PYC Therapeutics

14 November 2025

SUSTAINED VISION IMPROVEMENTS IN RP11 PATIENTS

- **PYC is developing an investigational drug candidate (known as VP-001) with the potential to become the first approved treatment option for patients with the blinding eye disease Retinitis Pigmentosa type 11 (RP11)[1]**

- **Patients receiving VP-001 in the ongoing Phase 1/2 clinical trials demonstrate sustained improvement in vision in the treated eye up to 18 months after initiation of treatment[2]**

- **The VP-001 treated eye outperforms both the 'fellow' (untreated) eye in patients as well as the natural history control group across all registrational endpoints measured[3] - including:**
  - **Low Luminance Visual Acuity – mean change from baseline;**
  - **Low Luminance Visual Acuity – proportion of patients achieving 10+ letter gains;**
  - **Microperimetry – mean whole grid sensitivity; and**
  - **Microperimetry – number of loci gaining 7db or more.**

- **VP-001 continues to demonstrate a favourable safety/tolerability profile with no serious adverse events reported in any patient who has received the drug candidate to date[4]**

- **PYC is preparing to engage the US Food and Drug Administration (FDA) to align on a registrational trial design ahead of expected commencement of this study in 2026[5]**

PERTH, Australia and SAN FRANCISCO, California – 14 November 2025

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 a drug candidate (known as VP-001) that addresses the underlying cause of Retinitis Pigmentosa type 11 (RP11). RP11 is a blinding eye disease of childhood caused by a mutation in a single gene. VP-001 is designed to rescue the gene expression deficit caused by this genetic mutation.

[1] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025
[2] See Figure 1 below
[3] See Figures 1 and 2 for supporting details
[4] No Treatment-Related Serious Adverse events as of 14 November 2025
[5] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025

PYC today announces that patients receiving VP-001 as part of the ongoing Phase 1/2 clinical trials[6] have sustained improvements in both functional vision and retinal sensitivity through 18 months of follow up (See Figures 1 and 2).

Figure 1. Low Luminance Visual Acuity (change from baseline) readings for all patients dosed with VP-001 at or above 30 micrograms per eye in the Single Ascending Dose (SAD) study and Open Label Extension (OLE) or the Multiple Ascending Dose (MAD) study[7]. Treated eye outcomes (in light blue) compared to the outcomes from PYC's natural history study (line of fit depicted in red with 95% confidence interval shaded in light red)[8] over time following first dose of the drug candidate[9].

