FOUR-YEAR OUTCOMES OF FARICIMAB IN DME: FIRST TIME SAFETY AND EFFICACY RESULTS FROM THE RHONE-X LONG-TERM EXTENSION TRIAL

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Financial Disclosures

- AMK: Consultant: 4D Molecular Therapeutics, AbbVie, Adverum, Alcon, Amgen, Annexin, Annexon, Apellis, Aviceda, Beacon Therapeutics, Boehringer Ingelheim, Clearside, Complement Therapeutics, Exegenesis Bio, EyePoint, Frontera, Genentech, Inc., Gyroscope, iLumen, Iveric Bio, Janssen, Kodiak Sciences, Kriya, Kyowa Kirin, Nanoscope, Novartis, Ocular Therapeutix, Oculis, Ocuphire, OcuTerra, Olives Bio, Opthea, Oxular, Oxurion, Perfuse, Ray Therapeutics, RecensMedical, Regeneron, Regenxbio, Revive, RevOpsis, Roche, Sanofi, Stealth, Thea, Unity, Vanotech, Vial; Research Support: 4D Molecular Therapeutics, Aviceda, Adverum, Alexion, Annexon, Apellis, Aviceda, Eluminex, EyePoint, Exegenesis, Genentech, Inc., Gyroscope, Iveric Bio, Janssen, Kodiak Sciences, Kyowa Kirin, Neurotech, Ocular Therapeutix, Oxular, Regenxbio; Stock options: Aviceda, Oculis, Opthea, PolyPhotonix, RecensMedical, Perfuse, RevOpsis, Vial; Board of Directors: Oculis

Study and Product Disclosures

- Faricimab is approved for the treatment of neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion in multiple countries worldwide. Faricimab is not currently approved for use outside these 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. for the study and third-party writing assistance, which was provided by Trishan Gajanand, PhD, of Envision Pharma Group

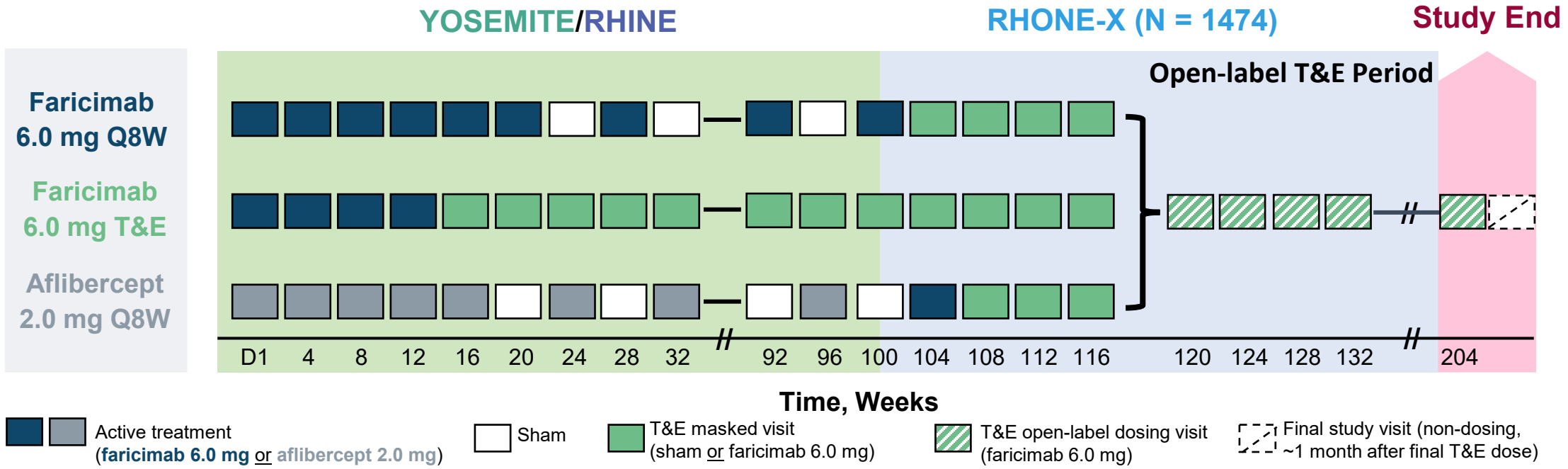
METHODS: RHONE-X Extension Trial Assessed the Long-Term Safety and Efficacy of Faricimab Treat & Extend in Patients With DME

