PYC Therapeutics

1 November 2024

FIRST ADOA PATIENT DOSED IN CLINICAL TRIAL

- **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 has recently progressed a drug candidate for the 1 in every 35,000 people[1] who suffer from a blinding eye disease called Autosomal Dominant Optic Atrophy (ADOA) into human trials[2]**
- **PYC has commenced a Single Ascending Dose (SAD) study in patients with ADOA to evaluate the safety/tolerability and efficacy profile of its drug candidate in this indication**
- **The first ADOA patient in this SAD trial has now received PYC's drug candidate**
- **This SAD study is scheduled to run for ~18 months and will:**
    - **provide initial insights on both the safety/tolerability and efficacy profile of this drug candidate in 1H 2025;**
    - **inform the design of a Multiple Ascending Dose (MAD) study scheduled to commence in 1H 2025; and**
    - **inform the design of a registrational trial (expected to commence in 2026) required for approval of this drug candidate with a New Drug Application planned for 2028[3]**

PERTH, Australia and SAN FRANCISCO, California – 1 November 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 an investigational drug candidate (known as PYC-001) that addresses the underlying cause of a blinding eye disease called Autosomal Dominant Optic Atrophy (ADOA). PYC-001 has previously attracted both Orphan Drug

[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 doi: 10.1016/j.ophtha.2009.12.038

[2] See ASX announcement of 15 August 2024

[3] Subject to the risks and uncertainties set out in the Company's ASX filings of 14 March 2024

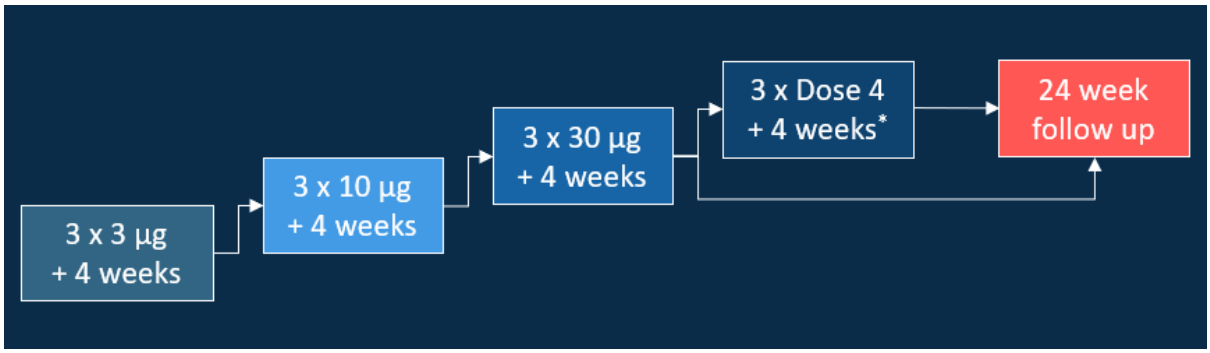
Designation[4] and Rare Pediatric Disease Designation[5] from the US Food and Drug Administration.

PYC today announces that the first ADOA patient enrolled in its Single Ascending Dose (**SAD**) study of PYC-001 has now received their initial dose of the drug candidate. The patient has received a 3 µg dose of PYC-001 in one eye via intravitreal administration.

Two more patients will be enrolled in this initial dose cohort and are expected to receive their first dose of PYC-001 soon.[6]

This is the second drug development program to utilise PYC's proprietary RNA conjugate platform to have advanced into human trials. The first program has recently provided positive safety and efficacy signals in patients with another form of blinding eye disease[7].

Figure 1. Schematic overview of the SAD study



*PYC may engage the regulator to discuss the inclusion of an additional dosing cohort (dose 4) in 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[8].

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 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[9].

[4] See ASX announcement of 24 May 2024
[5] See ASX announcement of 30 August 2024
[6] Refer ASX announcement 15 August 2024
[7] See ASX announcements of 5 and 12 August 2024
[8] 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
[9] Refer ASX announcement 4 October 2023

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**[10].

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[11]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024[12]

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[13]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024 and 2025[14]

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[15] 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[16]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[17]
- PYC will initiate Investigational New Drug (IND)-enabling studies in 2025 to facilitate progression into human trials

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,

[10] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232
[11] 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
[12] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[13] 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
[14] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[15] 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.
[16] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[17] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/

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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