PYC Therapeutics

5 August 2024

RP11 CLINICAL TRIAL UPDATE

- **PYC is developing the only clinical-stage investigational drug candidate designed for patients with the blinding eye disease Retinitis Pigmentosa type 11 (RP11)**
- **The Company previously presented encouraging early data demonstrating visual functional improvement in one RP11 patient 2-months after receiving a single dose of its drug candidate at the Association for Research in Vision and Ophthalmology conference in May[1]**
- **PYC today announces that:**
    - **The visual function in this patient has further improved at 4-months of follow-up[2];**
    - **A second patient from the same cohort (cohort 3) in the Single Ascending Dose (SAD) study has demonstrated an improvement in visual function at the same time point (4-months post dosing); and**
    - **Both patients have reached the threshold that is considered to be 'clinically significant' on this endpoint by the US Food and Drug Administration in the context of blinding eye diseases[3]**
- **Data from patients receiving a single higher dose of PYC's drug candidate will be generated in Q3 2024**
    - **Patient cohort 4 (75 microgram dose) in the SAD study will progress through the 3-month[4] visual function assessment in August**
- **Data from patients receiving multiple doses of PYC's drug candidate will start to be generated in Q3 and Q4 2024**
    - **The first patient enrolled in part B of the SAD study has now received their second dose of the drug candidate**

[1] See ASX announcement of 6 May 2024

[2] See Figure 1 and Figure 2 in this announcement for details on the week-15 time-point assessment for this patient

[3] Note that the FDA require this threshold to be reached in the context of pre-specified microperimetry grid points (which PYC has not done in this study) and at multiple timepoints - this will be the focus of PYC's repeat dose clinical trials in RP11. See 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 for further details and the discussion below under the heading 'Multiple patient responses – SAD cohort 3 (30 microgram dose)'

[4] PYC has now standardised the timing of microperimetry follow-up for patients enrolled in the SAD at 12-weeks after dosing to enable these patients to enrol in the recently announced part B extension of the SAD

- **Initial dosing of cohort 1 (30 microgram dose) in the Multiple Ascending Dose (MAD) study was completed in July and dosing in cohort 2 (75 microgram dose) in the MAD study is scheduled to commence in September 2024[5]**

- **PYC's near-term objective in the RP11 program is to establish clinical 'proof of concept' through these read-outs prior to initiation of a registrational study in 2025[6] that is directed towards enabling commercial launch of this drug candidate**

PERTH, Australia and SAN FRANCISCO, California – 5 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 assets[7] 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). These trials include a:

- Single Ascending Dose (SAD) study with an open-label repeat dose extension arm (part B of the SAD); and
- Multiple Ascending Dose (MAD) study.

Durability of response following a single dose of PYC's investigational drug candidate (SAD cohort 3 – 30 microgram dose)

PYC today announces that the improvement in retinal sensitivity observed 2-months after a single dose of PYC's drug candidate in one patient in cohort 3 of the SAD[8] has further improved at 4-months of follow up[9]. Visual functional improvement has been observed on microperimetry assessment across two dimensions in this patient:

1) A reduction in the number of points within the microperimetry grid that are not able to detect light stimuli at any frequency (known as 'scotomas'); and

2) The mean sensitivity to light detection of the points within the microperimetry grid that are immediately adjacent to a scotoma (known as 'Functional Transition Points')[10].

Figure 1. Microperimetry heatmap demonstrating a decrease in the number of central scotomas present in this patient following treatment with VP-001. The 4 central scotomas (coloured in black) present at baseline have decreased to 2 at 2-months of follow up and 1 at 4-months of follow-up.

[5] Subject to the risks set out in the Company's ASX disclosures of 14 March 2024
[6] Subject to the risks set out in the Company's ASX disclosures of 14 March 2024
[7] PYC owns 96% of the VP-001 program in partnership with the Lions Eye Institute who own the remaining 4%
[8] See ASX announcement of 6 May 2024
[9] See Figure 1 and Figure 2 in this announcement for details on the week-15 time-point assessment for this patient
[10] PYC imposes an additional criteria on Functional Transition Points in that they must score less than or equal to 12dB at baseline to be included in the assessment to avoid the 'ceiling effect'