Phase 3, multicenter, open-label, long-term extension trial

- Patients with DME who completed either the YOSEMITE or RHINE clinical trials without discontinuation of study treatment were included
- Patients were followed for an additional two years to assess the safety and efficacy of faricimab over 4 years

Faricimab treat & extend in RHONE-X

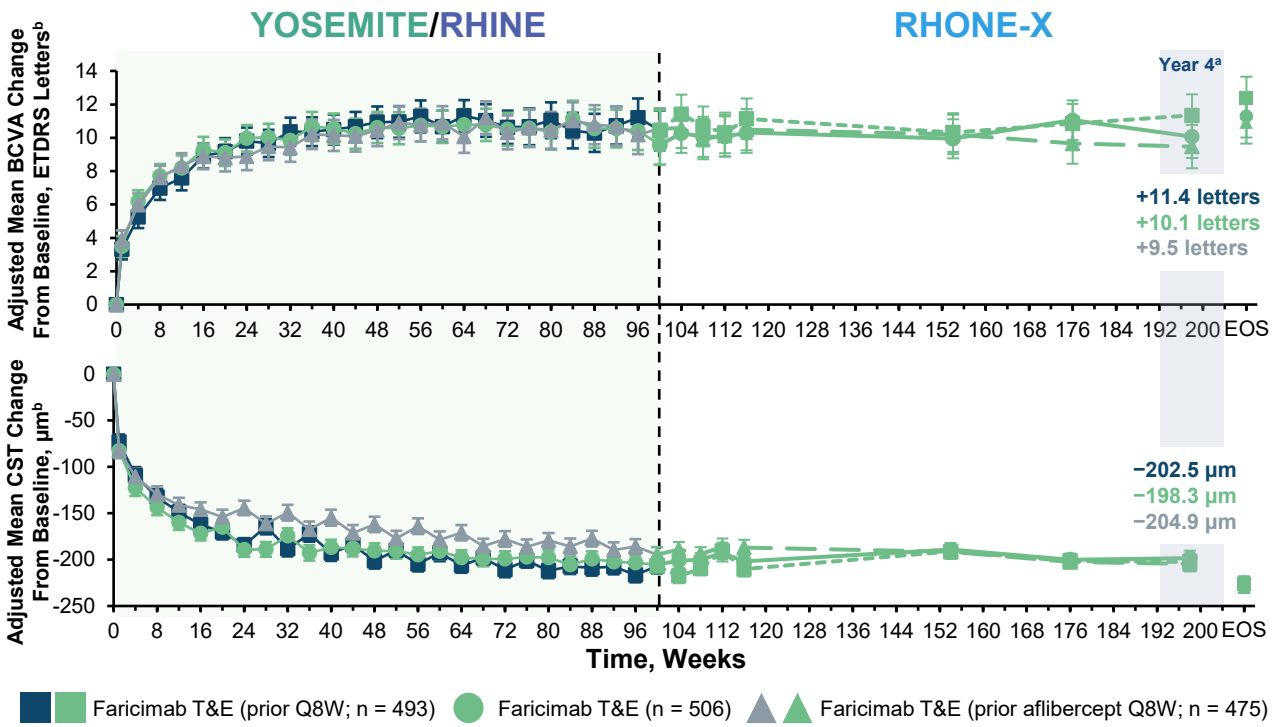
- Patients in RHONE-X attended monthly visits during the first 16 weeks (masked period) and subsequently only attended at T&E dosing visits (open label period)
- All patients received faricimab T&E up to Q16W



