the Port Delivery System with ranibizumab (PDS), dosed every six months or longer, show vision and anatomical outcomes in nAMD that are comparable to ranibizumab dosed every four weeks ^[2]**
- **Lowering the treatment burden in nAMD, through novel mechanisms and long acting delivery systems, has the potential to address under-treatment and improve patient outcomes**
- **Global phase III studies in Roche's ophthalmology portfolio have commenced – two for faricimab in diabetic macular edema (DME), and one for the PDS in nAMD**

Basel, 29 October 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the phase II STAIRWAY study which explored the extended durability of faricimab (RG7716) in the treatment of neovascular ("wet") age-related macular degeneration (nAMD), a leading cause of blindness globally in people aged 60 and over. ^[3] At 52 weeks, faricimab patients dosed either every 16 weeks or every 12 weeks demonstrated sustained vision outcomes comparable to ranibizumab dosed every four weeks. Results of the study were presented as a late-breaking oral presentation during the 2018 American Academy of Ophthalmology's (AAO) Annual Meeting in Chicago, Illinois, United States. ^[1]

"Because current anti-VEGF monotherapies for neovascular AMD are burdensome, requiring frequent clinic visits for eye injections, some people are under-treated and experience subsequent declining vision over time," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "The STAIRWAY data show the potential of faricimab to allow fewer injections while achieving and sustaining the same visual gains seen with a current standard of care. Based on these data, we will be initiating a global phase III programme for faricimab in neovascular AMD."

STAIRWAY is a 52 week study that assessed two extended dosing regimens of faricimab 6.0mg given every 16 weeks or every 12 weeks, compared to ranibizumab 0.5 mg every four weeks. At week 24 (three months after the last of four loading doses), patients randomised to faricimab every 16 weeks switched to 12-week dosing if they were shown to have active disease, per pre-defined criteria. At week 24, 65% (n=36/55) of people treated with faricimab had no active disease, highlighting the potential of 16 week dosing in nearly two-thirds of patients. Initial vision gains, as measured by Best Corrected Visual Acuity (BCVA), were fully maintained through to week 52 with both 16 and 12 week dosing regimens. People treated with faricimab dosed every 16 weeks experienced a mean improvement of 11.4 letters from baseline, compared to 10.1 letters in patients treated with faricimab dosed every 12 weeks, and 9.6 letters in patients treated with 0.5 mg ranibizumab dosed every four weeks. The three treatment regimens were similar in both the proportion of

patients gaining more than 15 letters and avoiding a loss of more than 15 letters. Comparable reductions in central retina thickness were also observed in people treated with both dosing intervals of faricimab and those treated with ranibizumab. ^[1] Faricimab was well tolerated with no new safety signals observed. ^[1]

In addition, data on the investigational Port Delivery System with ranibizumab (PDS) in patients with nAMD were also presented at the AAO Annual Meeting, comprising further data from the phase II Ladder study, and the trial design of the phase III Archway study. ^[2] The small, refillable eye implant, which is slightly longer than a grain of rice, is designed to allow most people with nAMD to go six months without needing a refill.

Topline results presented earlier this year showed the majority of PDS patients – including approximately 80% of patients in the high-dose PDS group – went six months or longer between the implantation and the first required refill of the device. Importantly, patients in the high-dose PDS group achieved similar visual outcomes as 0.5 mg ranibizumab dosed every four weeks. ^[4] Based on data from the phase II Ladder programme, the pivotal phase III Archway clinical trial and the Portal open label extension study were initiated in September 2018. These studies will evaluate the efficacy and safety of PDS with ranibizumab 100 mg/ml concentration in patients with nAMD at a fixed dosing interval of 24 weeks. ^[5;6]

Faricimab and the PDS are the two most advanced investigational treatments in Roche's robust ophthalmology pipeline. In addition to Archway, two pivotal phase III studies for faricimab are currently open and enrolling: RHINE and YOSEMITE. These two studies are designed to investigate the efficacy and safety of faricimab compared with aflibercept in people with diabetic macular edema (DME). ^[7;8] Based on STAIRWAY, a global phase III programme for faricimab in nAMD is anticipated to commence in 2019.

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About Neovascular (“wet”) Age-Related Macular Degeneration

AMD is a disease that impacts the part of the eye that provides sharp, central vision needed for activities like reading. ^[3] Neovascular AMD is an advanced form of the disease that can cause rapid and severe vision loss and affects 17 million people worldwide. ^[9;10] It is caused by the growth of abnormal blood vessels, also referred to as choroidal neovascularization (CNV), into the macula. These vessels leak fluid and blood and cause scar tissue that destroys the central retina. This process results in a deterioration of sight over a period of months to years.

Current standards of care for nAMD target vascular endothelial growth factor (VEGF) alone, which effectively addresses vessel permeability but only partially addresses the inflammatory component of the disease. Furthermore, people receiving anti-VEGF therapy may need as often as monthly eye injections, a burden that can lead to under-treatment of nAMD and, potentially, less than optimal vision outcomes. ^[11;12] There is a significant unmet need for efficacious, longer-lasting therapies for people with this condition.

