6 May 2024

PRESENTATION OF RP11 CLINICAL TRIAL DATA AT ARVO CONFERENCE

- **PYC is conducting clinical trials of the first investigational drug candidate with disease-modifying potential in a blinding eye disease of childhood called Retinitis Pigmentosa type 11 (RP11)**
- **PYC is currently evaluating the safety and efficacy profile of this drug candidate in these ongoing clinical trials prior to commencing a planned registrational trial in 2025[1] to support a potential New Drug Application anticipated in 2027[2]**
- **Data from PYC's ongoing clinical trials in RP11 will be presented by Associate Professor Fred Chen of the Lions Eye Institute in a podium presentation on Sunday 5 May 2024 at the Association for Research in Vision and Ophthalmology (ARVO) conference in Seattle, Washington**
- **The presentation includes:**
    - **safety data from PYC's ongoing dose escalation study demonstrating no treatment emergent serious adverse events across all three patient cohorts dosed to date; and**
    - **initial encouraging microperimetry data showing improvement in retinal sensitivity for one patient in cohort 3 (30 micrograms of the investigational drug candidate)**

PERTH, Australia and SAN FRANCISCO, California – 6 May 2024

PYC Therapeutics Limited (ASX:PYC) (**PYC** or the **Company**) today announces that Associate Professor Fred Chen of the Lions Eye Institute will make a podium presentation at the Association for Research in Vision and Ophthalmology (ARVO) in Seattle on Sunday 5 May 2024. The subject of A/Prof Chen's presentation will be 'A Phase 1 First In Human Study of VP-001 – A peptide conjugated oligonucleotide for the treatment of Retinitis Pigmentosa Type 11'. A copy of the presentation is attached to this announcement.

The presentation includes comprehensive safety and tolerability data for the investigational drug candidate known as VP-001 demonstrating that there have been no treatment emergent serious adverse events in any of the three patient cohorts dosed with VP-001 to date.

[1] Subject to ongoing successful results across safety/tolerability, efficacy and regulatory dimensions of the clinical trials process

[2] Subject to the risks set out in the Company's ASX filing of 14 March 2024

A/Prof. Chen will also present data from one patient within cohort 3 (30 micrograms of VP-001) of the Single Ascending Dose (SAD) study. This patient is notable for the fact that they are at an earlier stage of disease progression than the other patients enrolled in the SAD study. Assessment of the patient's visual function at both 4 and 8 week follow up visits demonstrates potential signs of early improvement in the patient's retinal sensitivity as assessed by microperimetry.

PYC has refined the inclusion criteria for the fourth cohort of patients scheduled to receive VP-001 at a 75 microgram dose within the SAD over the next 4 weeks to focus on patients with an earlier stage of disease progression. PYC will measure visual function and functional vision in these patients using multiple ocular measurements, in addition to microperimetry.

PYC is hosting an investor presentation on Thursday 9 May 2024 at 9am AWST (See ASX announcement of 1 May 2024). Investors can register for the event at the following link:

https://us02web.zoom.us/webinar/register/WN_Wn1FQCK_SWOS123Buf-EdQ

This announcement was approved for release by the Board of PYC Therapeutics Limited.

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 development**[3].

The Company was the first to progress a drug candidate for a blinding eye disease of childhood (Retinitis Pigmentosa type 11) into human trials. The Company is progressing a second drug program targeting a blinding eye disease (Autosomal Dominant Optic Atrophy) and a third program targeting Polycystic Kidney Disease which are anticipated to commence human trials in mid-2024 and early 2025 respectively.

For more information, visit pyctx.com, or follow us on LinkedIn and Twitter.

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.

[3] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

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.

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Phase 1 First-in-Human Study of VP-001

A Peptide Conjugated Oligonucleotide for the Treatment of Retinitis Pigmentosa Type 11

Dr Fred Chen

Lions Eye Institute, Perth, Australia

ARVO 2024

Executive Summary – Update on VP-001 for RP11

Introduction to VP-001 for RP11

1. RP11 is a progressive and blinding eye disease for which there are no treatments available for patients

2. RP11 is caused by insufficient expression of one gene *(PRPF31)* in the retina

3. VP-001 addresses the underlying genetic cause of RP11 and leads to functional benefits in patient-derived cell and organoid models

VP-001 is now generating data as the first drug candidate in clinical trials for RP11

4. VP-001 is safe in all dose cohorts tested to date in humans
   a. No serious adverse events observed; and
   b. No significant changes in any ocular measurements, indicating safety of the drug candidate

5. Encouraging signs of efficacy signal observed (microperimetry data) in patient who received 30 µg VP-001 – patient at earlier stage of disease progression than others in SAD

6. Protocol amendments filed with FDA to increase dosing of VP-001 in SAD and MAD

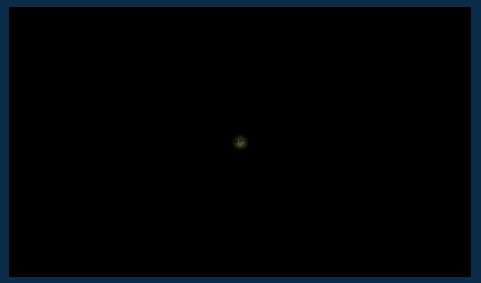
1. RP11 is a progressive and blinding eye disease for which there are no treatments available for patients

