A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib

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Financial Disclosures

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EYP-1901: A Novel Approach to Wet AMD Therapy

Vorolanib in Bioerodible Intravitreal Insert

Vorolanib

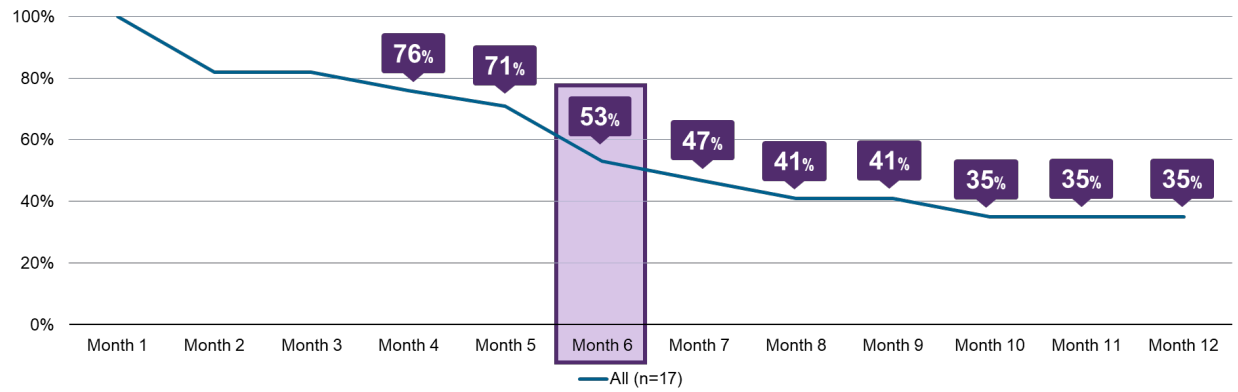
- Receptor-binding, small molecule pan-VEGFR inhibitor
- Activity against all VEGF and PDGF receptors,[1,2] no inhibition of the TIE2 receptor at clinically relevant doses[2]
- Oral vorolanib previously studied in wet AMD (wAMD) phase 1 and 2 programs[3,4]

EYP-1901

- Vorolanib formulated as a bioerodible intravitreal insert, designed to provide sustained, zero-order release

Phase 1 DAVIO Trial of EYP-1901 in wAMD demonstrated a median time to anti-VEGF treatment of 6 months and a 79% reduction in treatment burden at 6 months

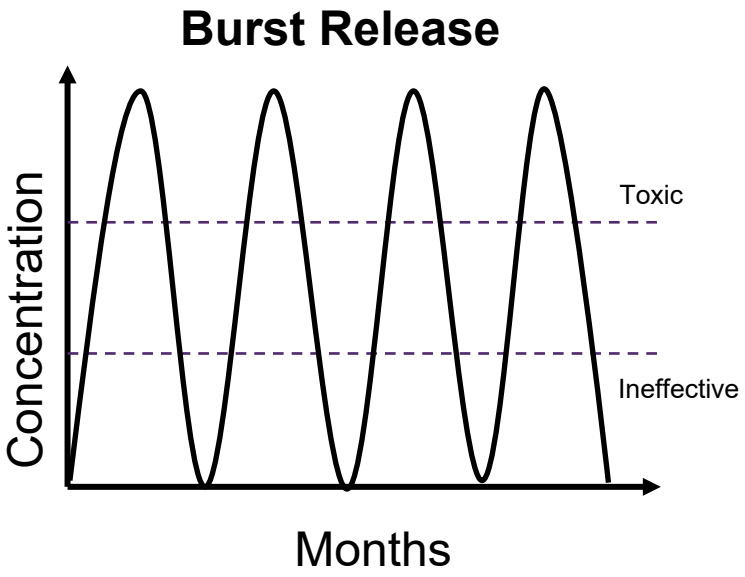
Anti-VEGF Treatment-free Rates Up to Each Visit in the Phase 1 DAVIO Trial

