PYC Therapeutics

21 July 2026

ADOA PROGRAM UPDATE

- **PYC is a precision medicine company dedicated to changing the lives of patients with genetic diseases who have no treatment options available**
- **The Company is progressing a drug candidate (known as PYC-001) that addresses the underlying cause of a blinding eye disease known as Autosomal Dominant Optic Atrophy (ADOA) through clinical trials[1]**
- **PYC today announces that:**
  - **Studies in Non-Human Primates (NHPs) demonstrate an increase in target gene expression in the retina 4 months after a single dose of PYC-001[2]; and**
  - **Patients who have received PYC-001 in the ongoing Phase 1/2 clinical trials demonstrate both sustained improvements in visual acuity and decreased retinal stress[3]**
- **The NHP data supports an extension of the dosing interval being evaluated in the ongoing clinical trials of PYC-001 beyond once every 4 months and PYC will now review and amend the clinical protocol accordingly[4]**
- **The latest data is also supportive of both the translational potential of PYC-001 in ADOA as well as other blinding eye diseases in which increased *OPA1* expression has potential to impact the disease course[5] - PYC is progressing the evaluation of this drug candidate in pre-clinical models of additional indications including glaucoma**

PERTH, Australia and SAN FRANCISCO, California – 21 July 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.

[1] Additional details on PYC's clinical studies of PYC-001 in ADOA available using the clinical trials identifiers: NCT06970106 and NCT06461286
[2] See Figure 1a below for a full description of the data
[3] As measured by Flavoprotein Fluorescence imaging (See Figure 3)
[4] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
[5] See, for example Stavropoulos, D.; Grewal, M.K.; Petriti, B.; Chau, K.-Y.; Hammond, C.J.; Garway-Heath, D.F.; Lascaratos, G. The Role of Mitophagy in Glaucomatous Neurodegeneration. Cells 2023, 12, 1969. https://doi.org/10.3390/cells12151969

The Company currently has three clinical-stage drug development programs including a drug candidate (known as PYC-001) that addresses the underlying cause of Autosomal Dominant Optic Atrophy (ADOA). PYC today announces that:

- Non-Human Primates treated with a single dose of PYC-001 at 15 micrograms (mcg / µg) per eye (Human Equivalent Dose of the 30 mcg dose currently being evaluated in the ongoing Phase 1a/1b human trials[6]) demonstrate a sustained increase in OPA1 protein expression in the retina 4 months after a single administration of the drug candidate (see Figure 1a); and
- ADOA patients in the ongoing clinical trials of PYC-001 demonstrate sustained improvement in both visual acuity and retinal stress following repeat doses of the drug candidate (see Figures 2 and 3).

Non-Clinical Data

Figure 1a. Time course evaluation of NHP retinal ganglion cell expression of OPA1 protein as measured by immunofluorescence (see Figure 1b) following administration of a single 15 microgram dose of PYC-001[7]