Degenerative sight of an RP11 patient

6 YEARS OLD

26 YEARS OLD

46 YEARS OLD



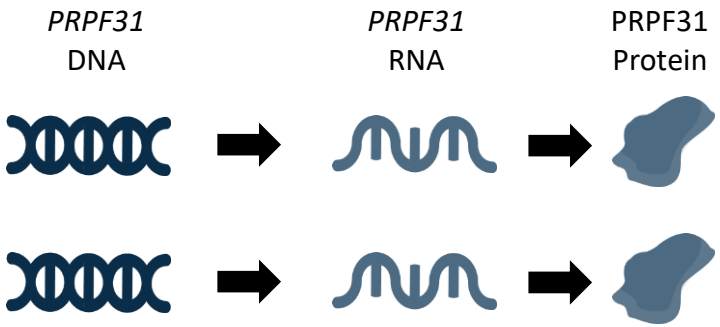
Retinitis Pigmentosa (RP)[1,2]

- A severe and progressive blinding eye disease that begins in childhood
- Affects 1 in every 3,500 people (RP11 accounts for ~3% of RP)
- Patients experience night blindness followed by tunnel vision and ultimately legal blindness
- There are no treatments available for patients with RP type 11 nor are there any in clinical development

1. Daiger S et al. 'Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa' Cold Spring Harb. Perspect. Med. 5 (2014)
2. Ellingford J et al. 'Molecular findings from 537 individuals with inherited retinal disease' J Med Genet 53, 761-776 (2016)

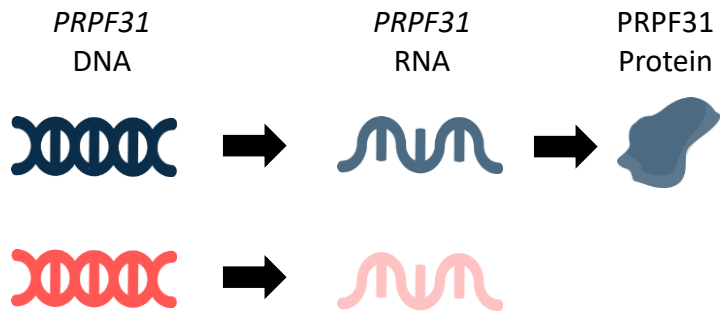
2. RP11 is caused by insufficient expression of one gene in the retina

Unaffected individual



Functional *PRPF31* expression = 100%

RP11 patient[1]



Functional *PRPF31* expression = ~50%

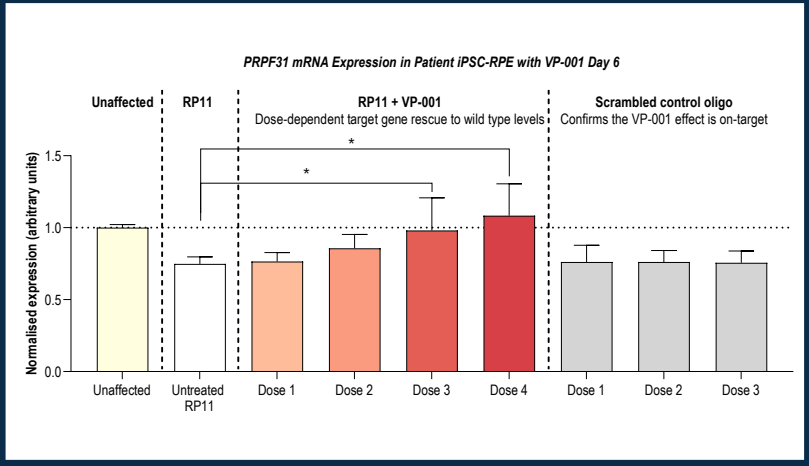
1. Hafler BP, et al. Course of Ocular Function in PRPF31 Retinitis Pigmentosa. Semin Ophthalmol. 2016;31:1-2

3. VP-001 addresses the underlying cause of RP11 and leads to functional benefit in patient-derived cell and organoid models

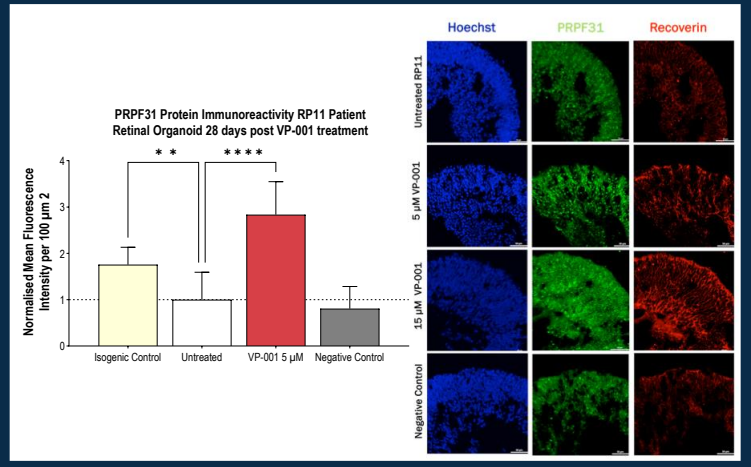
1. VP-001 is capable of completely rescuing the haploinsufficiency responsible for causing the disease in patient-derived models
    a) Upregulation of *PRPF31* mRNA in RP11 iPSC-RPE
    b) Upregulation of PRPF31 protein in RP11 3D organoid models

