Bioerodible EYP-1901 (vorolanib intravitreal insert) for Sustained Release of a Tyrosine Kinase Inhibitor for Retinal Exudative Disease

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Disclosures & Disclaimer

Presenter disclosures

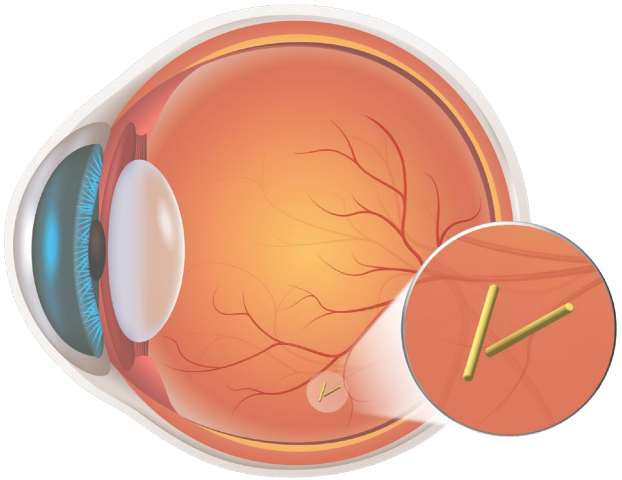
- Consultant: AbbVie, Alcon, Alkeus, Apellis, EyePoint, Genentech, Harrow, Neurotech, Ocular Therapeutix, Regeneron, Zeiss
- Speaker: AbbVie, Apellis, Harrow, Regeneron

Study disclosures

- Funding was provided by EyePoint for the study and third-party writing support by Dionne Turnbull, PhD, of Koahana, Inc.

EYP-1901 is an investigational product and its safety and efficacy has not been established. FDA has not approved EYP-1901 in the United States. The materials discussed in this presentation do not predict future FDA approval. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

EYP-1901 (vorolanib intravitreal insert) is Designed to Provide Sustained Release of the TKI Vorolanib for At Least 6 Months[1-5]



Each bioerodible IVT insert is:

- **94% drug** / 6% matrix
- **1/5000th** of vitreous volume

No PEG/PLGA

Sustained release of the TKI vorolanib via bioerodible intravitreal insert

- **Consistent daily dosing with drug release ≥ 6 months**
- **No free-floating drug particles**
- **No anterior chamber opacities**

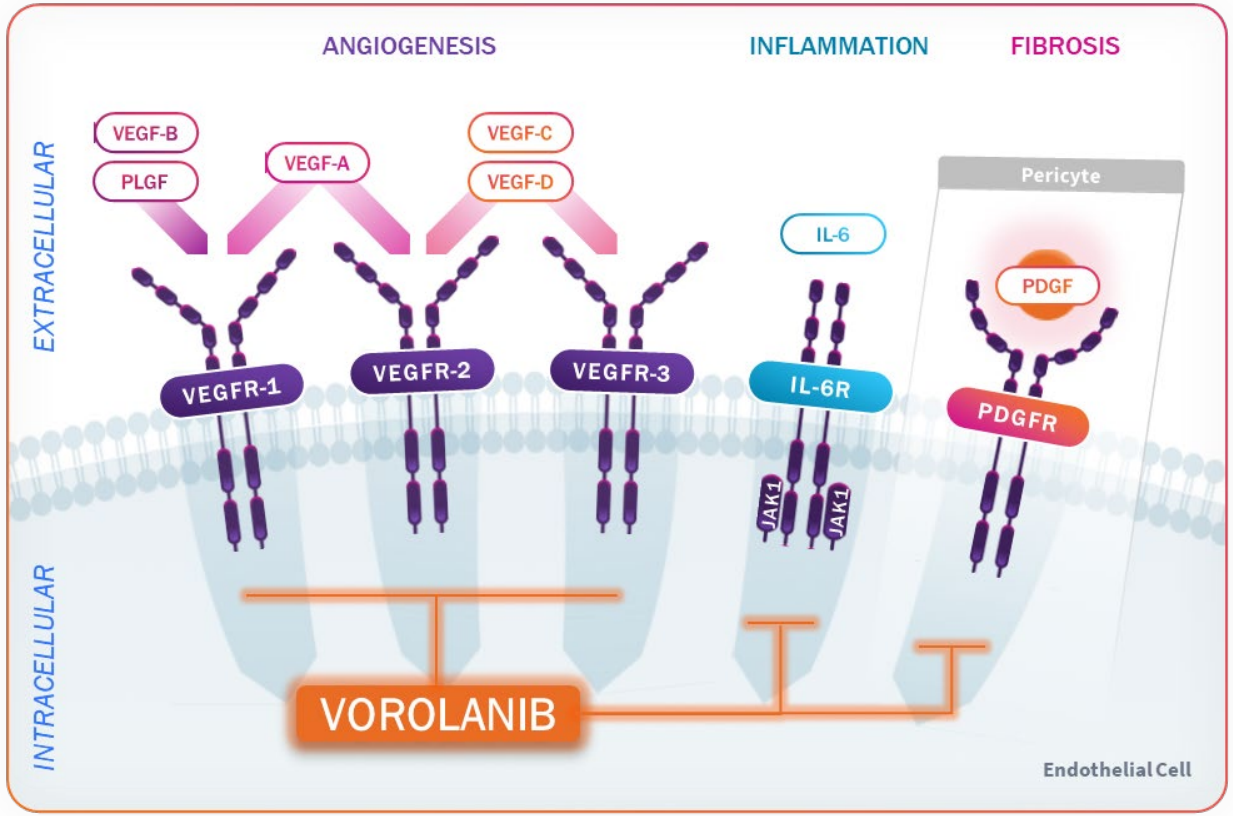
Evaluated in >400 patients to date, with no EYP-1901-related safety concerns