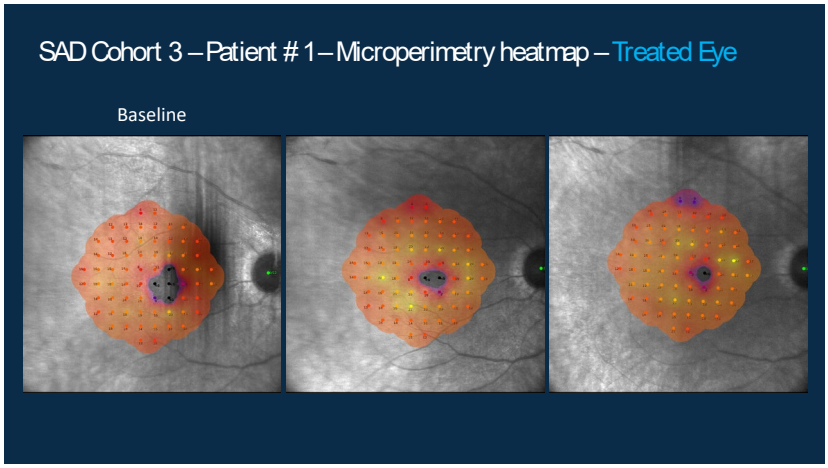


Figure 2. Change from baseline in the number of scotomas within the microperimetry grid in the VP-001 treated eye compared to the untreated eye over time - Patient #1 in cohort 3.

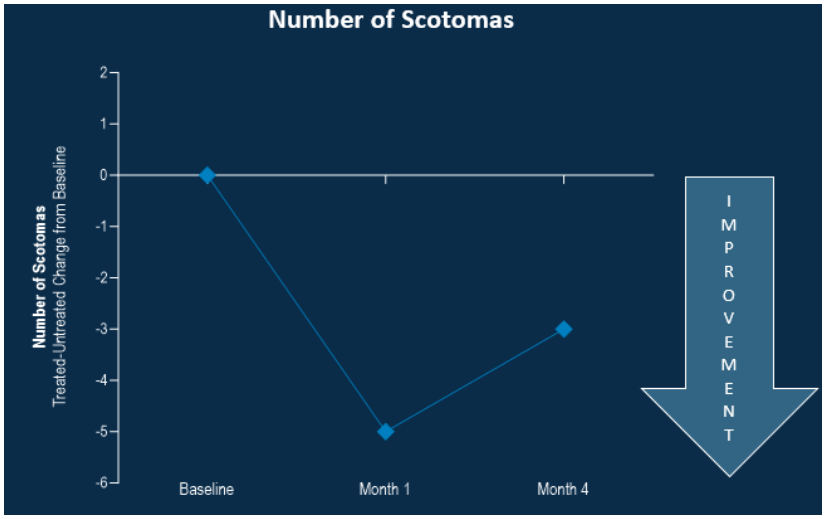
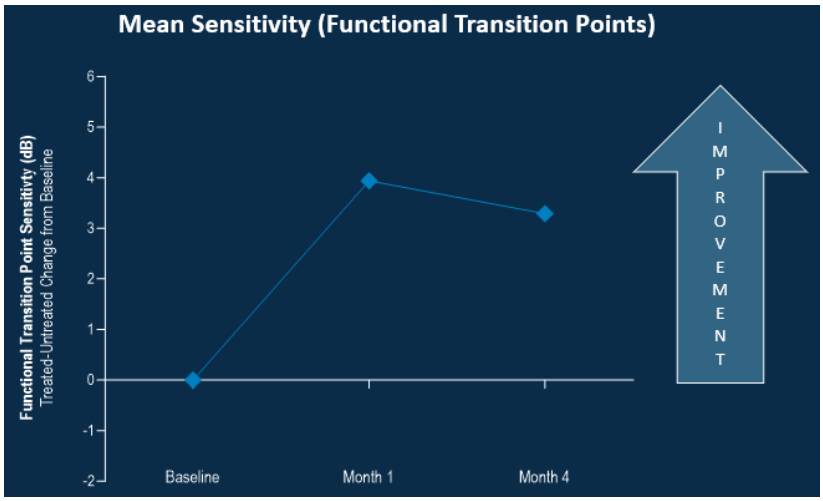


Figure 3. Mean sensitivity of Functional Transition Points within the microperimetry grid in the VP-001 treated eye when compared to the untreated eye over time - Patient #1 in cohort 3.



Data from the 2-month follow-up assessment of this patient was presented at the Association for Research in Vision and Ophthalmology conference in Seattle in May[11].