2. By correcting the *PRPF31* gene insufficiency, VP-001 rescues both the appearance and function of the affected cells in RP11 patient-derived models

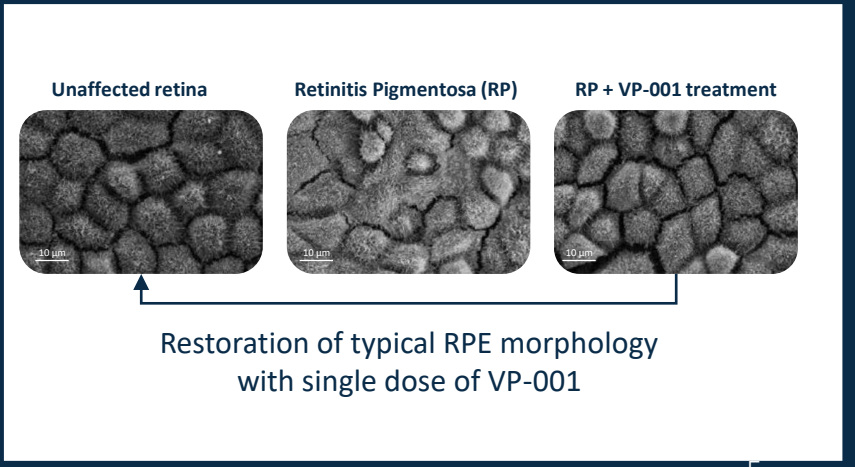
1a) *PRPF31* mRNA upregulation



1b) PRPF31 protein upregulation



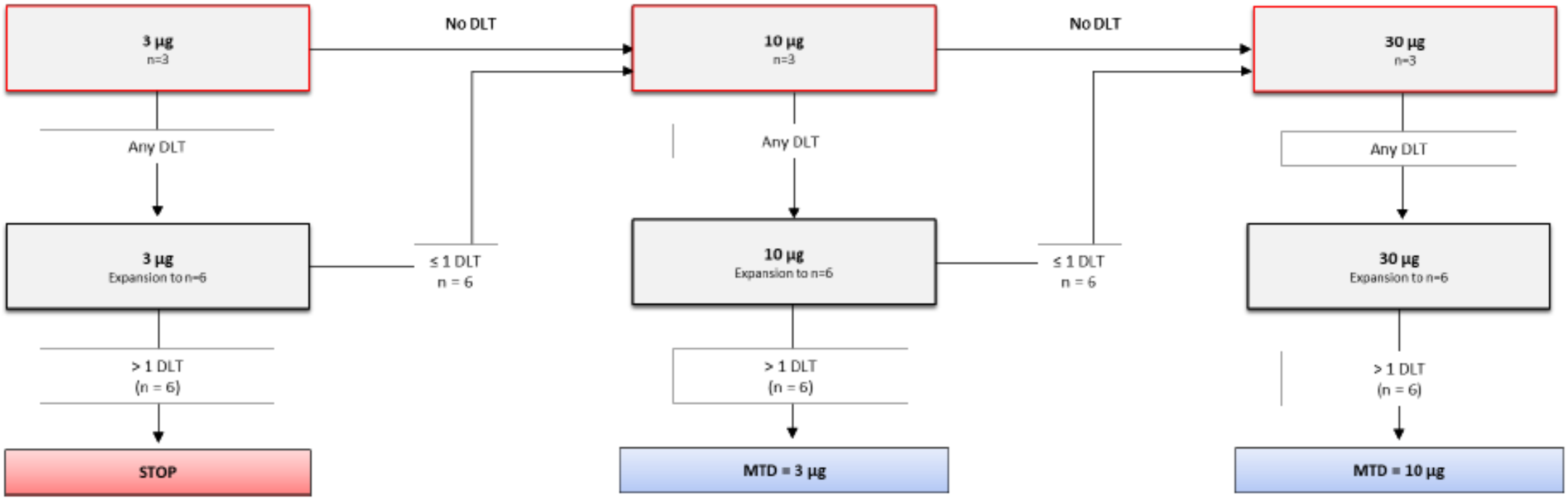
2) Functional rescue of RPE morphology



Phase 1 First-in-Human Study of VP-001

VP-001 is now generating data as the first drug candidate in clinical trials for RP11

PLATYPUS: Study Design



Abbreviations: DLT = dose limiting toxicity; MTD = maximum tolerated dose

PLATYPUS: Safety and Exploratory Efficacy Endpoints

Safety monitored by evaluation of:

- Ocular and non-ocular adverse events (AEs)
- Clinical chemistry parameters
- Best-corrected visual acuity (BCVA)
- Perimetry
- Microperimetry
- Slit lamp and fundus examination
- Fundus autofluorescence (FAF) imaging
- Spectral domain optical coherence tomography (SD-OCT)

Exploratory efficacy evaluated using:

- Perimetry
- Microperimetry
- BCVA
- SD-OCT
- Wide-field fundus photography
- Full-field Stimulus Threshold (FST)
- Quality of life questionnaires

