Phase II data support potential for Roche’s novel anti-VEGF/anti-angiopoietin-2 bispecific antibody, RG7716, for people with diabetic macular edema

- RG7716 is the first bispecific antibody designed specifically for the treatment of retinal eye diseases
- RG7716 demonstrated clinically meaningful visual acuity gains from baseline, and statistically significant improvements in visual acuity compared with ranibizumab
- Key secondary and exploratory anatomical outcomes were supportive of the primary outcome
- Phase III programme will be discussed with health authorities following data assessment from Phase II studies

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced encouraging results from the Phase II BOULEVARD study. In people with vision loss from diabetic macular edema (DME), treatment with intravitreal RG7716 resulted in clinically meaningful and statistically significant improvements in visual acuity gains compared with ranibizumab alone. Key secondary and exploratory anatomical outcomes – reduction of central retina thickness and improvements in diabetic retinopathy severity scores – were supportive of the primary outcome. RG7716 is the first bispecific, monoclonal antibody specifically designed for the eye that simultaneously binds to and inactivates vascular endothelial growth factor A (VEGF-A) and angiopoietin-2 (Ang-2). These data were presented at Angiogenesis, Exudation, and Degeneration 2018, a medical symposium presented by Bascom Palmer Eye Institute of the University of Miami Miller School of Medicine, part of the University of Miami Health System.¹

“For the first time in diabetic macular edema, a clinically meaningful and statistically significant improvement in visual acuity compared to anti-VEGF alone has been demonstrated by simultaneously neutralising both angiopoietin-2 and VEGF-A with a bispecific antibody,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. “These Phase II results show the potential of RG7716 for people living with diabetic macular edema, a leading cause of vision loss in working-age adults.
There remains a significant unmet medical need for more efficacious and longer lasting therapies for diabetic macular edema.”

BOULEVARD assessed two doses of RG7716 (1.5mg and 6mg) versus ranibizumab standard of care (0.3mg) given as monthly intravitreal injections. The study met its primary endpoint, demonstrating a significant improvement in adjusted Best Corrected Visual Acuity (BCVA) at week 24 for RG7716 versus ranibizumab in treatment-naïve patients: 6mg RG7716 resulted in an adjusted mean improvement of 13.9 chart letters from baseline, compared to 11.7 letters in patients treated with 1.5 mg RG7716, and 10.3 letters in patients treated with 0.3mg ranibizumab. The difference between 6mg RG7716 and 0.3mg ranibizumab was statistically significant with an adjusted mean difference of +3.6 letters (p=0.03, 80% CI 1.53–5.61, pre-specified significance level: p<0.2).

Secondary endpoints of the study included assessment of functional and anatomic measures versus ranibizumab standard of care. Both RG7716 arms achieved higher proportions of patients gaining more than two, and more than three, lines of visual acuity. Both RG7716 arms resulted in greater reduction of central retina thickness as well as a greater two-step improvement of diabetic retinopathy severity. RG7716 was well tolerated with no new safety signals observed. Additional data analyses of BOULEVARD are ongoing and will be presented at future medical meetings.

In addition to BOULEVARD, RG7716 is also being evaluated in the Phase II AVENUE and STAIRWAY studies in neovascular age-related macular degeneration (nAMD). All three studies have finished enrolment and are currently in follow-up. Roche is committed to presenting data from all Phase II studies at upcoming medical meetings, and we plan to discuss our Phase III programme with health authorities following data assessment.

A live audio webcast and conference call to discuss the data from the Phase II BOULEVARD study in DME will be held on Tuesday 13 February from 4:00 to 5:00 pm CET. This virtual event, independently organised by Roche, is open to analysts and investors. Further details are available here.

**About the BOULEVARD Study**

BOULEVARD (NCT02699450) is a Phase II study designed to assess the efficacy and safety of RG7716 compared with ranibizumab in people with diabetic macular edema (DME). This prospective, randomised, comparator-controlled, double-masked, multi-centre, multi-dose, three-arm study enrolled 229 participants.
in more than 90 sites across the United States. All patients were dosed monthly (28 days +/- 7 days) for 20 weeks. Subsequently, there is an observation period of up to 16 weeks for a total study length of 36 weeks. The primary objective of BOULEVARD was to demonstrate superior gains in visual acuity compared to ranibizumab injections at week 24 in anti-vascular endothelial growth factor (VEGF) treatment-naïve participants.

About RG7716

RG7716 is the first bispecific, monoclonal antibody specifically designed for the eye that simultaneously binds to and neutralises both angiopoietin-2 (Ang-2) and vascular endothelial growth factor A (VEGF-A) with high potency and specificity. In diabetic macular edema (DME), Ang-2 works synergistically with VEGF to drive biological pathways that cause vessel permeability and inflammation. Both of these contribute to vascular instability which results in vision loss.3,4 Therefore, simultaneous inhibition of both Ang-2 and VEGF may lead to improved outcomes, reduced treatment burden, or both.3,4

About diabetic macular edema (DME)

Diabetic macular edema (DME) affects over 21 million people globally and is associated with blindness and decreased quality of life when left untreated.5 Loss of visual function due to diabetes is the leading cause of adult onset blindness.6,7 The longer people have diabetes, especially if it is poorly managed, the higher their risk for developing DME. DME is one of the vision-threatening complications of diabetic retinopathy, in which chronic damage occurs to the fine blood vessels of the retina, the light-sensitive tissue at the back of the eye necessary for good vision.8

There is a significant unmet need for more efficacious and longer-lasting therapies for people with DME.9,10,11,12,13 DME is a multifactorial disease with a strong inflammatory component. While current anti-VEGF treatments effectively address vessel permeability, they only partially address the inflammatory component of the disease. DME causes or leads to central vision loss, limiting a person’s ability to perform tasks essential for daily life, potentially resulting in increased social isolation and decreased mental health.14

About Roche in ophthalmology

Roche is researching and developing new treatments for people living with a range of eye diseases that cause significant visual impairment and blindness, including neovascular age-related macular degeneration (AMD), diabetic macular edema (DME), diabetic retinopathy (DR), geographic atrophy (GA) and other retinal diseases. Roche is also investigating platforms for sustained ocular drug delivery.
Lucentis® (ranibizumab) was developed by Genentech, a member of the Roche Group. Genentech retains commercial rights in the US and Novartis has exclusive commercial rights for the rest of the world. Lucentis® is FDA-approved for the treatment of patients with wet age-related macular degeneration (AMD), macular edema after retinal vein occlusion (RVO), diabetic macular edema (DME), diabetic retinopathy (DR) and myopic choroidal neovascularization (mCNV).

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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row 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. Anti-VEGF/Anti-Angiopoietin-2 Bispecific Antibody RG7716 in Diabetic Macular Edema: Results from the Phase 2 BOULEVARD Clinical Trial. Presented by Dugel, P on 10th February during Session VII Diabetes, Retinal Degenerations, and Uveitis at the 2018 Angiogenesis, Exudation, and Degeneration meeting, Miami, Florida, USA.


