Faricimab for Macular Edema Due to Retinal Vein Occlusion: Rationale and Design of the Phase 3 BALATON and COMINO Trials

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Presented at the World Ophthalmology Congress | Virtual | 9–12 September 2022
Disclosures

Financial Disclosures

- HM: Consultant/Lecture Fees: Allergan/AbbVie, Apellis, Bayer, Novartis, Roche
- CD: Consultant: Adverum, Dutch Ophthalmic Research Center, Genentech, Inc., Iveric Bio, Novartis, Regeneron; Research Support: Adverum, Alexion, Bayer, Genentech, Inc., Gyroscope, Iveric Bio, Kodiak Sciences, Novartis, Regeneron, Regenxbio, Roche, Unity; Speaker: Genentech, Inc., Novartis
- LP, HL, FA, ZH: Employment: Genentech, Inc.
- NJ: Employment: Roche Products Ltd.
- L-OH: Consultant/Lecture Fees: Alcon, Allergan, Bausch + Lomb, Bayer, Novartis, Roche, ZEISS; Grants (Study Participation): Apellis, Novartis, Pixium Vision, Roche

Study and Product Disclosures

- As of August 2022, faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular edema in several countries in North America (including the United States), Europe and Asia-Pacific, and is being studied for the treatment of macular edema due to retinal vein occlusion. Please note that faricimab is not currently approved for use outside these countries, or for use outside its approved indications
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by F. Hoffmann-La Roche Ltd., Genentech, Inc., for the study and third-party writing assistance, which was provided by Nisha S. Yeotikar, PhD, of Envision Pharma Group
RVO Carries a High Treatment Burden

- Intravitreal **anti-VEGF** therapy is the first-line treatment for macular edema due to RVO

- Patients desire **fewer injections** and **fewer appointments** in their treatment regimen for the **same visual results**

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RVO, retinal vein occlusion; VEGF, vascular endothelial growth factor.
Patients With RVO in Real-world Studies Receive Fewer Anti-VEGF Injections Than Those in Clinical Trials

**BRVO**

**Mean injection number during year 1**

- Clinical Trials (BL–M12): 9.0
- Real-world Studies (BL–M12): 4.9
- LTE Trials (M12–M24): 2.1

**Mean injection number during year 2**

- Clinical Trials (BL–M12): 8.5
- Real-world Studies (BL–M12): 3.7

**Mean Injection Frequency (BL–M12)**

- Clinical Trials (BL–M12): 11.8
- Real-world Studies (BL–M12): 10.8
- LTE Trials (M12–M24): 5.1

**Mean Injection Frequency (M12–M24)**

- Clinical Trials (BL–M12): 11.1
- Real-world Studies (BL–M12): 8.1
- LTE Trials (M12–M24): 4.5

**CRVO**

**Mean injection number during year 1**

- Clinical Trials (BL–M12): 9.1
- Real-world Studies (BL–M12): 8.1
- LTE Trials (M12–M24): 3.5

**Mean injection number during year 2**

- Clinical Trials (BL–M12): 8.7
- Real-world Studies (BL–M12): 7.8
- LTE Trials (M12–M24): 3.3

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*LTE trials assessed from the baseline of the LTE trial (M12) and after 12 months (M24).

Danzig C et al. Presented at: American Society of Retina Specialists Annual Meeting; October 8-12, 2021; San Antonio, TX.

BL, baseline; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; LTE, long-term extension; M, month; RVO, retinal vein occlusion; VEGF, vascular endothelial growth factor.
Consequently, Patients With RVO in Real-world Studies Achieve Smaller Vision Gains Than Those in Clinical Trials

There is an unmet need for durable therapies that reduce treatment burden and optimise real-world outcomes in RVO.

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BRVO

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<tr>
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<th>Mean vision improvements during year 1</th>
<th>Mean vision maintenance during year 2</th>
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<td>LTE Trials (M12–M24)</td>
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CRVO

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<th>Mean vision improvements during year 1</th>
<th>Mean vision loss during year 2</th>
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<td>4.1</td>
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</tbody>
</table>

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LTE trials assessed from the baseline of the LTE trial (M12) and after 12 months (M24).

Danzig C et al. Presented at: American Society of Retina Specialists Annual Meeting; October 8-12, 2021; San Antonio, TX.

BCVA, best-corrected visual acuity; BL, baseline; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; ETDRS, Early Treatment Diabetic Retinopathy Study; LTE, long-term extension; M, month; RVO, retinal vein occlusion.
Faricimab, the First Intraocular Bispecific Antibody: 1-Molecule, 2-Disease Pathway Targets for Durable Efficacy

Ang-2 vitreous concentrations are elevated in retinal diseases, especially RVO

Dual inhibition of Ang-2 and VEGF-A with faricimab may stabilise vessels and reduce neovascularisation, leading to durable efficacy when treating retinal diseases.

Anti–Ang-2 Fab
- Stabilises vessels
- Reduces vascular leakage
- Reduces inflammation

Anti–VEGF-A Fab
- Reduces vascular leakage
- Inhibits neovascularisation

Modified Fc
- Reduces systemic exposure
- Reduces inflammatory potential

* $P = 0.0451$; **** $P < 0.0001$ versus control.


