Safety and Efficacy of OPGx-RHO Silence-and-Replace AAV Gene Therapy: Evidence Across Two Large Animal Models

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Retinal Therapeutics Innovation Summit

May 1, 2026

Disclosures and Forward-Looking Statements

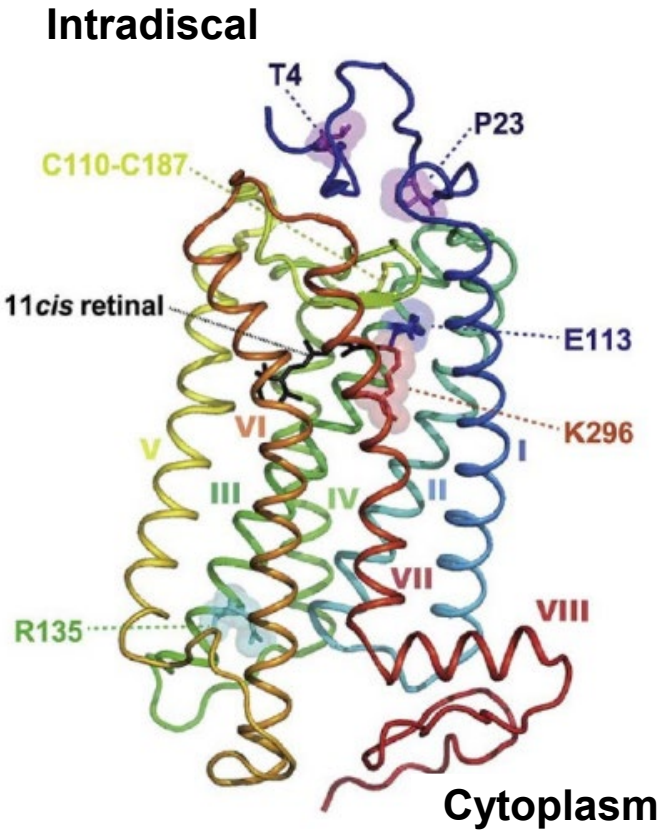
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning data from and future enrollment for our clinical trials and our pipeline of additional indications. These forward-looking statements relate to us, our business prospects and our results of operations and are subject to certain risks and uncertainties posed by many factors and events that could cause our actual business, prospects and results of operations to differ materially from those anticipated by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those described under the heading "Risk Factors" included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2025, June 30, 2025 and September 30, 2025 and in our other filings with the U.S. Securities and Exchange Commission (the "SEC"). Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this presentation. In some cases, you can identify forward-looking statements by the following words: "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "aim," "may," "ongoing," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. We undertake no obligation to revise any forward-looking statements in order to reflect events or circumstances that might subsequently arise. These forward-looking statements are based upon our current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: our clinical data related to gene therapies for the treatment of inherited retinal diseases is preliminary and related to a relatively small group of patients, and, as a result, data that initially appears promising may be revised, updated, or invalidated at a later data readout and/or may ultimately not be capable of duplication in additional patients; failure to successfully integrate our businesses following our acquisition of former Opus Genetics Inc. (the "Opus Acquisition") could have a material adverse effect on our business, financial condition and results of operations; the Opus Acquisition significantly expanded our product pipeline and business operations and shifted our business strategies, which may not improve the value of our common stock; our gene therapy product candidates are based on a novel technology that is difficult to develop and manufacture, which may result in delays and difficulties in obtaining regulatory approval; our planned clinical trials may face substantial delays, result in failure, or provide inconclusive or adverse results that may not satisfy the U.S. Food and Drug Administration (the "FDA") requirements to further develop our therapeutic products; delays or difficulties associated with patient enrollment in clinical trials may affect our ability to conduct and complete those clinical trials and obtain necessary regulatory approvals; changes in regulatory requirements could result in increased costs or delays in development timelines; we depend heavily on the success of our product pipeline; if we fail to find strategic partners or fail to adequately develop or commercialize our pipeline products, our business will be materially harmed; others may discover, develop, or commercialize products similar to those in our pipeline before or more successfully than we do or develop generic variants of our products even while our product patents remain active, thereby reducing our market share and potential revenue from product sales; we do not currently have any sales or marketing infrastructure in place and we have limited drug research and discovery capabilities; the future commercial success of our products could significantly depend upon several uncertain factors, including third-party reimbursement practices and the existence of competitors with similar products; product liability lawsuits against us or our suppliers or manufacturers could cause us to incur substantial liabilities and could limit commercialization of any product candidate that we may develop; failure to comply with health and safety laws and regulations could lead to material fines; we have not generated significant revenue from sales of any products and expect to incur losses for the foreseeable future; our future viability is difficult to assess due to our short operating history and our future need for substantial additional capital, access to which could be limited by any adverse developments that affect the financial services markets; raising additional capital may cause our stockholders to be diluted, among other adverse effects; we operate in a highly regulated industry and face many challenges adapting to sudden changes in legislative reform or the regulatory environment, which affects our pipeline stability and could impair our ability to compete in international markets; we may not receive regulatory approval to market our developed product candidates within or outside of the U.S.; with respect to any of our product candidates that receive marketing approval, we may be subject to substantial penalties if we fail to comply with applicable regulatory requirements; our potential relationships with healthcare providers and third-party payors will be subject to certain healthcare laws and regulations, which could expose us to extensive potential liabilities; we rely on third parties for material aspects of our business, such as conducting our nonclinical and clinical trials and supplying and manufacturing bulk drug substances, which exposes us to certain risks; we may be unsuccessful in entering into or maintaining licensing arrangements (such as our license agreement with Viatris, Inc.) or establishing strategic alliances on favorable terms, which could harm our business; our current focus on the cash-pay utilization for future sales of RYZUMVI may limit our ability to increase sales or achieve profitability with this product; inadequate patent protection for our product candidates may result in our competitors developing similar or identical products or technology, which would adversely affect our ability to successfully commercialize; we may be unable to obtain full protection for our intellectual property rights under U.S. or foreign laws; we may become involved in lawsuits for a variety of reasons associated with our intellectual property rights, including alleged infringement suits initiated by third parties; we are dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy; as we grow, we may not be able to operate internationally or adequately develop and expand our sales, marketing, distribution, and other corporate functions, which could disrupt our operations; the market price of our common stock is expected to be volatile; our common stock may be subject to delisting from the Nasdaq Capital Market, which could adversely affect our ability to access capital markets; factors out of our control related to our securities, such as securities litigation or actions of activist stockholders, could adversely affect our business and stock price and cause us to incur significant expenses; our business could experience an adverse impact from current or proposed tariffs on imported goods we purchase; our ability to utilize our common stock to finance future capital needs, or for other purposes, is limited by our authorized shares available for issuance; and instability and operational disruptions at government agencies, such as the FDA, may adversely impact our development and commercialization plans by causing delays and requiring the use of additional, unforeseen resources to obtain regulatory approval for trials or products in our pipeline.

The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive. Readers are urged to carefully review and consider the various disclosures made by us in this report and in our other reports filed with the SEC that advise interested parties of the risks and factors that may affect our business. All forward-looking statements contained in this presentation speak only as of the date on which they were made. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Rhodopsin-Mediated Autosomal Dominant Retinitis Pigmentosa

- **Retinitis pigmentosa is the most prevalent inherited retinal disease**
  - Results in bilateral degeneration of rod and cone photoreceptors, ultimately leading to night blindness and progressive visual impairment
- **Autosomal dominant RP is the most common autosomal dominant retinal disease**
  - *RHO* is the most common cause of adRP (~ 30% of cases)
- **Prevalence of adRP-RHO is approximately 11,000 in U.S. and EU**

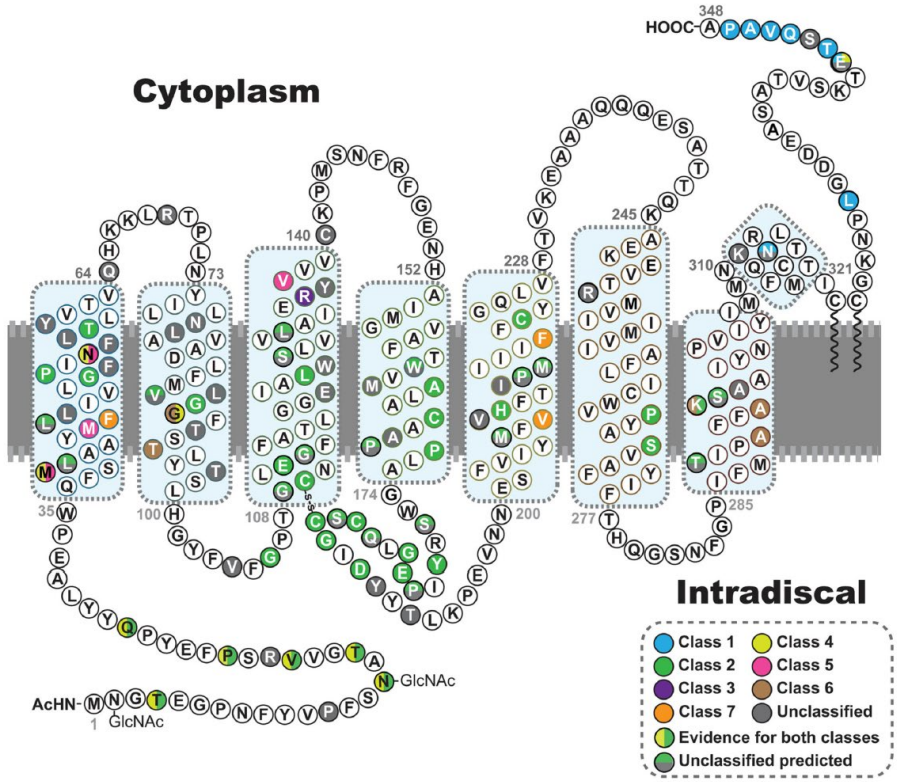
Rhodopsin



adRP, autosomal dominant retinitis pigmentosa; RHO, rhodopsin; RP, retinitis pigmentosa.

