PYC Therapeutics

24 March 2026

ADOA PROGRAM - PRESENTATION AT NANOS 2026

- **PYC is a precision medicine company dedicated to changing the lives of patients with genetic diseases who have no treatment options available**
- **One of PYC's clinical-stage programs is an investigational drug candidate (known as PYC-001) that targets the underlying cause of a blinding eye disease of childhood called Autosomal Dominant Optic Atrophy (ADOA)**
- **PYC today announces that safety and efficacy data from a Single Ascending Dose study of PYC-001 in ADOA patients[1] will be presented by Dr. Clare Fraser at the North American Neuro-Ophthalmology Society (NANOS) 2026 Conference in Boston, MA between 20-24 March 2026 – a copy of Dr. Fraser's presentation is attached to this announcement**
- **PYC has recently commenced a Multiple-Ascending Dose (MAD) study of PYC-001 in ADOA patients[2] with clinical safety and efficacy data from this repeat dose study expected to be presented in H2 CY26[3]**

PERTH, Australia and SAN FRANCISCO, California – 24 March 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 available for patients.

PYC today announces that clinical data from the Single Ascending Dose (SAD) study of PYC-001 in ADOA patients will be presented by Dr. Clare Fraser at the North American Neuro-Ophthalmology Society (NANOS) 2026 conference in Boston, Massachusetts. The presentation will highlight the safety/tolerability and efficacy results of single doses of PYC-001 demonstrated in the study.

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

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[1] Trial details available using the identifier NCT06461286
[2] See ASX announcement of 21 October 2025
[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

PYC recently commenced a repeat dose study of PYC-001 in ADOA patients and expects to present clinical safety and efficacy data from this study in H2 CY26[5].

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[6].

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 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 CEO of PYC Therapeutics Limited

CONTACT US

Investor relations and media contact
investor@pyctx.com

[5] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
[6] 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 1A Single Ascending Dose Study To Evaluate Safety Of PYC-001; A Peptide-Conjugated Oligonucleotide Designed To Treat OPA1 Mutation-Associated Autosomal Dominant Optic Atrophy

Clare Fraser

NANOS March 2026

Sundew

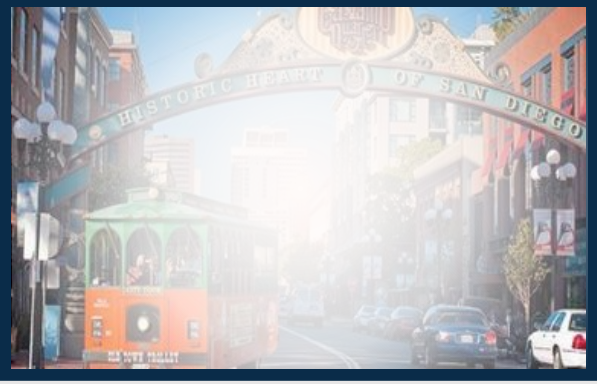
Disclosures: Clare Fraser – assistance with travel costs from PYC

