

PRESENTATION OF OPHTHALMOLOGY CLINICAL TRIAL DATA AT ARVO CONFERENCE

- **PYC is a precision medicine company dedicated to changing the lives of patients with genetic diseases who have no treatment options available**
- **PYC is developing two investigational drug candidates that have the potential to become the first approved treatment options for blinding eye diseases of childhood¹:**
 - **VP-001 for the treatment of Retinitis Pigmentosa type 11 (RP11); and**
 - **PYC-001 for the treatment of Autosomal Dominant Optic Atrophy (ADOA)**
- **PYC today announces that data from the ongoing Phase 1/2 trials in both RP11 and ADOA will be presented at the Association for Research in Vision and Ophthalmology (ARVO) conference in Denver, Colorado between 3 and 7 May 2026**
- **A copy of the presentation materials for each program is attached to this announcement**

PERTH, Australia and SAN FRANCISCO, California – 4 May 2026

PYC Therapeutics Limited (ASX:PYC) (PYC or the Company) is a precision medicine Company dedicated to changing the lives of patients with genetic diseases who have no treatment options available.

The Company currently has three clinical-stage drug development programs including two drug candidates that address the underlying cause of blinding eye diseases of childhood:

- PYC's drug candidate known as VP-001 is designed to correct the underlying genetic cause of a disease called Retinitis Pigmentosa type 11 (RP11); and
- PYC's drug candidate known as PYC-001 is designed to correct the underlying genetic cause of a disease called Autosomal Dominant Optic Atrophy (ADOA).

Both drug candidates are the most advanced assets in clinical development for their respective target diseases and hold first-in-indication potential.

¹ Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

PYC today announces that data from the ongoing Phase 1/2 trials of both VP-001 and PYC-001 in RP11 and ADOA respectively will be presented at the Association for Research in Vision and Ophthalmology (ARVO) conference in Denver, Colorado between 3 and 7 May 2026. The presentations will highlight the safety/tolerability and emerging efficacy profiles of both drug candidates established in the clinical trials completed to date. Details of each presentation on PYC's pipeline assets forming part of the ARVO conference are provided below:

- Dr. Patrick Yu-Wai-Man: SUNDEW: A Phase 1A Single Ascending Dose (SAD) Study to Evaluate the Safety and Tolerability of a Peptide-Conjugated Oligonucleotide (PYC-001) to Treat OPA1-Associated Autosomal Dominant Optic Atrophy
- Dr. Jessica Morgan: Adaptive optics imaging, microperimetry and optoretinography following intravitreal injection of VP-001 in patients with PRPF31-associated retinitis pigmentosa
- Dr. Fred Chen: A Phase 1B Multiple Ascending Dose Study of VP-001; a peptide conjugate of oligonucleotide designed to treat PRPF31-related Retinitis Pigmentosa
- Dr. Patrick Yu-Wai-Man: Innovative Therapies for Inherited Optic Neuropathies

A copy of the presentation materials for each of these presentations² is attached to this announcement.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a clinical-stage biotechnology company creating a new generation of RNA therapies to change the lives of patients with genetic diseases. The Company utilises its proprietary drug delivery platform to enhance the potency of precision medicines within the rapidly growing and commercially proven RNA therapeutic class. PYC's drug development programs target monogenic diseases – the indications with the highest likelihood of success in clinical development³.

For more information, visit pyctx.com, or follow us on [LinkedIn](#) and [X](#).

Forward looking statements

Any forward-looking statements in this ASX announcement have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations, and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside the Company's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this ASX announcement include known and unknown risks. Because actual results could differ materially to assumptions made and the Company's current intentions, plans, expectations, and beliefs about the future, you are urged to view all forward-looking statements contained in this ASX announcement with caution. The Company undertakes no obligation to publicly update any forward-looking statement whether as a result of new information, future events or otherwise.

This ASX announcement should not be relied on as a recommendation or forecast by the Company. Nothing in this ASX announcement should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

² The following presentation material is not attached - Dr. Patrick Yu-Wai-Man: Innovative Therapies for Inherited Optic Neuropathies

³ Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank
<https://doi.org/10.1101/2020.11.02.2022232>

This ASX announcement was approved and authorised for release by the Board of PYC Therapeutics Limited

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SUNDEW: A Phase 1A Single Ascending Dose Study of PYC-001; a peptide conjugated oligonucleotide designed to treat OPA1 mutation-associated Autosomal Dominant Optic Atrophy



Patrick Yu-Wai-Man¹, Clare Fraser², Doron Hickey³, Andrea Vincent⁴, George Mitchell⁵, Timothy Masarej⁵, Sri Mudumba⁵, Paula Cunningham⁵, Tracy Chai⁵, Fern Utama⁵, Jessica Stevenson⁵, Katherine Lee⁵, Janya Grainok⁵, Aishwarya Kundu⁵

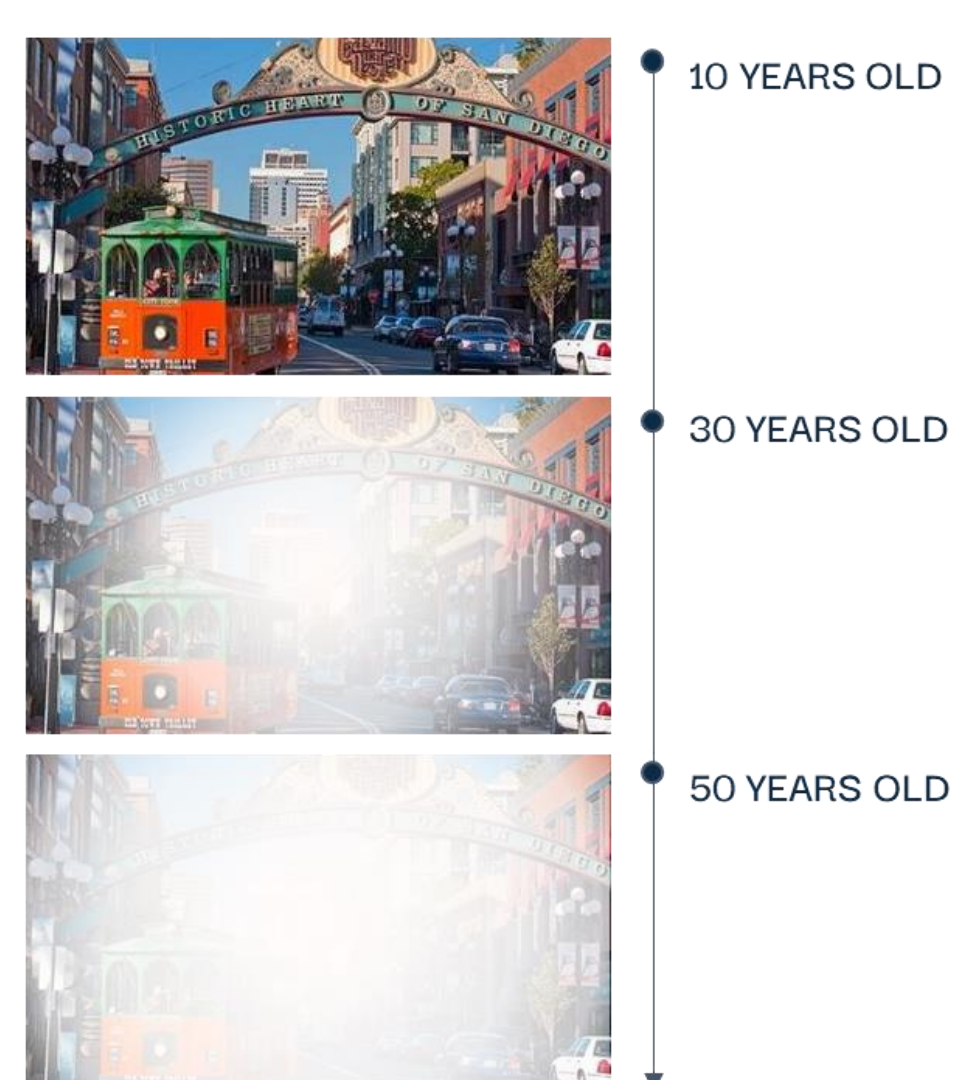
¹University of Cambridge and Moorfields Eye Hospital, ²Sydney Eye Hospital, ³The Royal Victorian Eye and Ear Hospital, ⁴University of Auckland, ⁵PYC Therapeutics, Harry Perkins Institute of Medical Research

ADOA is a progressive and blinding eye disease of childhood for which there are no available treatment options

Autosomal Dominant Optic Atrophy (ADOA) & PYC-001

- A progressive and irreversible blinding eye disease
- It is the most common inherited optic neuropathy with 9,000 – 16,000 affected individuals in the western world^{1,2}
- Median age of onset at 7 years of age, with 80% of patients symptomatic before age 10³
- There are no treatments available for patients with ADOA
- Caused by haploinsufficiency of the *OPA1* gene, resulting in the loss of Retinal Ganglion Cells (RGCs) whose axons form the optic nerve
- PYC-001 increases *OPA1* protein levels to restore the mitochondrial network and improve cellular bioenergetics in models derived from patients with ADOA in a mutation independent manner
- PYC is an intravitreally administered RNA-peptide drug conjugate that binds to *OPA1* mRNA

Deteriorating vision of an ADOA patient



The deficiency of OPA1 protein in ADOA patients triggers a cascade of bioenergetic deficits that culminate in RGC cell death and loss of vision

Unaffected bioenergetics

- Wild type *OPA1* protein expression (100%)
- Slim, and tight mitochondrial ultrastructure
- Elongated mitochondria
- Improved respiratory efficiency
- More resistant to cell death

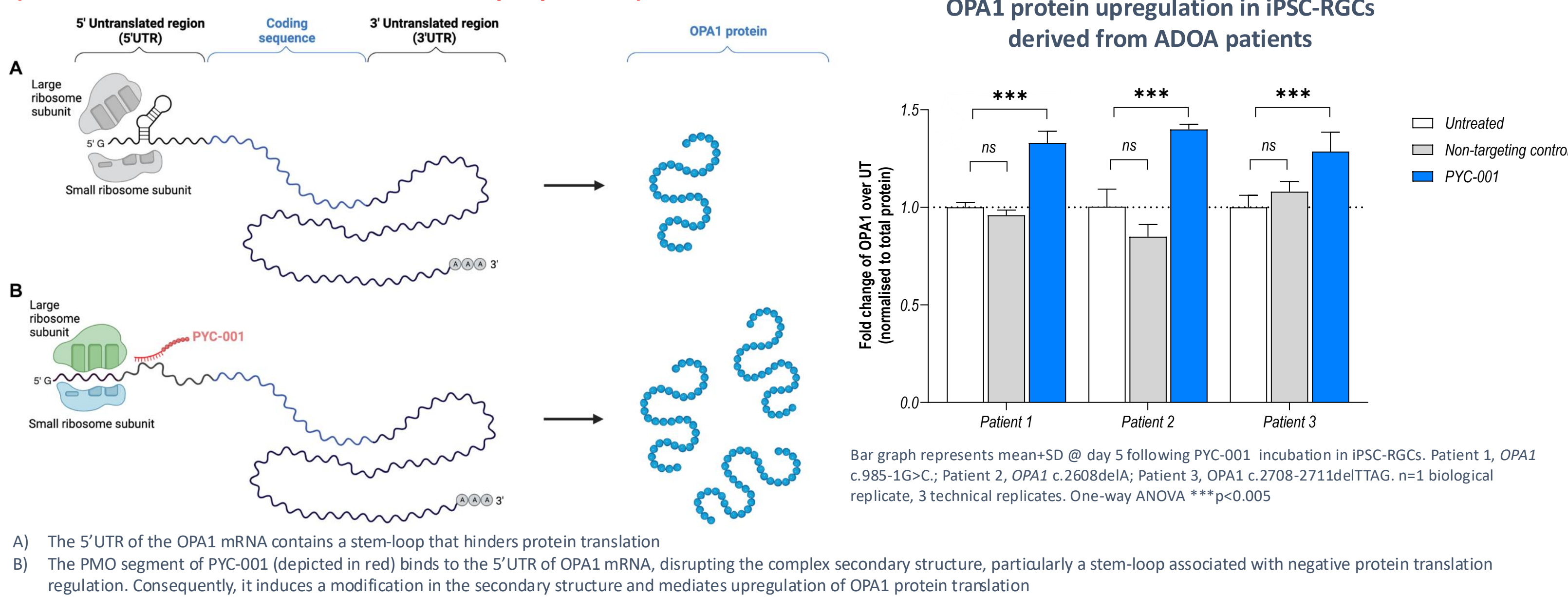
Bioenergetics in ADOA

- OPA1* haploinsufficient ~50-70% expression
- Disorganized, wide cristae and cristae junctions
- Fragmented mitochondria
- Lower respiratory efficiency
- Higher sensitivity to challenge

Loss of vision

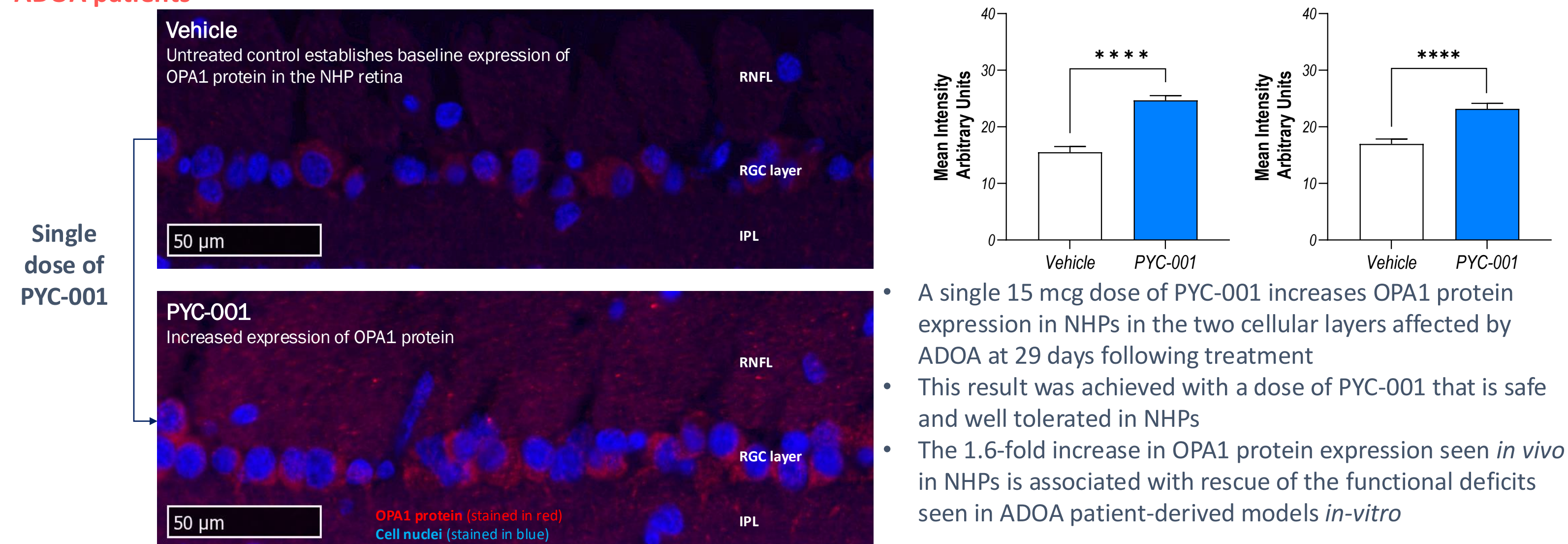
PYC-001 specifically addresses the underlying cause of ADOA by increasing *OPA1* protein expression

PYC-001 has demonstrated the potential to address the root cause of ADOA in a mutation independent manner (validated in material derived from multiple patients)



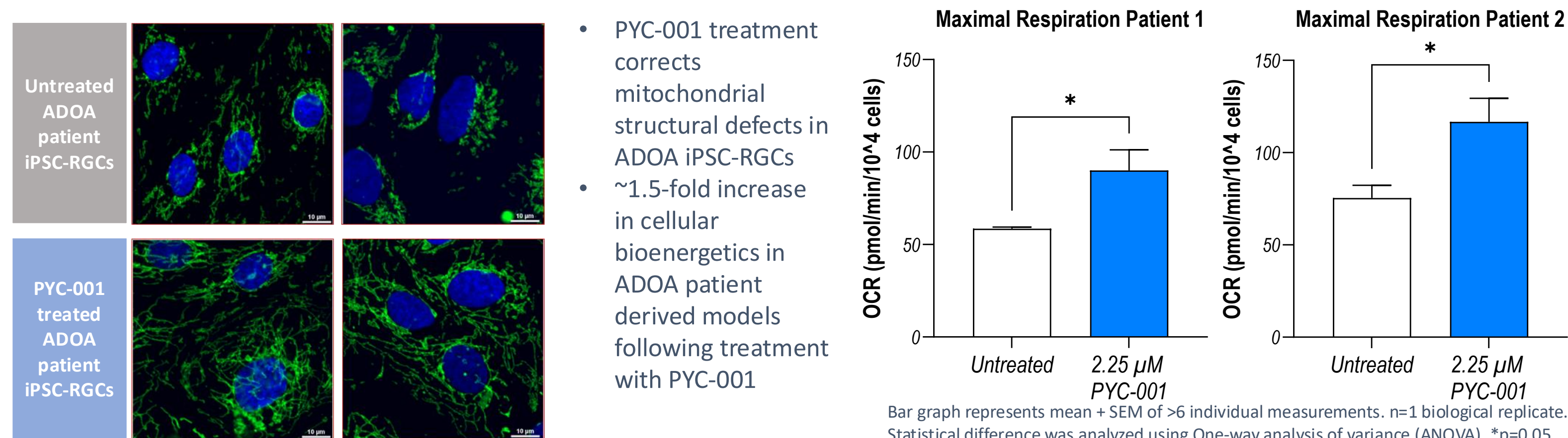
PYC-001 increases *OPA1* protein levels in the retina at safe and well-tolerated doses in Non-Human Primates

The RGC layer and Retinal Nerve Fibre Layer (RNFL) are the two cellular layers affected by insufficient *OPA1* protein expression in ADOA patients



Increasing *OPA1* protein levels rescues the functional deficits associated with ADOA in patient-derived models

PYC-001 treatment restores mitochondrial impairments and cellular bioenergetics in iPSC-RGCs derived from ADOA patients^{3,4}



Methods

Design of PYC-001

A translational enhancing oligonucleotide conjugated to a cell-penetrating peptide (PYC-001) was developed, designed to increase expression of the *OPA1* protein from the remaining wild-type allele in patients affected by Autosomal Dominant Optic Atrophy (ADOA)⁴.

In vitro preclinical efficacy data

Generated in iPSC-derived Retinal Ganglion Cells (RGCs) from multiple ADOA patients, confirmed mutation-agnostic intended mechanism of action in target cells, following treatment with PYC-001³.

In vivo preclinical efficacy data

Cynomolgus monkeys were dosed bilaterally with PYC-001 by IVT injections of 15 mcg/eye. Immunohistochemistry of the RGC and confirmed modulation of target gene expression in the affected cell type/layer in the retina with a single, safe and well tolerated dose⁴.

SUNDEW, a Phase 1 Single Ascending Dose (SAD) First-in-Human (FIH) study

Nine participants with genetically confirmed *OPA1* mutation-associated ADOA were recruited at 2 sites in Australia in 3 cohorts (3, 10 and 30 mcg). Each participant received a unilateral intravitreal injection of PYC-001 in the worst affected eye and were followed for adverse events. Dose escalation was approved by a Safety Review Committee (SRC). Safety and tolerability are assessed based on both ocular and non-ocular adverse events reporting in conjunction with clinical chemistry parameters, measures of visual function, functional vision and imaging. Exploratory efficacy was assessed using Visual Acuity.

MYRTLE, a Phase 1b Multiple Ascending Dose (MAD) study

Up to 18 participants with genetically confirmed *OPA1* mutation-associated ADOA were recruited at sites across APAC, into 5 cohorts (10 mcg Q8W, Q12W, 30 mcg Q8W, Q12W and a 60 mcg single dose cohort followed by repeat doses Q12W). Participants receive unilateral injections of PYC-001 and are followed for adverse events. Safety and tolerability are assessed based on both ocular and non-ocular adverse events reporting in conjunction with clinical chemistry parameters, measures of visual function, functional vision and imaging. Exploratory efficacy was assessed using visual acuity and Flavoprotein Fluorescence. Participants will receive at least 3 doses of PYC-001.

Clinical Data Generated in SUNDEW and MYRTLE

Safety/Tolerability Profile of Single Doses of PYC-001

- No Treatment Related-Serious Adverse Events (TR-SAEs) observed in any patient following injection of PYC-001 to date (3 mcg, 10 mcg, 30 mcg and 60 mcg)⁵
- Treatment-Emergent Adverse Events were mostly mild, and procedure related with no ongoing adverse events

Encouraging improvement in measures of visual acuity (relative to both control eye and baseline) have been observed in ADOA patients treated with PYC-001 in the SUNDEW and MYRTLE studies

Figure 1. Change from baseline in Low-Contrast Visual Acuity (LCVA) in *OPA1* ADOA patients treated with PYC-001[^]

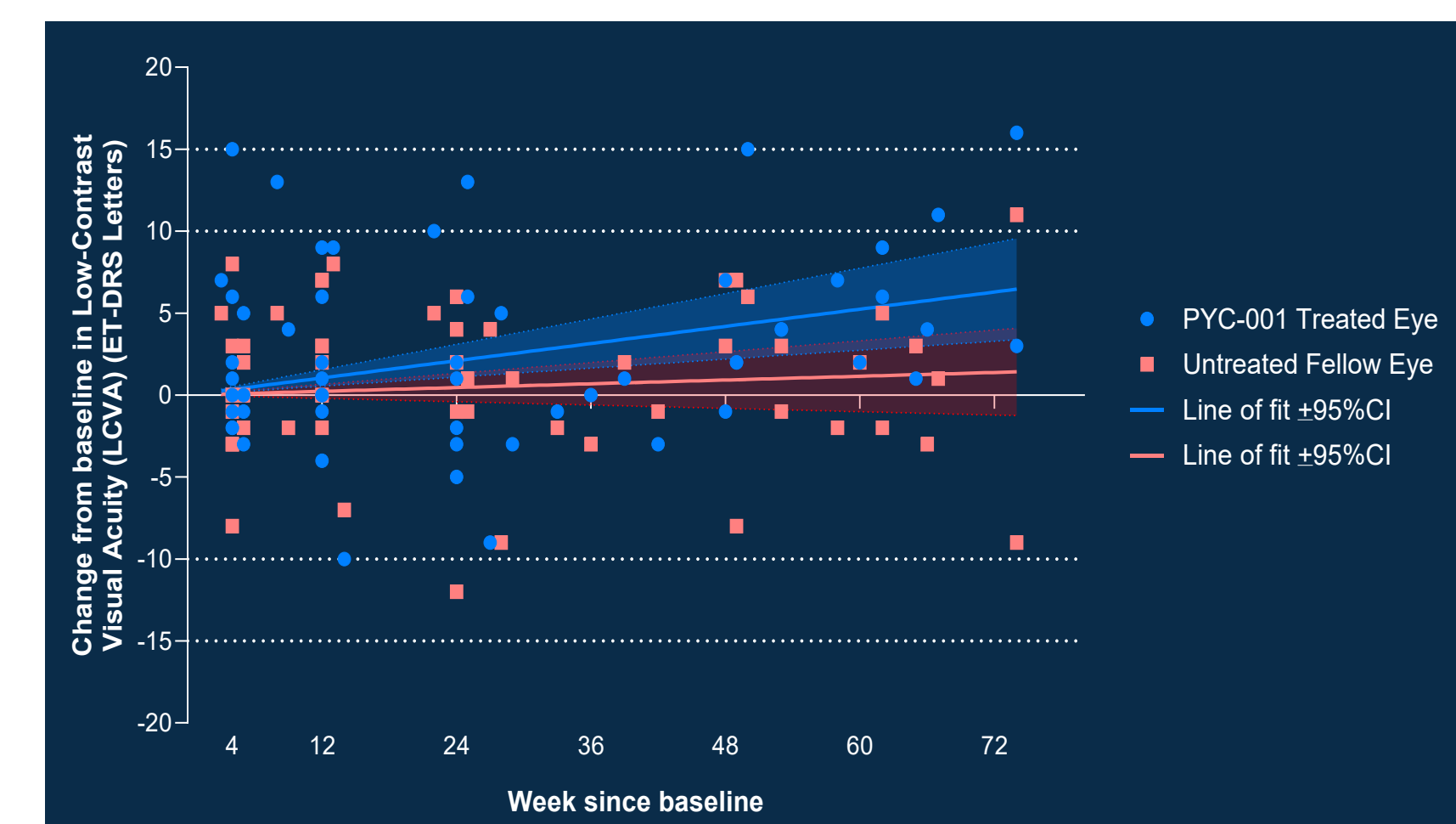
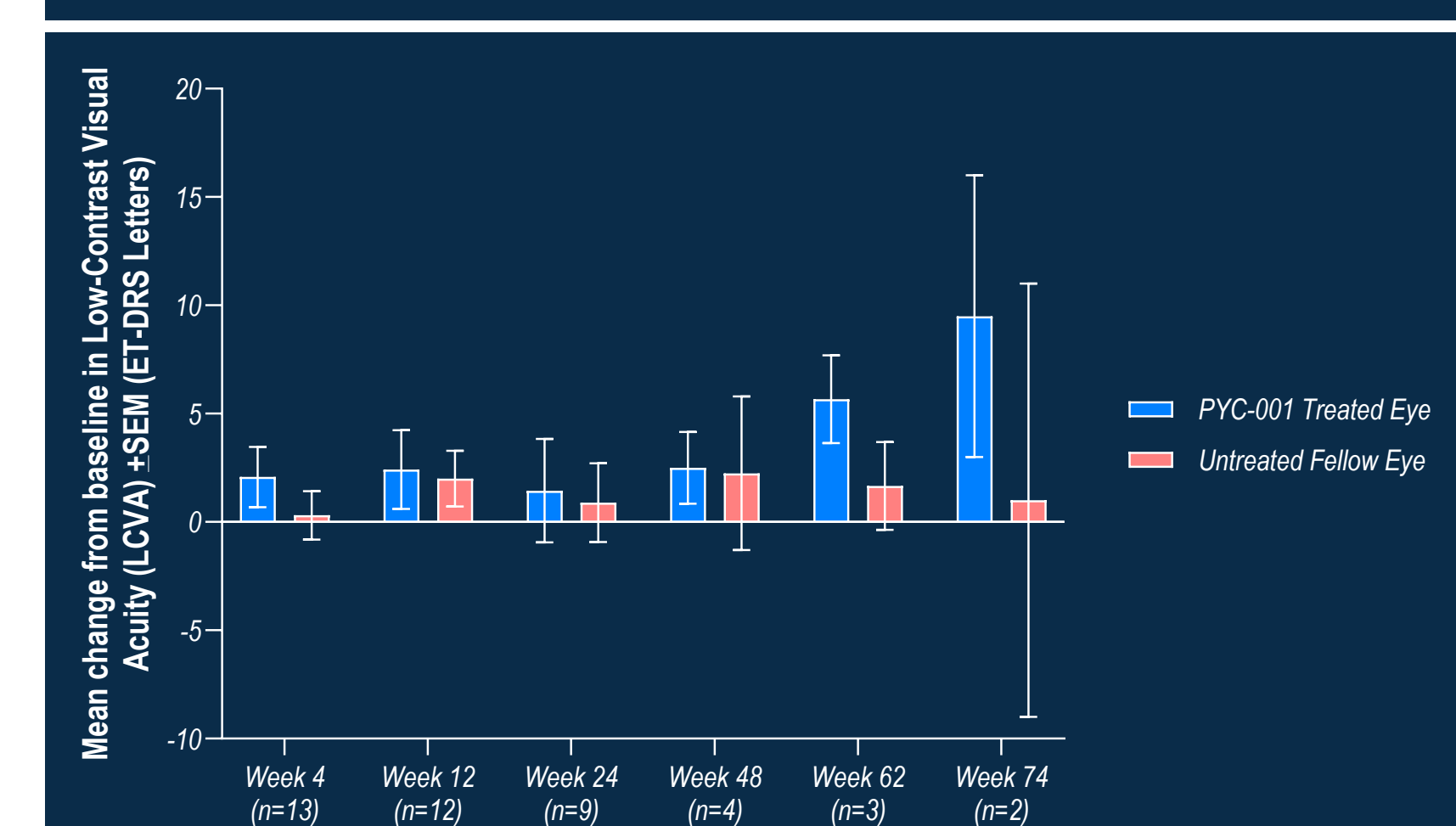


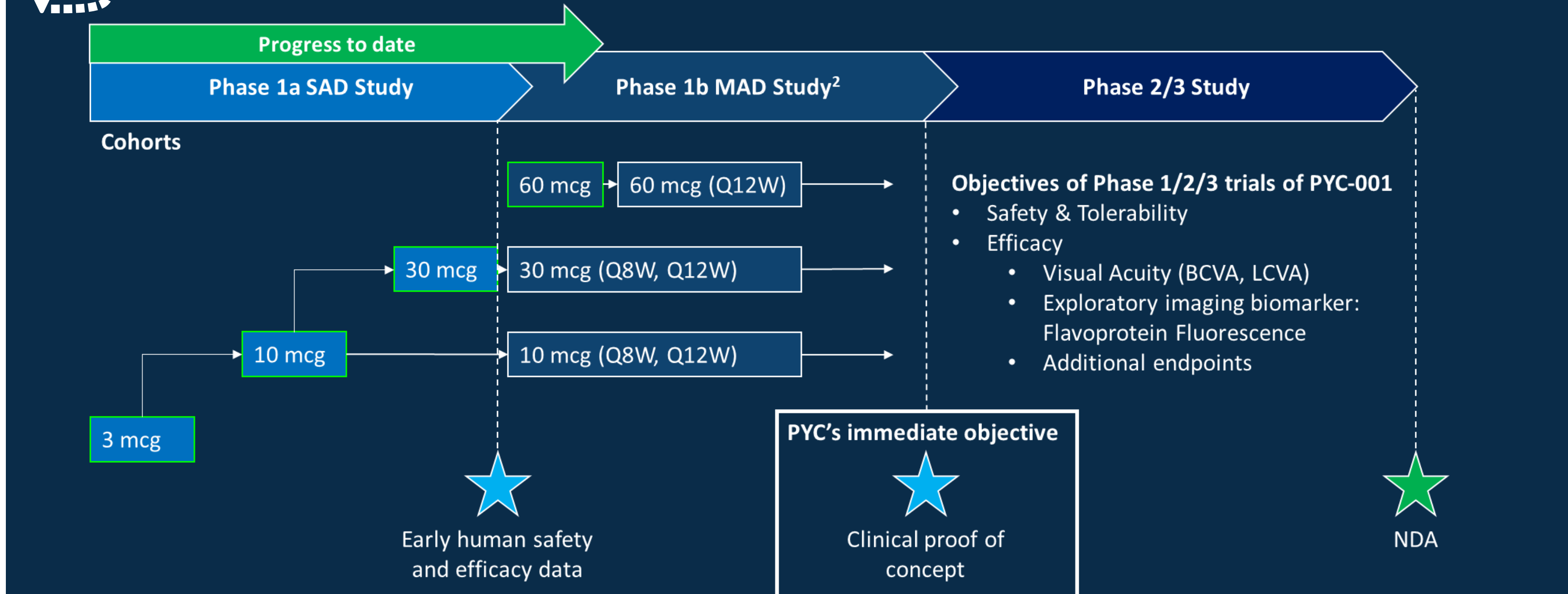
Figure 2. Mean change from baseline in Low-Contrast Visual Acuity (LCVA) (±SEM) in *OPA1* ADOA patients treated with PYC-001[^]



Select timepoints where n≥2

[^]All patients with data available from SUNDEW and MYRTLE at 17/4/26

PYC-001 has the potential to become the first approved treatment for patients with ADOA*



*PYC-001 is the most advanced drug candidate with disease-modifying potential in clinical development for ADOA based on publicly available information. Future development is subject to risks and uncertainties outlined in the Company's ASX filings of 2 February 2026.