Biology of RHO IRD (adRP)

- ***RHO* encodes for rhodopsin,** a rod photoreceptor 11-*cis*-retinaldehyde photopigment located in the outer segment, critical for phototransduction
  - Rhodopsin is a **G-protein coupled receptor**
- **> 150 *RHO* mutations** associated with adRP and CSNB
- Typical pattern of **rod degeneration beginning in childhood** (accompanied by night blindness) with **subsequent degeneration of cones**
- Dominant *RHO* mutations are typically **gain-of-function,** necessitating ablate (knockdown) and replace gene therapy strategies, or **dominant-negative,** which affects wild type rhodopsin protein function
- Pathogenic *RHO* mutations **affect multiple cellular functions:**
  - Class 1: Golgi trafficking and outer segment targeting
  - Class 2: Misfolding and ER retention
  - Class 3: Vesicular trafficking and endocytic pathways
  - Class 4: Altered post-translational modifications
  - Class 5: Altered transducin activation
  - Class 6: Constitutive activation
  - Class 7: inability to dimerize
  - Unclassified

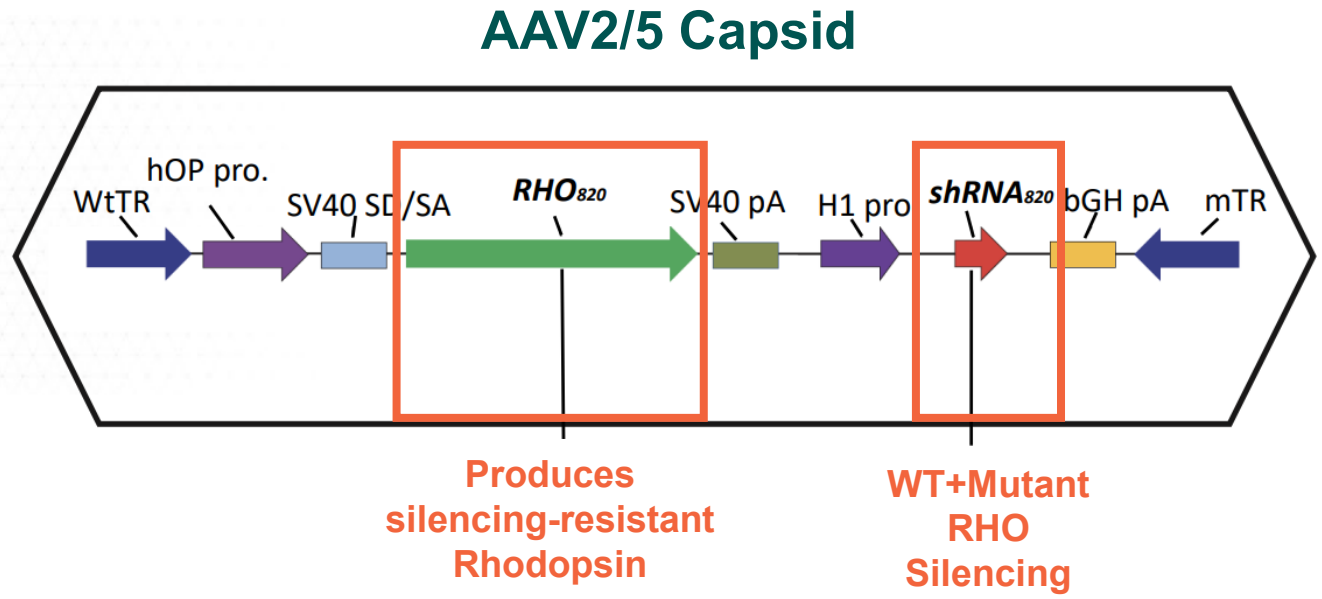


Athanasiou et al., PRER 2018

adRP, autosomal dominant retinitis pigmentosa; CSNB, congenital stationary night blindness; IRD, inherited retinal disease; RHO, rhodopsin.

Overview of Single AAV OPGx-RHO Silence-and-Replace Gene Therapy

Vector	scAAV5
Construct	scAAV2/5-H1p-shRNA$_{820}$-hOP-RHO$_{820}$, human opsin promoter
Delivery	Single subretinal injection



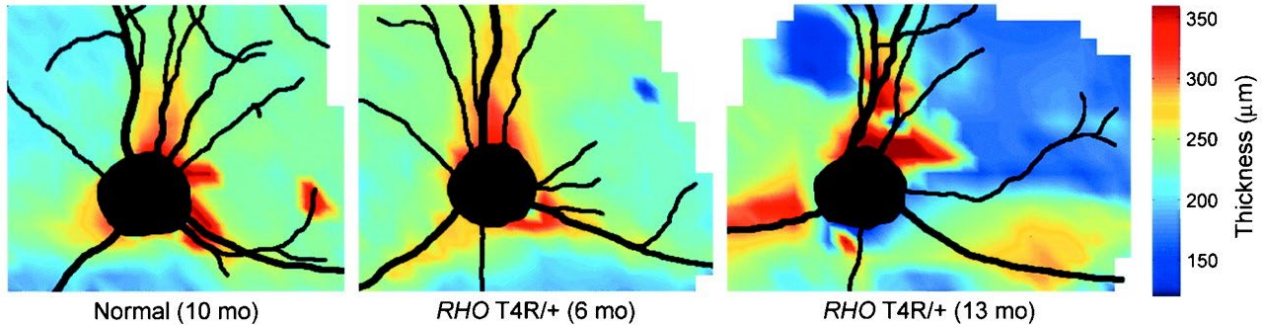
Therapeutic Efficacy of OPGx-RHO in a Canine Model of adRP-RHO

OPUS GENETICS®

Canine Model of *RHO* adRP as a Test Bed for Therapeutic Studies

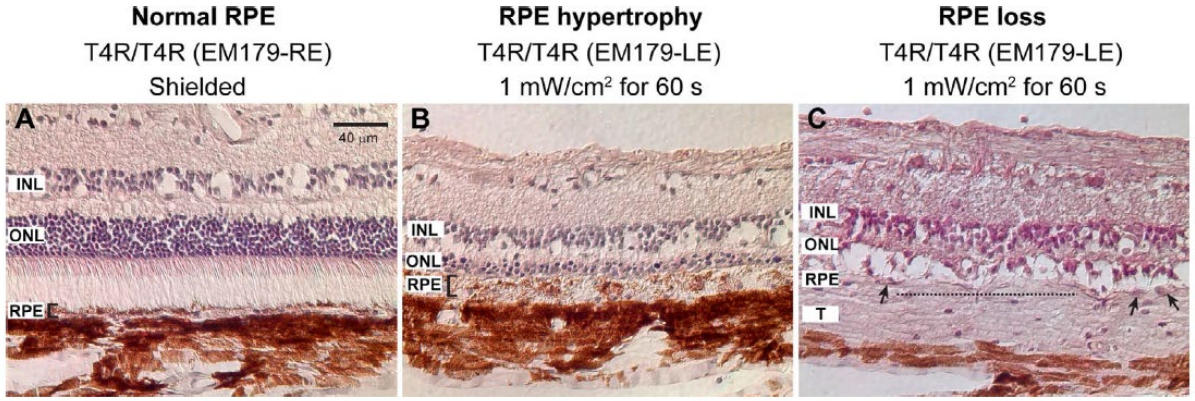
- **Canine model of *RHO*** with naturally-occurring heterozygous T4R mutation provides opportunity to test therapeutic interventions
  - Slow recovery of rod function after light exposure
  - Mirrors pattern of retinal degeneration in human adRP

- **Susceptible to light damage and subsequent PR cell death** → Acute light exposure can be used to accelerate pathology



Kijas et *al*.., PNAS 2002

Retinal topographic changes: Progressive thinning in superior temporal quadrants, reflecting scotomas in adRP patients

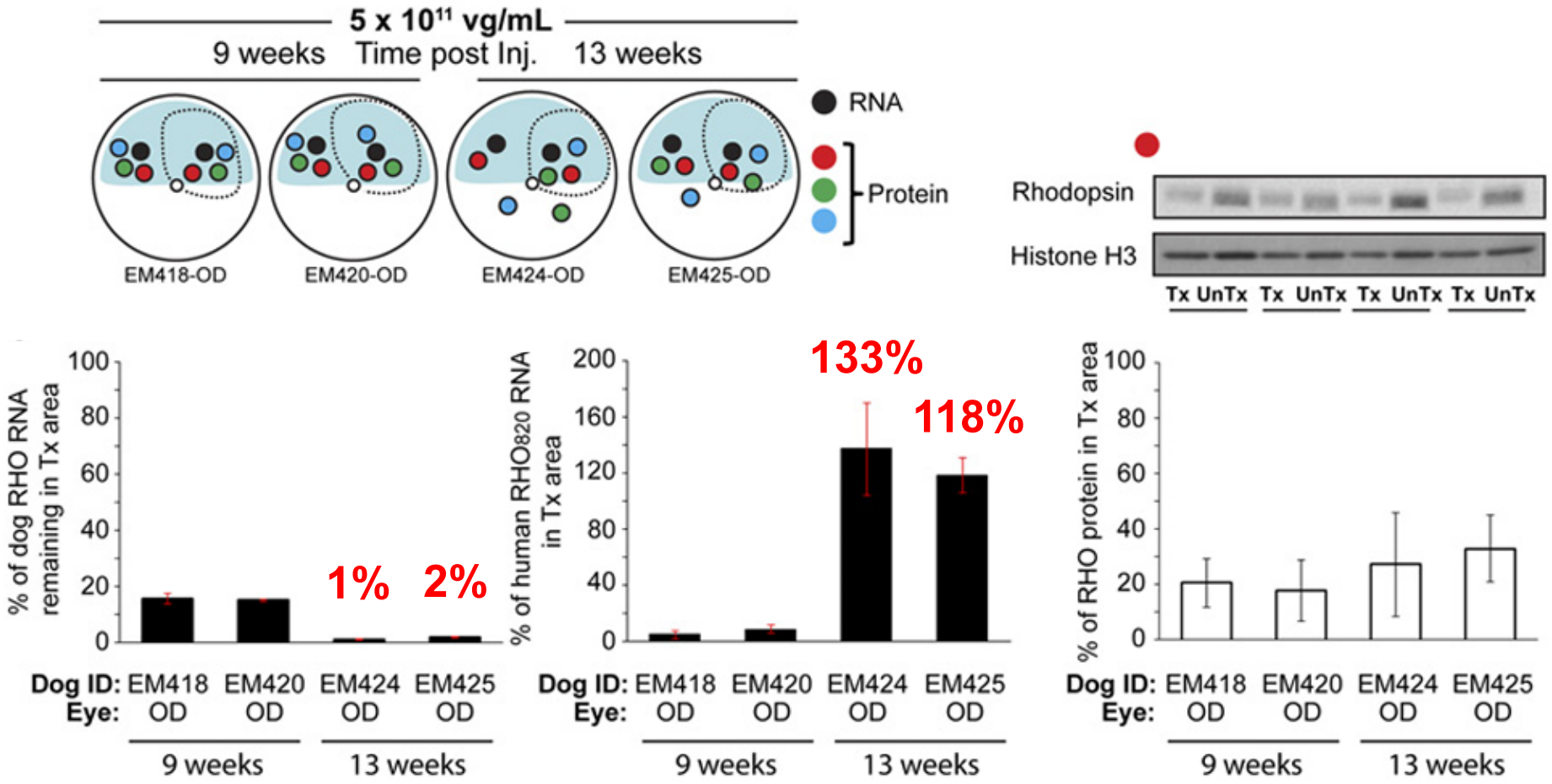


Sudharsan et *al*.., IOVS 2017

adRP, autosomal dominant retinitis pigmentosa; PR, photoreceptor; RHO, rhodopsin; RPE, retinal pigment epithelium.