Inserts not drawn to scale, for illustrative purposes only. The dose investigated in phase 3 trials is 2.686 mg (two inserts of 1.343 mg each) administered in a single injection. **1.** Bakri SJ, et al. *PLoS One.* 2024;19(6):e0304782. **2.** Singh R, et al. *Invest Ophthalmol Vis Sci.* 2026;67:3653. **3.** Lynch J, et al. *Invest Ophthalmol Vis Sci.* 2026;67:3638. **4.** Patel S, et al. *Ophthalmol Sci.* 2024;4(5):100527. **5.** Wykoff CC, et al. *J Vitreoretin Dis.* 2024;8(5):577-586. **IL-6(R)**, interleukin-6 (receptor); **IVT**, intravitreal; **JAK**, Janus kinase; **MoA**, mechanism of action; **PEG**, polyethylene glycol; **PDGF(R)**, platelet-derived growth factor (receptor); **PLGA**, poly lactic-co-glycolic acid; **PLGF**, placental growth factor; **TKI**, tyrosine kinase inhibitor; **VEGF(R)**, vascular endothelial growth factor (receptor).

Data on file. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

The TKI Vorolanib has a Multi-MoA with the Potential to Address Both Angiogenesis and Inflammation

Unlike anti-VEGFs, vorolanib works *intracellularly* at the receptor level



In nonclinical studies, vorolanib:

- Is a **potent pan-VEGFR inhibitor**, **suppressing VEGF-mediated angiogenesis**[1]
- Inhibits **IL-6-mediated inflammatory signaling** at clinically relevant doses by targeting **JAK1**[2]
- **Inhibits PDGFR** with potential antifibrotic effect[1,3]

1. Bakri SJ, et al. *PLoS One.* 2024;19(6):e0304782. **2.** Singh R, et al. *Invest Ophthalmol Vis Sci.* 2026;67:3653. **3.** Chakravarthy U, et al. "EYP-1901 (vorolanib intravitreal insert), a Bioerodible, Sustained-Delivery Intravitreal Insert for Neovascular Age-Related Macular Degeneration: Preclinical Development to Pivotal Phase 3 Trials." Presented at FLORetina ICOOR Meeting, December 5–8, 2024; Florence, Italy. **IL-6(R)**, interleukin-6 (receptor); **JAK**, Janus kinase; **MoA**, mechanism of action; **PDGF(R)**, platelet-derived growth factor (receptor); **PLGF**, placental growth factor; **TKI**, tyrosine kinase inhibitor; **VEGF(R)**, vascular endothelial growth factor (receptor).

