PYC Therapeutics

23 July 2024

EXTENSION OF RP11 SINGLE DOSE STUDY INTO MULTIPLE DOSE FORMAT

- **PYC is developing the only clinical-stage investigational drug candidate designed for patients with the blinding eye disease Retinitis Pigmentosa type 11 (RP11)**
- **PYC today announces that it has received Institutional Review Board (IRB) approval to extend the ongoing Single Ascending Dose (SAD) study in patients with RP11 into an open-label 'Part B' under which patients will receive multiple doses of PYC's investigational drug candidate**
- **This IRB approval enables PYC to increase the number of patients for whom safety and efficacy data will be available following repeat doses of the drug candidate[1]**
- **A protocol amendment in support of the Part B SAD extension was submitted to the US Food and Drug Administration in June**
- **Data read-outs from the SAD (including the part B extension study) and the ongoing 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[2] - anticipated to commence in 2025[3]**

PERTH, Australia and SAN FRANCISCO, California – 23 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[4] is a first-in-class drug candidate currently progressing through both a Single Ascending Dose (SAD) study and a Multiple Ascending Dose (MAD) study for patients with a blinding eye disease called Retinitis Pigmentosa type 11 (RP11).

PYC today announces that it has received approval from the Institutional Review Board (IRB) governing its ongoing clinical trials in RP11 to allow patients who have received a single dose of the drug candidate in the existing SAD study to rollover into an open-label extension arm of this study (known as Part B of the SAD) under which they will receive multiple doses of PYC's drug candidate.

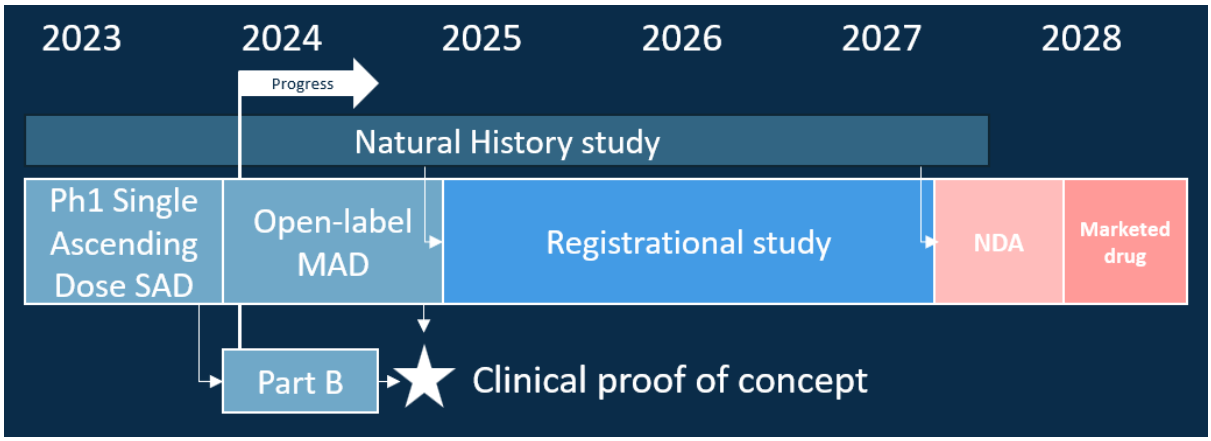
[1] Subject to the risks set out in the Company's ASX filing of 14 March 2024
[2] Subject to the risks set out in the Company's ASX filing of 14 March 2024
[3] Subject to the risks set out in the Company's ASX filing of 14 March 2024
[4] PYC owns 96% of the VP-001 program in partnership with the Lions Eye Institute who own the remaining 4%

The important details associated with extension of the SAD study into Part B include:

- **Dose**: Patients enrolling in this study will receive either 30 micrograms or 75 micrograms of the drug candidate in the previously treated eye as their repeat dose in Part B of the SAD;
- **Dose interval**: Patients are currently scheduled to receive two further doses of the drug candidate under Part B of the SAD, including:
    - a second dose of the drug candidate as close as possible to a 12-week dosing interval from their original dose (in the SAD study);
    - a third dose of the drug candidate ~8 weeks after the second dose (in Part B of the SAD study);
- **Endpoints**: Patients will be assessed on both safety/tolerability and efficacy endpoints throughout the course of the study; and
- **Read-outs**: Data from Part B of the SAD is expected before the end of the year.