4a. VP-001 is safe in all dose cohorts in SAD (no serious adverse events)

No Serious Adverse Events (SAEs) were observed (across all dose cohorts)

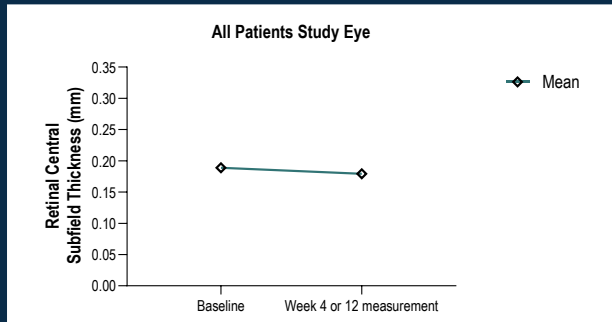
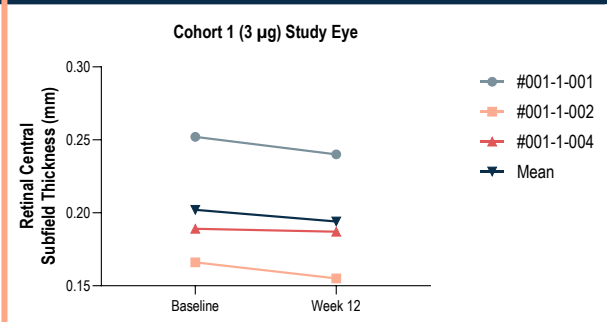
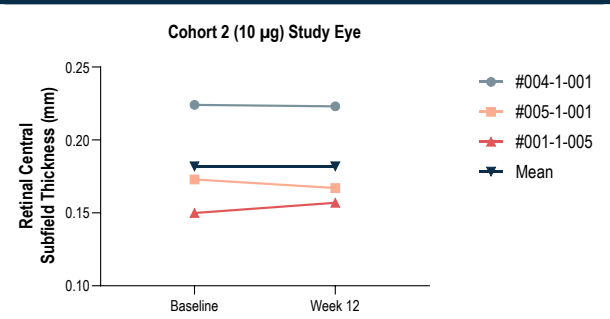
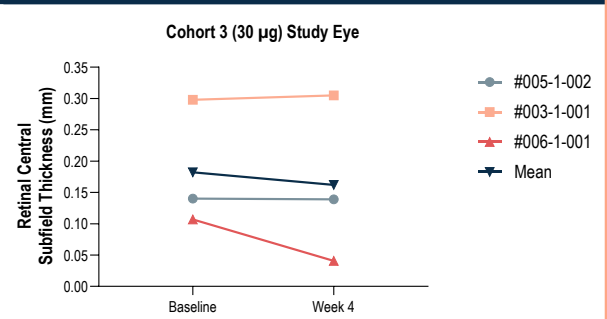
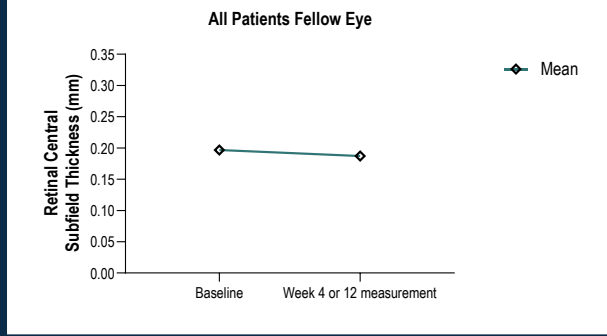
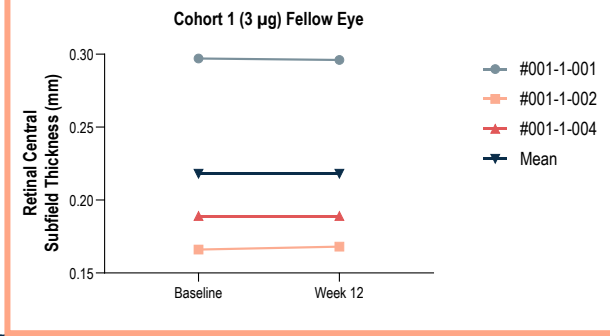
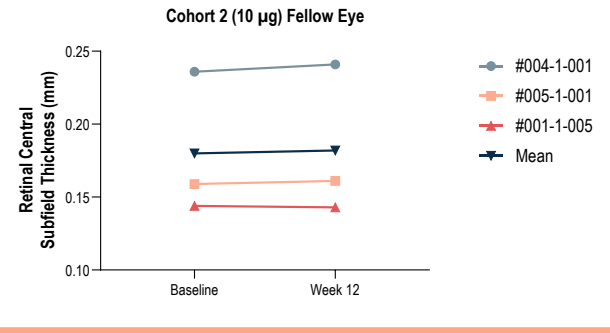
Dose (patient ID) and study eye	TEAE	Relationship to VP-001
3 mcg (001-1-001) OS	Vitreous floaters (OU) Vitreous opacities (OU) Vitreous consolidation (OS)	Not Related Not Related Not Related
3 mcg (001-1-002) OS	Pulled gluteus maximus left: Non-ocular Paronychia right thumb: Non-ocular Pulled hamstring muscle left: Non-ocular Shingles: Non-ocular Decreased foveal light reflex: OD Trace subconjunctival hemorrhage: OS Posterior vitreous detachment: OU Vitreous floaters: OU Photopsia: OS Photopsia:OD Vitreous Opacities:OU	Not Related Not Related Not Related Not Related Not Related Not Related Not Related Not Related Possible Not Related Not Related
3 mcg (001-1-004) OS	Eye soreness: OS Headache: Non-ocular Myokymia: OS	Not Related Possible Not suspected
10 mcg (001-1-005) OD	Covid-19: Non-ocular Subconjunctival hemorrhage: OD Dull ache near injection: OD Rare anterior chamber cells (0.5+): OD Intermittent and brief dull ache around eye: OD Attenuated retinal vessels: OS	Not Related Not Related Not Related Possible Not suspected Not Related
10 mcg (004-1-001) OS	Feeling of eye swelling: OS Frequent tearing: OS	Not Related Not Related
10 mcg (005-1-001) OS	Facial tendonitis: Non-ocular	Not Related
30 mcg (005-1-002) OD	Subconjunctival hemorrhage: OD Low glucose: Non-ocular	Not Related Not Related