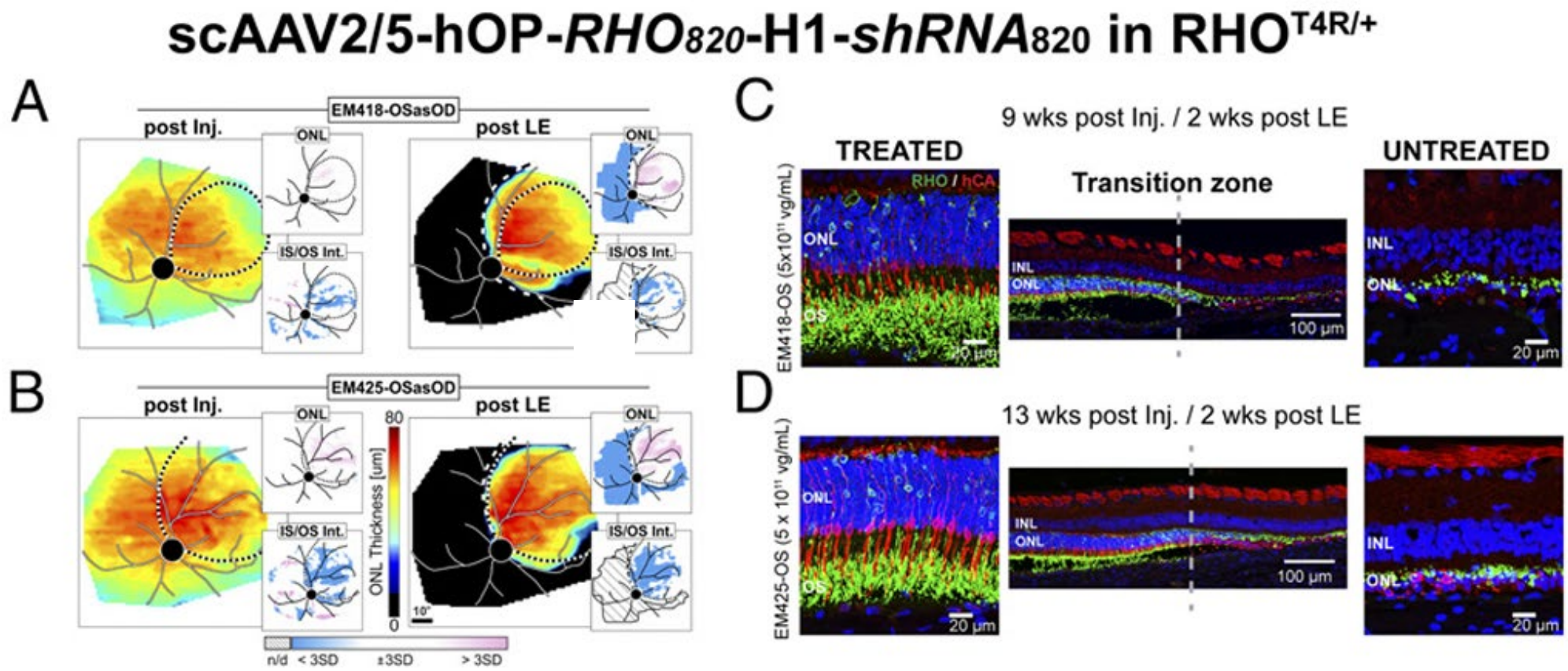
OPUS GENETICS

OPGx-RHO: Knockdown and Replacement in T4R adRP-RHO Canines



Cideciyan AV, et al. *Proc Natl Acad Sci* USA. 2018;115:E8547-E8556.

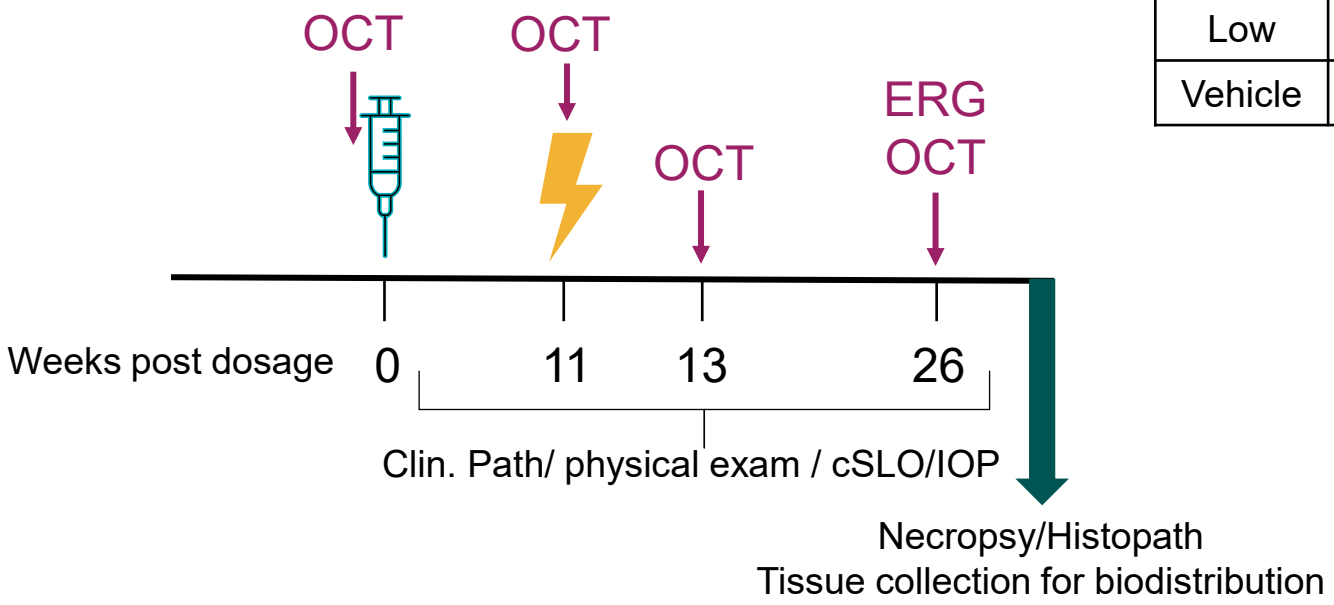
OPGx-RHO: Knockdown and Replacement in T4R adRP-RHO Canines



Cideciyan AV, et al. *Proc Natl Acad Sci* USA. 2018;115:E8547-E8556.

OPGx-RHO IND-Enabling Study Design

- RHO T4R/+ mutation is naturally occurring in English Mastiff canine model and causes retinal dysfunction and degeneration that mimics human dominant RP
- OPGx-RHO vector dosage BEFORE onset of retinal degeneration



		Dose Level (OD only)		
Dose	Number of animals	Vector concentration (vg/mL)	Total dose (vg per eye)	Injection volume (µL)
High	3	1.0×10^{12}	1.5×10^{11}	~150
Mid	3	3.16×10^{11}	4.74×10^{10}	~150
Low	3	1.0×10^{11}	1.5×10^{10}	~150
Vehicle	3	0	0	~150

Subretinal injection (1 eye)

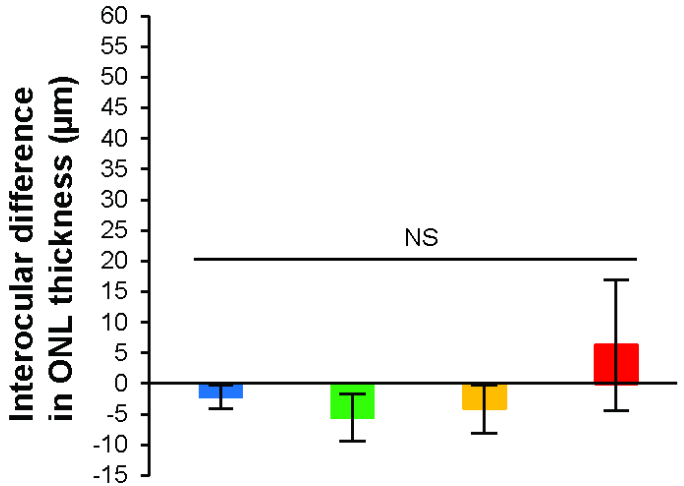
Light damage OU (high dose light)

cSLO, confocal scanning laser ophthalmoscopy; ERG, electroretinogram; IOP, intraocular pressure; OCT, optical coherence tomography; OD, right eye; OU, both eyes; RD retinal dystrophy; RP, retinitis pigmentosa.

