PYC Therapeutics

3 September 2026

ADOA PROGRAM - DATA PRESENTATION AT NOSA 2026

- **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 safety and efficacy data[2] for this program will be presented by Dr. Clare Fraser at the Neuro-Ophthalmology Society of Australia (NOSA) conference in Melbourne, Australia between 3 and 5 September 2026 – a copy of Dr. Fraser's presentation is attached to this announcement**
- **PYC-001 is progressing through a global Phase 1/2 Multiple Ascending Dose (MAD) study with the objective of establishing clinical proof-of-concept prior to progression into a global registrational trial directed towards supporting a New Drug Application (NDA) in ADOA[3]**

PERTH, Australia and SAN FRANCISCO, California – 3 September 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 a drug candidate (known as PYC-001) that addresses the underlying cause of Autosomal Dominant Optic Atrophy (ADOA). ADOA affects 1 in every 35,000[4] people and there are currently no approved treatment options for patients.

PYC today announces that the latest data for this program will be presented by Dr. Clare Fraser between 3 and 5 September at the Neuro-Ophthalmology Society of Australia (NOSA) Annual Scientific Meeting.

A copy of the NOSA presentation material is attached to this announcement.

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[1] Additional details on PYC's clinical studies of PYC-001 in ADOA available using the clinical trials identifiers: NCT06970106 and NCT06461286
[2] Refer PYC ASX Announcement of 21 July 2026
[3] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
[4] Yu-Wai-Man, P. et al. The Prevalence and Natural History of Dominant Optic Atrophy Due to OPA1 Mutations Ophthalmology. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038

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[5].

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

CONTACT US

Investor relations and media contact
investor@pyctx.com

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

A Phase 1B Open-Label, Randomized, Single Dose and Repeat Dose Study to Evaluate the Single and Repeat Dose Safety and Tolerability of Intravitreally Administered PYC-001 in Participants with Confirmed OPA1 Mutation-Associated Autosomal Dominant Optic Atrophy

NOSA 2026

Clare Fraser

Disclosures: – assistance with travel costs to NANOS 2026

PYC-001 in Confirmed OPA1

Sundew (single dose)

Myrtle (multi dose)

NOSA 2026

Clare Fraser

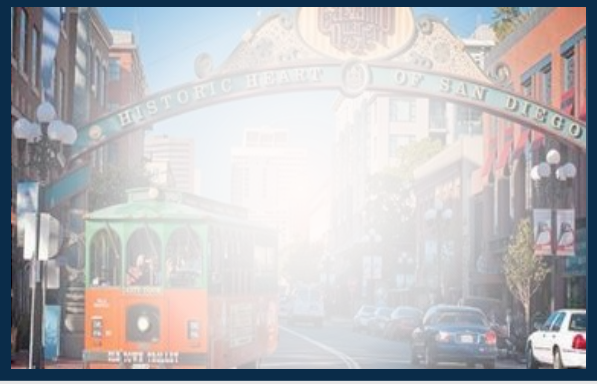
Disclosures: – assistance with travel costs to NANOS 2026 from PYC

Overview

- ADOA is a progressive and irreversible blinding eye disease with onset in childhood
- ADOA affects 1 in every 35,000 people[1-2]

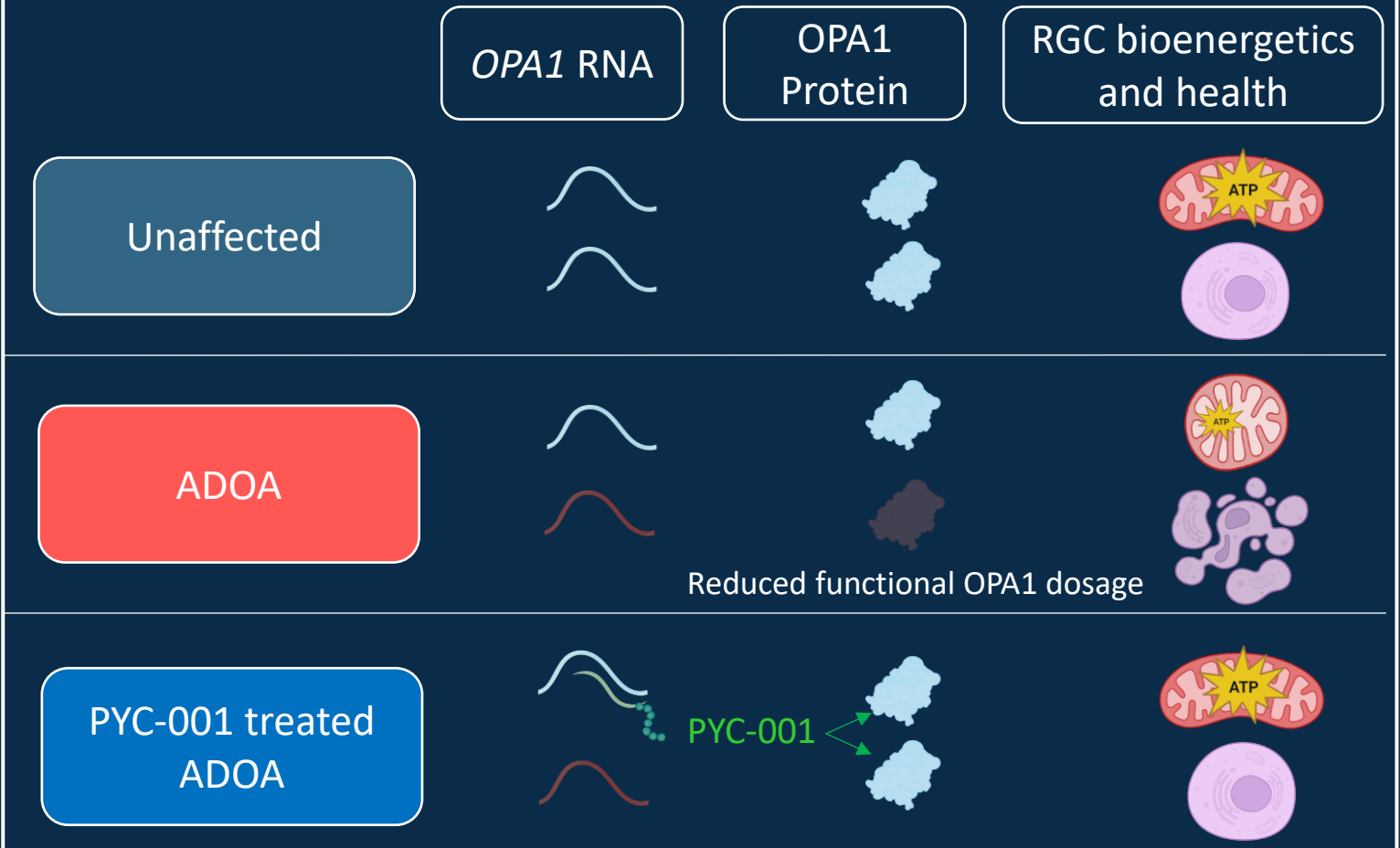
Typical visual profile of an ADOA patient at age 10