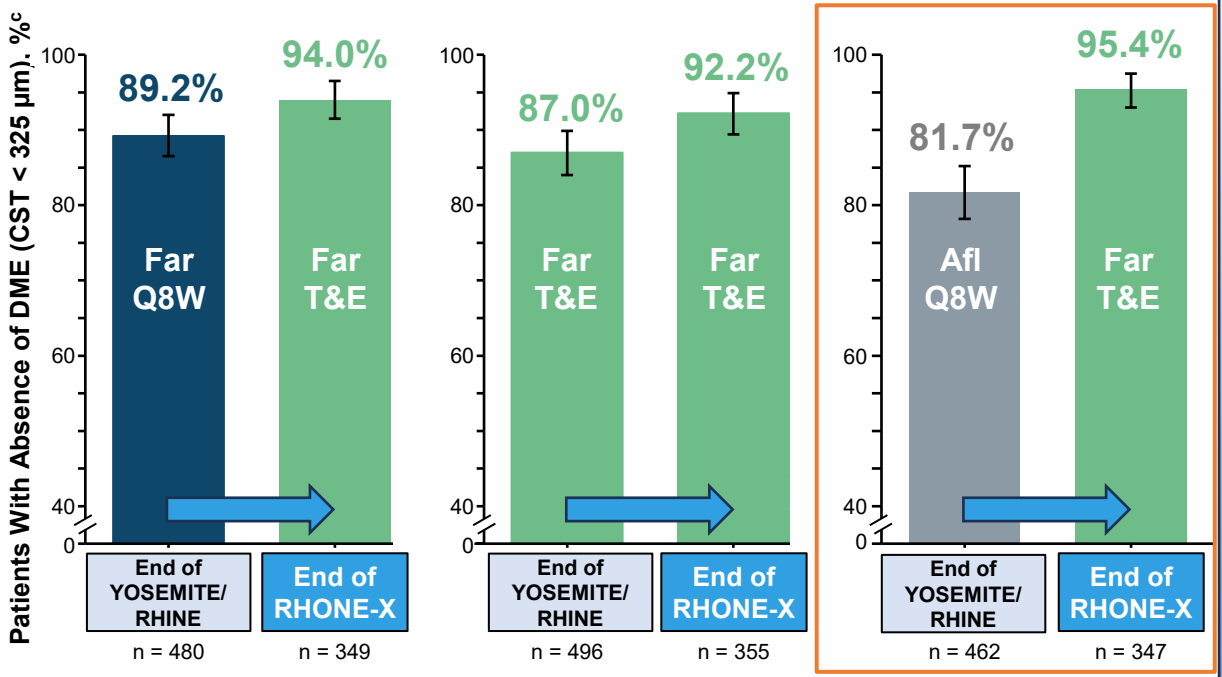
YOSEMITE (NCT03622580); RHINE (NCT03622593); RHONE-X (NCT04432831). Personalized T&E–based dosing regimen: stable CST + BCVA, dosing extended (by 4 weeks, max Q16W); worsening CST ± BCVA, dosing reduced (by 4 or 8 weeks, min Q4W); extension or reduction criteria not met: dosing maintained. Faricimab T&E regimen started at week 100/day 1 of RHONE-X for faricimab Q8W and aflibercept Q8W but not all patients received faricimab at week 100.
BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; DME, diabetic macular edema; Q4W, every 4 weeks; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat & extend.

RESULTS: Robust Vision and CST Improvements Were Maintained in RHONE-X With >90% of Patients Achieving Absence of DME (CST< 325 µm) with Faricimab up to Q16W by End of Study

Safety: Faricimab was well tolerated through years 3 and 4 of RHONE-X with the nature of AEs consistent with the YOSEMITE/RHINE parent trials



Absence of DME was achieved by >90% of patients by the end of RHONE-X regardless of prior treatment arm



~80% of patients achieved ≥Q12W dosing at the end of RHONE-X

Faricimab T&E regimen started at week 100/day 1 of RHONE-X for faricimab Q8W and aflibercept Q8W but not all patients received faricimab at week 100. Estimates for year 3 and 3.5 are averaged over weeks 144 to 164 and 168 to 188, respectively. [a]Adjusted mean change from baseline at year 4 of RHONE-X, averaged over weeks 192 to 204. EOS minimum of 28 days after the final faricimab dose. [b]Analysis of Covariance model was adjusted for parent study treatment group, visit, visit-by-treatment group interaction, baseline BCVA (continuous) or baseline CST (continuous) as applicable, baseline BCVA (< 64 vs ≥ 64 ETDRS letters), prior intravitreal anti-VEGF therapy (yes vs no), region (US and Canada, and the rest of the world). [c]Weighted estimates were based on CMH test stratified by baseline BCVA score (< 64 letters vs. ≥64 letters), prior intravitreal anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. the rest of the world). Missing data were not imputed. Estimates < 0% or > 100% were imputed as 0% or 100% respectively. 95% CI error bars are shown.