Overview

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

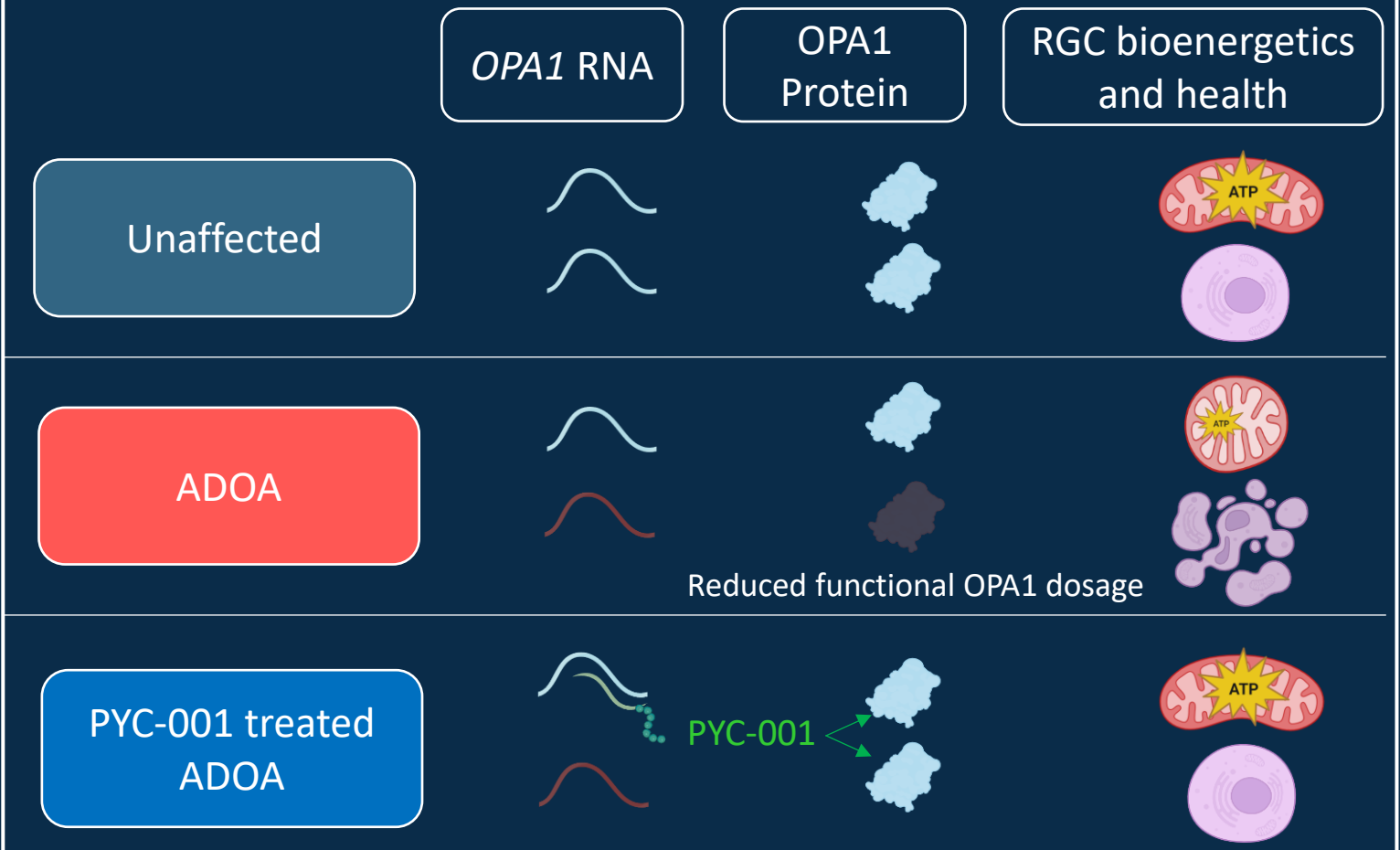
Typical visual profile of an ADOA patient at age 10

Typical visual profile of an ADOA patient at age 30



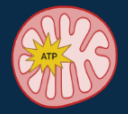
PYC-001 is a disease-modifying drug candidate for ADOA in clinical trials

PYC-001 is a peptide-conjugated oligonucleotide administered intravitreally



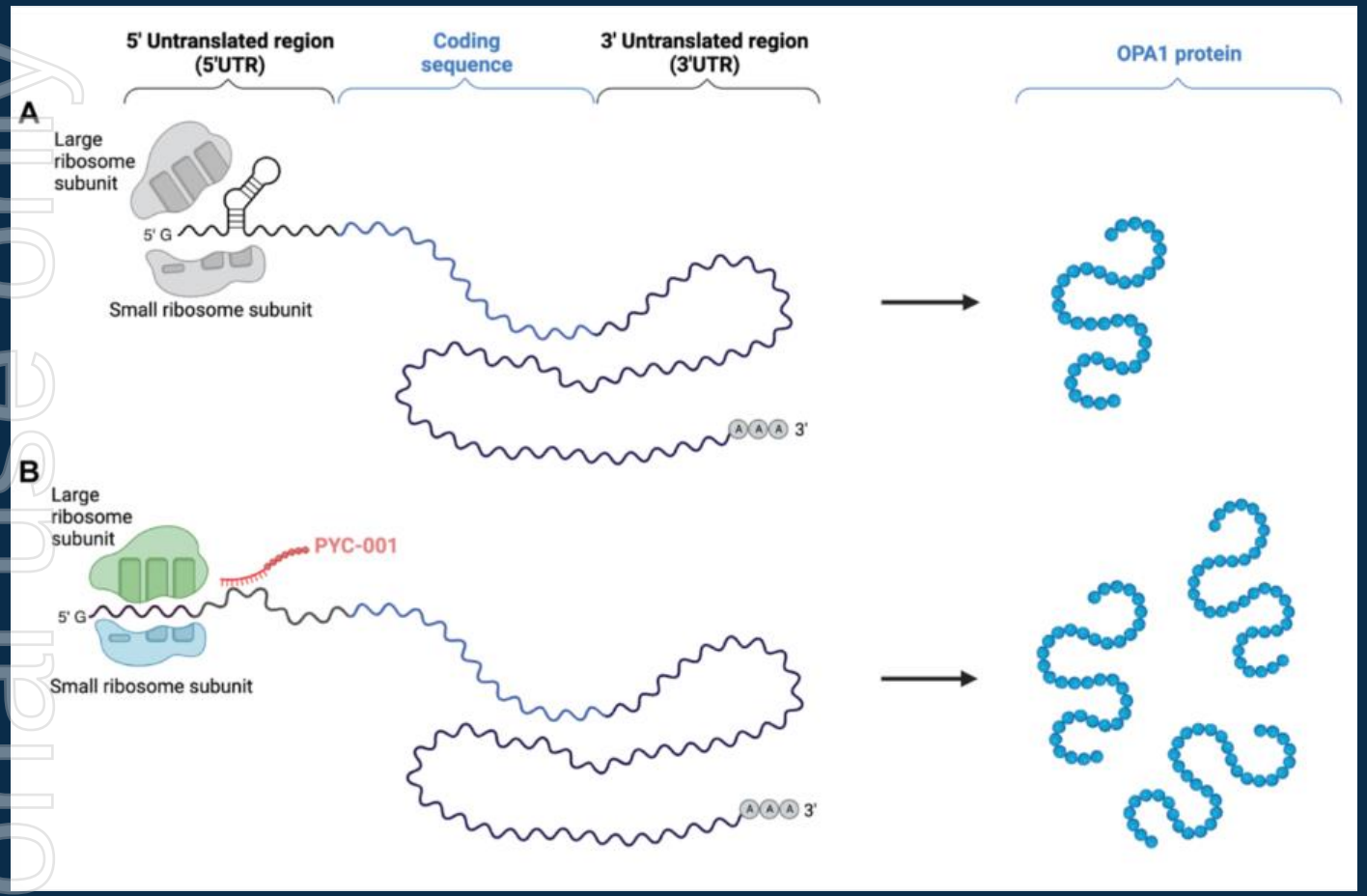
1. In 65-90% of cases - Yu-Wai-Man, P. et al. Ophthalmology. The prevalence and natural history of dominant optic atrophy due to OPA1 mutations. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038
2. Amati-Bonneau, P. et al. OPA1-associated disorders: phenotypes and pathophysiology. The international 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