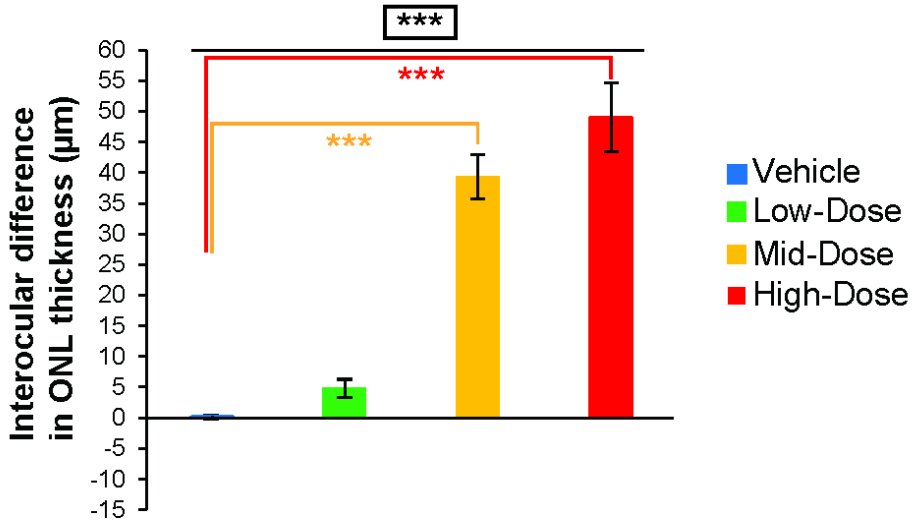
Preservation of ONL Thickness in OPGx-RHO Treated Retinas

- Differences in ONL thickness between injected (OD) and equivalent uninjected areas (OS) at 11 and 25 weeks post-dosage from OCT-derived ONL maps
- Dose-dependent preservation of ONL thickness in mid- and high-dose groups

11 wks post dosage (pre light exposure)



25 wks post dosage (14 wks post light exposure)

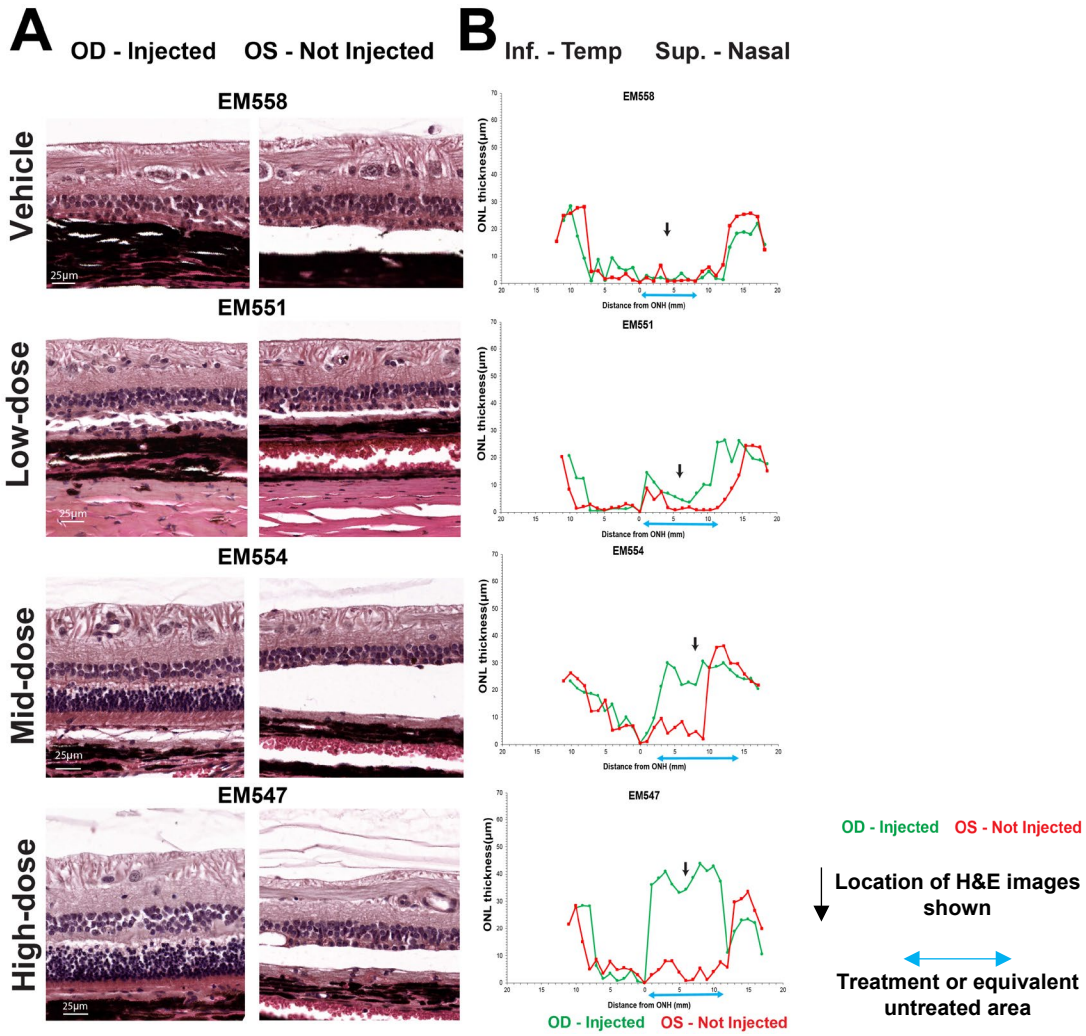


*** = p ≤ 0.001

LE, light exposure; OCT, optical coherence tomography; OD, right eye; ONL, outer nuclear layer; OS, left eye; NS, non-significant.

Preservation of ONL Thickness in OPGx-RHO Treated Retinas

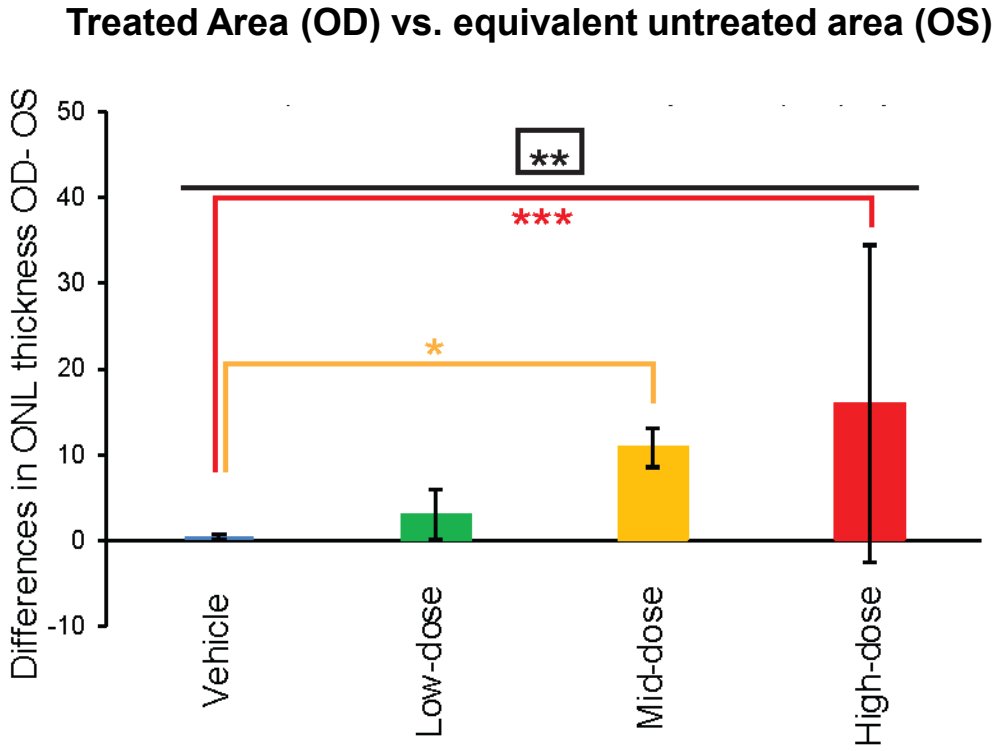
- Representative histology and quantification of ONL thickness from ONH -> peripheral ora serrata along inf-temp and sup-nas quadrants
- **27 weeks post dosage** in OD (injected) and OS (untreated, contralateral) retinas
- In 12/12 uninjected eyes, ONL thickness at Study Week 27 was reduced to < 10 µm (0-2 nuclei) in the central to mid-peripheral retina
- Mid and high dose injected retinas exhibited protection against light-induced ONL thinning



OCT, optical coherence tomography; OD, right eye; ONL, outer nuclear layer; OS, left eye.

Preservation of ONL Thickness in OPGx-RHO Treated Retinas

- Quantitative analysis of the retention of ONL thickness in the treated area measured by histology at 27 weeks post-dosage
- Mid and high dose injected retinas exhibited protection against light-induced ONL thinning