Multiple patient responses (SAD cohort 3 – 30 microgram dose)

A second patient from cohort 3 of the SAD has now completed a visual functional assessment at 4-months post-dosing[12] and has also demonstrated improved visual function in the treated eye[13].

Figure 4. Change from baseline in the number of scotomas within the microperimetry grid in the VP-001 treated eye compared to the untreated eye over time - Patient #2 in cohort 3.

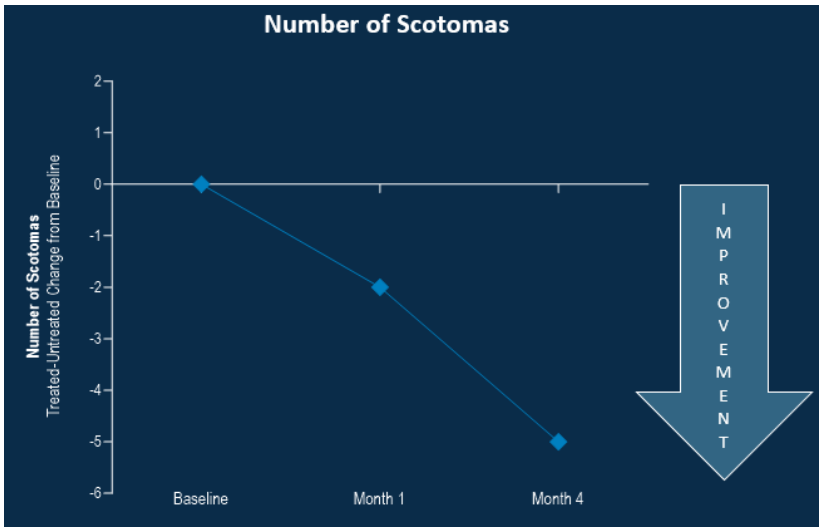
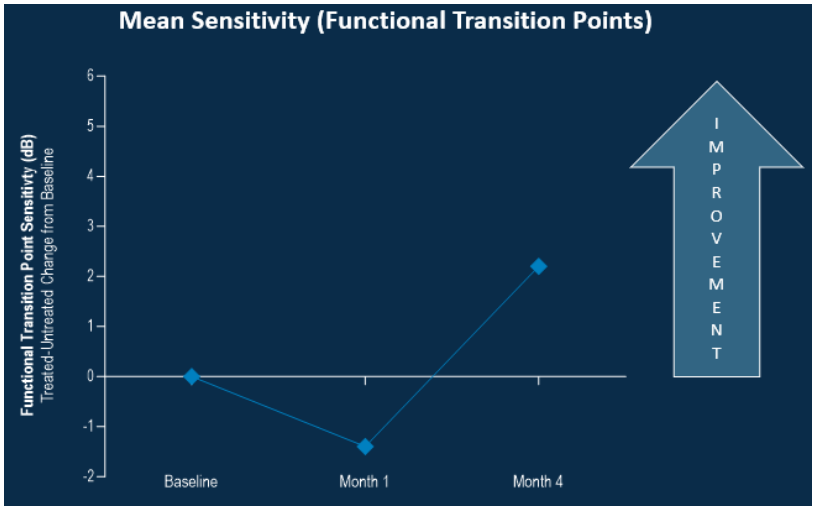