OPA1 protein deficiency triggers a cascade of bioenergetic deficits leading to vision loss in ADOA patients

Unaffected individual			ADOA patient
Wild type OPA1 protein expression (100%)		OPA1	 Haploinsufficient ~50-70% expression
Slim and tight mitochondrial ultrastructure		Cristae ultrastructure	 Disorganized, wide cristae and cristae junctions
Elongated mitochondria		Morphology	 Fragmented mitochondria
Improved respiratory efficiency		Bioenergetics	 Lower respiratory efficiency
More resistant to cell death		Cell-death	 Higher sensitivity to challenge

Loss of vision

PYC-001 Mechanism of action



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

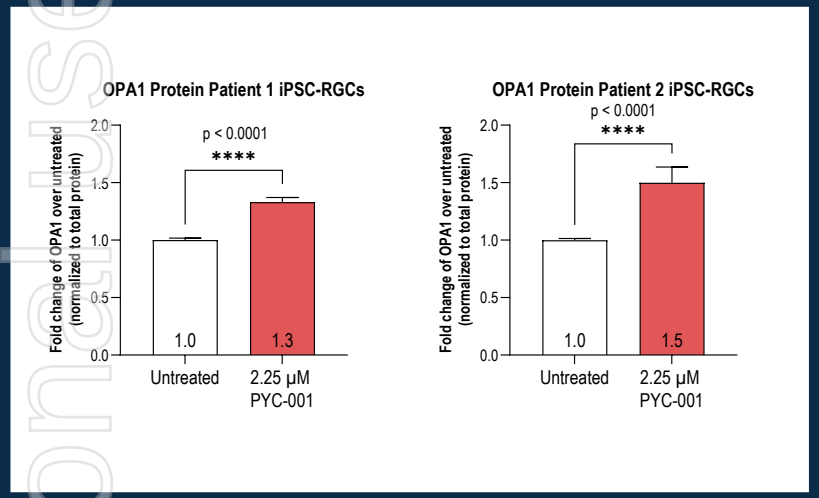
B) The phosphorodiamidate morpholino oligonucleotide (PMO) structure of PYC-001 (depicted in red) binds to the 5'UTR of OPA1 mRNA, disrupting the stem-loop structure, facilitating more efficient ribosomal access

