PYC Therapeutics

10 July 2024

COMMENCEMENT OF RP11 MULTIPLE DOSE TRIAL

- **PYC has commenced a Multiple Ascending Dose (MAD) study to evaluate the safety and efficacy profile of its investigational drug candidate designed for patients with the blinding eye disease Retinitis Pigmentosa type 11 (RP11)**
- **PYC has progressed into this MAD study following recent positive results in a Single Ascending Dose (SAD) study of this drug candidate[1] in patients with RP11**
- **Patients in the MAD study will be assessed on both safety and efficacy endpoints after receiving repeat doses of the two highest doses of PYC's drug candidate that were established as being safe and well tolerated in the SAD study (30 µg and 75 µg per eye)[2]**
- **Safety and efficacy read-outs from the MAD are expected before the end of the year and will help inform the design of the registrational trial required to support a New Drug Application for this drug candidate[3] - expected to commence in 2025[4]**

PERTH, Australia and SAN FRANCISCO, California – 10 July 2024

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating precision therapies for patients with genetic diseases and no treatment options available. One of the Company's assets[5] is a first-in-class drug candidate currently progressing through a Phase 1 Single Ascending Dose (SAD) study for patients with a blinding eye disease called Retinitis Pigmentosa type 11 (RP11).

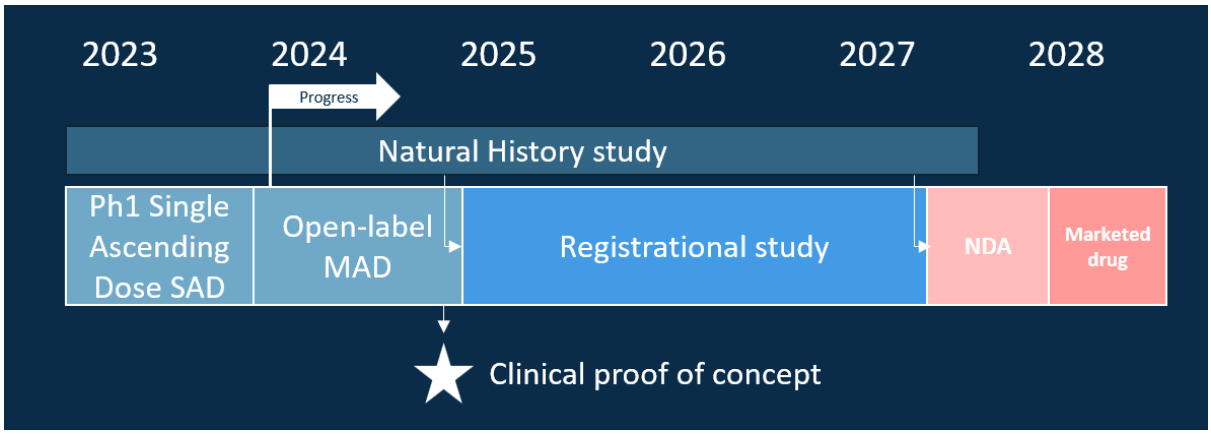
PYC today announces that it has completed dosing of the first patient with RP11 in a Multiple Ascending Dose (**MAD**) study of this investigational drug candidate (known as VP-001). This open-label trial will utilise doses of VP-001 that have been established as safe and well-tolerated in the Single Ascending Dose (**SAD**) study[6] and are anticipated to be in the therapeutic range.

The MAD study will assess the safety/tolerability and efficacy of VP-001 in the context of repeat dosing. Data from the SAD and MAD studies are expected to inform the design of

[1] See ASX announcements of 6 May 2024 and 1 July 2024
[2] See ASX announcement of 1 July 2024 and noting that PYC may add further doses (above 75 micrograms per eye) into the MAD study protocol at a later point in time
[3] Subject to the risks set out in the Company's ASX filing of 14 March 2024
[4] Subject to the risks set out in the Company's ASX filing of 14 March 2024
[5] PYC owns 96% of the VP-001 program in partnership with the Lions Eye Institute who own the remaining 4%
[6] See ASX announcement of 1 July 2024

a registrational trial that is set to commence in 2025[7] and is directed towards supporting a New Drug Application and commercial launch of VP-001. If successful, this would mark the first approved therapy within the major unmet need of RP11.