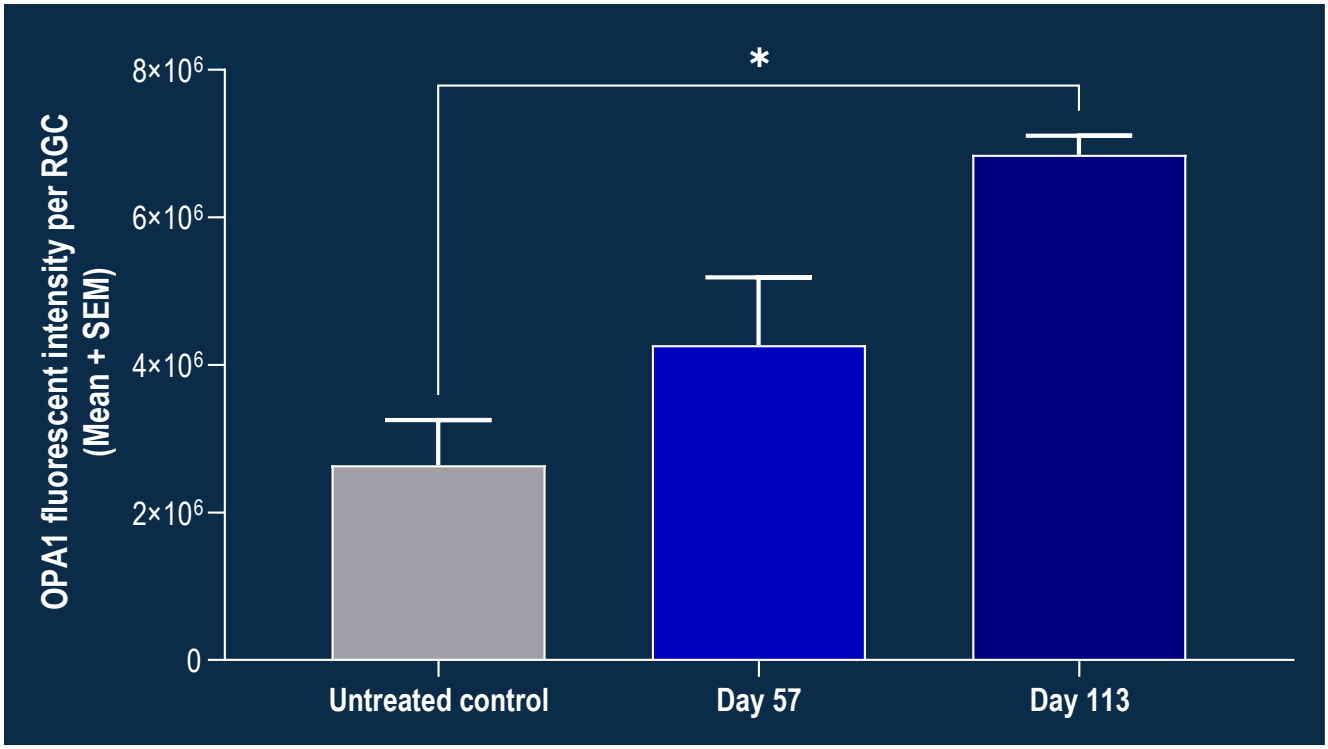
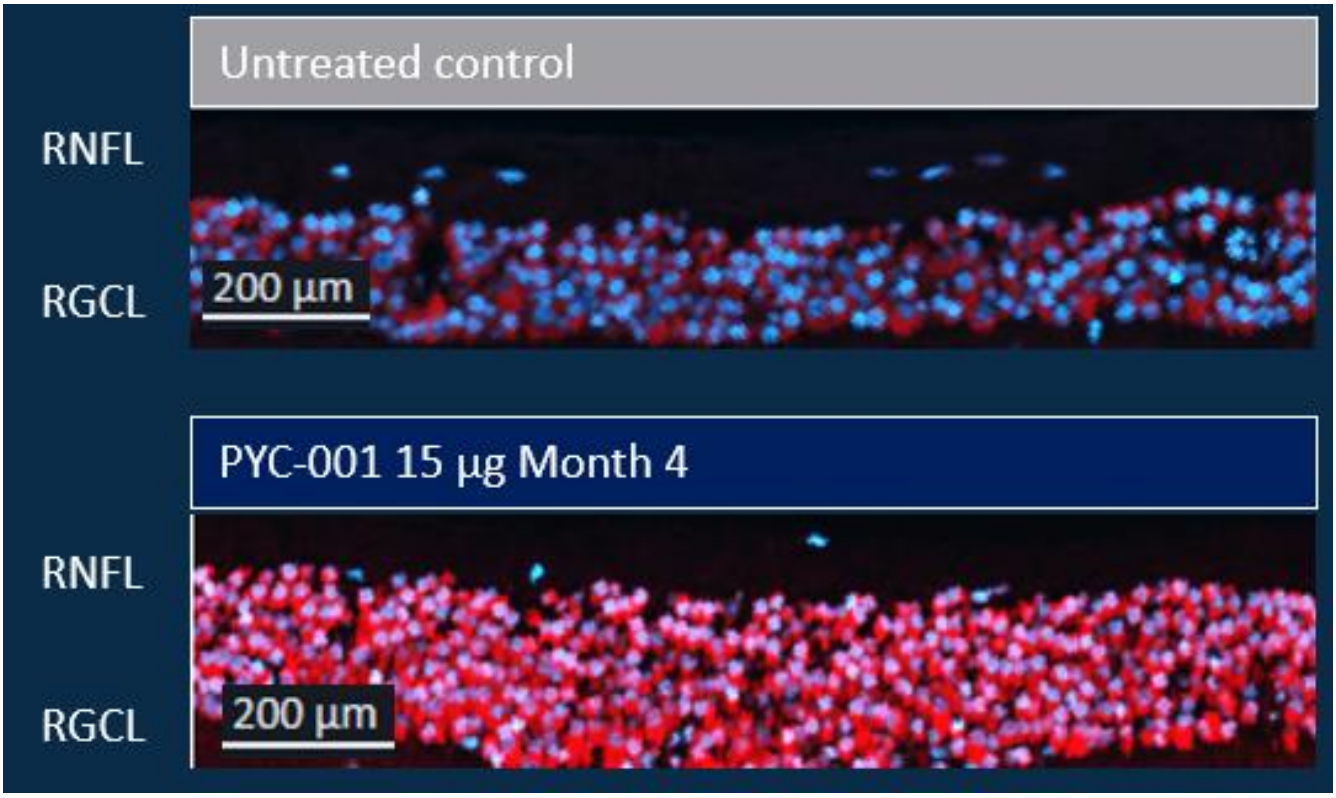