Conclusions

- Clinical and pre-clinical data support continued development of PYC-001
- PYC-001 is the first precision therapy to be dosed in patients with *OPA1* ADOA with disease-modifying observed potential in clinical development for ADOA
- No Treatment-Related Serious Adverse Events (TR-SAEs) were observed in any patient who received a single dose of PYC-001 to date (doses of 3, 10, 30 and 60 mcg)
- Preliminary data indicate improvements in visual acuity for patients with *OPA1* ADOA who have received PYC-001
- Pre-clinical data: PYC-001 restored mitochondrial function in patient-derived models of *OPA1* ADOA and the doses were found to be safe and effective in NHPs
- Next steps: PYC is progressing PYC-001 through a repeat dose study (MYRTLE – Phase 1b) in patients with *OPA1* ADOA to demonstrate clinical proof of concept



Adaptive optics imaging, microperimetry and
optoretinography following intravitreal injection of VP-001 in
patients with *PRPF31*-associated retinitis pigmentosa

Jessica I. W. Morgan

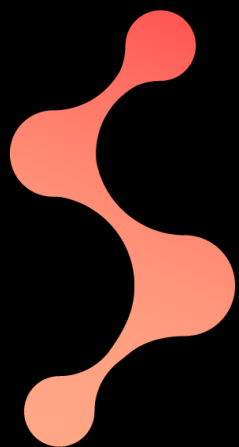
**Nivedhitha Govindasamy, Peiluo Xu, Yu You Jiang,
Raymond L. Warner, Thiran Jayasundera,
Sandeep Grover, George Mitchell, Sri Mudumba**

ARVO 2026

jwmorgan@penntermedicine.upenn.edu



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PYC
Therapeutics



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NIH P30EY001583



Research to
Prevent
Blindness



Center for Advanced Retinal & Ocular Therapeutics
PennCAROT



The people who make it happen!

Jing Zhang

Yu You Jiang

Peiluo (Angela) Xu

Nivedhitha Govindasamy

Shaofeng Huang

Raymond L. Warner

Thanks to Alfredo Dubra for sharing the AOSLO optical design and software and Austin Roorda for sharing AO microperimetry technology.



Disclosure: I am an inventor on a patent for optoretinography and receive funding for the lab from PYC Therapeutics and Beacon Therapeutics.

Retinitis Pigmentosa

- Affects 1 in 3,000-5,000 individuals
- Rods degenerate initially with subsequent degeneration of cones and RPE

6 years old



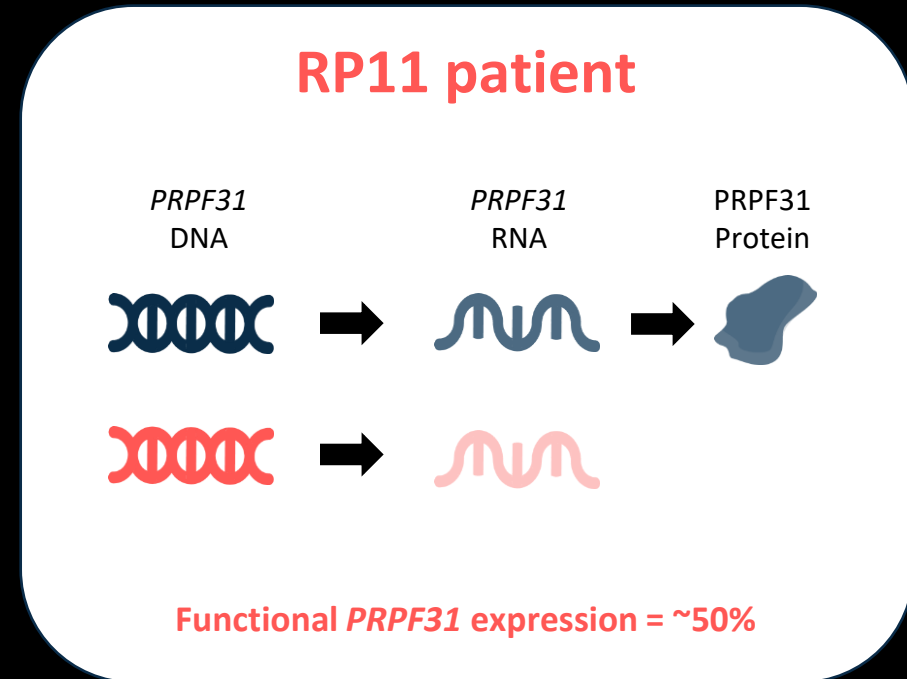
26 years old



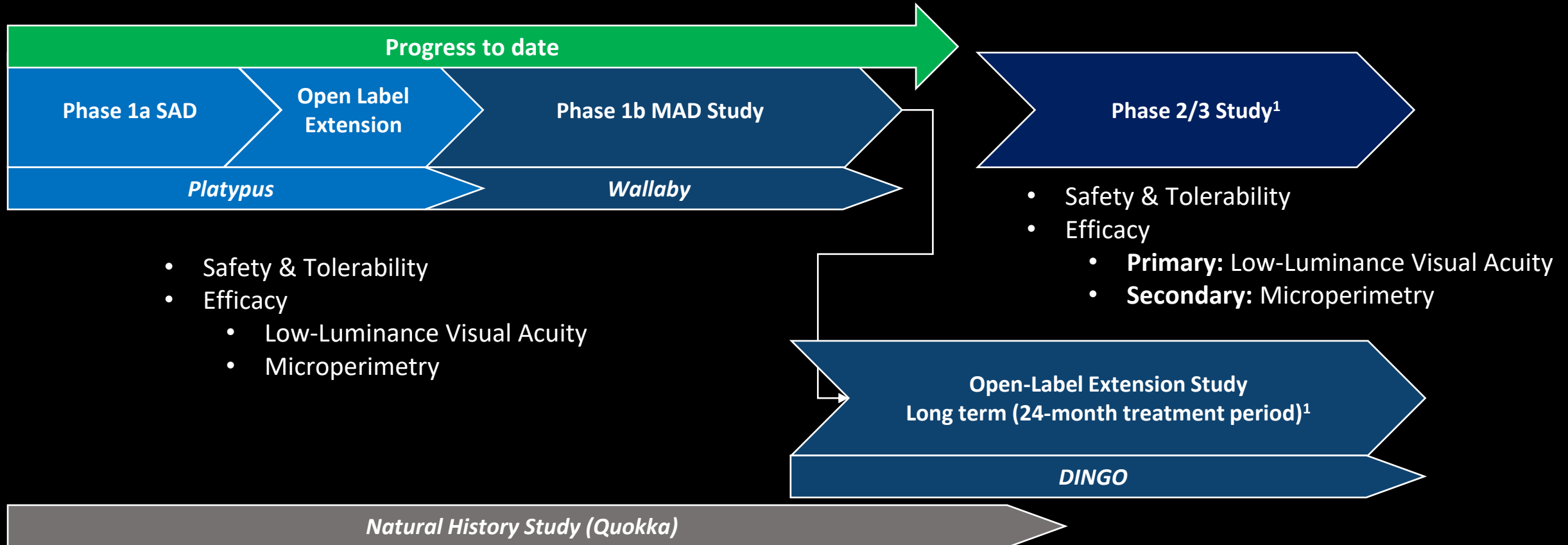
Patients experience night blindness followed by loss of peripheral and then central vision - legal blindness occurs in the 4th or 5th decade of life¹⁻³

Retinitis Pigmentosa type 11

- 1-3% of RP
- Caused by mutations on the *PRPF31* gene
- Autosomal dominant inheritance
- VP-001: a RNA therapeutic that leads to upregulation of *PRPF31*



Experimental treatment of RP11 using VP-001



Chen *et al.* Presentation 5499
Thursday, May 7 11:45-12:00
Bluebird Ballroom 1B

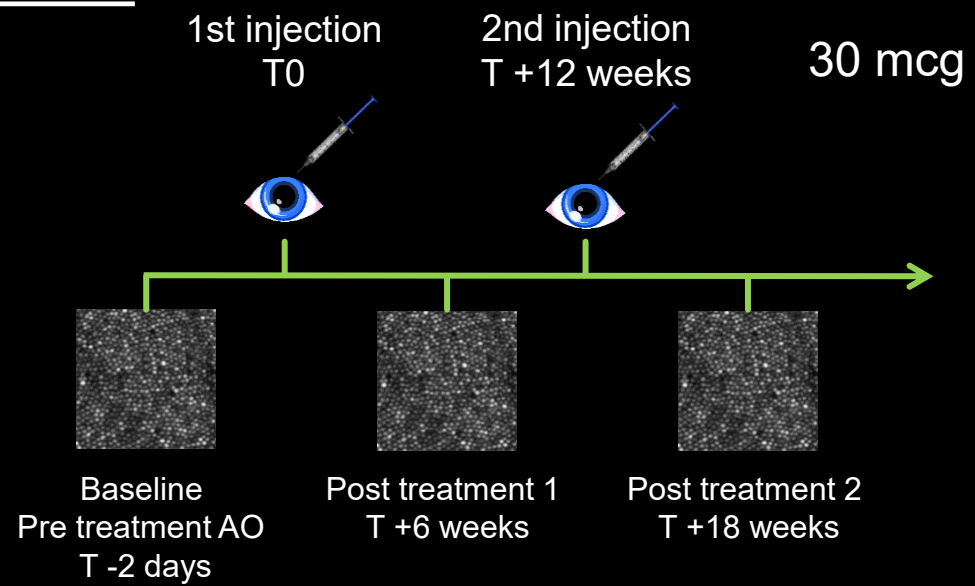
1. Subject to the risks and uncertainties outlined in PYC Therapeutics' ASX disclosures of 2 February 2026

2. Based on an analysis of publicly-available information including clinicaltrials.gov

3. See PYC Therapeutics' ASX disclosures of 16 March 2026

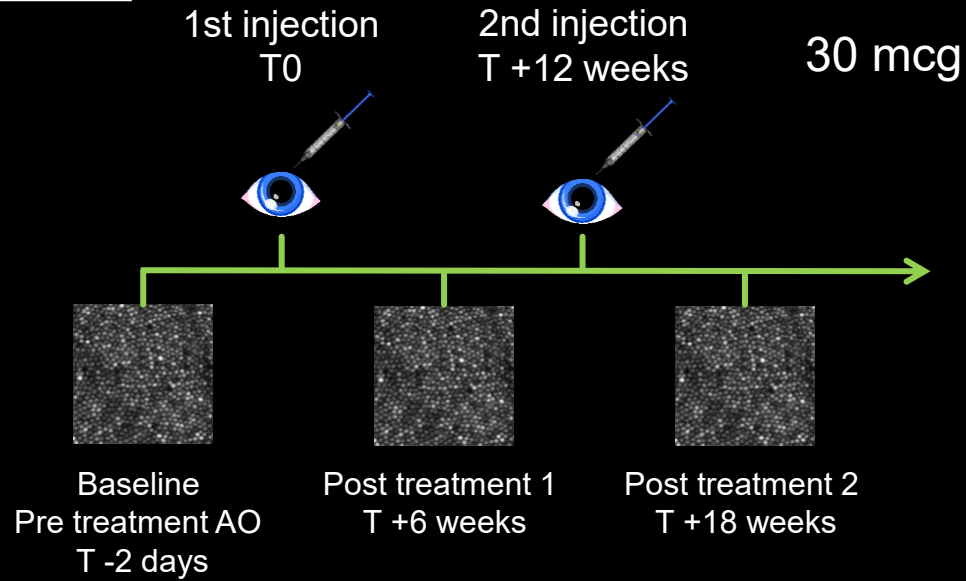
Patient 1

(005-1-002, Platypus/Dingo)



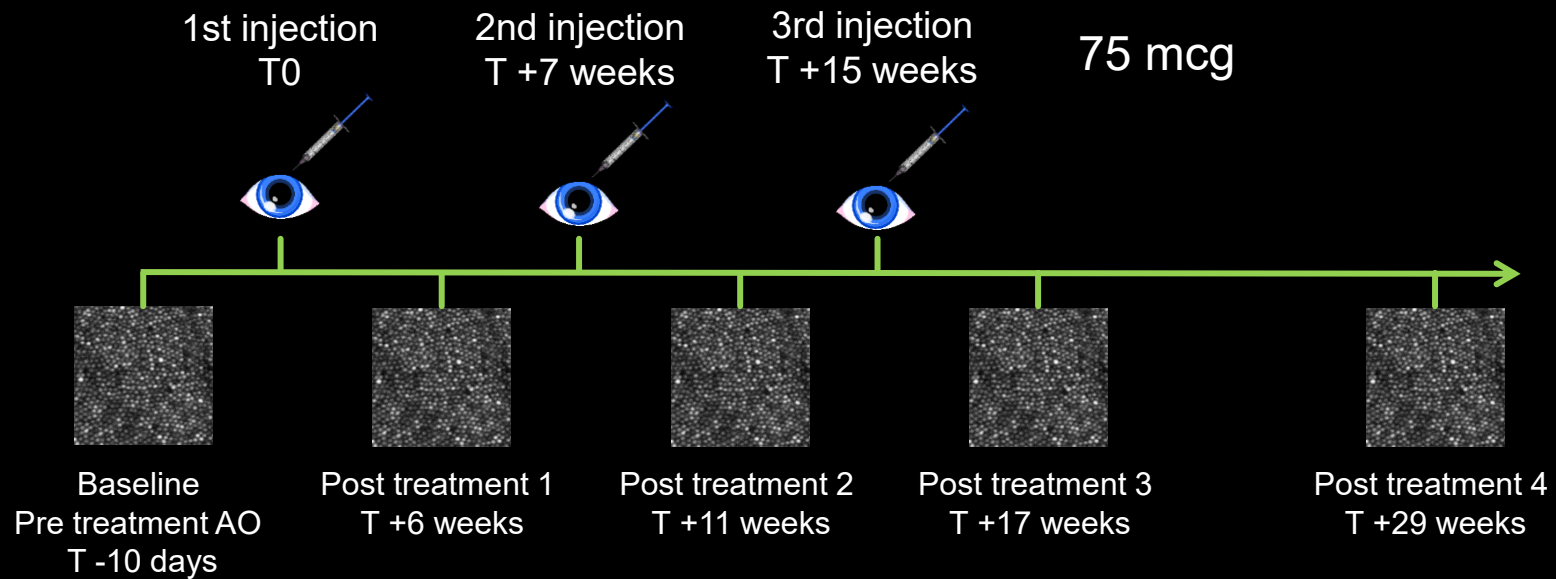
Patient 1

(005-1-002, Platypus/Dingo)



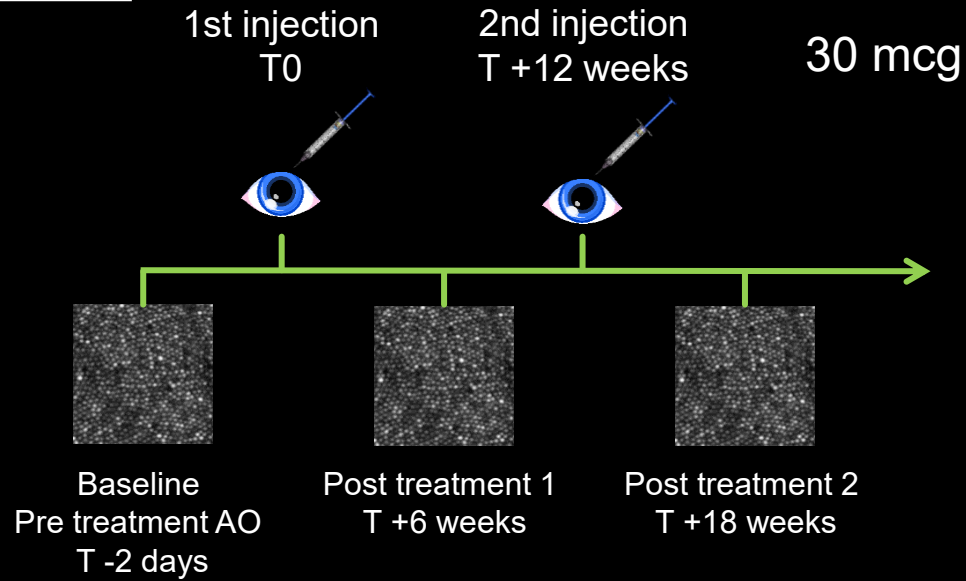
Patient 2

(003-1-003, Wallaby/Dingo)



Patient 1

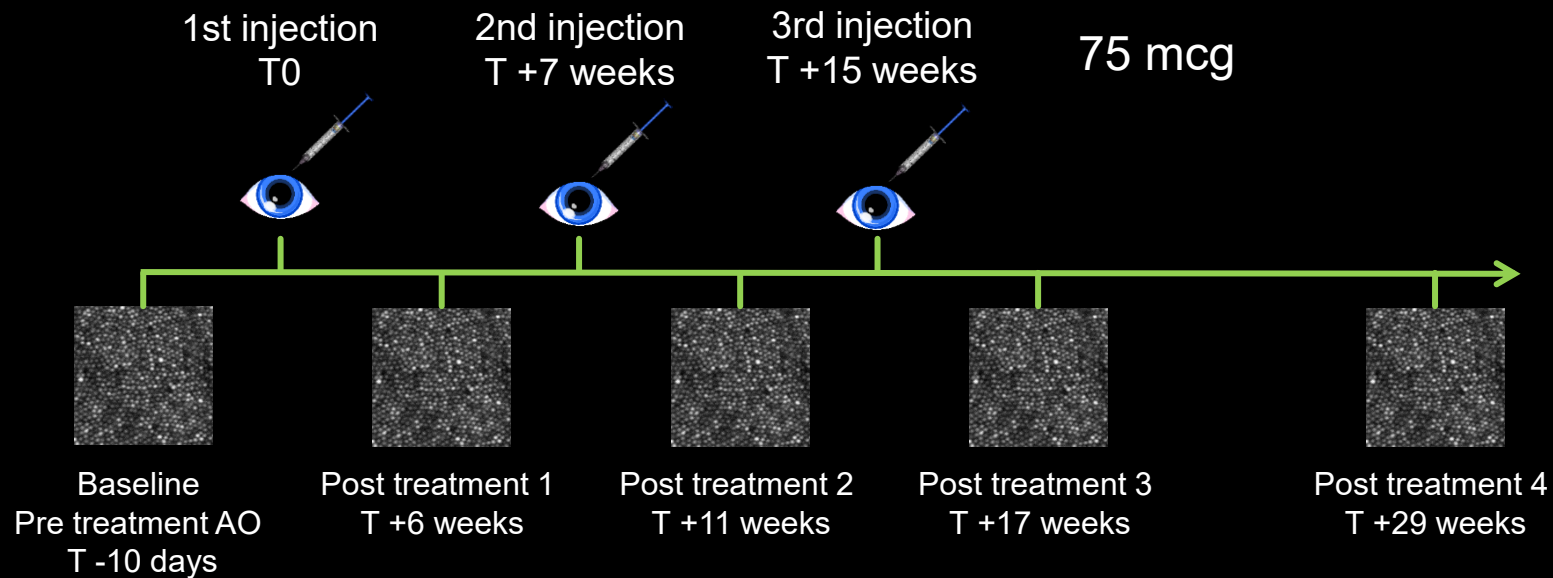
(005-1-002, Platypus/Dingo)



- Adaptive optics scanning light ophthalmoscopy
- Optoretinography
- Adaptive optics microperimetry
- OCT

Patient 2

(003-1-003, Wallaby/Dingo)



Evaluate retinal structure and function in *PRPF31*-associated retinitis pigmentosa before and after unilateral treatment with experimental VP-001

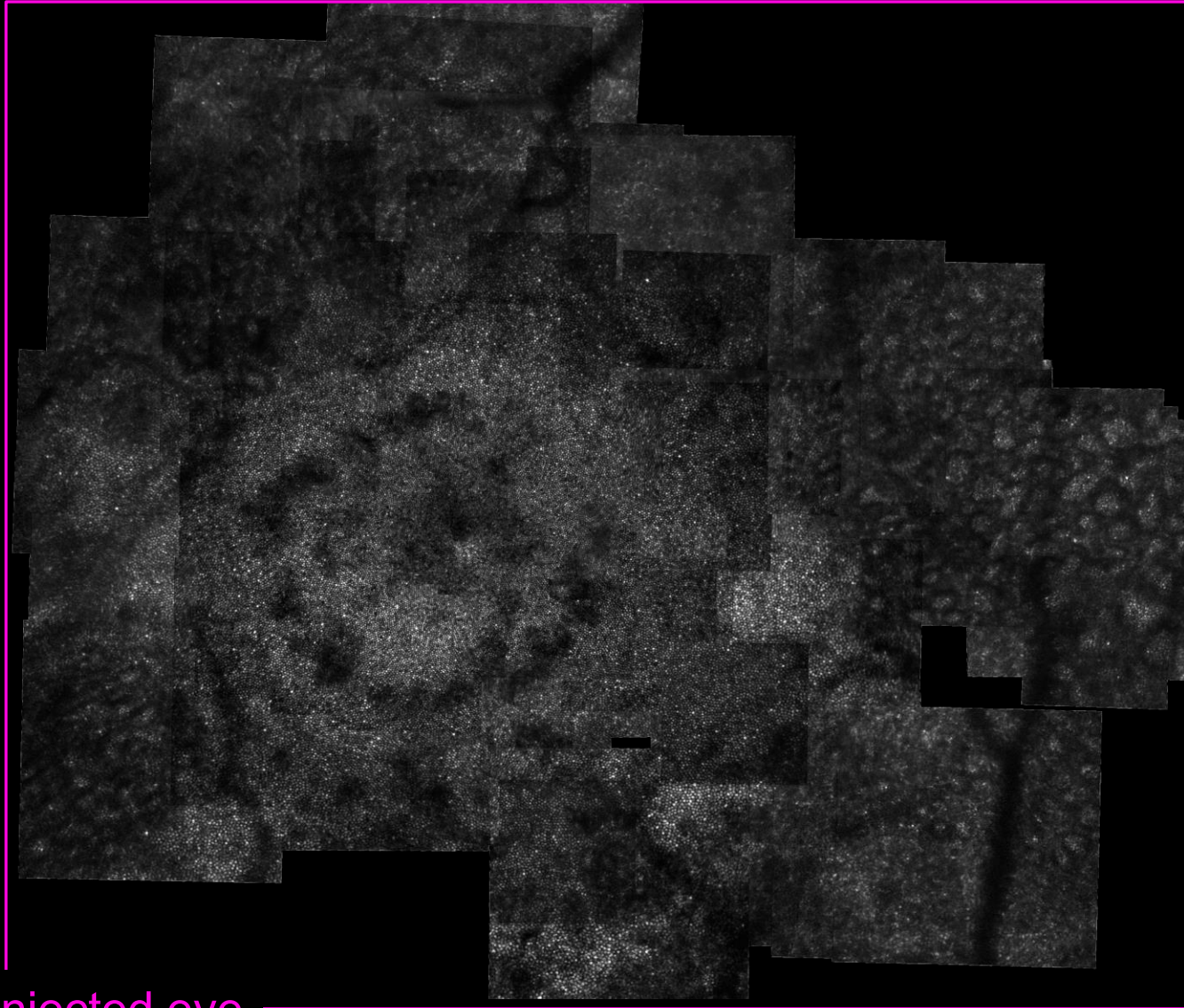
Patient 2

Baseline, Pre-treatment



Patient 2: Degenerative microcysts over time

Baseline, Pre-treatment



Injected eye

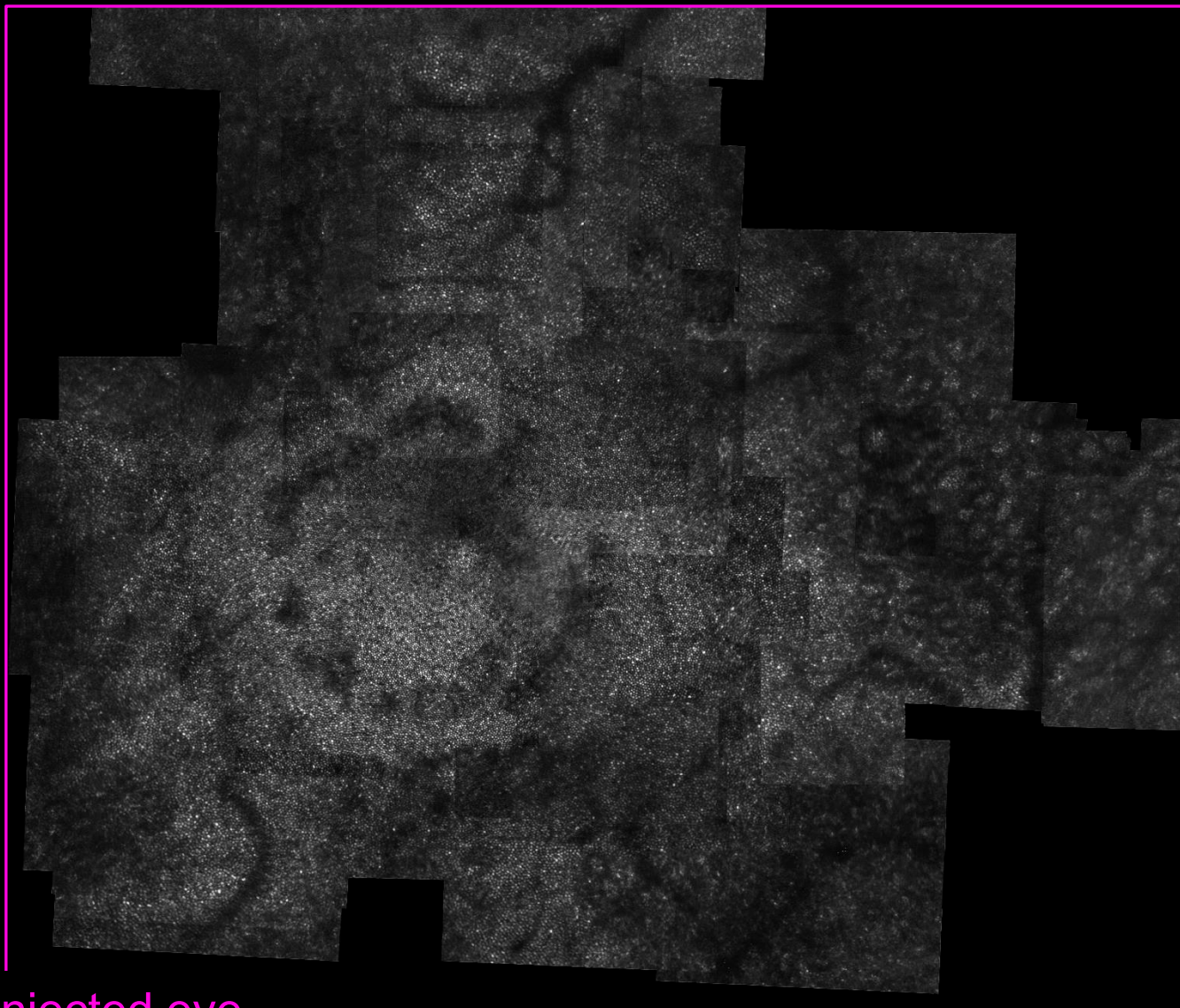
Patient 2: Degenerative microcysts over time