Typical visual profile of an ADOA patient at age 30



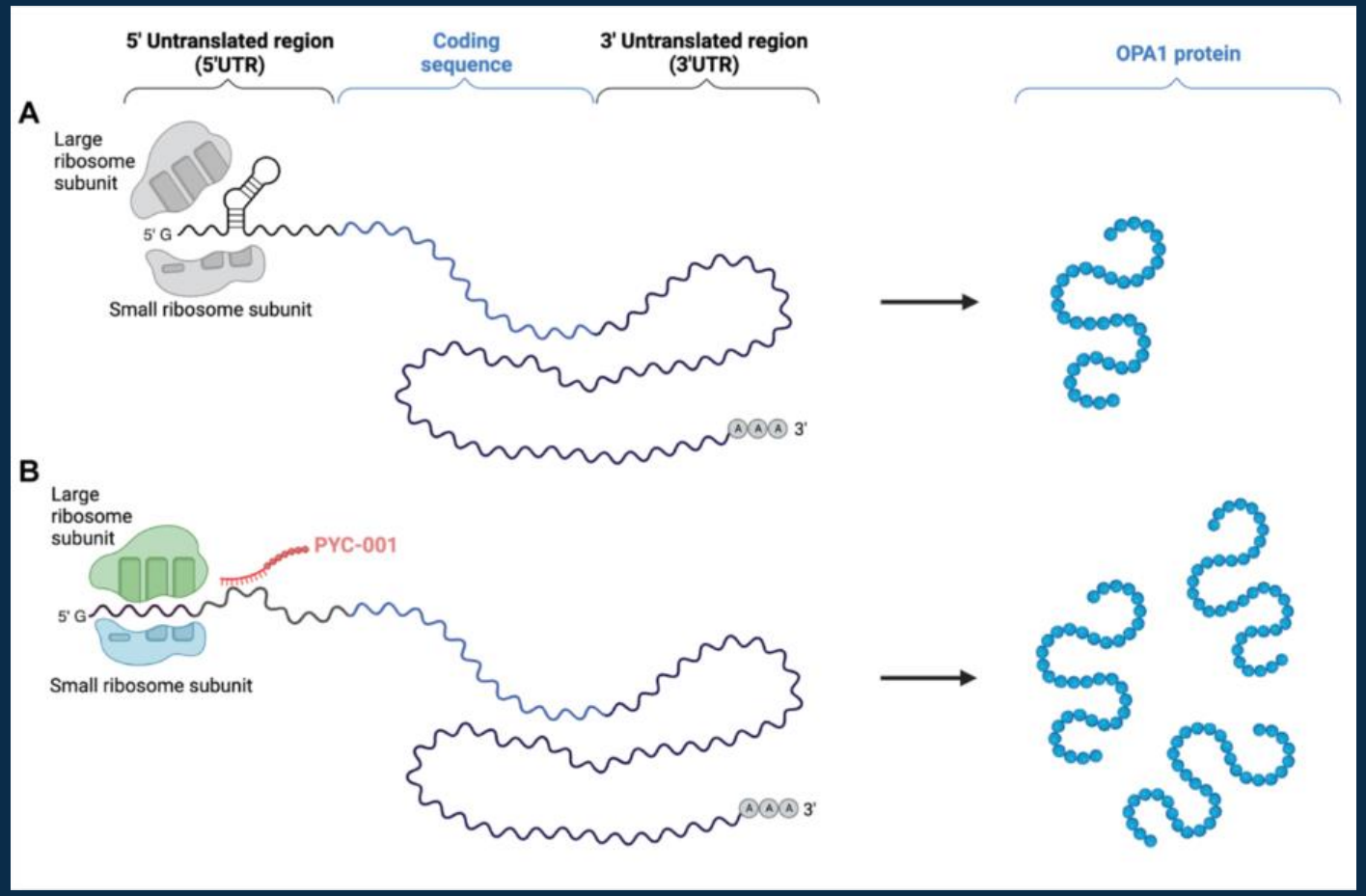
PYC-001 is a disease-modifying drug candidate for ADOA in clinical trials