Figure 1b. Representative images of NHP retinal expression of OPA1 protein (stained in red with cell nuclei stained in blue) following administration of a single 15 microgram dose of PYC-001 at Month 4 as compared to untreated control NHP[8]

[6] Based on volumetric scaling from the NHP eye to human eyes with a scaling factor of ~2.2

[7] Quantification of OPA1 protein by immunofluorescence in Retinal Ganglion Cells (RGC) in NHPs with and without treatment with PYC-001. The results show a statistically significant (Welch's t-test, *p<0.05) increase in intensity of OPA1 signal in the PYC-001 group at Day 113 (Month 4) following a single safe and well-tolerated 15 mcg dose of PYC-001 (N=3 untreated control NHPs, N=4 NHPs in each PYC-001 treated group). Each data point is a biological replicate representing the average of multiple technical replicates serially sampled from different regions of the retina. Data presented includes untreated control animals necropsied on Day 3 and PYC-001 treated animals sampled at Day 57 (Month 2) and Day 113 (Month 4).

[8] Representative images of central retina. RGCL = Retinal Ganglion Cell Layer. RNFL = Retinal Nerve Fiber Layer.



The sustained increase in OPA1 protein expression is supportive of both the disease-modifying potential of PYC-001[9] (given that decreased *OPA1* expression is the root cause of ADOA) and an extended dosing interval in the ongoing clinical trials. Patients are currently receiving the drug candidate once every 2-3 months whereas this data supports an extension of the dosing interval to once every ≥4 months. PYC will now review the clinical protocol for the ongoing studies with a view to extending the dosing interval in these trials.

Clinical Data

Complementing this non-clinical data in support of PYC-001's translational potential is updated data from the ongoing phase 1/2 trials in ADOA patients demonstrating improved visual acuity (see Figure 2) and decreased retinal stress (see Figure 3) following repeat dose administration of the drug candidate.

These improvements in vision have been achieved in the context of a favourable safety/tolerability profile with continuation of the absence of any Treatment Related-Serious Adverse Events in any patient who has received PYC-001 to date, including those who have received multiple doses of the drug candidate[10].

