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

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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 RP11[1] – 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. As at 21 April 2026

1) Patients with RP11 experience progressive and irreversible vision loss beginning in childhood[1-3]

Illustration of the degeneration in sight experienced by an RP11 patient[1-3]

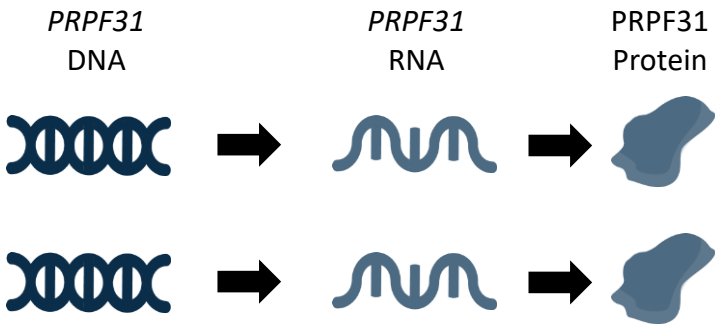
6 years old → **26 years old** → **46 years old**

Patients experience night blindness followed by loss of peripheral and then central vision - legal blindness occurs in the 4th or 5th decade of life[1-3]

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)

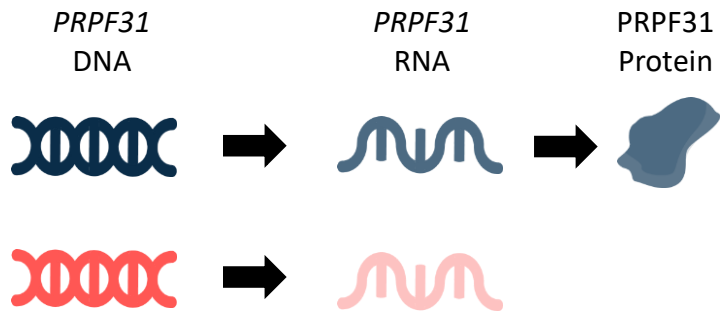
2) RP11 is caused by a haploinsufficiency of one gene (*PRPF31*) in the retina

Unaffected individual



Functional *PRPF31* expression = 100%

RP11 patient



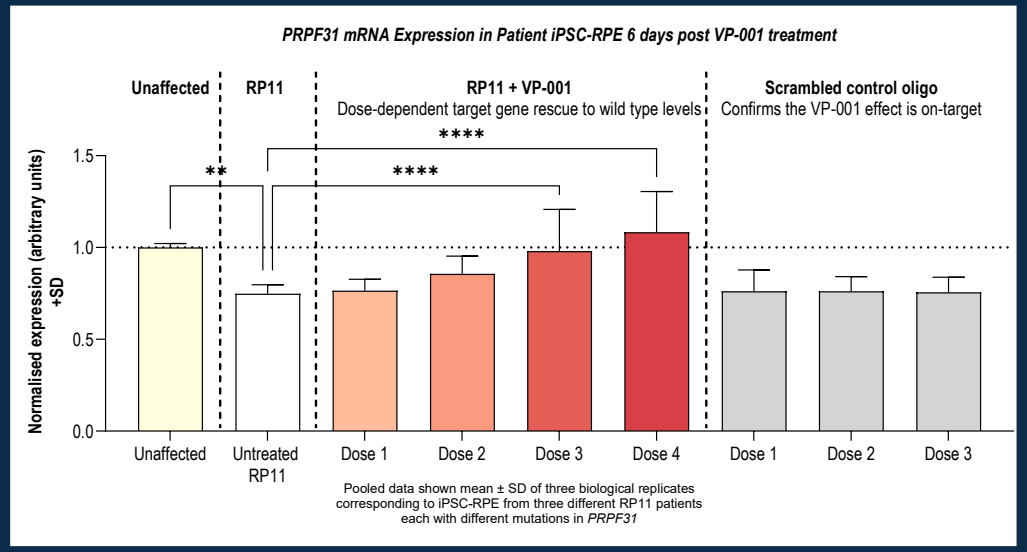
Functional *PRPF31* expression = ~50%

PRPF31 is a crucial splicing factor in the retina and regulates the synthesis of key proteins involved in vision, including Rhodopsin[2]