PYC-001 is a peptide-conjugated oligonucleotide administered intravitreally



1. In 65-90% of cases - Yu-Wai-Man, P. et al. Ophthalmology. The prevalence and natural history of dominant optic atrophy due to OPA1 mutations. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038
2. Amati-Bonneau, P. et al. OPA1-associated disorders: phenotypes and pathophysiology. The international journal of biochemistry & cell biology, 2009;41(10), 1855–1865. doi: 10.1016/j.biocel.2009.04.012
3. Image and caption sourced from Gene Vision. Available; https://gene.vision/knowledge-base/dominant-optic-atrophy-for-patients/#condition

PYC-001 Mechanism of action

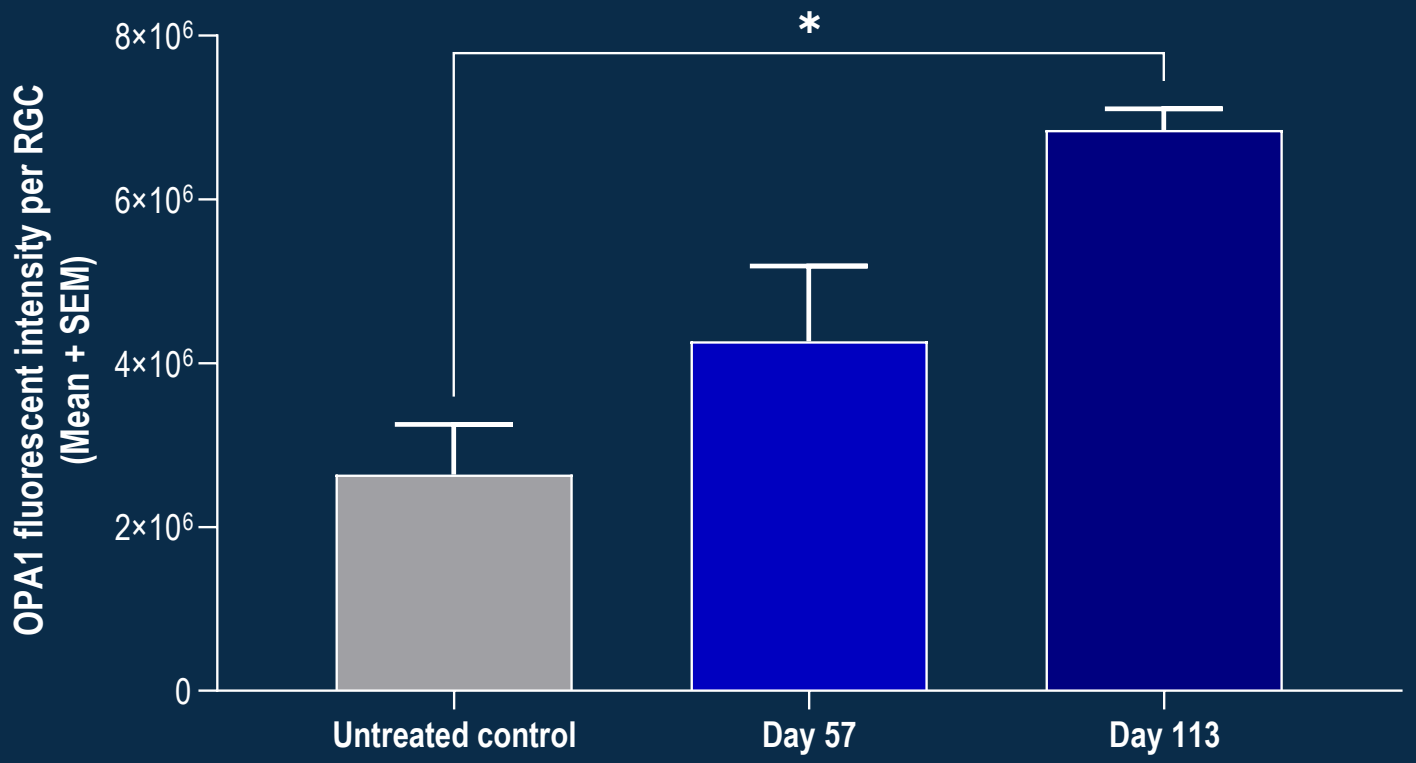


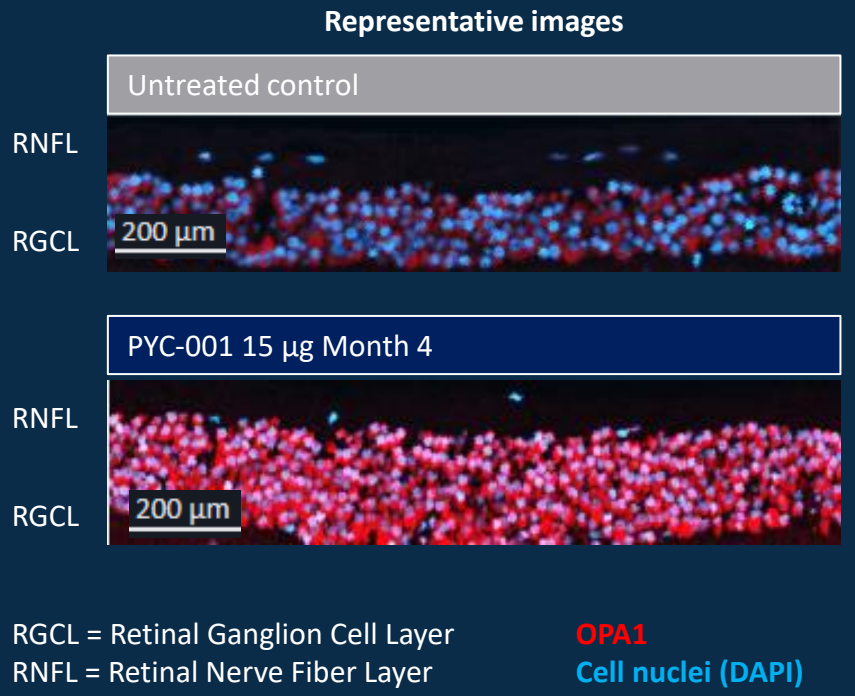
A) The 5'UTR of the OPA1 mRNA contains a stem-loop structure that hinders protein translation