Baseline, Pre-treatment

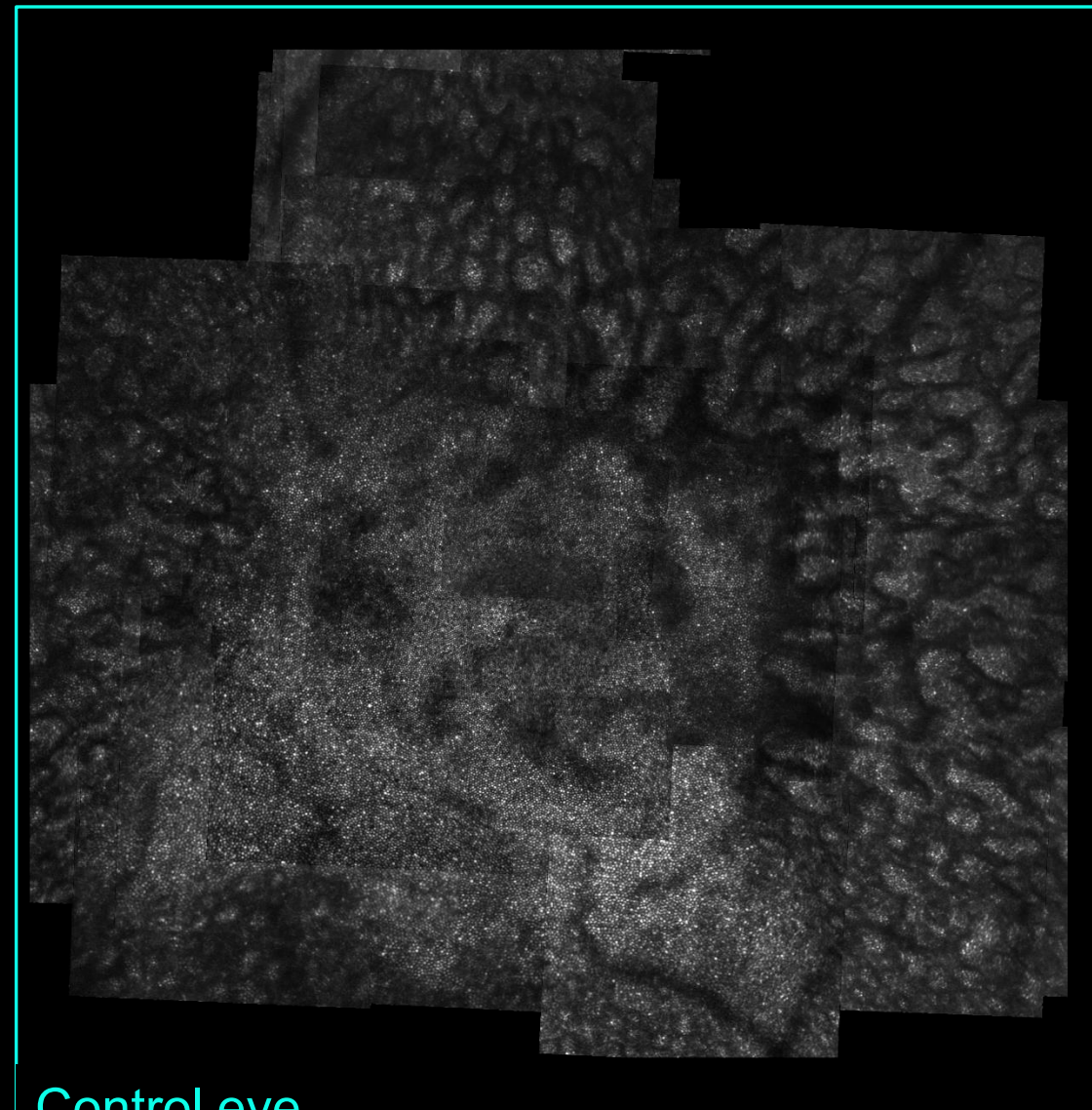


Patient 2: Degenerative microcysts over time

Post-injection 3, 17 weeks



Injected eye

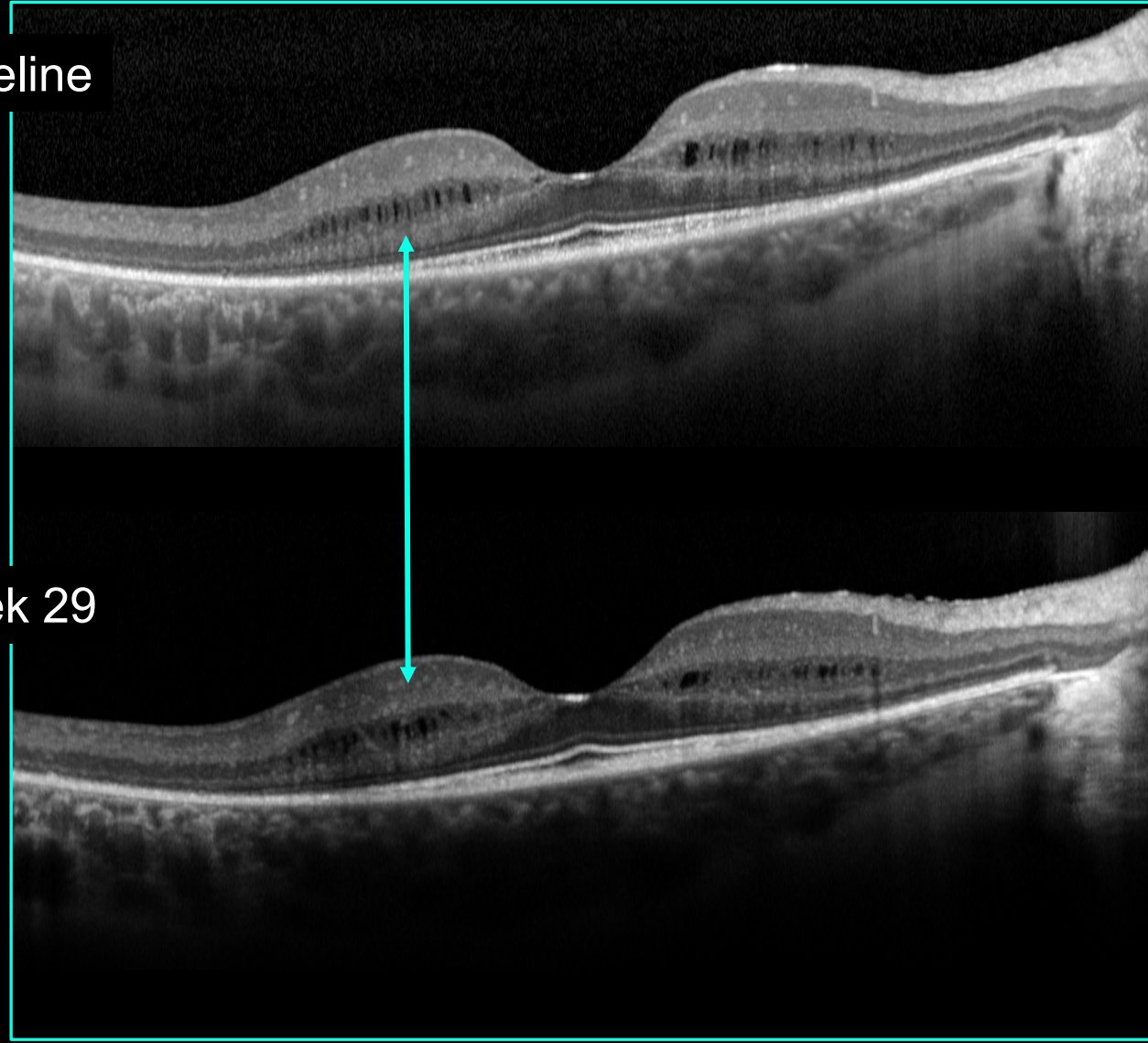
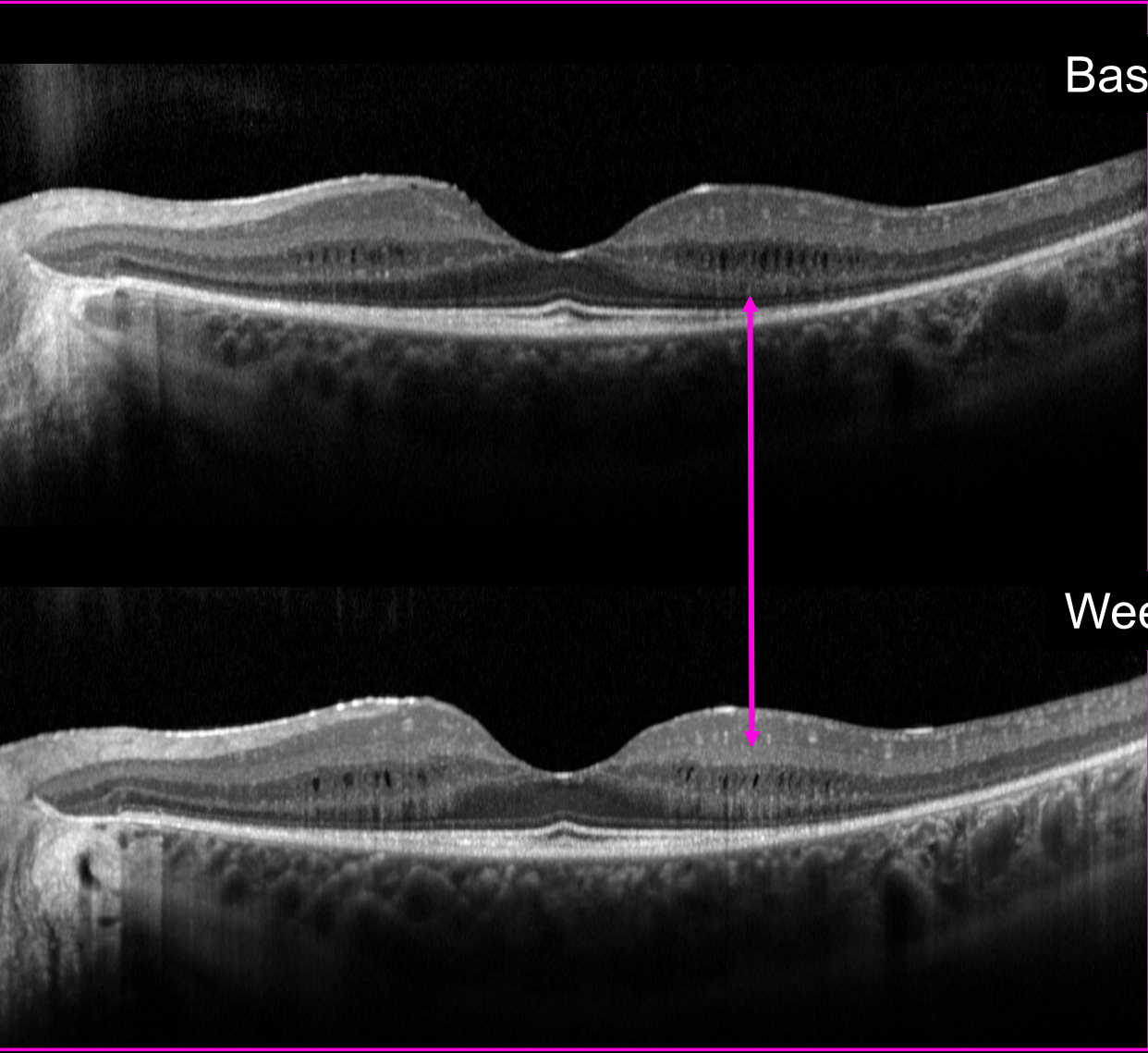


Control eye

Patient 2: Degenerative microcysts over time

Baseline

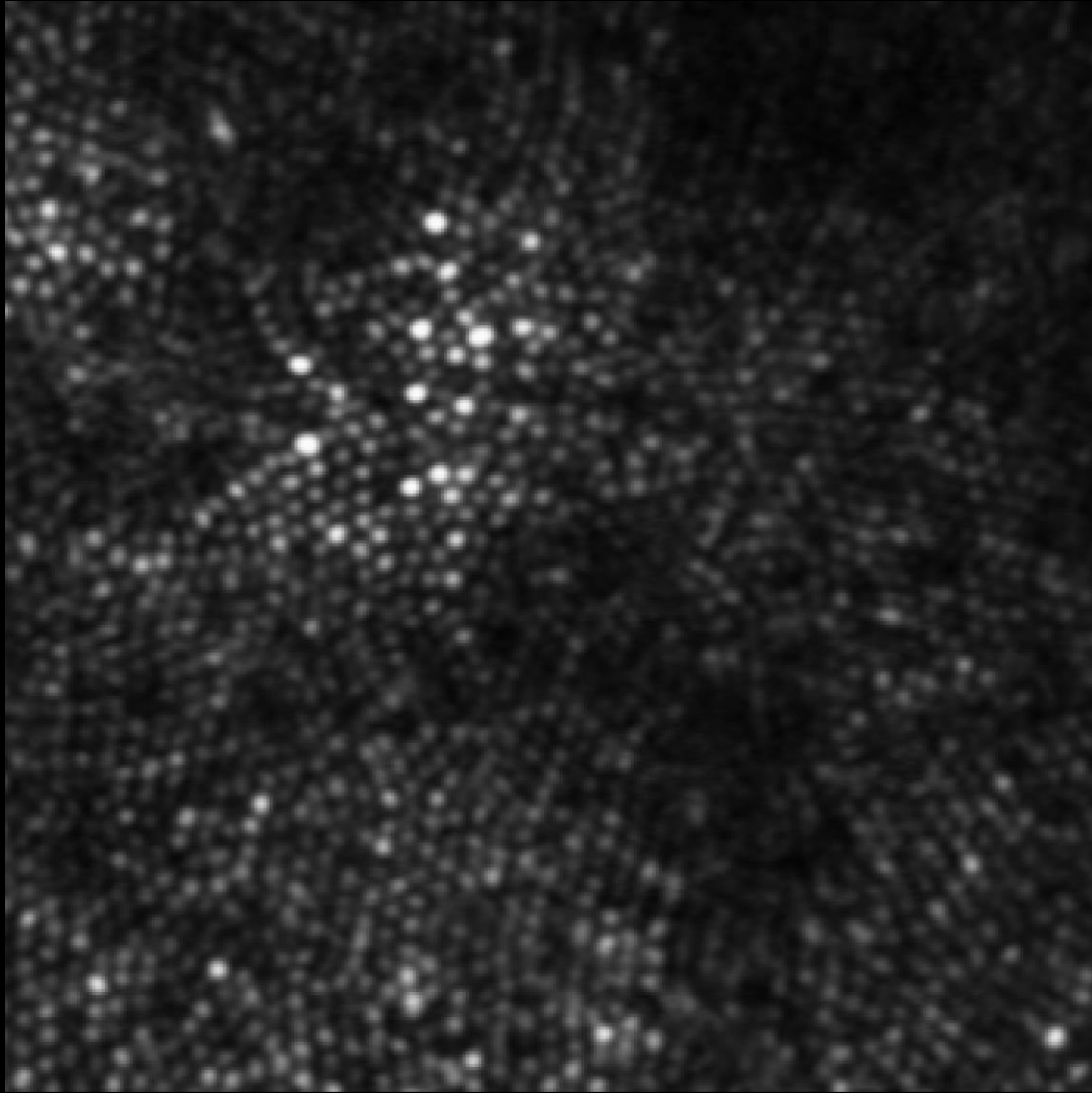
Week 29



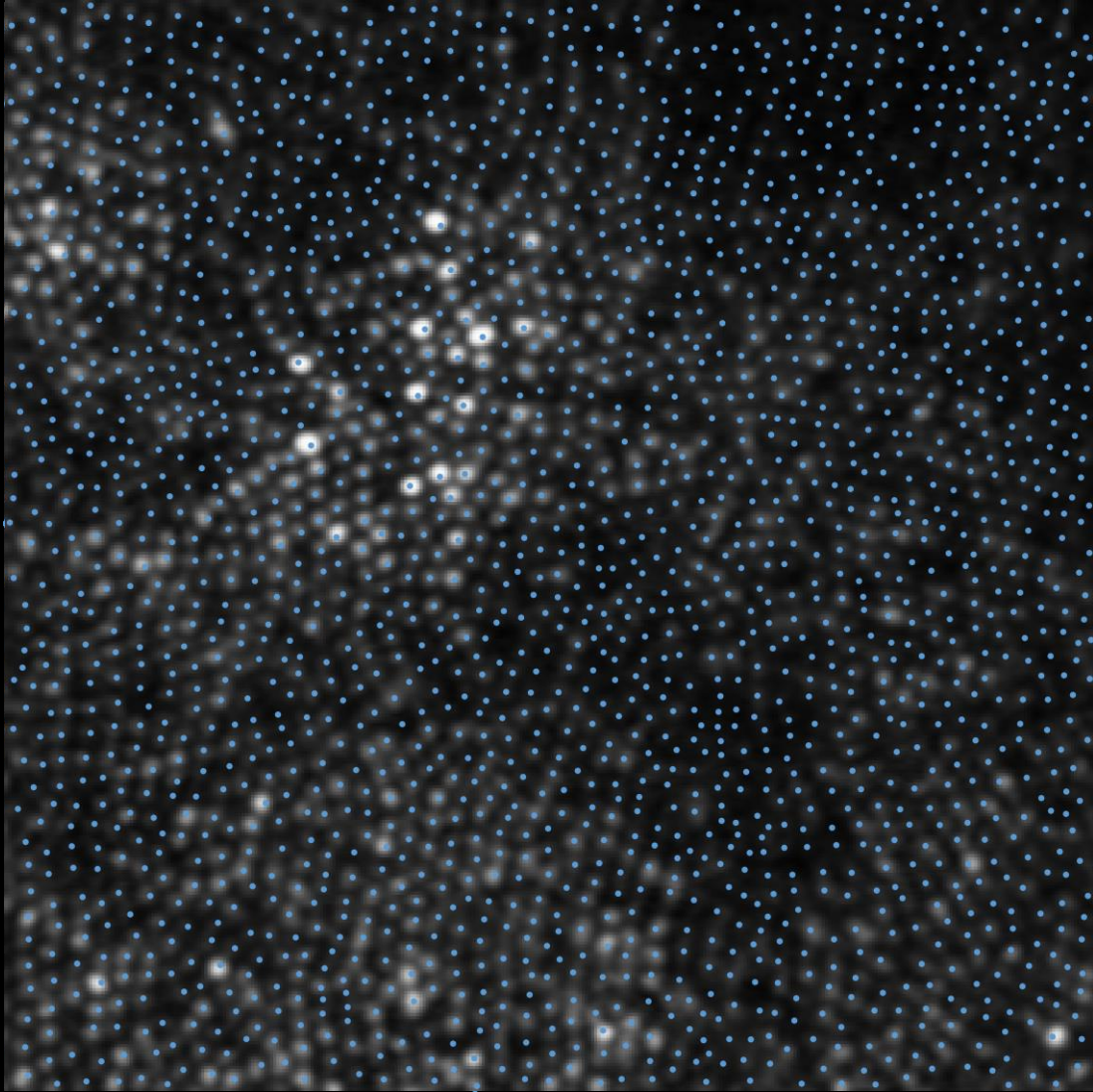
Injected eye

Control eye

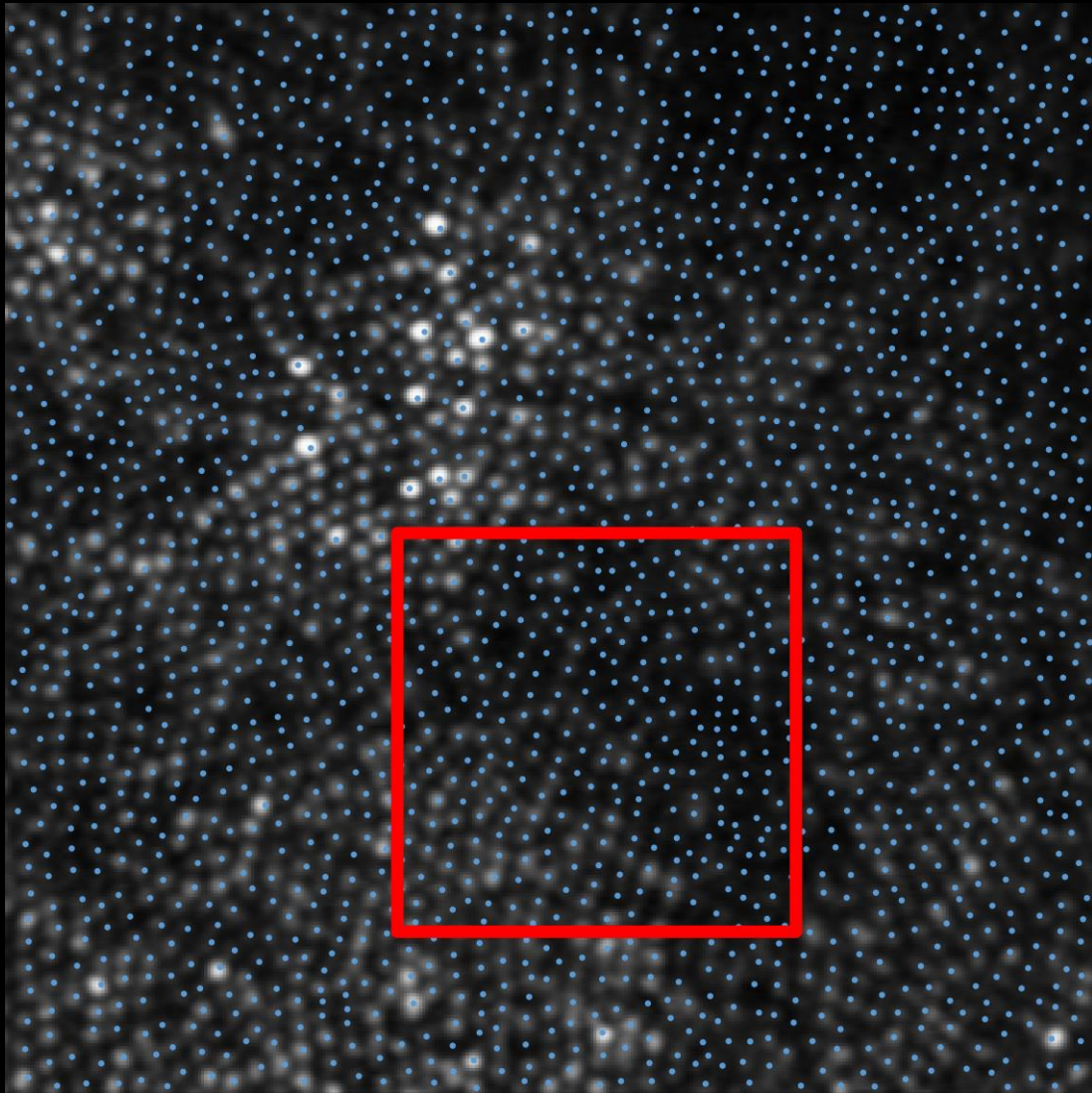
Patient 2: Peak cone density over time



Patient 2: Peak cone density over time

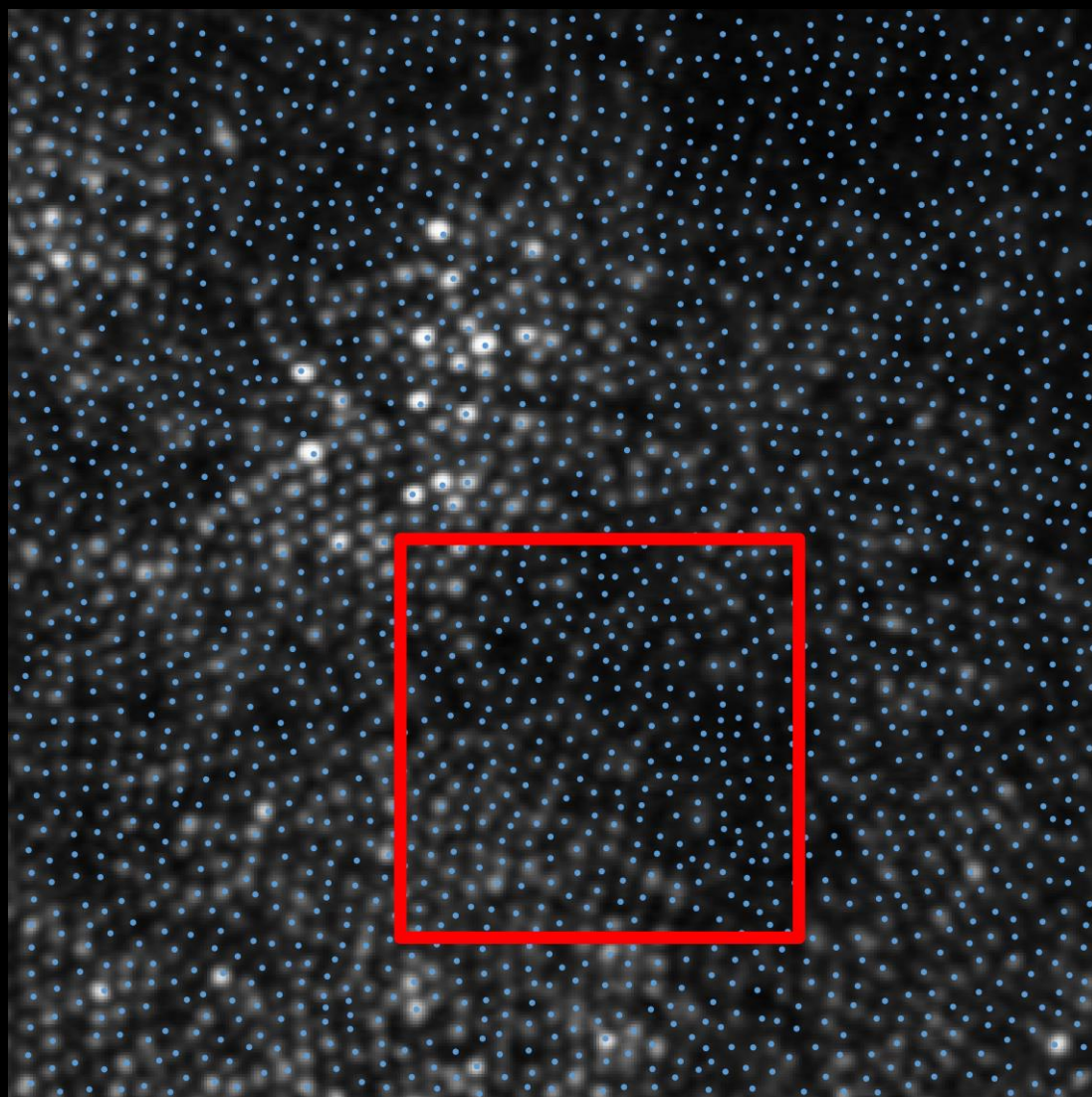


Patient 2: Peak cone density over time

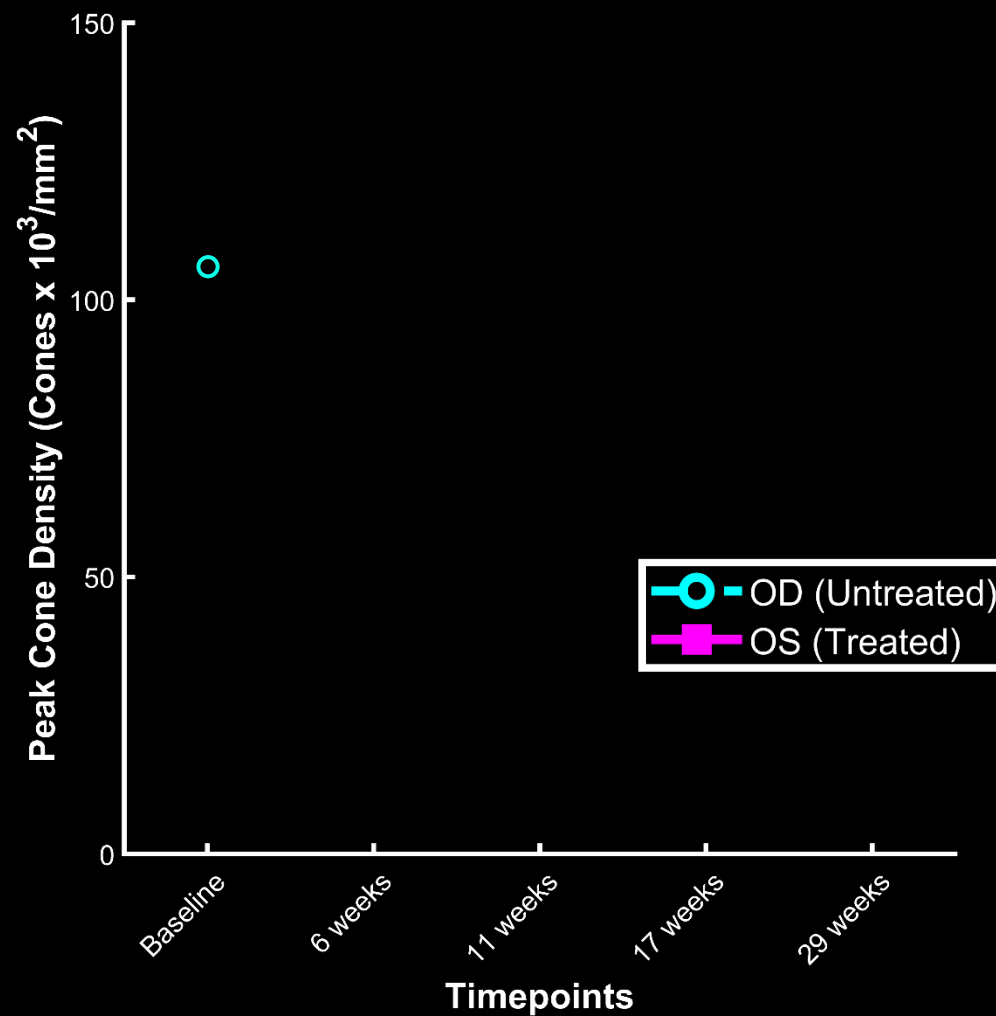


106,039 cones/mm²

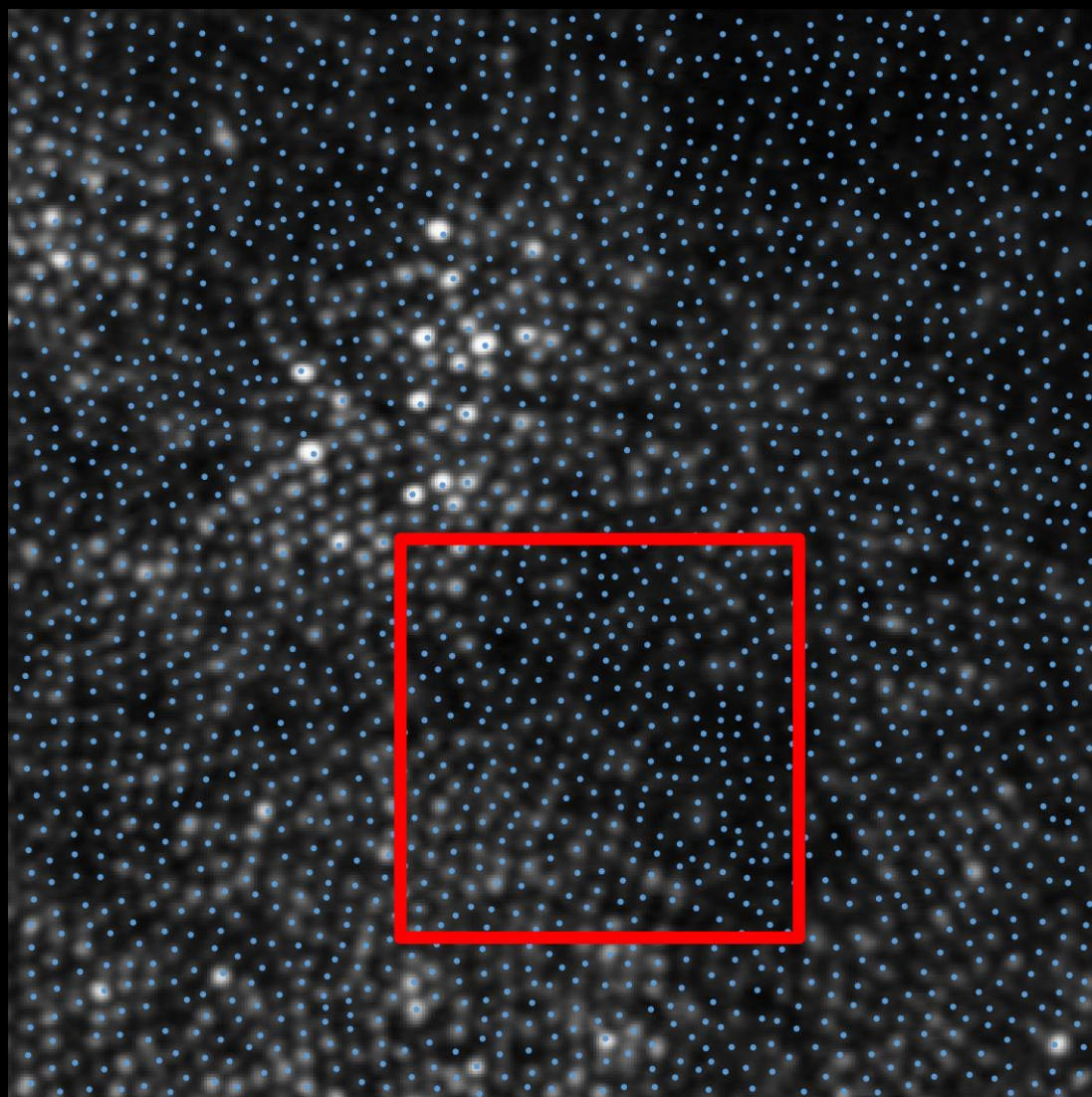
Patient 2: Peak cone density over time



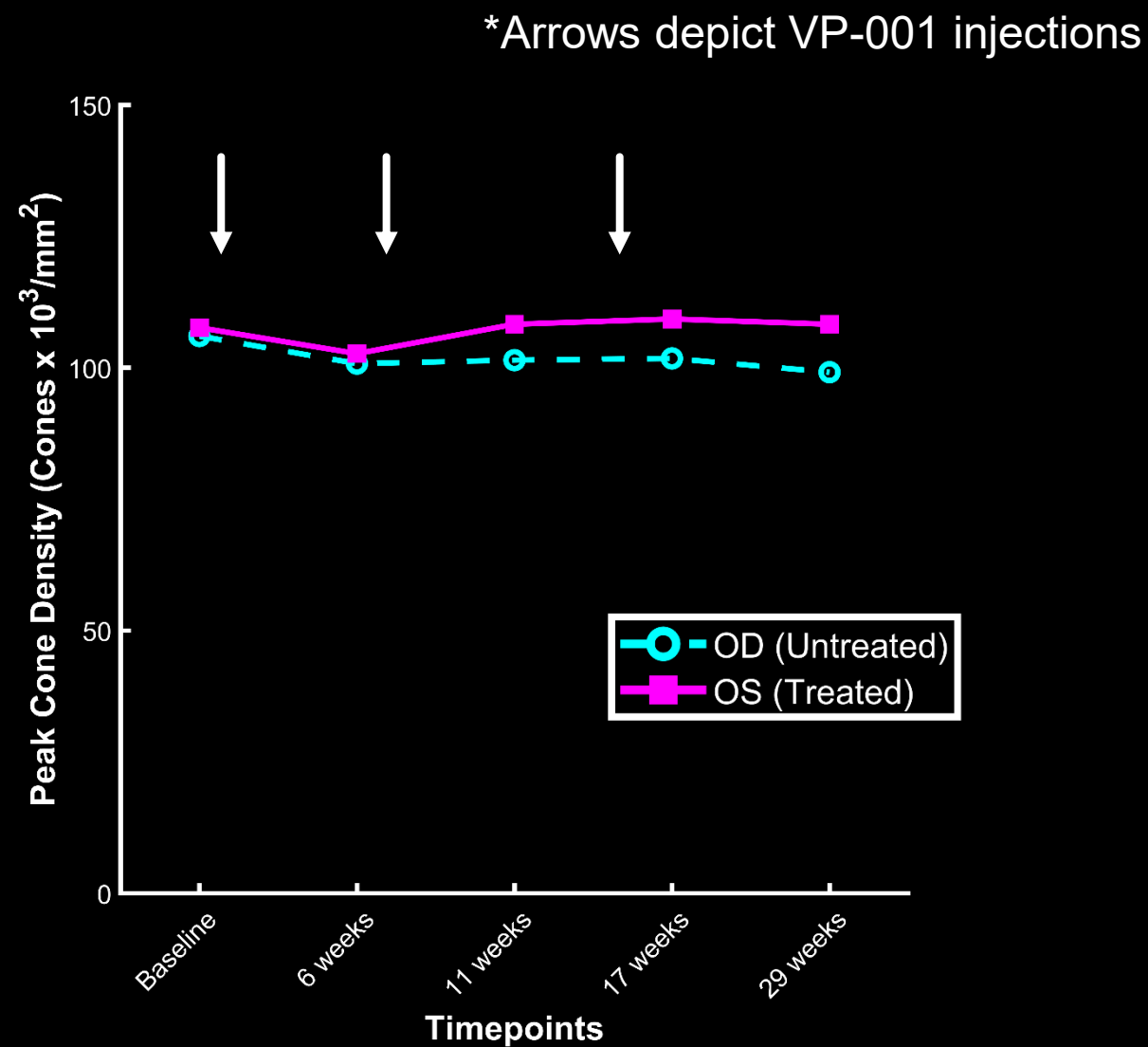
106,039 cones/mm²



Patient 2: Peak cone density over time



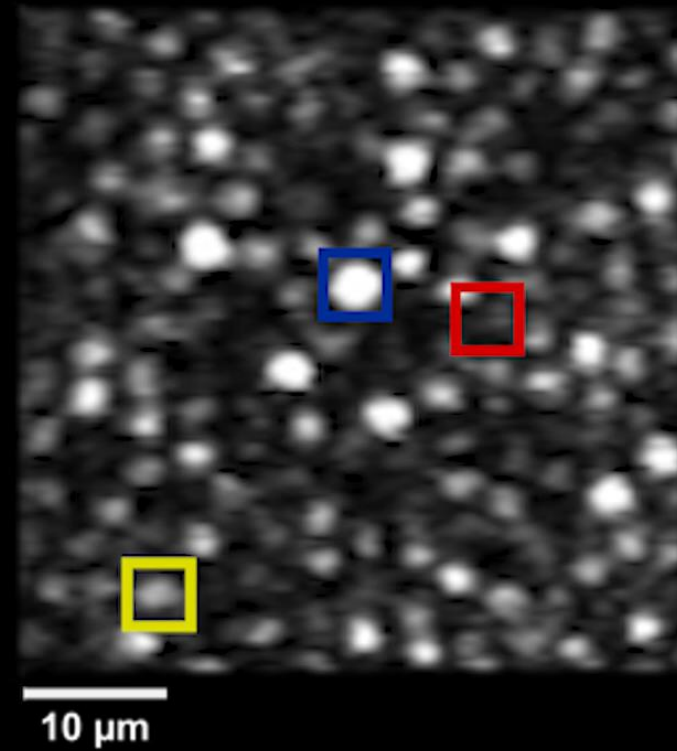
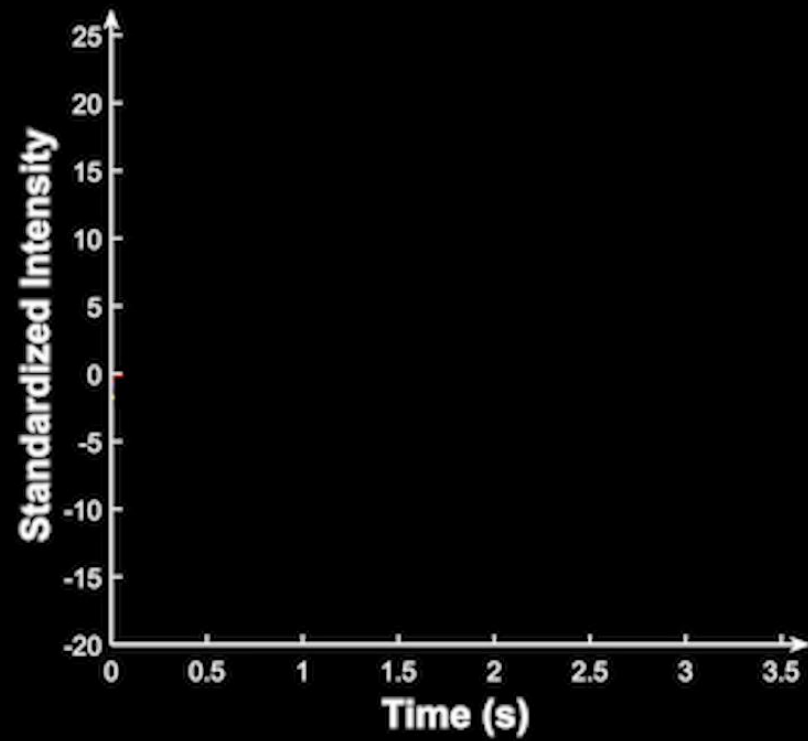
106,039 cones/mm²