[9] ADOA is caused by a ~50% reduction in *OPA1* expression in the retinal ganglion cells
[10] Accurate as at the date of this announcement

Figure 2. Improvements in Low Contrast Visual Acuity (LCVA) in ADOA patients enrolled in PYC's ongoing clinical trials following administration of PYC-001[11]

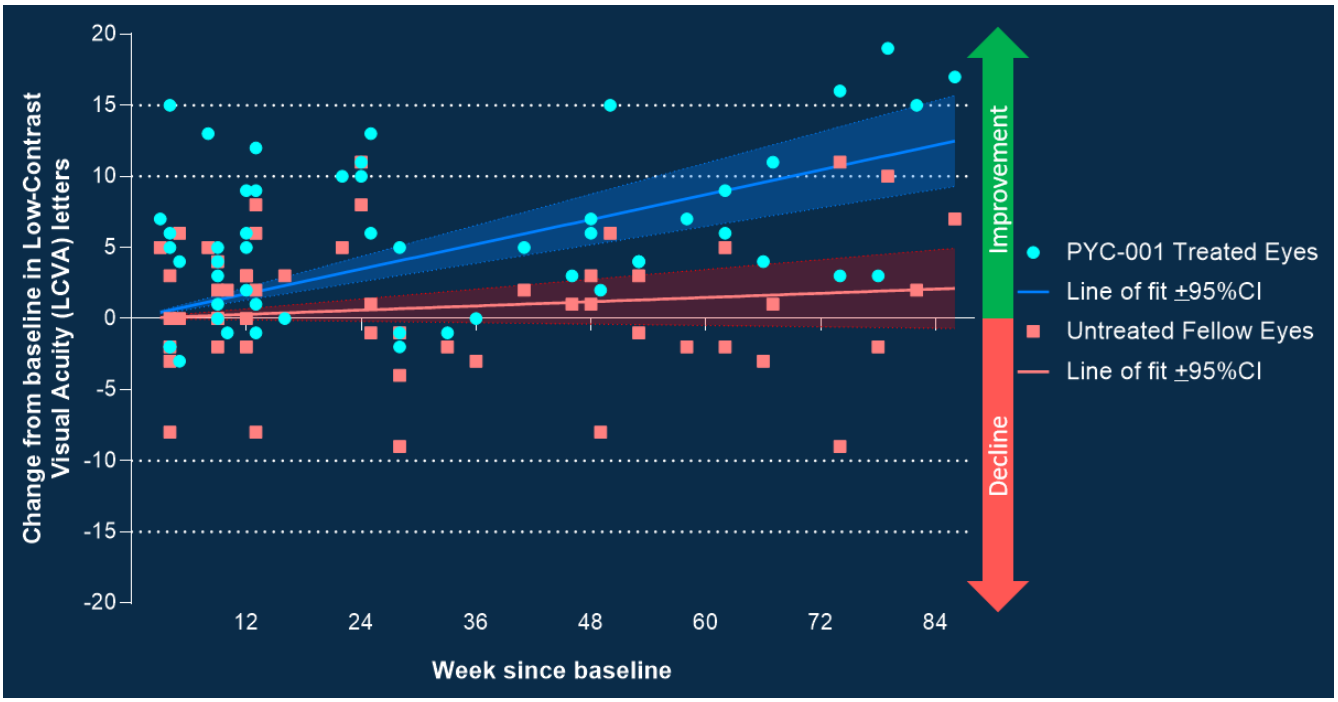
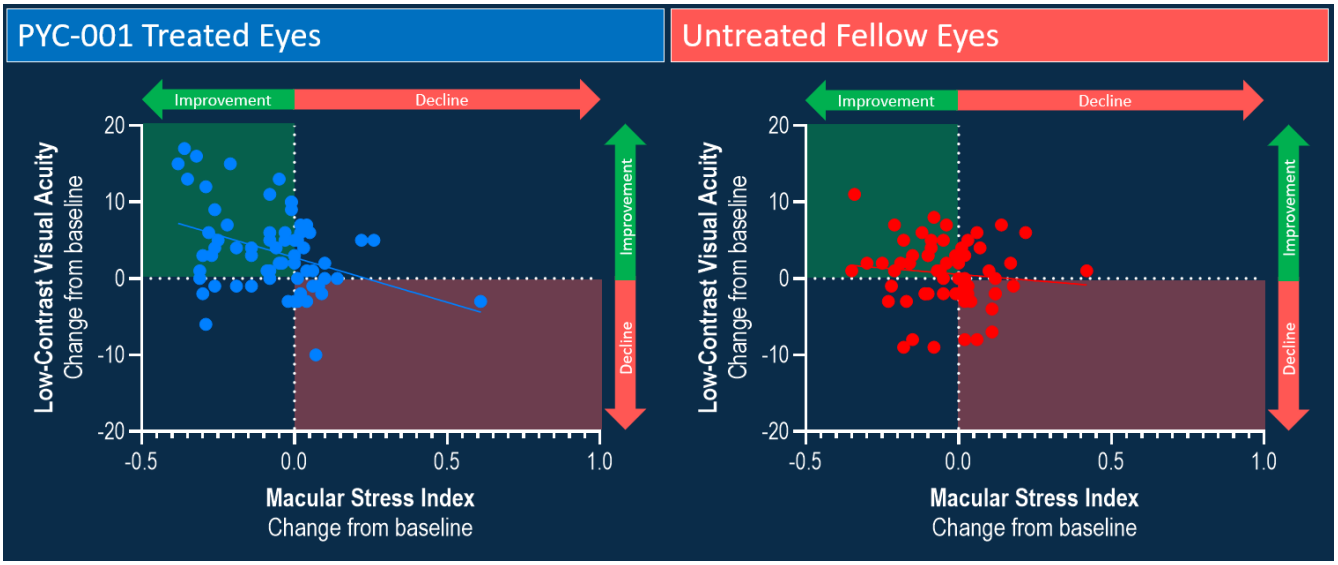