B) The PMO structure of PYC-001 (depicted in red) binds to the 5'UTR of OPA1 mRNA, disrupting the complex secondary structure, particularly the stem-loop structure – facilitating more efficient ribosomal access

This induced modification in the complex secondary structure allows for augmented OPA1 protein translation

PYC-001: Updated NHP research





RGCL = Retinal Ganglion Cell Layer
RNFL = Retinal Nerve Fiber Layer

OPA1
Cell nuclei (DAPI)

A single dose of PYC-001 sustains a 2-fold increase in OPA1 protein expression through 4 months in the NHP retina[1]

1. Refer ASX Announcement of 21 July 2026. 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).

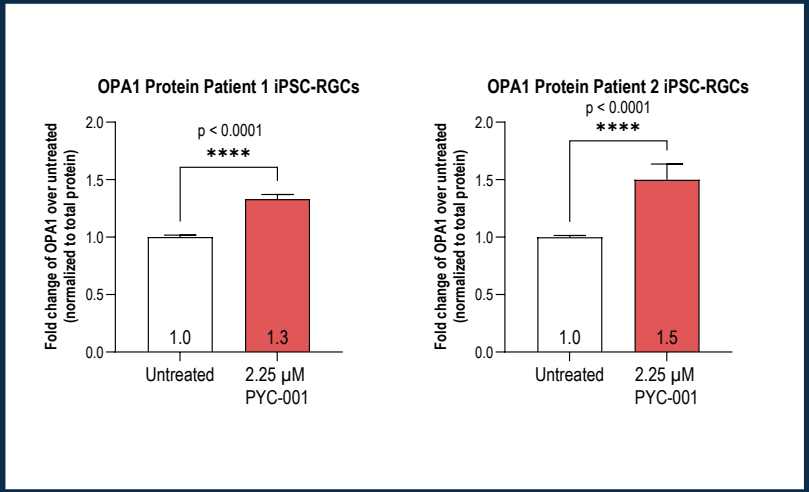
PYC-001: Background human in-vitro research

In ADOA patient-derived induced pluripotent stem cells (iPSC-RGC) [1]

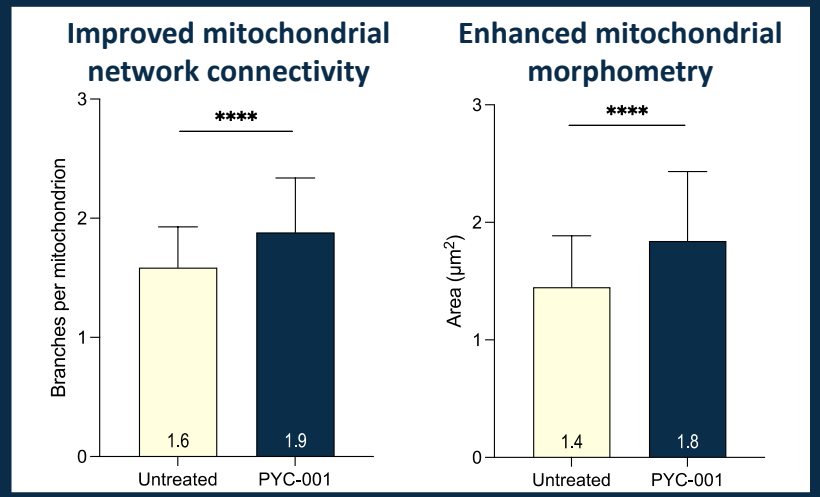
a) Upregulates OPA1 protein in a mutation agnostic manner