AE, adverse event; Afl, aflibercept 2 mg; BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; CST, central subfield thickness; DME, diabetic macular edema; EOS, end of study; ETDRS, Early Treatment Diabetic Retinopathy Study; Far, faricimab; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat & extend; VEGF, vascular endothelial growth factor.

DISCUSSION: Long-term Safety and Efficacy Outcomes in DME With Faricimab

- RHONE-X is the **largest DME long-term extension study** to date and had **excellent patient retention (81.7%)**
- Faricimab was **well tolerated** with a safety profile that was **consistent** with the YOSEMITE/RHINE parent trials
- BCVA and CST **improvements** achieved in the YOSEMITE/RHINE trials were **maintained** with ~80% of patients on ≥Q12W dosing intervals at the end of study
- **Absence of DME** (CST <325 µm) was achieved in **over 90% of patients** by the end of the study
- RHONE-X demonstrated the long-term safety and efficacy of **dual Ang-2/VEGF-A inhibition** with faricimab in DME

Ang-2, angiopoietin-2 ; CST, central subfield thickness; DME, diabetic macular edema; Q12W, every 12 weeks; VEGF, vascular endothelial growth factor.

Backup: Faricimab Was Well Tolerated Through Years 3 and 4 of RHONE-X With the Nature of AEs Consistent With the YOSEMITE/RHINE Parent Trials

AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]	Faricimab T&E (prior Q8W) n = 491	Faricimab T&E n = 500	Faricimab T&E (prior aflibercept) n = 473
Ocular AEs[b]	219 (44.6%)	188 (37.6%)	197 (41.6%)
Serious ocular AEs[b]	31 (6.3%)	15 (3.0%)	26 (5.5%)
Ocular AEs of special interest[c]	30 (6.1%)	14 (2.8%)	24 (5.1%)
Intraocular inflammation events[d]	7 (1.4%)	7 (1.4%)	5 (1.1%)
Uveitis	3 (0.6%)	1 (0.2%)	0
Iritis	2 (0.4%)	4 (0.8%)	1 (0.2%)
Iridocyclitis	0	2 (0.4%)	3 (0.6%)
Vitritis	1 (0.2%)	1 (0.2%)	2 (0.4%)
Post-procedural inflammation	1 (0.2%)	0	0
Endophthalmitis events	2 (0.4%)	0	1 (0.2%)
Retinal vasculitis/retinal occlusive vasculitis events	0	0	0
Retinal vascular occlusion events (not associated with inflammation)			
Retinal vein occlusion	4 (0.8%)	4 (0.8%)	1 (0.2%)
Retinal artery occlusion	0	1 (0.2%)	2 (0.4%)
Retinal artery embolism	0	0	0
Arterial occlusive disease	0	0	0
Serious non-ocular AEs	122 (24.8%)	100 (20.0%)	112 (23.7%)
APTC events[e]	27 (5.5%)	24 (4.8%)	26 (5.5%)

Safety data are presented only for the safety evaluation population from RHONE-X who are defined as patients who received at least one dose of faricimab in the RHONE-X long-term extension study. Includes AEs with onset from the first dose of study drug through study end. [a] Percentages are based on n values in the column headings; multiple occurrences of the same AE in an individual are counted only once. [b] Ocular AEs in the study eye only are presented. [c] Ocular AEs of special interest were defined as events associated with severe intraocular inflammation, events requiring surgical or medical intervention to prevent permanent loss of sight or events associated with BCVA loss of ≥ 30 letters for > 1 hour. [d] Excluding endophthalmitis. [e] APTC events were adjudicated by an external independent committee; all other events were investigator reported.

AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BCVA, best-corrected visual acuity; T&E, treat-and-extend; Q8W, every 8 weeks.