AMD, age-related macular degeneration; Ang-2, angiopoietin-2; DR, diabetic retinopathy; Fab, fragment antigen binding; Fc, fragment crystallisable; pDR, proliferative diabetic retinopathy; RVO, retinal vein occlusion; VEGF-A, vascular endothelial growth factor-A.
In Phase 3 Trials, Faricimab Demonstrated Durable Efficacy Through Disease Control With Up to Q16W Dosing in Patients With DME and nAMD

- **Durable vision gains**
  - Comparable BCVA gains with faricimab Q8W or treat-and-extend–based PTI up to Q16W versus aflibercept Q8W\(^1\) were maintained through year 2

- **Disease control outcomes**
  - Durable efficacy with faricimab up to Q16W dosing\(^a\)
  - Improved anatomic outcomes with faricimab up to Q16W versus aflibercept Q8W were maintained over 2 years\(^b\)

- **Safety outcomes**
  - Faricimab was well tolerated through study end
    - No cases of retinal vasculitis or occlusive retinal vasculitis were reported

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**YOSEMITE and RHINE (DME)**

- ≥ Q12W dosing: 78%
- Q16W dosing: 62%

**TENAYA and LUCERNE (nAMD)**

- ≥ Q12W dosing: 78%
- Q16W dosing: 63%

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YOSEMITE: NCT03622580; RHINE: NCT03622593; TENAYA: NCT03823287; LUCERNE: NCT03823300. 1. Wykoff CC et al; YOSEMITE and RHINE Investigators. Lancet. 2022;399(10326):741-755. 2. Heier JS et al; TENAYA and LUCERNE Investigators. Lancet. 2022;399(10326):729-740. 3. Proportion of patients in the pooled faricimab PTI arms who achieved ≥ Q12W or Q16W dosing at week 96, among those who had not discontinued the study at the week 96 visit (YOSEMITE, n = 270; RHINE, n = 287). 4. In general, patients receiving faricimab achieved greater reductions in CST over time compared with aflibercept (not a statistically significant difference). In general, a numerically greater proportion of patients receiving faricimab achieved absence of DME (CST < 325 μm) or absence of IRF over time compared with aflibercept. 5. Percentages are based on the number of patients randomised to the faricimab arm who have not discontinued the study at that visit, and treatment interval at week 112 is calculated using data recorded at week 108 (TENAYA, n = 271; LUCERNE, n = 287). BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; IRF, intraretinal fluid; nAMD, neovascular age-related macular degeneration; PTI, personalised treatment interval; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.
BALATON and COMINO: 2 Global, Randomised, Double-Masked, Active Comparator–Controlled, Phase 3 Trials of Faricimab in RVO

BALATON: NCT04740905; COMINO: NCT04740931.
RVO, retinal vein occlusion.
BALATON and COMINO Phase 3 Study Design

- BALATON (BRVO; N = 553)
- COMINO (CRVO/HRVO; N = 730)

Key Inclusion Criteria:
- Treatment-naïve patients with macular edema due to RVO
- BCVA of 73 ETDRS letters (20/40) to 19 ETDRS letters (20/400)
- CST of ≥ 325 μm (Spectralis or ZEISS) or ≥ 315 μm (Cirrus or Topcon)

**Arm A**
Faricimab 6.0 mg 6 × Q4W followed by faricimab PTI

**Arm B**
Afibercept 2.0 mg 6 × Q4W followed by faricimab PTI

**Treat-and-Extend-Based PTI Dosing**
- Dosing intervals of Q4W–Q16W based on DA at previous visits
- First possible extension at week 24
- IxRS-guided PTI criteria

**BCVA**, best-corrected visual acuity; **BRVO**, branch retinal vein occlusion; **CRVO**, central retinal vein occlusion; **CST**, central subfield thickness; **DA**, disease activity; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **HRVO**, hemiretinal vein occlusion; **IxRS**, interactive web or voice response system; **PTI**, personalised treatment interval; **Q4W**, every 4 weeks; **Q16W**, every 16 weeks; **RVO**, retinal vein occlusion.
BALATON and COMINO Study Efficacy Endpoints

Primary Endpoint
BCVA change from baseline at week 24

Key Secondary Efficacy Objectives

Part 1 (Through Week 24)
- BCVA change from baseline over time
- Proportion of patients gaining or avoiding BCVA loss over time
- CST change from baseline over time
- NEI VFQ-25 composite score change from baseline over time

Part 2 (PTI Phase From Week 24 Through Week 72)
- Proportion of patients on Q4W, Q8W, Q12W or Q16W dosing intervals at week 68
- Same endpoints as part 1 through to week 72

BCVA, best-corrected visual acuity; CST, central subfield thickness; NEI VFQ-25, National Eye Institute Visual Function Questionnaire-25; PTI, personalised treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.
Conclusions

• BALATON and COMINO will evaluate whether dual Ang-2/VEGF-A pathway inhibition with faricimab may promote vascular stability and durable efficacy beyond anti-VEGF therapies for macular edema due to RVO.

• Treat-and-extend–based PTI dosing will examine the potential for individualised faricimab therapy, tailored according to patient needs, to reduce treatment burden while maintaining efficacy.