b) Restores mitochondrial structural defects

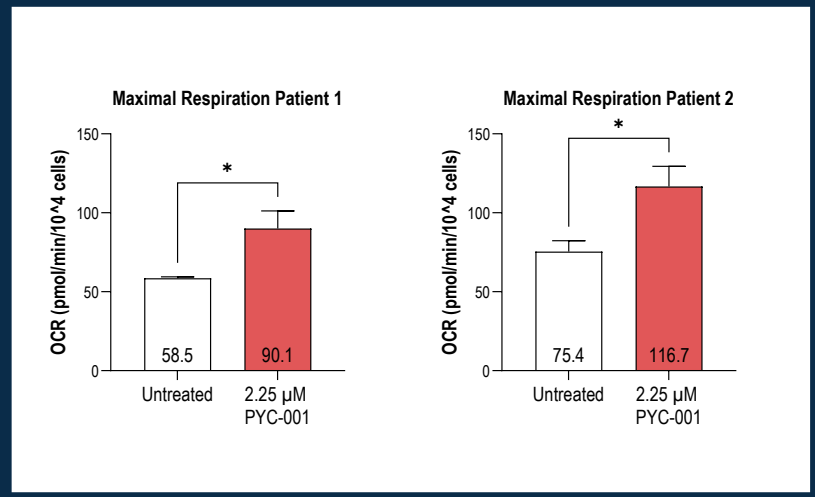
c) Restores cellular bioenergetics



a) OPA1 protein upregulation



b) Restoration of mitochondrial defects



c) Restoration of cellular bioenergetics

= Effectively rescuing OPA1 haploinsufficiency

1. Refer PYC Therapeutic's ASX Announcements: 3 April 2023 and 4 October 2023

By restoring OPA1 protein expression, PYC-001 could address the underlying cause of ADOA

	ADOA Patient		ADOA Patient + PYC-001	
Haploinsufficient ~50-70% expression		OPA1		Restoration towards 100%
Disorganized, wide cristae and cristae junctions		Cristae ultrastructure		Slim, tight and narrow
Fragmented		Morphology		Elongated
Lower respiratory efficiency		Bioenergetics		Improved respiratory efficiency
Higher sensitivity to challenge		Cell-death		More resistant to cell death

Functional outcome

OPA1 protein restoration

↓

Mitochondrial structural defect correction

↓

Mitochondrial respiratory improvement

↓

Protection against cell death (loss of RGCs)

Created with Biorender

PYC-001: Patient overview

- >18 years
- haplo-insufficiency OPA1 mutation
- vision between 20/40 and 20/200
- mild to moderate RNFL loss (1-3 sectors) on Spectralis glaucoma module
- not on idebenone, CoQ10, B vitamin supplements or other nutraceuticals

PYC-001: Safety outcomes

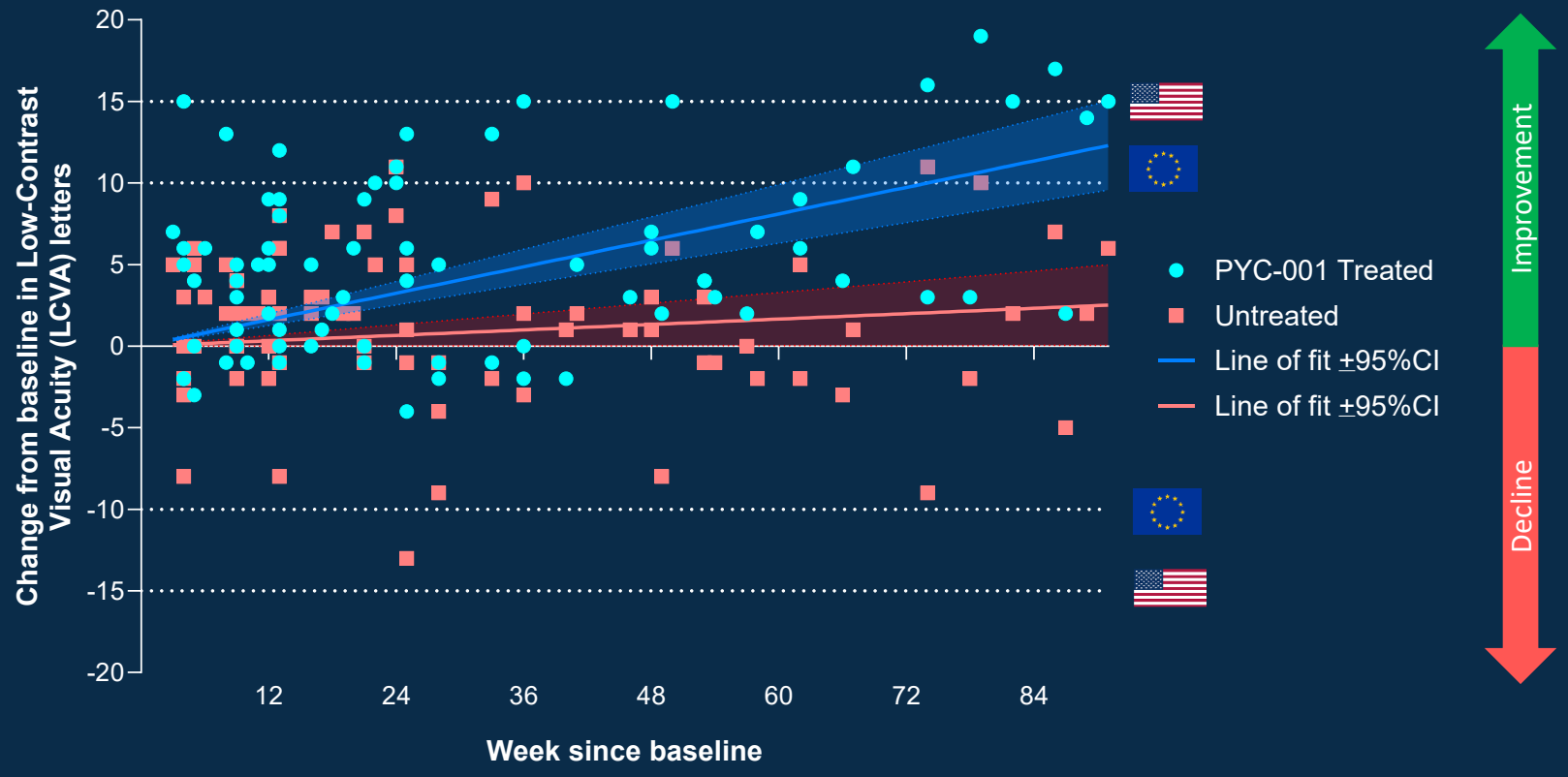
- ✓ **PYC-001 has been shown to be safe and well-tolerated in ADOA patients[1]**
- ✓ **No Treatment Related-Serious Adverse events (TR-SAEs) observed in any subject dosed with PYC-001 to date[1]**
- ✓ **No Treatment Related-Adverse Events (TR-AEs) observed in any subject dosed with PYC-001 to date[1]**
- ✓ **The outcomes listed above include patients who have received multiple doses of PYC-001 to date[1]**

