15 August 2024

PYC TO START HUMAN TRIALS IN SECOND BLINDING EYE DISEASE

- **PYC today announces that it has received Human Research Ethics Committee (HREC) approval to commence clinical trials of its drug candidate in patients with Autosomal Dominant Optic Atrophy (ADOA)**
- **The Company has lodged a Clinical Trial Notification with the Therapeutic Goods Administration and will now commence first in human studies of this drug candidate in Australia with first patient dosing expected to occur this quarter**
- **The ADOA program enters human trials after PYC recently demonstrated the safety and initial efficacy profile of its RNA conjugate modality in a human eye for the first time in the Company's lead Retinitis Pigmentosa type 11 drug program[1]**
- **PYC's ADOA drug candidate is designed for the 1 in every 35,000 people who suffer from this irreversible blinding eye disease[2] who currently have no treatment options available**
- **PYC expects to establish clinical 'proof of concept' data (initial human safety and efficacy data) for this drug candidate in 2025 prior to initiating a registrational study in 2026[3]**

PERTH, Australia and SAN FRANCISCO, California – 15 August 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 available. One of the Company's assets is a first-in-class drug candidate for patients with a blinding eye disease called Autosomal Dominant Optic Atrophy (ADOA). This drug candidate is known as PYC-001. PYC-001 has been granted Orphan Drug Designation by the US Food and Drug Administration[4].

PYC today announces that it has received all required regulatory approvals to commence first in human trials of PYC-001. The Company will now proceed to dosing ADOA patients with PYC-001 in a Single Ascending Dose (**SAD**) study. An overview of this SAD study design is outlined below (See Figure 1). ADOA patients enrolled in the SAD will receive a

[1] See ASX announcements of 1 July 2024, 5 and 12 August 2024
[2] 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
[3] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 14 March 2024
[4] Refer ASX announcement 24 May 2024

single dose of PYC-001 into one eye via intravitreal administration. The primary endpoint of the study will be Treatment Emergent Adverse Events (TE-AEs) and Treatment Emergent Serious Adverse Events (TE-SAEs). Patients will also be monitored for changes in visual function and functional vision throughout the course of the trial.

Study Overview

The open label study will be conducted in Australia at 2 sites and will recruit patients over the age of 18 with a confirmed OPA1 mutation-associated autosomal dominant optic atrophy. The study is being conducted in accordance with Good Clinical Practices (GCP) and PYC-001 has been manufactured to Good Manufacturing Practice (GMP) standard.

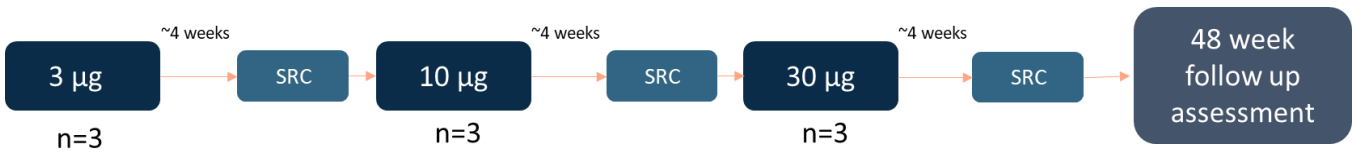
The study will consist of three cohorts (3µg, 10µg and 30µg) with each cohort consisting of 3 patients. Patients will receive a single dose of PYC-001 into one eye via intravitreal administration. The Safety Review Committee will review the 4 week safety data of each cohort before approving progression to the next dose level.

The primary endpoint of the study will be Treatment Emergent Adverse Events (TE-AEs) and Treatment Emergent Serious Adverse Events (TE-SAEs). The study will also collect data on exploratory efficacy endpoints to measure structural and functional changes in the patient's vision. These include, but are not limited to, standard visual acuity assessments, visual field sensitivity by Static Perimetry and Mitochondrial function. Detection of Apoptotic Retinal Cells (DARC) is also being used as an exploratory biomarker of disease progression with and without treatment.

Data collected from the exploratory efficacy endpoints, in conjunction with the data collected from the concurrent Natural History Study, will inform the design of the registrational study expected to commence in 2026.[5]

This SAD study forms the basis for the clinical trial pathway previously aligned with the US Food and Drug Administration (refer to ASX announcement 6 November 2023).

Figure 1. Schematic overview of the SAD study



About PYC-001 – a first-in-class drug candidate with disease-modifying potential in ADOA

ADOA is a blinding eye disease that begins in childhood and ultimately leads to legal blindness in middle age in most patients. The disease affects ~1 in every 35,000 people and is caused by insufficient expression of the *OPA1* gene in the retina.

There are currently no treatment options available for patients with ADOA which represents an estimated >$2 billion p.a. addressable market[6].

PYC-001 is a precision therapy that aims to restore the expression of the *OPA1* gene back to levels required for the normal function of the retina. PYC-001 utilises PYC's proprietary

[5] Assuming successful completion of SAD and Multiple Ascending Dose study and receipt of required regulatory approvals.
[6] Estimated market in Australian dollars based on a target patient population of 7,500 in the Western World and median orphan drug pricing of US$150,000 per patient per annum

drug delivery technology to overcome the major challenge for RNA drugs by ensuring that sufficient drug reaches its target inside the cells affected by ADOA. PYC-001 is effective at addressing the underlying cause of ADOA in both patient-derived 'retina in a dish' and Non-Human Primate models[7].

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**[8].

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[9]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024[10]

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[11]
- Now entering clinical trials with human safety and efficacy read-outs anticipated in 2024 and 2025[12]

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[13] that leads to renal failure and the need for organ transplantation in the majority of patients
- Clinical trials are expected to commence in early 2025 with human safety and efficacy data anticipated in 2025 and 2026[14]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[15]
- PYC will initiate Investigational New Drug (IND)-enabling studies in 2025 to facilitate progression into human trials

[7] Refer ASX announcement 4 October 2023
[8] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232
[9] Sullivan L, et al. Genomic rearrangements of the PRPF31 gene account for 2.5% of autosomal dominant retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2006;47(10):4579-88
[10] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[11] 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
[12] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[13] Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [Updated 2022 Sep 29]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews. Seattle (WA): University of Washington, Seattle; 1993-2023.
[14] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[15] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/

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 Board of PYC Therapeutics Limited

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