Common AEs seen with the study eye are highlighted. No adverse events were seen in 2 of 3 patients who received 30 µg dose of VP-001 in SAD.

4b. VP-001 is safe in all dose cohorts in SAD (no significant change in any ocular measurements of safety)

No significant changes in any ocular measurements indicating safety (across all cohorts)

Retinal Central Subfield Thickness Measurements (used as representative data)

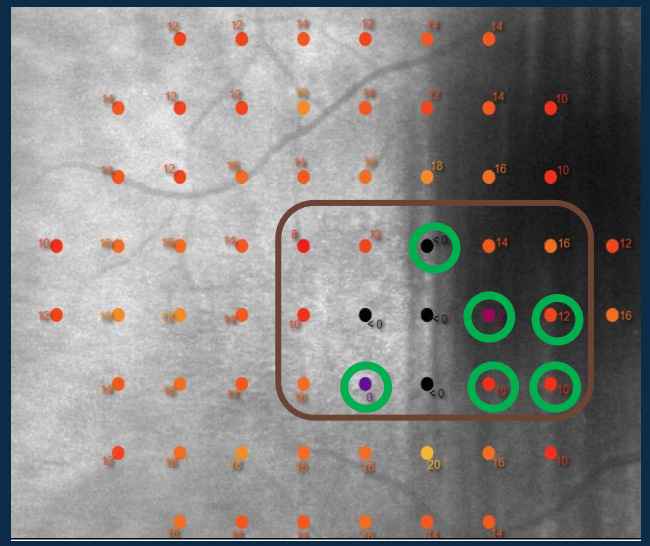
	All Cohorts Pooled	Cohort 1 (3 µg)	Cohort 2 (10 µg)	Cohort 3 (30 µg)
Study Eye				
Fellow Eye				

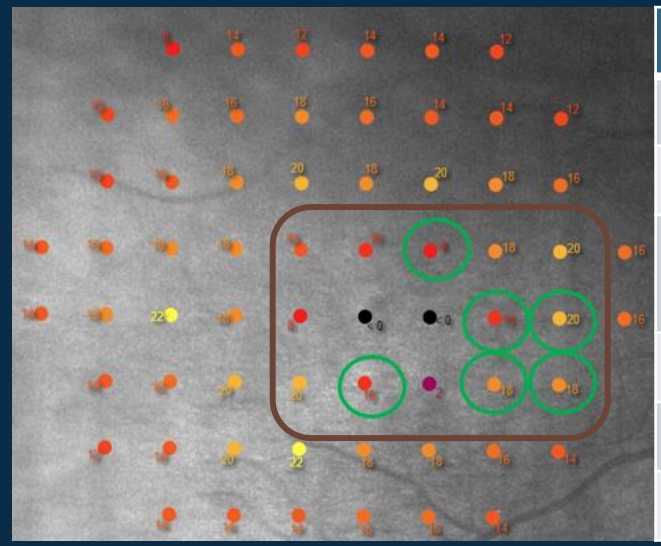
n=9

5. Encouraging signs of efficacy signal (microperimetry data) in patient treated with 30 µg VP-001 (8 week follow up comparison to fellow eye)

Baseline (December 2023) | Week 8 Post-Dosing | Findings

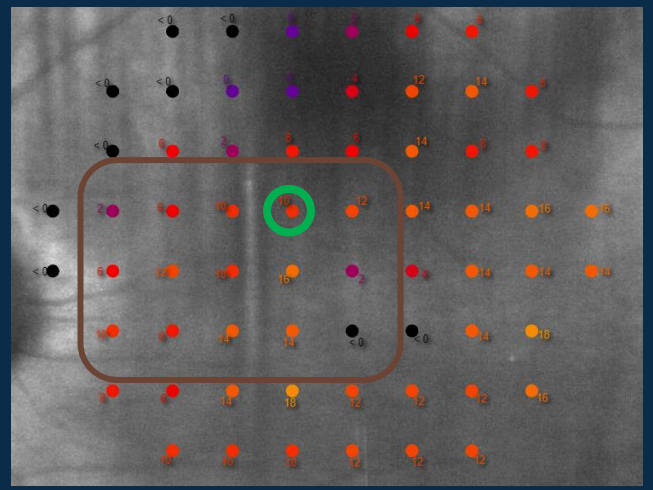
Study Eye (30 µg VP-001)