Dose of PYC-001 (number of patients that have received)[1,2]	Number of patients with TR-SAE (%)
3 mcg (n=3)	0 (0%)
10 mcg (n=8)	0 (0%)
30 mcg (n=10)	0 (0%)
60 mcg (n=5)	0 (0%)

1. Accurate as at 1 September 2026. Safety outcomes may be subject to change following future Safety Review Committee (SRC) review of data collected over the course of the ongoing clinical studies. Treatment-related adverse events defined based on relationship to study agent/investigational drug.
2. Number of patients that have received at least one dose at this level (SUNDEW and MYRTLE data). Roll-over patients contribute to safety outcomes for each dose level they received (total of 23 ADOA patients have received PYC-001).

PYC-001: Results LCVA over time

Low-Contrast Visual Acuity data for ADOA patients enrolled in MAD meeting proposed registrational trial inclusion criteria[1]



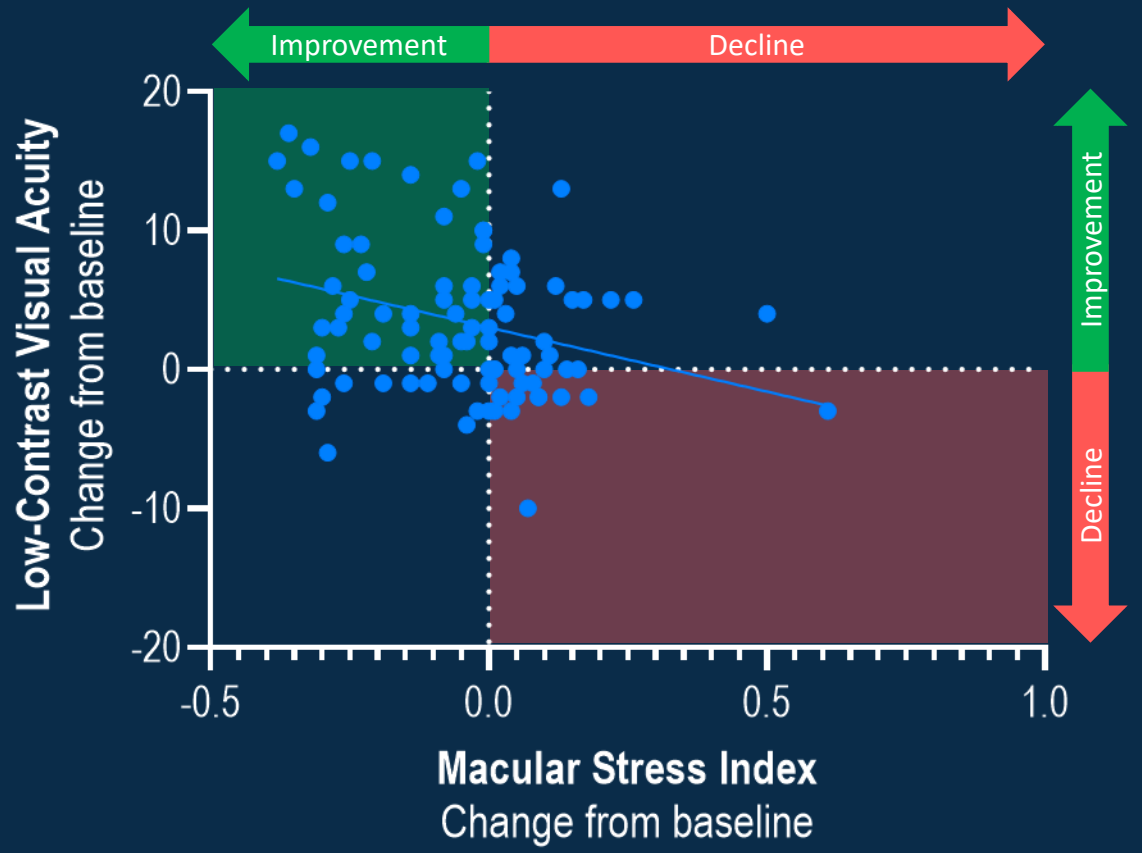
Clinically meaningful changes in LCVA in treated eyes (both ≥10 and ≥15-letter threshold)[2]