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

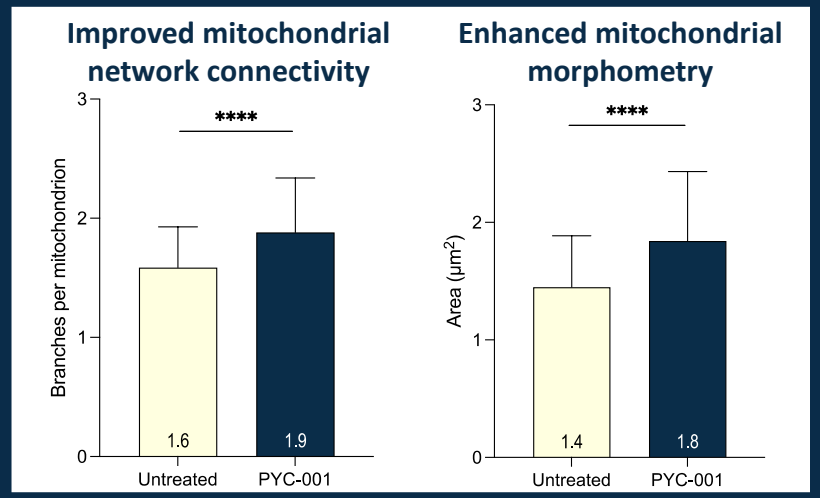
PYC-001 Background research

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

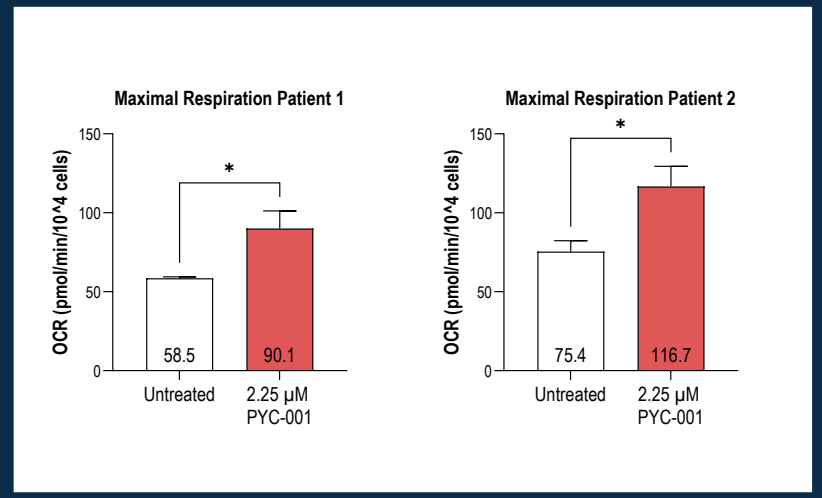
a) Upregulates OPA1 protein in a mutation agnostic manner
b) Restores mitochondrial structural defects
c) Restores cellular bioenergetics



a) OPA1 protein upregulation



b) Restoration of mitochondrial defects



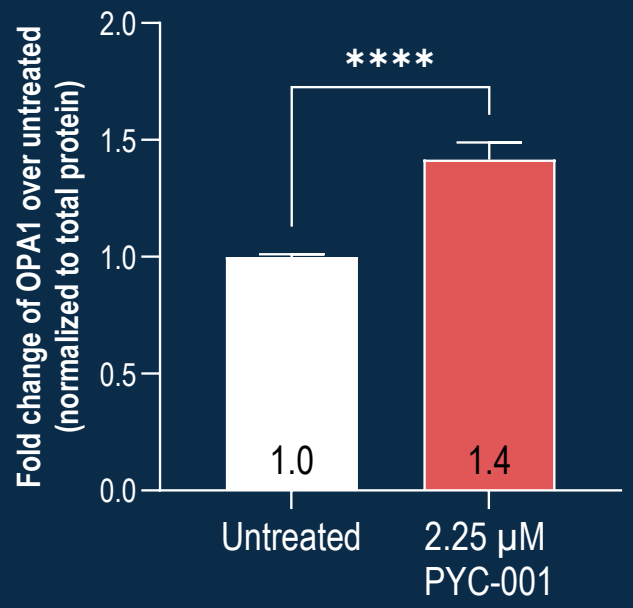
c) Restoration of cellular bioenergetics