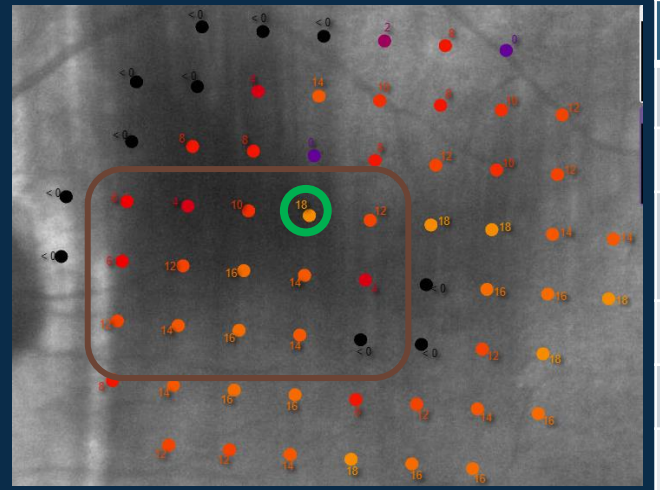




Microperimetry measurements (#005-1-002)	
Mean threshold (baseline)	12.5
Mean threshold (week 4)	13.1
Number of Loci with > 7 dB Improvement	**6**
CFB in number of Scotomatous points	**-2**
Mean threshold 15 loci ROI (baseline)	**7.3**
Mean threshold 15 loci ROI (week 8)	**11.8**