Greater mean change from baseline as compared to untreated fellow eyes

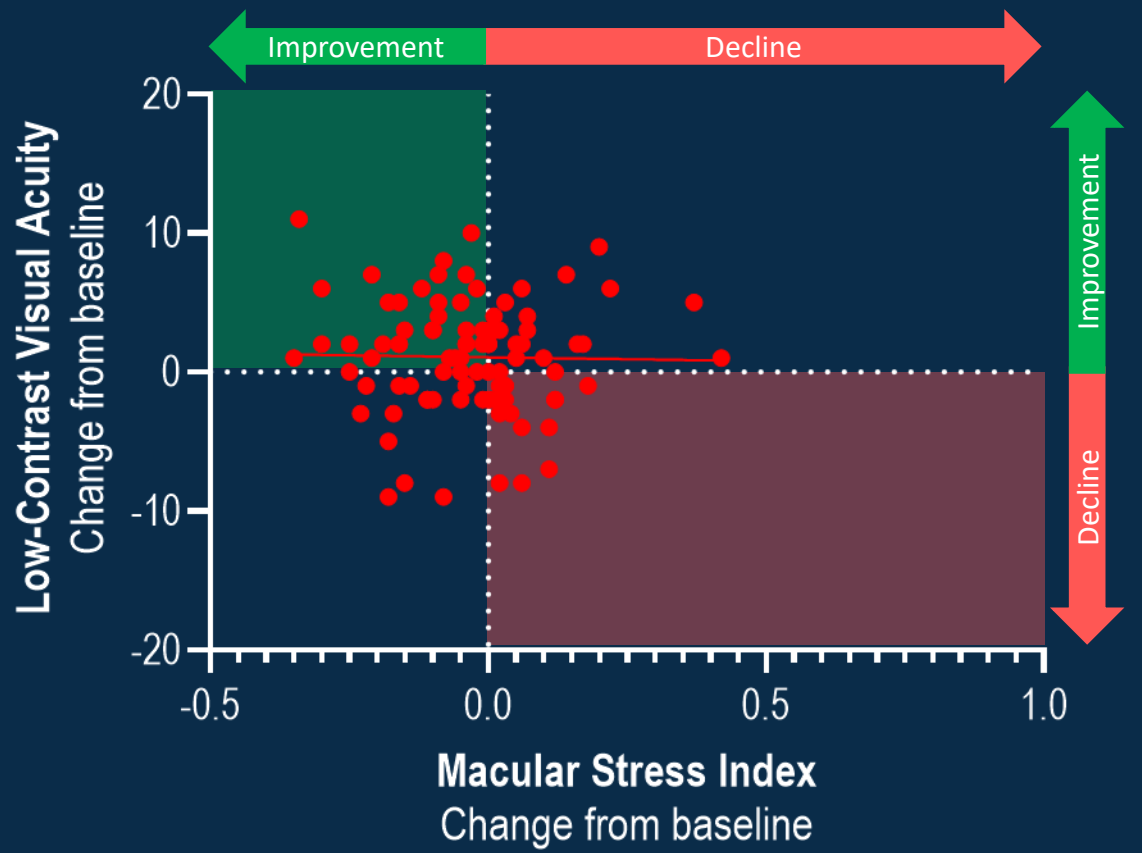
1. All data from MYRTLE patients that have received 10 mcg or more of PYC-001 with LCVA ≤50 in treated eye at baseline with at least 1 follow up visit with LCVA recorded. Data extracted as accessible on 01 September 2026. Subject to the risks and uncertainties outlined in this document and the Company's ASX disclosures of 2 February 2026
2. 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