= Effectively rescuing OPA1 haploinsufficiency

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

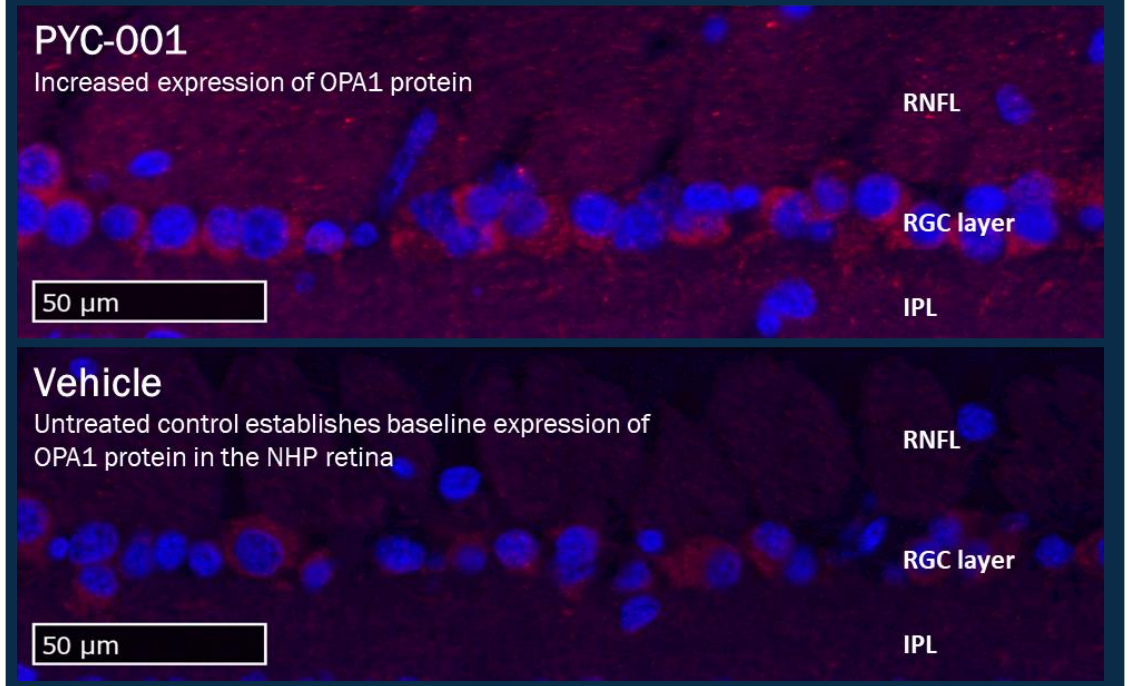
PYC-001 Background research

PYC-001 increases OPA1 protein in iPSC-RGCs



A 1.4-fold increase in OPA1 levels is expected to protect RGCs[3]

Single dose of PYC-001 increased OPA1 protein (stained **red**) expression 1.6-fold in NHP retina



PYC-001 has a fully-integrated PK/PD/safety profile *in vivo*[2] *in non-human primates*

1. Refer PYC Therapeutic's ASX Announcement: 3 April 2023 2. Refer PYC Therapeutic's ASX Announcement: 4 October 2023
3. Based on the effect of PYC-001 in restoring mitochondrial morphology and cellular bioenergetics upstream in the disease-causing cascade that leads to RGC death (in ADOA patient-derived models)

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)

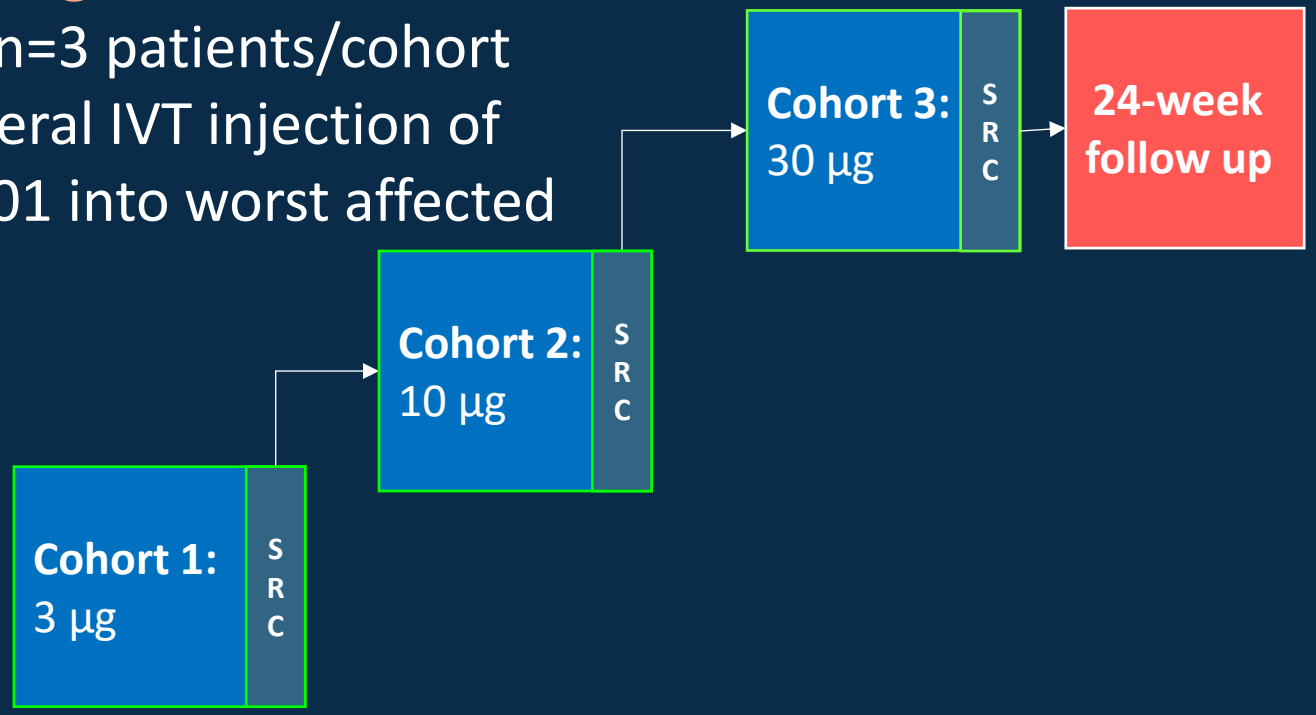
Created with Biorender

SUNDEW: Phase 1A First-In-Human study of PYC-001 in OPA1 mutation associated ADOA patients