Figure 1: Clinical trial pathway for PYC's RP11 drug candidate[8]



The MAD study will be conducted in the USA across 5 sites and will involve intravitreal administration of VP-001 to a single study eye in participants over the age of 12 with confirmed *PRPF31* mutation-associated retinal dystrophy (RP11). The study is being conducted in accordance with Good Clinical Practices (GCP) and the VP-001 batch to be used in the study has been manufactured to Good Manufacturing Practice (GMP) standard.

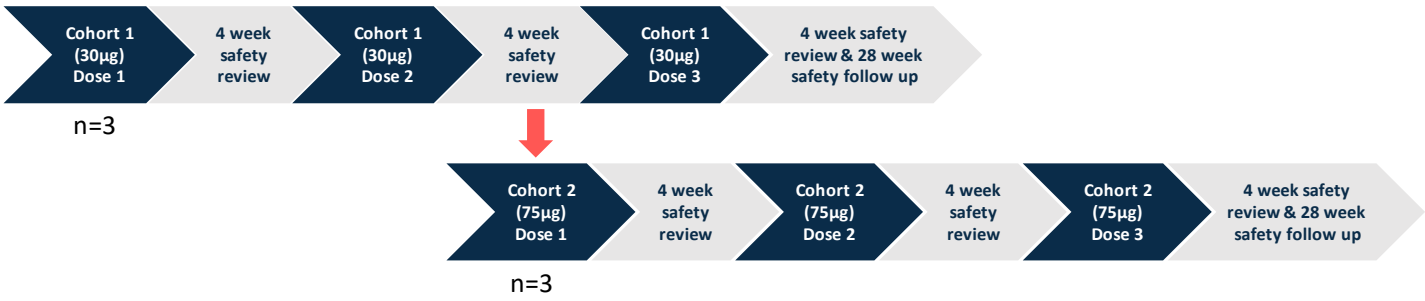
The study will consist of two cohorts (30µg and 75µg[9]) with each cohort consisting of 3 patients. Each patient will receive a total of 3 doses of the relevant dose for their cohort with doses administered 8 weeks apart. A Safety Review Committee (SRC) will meet 4 weeks after the completion of each dose to review the safety data collected from the study and approve progression to subsequent doses (both within and across cohorts).

The primary endpoints of the study are Treatment Emergent Ocular Adverse Events (TE-AEs) and Treatment Emergent Serious Adverse Events (TE-SAEs) in the study eye over a 52-week period. The 75µg dose cohort will commence upon review of the 4-week safety data of the second dose of the 30µg cohort in the MAD study. On completion of the last (3rd) dose for the cohort, patients will be followed for a 28-week safety follow up period.

Data will be collected for secondary and exploratory endpoints, including efficacy, to support the design of a proposed registrational study expected to commence in 2025[10].

[7] Subject to completion of current studies and regulatory approval
[8] Management forecast as of February 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.
[9] Commencement of 75µg dose cohort is subject to Safety Review Committee approval following 4 week follow up of 75µg single dose cohort in the SAD Phase 1 trial (Refer to ASX announcement of 24 April 2024) and SRC approval of dose 2 of the 30µg dose cohort in the MAD study. PYC may add a third cohort of patients in to the MAD at a dose above 75 micrograms per eye.
[10] Subject to the risks set out in the Company's ASX filing of 14 March 2024

Figure 2. Schematic overview of the open-label MAD study



The MAD study and the concurrent SAD study are expected to have concluded in 2025, at which time the Company will evaluate the safety/tolerability and efficacy profile of VP-001 before progressing into a registrational trial in the event of successful outcomes.