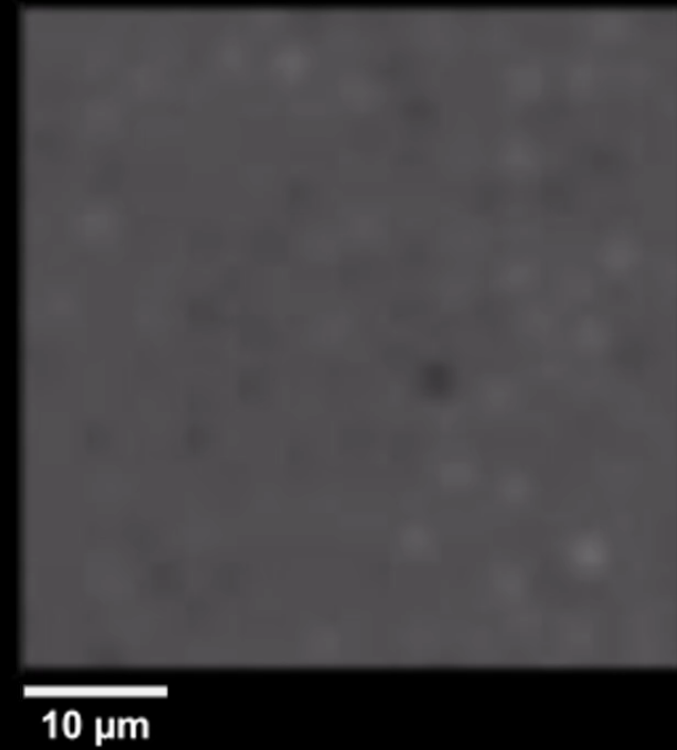
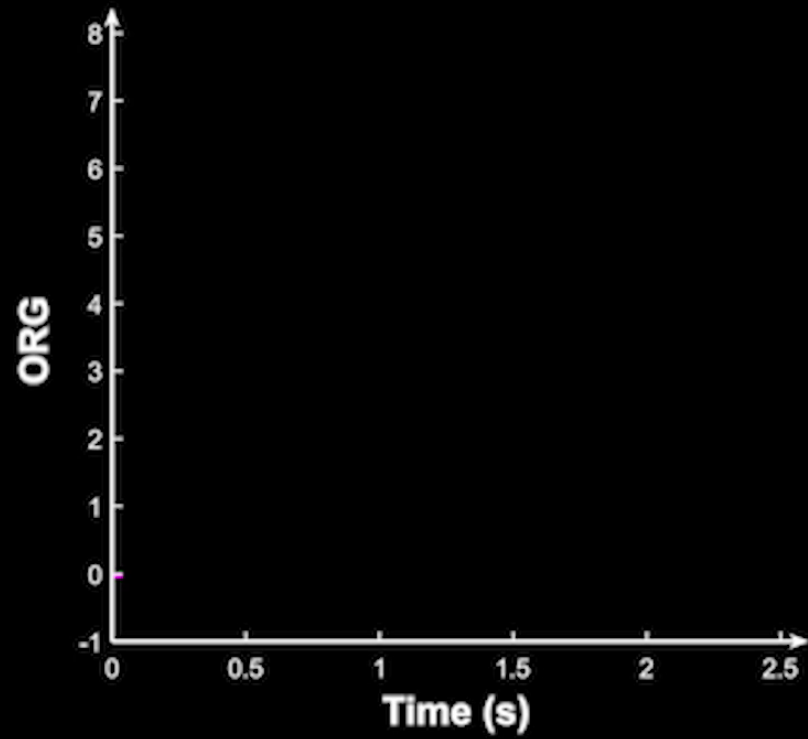
Optoretinography

- Objective measure of photoreceptor function.
- An optical signal that occurs in response to a visible stimulus.

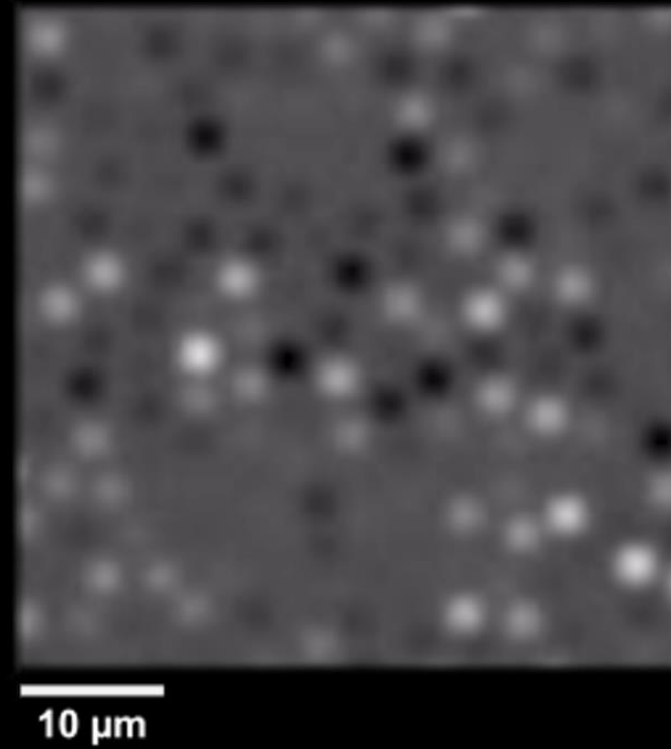
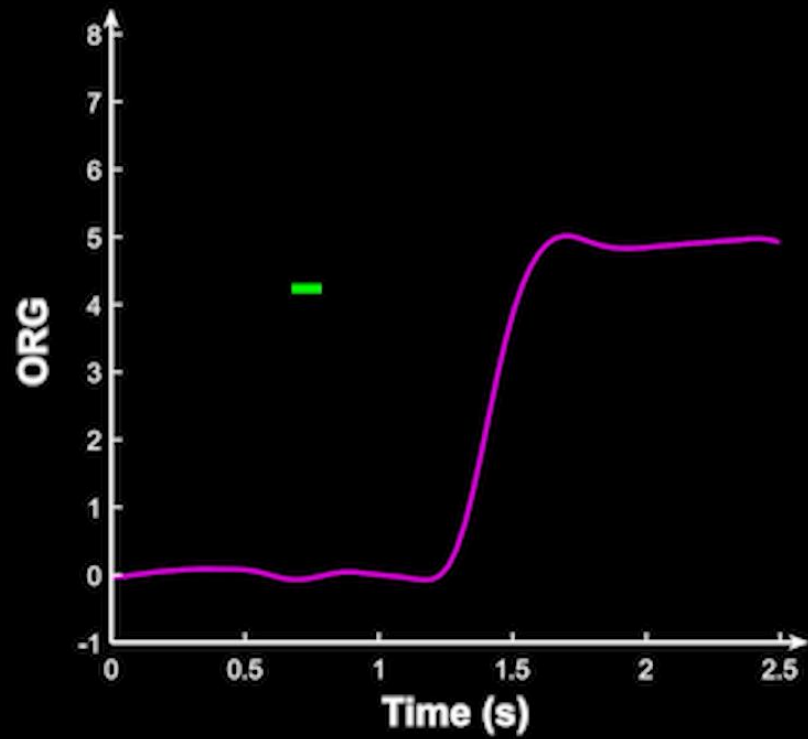
Optoretinography



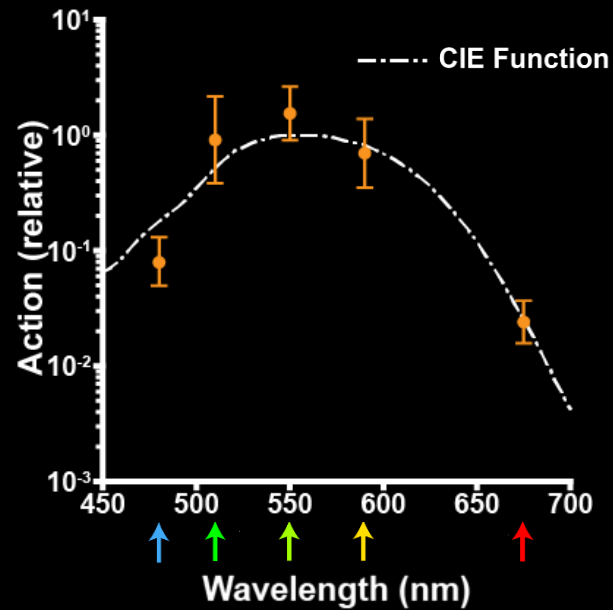
Optoretinography



Optoretinography



Optoretinography



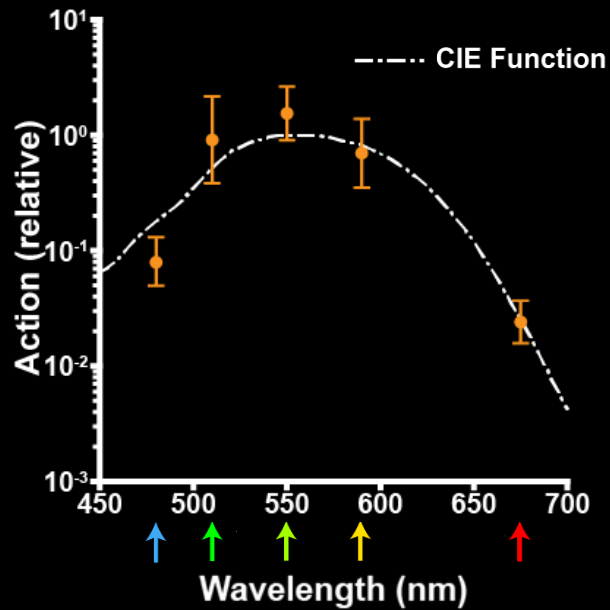
Research Article Vol. 8, No. 11 | 1 Nov 2017 | BIOMEDICAL OPTICS EXPRESS 5098

Biomedical Optics EXPRESS

Non-invasive assessment of human cone photoreceptor function

ROBERT F. COOPER,^{1,2} WILLIAM S. TUTEN,^{1,2} ALFREDO DUBRA,³ DAVID H. BRAINARD,² AND JESSICA I. W. MORGAN^{1,4,*}

Optoretinography

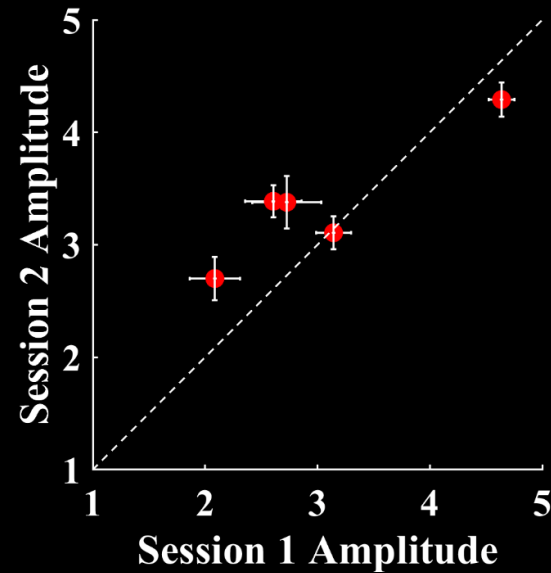


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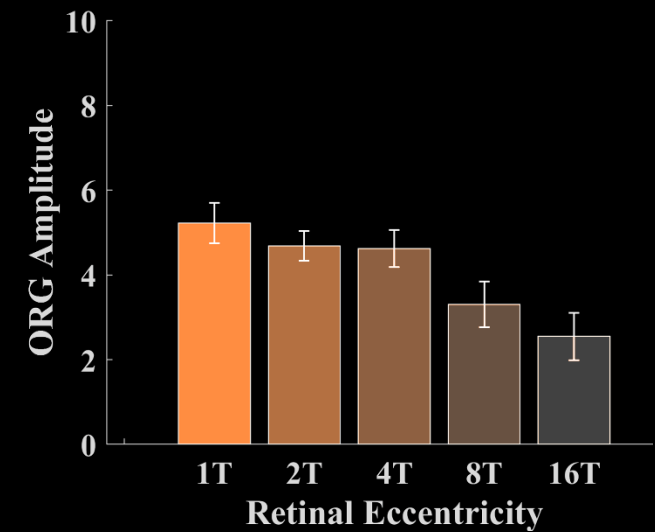
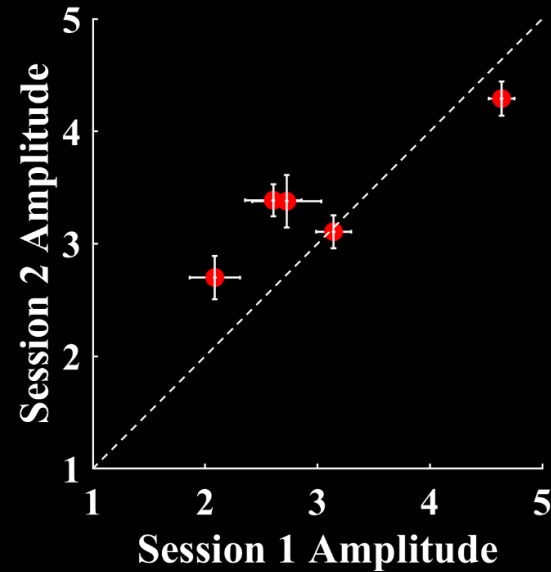
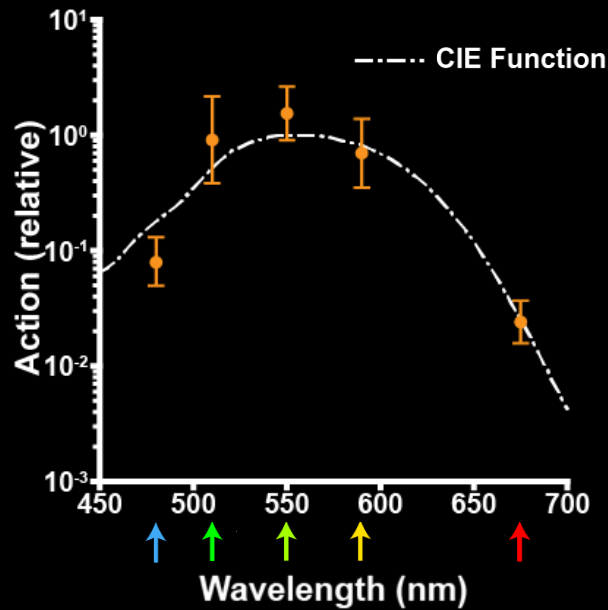
Research Article Vol. 13, No. 12/1 Dec 2022 | Biomedical Optics Express 6561

Biomedical Optics EXPRESS

Repeatability and reciprocity of the cone optoretinogram

R. L. WARNER,¹ D. H. BRAINARD,² AND J. I. W. MORGAN^{1,3,*}

Optoretinography

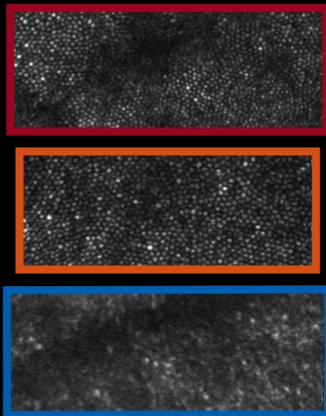
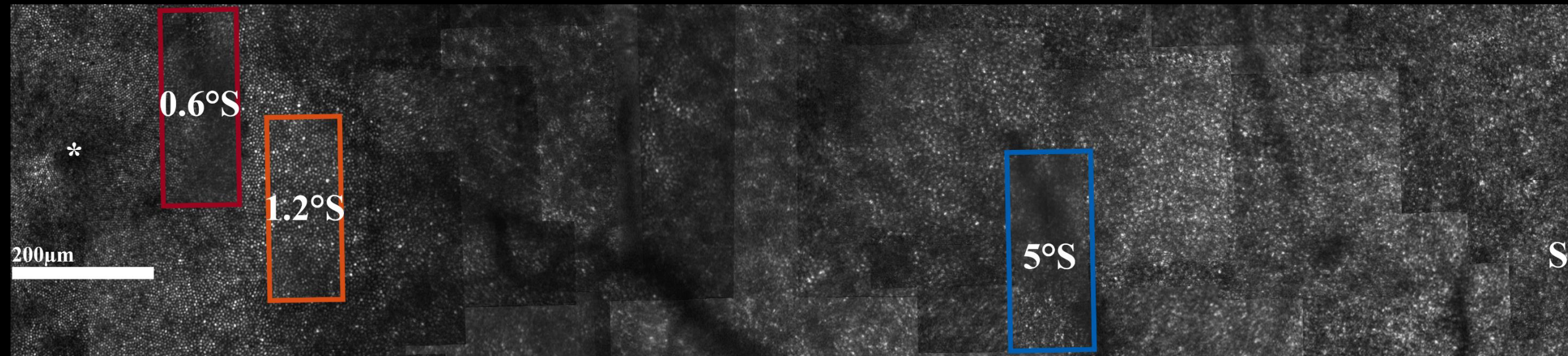


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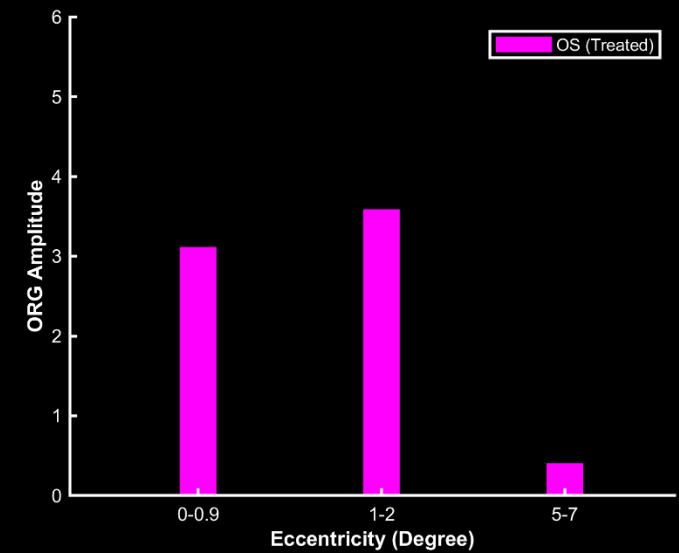
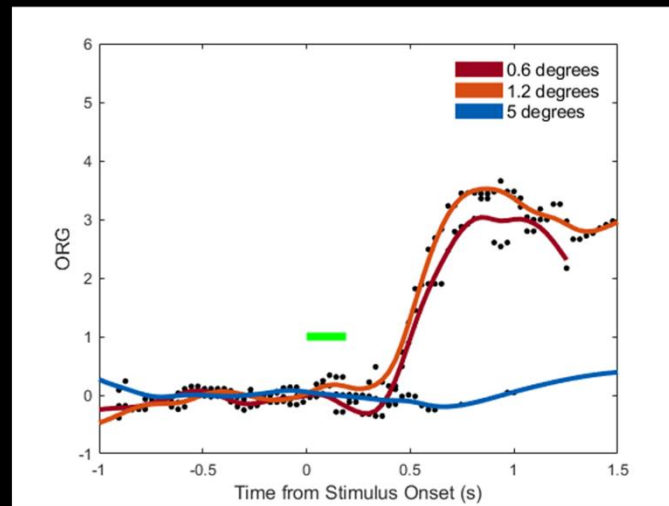
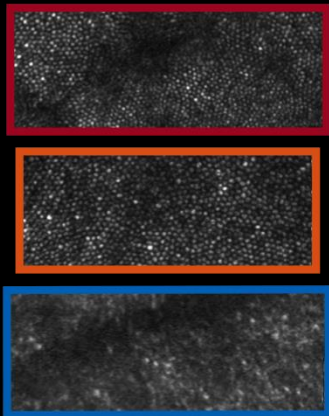
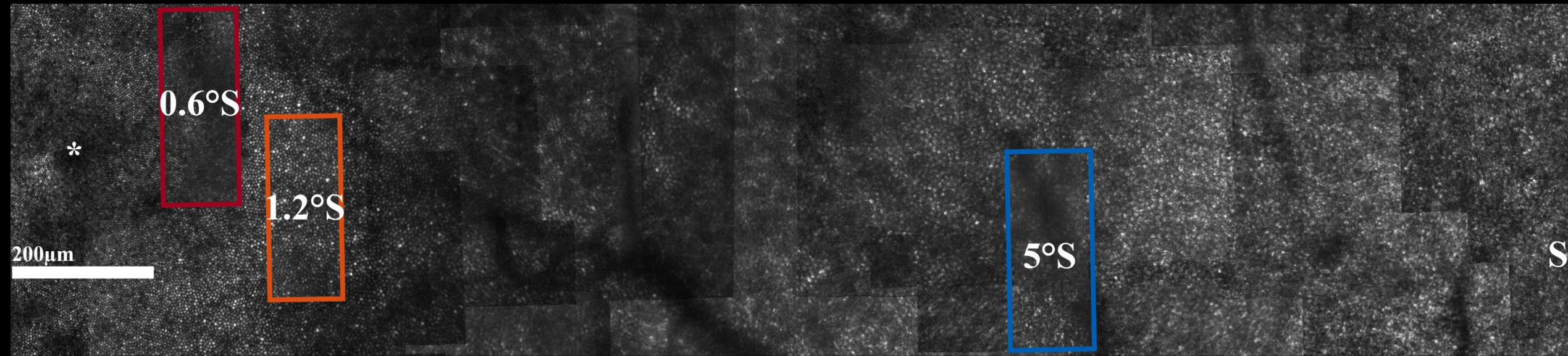
Research Article Vol. 13, No. 12/1 Dec 2022 | Biomedical Optics Express 6561
Biomedical Optics EXPRESS
Repeatability and reciprocity of the cone optoretinogram
 R. L. WARNER,¹ D. H. BRAINARD,² AND J. I. W. MORGAN^{1,3,*}

hv photonics MDPI
 Article
The Cone Optoretinogram as a Function of Retinal Eccentricity[†]
 Raymond L. Warner¹, Peiluo Xu², David H. Brainard³ and Jessica I. W. Morgan^{1,4,*}

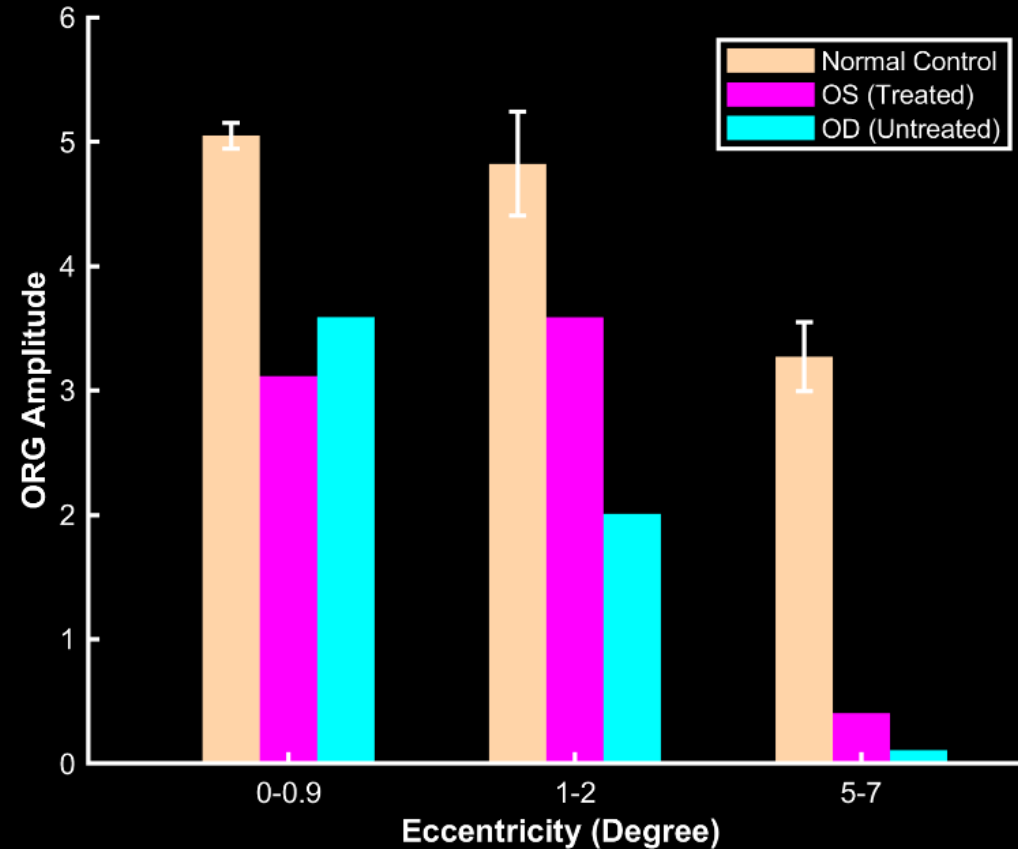
Optoretinography, Patient 2 Baseline, OS



Optoretinography, Patient 2 Baseline, OS

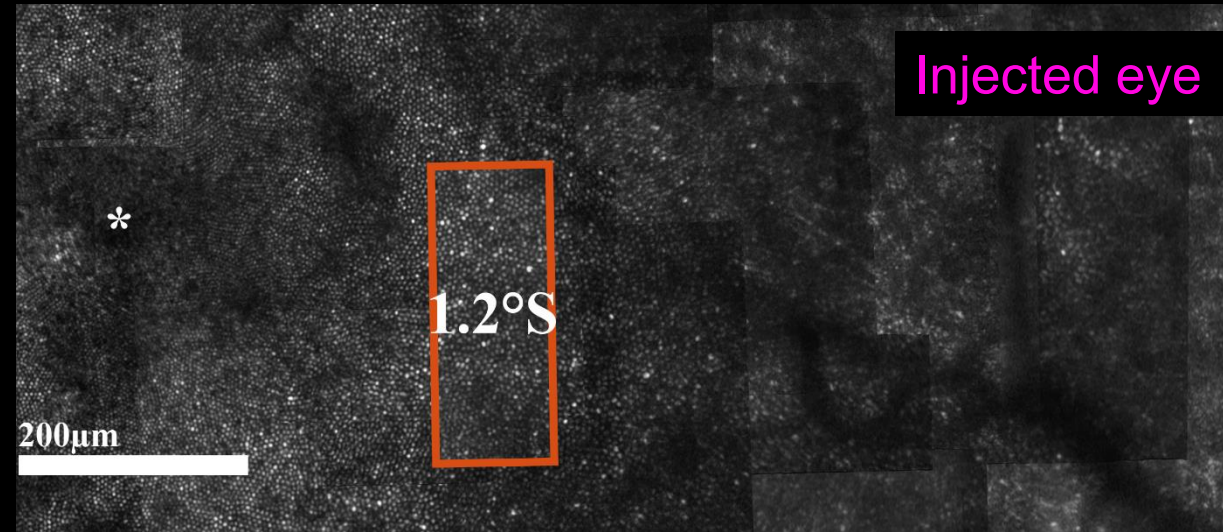


Optoretinography, Patient 2 Baseline

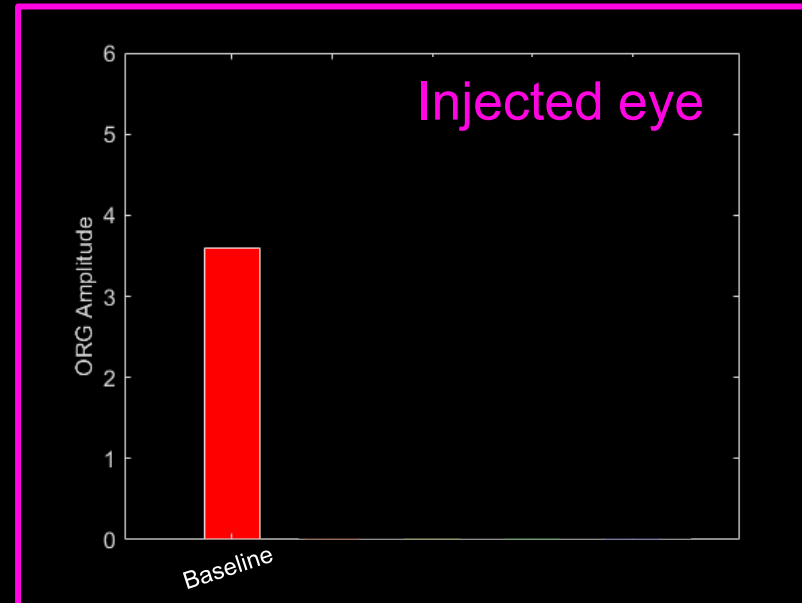
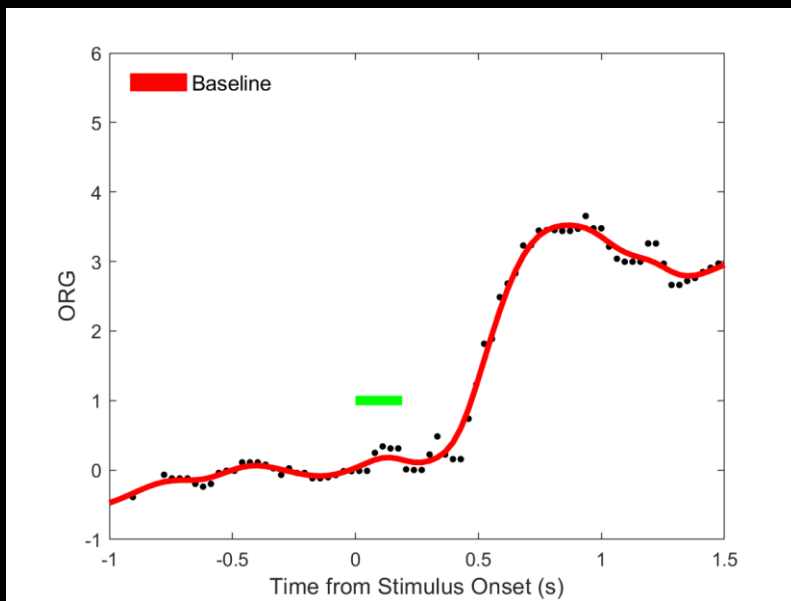
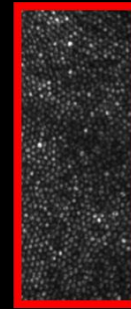


Baseline ORG amplitude is reduced from normal.