This approval will enable PYC to expand the number of patients for whom safety and efficacy data will be available following repeat doses of the drug candidate. Data from the SAD, Part B extension study and the ongoing MAD is expected to inform the design of a registrational trial that is set to commence in 2025[5] 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[6]



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[7] (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)

[5] Subject to completion of current studies and regulatory approval
[6] 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.
[7] See ASX Announcement of 7 October 2020

- 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[8]

- RP11 represents an estimated >$1 billion p.a. addressable market[9]

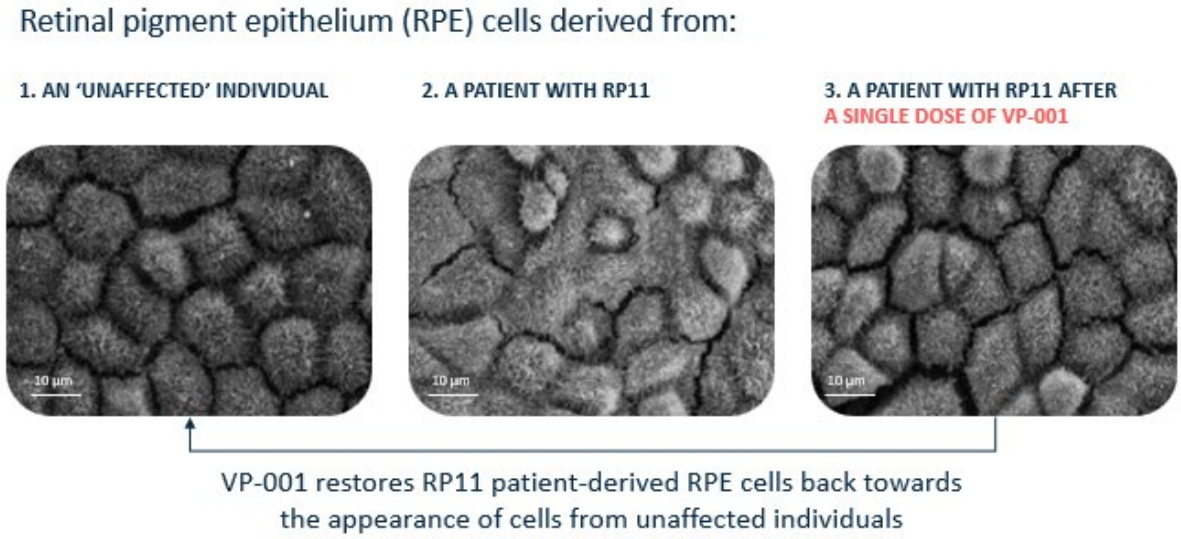
Pre-clinical data supporting PYC's RP11 drug candidate

- High Concentration in the Non-Human Primate (NHP) retina (>4,500 ng/g following a 30 µg dose)[10]

- Safe and well-tolerated in NHPs (No Observable Adverse Event Level of 50 µg /eye)[11]

- Effective in patient-derived models[12] (see Figure 2 below)

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**[13].

[8] FDA: US Food and Drug Administration. Refer to ASX announcement 2 August 2023
[9] 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)
[10] See ASX Announcement of 7 November 2022
[11] See ASX Announcement of 7 November 2022
[12] See ASX Announcement of 16 December 2020
[13] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[14]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024[15]

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[16]
- Now entering clinical trials with human safety and efficacy read-outs anticipated in 2024 and 2025[17]

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[18] 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[19]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[20]
- 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.

[14] 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

[15] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

[16] 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

[17] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

[18] 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.

[19] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

[20] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/

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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