PYC-001: Results

PYC-001 Treated Eyes



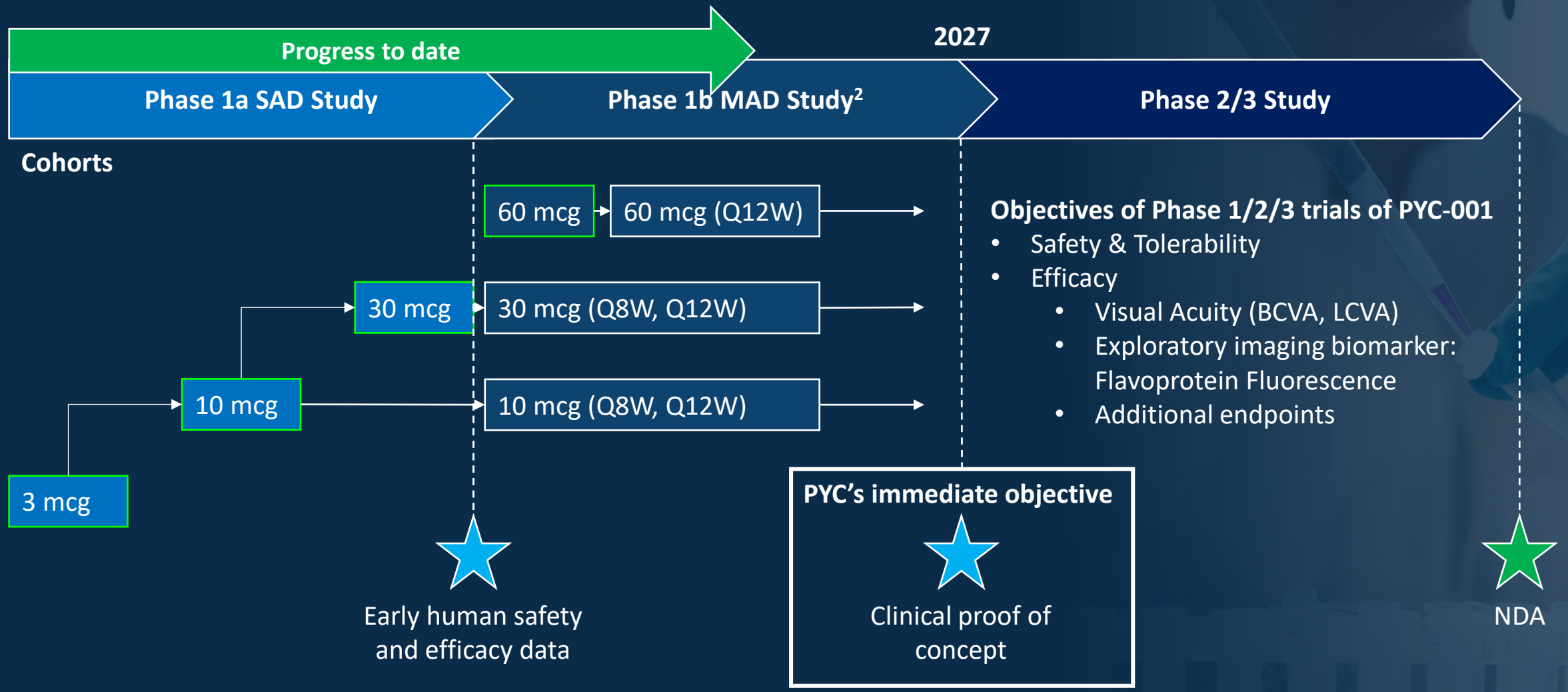
Untreated Fellow Eyes



Reduced macular stress (FPF) correlates to improved LCVA[1]

1. 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. Data extracted as accessible on 01 September 2026. Not all patients have had the same number of follow-up visits.

Planned progress: registrational trial to support the first approval in ADOA[1]



1. PYC-001 is the most advanced drug candidate with disease-modifying potential in clinical development for ADOA based on publicly available information. Subject to the risks and uncertainties outlined in this document and the Company's ASX disclosures of 2 February 2026 as well as changes in the treatment landscape in ADOA
2. PYC may engage with regulatory authorities to discuss the potential for an open-label extension of the 'Phase 1b MAD study' to provide data for longer-term dosing of PYC-001 in ADOA patients ahead of initiating registrational trials

FDA special designations intended to accelerate the path to approval

FDA Special Designation	Status	Benefits
Orphan Drug Designation	Granted for OPA1-associated vision loss[1,2]	• Tax credits for qualified clinical trials • Exemptions from some regulatory fees • Potential for 7 years of market exclusivity post-approval
Rare Pediatric Disease Designation	Granted for OPA1-associated vision loss[2,3]	• Clearer regulatory guidance • Eligible to receive a Priority Review Voucher (PRV) upon approval of PYC-001 – used to expedite the review of another product
Fast Track Designation	Potentially eligible[4]	• Increased frequency of regulatory meetings • Eligibility for Accelerated Approval and Priority Review, if relevant criteria are met; and • The potential for a Rolling Review in support of a New Drug Application
Breakthrough Drug Designation	Potentially eligible[5]	• All Fast Track Designation features; • Intensive guidance on an efficient drug development program; and • Organizational commitment involving senior managers

1. Refer ASX Announcement 24 May 2024
2. ADOA is not the only indication in which *OPA1* mutations are associated with vision loss
3. Refer ASX Announcement 30 August 2024
4. US FDA. Fast Track designation explanation available on the FDA website
5. US FDA. Breakthrough Drug Designation explanation available on the FDA website

PYC-001: Conclusions

- PYC-001 is a drug candidate with first in indication potential for the treatment of ADOA[1]
- A single dose of PYC-001:
  - 2-fold increase in OPA1 protein expression through 4 months in the NHP retina
  - Rescues the functional deficits associated with the ADOA phenotype in patient-derived models
- Early clinical data shows improved LCVA and reduced macular stress after treatment
- Demonstrated a highly favourable safety profile to date
- PYC is preparing to progress the candidate into a registrational trial aimed at supporting the first approval in ADOA[1]

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