

VISION IMPROVEMENT IN MULTIPLE RP11 PATIENTS

- **PYC is developing the only clinical-stage investigational drug candidate designed specifically for patients with the blinding eye disease Retinitis Pigmentosa type 11 (RP11)**
- **The Company recently reported an improvement in vision in 2 patients with RP11 after they received a single 30 microgram dose of this drug candidate (known as VP-001)¹**
- **PYC today announces an improvement in vision in 2 additional patients with RP11 after they received a single 75 microgram dose of VP-001²**
- **PYC will announce further results from the ongoing multiple dose studies of VP-001 in Q4 2024³**
- **PYC is now preparing for a registrational trial (scheduled to commence next year) that will be designed to support a new drug application and commercial launch of this drug candidate⁴**

PERTH, Australia and SAN FRANCISCO, California – 12 August 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 assets⁵ is a drug candidate (known as VP-001) currently progressing through multiple concurrent clinical trials in patients with a blinding eye disease called Retinitis Pigmentosa type 11 (RP11).

Vision improvement in multiple RP11 patients in SAD cohort 4

PYC today announces results for the 3 patients enrolled in cohort 4 of the ongoing Single Ascending Dose (SAD) study at 3-months of follow-up. These 3 patients received a single 75 microgram dose of VP-001 in their worst affected eye.

Two out of the three RP11 patients in this cohort had enhanced retinal sensitivity across the entire macula at 3 months of follow up when compared to baseline⁶. The macula is an important part of the retina that is densely populated by photoreceptors (the specialised

¹ As assessed by microperimetry – see ASX announcement of 5 August 2024 for further details

² As assessed by microperimetry – see the body of this announcement for further details

³ See ASX announcements of 23 July and 10 July for details on the part B extension of the SAD study and the MAD study respectively

⁴ Subject to the risks and uncertainties set out in the Company's ASX disclosures 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 As assessed by whole grid sensitivity on microperimetry and compared to the relevant patient's baseline

cells that create the visual signal) and is responsible for central vision, most colour-vision and our ability to perceive fine visual details.

Figure 1. Correlation between sensitivity on microperimetry (measured in dB) and fold-change in sensitivity to light⁷

Decibel change (dB)	1	2	3
Fold-change in sensitivity to light (intensity of stimulus luminance)	1.26	1.6	2.0

The results include:

- A +1.1 dB improvement over baseline as assessed by whole-grid mean retinal sensitivity in patient 1 at 3-months of follow-up (the change in the treated eye over this time-period also outperformed the change in the untreated eye by +2.1 dB);
- A +1.0 dB improvement over baseline as assessed by whole-grid mean retinal sensitivity in patient 2 at 3-months of follow-up (the change in the treated eye over this time-period also outperformed the change in the untreated eye by +0.3 dB); and
- The third patient in cohort 4 of the SAD study has mutations in two different genes responsible for causing Retinitis Pigmentosa⁸. This patient saw disease progression in both the treated and the untreated eye at 3 months of follow-up⁹.

SAD cohort 4 - part B extension study enrolment

All three patients from cohort 4 in the SAD have enrolled in the part B extension study and will receive multiple doses of VP-001 (75 micrograms in the study eye).

Patient 1 was the first patient to enrol in the part B extension study and has already received a second dose of the drug candidate in their study eye¹⁰.

Patient 2 has enrolled in the extension study and their second dose is currently being scheduled.

Patient 3 (who has not seen a quantifiable visual functional improvement on microperimetry assessment) is reporting visual functional improvement in the VP-001 treated eye and has consequently enrolled in the part B extension study. This patient has now received their second dose of VP-001.

Additional data point for SAD patient cohort 3

The third patient in cohort 3 of the SAD (whose results were not included in the announcement of 5 August because they did not undergo microperimetry assessment at 3-4 months post-dosing) has now completed their 6-month follow-up visit including assessment on microperimetry. The results show a marginally slower rate of disease progression in the treated eye (-0.5 dB) when compared to the untreated eye (-0.7 dB) on whole grid mean retinal sensitivity at this time-point.

⁷ See section 2.1.1 from Pfau et. al. Fundus controlled perimetry (microperimetry): Application as outcome measure in clinical trials in Progress in Retinal and Eye Research. Volume 82, May 2021, 100907

⁸ The third patient in cohort 4 of the SAD has mutations in both *PRPF31* (causing RP type 11) and *USH2A* (causing Usher's Syndrome)

⁹ As assessed by whole grid mean retinal sensitivity on microperimetry

¹⁰ See ASX announcement of 5 August 2024

SAD cohort 3 - part B extension study enrolment

Patients 1 and 2 in cohort 3 of the SAD have now also enrolled in the part B extension study and scheduling for their second dose of VP-001 (30 micrograms) in their study eye is in progress.

Data from visual functional assessment in all 5 patients enrolled in the part B extension of the SAD study after multiple doses of VP-001 is anticipated in Q4¹¹.

