PYC Therapeutics

14 May 2024

GLP TOX RESULTS CLEAR PATH FOR SECOND BLINDING EYE DISEASE DRUG TO ENTER HUMAN TRIALS

- PYC is a clinical-stage biotechnology company developing a pipeline of first-in-class precision medicines for patients who have genetic diseases and no treatment options available today
- The Company is currently preparing for a clinical trial of one of its drug candidates in a blinding eye disease of childhood called Autosomal Dominant Optic Atrophy (ADOA) – a genetic condition affecting 1 in every 35,000 people and for which there are no available treatments[1]
- This drug candidate is effective in addressing the underlying cause of ADOA in both Non-Human Primate (NHP) and patient-derived 'retina in a dish' models[2]
- The safety profile of this drug candidate has now been established in Good Laboratory Practice (GLP) toxicology studies in NHPs – clearing the path for a regulatory submission to enable human trials to commence
- PYC will progress directly into ADOA patients in the upcoming Single Ascending Dose (SAD) study – enabling initial human safety and efficacy data for this program to be delivered in 2025[3] prior to a planned New Drug Application in 2028[4]

PERTH, Australia and SAN FRANCISCO, California – 14 May 2024

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating first in class precision therapies for patients with genetic diseases and no treatment options. One of the Company's assets is a drug candidate that addresses the underlying cause of a blinding eye disease of childhood called Autosomal Dominant Optic Atrophy (ADOA). This drug candidate has demonstrated disease-modifying potential in 'retina in a dish' models derived from patients with ADOA as well as in animal models[5]. The drug candidate has now also demonstrated a suitable safety profile for progression into human trials following completion of Good Laboratory Practice (GLP) toxicology studies in Non-Human Primates (NHPs).

[1] 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, 46 e1.
[2] See ASX announcement of 3 April 2023
[3] Subject to the risks set out in the Company's ASX filing of 14 March 2024
[4] Management forecast as of May 2024. Progression of the drug candidate on these timelines is subject to ongoing success of the development program and includes all risks customary to an early-stage biotechnology company including regulatory risks.
[5] See ASX announcement of 4 October 2023

The results of the GLP toxicology studies in NHPs demonstrate that PYC's investigational drug candidate for ADOA (known as PYC-001) was safe and well-tolerated at all doses tested with a No Observable Adverse Event Limit (NOAEL) of 30 micrograms per eye – the highest dose of PYC-001 evaluated in these studies.

PYC now has all of the information required to submit a regulatory application to progress into human trials for PYC-001.

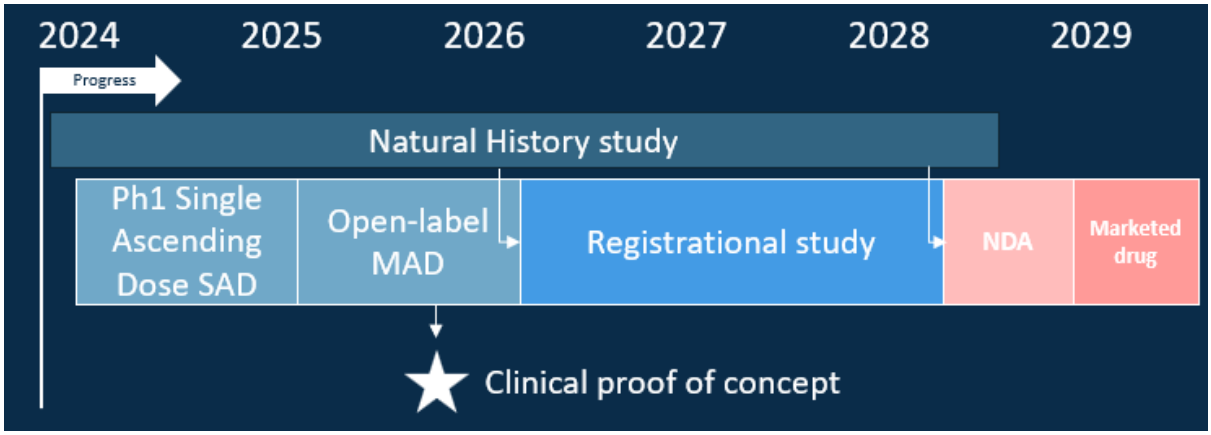
Table 1: Results of GLP single dose toxicology study for PYC-001 in NHPs

A single-dose GLP toxicology study was conducted in NHPs. Low, medium and high doses of PYC-001 were administered and evaluated in addition to a control group. All dosing was bilateral, and administration of PYC-001 was by injection into the vitreous of the eye, the same route of administration anticipated to be used in human clinical trials. The single-dose NHP evaluations were conducted for a duration of 12 weeks. The information reported here contains data through completion of the studies at week 12 following single doses of PYC-001 at each of the three doses assessed in NHPs.

