PYC Therapeutics

1 July 2024

RP11 DRUG CANDIDATE SAFE AND WELL TOLERATED

- **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 is currently conducting clinical trials of the first drug candidate with disease-modifying potential in a blinding eye disease of childhood called Retinitis Pigmentosa type 11 (RP11)**
- **Four cohorts of patients have now been dosed with this drug candidate in a Single Ascending Dose (SAD) study with no evidence of Treatment Emergent Serious Adverse Events in any patient at 4-weeks of follow up post-dosing**
- **Importantly, there were no Treatment Emergent Adverse Events of any nature in patients in cohort #4 of the SAD who received the highest dose of PYC's investigational drug candidate (75 micrograms per eye)**
- **PYC is now progressing this drug candidate into a Multiple Ascending Dose (MAD) study with the two highest doses from the SAD expected to be utilised in the MAD[1]**
- **Successful results in the SAD and MAD trials will lead to initiation of a registrational trial in 2025 aimed at supporting the first New Drug Application in Retinitis Pigmentosa type 11[2]**

PERTH, Australia and SAN FRANCISCO, California – 1 July 2024

PYC Therapeutics Limited (ASX:PYC) (**PYC** or the **Company**) today announces that the Safety Review Committee (SRC) governing the Company's Single Ascending Dose (SAD) study in patients with Retinitis Pigmentosa type 11 (RP11) has met and reviewed the 4-week safety data from patient cohort #4 and recommended continuing with the clinical trial as planned.

Each patient in cohort #4 received a single 75 µg intravitreal dose of PYC's investigational drug candidate for RP11 (known as VP-001) in one eye. VP-001 was considered safe and well-tolerated at 4-weeks of follow up in all four patient cohorts who have received the drug to date with no evidence of Treatment Emergent Serious Adverse Events (TE-SAEs).

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

Importantly, there were also no Treatment Emergent Adverse Events (TE-AEs) in any patient in cohort 4 of the SAD.

"*We are very pleased to have now established a clean safety profile for VP-001 across multiple doses that we anticipate having therapeutic activity*" commented PYC's CEO Dr. Rohan Hockings. "*Not only does this enable us to progress to a multiple dose study in RP11 with high conviction but it also has important read-through implications for the remainder of our ocular pipeline as this is the first time the RNA conjugate modality has ever been used in a human eye*."

PYC will now progress to a Multiple Ascending Dose (MAD) study with the two highest doses established as being safe and well-tolerated in the SAD (30 and 75 µg respectively) to be administered in a repeat dose format in the MAD. The Company anticipates dosing cohort #1 (30 micrograms of VP-001) in the MAD study in July. Progression to cohort #2 (75 micrograms of VP-001) in the MAD will commence after patients in cohort #1 have received multiple doses of the drug candidate[3].

PYC is currently evaluating a further dose escalation of VP-001 in the context of the safety/tolerability profile of this drug candidate observed to date. The Company will make a final decision as to whether to include higher doses (above 75 micrograms) of VP-001 in the MAD after reviewing both the safety and efficacy data that will be generated in the SAD and MAD studies through H2 2024.

Both studies 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.

This announcement was approved for release by the Board of PYC Therapeutics Limited.

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**[4].

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[5]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2024[6]

[3] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[4] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232
[5] 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
[6] 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[7]
- Now entering clinical trials with human safety and efficacy read-outs anticipated in 2024 and 2025[8]

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[9] 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[10]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[11]
- 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.

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[7] 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
[8] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[9] 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.
[10] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[11] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/