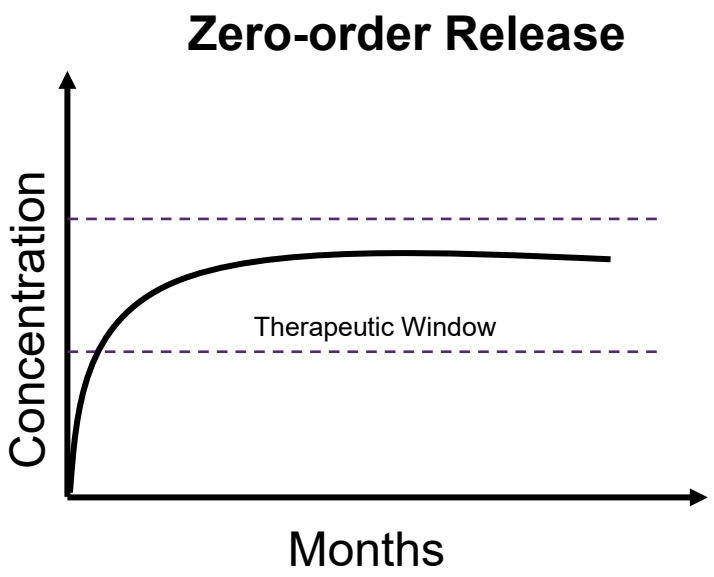


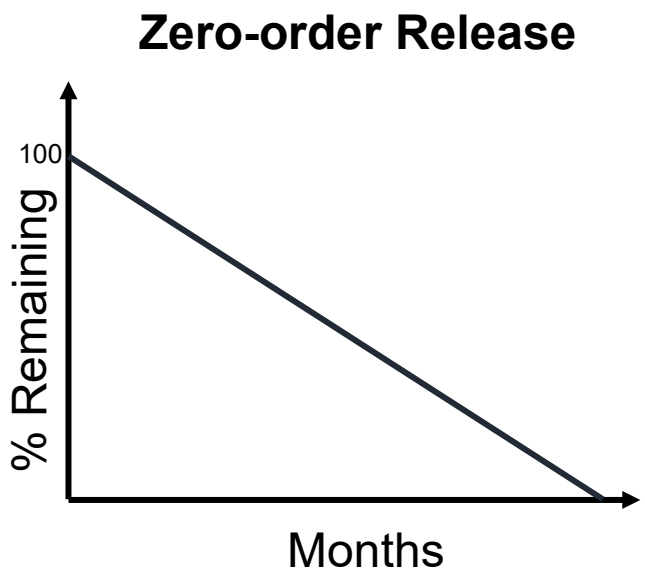
PDGFR = platelet-derived growth factor receptor; VEGFR = vascular endothelial growth factor receptor.

1. Bendell JC, et al. *Oncologist.* 2019;24(4):455-e121. 2. Data on file. EyePoint Pharmaceuticals. 3. Jackson TL, et al. *JAMA Ophthalmol.* 2017;135(7):761-767. 4. Cohen MN, et al. *Br J Ophthalmol.* 2021;105(5):716-722.