Phase 1a Single Ascending Dose Study

Study Design

- N=9 ; n=3 patients/cohort
- Unilateral IVT injection of PYC-001 into worst affected eye



Ocular Assessments

Objective	Subjective
1. Flavoprotein fluorescence – Ocumet Beacon	1. BCVA 2. LCVA (ETDRS letters)
2. SD-OCT - RNFL - GCL	3. Pelli Robson Contrast sensitivity
3. Multi-focal VEP	4. Color vision (HRR plates)
	5. Static Perimetry (HVF 24-20)

Primary Outcome: Safety & Tolerability

Secondary Outcomes: Evaluate treatment effect on ocular structure and function

Sundew – 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

Cohort	Dose	Average age	Sex composition		Average baseline BCVA		Average baseline LCVA	
			Male	Female	Treated	Untreated	Treated	Untreated
1 (n=3)	3 mcg	50	2	1	63	63.3	44.3	49
2 (n=3)	10 mcg	50.3	2	1	52.7	53	51	44.3
3 (n=3)	30 mcg	52.3	2	1	56	55.3	44	43

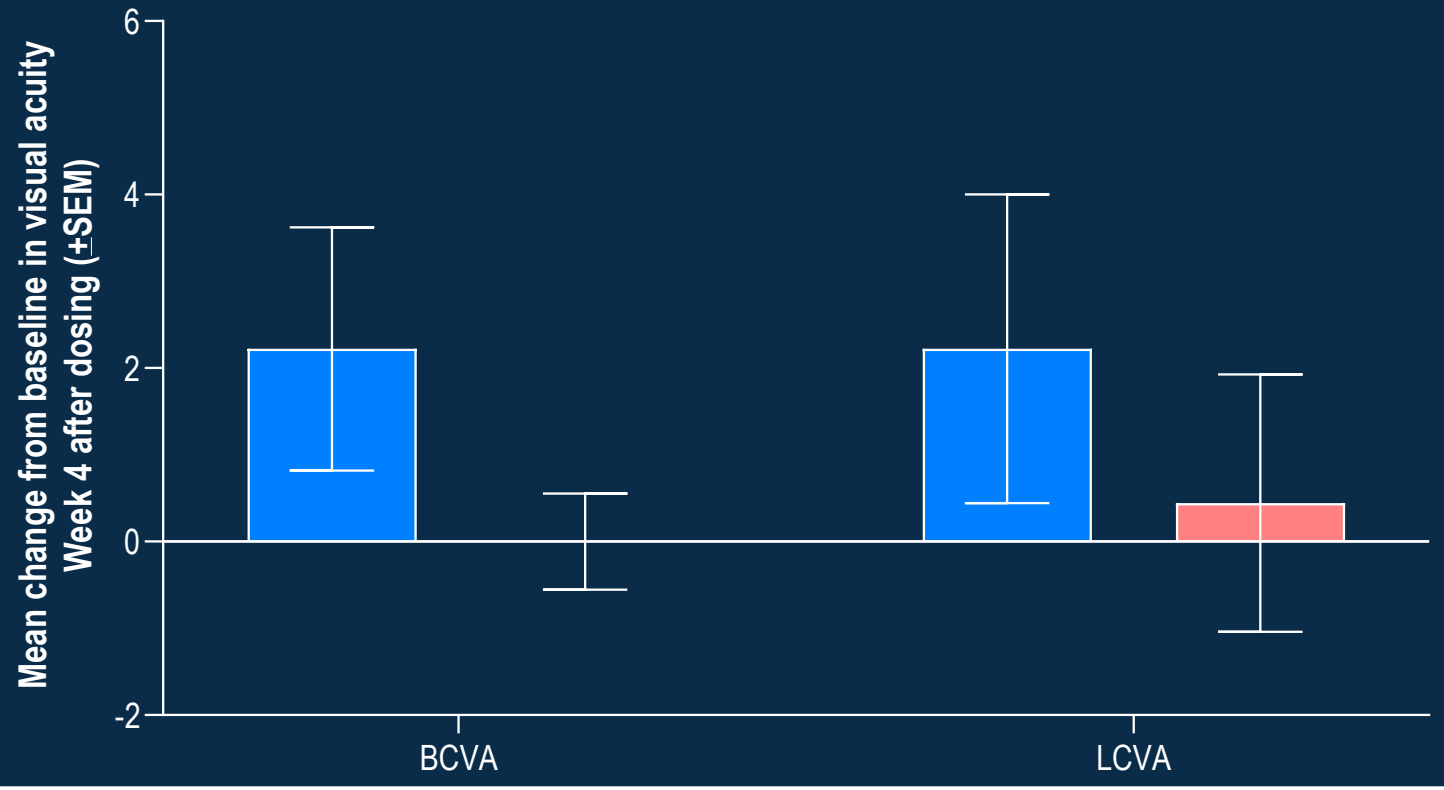
Sundew – safety outcomes