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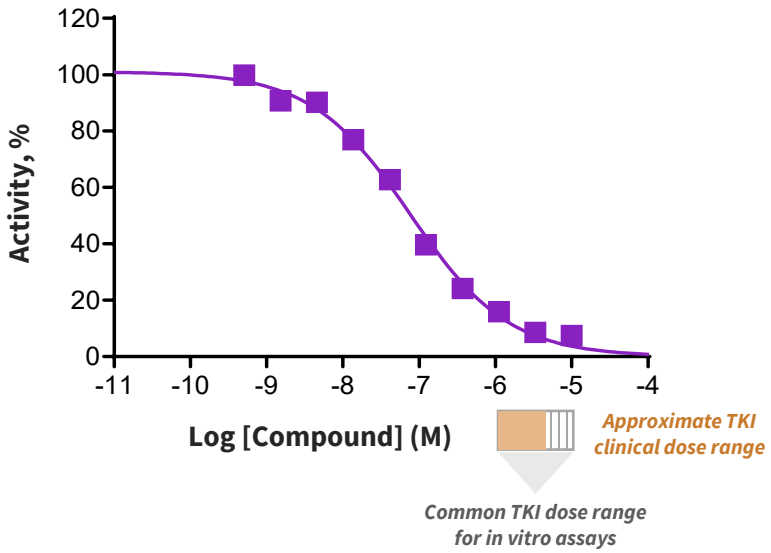
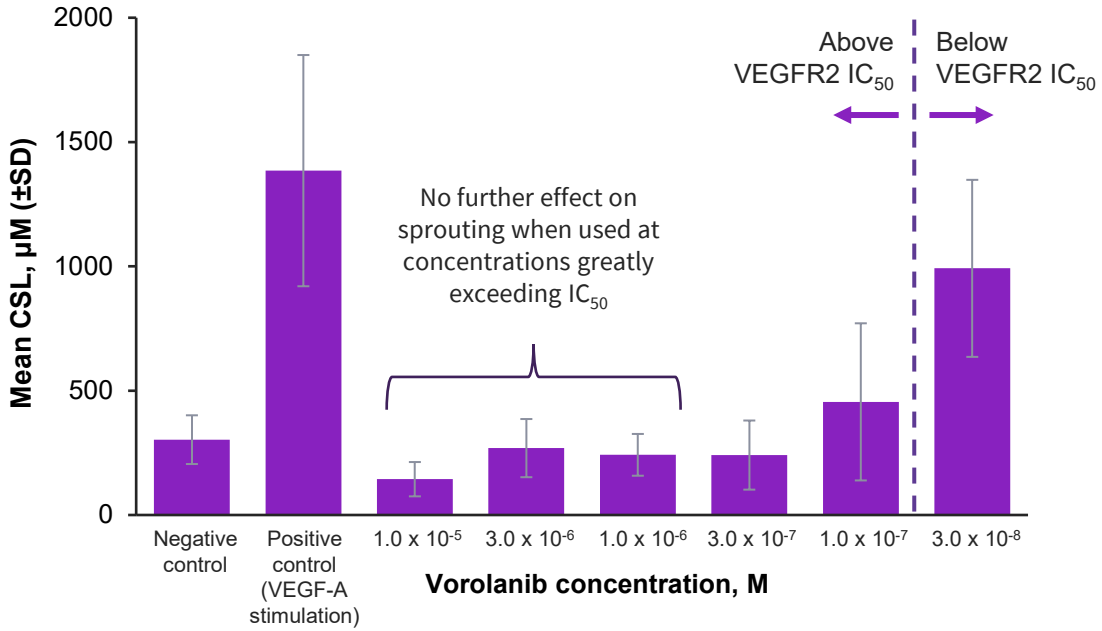
Vorolanib is a Potent Pan-VEGFR Inhibitor with Anti-Angiogenic Activity *In Vitro*

