PYC Therapeutics

29 April 2024

RP11 DRUG CANDIDATE SAFE AND WELL TOLERATED – PROGRESSING TO MID-STAGE HUMAN TRIALS

- **PYC is conducting a Single Ascending Dose (SAD) study of the first investigational drug candidate to have progressed to human trials in a blinding eye disease of childhood called Retinitis Pigmentosa type 11 (RP11)**
- **The Safety Review Committee (SRC) governing this clinical trial has met to review the data for the 3 patient cohorts who have received PYC's drug candidate to date**
- **All 3 doses have been determined to be safe and well tolerated by the SRC – opening up a pathway for PYC to:**
    - **initiate a Multiple Ascending Dose (MAD) study now that the dose at which RP11 patients are expected to derive a benefit from this drug candidate has been reached; and**
    - **continue to escalate dosing in the SAD to identify the dose at which RP11 patients derive maximum benefit from the drug candidate prior to initiation of a registrational trial[1]**
- **PYC expects to commence the MAD study in Q2 2024[2]**
- **The Company has amended the SAD protocol to allow for higher dosing and patients in cohort #4 are expected to receive the drug candidate in May 2024**
- **Successful results in the SAD and MAD trials will lead to the initiation of a registrational trial in 2025 aimed at supporting the first New Drug Application within the major unmet need of RP11 patients – expected to occur in 2027[3]**

PERTH, Australia and SAN FRANCISCO, California – 29 April 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 approved

[1] Subject to ongoing successful results across safety/tolerability, efficacy and regulatory dimensions of the clinical trials process
[2] PYC will provide an overview of the study protocol for this MAD trial prior to initiation of the trial next month
[3] Subject to the risks set out in the Company's ASX filing of 14 March 2024

escalation in dosing to a fourth patient cohort. This fourth patient cohort will receive the investigational drug candidate known as VP-001 at a dose of 75 micrograms per eye. The approval comes following review of the safety and tolerability data for patients in:

- cohort 1 (3 micrograms per eye);
- cohort 2 (10 micrograms per eye); and
- cohort 3 (30 micrograms per eye).

PYC's Chief of Research and Development, Dr. Sri Mudumba, commented on the outcome of the SRC review:

"*We have reached a dose at which we expect to see activity of the drug candidate in patients with RP11. This has triggered us to commence the repeat dose study in order to gain greater insight on the efficacy profile of this drug candidate following an extended exposure window in the retina of RP11 patients.*

At the same time, the safety and tolerability profile of the drug candidate observed to date allows for higher dosing. We have therefore amended the SAD study protocol to escalate dosing further and we will convert these doses into the MAD study following confirmation that VP-001 is safe and well-tolerated at these higher doses too."

Patients are expected to receive the 75 microgram dose of VP-001 in the updated SAD study before the end of May. A Multiple Ascending Dose (MAD) study is expected to commence in May and PYC will provide a detailed overview of the study design prior to initiation of this clinical trial.

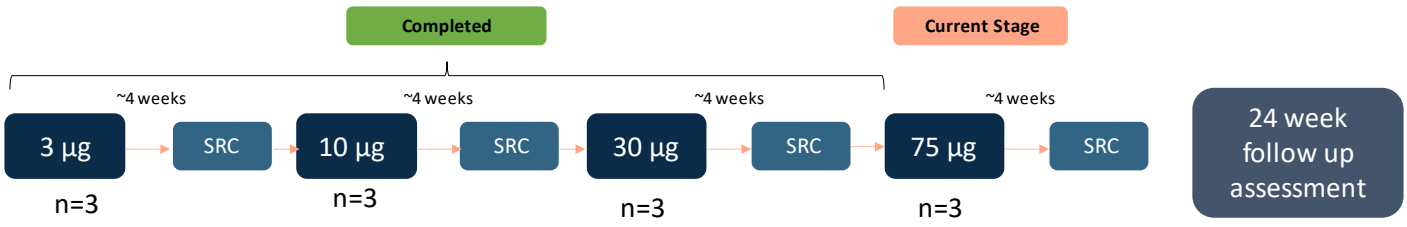
Both studies are expected to have concluded in early 2025, at which time the Company will evaluate the safety/tolerability and efficacy profile of VP-001 before progressing into a registrational trial in the event of successful outcomes[4].

About the Platypus Phase 1 Single Ascending Dose (SAD) Study

The Phase 1 open label study will be conducted to evaluate the safety and tolerability of a single dose of VP-001 to a single eye administered intravitreally in participants over the age of 18 with confirmed PRPF31 mutation-associated retinal dystrophy (RP11 patients).

Four groups of patients will be administered a single dose (3µg, 10µg, 30µg & 75µg) with each cohort consisting of 3 patients with RP11. The Safety Review Committee (SRC) for the study will review the safety data for each cohort of patients dosed with VP-001, 4 weeks after dosing is administered. When the final patient in the relevant cohort has progressed through the SRC, the trial will progress to the next cohort/dosing group.

On completion of the dosing of the highest tolerated dose cohort, a 24-week safety follow-up assessment will be conducted to assess treatment-emergent adverse events.



Refer to ASX announcement 26 April 2023 for further information on the Phase 1 trial.

[4] PYC will provide further detail on the objectives of the MAD prior to initiation of the study in May 2024

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**[5].

The Company was the first to progress a drug candidate for a blinding eye disease of childhood (Retinitis Pigmentosa type 11) into human trials. The Company is progressing a second drug program targeting a blinding eye disease (Autosomal Dominant Optic Atrophy) and a third program targeting Polycystic Kidney Disease which are anticipated to commence human trials in mid-2024 and early 2025 respectively.

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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[5] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232