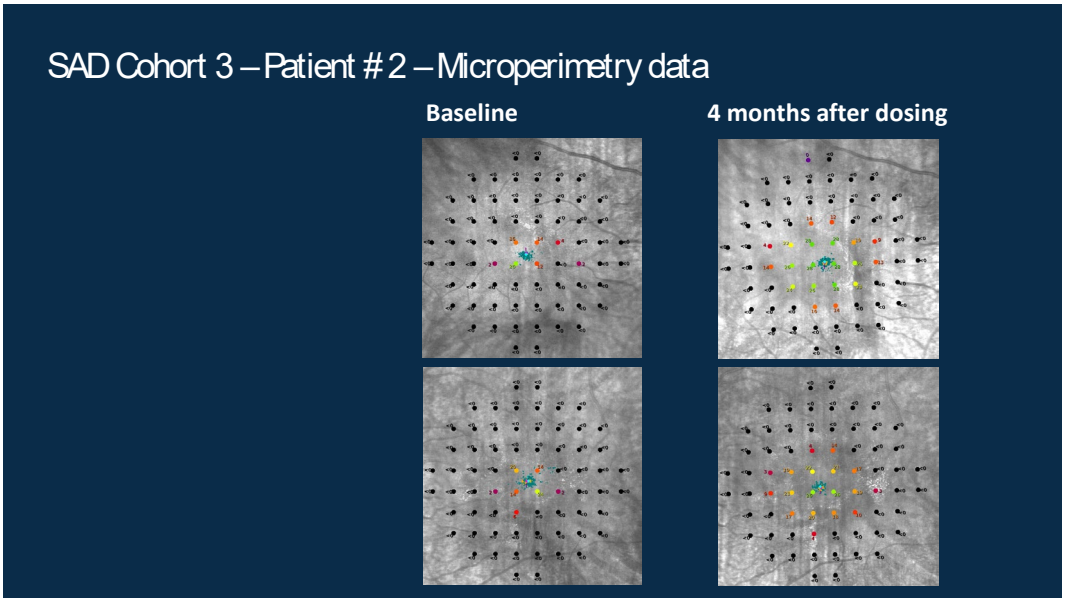
Figure 5. Mean sensitivity of Functional Transition Points within the microperimetry grid in the VP-001 treated eye when compared to the untreated eye over time - Patient #2 in cohort 3.



[11] See ASX announcement of 6 May 2024
[12] See Figure 3 and Figure 4 in this announcement for details on the week-16 time-point assessment for this patient
[13] Assessed by microperimetry – see Figures 4, 5 and 6

The FDA has previously issued guidance on the extent of improvement required on microperimetry assessment to be considered clinically meaningful in the context of blinding eye diseases[14]. Both patients in cohort 3 of the SAD described here have exceeded these criteria[15].

Figure 6. Microperimetry data for patient 2 in cohort 3 of the SAD at 4 months of follow-up post dosing with VP-001



PYC's CEO, Dr. Rohan Hockings, commented on this data: "*It is exciting to see VP-001's ability to address the root cause of RP11 in 'retina in a dish' models now translating to improved visual function in RP11 patients*".

First patient receives multiple doses of VP-001 (SAD part B)

PYC also advises that it has completed repeat dosing of the first patient in part B of the SAD study. The first patient to enrol in cohort 4 of the SAD study has completed their 12-week evaluation following their first dose of VP-001 and has now enrolled in the part B extension of the SAD. This patient has received their second 75 microgram dose of VP-001 in their study eye marking the first patient to have received multiple doses of this drug candidate.

Upcoming data read-outs (SAD cohort 4 and 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 in cohort 4 of the SAD study[16] who will progress through a 3-month visual function assessment in July and August;

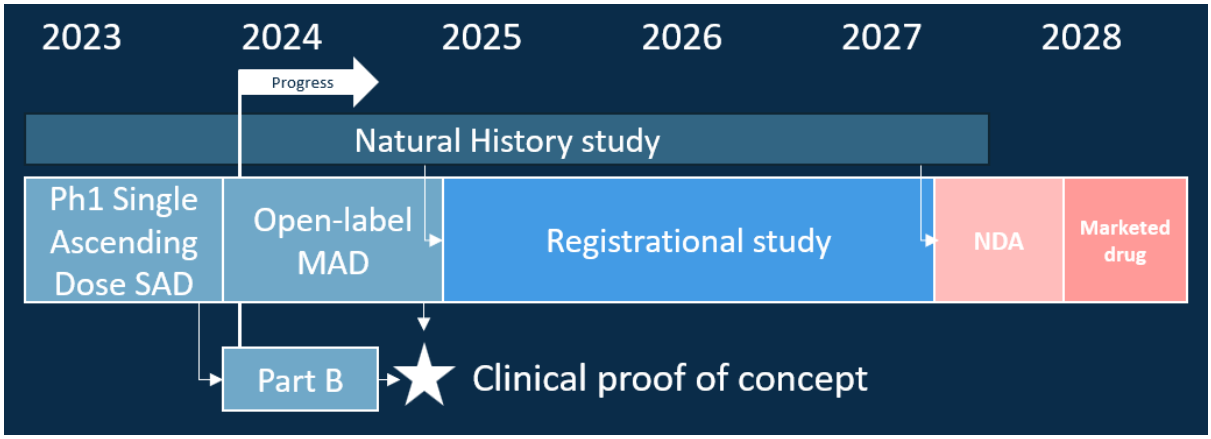
[14] See footnote 3 for further detail and section 2.4.7 in Pfau et. al. Fundus-controlled perimetry (microperimetry): Application as outcome measure in clinical trials in Progress in Retinal and Eye Research. Volume 82, May 2021, 100907
[15] See ASX announcement of 6 May 2024 in relation to patient 1 and Figure 5 in relation to patient 2
[16] See ASX announcement of 16 May 2024