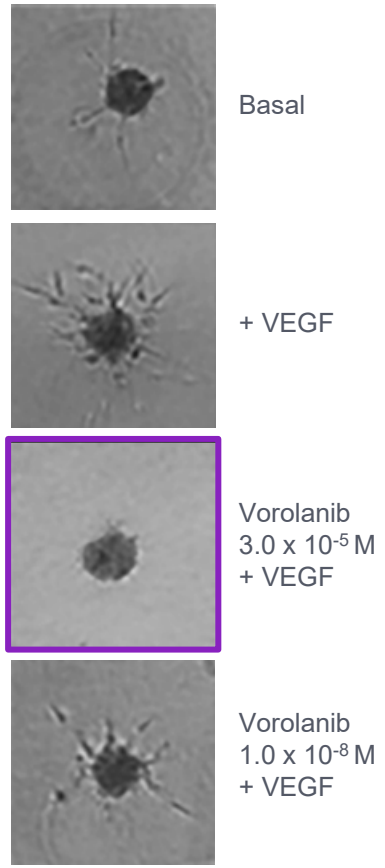
Independent Third-Party[a] Nonclinical Assays

Potent VEGFR2 inhibition at clinically relevant concentrations



Effective inhibition of VEGF-induced angiogenesis at concentrations ≥VEGFR2 IC_{50}





Vorolanib IC_{50} data for VEGFR2

HUVEC sprouting assay[1,b]

[a] Non-clinical assays were performed by Millipore Corporation (Dundee, Scotland) and Reaction Biology Corporation (Malvern, PA, USA/Freiburg, Germany); funded by EyePoint. [b] Results are (mean ± SD) for the quantitative analysis of the CSL per spheroid for each TKI at the different test concentrations. Negative control was basal medium, and positive control was VEGF-A stimulation.

1. Bakri SJ, et al. *PLoS One.* 2024;19(6):e0304782.

CSL, cumulative sprout length; **HUVEC**, human umbilical vein endothelial cell; **IC_{50}**, half maximal inhibitory concentration; **TKI**, tyrosine kinase inhibitor; **VEGF(R)**, vascular endothelial growth factor (receptor).

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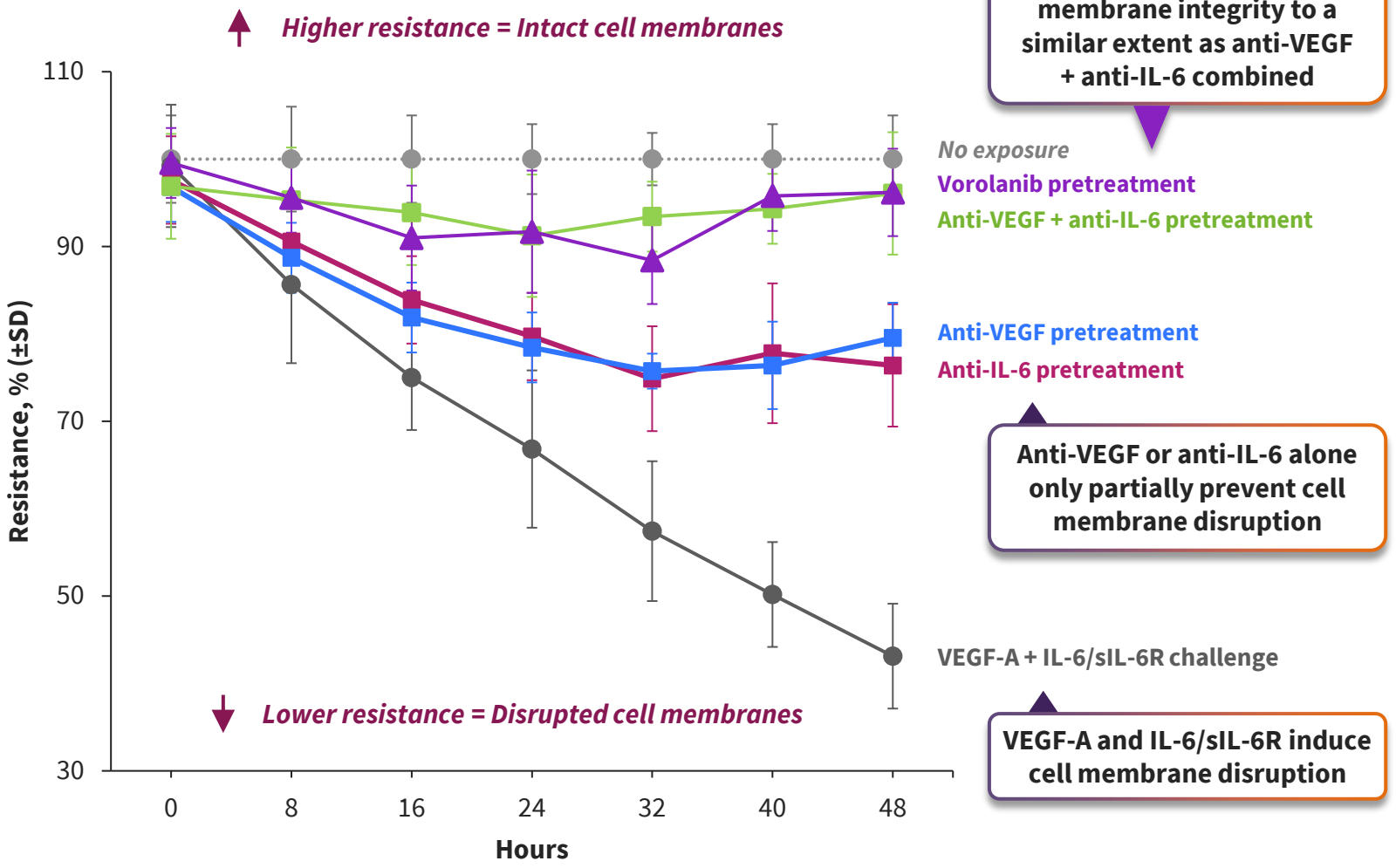
Vorolanib Maintains Cell Membrane Junctions *In Vitro*, with the Potential to Reduce Vascular Leakage