About STAIRWAY and faricimab

Faricimab is the first bispecific antibody designed specifically for intravitreal use to simultaneously bind to and neutralise both angiopoietin-2 (Ang-2) and VEGF-A with high potency and specificity. In nAMD, Ang-2 works synergistically with VEGF to drive pathologic blood vessel permeability and destabilisation, abnormal blood vessel growth and fluid leakage, which contribute to vision loss. Ang-2 also plays an important role in multiple aspects of inflammation in nAMD. ^[13;14]

STAIRWAY is a phase II, multicentre, randomised, comparator-controlled, parallel group clinical trial investigating the efficacy, safety and pharmacokinetics of faricimab administered with extended dosing regimens in 76 treatment-naïve people with nAMD. ^[1]

About Ladder, Archway and the investigational PDS

The investigational PDS is a small, refillable device, slightly longer than a grain of rice, surgically implanted in the eye during a procedure performed under local anaesthesia. The PDS is uniquely designed to continuously deliver a specialised formulation of ranibizumab over time. The 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 nAMD and other retinal diseases.

Ladder is a phase II, multicentre, randomised, interventional, active treatment-controlled study designed to evaluate the efficacy and safety of the PDS in people with nAMD who have previously responded to treatment with anti-VEGF therapies. ^[3]

Archway will evaluate the efficacy and safety of the PDS in patients with nAMD at a fixed dosing interval of 24 weeks. ^[5] In the trial, patients will be randomised into one of two arms: Arm A will receive the PDS 100 mg/mL and refills at fixed 24-week intervals; Arm B will receive monthly intravitreal injections of ranibizumab 0.5 mg. The primary endpoint of Archway is the change from baseline in BCVA at weeks 36 and 40. Additional data analyses of the Ladder study are ongoing and will be presented at future medical meetings.

About Roche in ophthalmology

Roche is committed to developing pioneering, transformative therapies for people living with a range of eye diseases that cause significant visual impairment and blindness, including nAMD, DME, diabetic retinopathy (DR), geographic atrophy (GA) and other retinal diseases. Roche is also investigating innovative platforms for sustained ocular drug delivery, including the PDS.

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.

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 under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

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. 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. 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 tenth consecutive year, Roche has been recognised as the most sustainable company 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 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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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References

- [1] Khanani AM, et al. Simultaneous Inhibition of VEGF and Ang-2 with Faricimab in Neovascular AMD: STAIRWAY Phase 2 Results. Presented at the 2018 American Academy of Ophthalmologists (AAO) Annual Meeting; 2018 Oct 26; Chicago, United States.
- [2] Pieramici D, et al. Port Delivery System With Ranibizumab (PDS): From Dose Ranging in Ladder Phase 2 to Archway Phase 3 Study Design. Presented at the 2018 American Academy of Ophthalmologists (AAO) Annual Meeting; 2018 Oct 27; Chicago, United States.
- [3] National Institutes of Health Medline Plus. Leading causes of blindness. [Internet; cited 2018 October]. Available from: <https://medlineplus.gov/magazine/issues/summer08/articles/summer08pg14-15.html>.
- [4] Awh C, et al. Ladder trial of the Port Delivery System for ranibizumab: Initial study results. Presented at the 36th Annual Meeting of the American Society of Retina Specialists (ASRS); 2018 Jul 20-25; Vancouver, British Columbia, Canada.
- [5] ClinicalTrials.gov. A Phase III Study to Evaluate the Port Delivery System Implant With Ranibizumab Compared With Monthly Ranibizumab Injections in Participants With Wet Age-Related Macular Degeneration (Archway). [Internet; cited 2018 October]. Available from: <https://clinicaltrials.gov/ct2/show/study/NCT03677934>.
- [6] ClinicalTrials.gov. Extension Study for the Port Delivery System With Ranibizumab (Portal). [Internet; cited 2018 October]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03683251>.
- [7] ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of RO6867461 in Participants With Diabetic Macular Edema (RHINE). [Internet; cited 2018 October]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03622593>.
- [8] ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of RO6867461 in Participants With Diabetic Macular Edema (YOSEMITE). [Internet; cited 2018 October]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03622580>.
- [9] Pennington KL, DeAngelis MM. Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors. *Eye and Vision*. 2016; 3:34.
- [10] Bright Focus Foundation. Age-related macular degeneration: facts & figures. [Internet; cited 2018 October]. Available from: <https://www.brightfocus.org/macular/article/age-related-macular-facts-figures>.

- [11] Holz FG, Tadayoni R, Beatty S, et al. Multi-country real-life experience of anti-vascular endothelial growth factor therapy for wet age-related macular degeneration. *British Journal of Ophthalmology*. 2015; 99:220-226.
- [12] Rao P, Lum F, et al. Real-world vision in age-related macular degeneration patients treated with single anti-VEGF drug type for 1 year in the IRIS registry. *Ophthalmology*. 2018; 125: 522-528.
- [13] Chakravarthy U BC, Brown D, Campochiaro P, et al. Phase 1 trial of anti-vascular endothelial growth factor/antiangiopoietin 2 bispecific antibody RG7716 for neovascular age-related macular degeneration. *Ophthalmology Retina* 2017; 1: 474-485
- [14] Rangasamy S, Srinivasan R, Maestas J, et al. A potential role for angiopoietin 2 in the regulation of the blood-retinal barrier in diabetic retinopathy. *Invest Ophthalmol Vis Sci* 2011; 52:3784-3791

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