Dose of PYC-001	(µg/eye)	# of eyes dosed	No findings of adverse tolerability at week 12 (conclusion of study) # of eyes (% of population)	Findings of adverse tolerability at week 12 (conclusion of study) # of eyes (% of population)
Control	0 µg	12	12 *(100%)*	0 *(0%)*
Low	3 µg	12	12 *(100%)*	0 *(0%)*
Medium	10 µg	12	12 *(100%)*	0 *(0%)*
High	30 µg	12	12 *(100%)*	0 *(0%)*

In addition to the detailed safety/tolerability assessment of the NHP eyes, there were also no signs of systemic tolerability issues including drug-related mortality, changes in health and behaviour or visual function observed through the 12-week study period.

Figure 2: Clinical trial pathway for PYC-001[6]



[6] Management forecast as of May 2024. Progression of the drug candidate on these timelines is subject to ongoing success of the development program and includes all risks customary to an early-stage biotechnology company including regulatory risks.

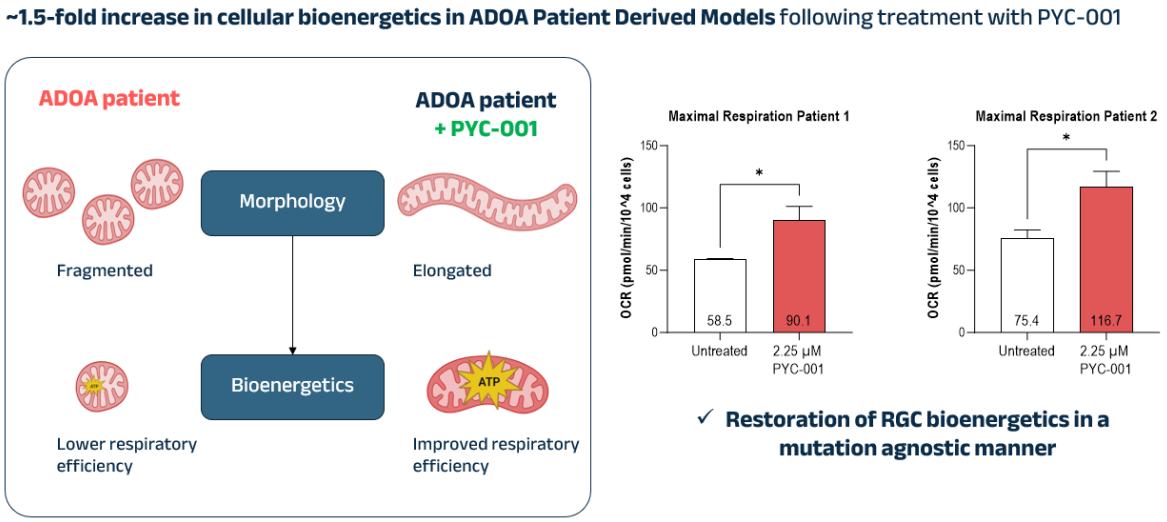
PYC's ADOA Program Overview

- Autosomal Dominant Optic Atrophy (ADOA) is a blinding disease of childhood affecting 1 in every 35,000 people
- ADOA is caused by a mutation in 1 copy of the *OPA1* gene leading to a protein insufficiency in Retinal Ganglion Cells (RGCs)
- PYC-001 increases expression of *OPA1* back towards wild-type ('unaffected') levels in ADOA patient-derived retinal organoids
- PYC-001 increases OPA1 expression in the NHP retina following a single safe and well-tolerated dose (15 µg/eye)
- ADOA represents an estimated >$2 billion p.a. addressable market[7] with no treatment options available for patients today

Pre-clinical data supporting PYC's ADOA drug candidate

- High Concentration in the Non-Human Primate (NHP) retina (>1,500 ng/g at Day 15 following a single 15 µg dose)[8]
- Effective with a safe and well-tolerated dose of 15 µg/eye in NHPs (No Observable Adverse Event Level of 30 µg/eye)[9]
- Effective in patient-derived models[10] (see Figure 2 below)

Figure 2. PYC-001 is effective in patient-derived models



[7] Estimated market in Australian dollars based on a target patient population of 10,000 in the Western World and median orphan drug pricing of US$150,000 per patient per annum (EvaluatePharma. Orphan Drug Report. 2019.)
[8] Refer ASX Announcement 4 October 2023
[9] Refer ASX Announcement 4 October 2023
[10] Refer ASX Announcement 3 April 2023

PYC-001 non-clinical progress checklist

Dimension	Supporting Data Available	ASX announcement
Biodistribution	✓	4 October 2023
Safety/Tolerability (non-GLP)	✓	4 October 2023
Durability *in vivo*	✓	4 October 2023
Efficacy *in vivo*	✓	4 October 2023
Functional rescue of disease (Patient-derived model)	✓	3 April 2023
Safety/Tolerability (GLP)	✓	14 May 2024

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 RNA therapeutic class. PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**[11].

The Company was the first to progress a drug candidate for a blinding eye disease of childhood into human trials. PYC is progressing two more drug candidates with disease-modifying potential into human studies in 2024[12].

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

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

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

[12] Management forecast as of May 2024. Progression of the drug candidate on these timelines is subject to ongoing success of the development program and includes all risks customary to an early-stage biotechnology company including regulatory risks.

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