PYC's RP11 Program Overview

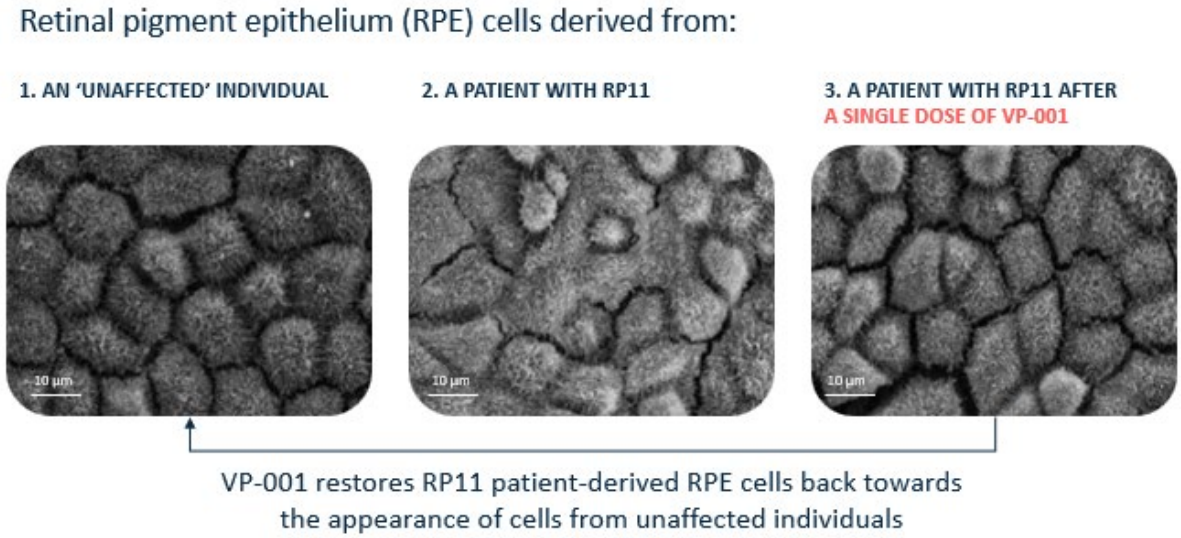
- Retinitis Pigmentosa type 11 (RP11) is a blinding disease of childhood affecting 1 in every 100,000 people
- RP11 is caused by a mutation in 1 copy of the *PRPF31* gene leading to a protein insufficiency in photoreceptor and Retinal Pigment Epithelial (RPE) cells
- VP-001 increases expression of *PRPF31* back to wild-type ('unaffected') levels in RP11 patient-derived retinal organoids and iPSC-RPE[11] (RPE grown from patients after turning a skin sample from the patient into an induced Pluripotent Stem Cell (iPSC) and then into the specific cell type in the eye that is affected by the disease to provide a human model of the disease-affected eye outside of a human)
- VP-001 is the first drug candidate to have progressed into human trials for RP11 and has been granted fast track status by the FDA[12]
- RP11 represents an estimated >$1 billion p.a. addressable market[13]

Pre-clinical data supporting PYC's RP11 drug candidate

- High Concentration in the Non-Human Primate (NHP) retina (>4,500 ng/g following a 30 µg dose)[14]
- Safe and well-tolerated in NHPs (No Observable Adverse Event Level of 50 µg /eye)[15]
- Effective in patient-derived models[16] (see Figure 2 below)

[11] See ASX Announcement of 7 October 2020
[12] FDA: US Food and Drug Administration. Refer to ASX announcement 2 August 2023
[13] Market valuation informed by patient prevalence (See: 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) and median orphan drug pricing of $150k p.a. (Evaluate Pharma. Orphan Drug Report. 2019)
[14] See ASX Announcement of 7 November 2022
[15] See ASX Announcement of 7 November 2022
[16] See ASX Announcement of 16 December 2020

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



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**[17].

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[18]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024[19]

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[20]
- Now entering clinical trials with human safety and efficacy read-outs anticipated in 2024 and 2025[21]

[17] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232
[18] 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
[19] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[20] 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
[21] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[22] 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[23]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[24]
- 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, 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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[22] 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.
[23] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[24] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/