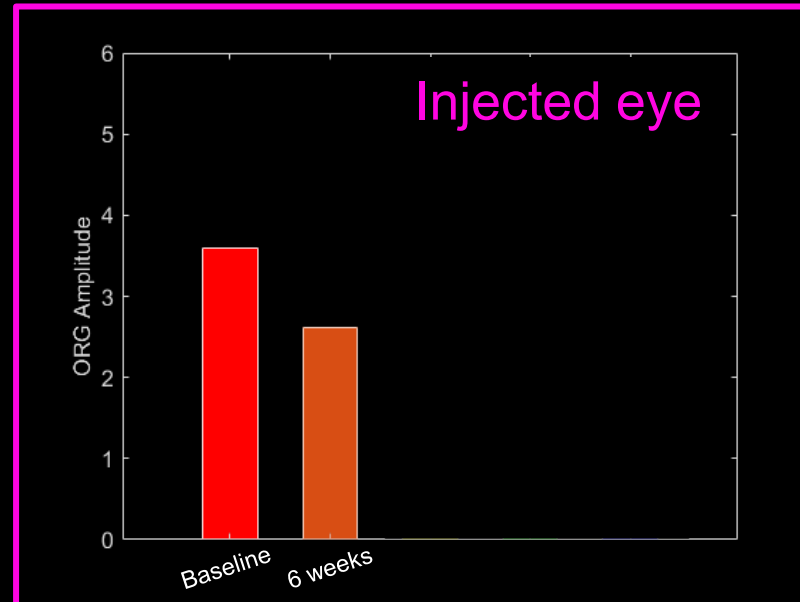
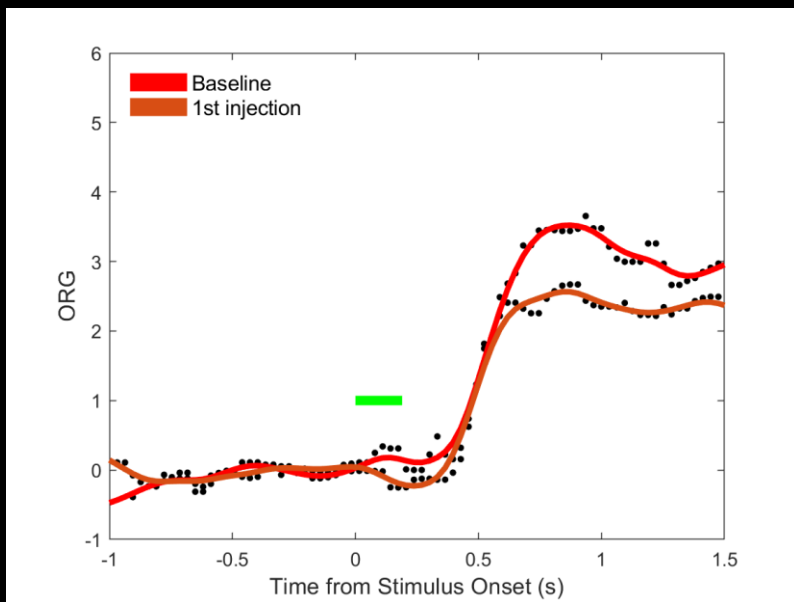
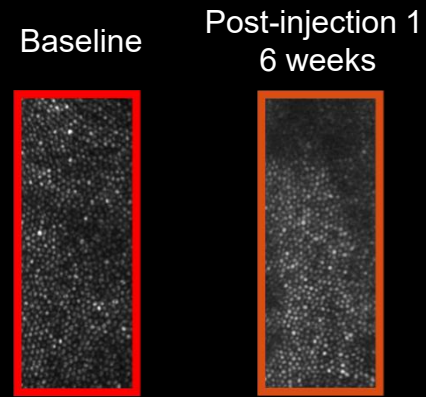
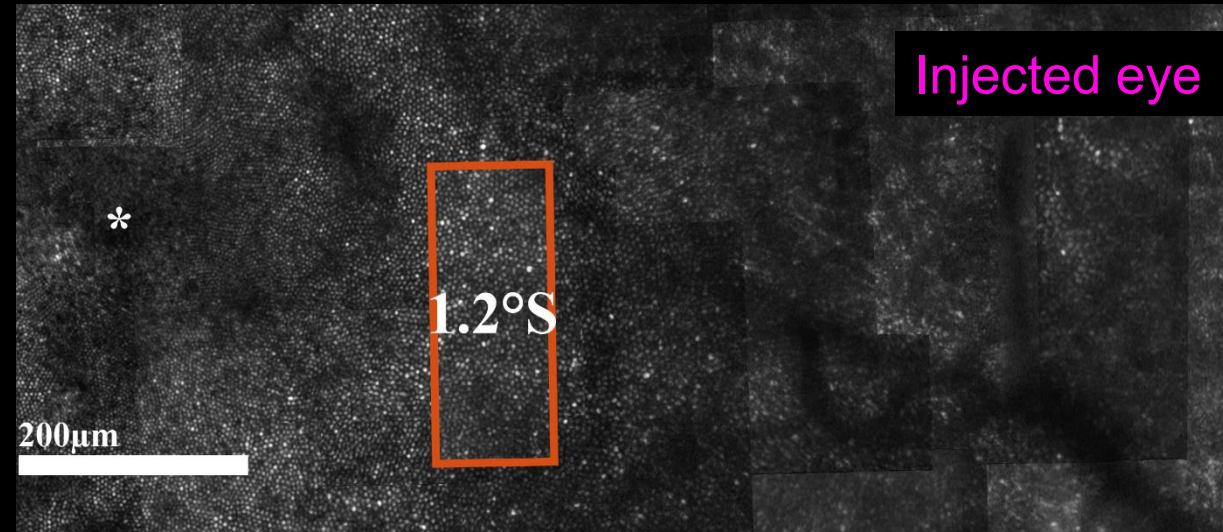
Optoretinography, Patient 2 over time



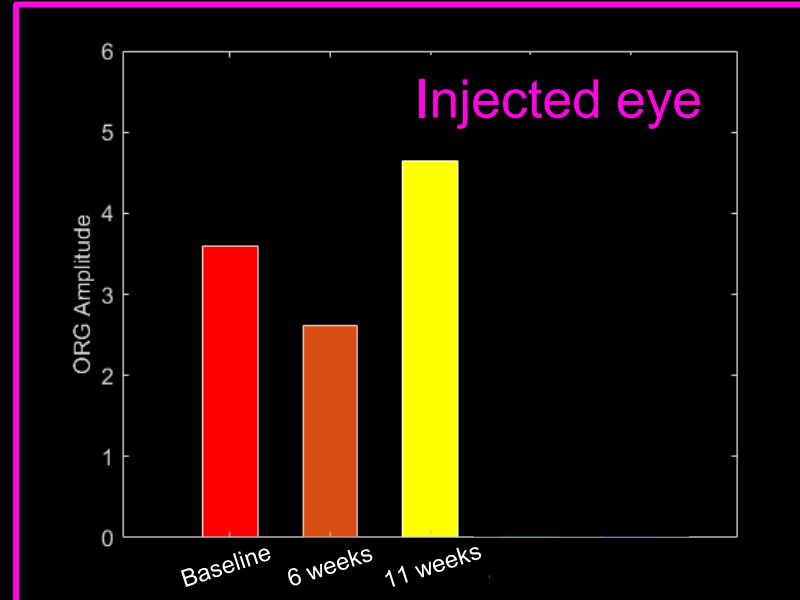
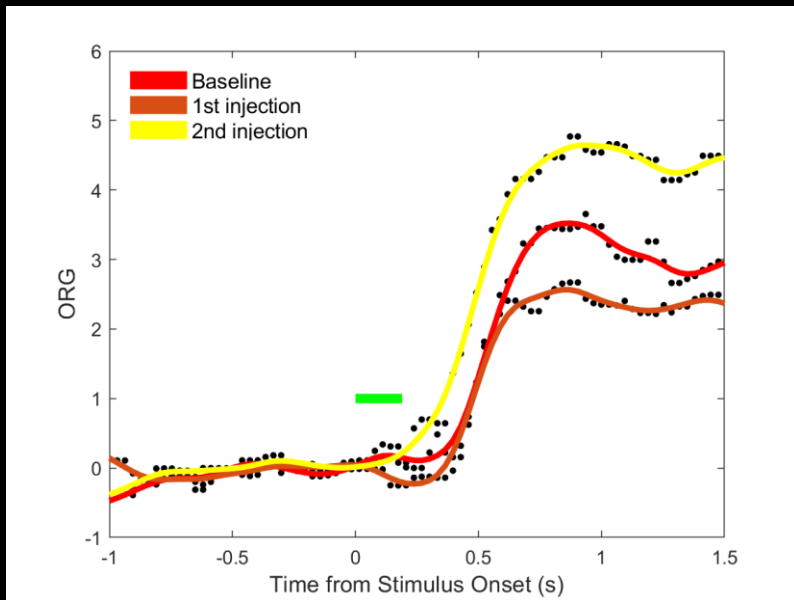
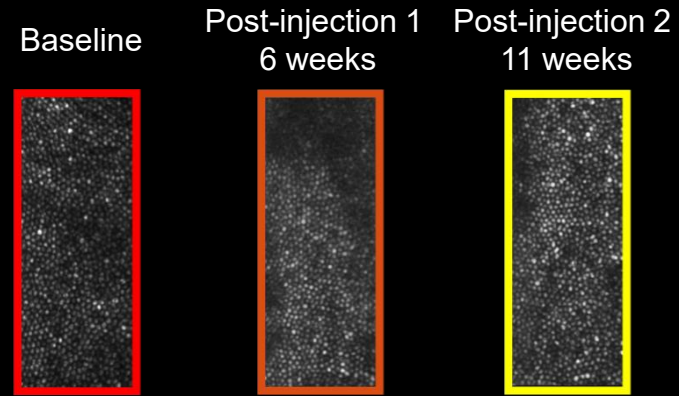
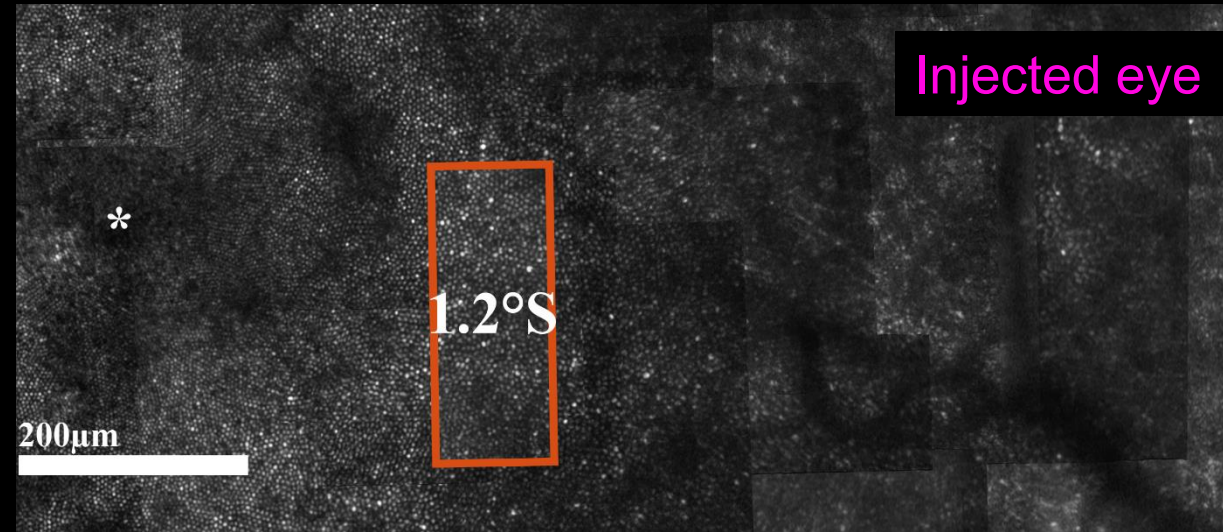
Baseline



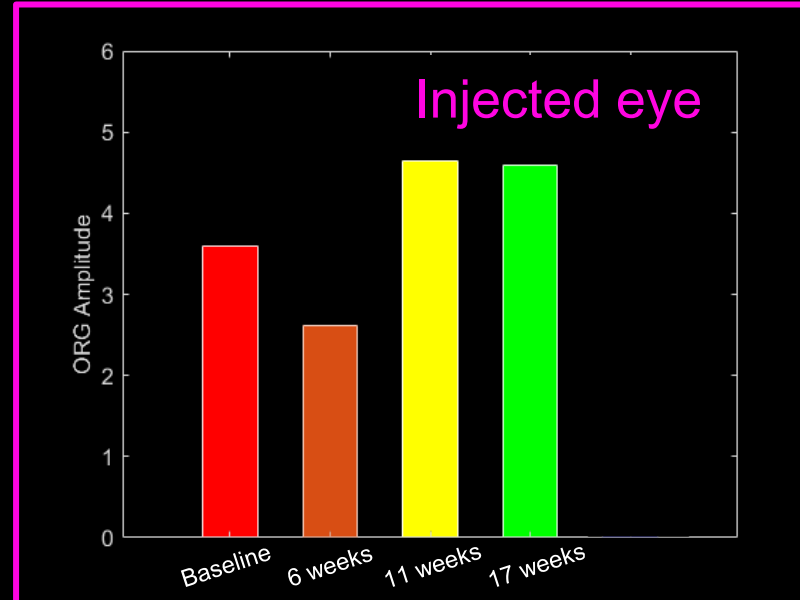
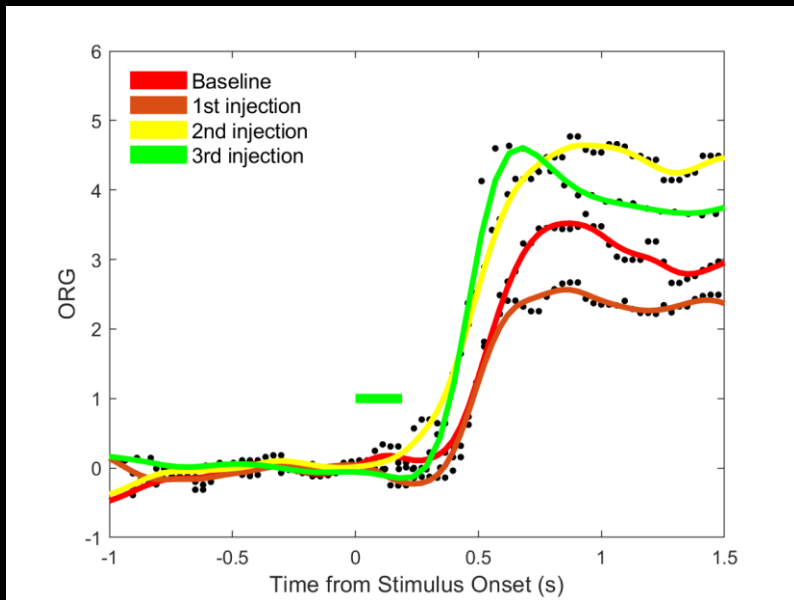
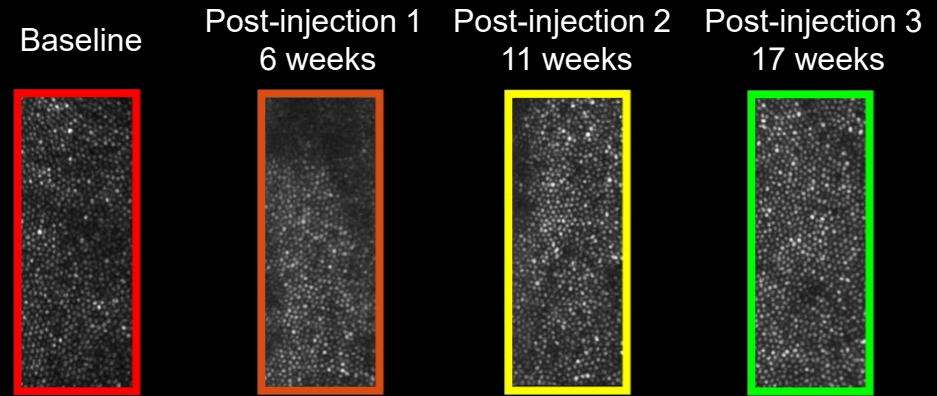
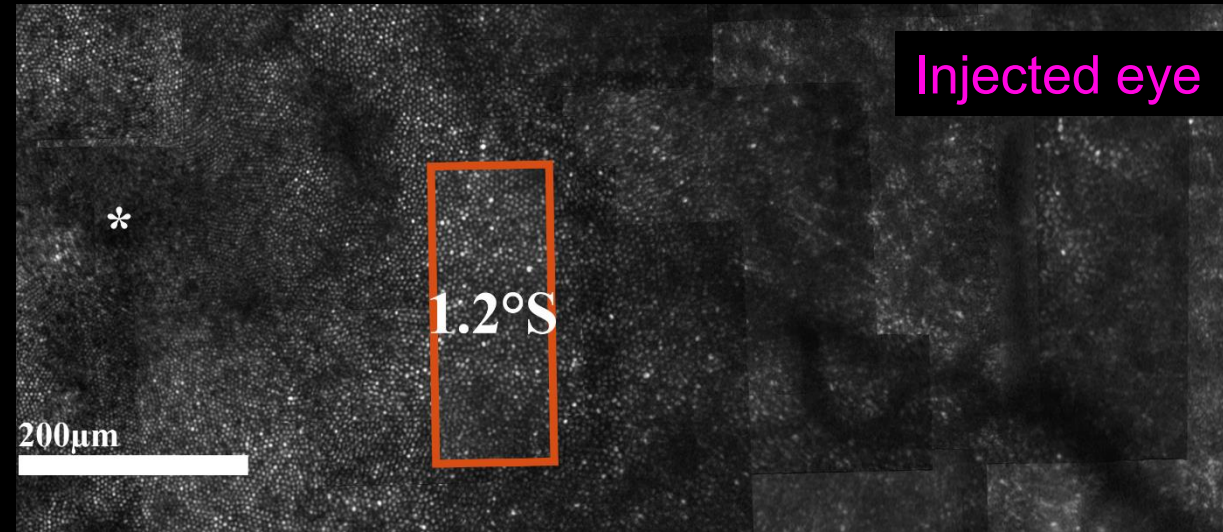
Optoretinography, Patient 2 over time



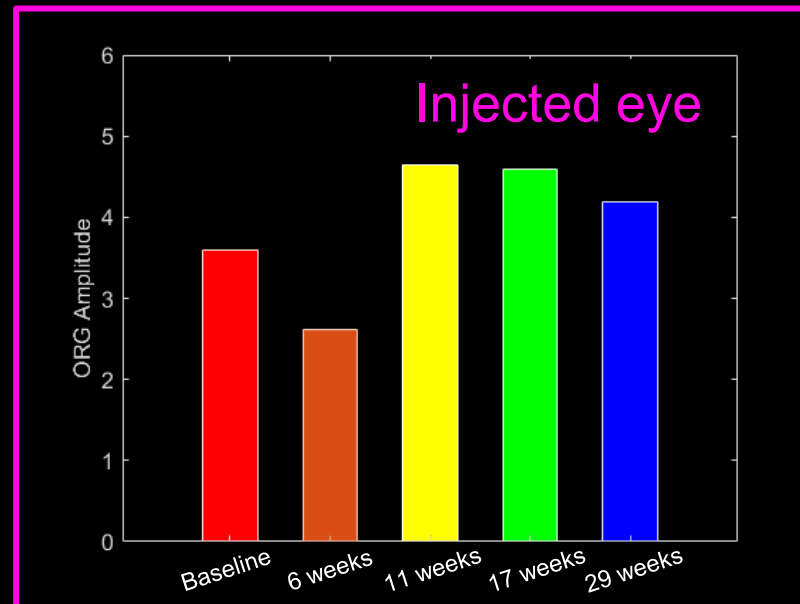
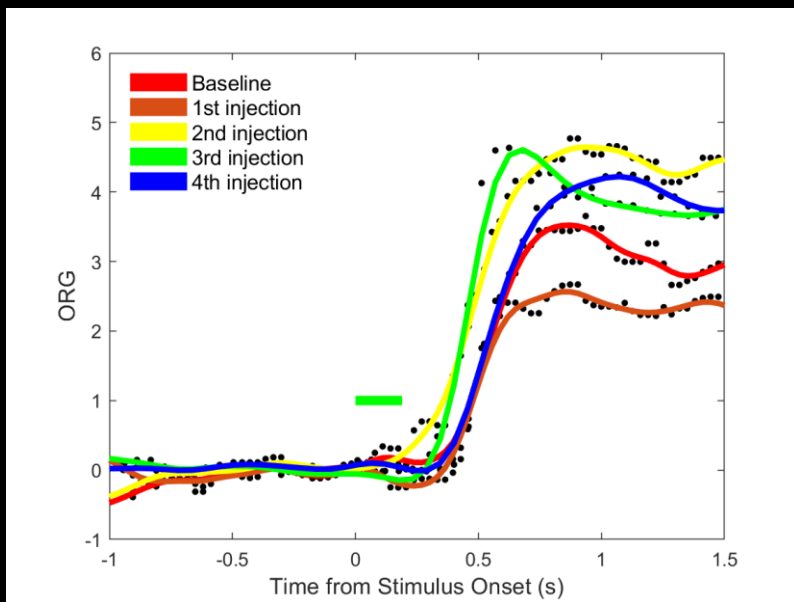
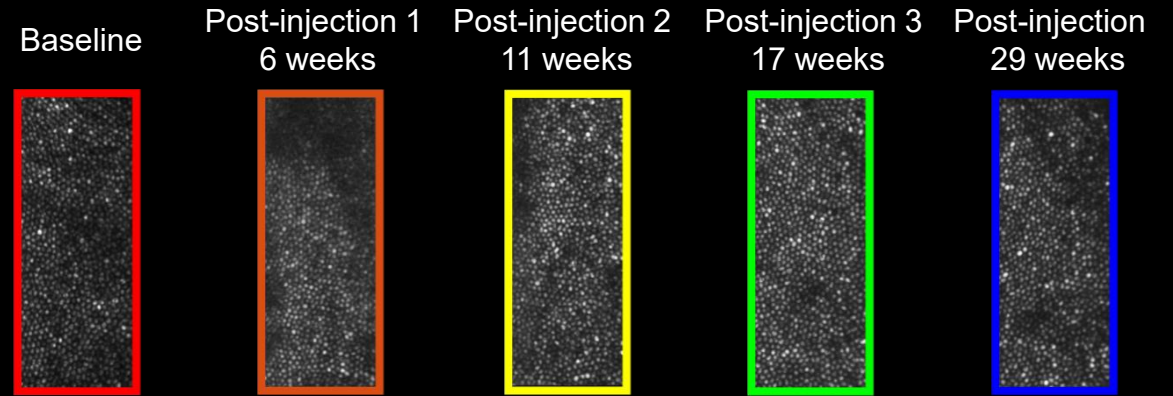
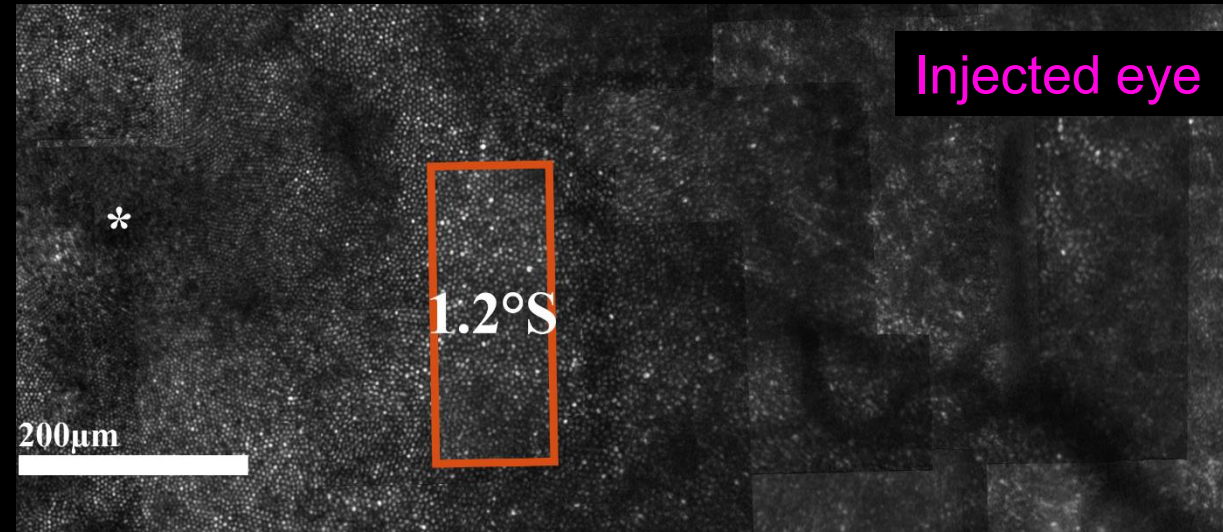
Optoretinography, Patient 2 over time



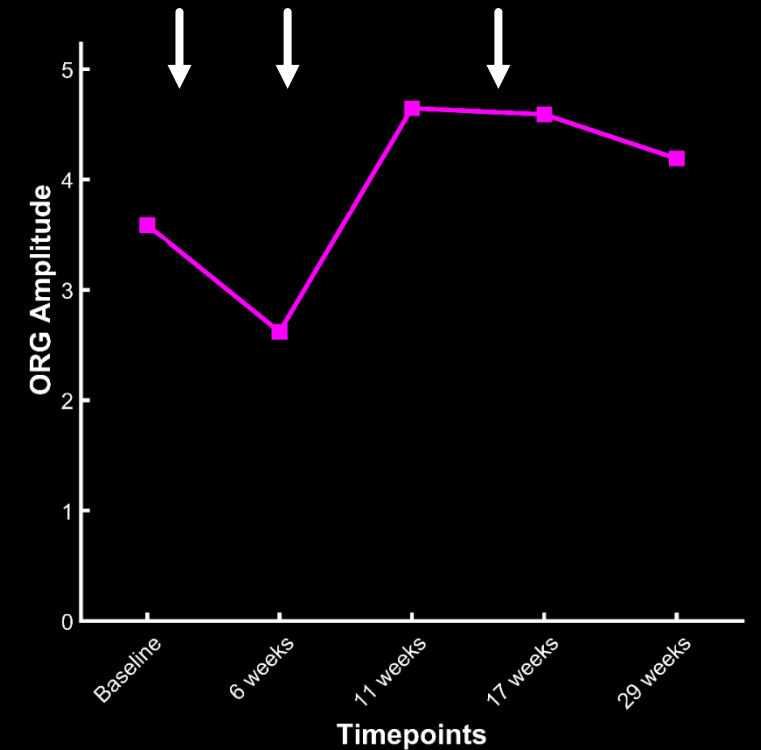
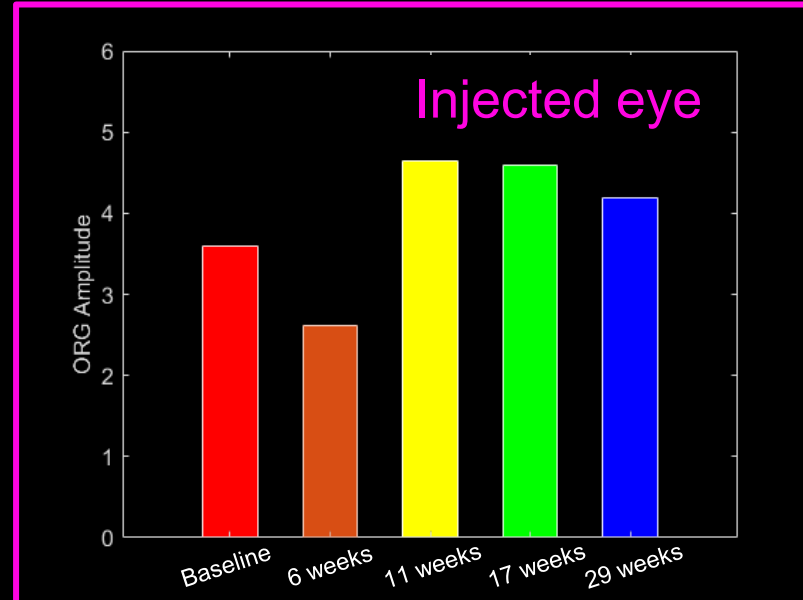
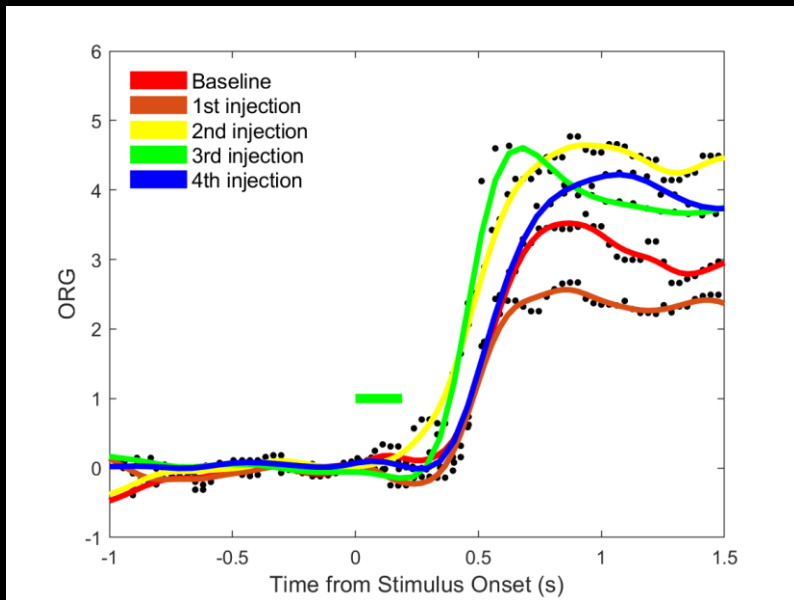
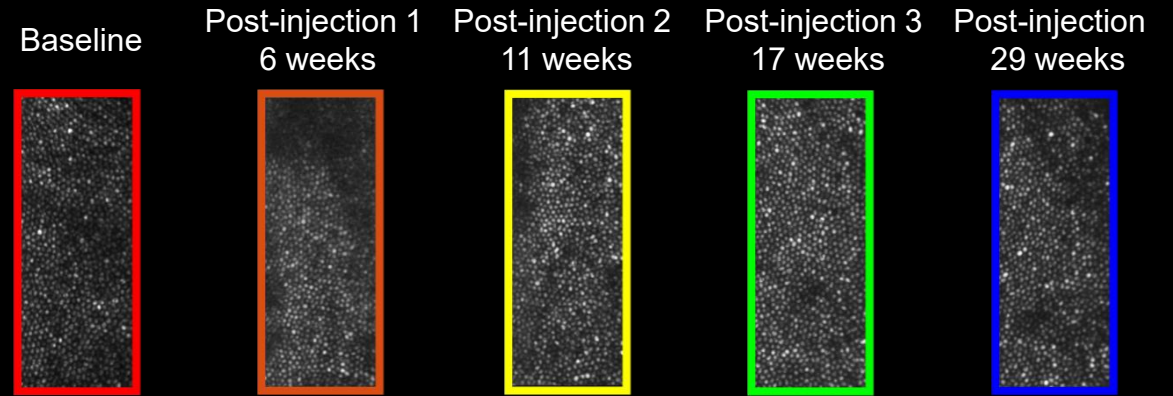
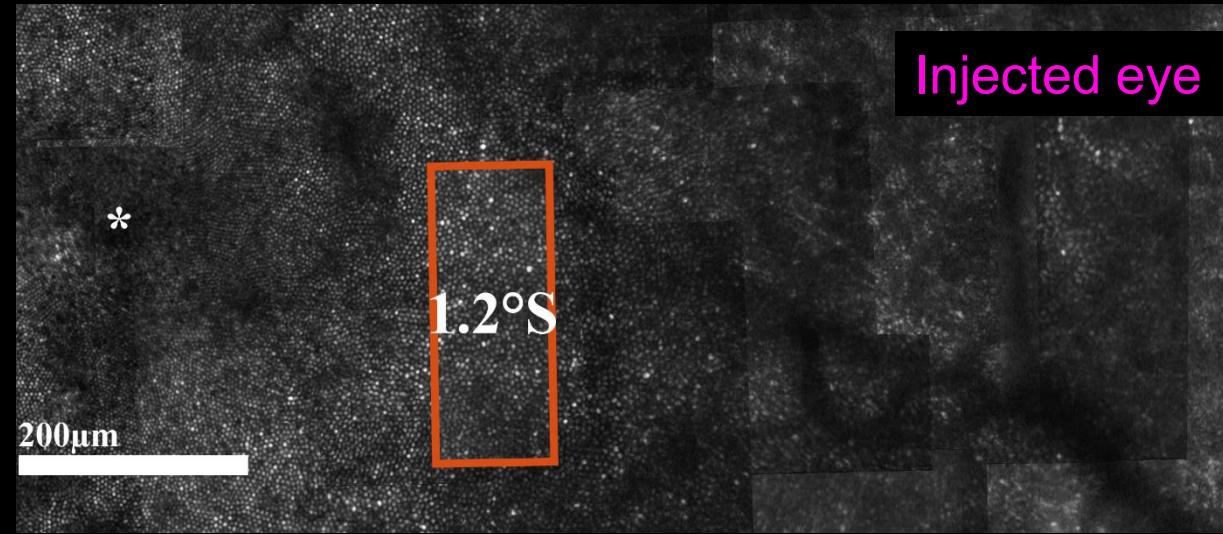
Optoretinography, Patient 2 over time