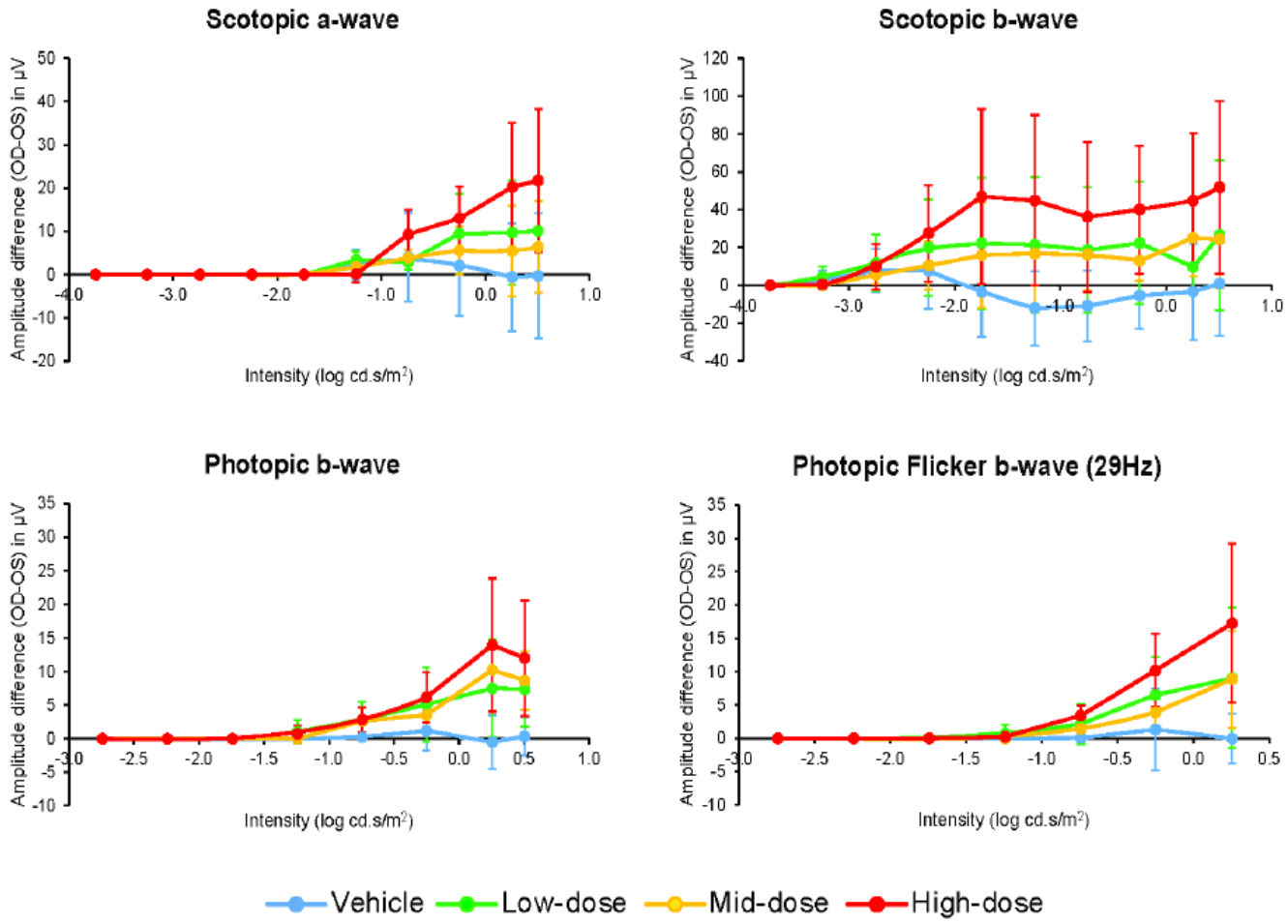


* = p ≤ 0.05, ** = p ≤ 0.01, and *** = p ≤ 0.001

OCT, optical coherence tomography; OD, right eye; ONL, outer nuclear layer; OS, left eye.

Comparison of ERG Amplitudes Across Treatment Groups at 26 Weeks Post-Dosage

- **Mean differences in scotopic a- and b-wave, photopic b-wave and 29 Hz flicker amplitudes** between the injected (OD) and uninjected (OS) eyes as a function of intensity of light stimulus
- Although the amplitude differences were higher in all three test-article treatment groups than in the vehicle-injected group, the overall difference across groups did not reach statistical significance



OD, right eye; OS, left eye.

adRP-RHO Canine Model IND-Enabling Study Informs Clinical Trial Design: OPGx-RHO Clinical Dosing Established

- **No systemic toxicity or test article-related effects** on body weight, IOP, clinical pathology parameters, organ weights, or macroscopic findings were seen during the 27-week in life phase of study
- **Dose-dependent structural preservation of the ONL and IS/OS was observed**
- **Low dose was well tolerated** and did not exhibit significant nonclinical findings
- **Mid dose was associated with minimal clinical signs of retinal inflammation** detected by OCT; Minimal subclinical retinal perivascular inflammatory cell infiltrates were noted in 1 out of 3 dogs
- **High dose was associated with clinical signs of retinal inflammation** by OCT, corresponding histologically to severe retinal perivascular inflammatory cell infiltrates and retinitis in 1 out of 3 dogs, as well as moderate subclinical retinal perivascular inflammatory cell infiltrates in another 1 out of 3 dogs
- **NOAEL of OPGx-RHO** established in this study: 4.74×10^{10} vg/eye (150 µL, 3.16×10^{11} vg/mL, mid dose)

cSLO, confocal scanning laser ophthalmoscopy; IOP, intraocular pressure; OCT, optical coherence tomography.

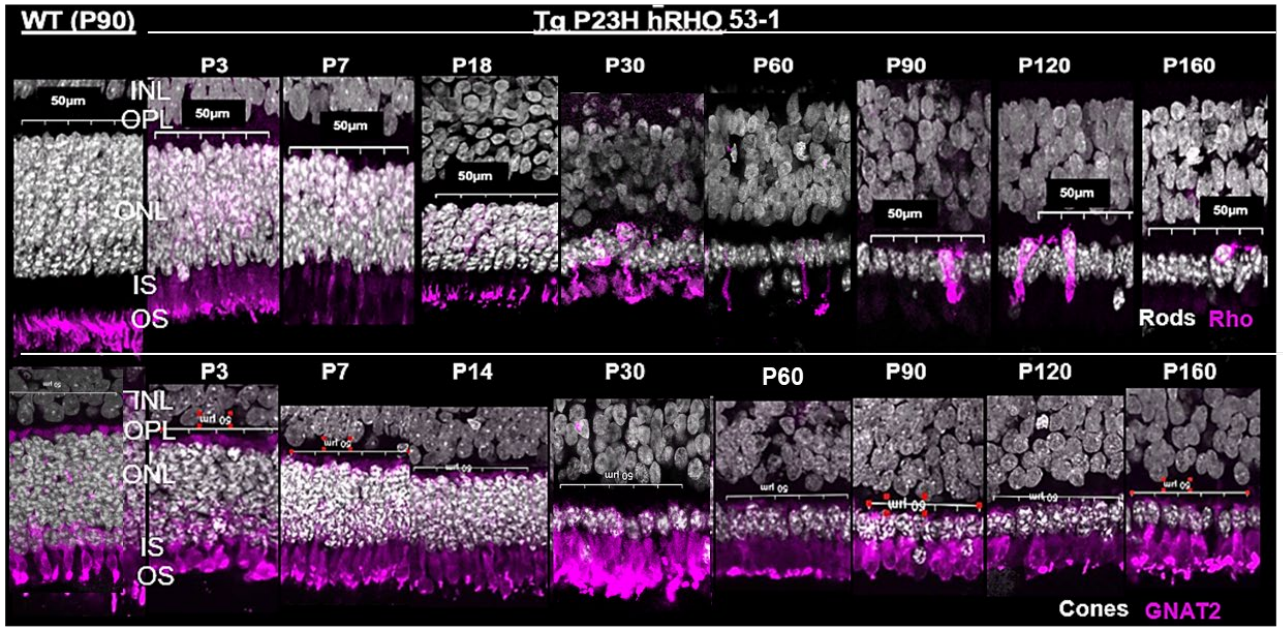
Therapeutic Efficacy of a OPGx-RHO in a Swine Model of adRP-RHO

Archana Jalligampala, Ph.D.

adRP, autosomal dominant retinitis pigmentosa..

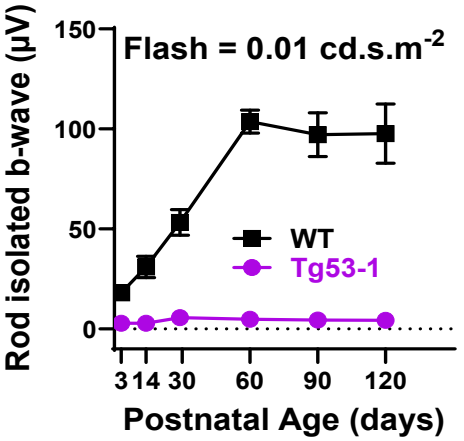
Transgenic P23H humanized RHO Swine Model of adRP

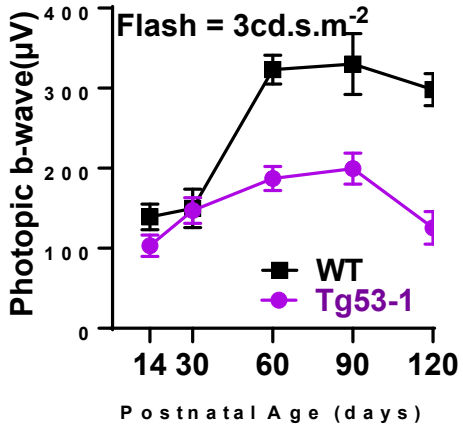
- No rod isolated ERG function from birth
- Viable rods detectable in P7 to test therapeutic interventions
- Persistence of cone viability and cone function through 5 years age