Zero-order Drug Release is Ideal for Intraocular Products





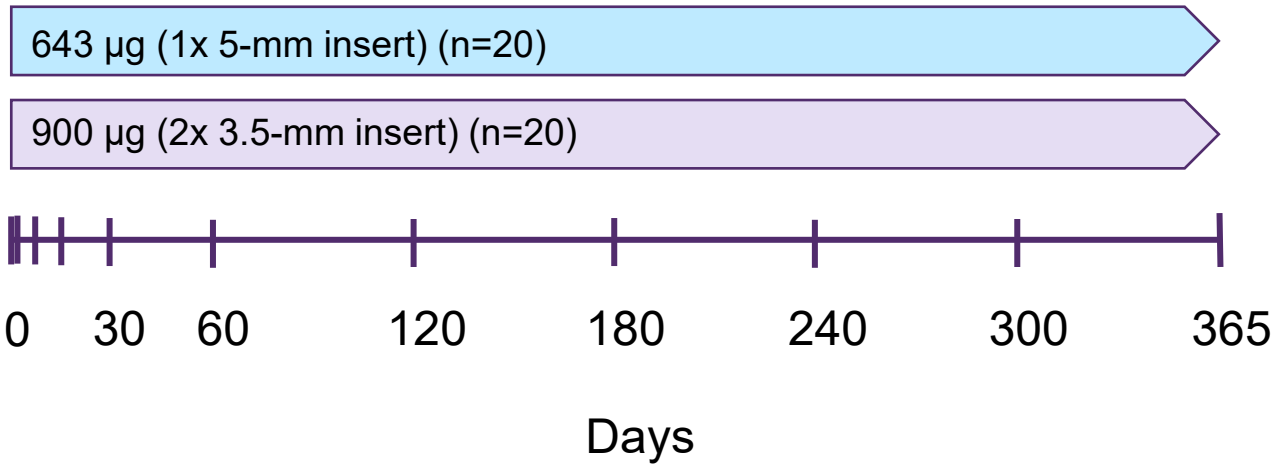


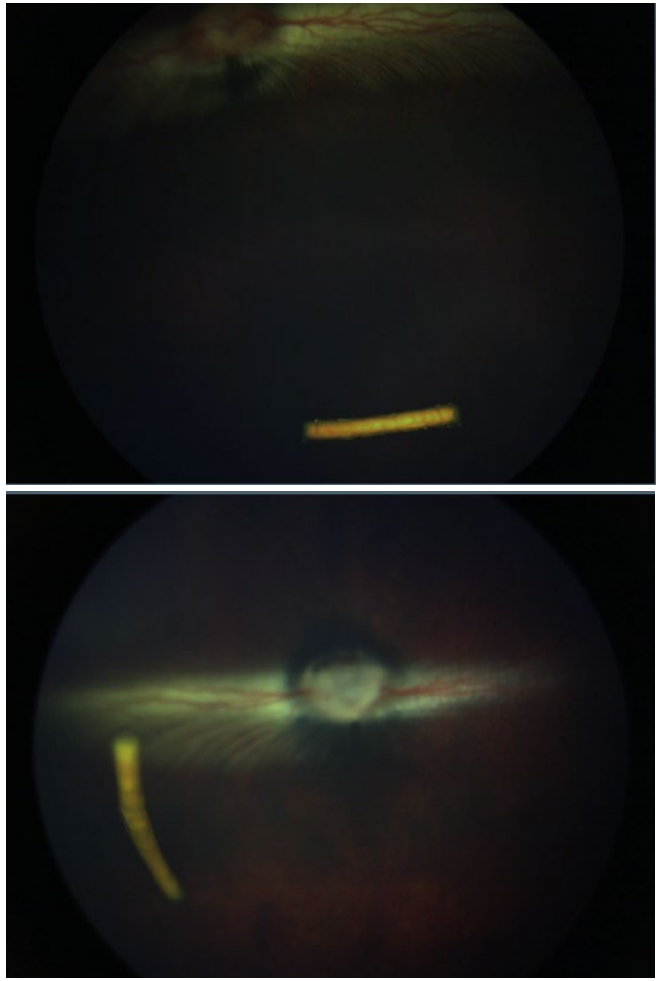
- Burst release can lead to periods of undertreatment or overtreatment resulting in a sawtooth pattern
- Zero-order drug release occurs at a constant rate over an extended period within a therapeutic window to **prolong the maximum therapeutic effect and minimize side effects**
- Zero-order release formulations provide the optimal approach to reaching a therapeutic level and maintaining a consistent exposure through the period of drug release

Preclinical Study Design and Methodology

Purpose: 12-month, intravitreal, single-dose, ocular PK study of EYP-1901 bilateral injection in Dutch Belted rabbits

- Sampling timepoints at Day 2, 7, 14, 30, 60 and then every 2 months
- Vorolanib concentrations reported for vitreous, retina, aqueous humor, and plasma
- Implants collected at each timepoint and evaluated for remaining vorolanib content