Fellow Eye

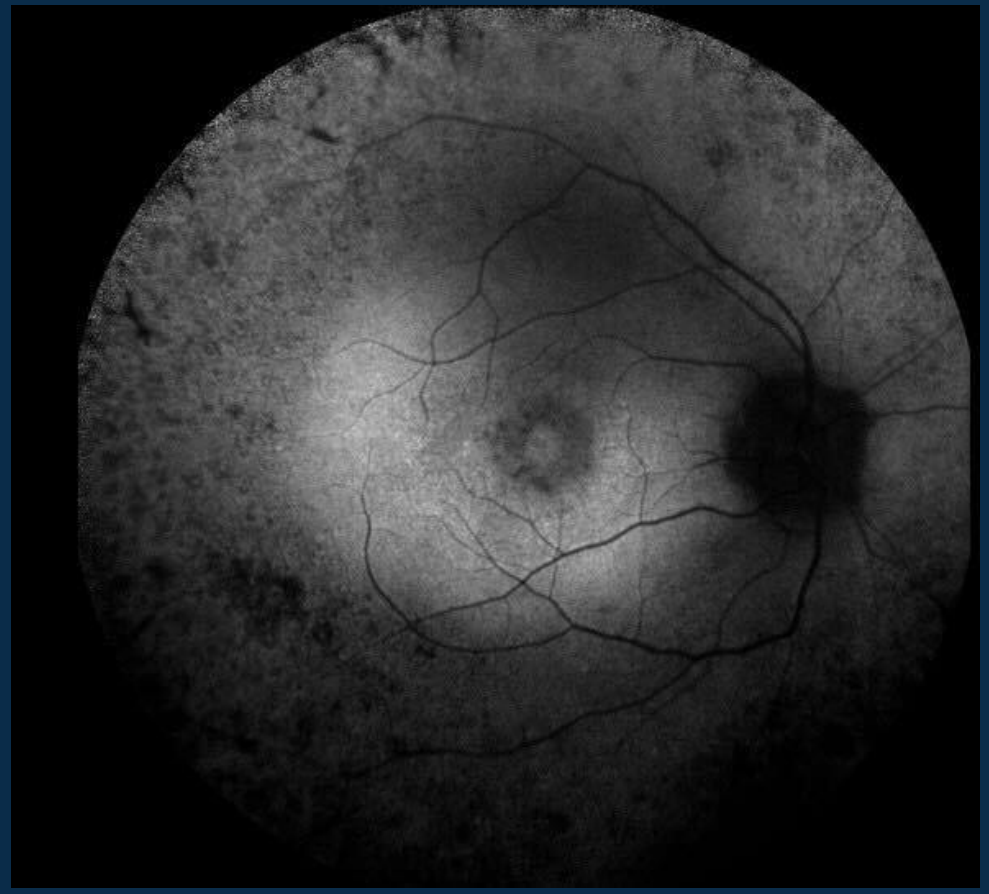


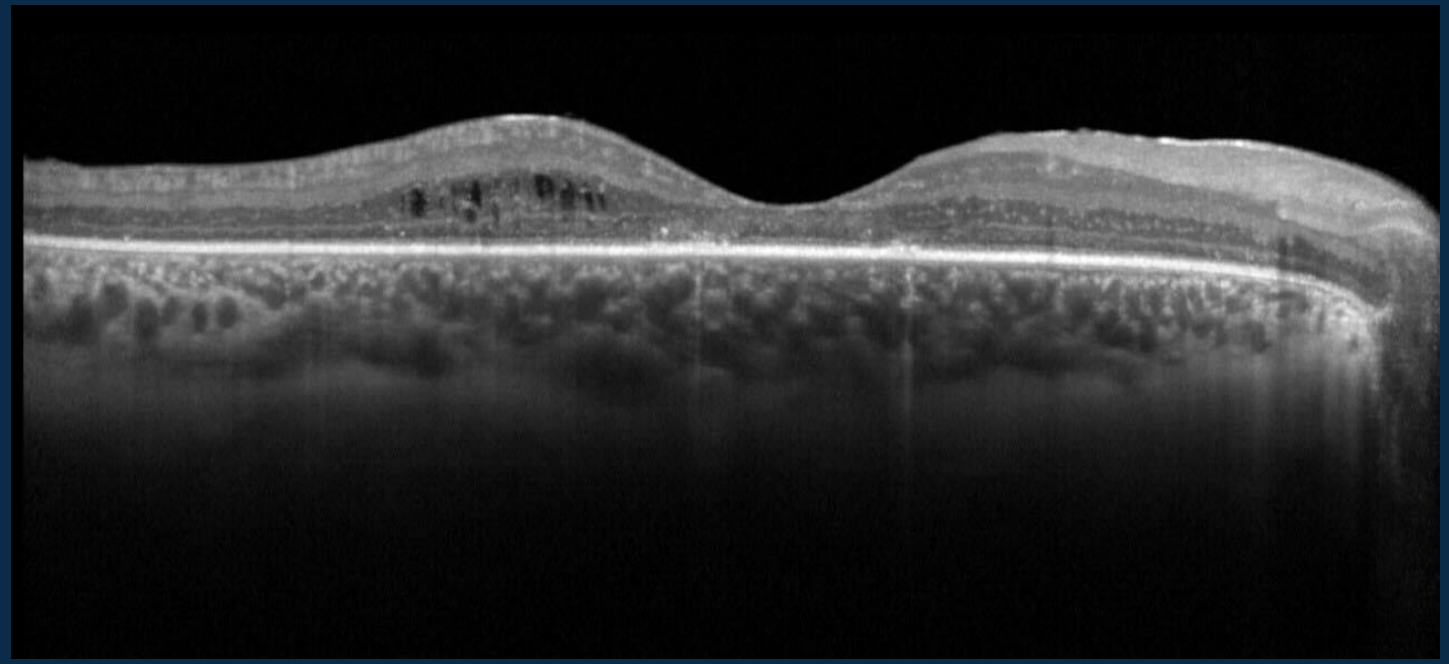


Microperimetry measurements (#005-1-002)	
Mean threshold (baseline)	8.1
Mean threshold (week 4)	8.9
Number of Loci with > 7 dB Improvement	**1**
CFB in number of Scotomatous points	**+2**
Mean threshold 15 loci ROI (baseline)	**8.8**
Mean threshold 15 loci ROI (week 8)	**10.5**

This patient is at earlier stage of disease progression than other patients in SAD

Microperimetry – Subject #005-1-002, Study Eye, PLATYPUS, Week 8 Post-Dosing – FAF & OCT



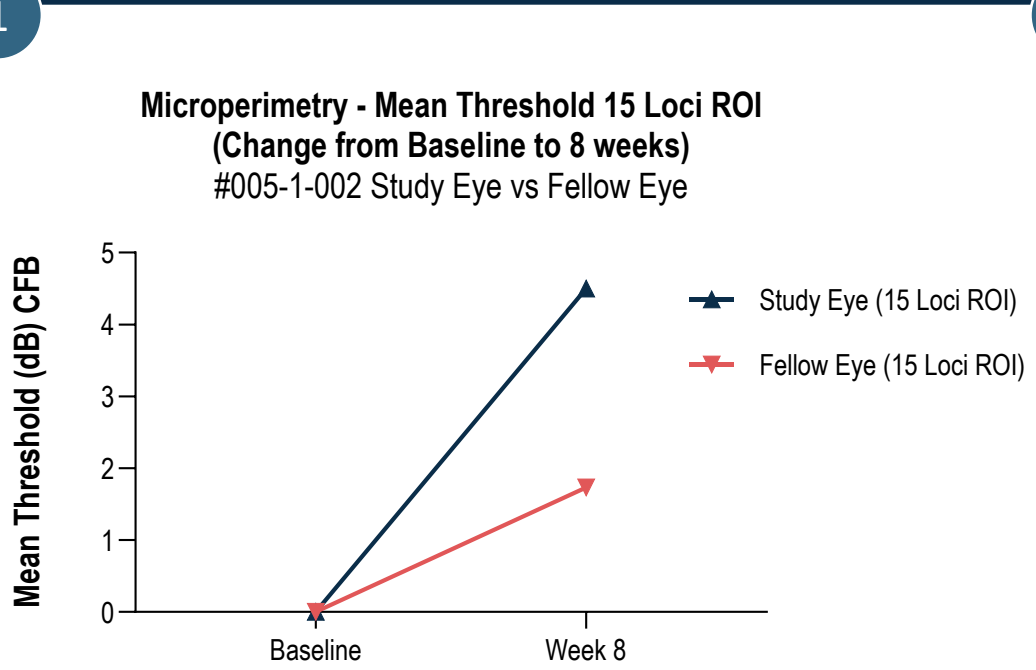


5. Encouraging signs of efficacy signal (microperimetry data) in patient treated with 30 µg VP-001 (8 week follow up comparison to fellow eye)