Rods

Cones



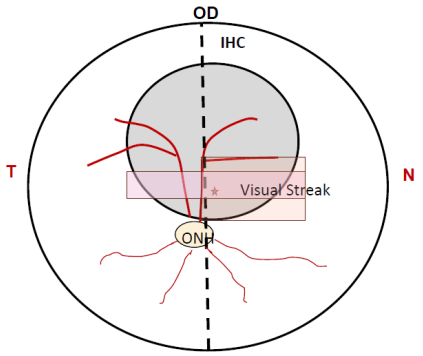


OPGx-RHO Study Design

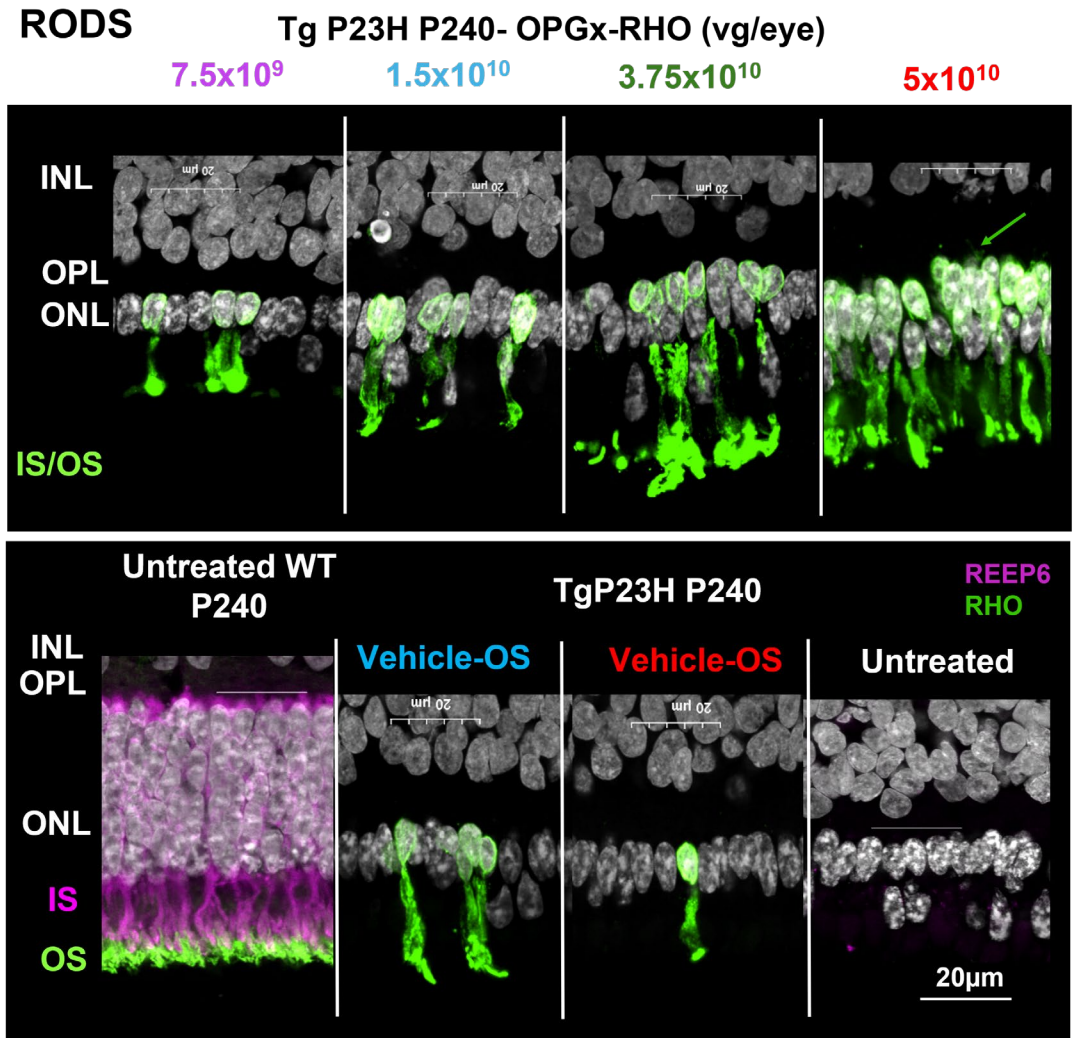
Treatment	Low	Mid-Low	Mid-High	High	Vehicle
Concentration	7.50E+09	1.50E+10	3.75E+10	5.00E+10	N/A
Number of eyes injected	5	7	5	5	23
Number of eyes to date	4	4	2	4	14

OPGx- RHO Maintains Rod Morphology in TgP23H Retinas

- Dose-dependent preservation of rod morphology 20-31 weeks post injection of OPGX-RHO

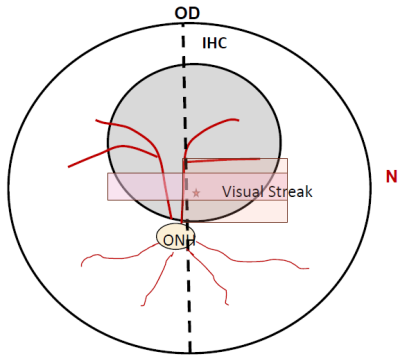


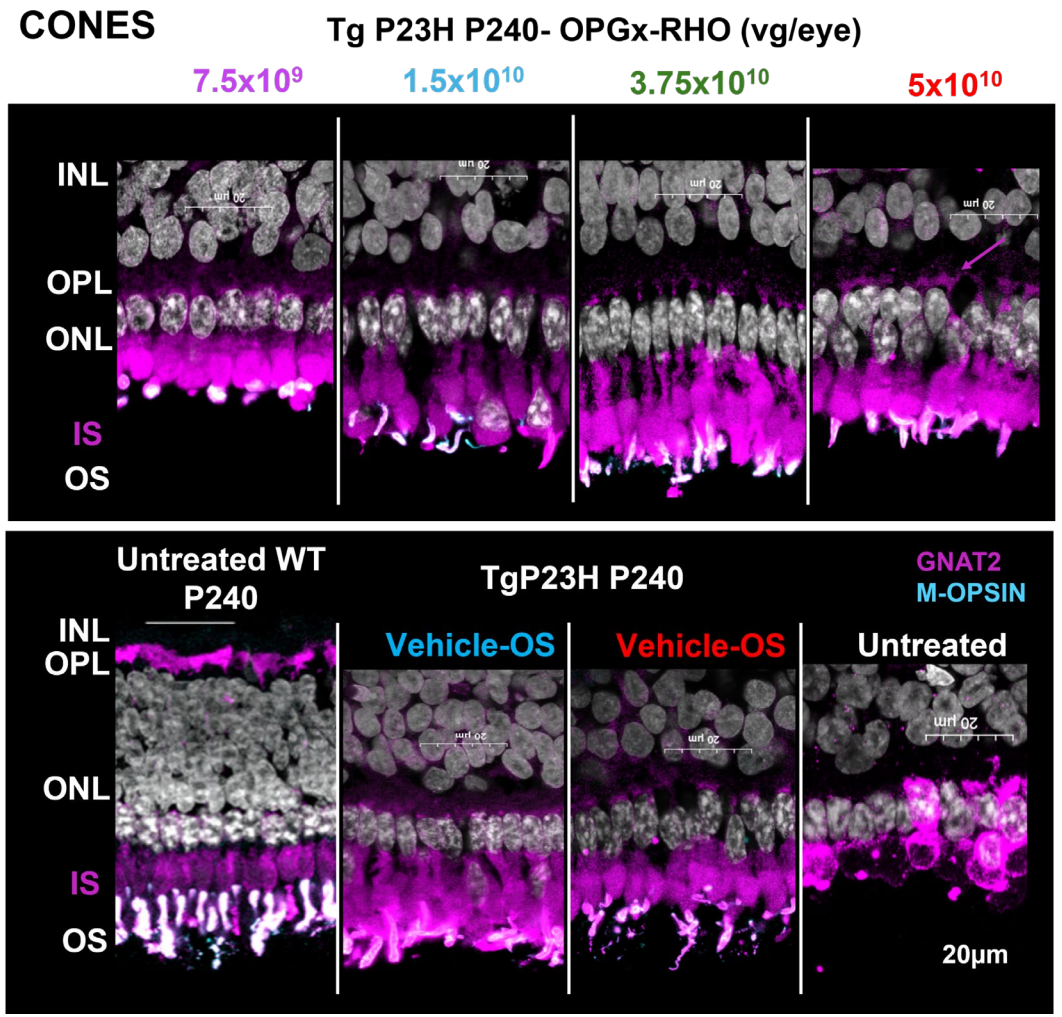
- 1.5 x 10^{10} vg/eye (“mid-low dose”) estimated to be minimal effective dose for rod preservation using immunofluorescence analysis



OPGx- RHO Maintains Cone Morphology in TgP23H Retinas

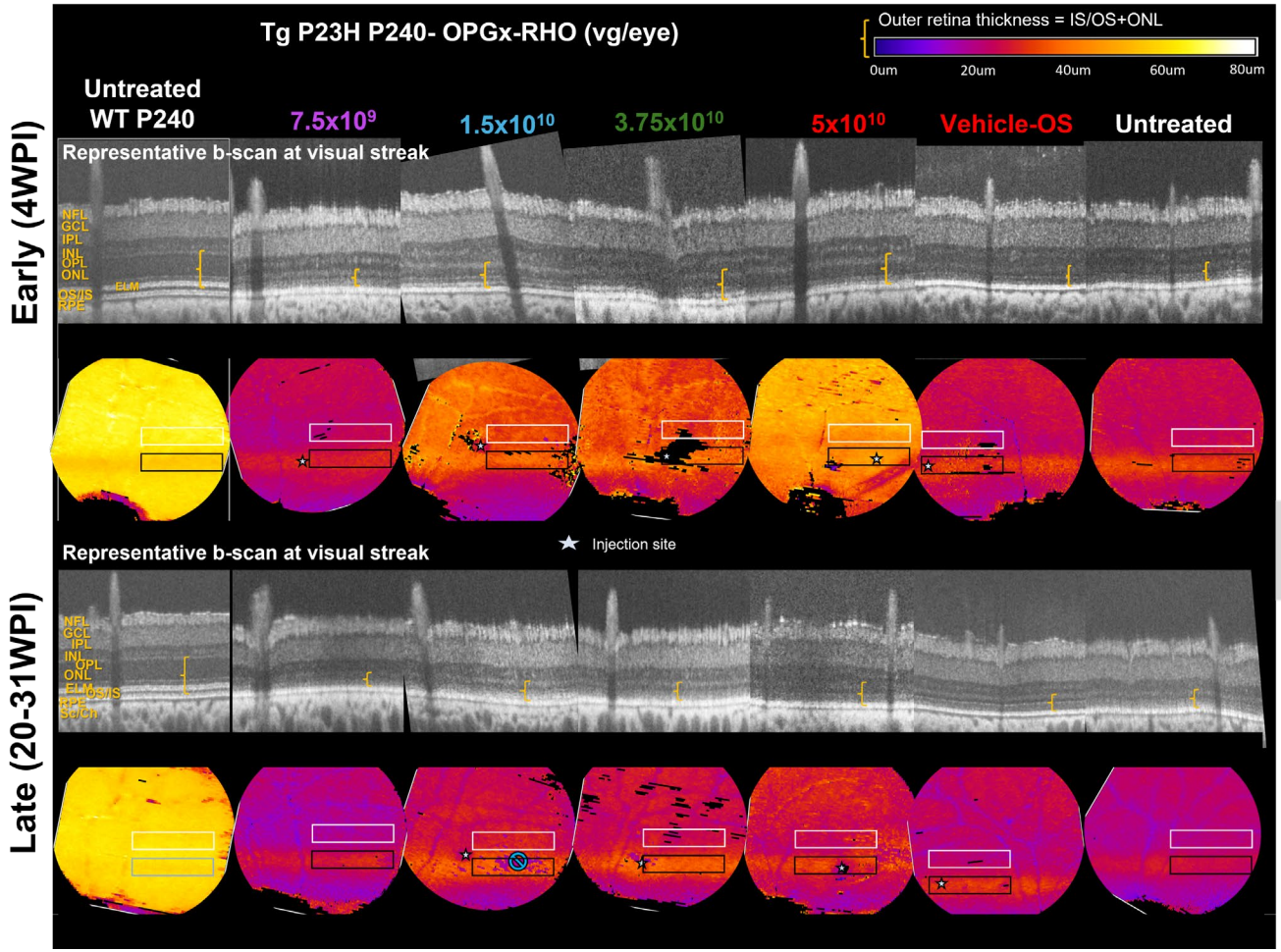
- Dose-dependent preservation of cone morphology 20-31 weeks post injection of OPGX-RHO
- 1.5 x 10^{10} vg/eye (“mid-low dose”) estimated to be minimal effective dose for cone preservation using immunofluorescence analysis