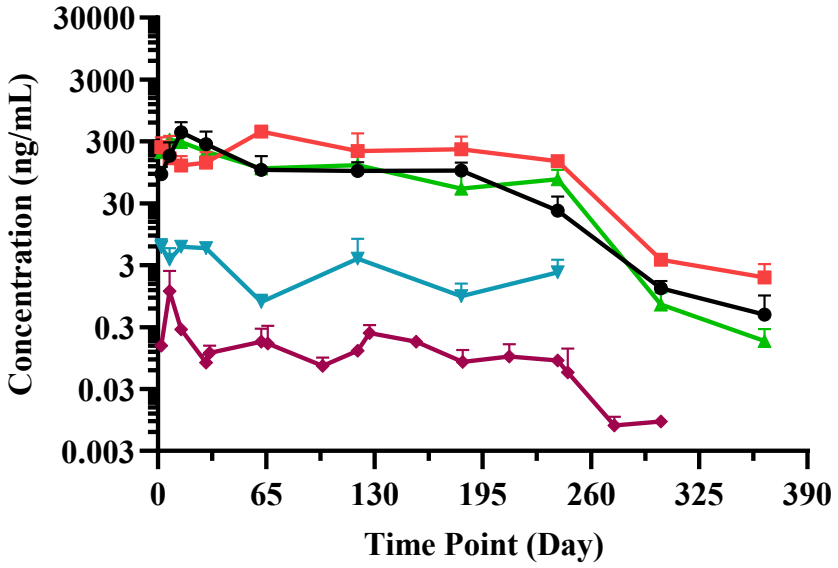




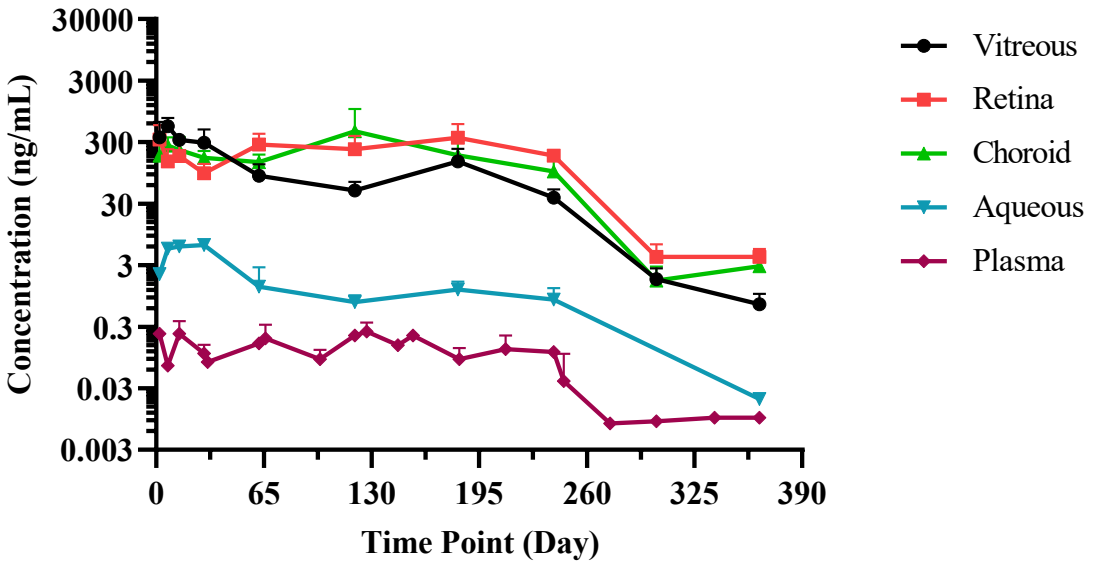
Ocular PK Demonstrated Initial Burst Followed by Extended Steady State Above IC_{50} in Target Tissues

- Reached steady state in all tissues quickly and maintained steady state until inserts neared depletion
- Inserts were depleted between 240 and 270 days
- Target tissues of retina and choroid were consistently above IC_{50} of 23 ng/mL for VEGFR2 through Day 240
- Plasma and aqueous humor levels were consistently below IC_{50} of 23 ng/mL for VEGFR2 throughout the study
- Lower limit of detection = 5 pg/mL