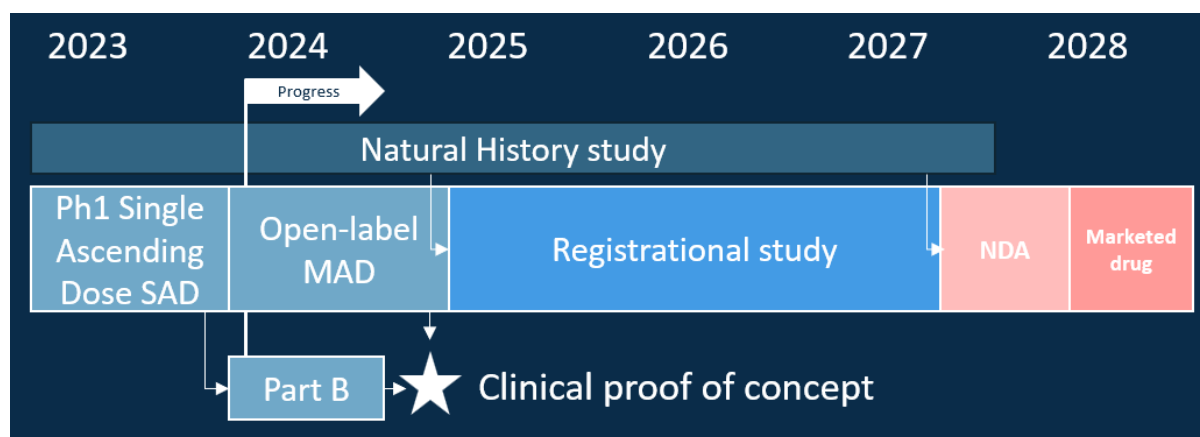
Upcoming data read-outs in repeat dose studies

PYC is seeking to establish clinical proof of concept for VP-001 through its ongoing clinical trials in patients with RP11. Multiple patient cohorts will progress through the visual functional assessments required to reach this milestone through the remainder of 2024 including:

- i) patients enrolled in the Part B extension of the SAD study¹²; and
- ii) patients enrolled in the concurrent Multiple Ascending Dose (MAD) study¹³.

Successful realisation of this objective will lead to initiation of a registrational trial for this drug candidate in 2025¹⁴ directed towards supporting regulatory approval and market launch of the first potential therapy for patients with RP11.

Figure 2. Clinical trial pathway for PYC’s RP11 drug candidate¹⁵



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-RPE¹⁶ (RPE grown from patients

¹¹ Subject to all of the risks and uncertainties outlined in the Company's presentation of 14 March 2024

¹² See ASX announcement of 23 July 2024 for details on the Part B extension of the SAD study

¹³ See ASX announcement of 10 July 2024 for details on the MAD study

¹⁴ Subject to the risks outlined in the Company's ASX disclosures of 14 March 2024

¹⁵ Management forecast as of July 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.

¹⁶ See ASX Announcement of 7 October 2020

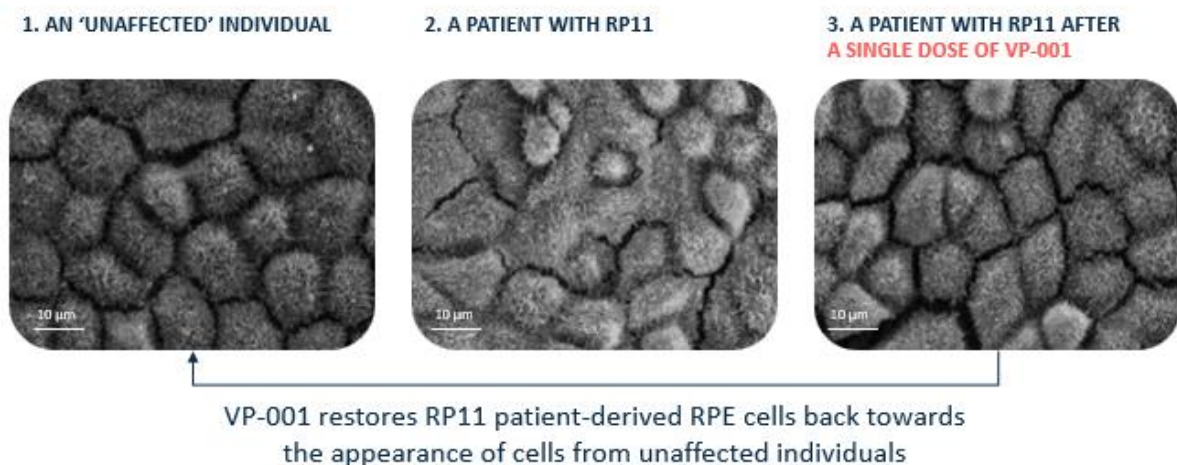
after turning a skin sample from the patient into an induced Pluripotent Stem Cell (iPSC) and then into the specific cell type in the eye that is affected by the disease to provide a human model of the disease-affected eye outside of a human)

- VP-001 is the first drug candidate to have progressed into human trials for RP11 and has been granted fast track status by the FDA¹⁷
- RP11 represents an estimated >\$1 billion p.a. addressable market¹⁸

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)¹⁹
- Safe and well-tolerated in NHPs (No Observable Adverse Event Level of 50 µg /eye)²⁰
- Effective in patient-derived models²¹ (see Figure 3 below)

Figure 3. VP-001 is effective in patient-derived models
Retinal pigment epithelium (RPE) cells derived from:



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**²².

¹⁷ FDA: US Food and Drug Administration. Refer to ASX announcement 2 August 2023

¹⁸ 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)

¹⁹ See ASX Announcement of 7 November 2022

²⁰ See ASX Announcement of 7 November 2022

²¹ See ASX Announcement of 16 December 2020

²² Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank
<https://doi.org/10.1101/2020.11.02.2022232>

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people²³
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024²⁴

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people²⁵
- Now entering clinical trials with human safety and efficacy read-outs anticipated in 2024 and 2025²⁶

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people²⁷ 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 2026²⁸

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people²⁹
- 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.

²³ 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

²⁴ Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

²⁵ 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

²⁶ Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

²⁷ Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [Updated 2022 Sep 29]. In: Adam MP, Feldman J, Mirzazadeh GM, et al., editors. GeneReviews. Seattle (WA): University of Washington, Seattle; 1993-2023.

²⁸ Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

²⁹ 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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