- ✓ **PYC-001 was safe and well-tolerated in ADOA patients**
- ✓ No Treatment Emergent-Serious Adverse events (TE-SAEs) observed in any subject dosed with PYC-001 to date[1]
- ✓ Treatment-Emergent Adverse Events (TE-AEs) were primarily mild and procedure related[1]
- ✓ No TE-AEs leading to treatment discontinuation[2]

1. Refer PYC Therapeutic's ASX Announcement: 5 September 2025
2. Accurate as at 12 January 2026 for the absence of TE-AE related treatment discontinuations

ADOA eyes treated with PYC-001 show improvement in visual acuity

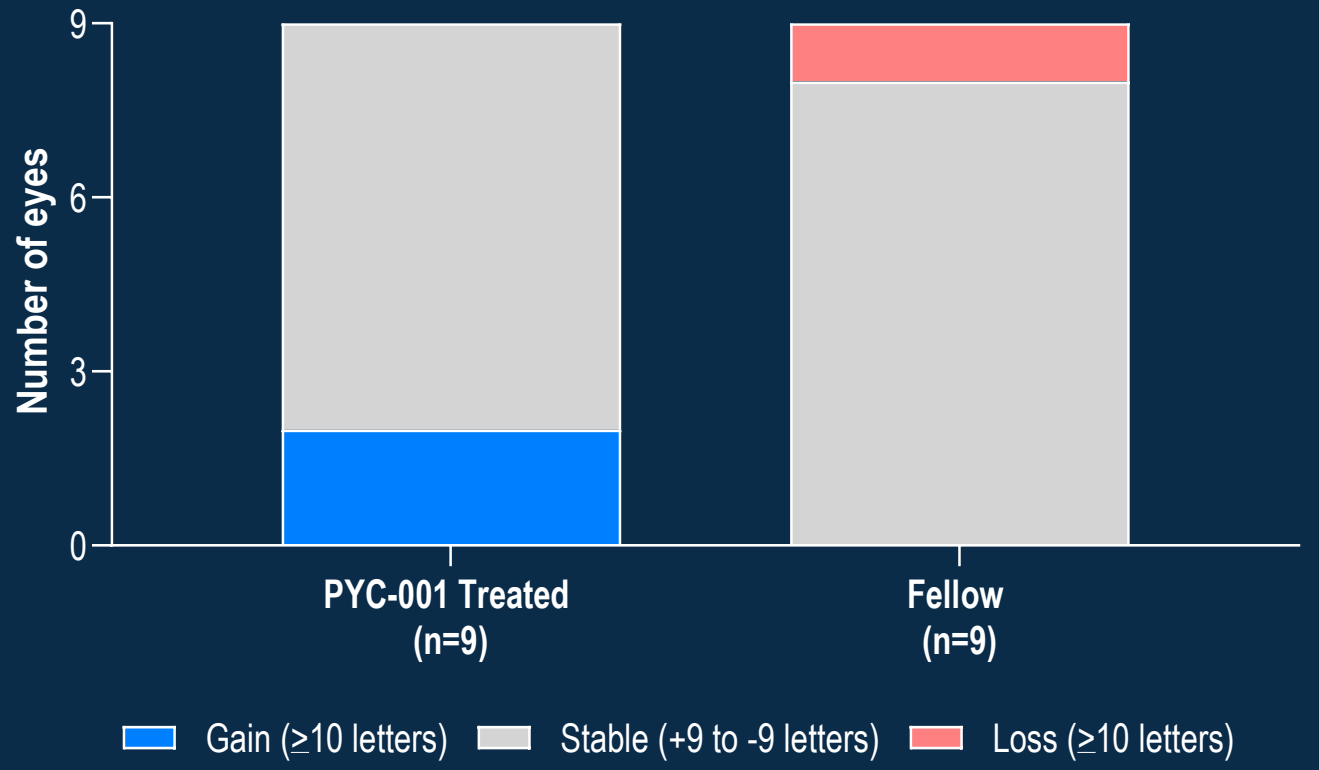
Mean change in Visual Acuity (best corrected and low contrast ETDRS letters) at Week 4 [1]



1. All *SUNDEW* patients with Week 4 data available (n=9, 3 patients from 3 mcg cohort, 3 patients from 10 mcg cohort and 3 patients from 30 mcg cohort), LCVA = Low Contrast Visual Acuity and BCVA = Best-Corrected Visual Acuity.