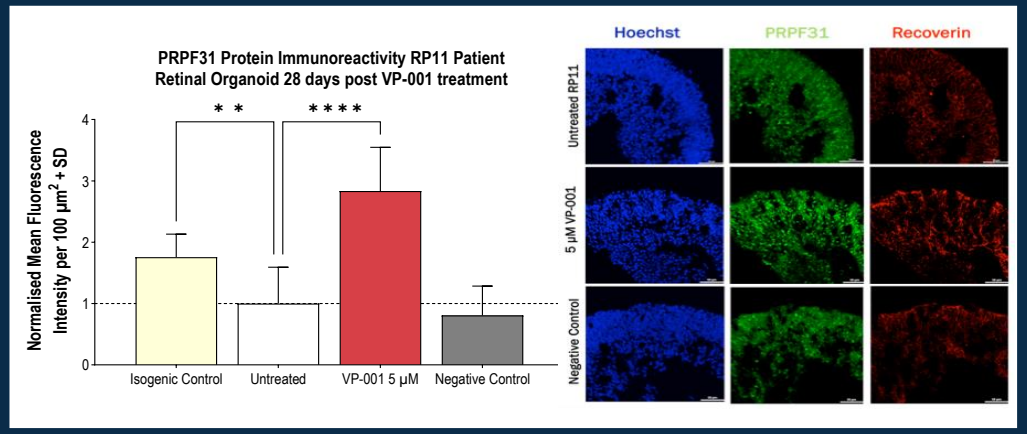
1. Hafler BP, et al. Course of Ocular Function in PRPF31 Retinitis Pigmentosa. Semin Ophthalmol. 2016;31:1-2
2. Yuan L, et al. Mutations in PRPF31 Inhibit Pre-mRNA Splicing of Rhodopsin Gene and Cause Apoptosis of Retinal Cells. Journal of Neuroscience. 2005 Jan 19;25(3):748–57.

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

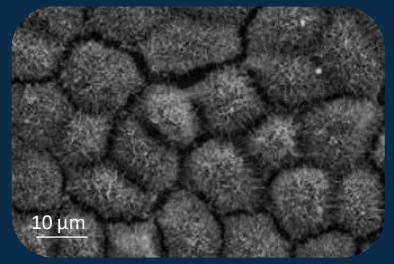
1) Upregulates *PRPF31* **mRNA** in RP11 iPSC-RPE



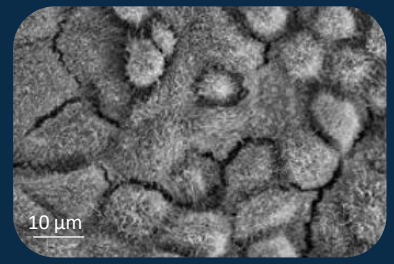
2) Upregulates PRPF31 **protein** in RP11 3D retinal organoid models



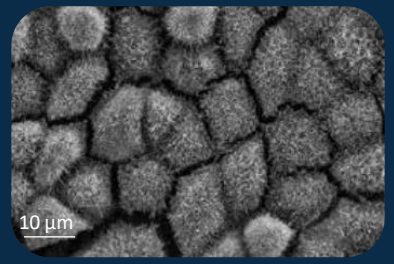
3) Rescues **appearance** and Structure of the affected cells (RPE)