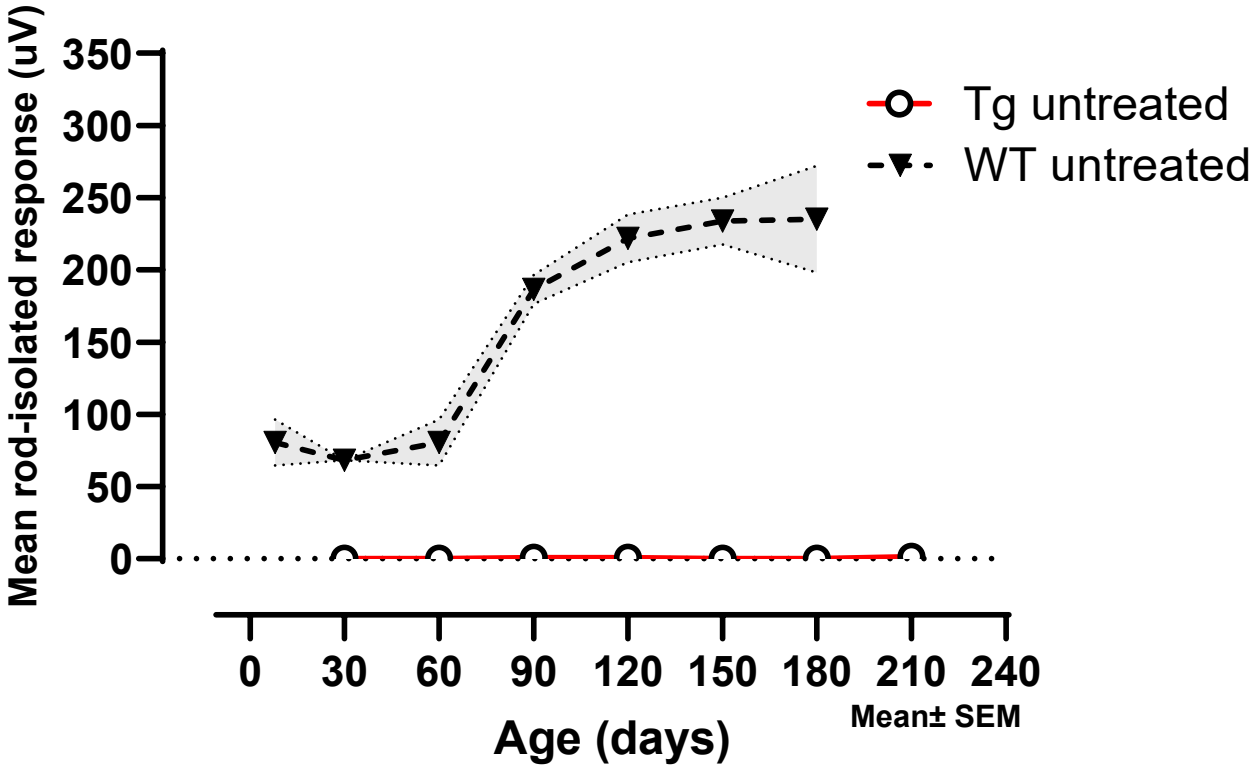
OCT Confirmation of Histologic Observations: OPGx-RHO Maintains Outer Retinal Integrity vs. Untreated TgP23H Retinas

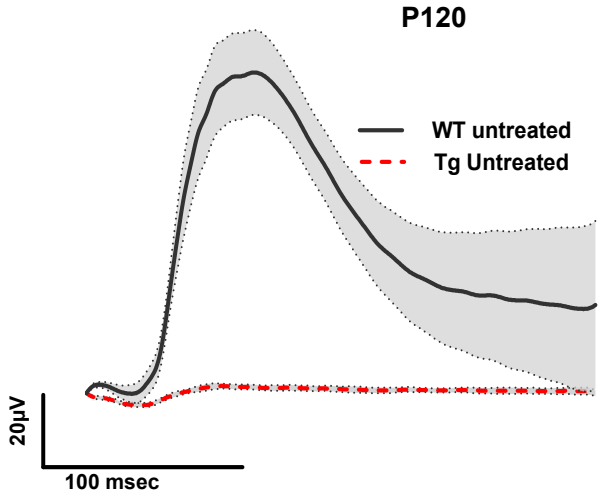
- Observations of OCT thickness maps at 4 and 20-31 weeks post injection of OPGx-RHO:
  - Limited outer retinal thinning between early and late timepoints supportive of cone maintenance
  - Dose-dependent preservation of rods



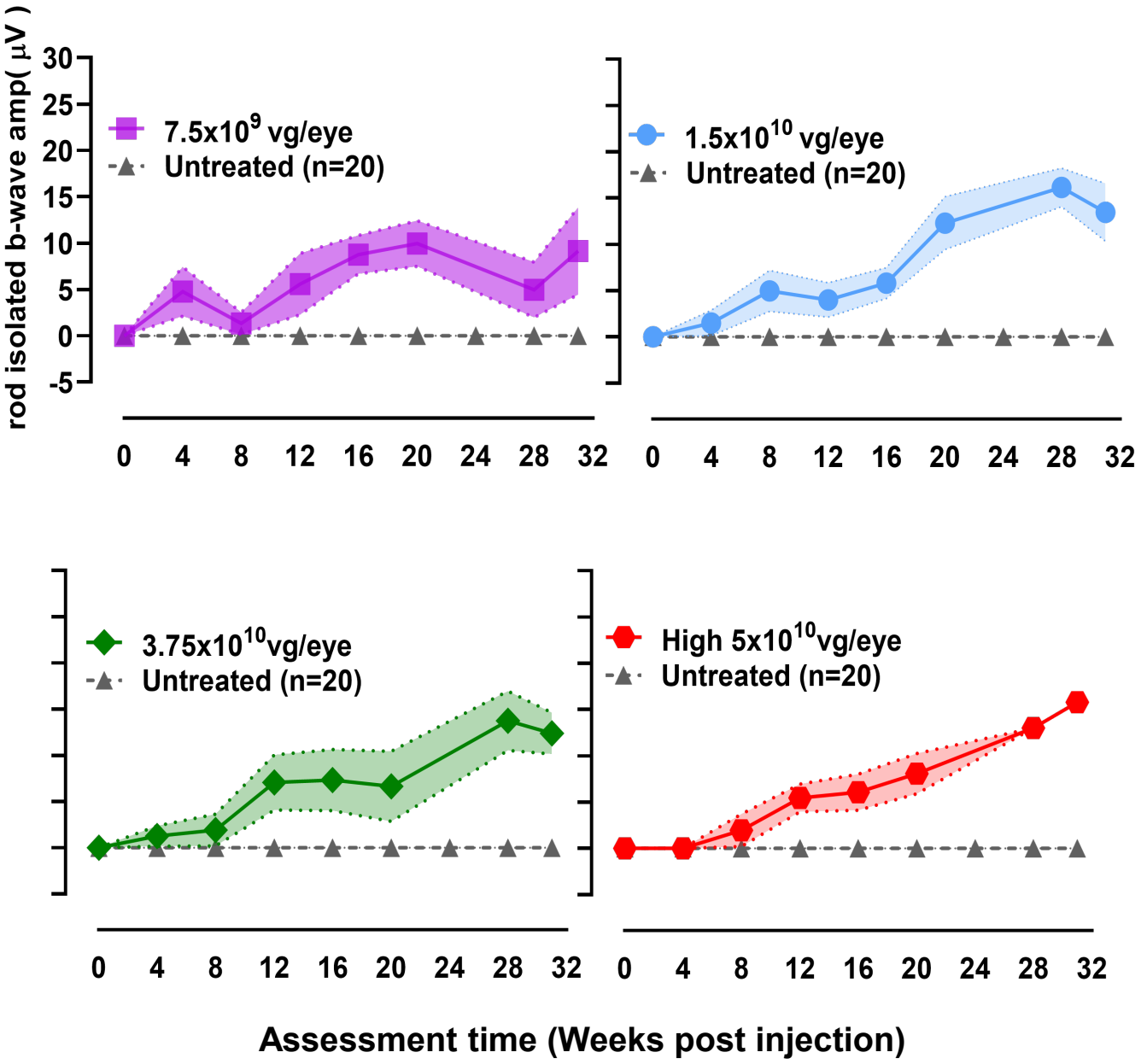
ERG: Rod-isolated Response (Untreated)