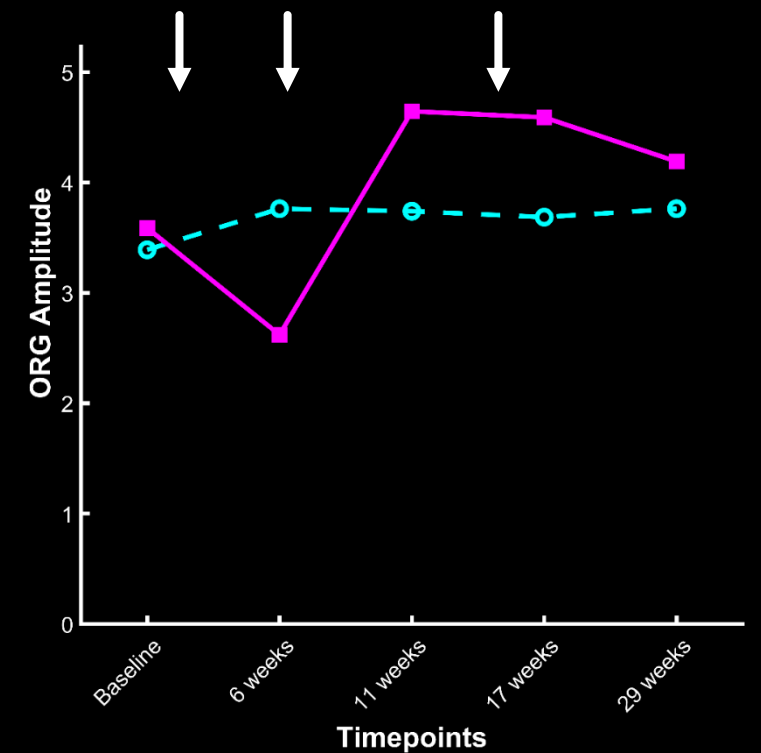
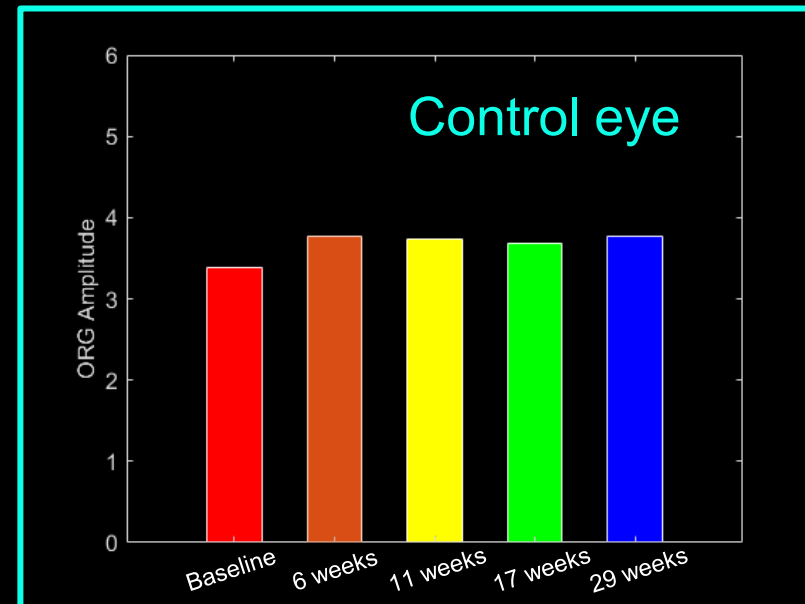
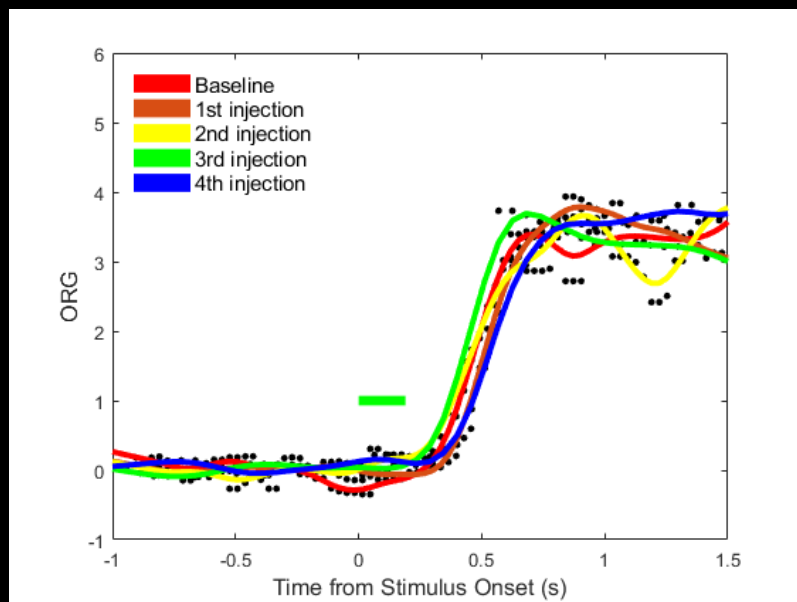
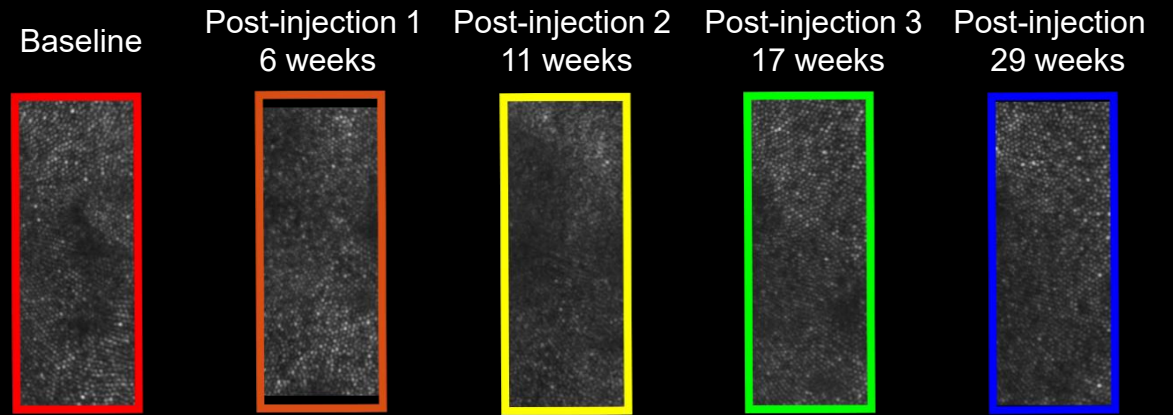
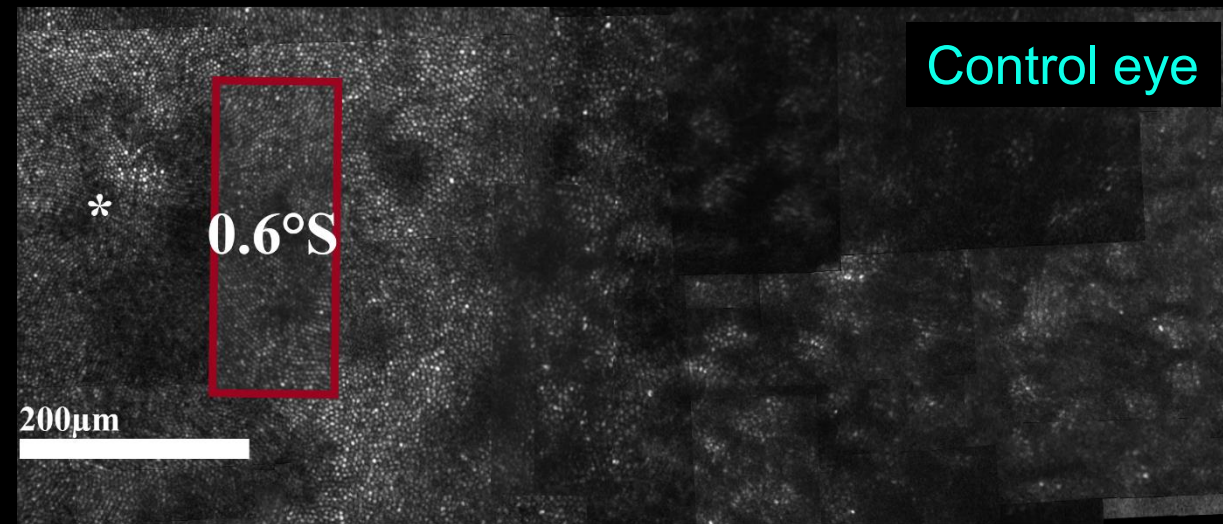
Optoretinography, Patient 2 over time



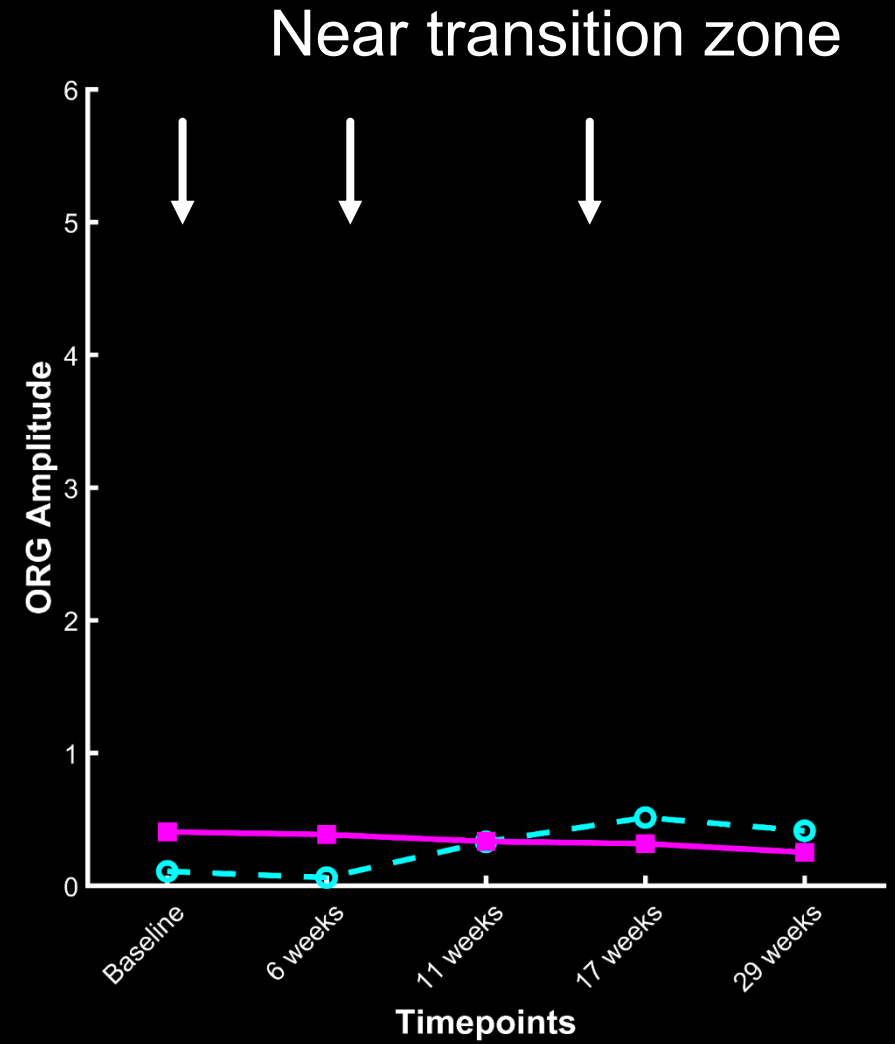
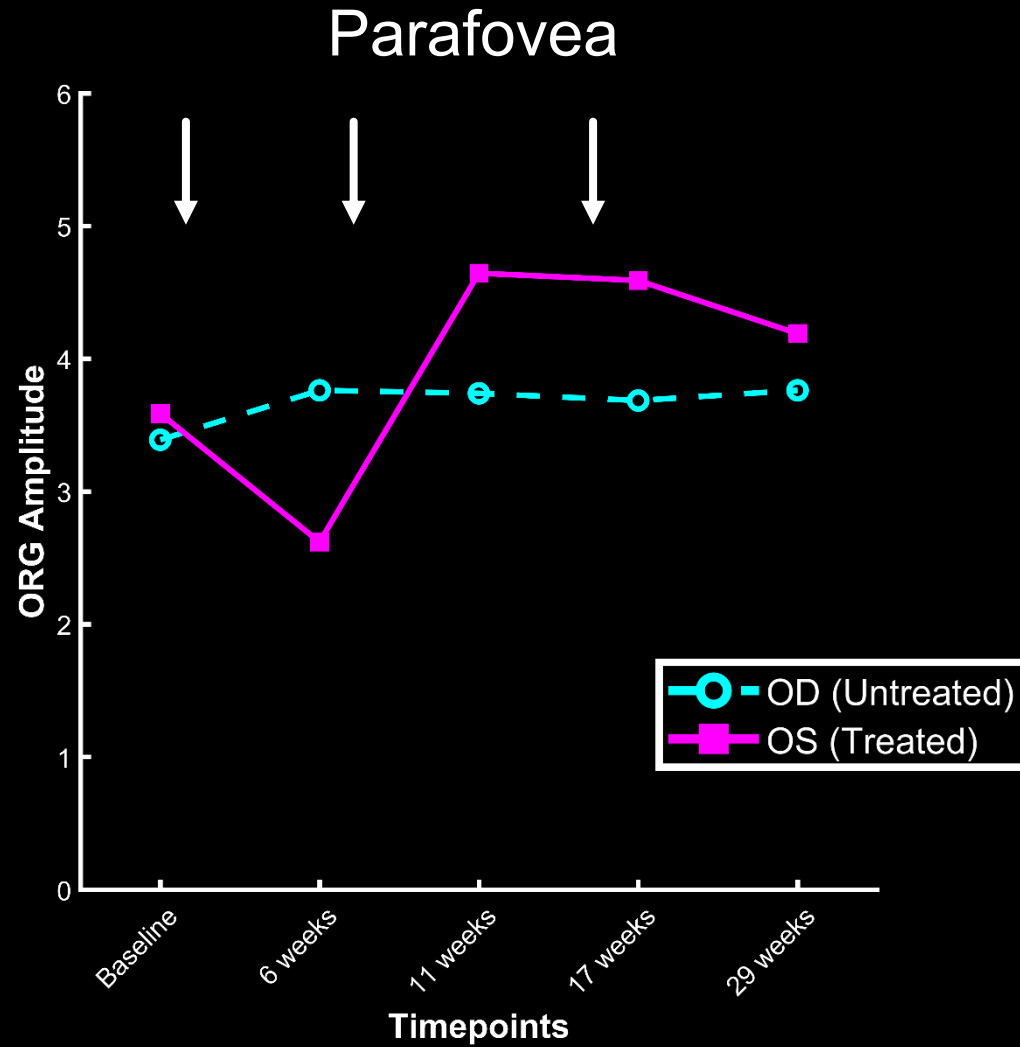
Optoretinography, Patient 2 over time



Optoretinography, Patient 2 over time



Optoretinography, Patient 2 over time



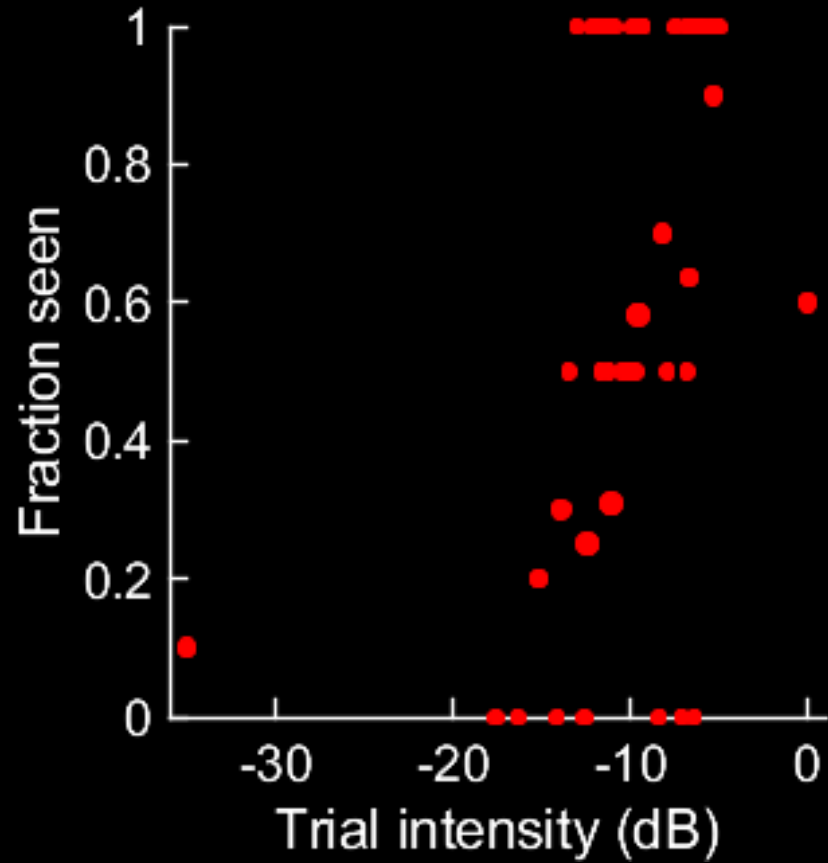
AO microperimetry

AO microperimetry



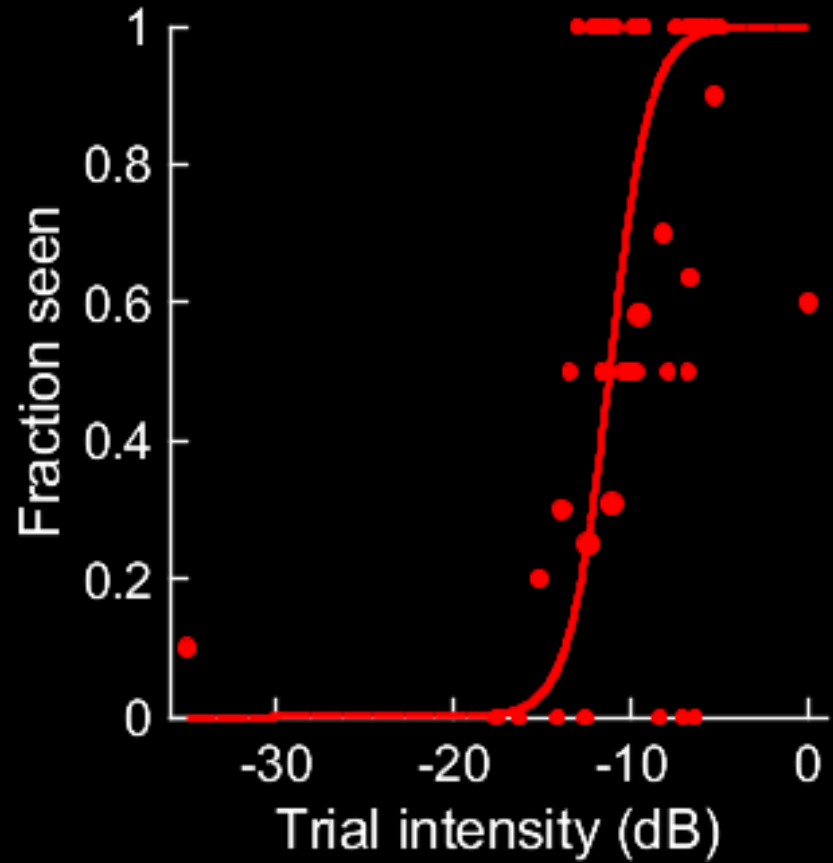
- Image the retina with infrared illumination with AOSLO.
- Deliver a 550 nm stimulus to targeted locations, repeatedly.
- Stimulus size varied by eccentricity but remained the same across time points for all locations.
- Yes/No response for each trial.
- QUEST adaptive staircase of 20 trials, 3 times.
- 100 trials using MOCS for intensities around the expected sensitivity.

AO microperimetry



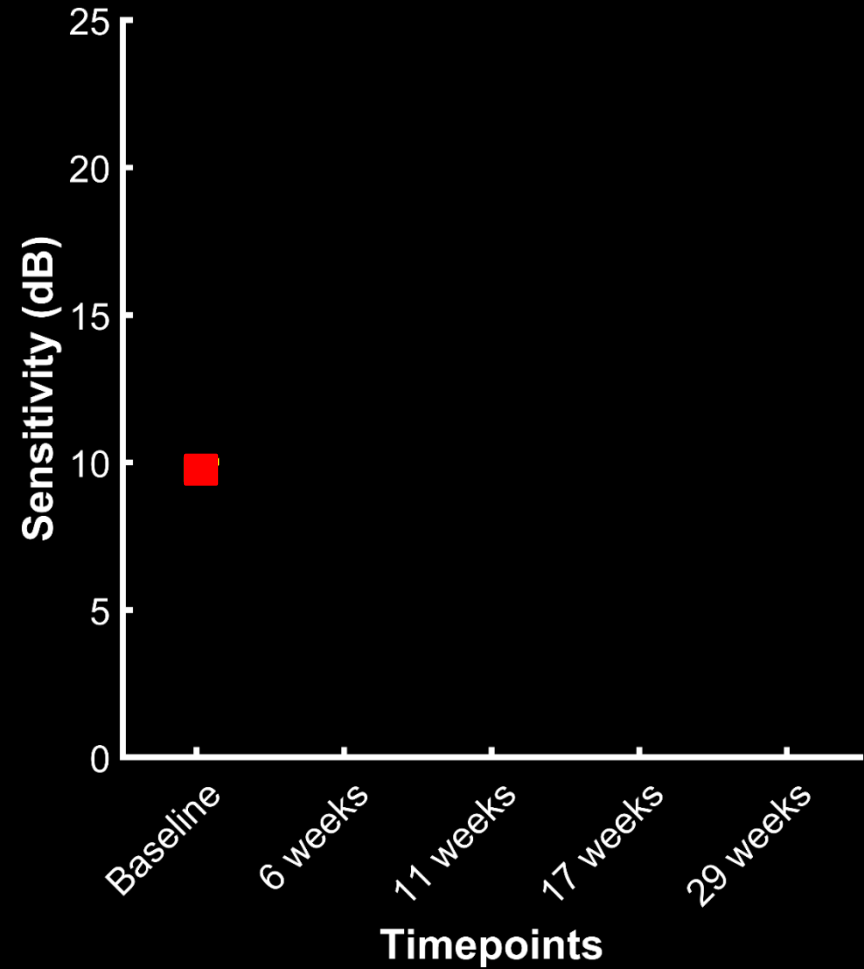
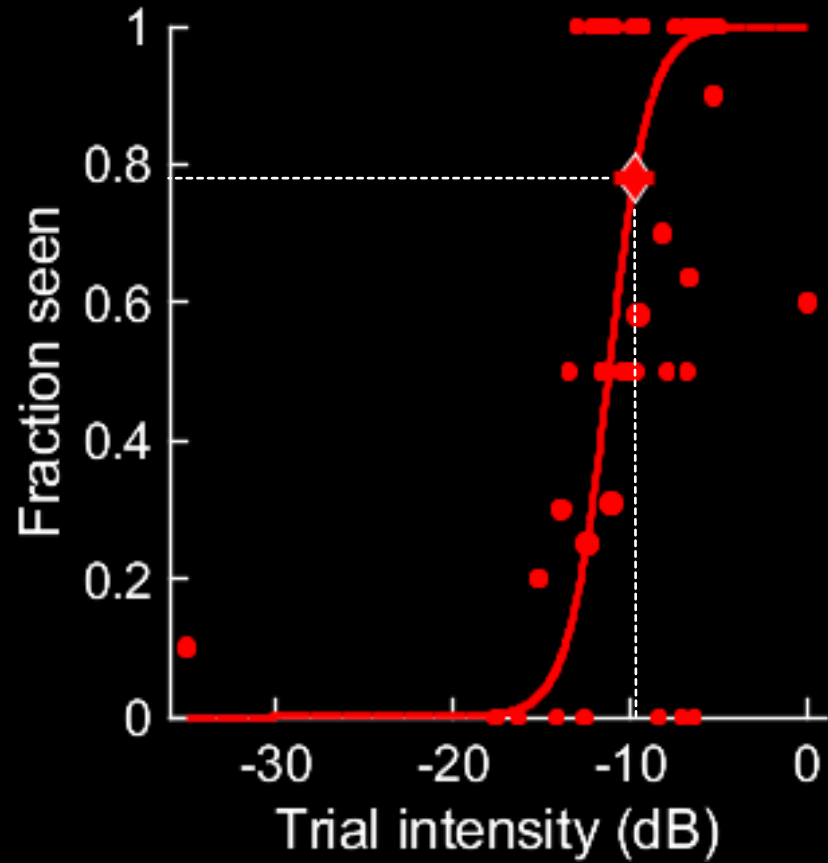
Baseline

AO microperimetry



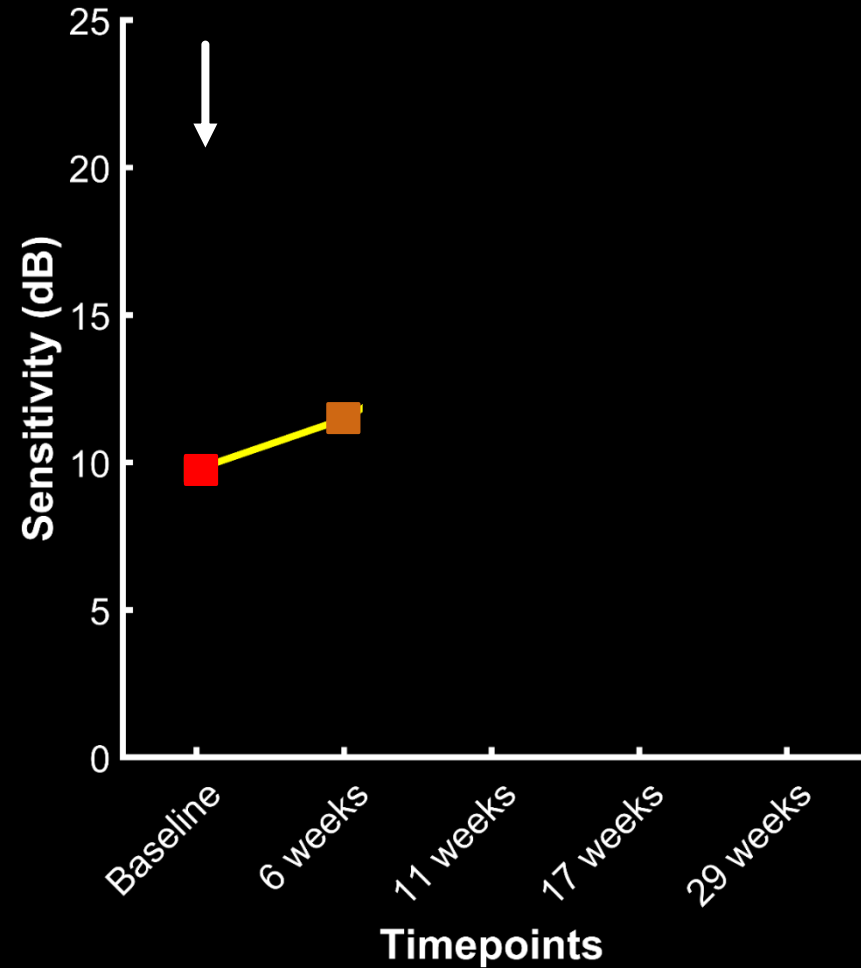
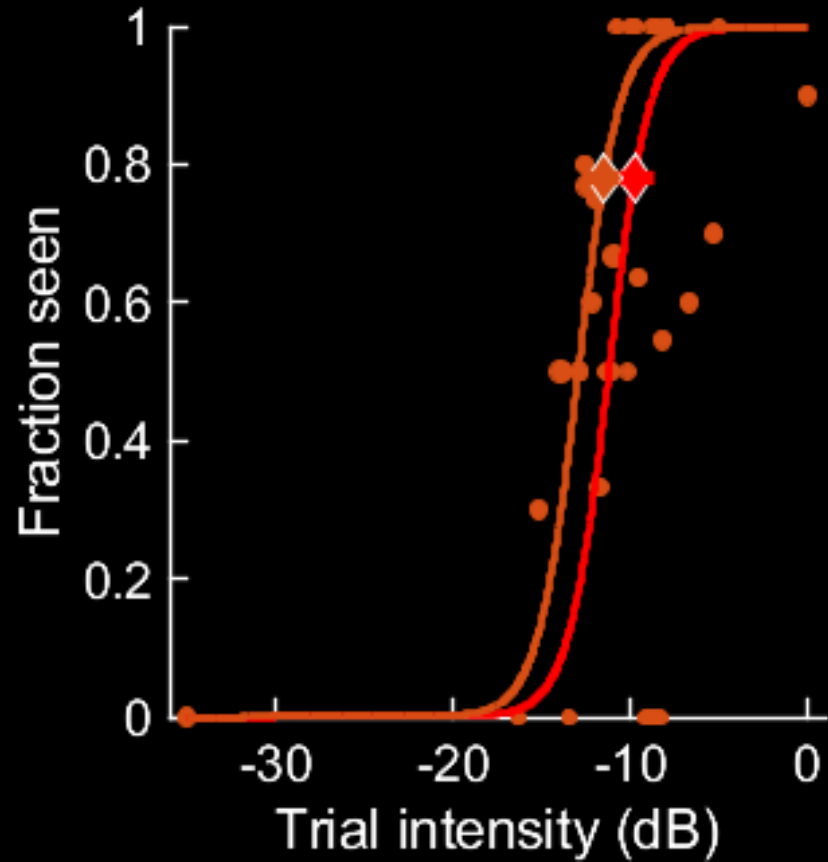
Baseline