Unaffected retina

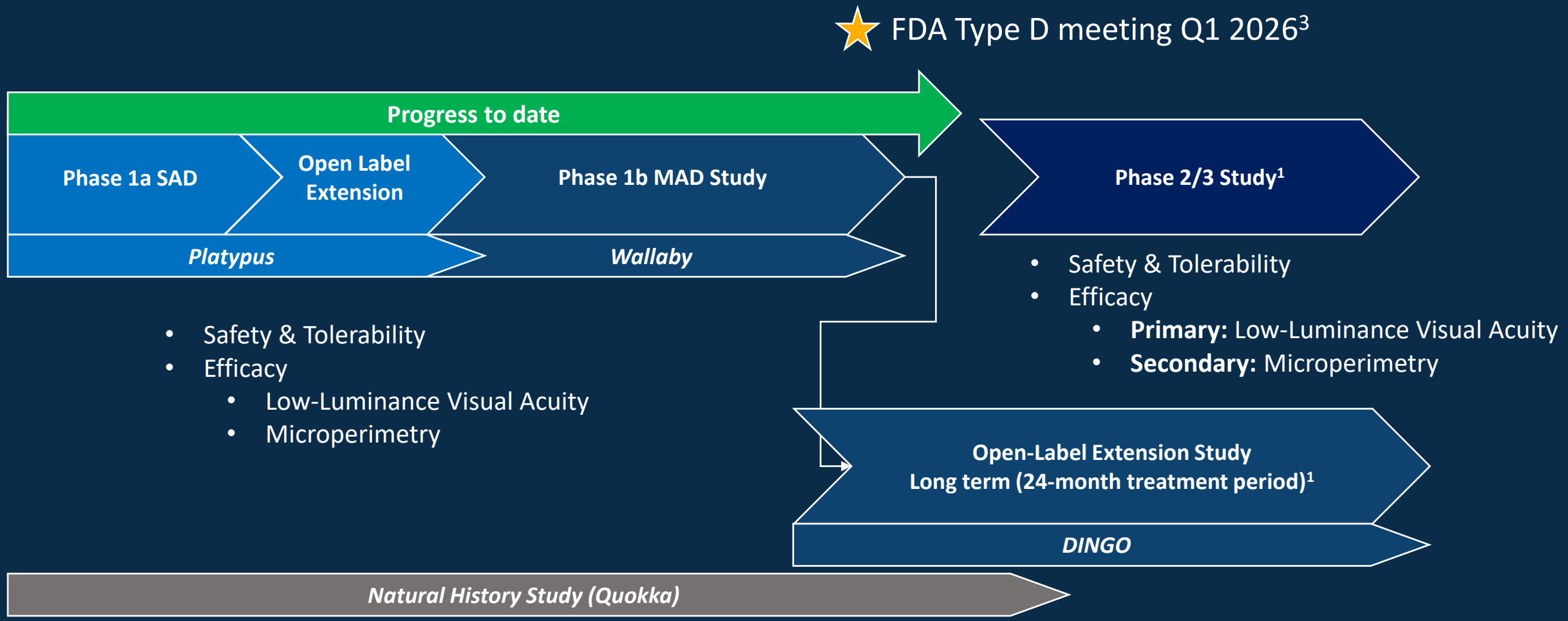


Retinitis Pigmentosa (RP)



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]



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 outcomes[1]	• 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

1. Accurate as at 21 April 2025

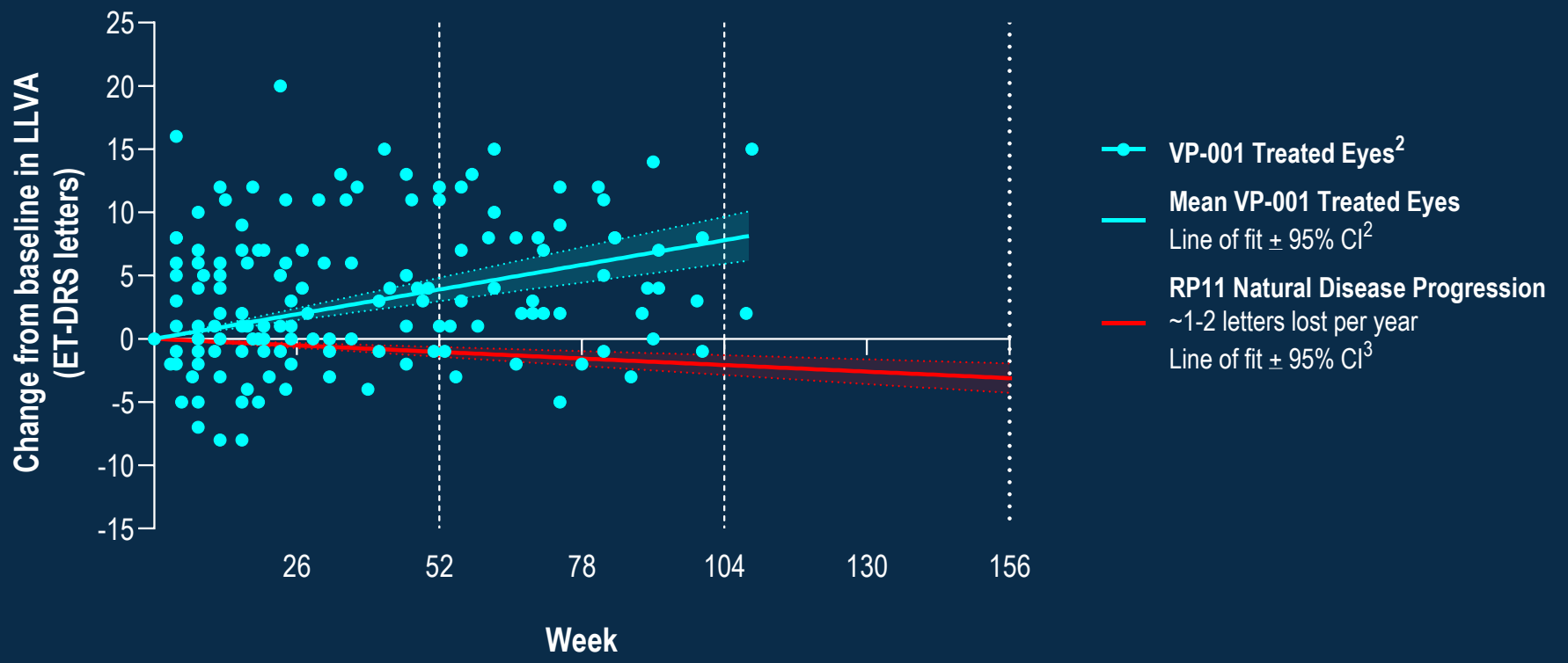
6) The efficacy of VP-001 is being evaluated using endpoints that matter most for patients with RP11