643 µg/eye, bilateral

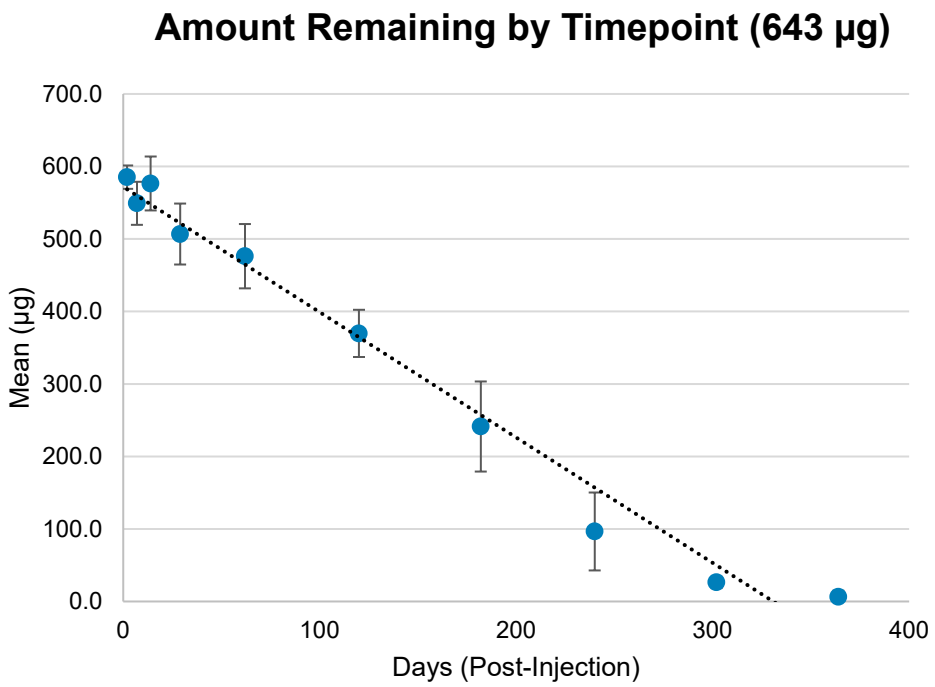


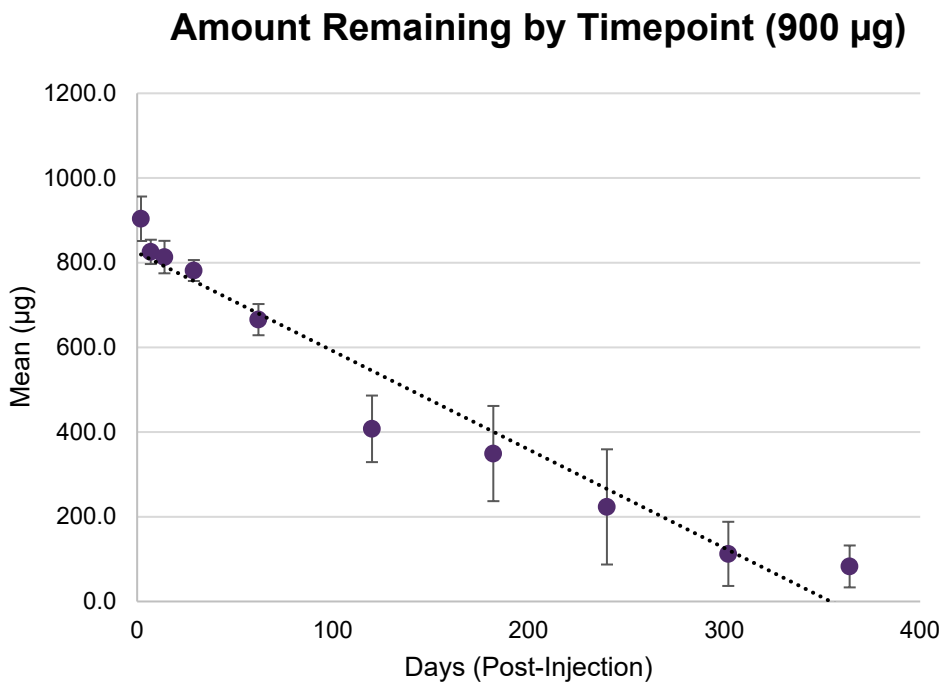
900 µg/eye, bilateral



Zero-order Release of Vorolanib at a Consistent Daily Microdose (µg/Day) Through 8-10 Months

- EYP-1901 inserts were collected at necropsy and tested for remaining vorolanib content
- Group 1 inserts (1 insert of 643 µg) released at average rate of 1.73 µg/day or 52.08 µg/month
- Group 2 inserts (2 inserts of 900 µg) released at average rate of 2.33 µg/day or 70.20 µg/month
- Demonstrated dose-proportional, zero-order kinetics





Summary of Results

Key findings:

- In this study, vorolanib formulated as a bioerodible EYP-1901 intravitreal insert demonstrated zero-order, sustained release over an 8-month period
  - Inserts showed depletion at 8-9 months
- At Day 240, vorolanib levels in retina and choroid remained above the IC_{50} of VEGFR2 (23 ng/mL)
  - Plasma and aqueous humor levels were below IC_{50} levels throughout the study
- By Day 270, vorolanib levels in all tissues were below the IC_{50} of VEGFR2

Clinical Relevance:

- Vorolanib is a pan-VEGFR inhibitor with a well-established mechanism of action
- EYP-1901 is designed to consistently deliver daily microgram doses of vorolanib over 6 months or more
- EYP-1901 is under Phase 2 clinical evaluation for the treatment of VEGF-mediated retinal diseases (DAVIO2 and PAVIA)