Figure 3. Decreased retinal stress as measured by Flavoprotein Fluorescence (FPF)[12] in ADOA patients enrolled in PYC's ongoing clinical trials following administration of PYC-001 is associated with the improvements in visual acuity described in Figure 2[13]



[11] All data from ADOA patients enrolled in the MYRTLE trial that have received 10 mcg or more of PYC-001 with LCVA ≤50 in treated eye at baseline with at least 1 follow up visit with LCVA recorded (11 out of the 15 patients enrolled in the study meet these criteria) - accurate as at 30 June 2026. CI = Confidence Interval. Not all patients have had the same number of follow-up visits.

[12] OcuMet Beacon quantifies mitochondrial Flavoprotein Fluorescence (FPF), a precursor of retinal cell death (See: Chen AX, et al. Functional imaging of mitochondria in retinal diseases using flavoprotein fluorescence. *Eye (Lond)*. 2021 Jan;35(1):74-92). Under oxidative stress, mitochondrial flavoproteins emit increased fluorescence when stimulated with blue light and OcuMet Beacon quantifies this fluorescence thereby acting as a promising biomarker of mitochondrial stress. FPF reveals higher mitochondrial dysfunction in patients with ADOA (See: FALCON ADOA Natural History Study Presentation – Raghu Mudumbai (NANOS, 2025)). The macula is a primary region of interest on FPF as it contains ~50% of all the Retinal Ganglion Cells (the affected cell type in ADOA) and accounts for just ~7% of total retina area (See: Curcio CA, Allen KA. Topography of ganglion cells in human retina. Journal of Comparative Neurology. 1990;300:5–25. doi: 10.1002/cne.903000103).

[13] All data from MYRTLE patients that have received 10 mcg or more of PYC-001 with at least one follow up visit with LCVA recorded accurate as at June 30 2026. Not all patients have had the same number of follow-up visits.

Next Steps

The combination of these updated data sets supports both an extension of the dosing interval in PYC's ongoing clinical trials in ADOA as well as exploration of the utility of the investigational drug candidate in other blinding eye diseases. PYC is currently evaluating the utility of PYC-001 in pre-clinical models of glaucoma with a view to initiating a Phase 2 study in glaucoma patients if these are successful[14].

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[15].

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

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.

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

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[14] Subject to alignment with regulatory authorities and final outcomes of the ongoing clinical trials in the ADOA patient population. Glaucoma patients are sensitive to the frequency of dosing of drug candidates hence the extended gene expression response in the NHP studies is particularly important in this setting. There is existing evidence in pre-clinical models of glaucoma that increased *OPA1* gene expression is protective of the retinal ganglion cells that cause the vision loss in this setting and PYC will now seek to complement this with data supportive of PYC-001 being able to achieve this outcome in pre-clinical models that closely recapitulate the human disease process.
[15] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232