ii) patients enrolling in the Part B extension of the SAD study[17] (visual function assessment over multiple time-points is expected for these patients in Q3 and Q4); and

iii) patients enrolled in the MAD study[18] (visual function assessment over multiple time-points is expected for these patients in Q4).

Successful realisation of this objective will lead to initiation of a registrational trial for this drug candidate in 2025[19] directed towards supporting regulatory approval and market launch of the first potential therapy for patients with RP11.

Figure 7. Clinical trial pathway for PYC's RP11 drug candidate[20]



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[21] (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[22]

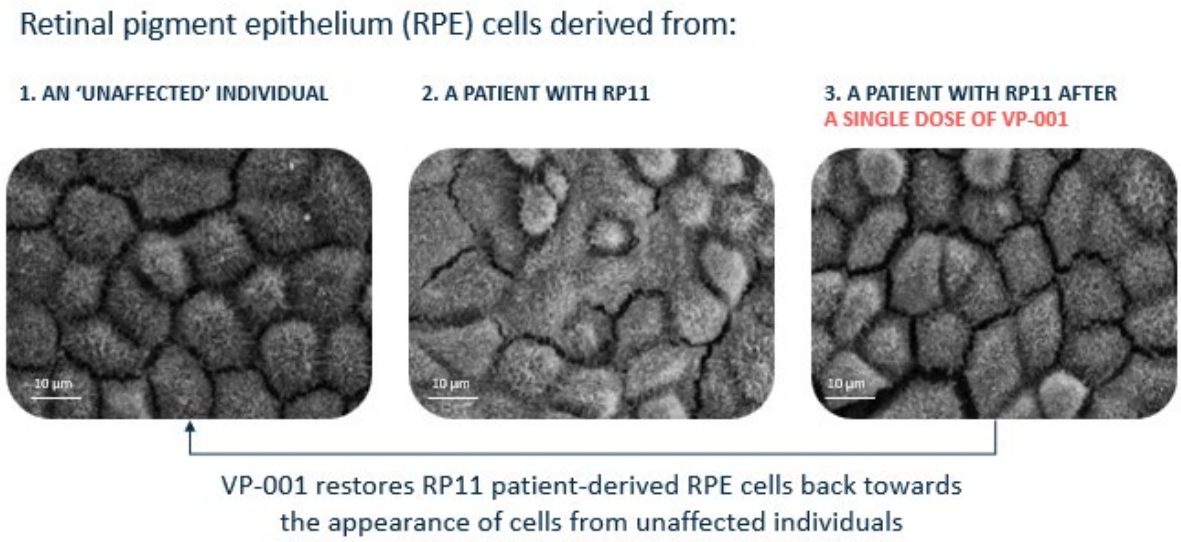
- RP11 represents an estimated >$1 billion p.a. addressable market[23]

[17] See ASX announcement of 23 July 2024 for details on the Part B extension of the SAD study
[18] See ASX announcement of 10 July 2024 for details on the MAD study
[19] Subject to the risks outlined in the Company's ASX disclosures of 14 March 2024
[20] 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.
[21] See ASX Announcement of 7 October 2020
[22] FDA: US Food and Drug Administration. Refer to ASX announcement 2 August 2023
[23] 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)

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)[24]
- Safe and well-tolerated in NHPs (No Observable Adverse Event Level of 50 µg /eye)[25]
- Effective in patient-derived models[26] (see Figure 8 below)

Figure 8. 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**[27].

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[28]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024[29]

[24] See ASX Announcement of 7 November 2022
[25] See ASX Announcement of 7 November 2022
[26] See ASX Announcement of 16 December 2020
[27] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232
[28] 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
[29] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[30]
- Now entering clinical trials with human safety and efficacy read-outs anticipated in 2024 and 2025[31]

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[32] 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[33]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[34]
- 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

[30] 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

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

[32] 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.

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

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

CONTACTS:

INVESTORS and MEDIA
info@pyctx.com