AO microperimetry



Baseline

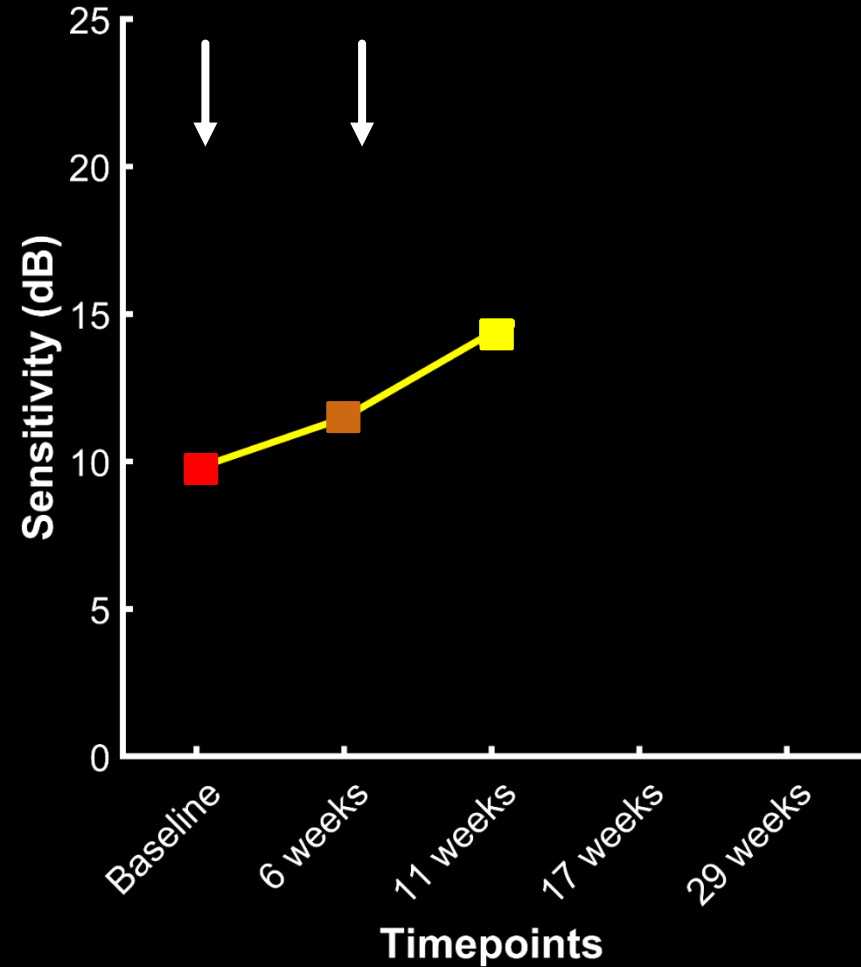
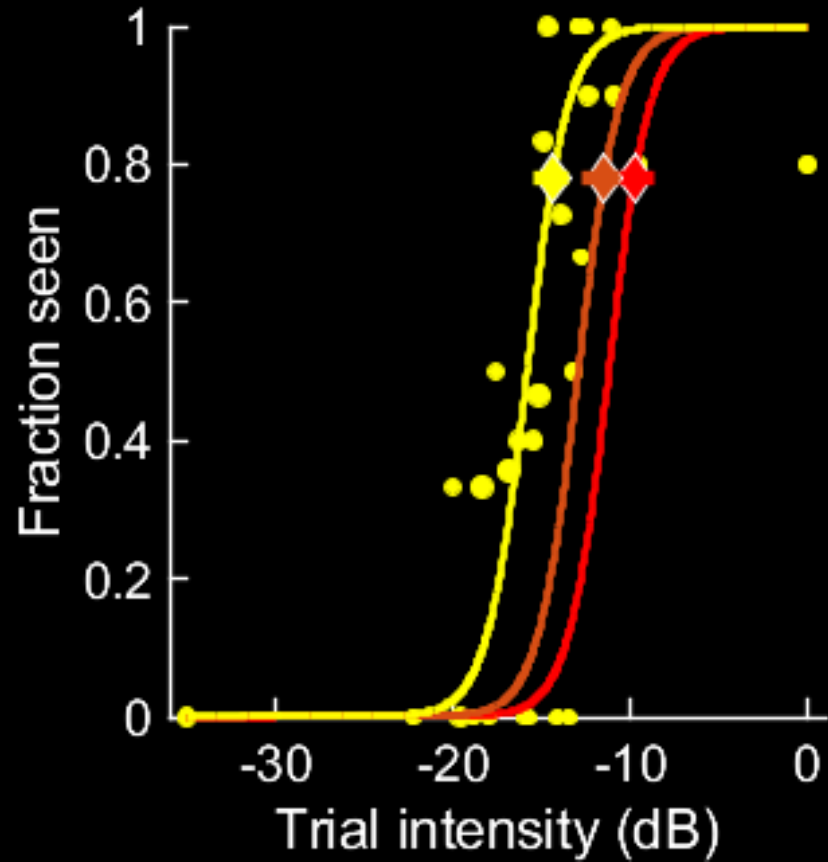
AO microperimetry – sensitivity over time



Baseline

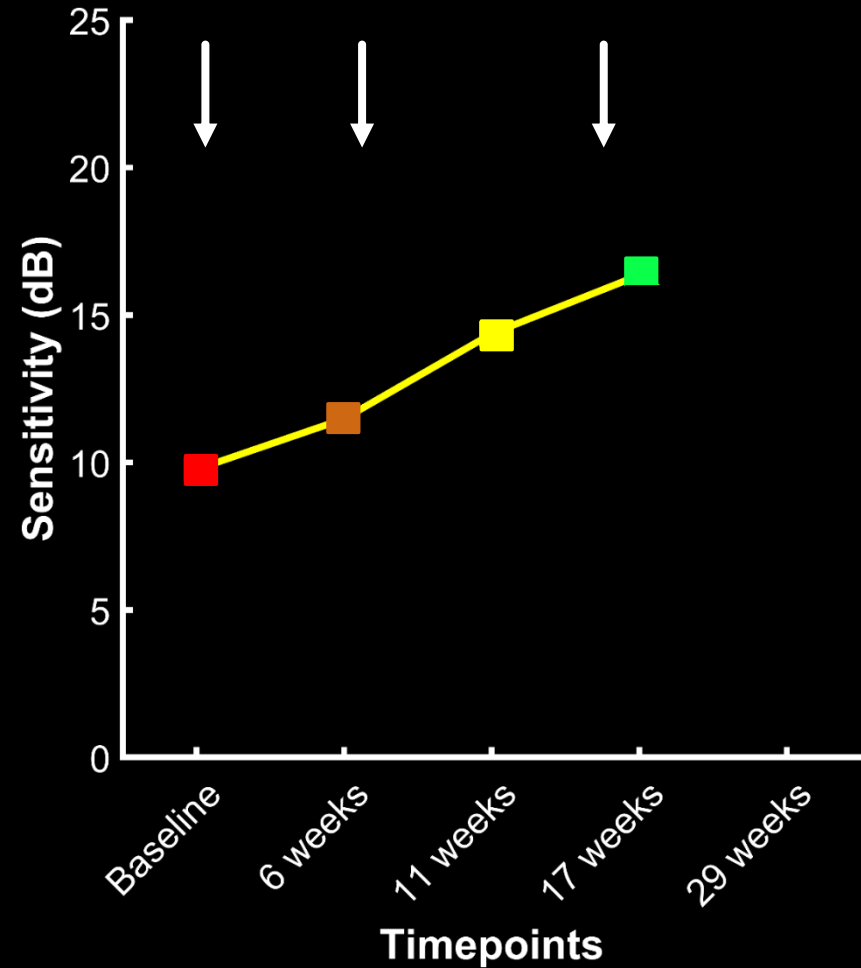
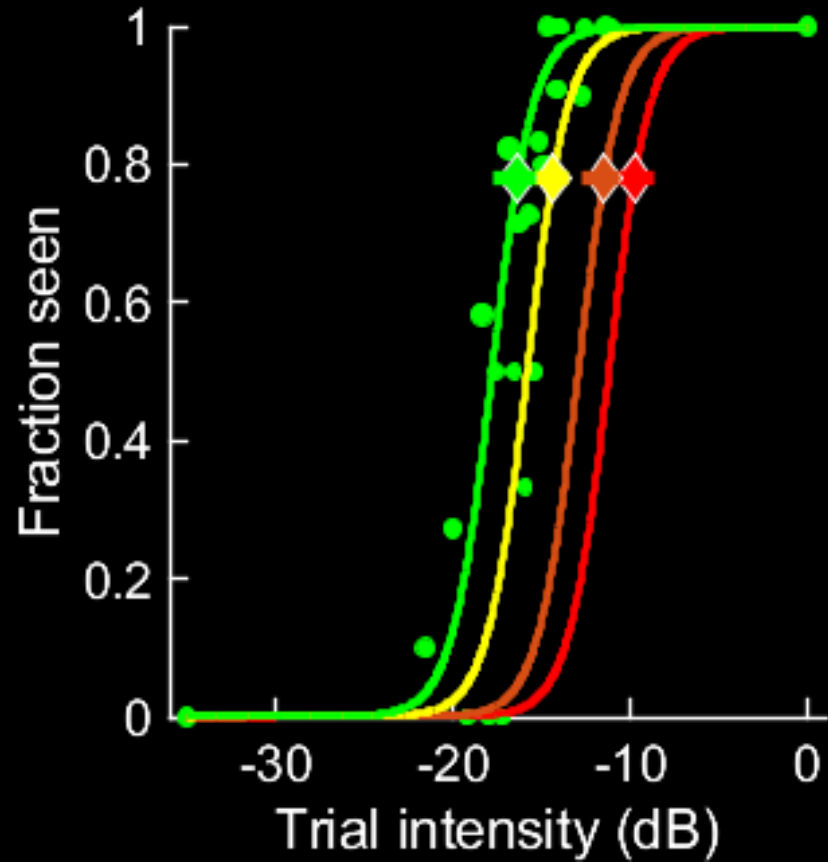
Post-injection 1
6 weeks

AO microperimetry – sensitivity over time



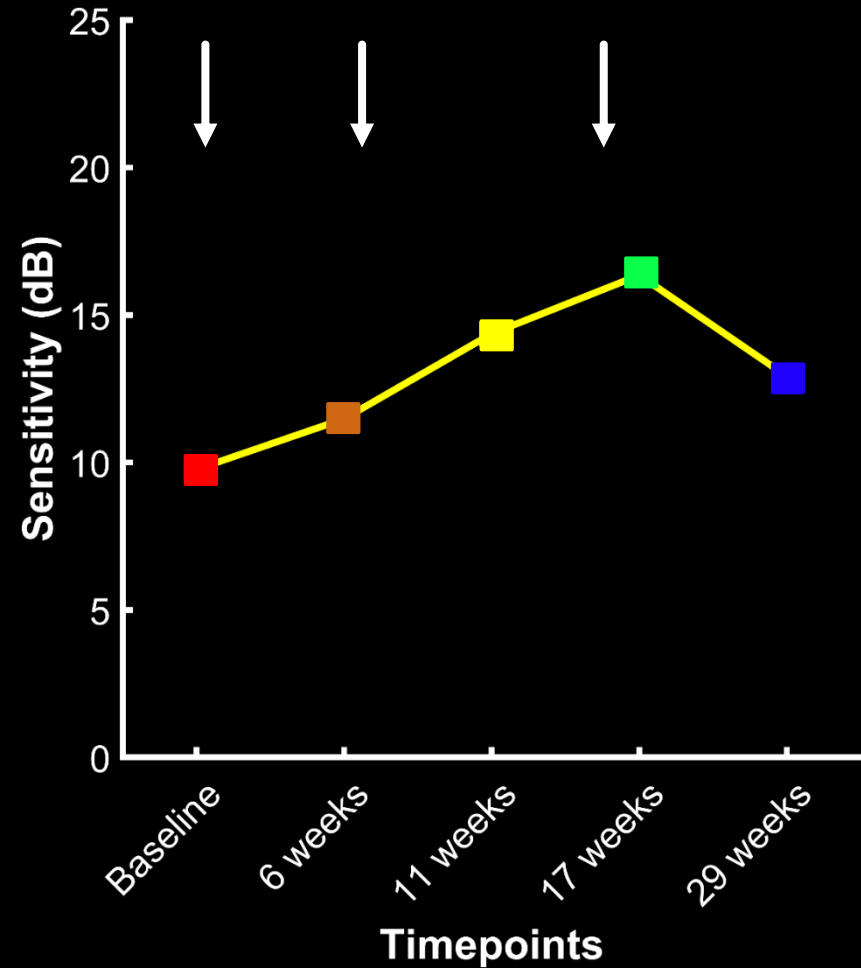
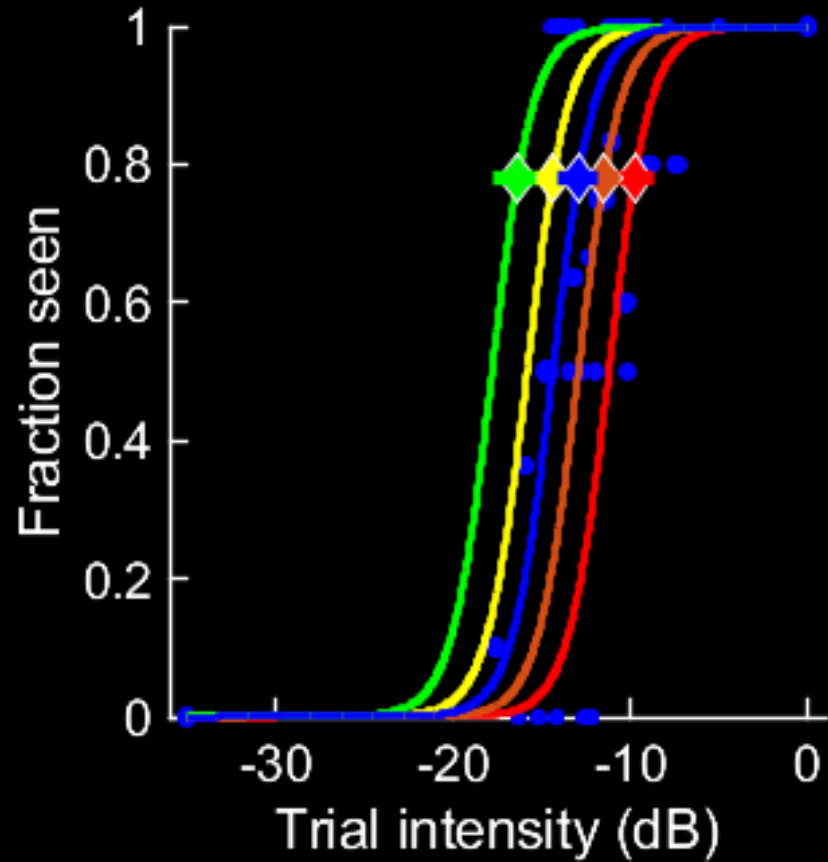
Baseline
Post-injection 1 6 weeks
Post-injection 2 11 weeks

AO microperimetry – sensitivity over time



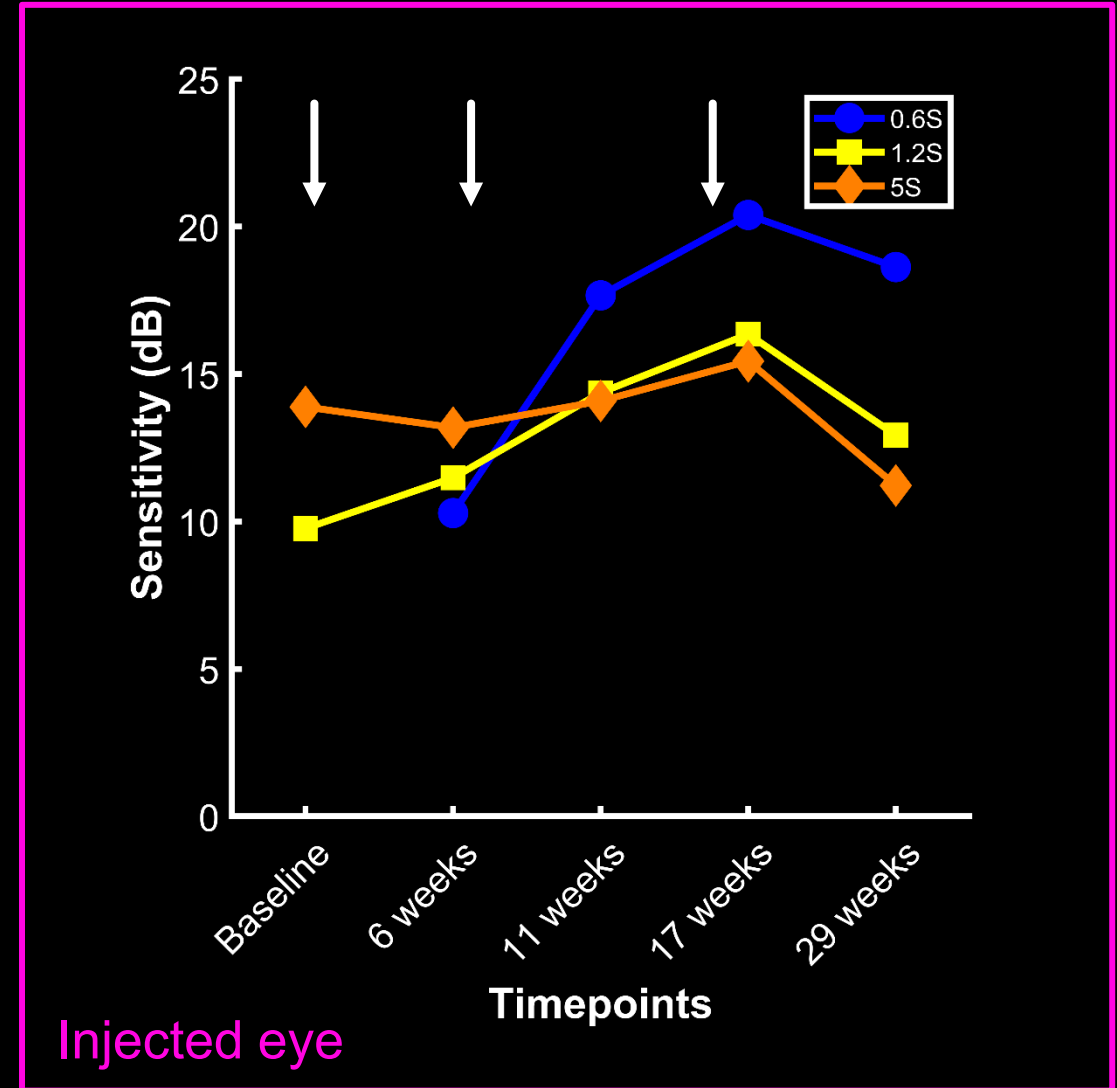
Baseline Post-injection 1 Post-injection 2 Post-injection 3
6 weeks 11 weeks 17 weeks

AO microperimetry – sensitivity over time

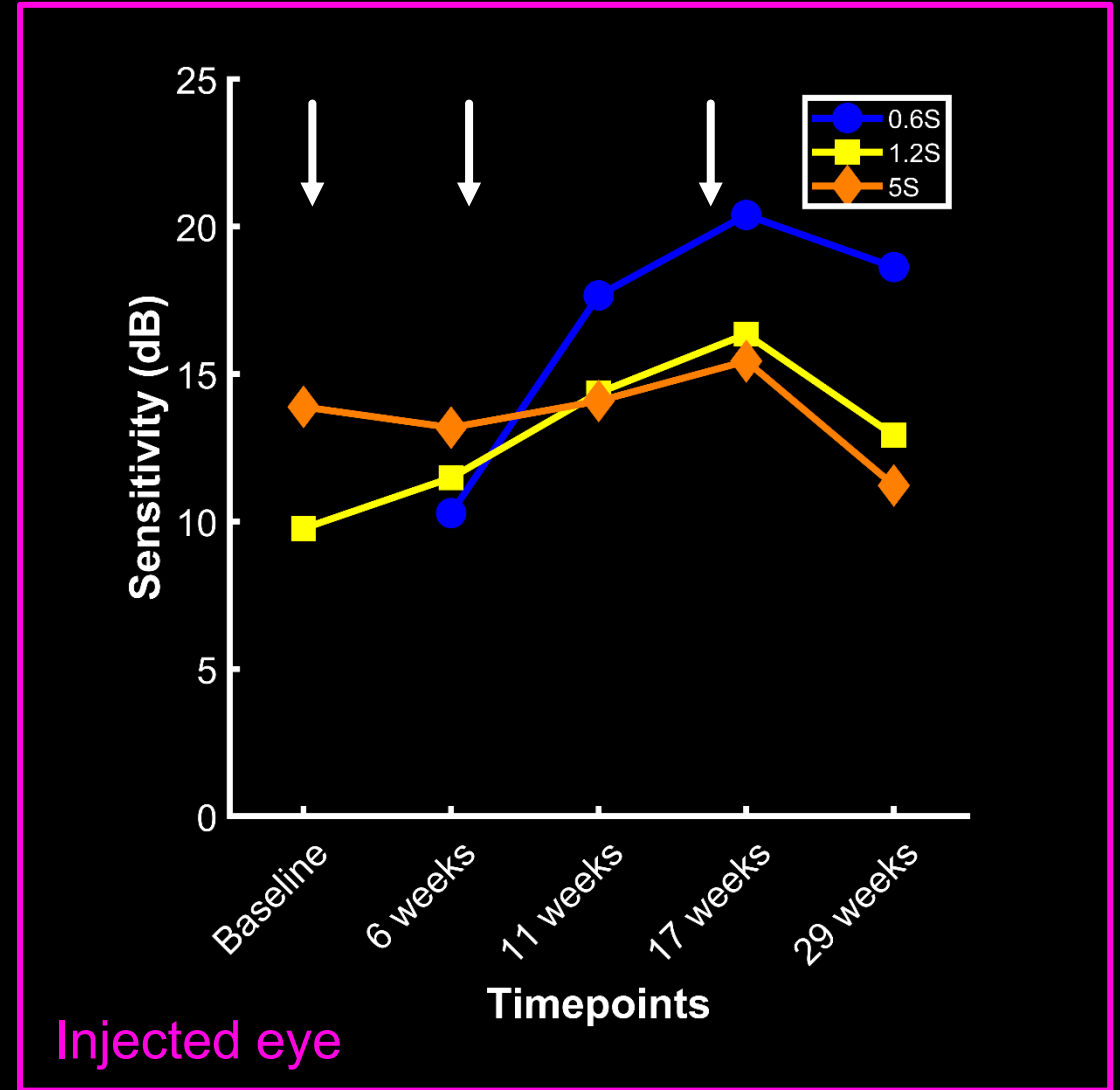
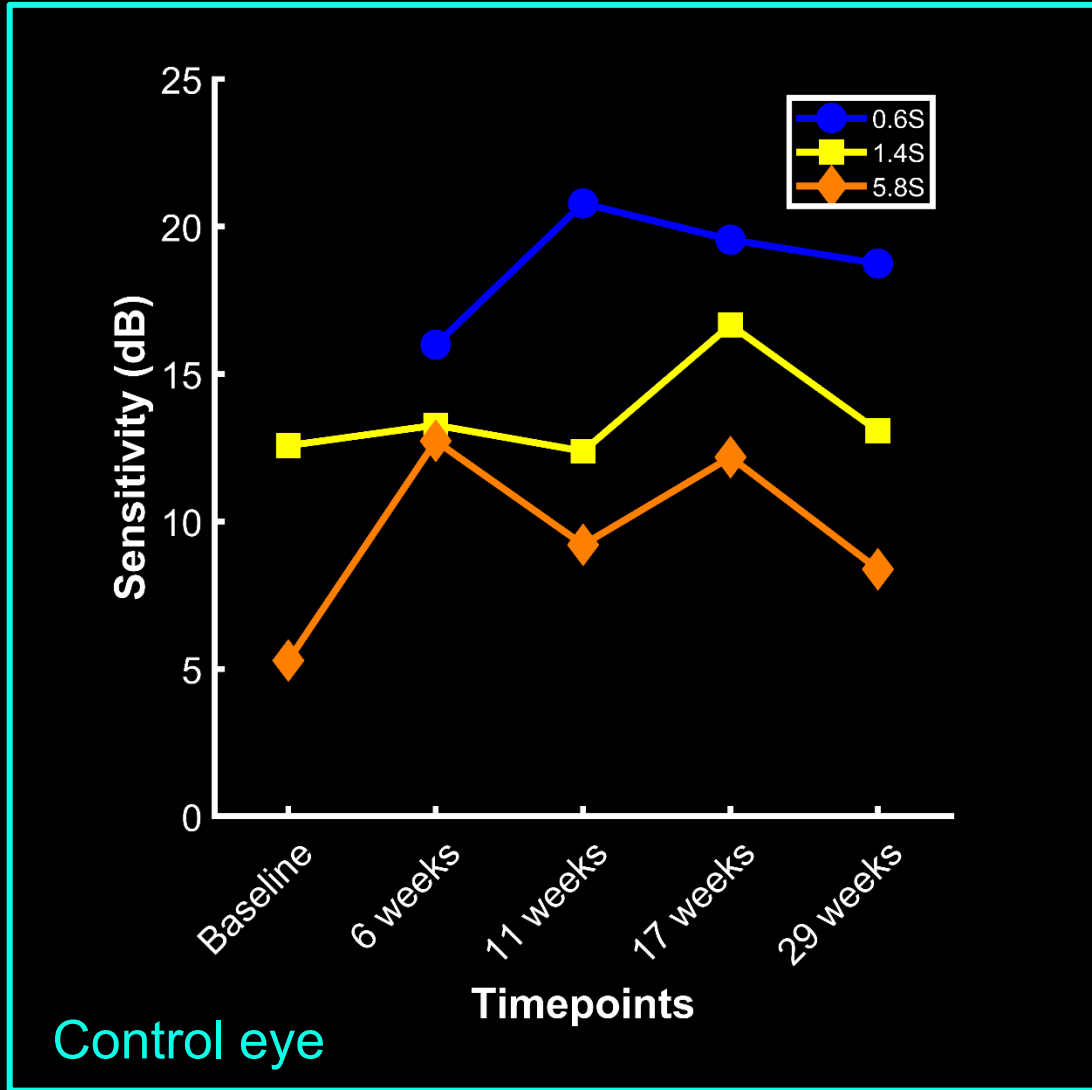


Baseline Post-injection 1 Post-injection 2 Post-injection 3 Post-injection
6 weeks 11 weeks 17 weeks 29 weeks

Sensitivity over time, Patient 2



Sensitivity over time, Patient 2



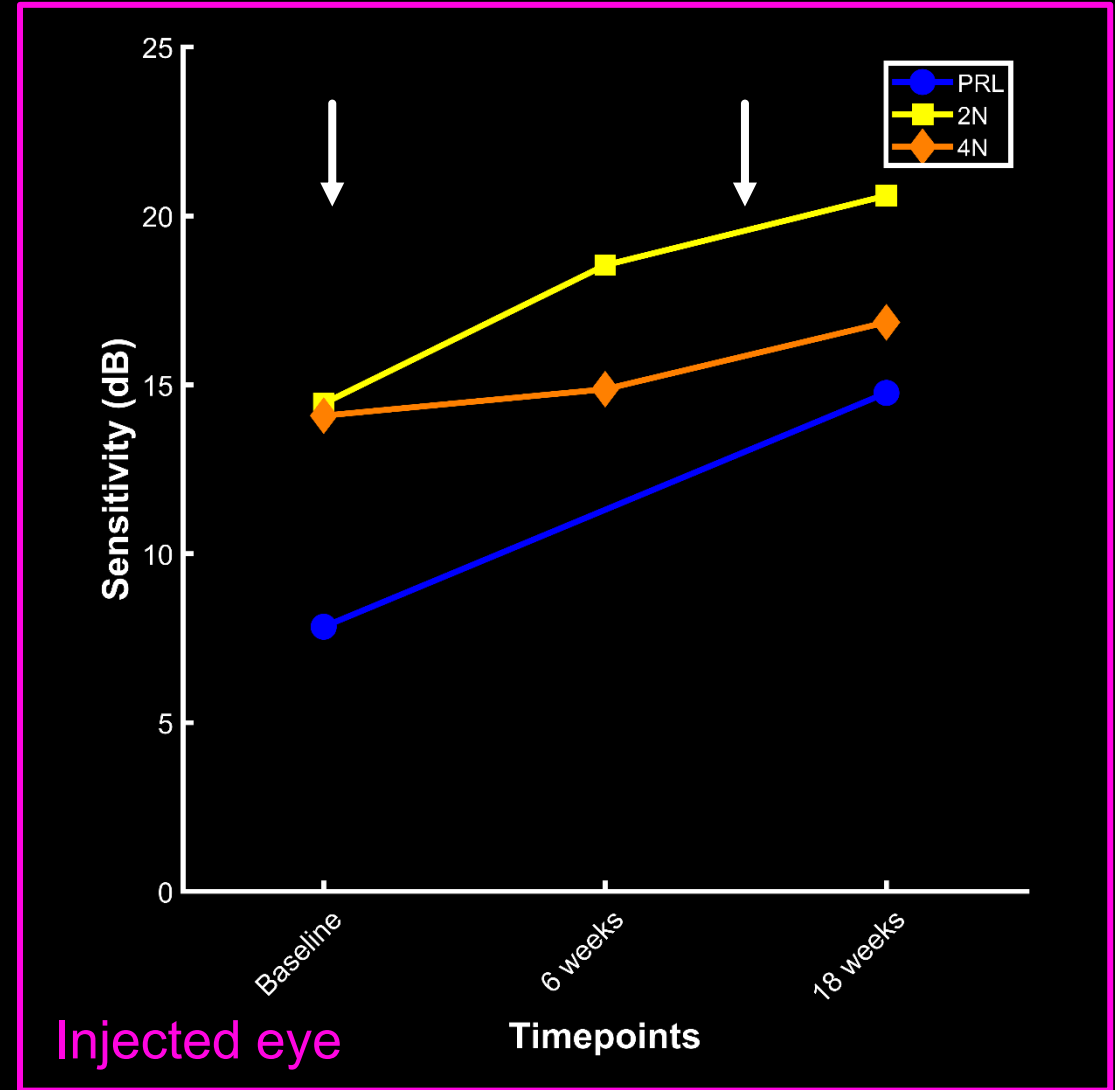
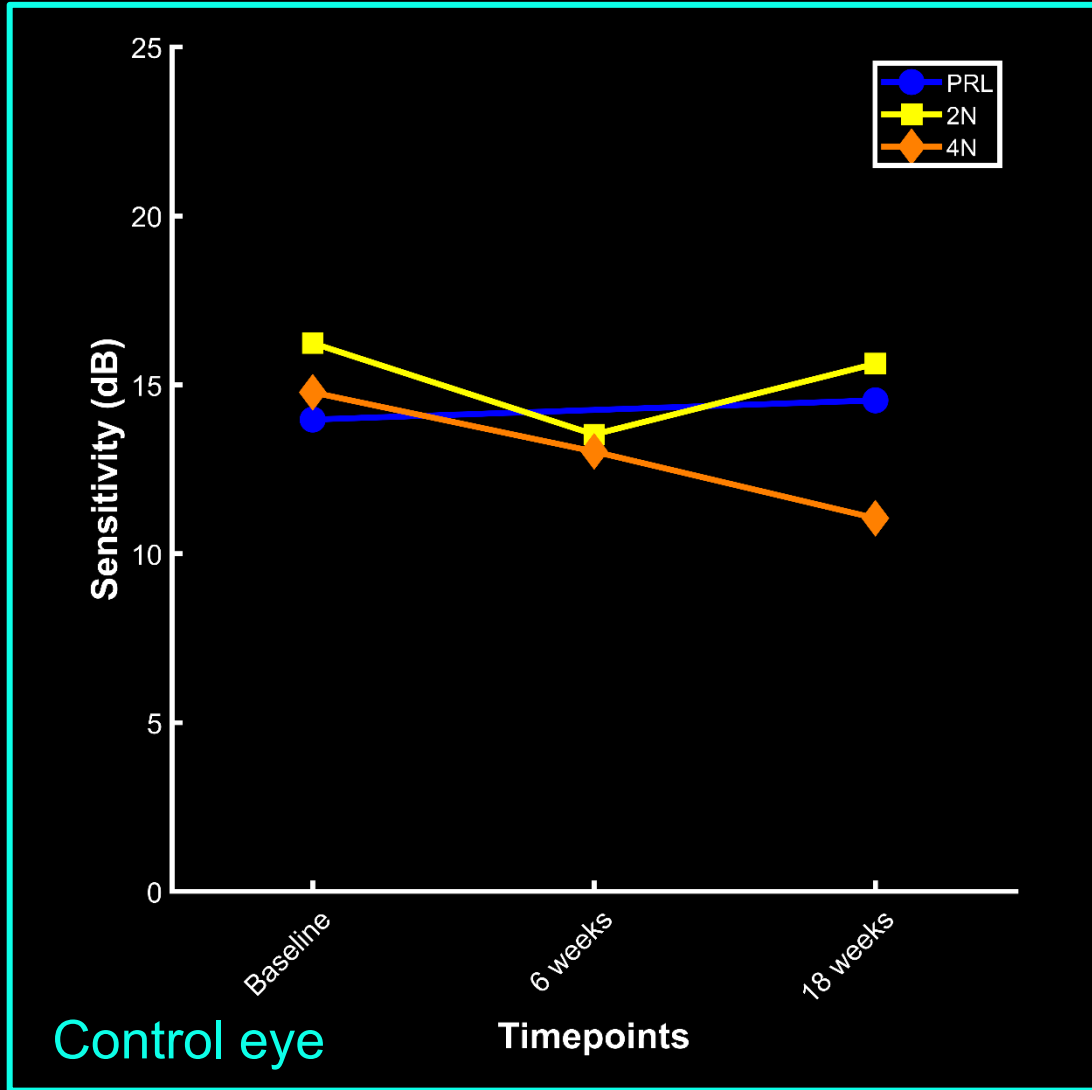
Patient 1