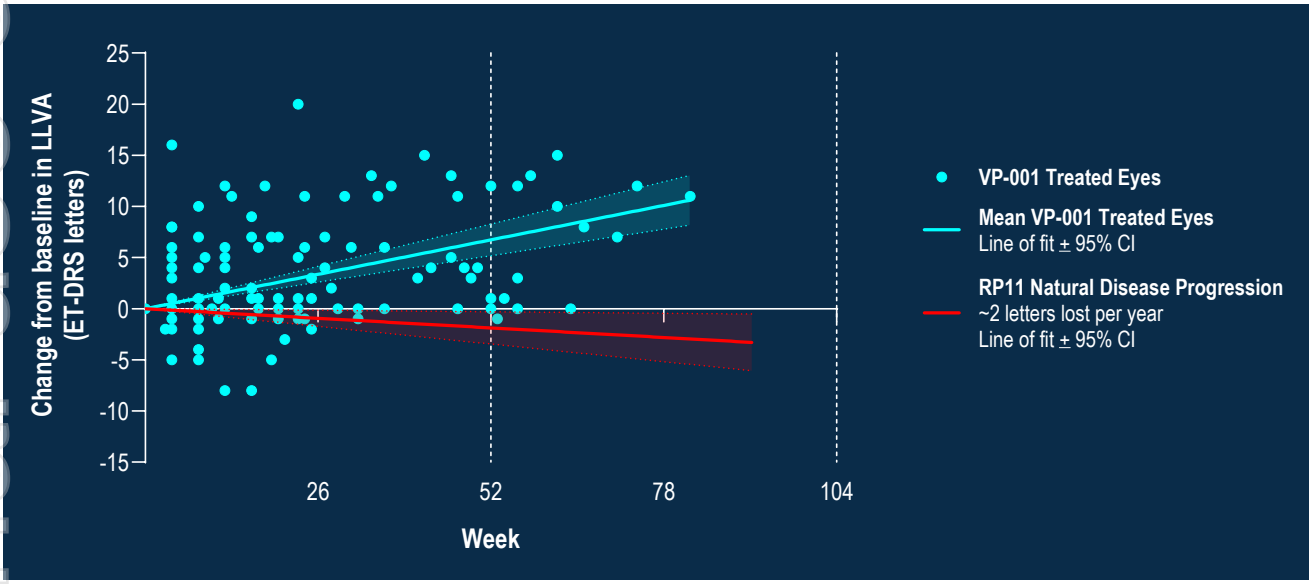

Figure 2. Performance of the VP-001 treated eye relative to the 'fellow' (untreated) eye in patients participating in the SAD study and OLE or MAD study at or above 30 microgram doses of the drug candidate[10]

[6] Including the Open Label Extension (OLE) of the single dose study, multiple dose study and OLE of the multiple dose study at doses of 30 micrograms and above

[7] Analysis of all data available for the treated eyes of all patients who received 30 mcg or more of VP-001 in PYC's Platypus and Wallaby studies (n=14). The line of fit accommodates data points from both the MAD and OLE studies and is used to illustrate the trajectory of visual function over time. Individual data points contributing to the line have been disclosed in PYC's ASX announcement on 28 April 2025. The line does not account for the time in which patients were not receiving the drug candidate (see Footnote 9).

[8] Line of fit of data collected from RP11 patients enrolled in PYC's Natural History Study followed for at least 52 weeks (n=16 eyes)

[9] Note that dosing has not been continuous throughout the evaluation period due to: i) some patients not being eligible for the OLE study; and ii) others having an extended temporal interval between SAD and OLE dosing.

[10] Analysis of patient data ~8 weeks post each dose of VP-001 (patients who received 30 mcg or more of VP-001). If 8-week post dose data was not available, data from nearest relevant timepoint was used in analysis. Patient with *USH2A* mutation has been excluded from analysis and patient with treated eye LLVA = 0 at baseline excluded from mean change analysis of both endpoints. N=12 patients followed for LLVA assessments. N=11 patients followed for microperimetry assessments (one patient did not have microperimetry data available at relevant timepoints), data not included if patient eye had unstable fixation. P-values calculated using paired t-test (two-tailed) comparing change from baseline treated eyes to fellow eyes.

	Mean change from baseline in treated eye	Mean change from baseline in fellow eye	P-value of difference (Paired t-test) or odds ratio
Low-Luminance Visual Acuity (mean)	3.63	1.8	*p = 0.0309
LLVA Proportion of eyes ≥10 letters (at multiple timepoints)	25%	8.3%	3.67
Microperimetry whole grid (mean)	0.87	0.56	p = 0.0994
Microperimetry (mean number of loci improved ≥7dB)	5.15	2.88	***p = 0.0003

In addition to the efficacy data set out above, VP-001 continues to demonstrate a favourable safety/tolerability profile with no treatment-related serious adverse events reported in any patient dosed with the drug candidate to date[11]. These results help inform PYC's final proposed design for the registrational trial of VP-001 in patients with RP11. The Company will meet with the US FDA in Q1 2026 to align on the data required to support a New Drug Application for VP-001 in RP11.

PYC will present an update on both its RP11 program and its Autosomal Dominant Optic Atrophy (ADOA) drug development program at the Royal Australian and New Zealand College of Ophthalmology (RANZCO) meeting in Melbourne, Australia between 14 and 17 November 2025.

Next Steps

PYC is in the final stages of preparing for a Type D meeting with the US FDA to align on a registrational trial pathway in RP11. The Company expects to initiate the registrational trial in 2026 following completion of the Type D meeting in Q1 2026[12].

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[13].

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

[11] Accurate as at 14 November 2025
[12] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025
[13] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

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.

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

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