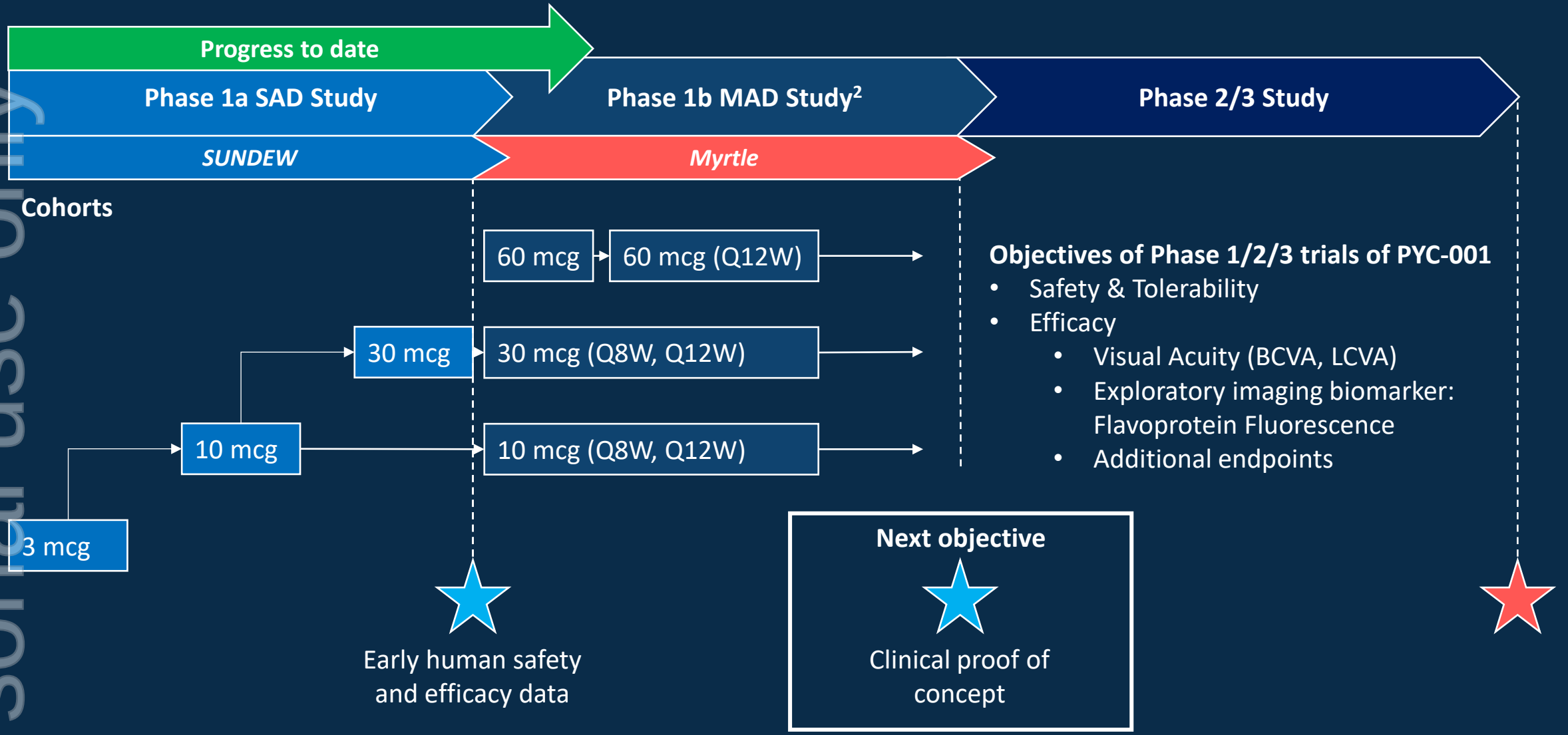
Week 24 follow-up

Number of eyes showing clinically meaningful[1] change in LCVA (ETDRS letters) at Week 24[2]



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. All *SUNDEW* patients with Week 24 data available (n=9, 3 patients from 3 mcg cohort, 3 patients from 10 mcg cohort and 3 patients from 30 mcg cohort), LCVA = Low Contrast Visual Acuity.

MYRTLE: Phase 1b multi-ascending dose trial is now underway



Objectives of Phase 1/2/3 trials of PYC-001

- Safety & Tolerability
- Efficacy
  - Visual Acuity (BCVA, LCVA)
  - Exploratory imaging biomarker: Flavoprotein Fluorescence
  - Additional endpoints

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 PYC Therapeutic's (The Company's) ASX disclosures of 2 February 2026 as well as changes in the treatment landscape in ADOA
2. PYC Therapeutics 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

Questions

Myrtle