- ***Vorolanib maintains cell membrane integrity to a similar extent as anti-VEGF + anti-IL-6 combined***

A TEER assay quantifies the integrity of intracellular junctions by measuring electrical resistance across a cell monolayer to demonstrate drug efficacy

Cell-based TEER assay in HUVECs[a]

Independent Third-Party[b] Nonclinical Assay



Vorolanib maintains cell membrane integrity to a similar extent as anti-VEGF + anti-IL-6 combined

Anti-VEGF or anti-IL-6 alone only partially prevent cell membrane disruption

VEGF-A and IL-6/sIL-6R induce cell membrane disruption

Singh R, et al. *Invest Ophthalmol Vis Sci.* 2026;67:3653.

[a] Immortalized HUVECs were pretreated with vorolanib, anti-IL-6 (siltuximab), anti-VEGF (aflibercept), or anti-VEGF + anti-IL-6 prior to stimuli challenge with hyper-VEGF-A + IL-6/sIL-6R. Integrity and maintenance of the cell junctions were monitored over time. [b] Non-clinical assays were performed by Creative Bioarray (NY, USA) and funded by EyePoint.

IL-6, interleukin 6; **sIL-6R**, soluble IL-6 receptor; **TEER,** trans-epithelial/endothelial electrical resistance; **VEGF**, vascular endothelial growth factor.