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

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 acuity[1]

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.

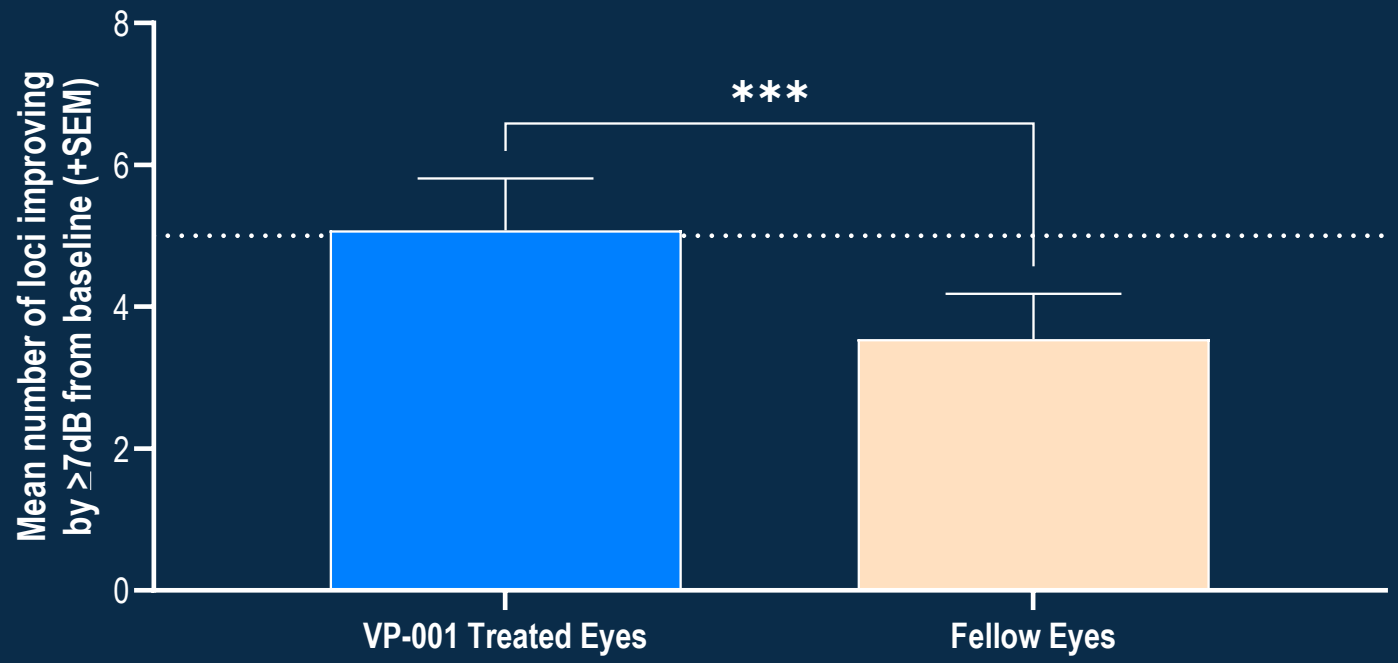
6(a)(ii) A greater proportion of RP11 eyes treated with VP-001 show clinically meaningful[1] improvements in LLVA

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 meaningful[1] improvements in retinal sensitivity (as assessed by microperimetry)

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



5 loci improving by ≥ 7dB is considered clinically meaningful[1]

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 trial[1]

"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."*

1. Comments reflect patient reported outcomes following treatment with VP-001 in an open-label study (meaning they may be subject to a 'placebo-effect' or bias) and communicated to the treating clinician (Principal Investigator) and relayed voluntarily to PYC

7) Long-term data from the ongoing Phase 2 study will be used to finalise the design of a potential registrational trial in RP11[1]

PYC Therapeutics

- It is expected that the final registrational trial will involve[2]:
  - **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