This patient is at earlier stage of disease progression than other patients in SAD

1. Greater microperimetry sensitivity improvements in treated eye (in 15 loci region of interest)
2. Reduction (improvement) in number of scotomatous points, compared to increase in fellow eye
3. Six loci improved >7dB in the VP-001 treated eye, compared to one in the fellow eye

1



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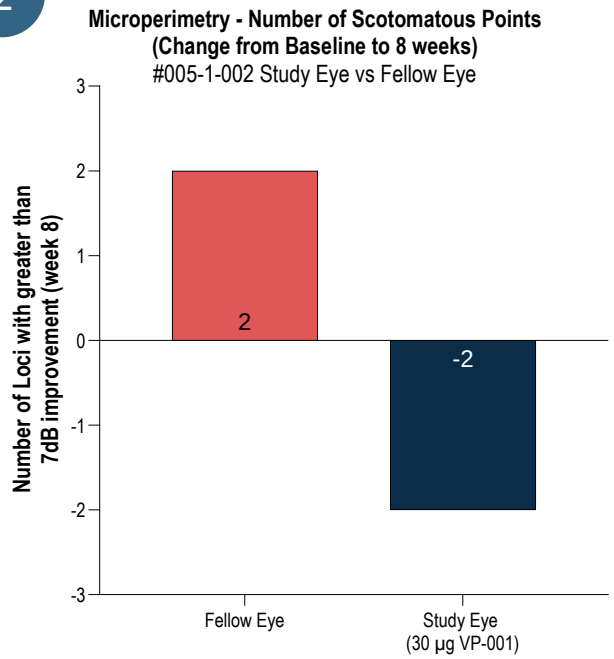

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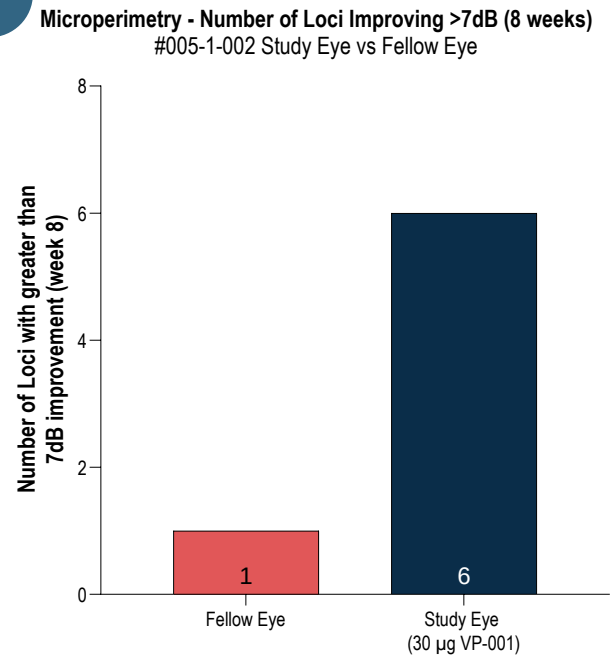

6. Protocol amendments filed with FDA to increase dosing of VP-001

- Protocol amendments to increase doses, filed with FDA for:
  - Addition of Cohort 4 (75 µg) to SAD study
  - Multiple-Ascending Dose (MAD) study to include repeat dosing of 30 µg and 75 µg

- Both protocol amendments have revised inclusion criteria:
  - Visual function in the eye to be treated as follows (a or b or c or d):
    a) V4e visual field >1000 degree2, per kinetic perimetry; or
    b) Mean microperimetry threshold: >5 decibel (dB) to <15dB; or
    c) Ellipsoid zone length >1000 microns, of which 500 microns is contiguous, by SD-OCT; or
    d) Full-field stimulus threshold; better than -20 dB for white, blue and red lights

Phase 1 First-in-Human Study of VP-001

Conclusion

Conclusion – VP-001 is safe and shows encouraging signs of efficacy

- VP-001 is safe in all dose cohorts tested to date
  - No serious adverse events observed, no significant changes in ocular measurements indicating safety

- Encouraging signs of efficacy signal observed (microperimetry data)
  - In a single patient who received 30 µg dose IVT of VP-001
  - Patient at earlier stage of disease progression than all other patients in SAD
  - Observation is consistent with faster rate of peripheral vision loss early in disease

- Protocol amendments to increase doses, filed and accepted by FDA for:
  - Addition of Cohort 4 (75 µg) to SAD study
  - Multiple-Ascending Dose (MAD) study to include repeat dosing of 30 µg and 75 µg
  - Both protocol amendments have revised inclusion criteria

Acknowledgements

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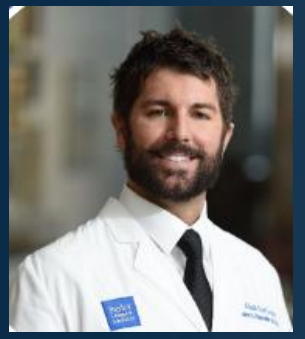

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