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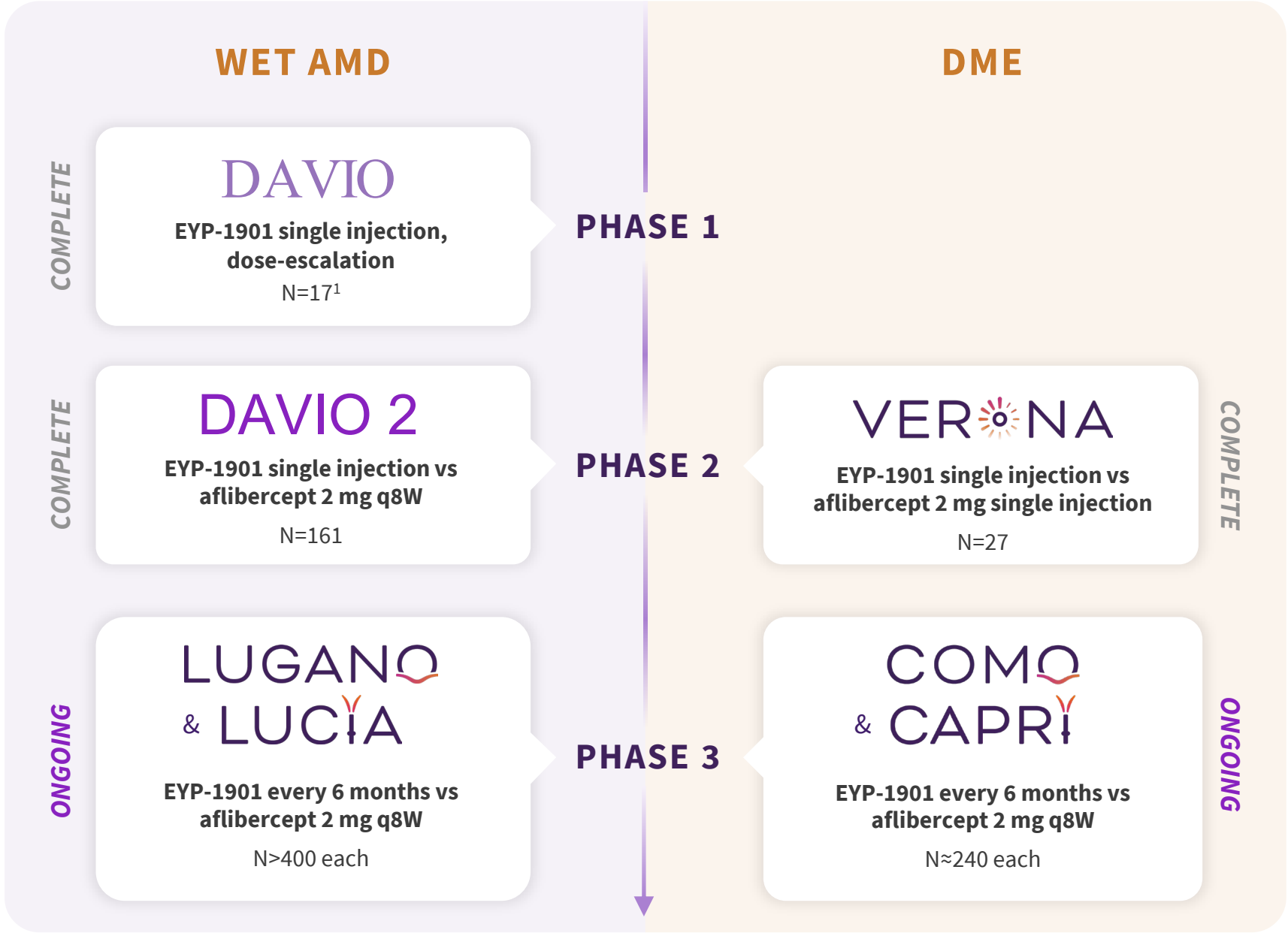
Clinical Trials of EYP-1901 in Wet AMD and DME

Phase 3 trials in wet AMD and DME fully enrolled and ongoing



1. Patel S, et al. *Ophthalmol Sci.* 2024;4(5):100527.
AMD, age-related macular degeneration; **DME**, diabetic macular edema; **q8W**, every 8 weeks.
Clinicaltrial.gov identifiers: DAVIO NCT04747197; DAVIO 2 NCT05381948; LUGANO NCT06668064; LUCIA NCT06683742; VERONA NCT06099184; COMO NCT07449936; CAPRI NCT07449923.
Data on file. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

EYP-1901 has the Potential to Fulfill Unmet Needs in Wet AMD and DME

- **Potent intracellular inhibition** of **VEGFRs**, **PDGFR**, and **IL-6 signaling** by vorolanib in nonclinical studies[1,2]
- **EYP-1901 demonstrated safety and efficacy** in phase 2 trials in wet AMD and DME
- **Phase 3 trials ongoing:** LUCIA (wet AMD) anticipated Q4 2026; COMO and CAPRI (DME) anticipated Q4 2027

***COMING UP NEXT:* FIRST PRESENTATION OF TOPLINE PHASE 3 LUGANO RESULTS OF EYP-1901 vs ON-LABEL AFLIBERCEPT 2 mg Q8W IN WET AMD**

1. Bakri SJ, et al. *PLoS One.* 2024;19(6):e0304782. **2.** Singh R, et al. *Invest Ophthalmol Vis Sci.* 2026;67:3653. **AMD**, age-related macular degeneration; **DME**, diabetic macular edema; **IL-6**, interleukin 6; **PDGFR**, platelet-derived growth factor receptor; **VEGFR**, vascular endothelial growth factor receptor. Clinicaltrial.gov identifiers: COMO, NCT07449936; CAPRI, NCT07449923; LUGANO, NCT06668064; LUCIA, NCT06683742.

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