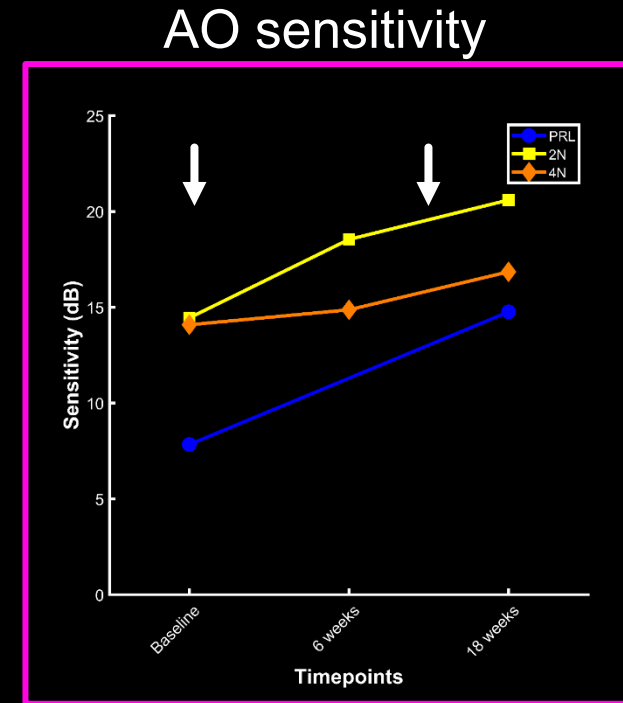
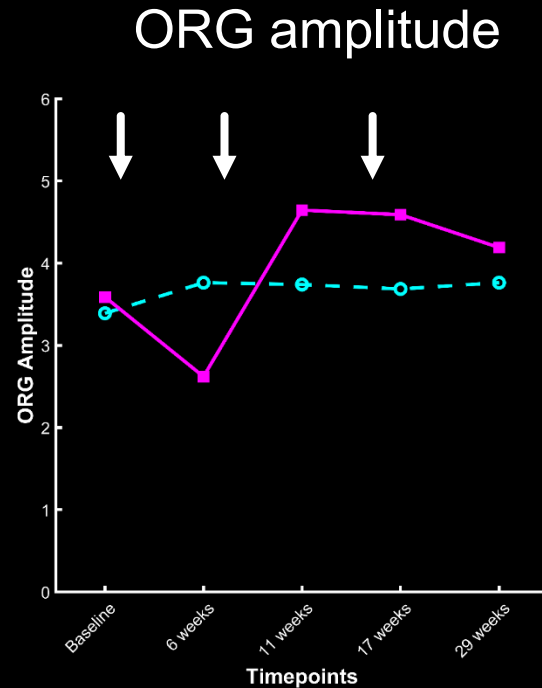
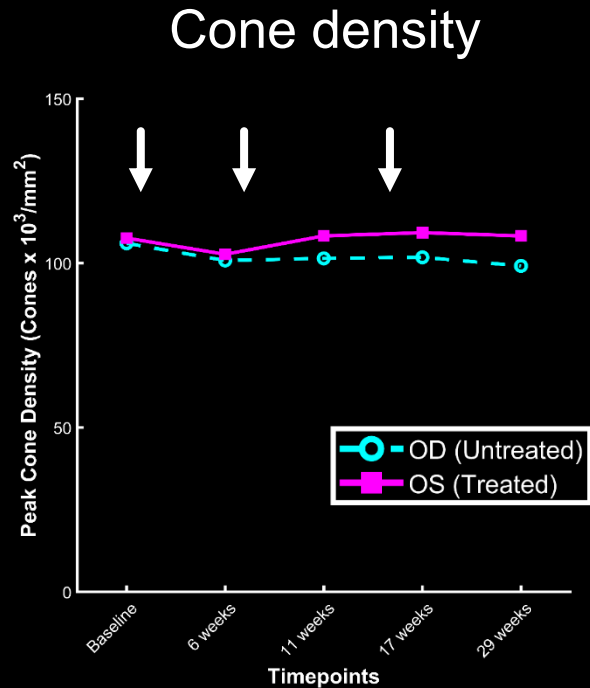
Patient 1



Sensitivity over time, Patient 1



Summary



- Cone density, ORG amplitude, and AO sensitivity can be used to assess experimental therapies for retinal disease.
- Cone structure and function were maintained or improved following treatment with VP-001.
- The data support future studies to assess VP-001 efficacy in additional RP11 patients.

A Phase 1B Multiple Ascending Dose Study of VP-001; a peptide conjugate of oligonucleotide designed to treat PRPF31-related Retinitis Pigmentosa

Dr. Fred Chen

Lions Eye Institute, Perth, Australia

ARVO 2026



VP-001 for the treatment of Retinitis Pigmentosa type 11 (RP11)

Introduction to RP11 and VP-001

- 1) Patients with RP11 experience progressive and irreversible vision loss beginning in childhood – there are no treatment options available
- 2) RP11 is caused by a haploinsufficiency of one gene (PRPF31) in the retina
- 3) VP-001 shows the ability to rescue the haploinsufficiency causing RP11 in patient-derived models

Clinical status and data generated to date

- 4) **Status:** VP-001 is the first clinical stage drug candidate for RP11 and is currently being evaluated in a Phase 2 Open-Label Extension study called DINGO
- 5) **Safety:** VP-001 is safe and well-tolerated in patients with RP11¹ – including patients who have received multiple doses of the drug candidate
- 6) **Efficacy:** RP11 patients treated with VP-001 have shown:
 - a) Clinically meaningful improvements in Low-Luminance Visual Acuity (LLVA);
 - b) Clinically meaningful improvements in retinal sensitivity (as assessed by microperimetry); and
 - c) Improved vision and quality of life after treatment with VP-001 (via patient/clinician reports)
- 7) **Future development:** Long-term follow up data from the ongoing Phase 2 study will be used to finalise the design of a potential registrational trial in RP11

1) Patients with RP11 experience progressive and irreversible vision loss beginning in childhood¹⁻³

Illustration of the degeneration in sight experienced by an RP11 patient¹⁻³

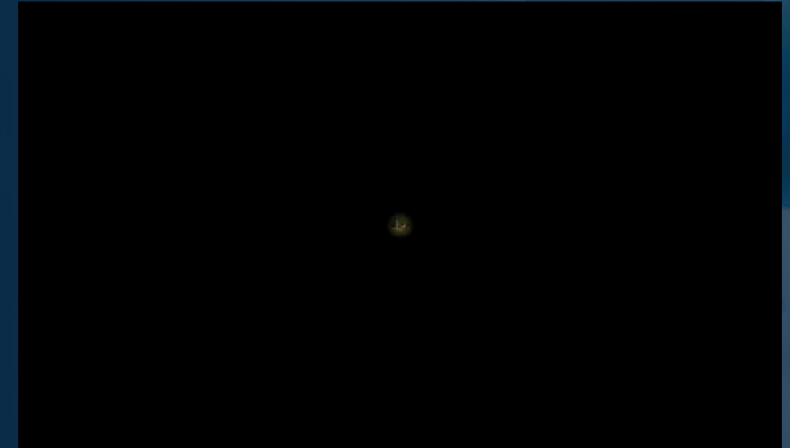
6 years old



26 years old



46 years old

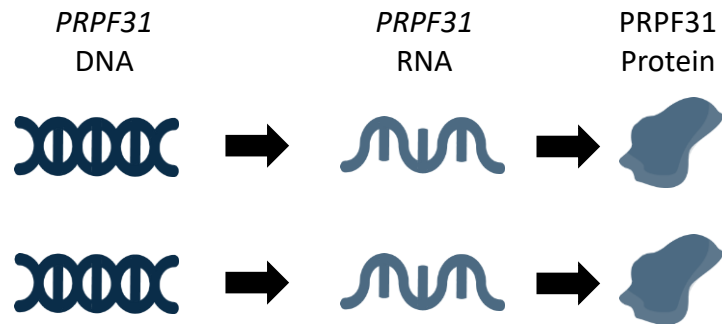


Patients experience night blindness followed by loss of peripheral and then central vision - legal blindness occurs in the 4th or 5th decade of life¹⁻³

1. Lisbjerg K, et al. Disease progression of retinitis pigmentosa caused by PRPF31 variants in a Nordic population: a retrospective study with up to 36 years follow-up. *Ophthalmic Genet.* 2023 Apr;44(2):139-146
2. Daiger S et al. 'Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa' *Cold Spring Harb. Perspect. Med.* 5 (2014)
3. Ellingford J et al. 'Molecular findings from 537 individuals with inherited retinal disease' *J Med Genet* 53, 761-776 (2016)

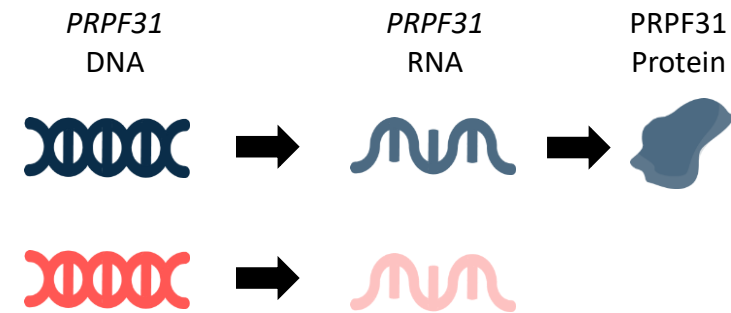
2) RP11 is caused by a haploinsufficiency of one gene (*PRPF31*) in the retina

Unaffected individual



Functional *PRPF31* expression = 100%

RP11 patient



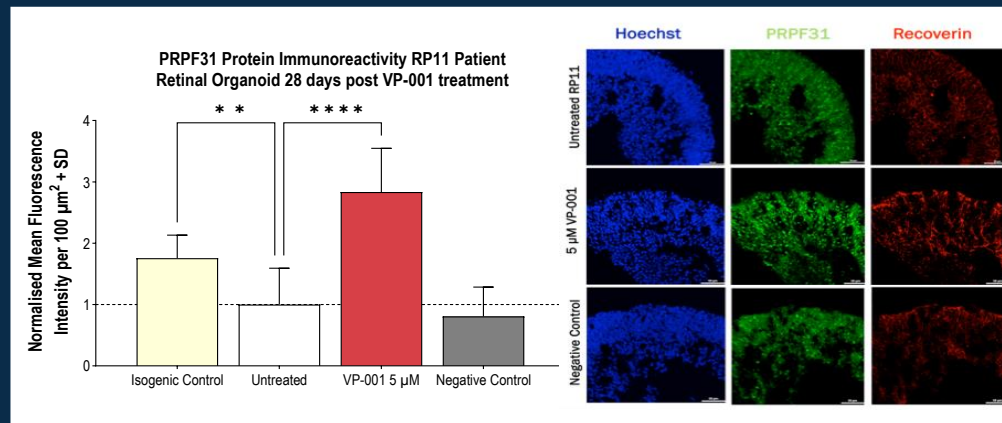
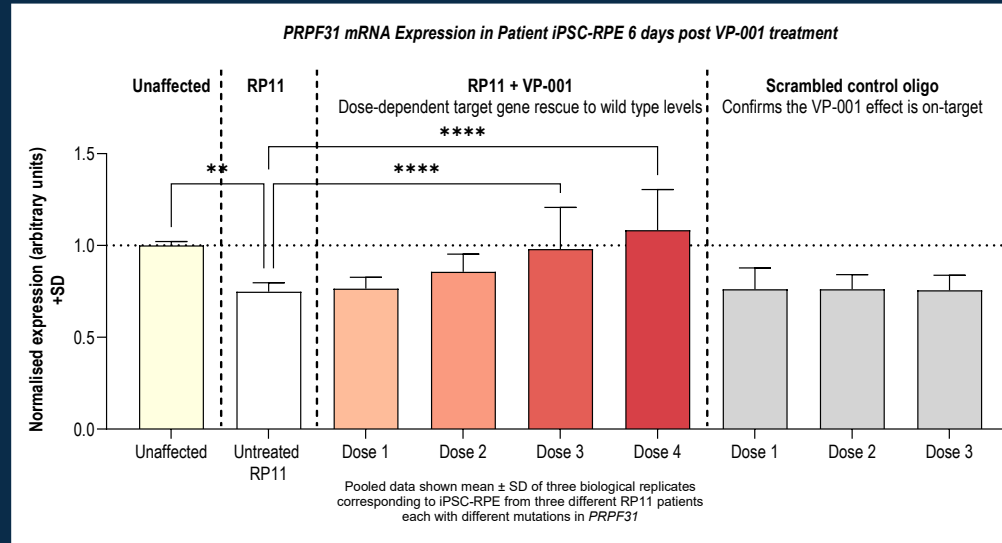
Functional *PRPF31* expression = ~50%

PRPF31 is a crucial splicing factor in the retina and regulates the synthesis of key proteins involved in vision, including Rhodopsin²

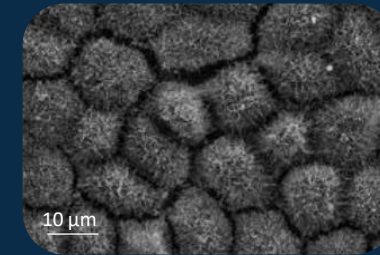
3) VP-001 shows the ability to rescue the haploinsufficiency causing RP11 in patient-derived models

1) Upregulates *PRPF31* mRNA in RP11 iPSC-RPE

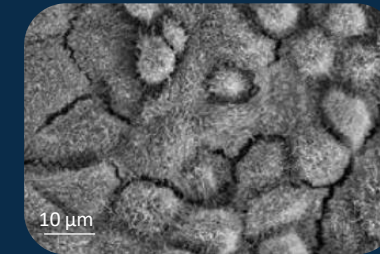
2) Upregulates PRPF31 protein in RP11 3D retinal organoid models



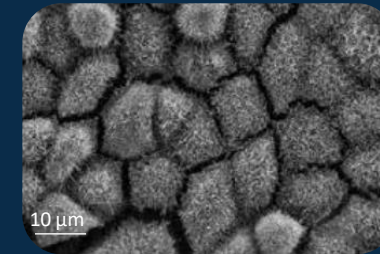
3) Rescues appearance and Structure of the affected cells (RPE)



Unaffected retina



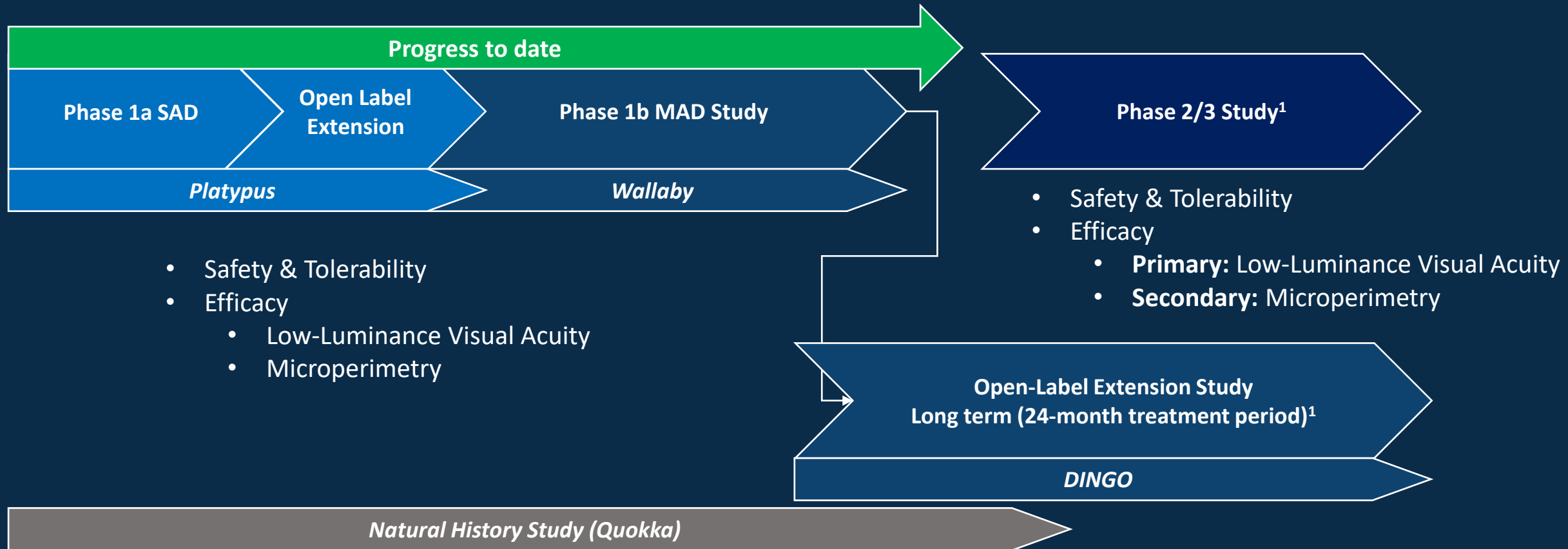
Retinitis Pigmentosa (RP)



RP + VP-001 treatment

4) VP-001 is the first clinical stage drug candidate for RP11 and has the potential to become the first approved treatment option^{1,2}

★ FDA Type D meeting Q1 2026³



1. Subject to the risks and uncertainties outlined in PYC Therapeutics' ASX disclosures of 2 February 2026

2. Based on an analysis of publicly-available information including clinicaltrials.gov

3. See PYC Therapeutics' ASX disclosures of 16 March 2026

5) VP-001 is safe and well-tolerated in RP11 patients

Safety outcomes¹

- No Treatment Related-Serious Adverse events observed in any subjects dosed with VP-001 to date
 - Including subjects who have received repeat doses of VP-001
- Treatment-Emergent Adverse Events were mostly mild, and procedure related

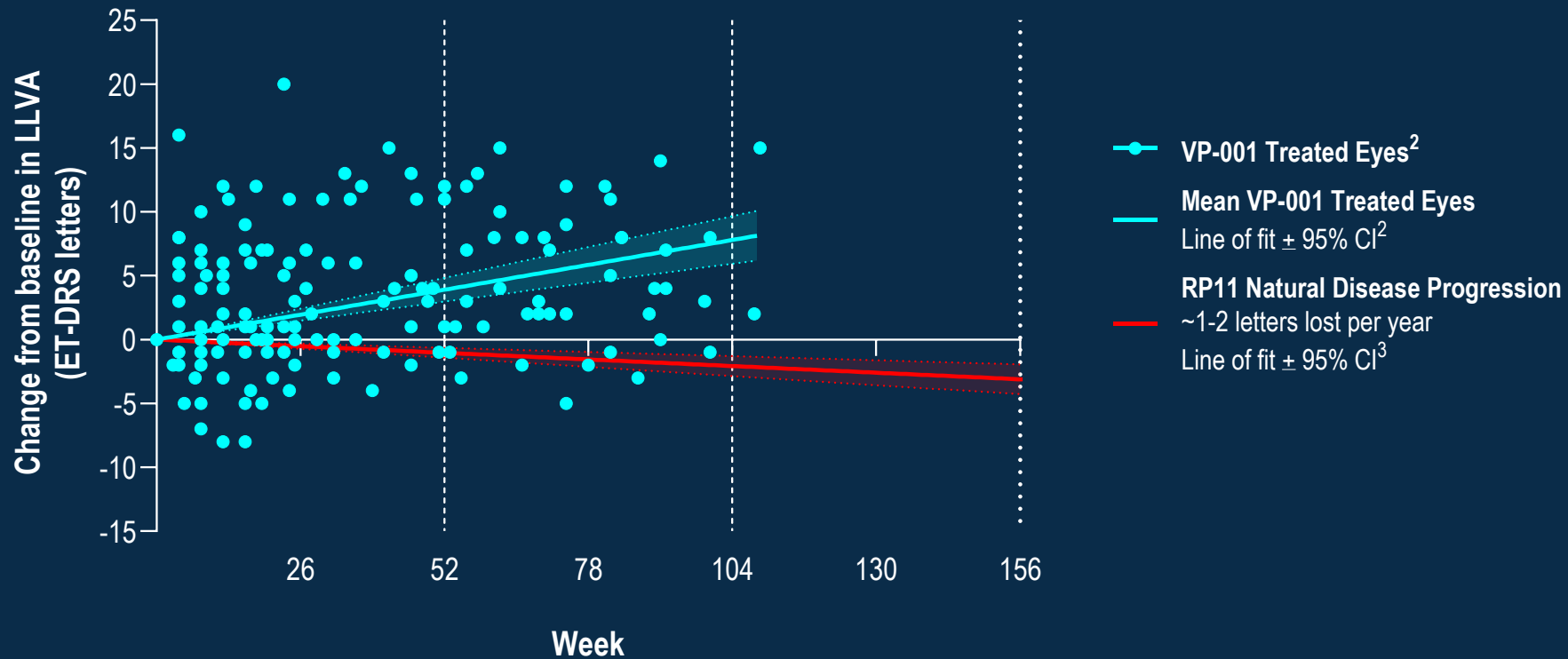
6) The efficacy of VP-001 is being evaluated using endpoints that matter most for patients with RP11

<p>1</p> <p>Low-Luminance Visual Acuity (LLVA)</p>	<p>Assessment of a patient's ability to see in low-light conditions - providing a direct assessment of rod function</p> <p>LLVA is a more sensitive marker of impaired central vision than BCVA and has been linked to higher experienced disability in Retinitis Pigmentosa¹⁻³</p>
<p>2</p> <p>Microperimetry (MP)</p>	<p>Used to characterise functional vision in a wide range of retinal conditions and enables disease progression tracking over short time periods</p> <p>Microperimetry correlates with LLVA and experienced disability in Retinitis Pigmentosa & can detect subtle defects in retinal sensitivity that precede changes in visual acuity³⁻⁵</p>

1. Low Luminance Visual Acuity and Low Luminance Deficit in Choroideremia and RPGR-Associated Retinitis Pigmentosa. (Wood et. al, 2021) doi:10.1167/tvst.10.2.28
2. Endpoints for clinical trials in ophthalmology (Schmetterer et. al, 2023) doi: 10.1016/j.preteyeres.2022.101160
3. Karuntu JS, Nguyen X-T-A, Boon CJF. Mesopic microperimetry is correlated with vision-related quality of life in patients with retinitis pigmentosa. Investigative Ophthalmology & Visual Science. 2023;64(8):4639-.
4. Clinical Perspectives and Trends: Microperimetry as a Trial Endpoint in Retinal Disease (Yang and Dunbar, 2021) doi: 10.1159/000515148
5. Clinical applications of microperimetry in RPGR-related retinitis pigmentosa: a review (Buckley et. al, 2021) doi: 10.1111/aos.14816

6(a)(i) RP11 patients treated with VP-001 have shown clinically meaningful improvements in visual acuity¹

Human efficacy: Change in Low-Luminance Visual Acuity (LLVA) in RP11 patients^{2,3}



1. A ≥ 10 letter change in visual acuity is considered clinically meaningful and ≥ 15 letter change has become a standard outcome measure in clinical trials – See Roy W. Beck MD et al. (2007) Visual acuity as an outcome measure in clinical trials of retinal diseases, Ophthalmology. Doi: 10.1016/j.ophtha.2007.06.047

2. Analysis of all data (n=16) available for the treated eyes of patients who received 30 mcg or more of VP-001 in PYC’s Platypus, Wallaby and DINGO studies with LLVA >0 at baseline. Data as at 21 April 2026. One patient has not been included in analysis due to breach of trial protocol.

3. Line of fit data for NHS patients with LLVA > 0 at baseline in both eyes and for which the difference between baseline and follow-up visit 1 was less than 15 letters (n=96 eyes). Data as at 25 March 2026.

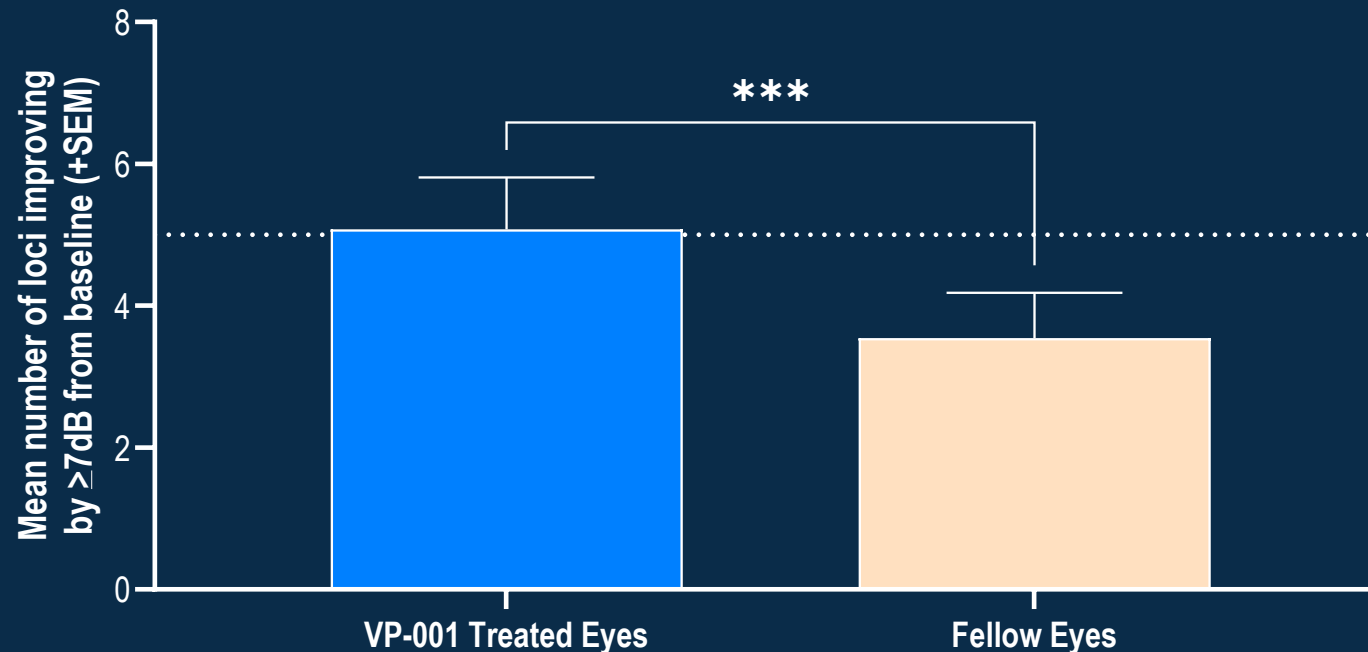
6(a)(ii) A greater proportion of RP11 eyes treated with VP-001 show clinically meaningful¹ improvements in LLVA

Trial(s)	Eye (analysis eligible 'n')	≥10 letter gain at multiple timepoints ³	% of eyes	≥10 letter loss at multiple timepoints ³	% of eyes	Stable (between +9 and -9 at all ⁵ timepoints) ³	% of eyes
VP-001 Interventional ²	VP-001 Treated Eyes (n=14) ³	3	21.4%	0	0%	11	78.6%
	Untreated Fellow Eyes (n=14) ³	1	7.1%	0	0%	13	92.9%
Natural History Study	Eligible Eyes (96) ⁴	3	3.1%	11	11.5%	82	85.4%

1. A ≥10 letter change in visual acuity is considered clinically meaningful and ≥15 letter change has become a standard outcome measure in clinical trials – See Roy W. Beck MD et al. (2007) Visual acuity as an outcome measure in clinical trials of retinal diseases, Ophthalmology. Doi: 10.1016/j.ophtha.2007.06.047
2. Change from baseline/screening
3. Analysis of all data available for patients who have received 30 mcg or more VP-001 in Platypus, Wallaby and Dingo with data for at least 2 follow up timepoints. Both eyes for patient with *USH2A* mutation and patient with treated eye LLVA = 0 at baseline have been excluded from analysis. Data as at 21 April 2026. One patient has not been included in analysis due to breach of trial protocol.
4. Data for NHS patients with LLVA > 0 at baseline in both eyes and for which the difference between baseline and follow-up visit 1 was less than 15 letters (n=96 eyes). Data as at 25 March 2026.
5. Includes eyes where a 10-letter change recorded at only one timepoint

6(b) RP11 patients treated with VP-001 have shown clinically meaningful¹ improvements in retinal sensitivity (as assessed by microperimetry)

Bar graphs showing mean number of loci improved by ≥ 7 dB from baseline for patients enrolled in DINGO^{2,3}



5 loci improving by ≥ 7 dB is considered clinically meaningful¹

1. Yaghy A, et al. Addressing Multiplicity in Retinal Sensitivity Analysis: An Alternative Approach to Assessing Gene Therapy Efficacy in Inherited Retinal Diseases. *Transl Vis Sci Technol.* 2025 Mar 3;14(3):25. doi: 10.1167/tvst.14.3.25.
2. Analysis of data available for patients who have received at least four doses of 30 mcg or more of VP-001 in PYC's PLATYPUS, WALLABY and DINGO studies. P-value calculated using paired t-test comparing change from baseline in VP-001 treated eyes to the fellow contralateral control eye ~8 weeks (or nearest relevant timepoint) post each dose of VP-001 ≥ 30 mcg (***) $p < 0.001$. Both eyes for patient with *USH2A* mutation and patient with treated eye LLVA = 0 at baseline have been excluded from analysis. One patient has not been included in analysis due to breach of trial protocol. Data as at 21 April 2026.
3. Microperimetry data not included if measurement 'unstable' or 'unreliable' as per - Josan AS, et al. Microperimetry Reliability Assessed From Fixation Performance. *Transl Vis Sci Technol.* 2023 May 1;12(5):21. doi: 10.1167/tvst.12.5.21.

6(c) Multiple RP11 patients have reported improved vision and quality of life after treatment with VP-001

Reported feedback from patients in PYC's RP type 11 Phase 1/2 clinical trial¹

"I see airplanes in the sky (never have before), stars at night, animals/creatures along the road..."

- *"My central vision was clearer... there was less haze. I was amazed!"*
- *"It was actually so clear that my existing eyeglass prescription was too strong for my treated eye thus making things a little distorted. I had an eye exam and got a new lens"*
- *"I honestly think the treatment helps quicker than the decline occurs"*

- *"I had become accustomed to finding my Starbuck's cup by feel... when I only had my left eye open (my non-treated eye), the cup disappeared. When I had only my right eye open (my treated eye), the cup appeared. It is a moment I'll always remember. It is the first moment since being diagnosed, that I felt like it was possible I may be able to see even as I get older... even as my kids grow up."*
- *"The other change is harder to describe. But, when walking down the hallways at work, there is simply more clarity in a wider range of my right eye. On my right side, I have more "breathing room." I can see more."*

7) Long-term data from the ongoing Phase 2 study will be used to finalise the design of a potential registrational trial in RP11¹



- It is expected that the final registrational trial will involve²:
 - **Primary endpoint** – mean change in Low Luminance Visual Acuity (LLVA)
 - Supported by key secondary endpoint of proportion of subjects demonstrating clinically meaningful change (15 letters) in LLVA
 - **Duration** – 48 months in total: 12-month enrolment + 36 months of treatment
 - **Size** – 90 patients in total (30 patients per cohort randomised to one of two active arms (30 and 75 mcg doses) or a sham control)

1. Subject to risks and uncertainties outlined in PYC Therapeutics' ASX announcement of 2 February 2026

2. Final timing and trial design subject to alignment with the FDA