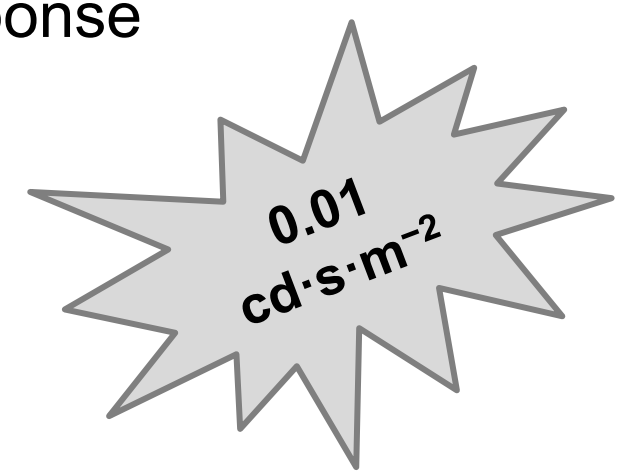
0.01 cd·s·m^{-2}





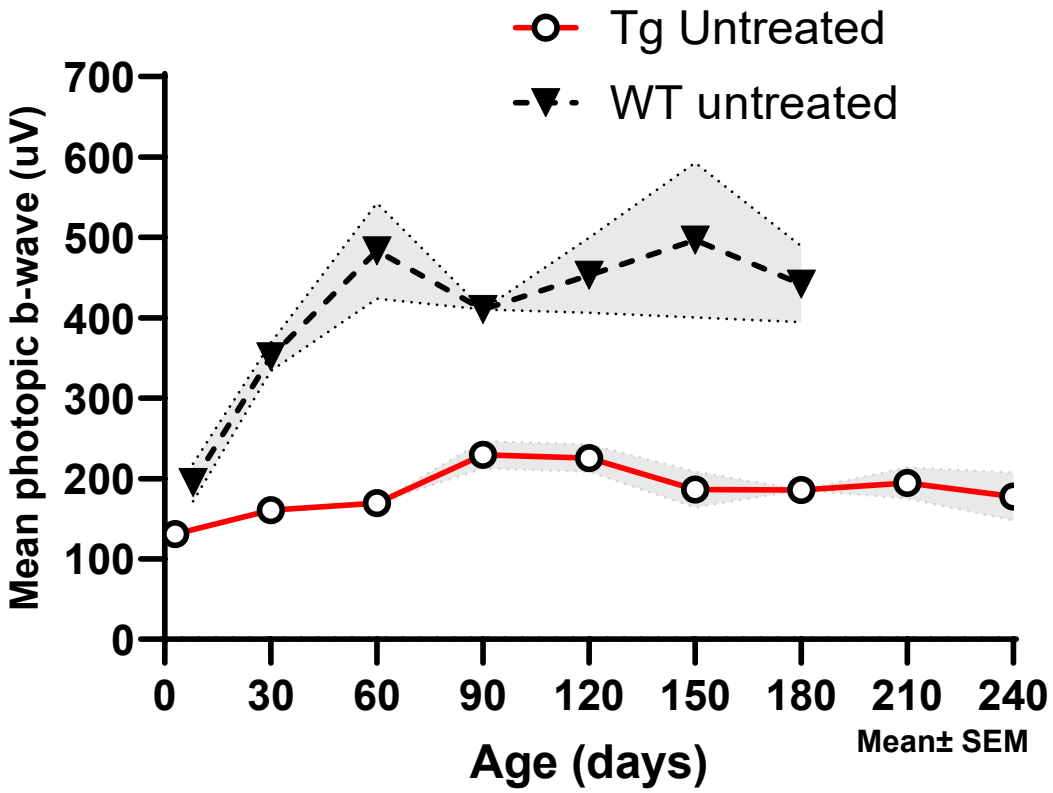
OPGx-RHO induced rod-isolated ffERG response

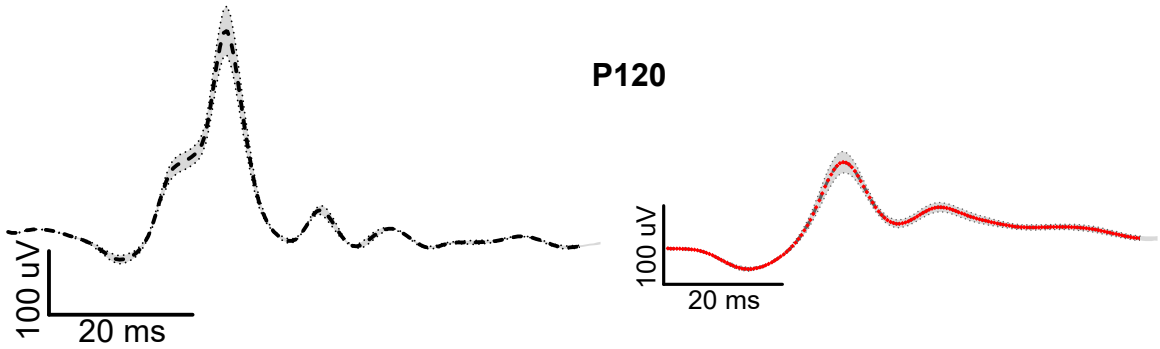




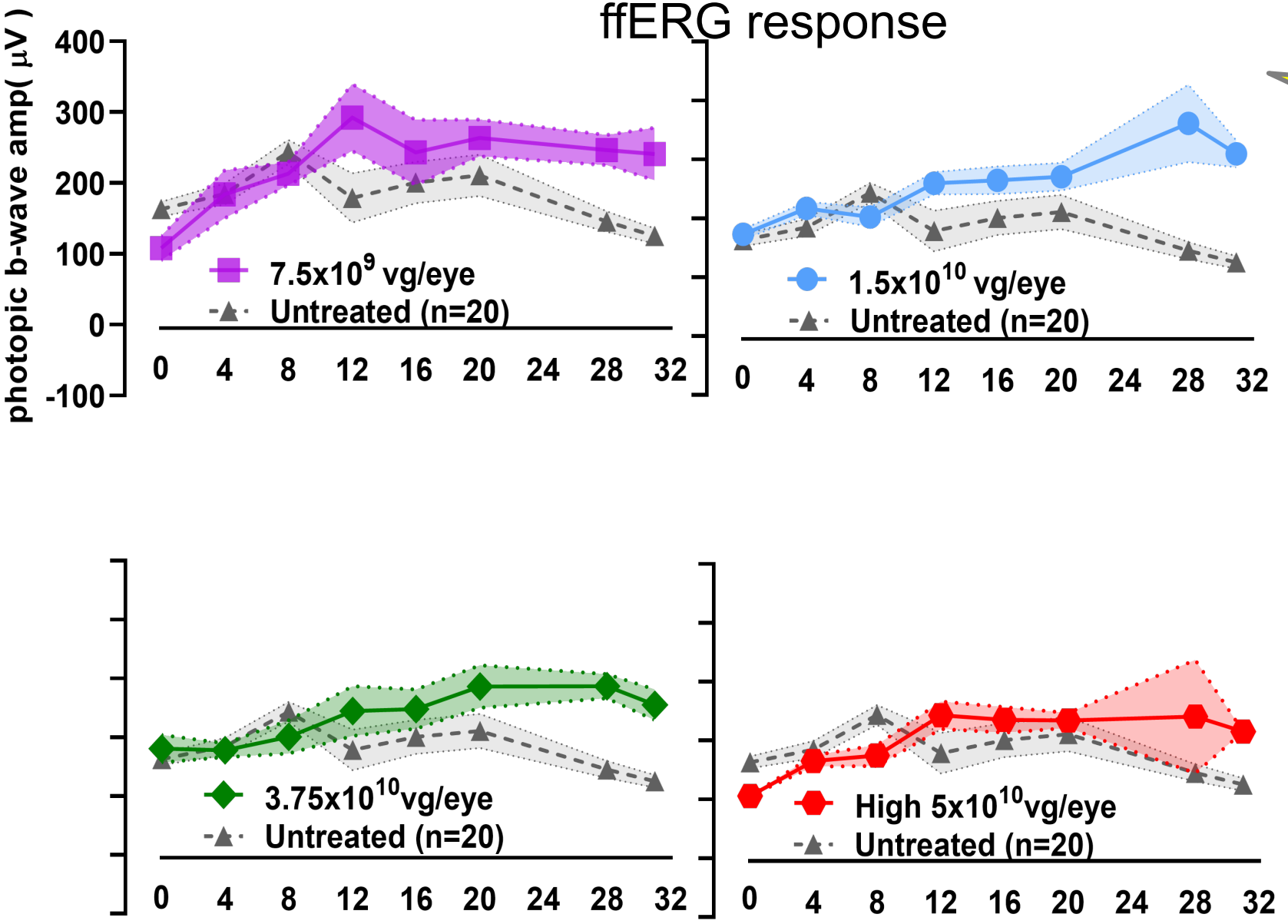
ERG: Photopic Response (Untreated)

3 cd·s·m^{-2}





OPGx-RHO mediated maintenance of cone-mediated ffERG response



3.0 cd·s·m^{-2}

Safety and Efficacy of OPGx-RHO Demonstrated in a Humanized Pig Model of P23H adRP-RHO

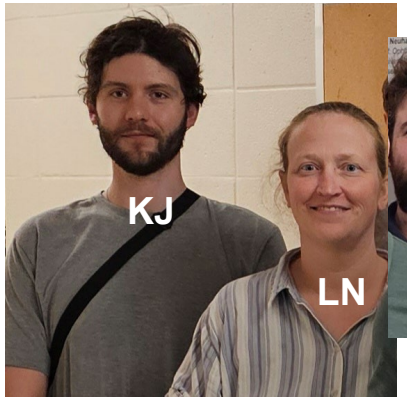
- **ERGs:**
  - Induction of rod isolated responses with preservation of cone responses
- **OCT:**
  - Dose-dependent maintenance of ONL thickness
- **IHC:**
  - Dose-dependent preservation of rod morphology
  - Cone structure remained preserved with prominent pedicles and IS/OS

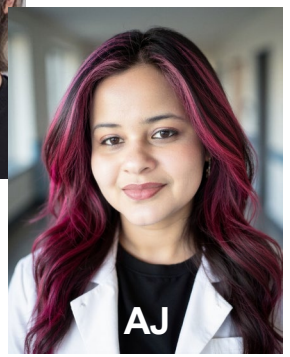
Opus Genetics

Multi-asset pipeline with significant projected data readouts and milestones

- **OPGx-LCA5:** Phase 3 dosing in H2 2026
- **OPGx-BEST1:** Phase 1/2, Cohort 1 three-month results mid-year 2026
- **Two additional gene therapy programs** to enter clinical testing
- **Phentolamine ophthalmic solution 0.75%**
  - **Presbyopia:** FDA PDUFA date of 10/17/26
  - **Dim light disturbances:** Phase 3 topline results in H1 2026

Acknowledgements





- Archana Jalligampala, Ph.D.
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Related OPGx-RHO ARVO Presentations

- Title: **Nonclinical efficacy and toxicity study of GMP-grade vector OPGx-RHO (scAAV2/5-RHO820-shRNA820) delivered by subretinal injection in a canine model of RHO-adRP** (Dufour V et al.)

- Presentation Number - Posterboard Number: **5746 - 0459**
  Session Number: 538
  Session Date/Times: **May 7, 2026 from 11:45 AM to 1:30 PM**

- Title: **Therapeutic efficacy of a mutation-independent AAV knockdown and replacement approach in a swine animal model of autosomal-dominant retinitis pigmentosa (adRP)** (Jalligampala A et al.)

- Presentation Number - Posterboard Number: **1536 - 0197**
  Session Number: 219
  Session Date/Times: **May 4, 20 26 from 11:15 AM to 1:00 PM**

Every patient's eyes tell a story

Images of real patients with IRDs.