PYC Therapeutics

5 November 2024

RP11 SAFETY REVIEW COMMITTEE APPROVES DOSE ESCALATION TO FINAL PATIENT COHORT

- **PYC is developing the first drug candidate (VP-001) for a blinding eye disease of childhood called Retinitis Pigmentosa type 11 (RP11)**
- **PYC has two ongoing multiple dose studies of VP-001 in patients with RP11:**
    - **An open label extension to the Single Ascending Dose (SAD) study; and**
    - **A Multiple Ascending Dose (MAD) study.**
- **RP11 patients enrolled in both ongoing Phase 1/2 studies have seen disease progression arrested and improved vision following treatment with VP-001[1]**
- **PYC today announces that the Safety Review Committee governing the MAD study has approved escalation in dosing to the final patient cohort (75 mcg) in this trial**
- **PYC expects to have data from all patients enrolled in these multiple dose studies available in Q1 2025 prior to engaging with the FDA on the design of the registrational study required to support a New Drug Application for VP-001[2]**

PERTH, Australia and SAN FRANCISCO, California – 5 November 2024

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating first in class precision therapies for patients with genetic diseases and no treatment options available. One of the Company's assets[3] is a drug candidate (known as VP-001) that addresses the underlying cause of a blinding eye disease called Retinitis Pigmentosa type 11 (RP11).

PYC today announces that the Safety Review Committee (SRC) governing the Company's ongoing multiple dose studies in patients with RP11 has met to review the safety/tolerability profile of VP-001 in patients who have received repeat doses of the drug candidate. Following a review of the data, the SRC has approved escalation in dosing to the final patient cohort in these combined phase 1/2 studies. Patients in the 75 mcg cohort

[1] As assessed by both microperimetry and Low Luminance Visual Acuity - See ASX announcements of 5 August, 12 August, 22 and 31 October 2024
[2] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 14 March 2024
[3] PYC owns 96.2% of VP-001 with the remaining 3.8% owned by the Lions Eye Institute

of the Multiple Ascending Dose (MAD) study can now be enrolled in the trial and are expected to receive their first dose of VP-001 before the end of the month.

Importantly, patients in the open label extension of the Single Ascending Dose (SAD) study have already progressed to repeat dosing at the 75 mcg dose and there have been no Treatment Emergent-Serious Adverse Events (TE-SAEs) in patients who have now received three 75 mcg doses of VP-001[4].

Data from this final patient cohort in the MAD study at 8 and 12 weeks of follow up is expected to be available in Q1 2025 and will help inform an engagement with the US Food and Drug Administration (FDA) on the design of the registrational study required to support a New Drug Application for VP-001[5].

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[6] (RPE cells 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 and orphan drug status by the FDA[7]

- RP11 represents an estimated >$1 billion p.a. addressable market[8]

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 RNA therapeutic class. PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**[9].

The Company has multiple ongoing clinical trials and is set to deliver human efficacy data for first-in-class drugs with disease modifying potential across multiple indications within the coming 12 months. The Company's existing drug development pipeline includes four programs addressing indications affecting 1 in every 1,000 people. PYC continues to conduct drug discovery activities to scale its platform technology into additional diseases of the eye, central nervous system, kidney and beyond.

[4] As at the date of this announcement. See also ASX announcement of 22 October 2024
[5] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 14 March 2024
[6] See ASX Announcement of 7 October 2020
[7] FDA: US Food and Drug Administration. Refer to ASX announcements of 2 August 2023 and 21 October 2024
[8] 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)
[9] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

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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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