26 May 2025

APPROVAL TO ESCALATE DOSING IN POLYCYSTIC KIDNEY DISEASE CLINICAL TRIAL

- **PYC is developing a clinical-stage drug candidate (known as PYC-003) for the treatment of Polycystic Kidney Disease (PKD)**
- **More than 10 million people worldwide suffer from PKD and have no treatment options available to them today[1]**
- **PYC is currently conducting Part A of a Phase 1a Single Ascending Dose (SAD) study of PYC-003 in healthy volunteers**
- **The Safety Review Committee (SRC) governing this trial has reviewed the 4-week safety data from cohort 1 (0.4 mg/kg dose) and has approved an escalation in dosing to cohort 2 (1.2 mg/kg dose)[2]**
- **The SRC is scheduled to meet again in July to review the 4-week safety data from cohort 2 with a successful outcome set to trigger both:**
    - **Further escalation of dosing (to 2.4 mg/kg) in healthy volunteers (in Part A of the Phase 1a study); and**
    - **Initiation of dosing at 0.4 mg/kg in patients with Polycystic Kidney Disease[3] (in Part B of the Phase 1a study)**

PERTH, Australia and SAN FRANCISCO, California – 26 May 2025

PYC Therapeutics Limited (ASX:PYC) (**PYC** or the **Company**) is a precision medicine Company dedicated to changing the lives of patients with genetic diseases who have no treatment options available.

The Company currently has three clinical-stage drug development programs including a drug candidate (known as PYC-003) that addresses the underlying cause of Polycystic Kidney Disease (PKD). PYC today announces that it has completed dosing in the first cohort of healthy volunteers in a Single Ascending Dose (SAD) study of PYC-003 and that the

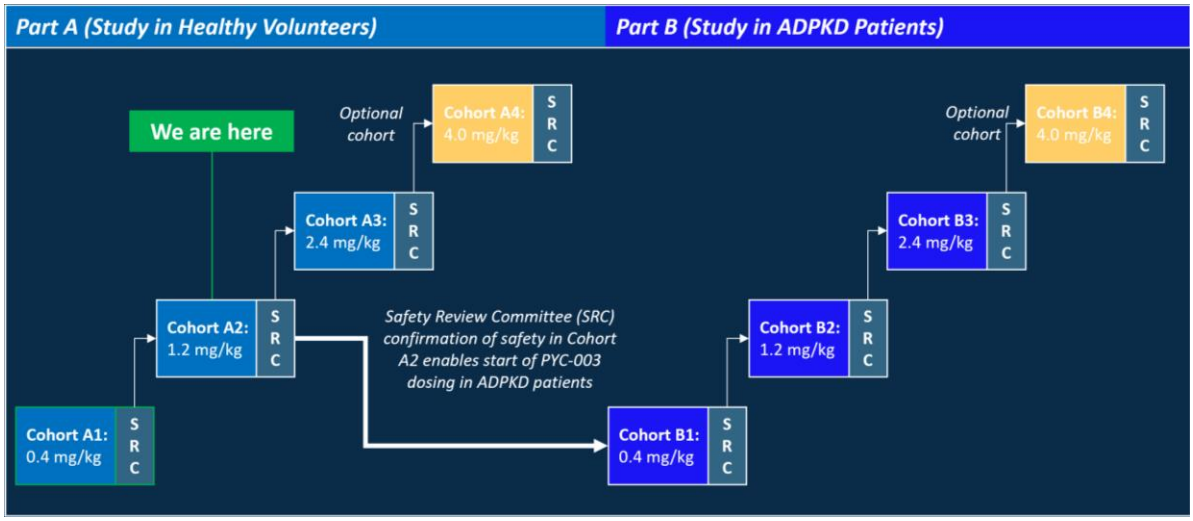
[1] Chapman, A. B., et al. (2015). "Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference." Kidney Int 88(1): 17-27

[2] Healthy volunteers in cohort 1 of the study received a dose of 0.4 mg/kg and participants in cohort 2 will be dosed at 1.2 mg/kg of PYC-003. See Figure 1 for more details

[3] See Figure 1 for more details. Subject to the risks and uncertainties outlined n the Company's ASX disclosures of 17 February 2025

Safety Review Committee (SRC) governing this clinical trial has reviewed the 4-week safety data from this first cohort and approved escalation of dosing to cohort 2[4].

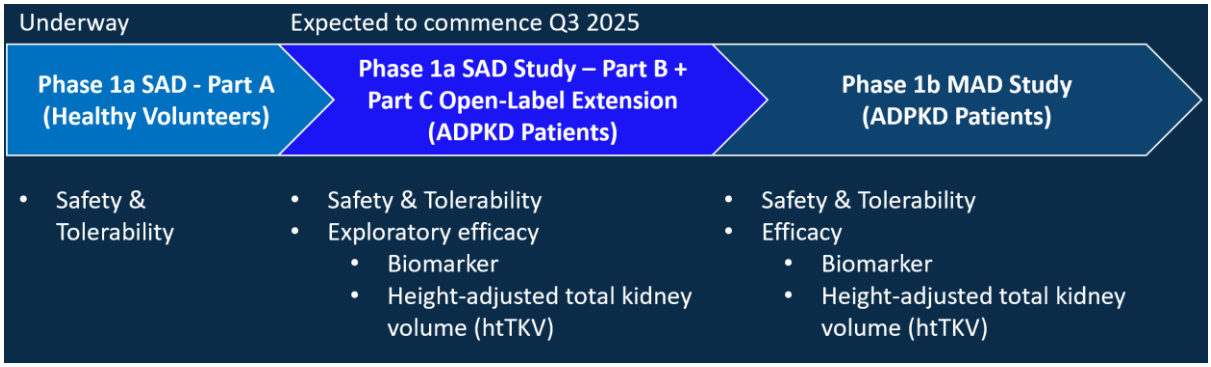
Figure 1. Phase 1a SAD study overview for PYC-003



PYC has now commenced dosing in cohort 2 of part A of the SAD. The Company anticipates initiating part B of the SAD in patients with PKD in Q3 upon successful review of the safety/tolerability data from cohort 2 in part A of the study by the SRC[5].

Parts A and B of the SAD study will be followed by an Open-Label Extension (OLE) study facilitating repeat dosing and evaluation of the optimal dosing regimen of PYC-003 alongside a Phase 1b Multiple Ascending Dose (MAD) randomised controlled trial to evaluate the safety/tolerability and efficacy profile of PYC-003 (See Figure 2 for an overview of the integration of the different elements of the Phase 1a/1b clinical trials of PYC-003[5]).

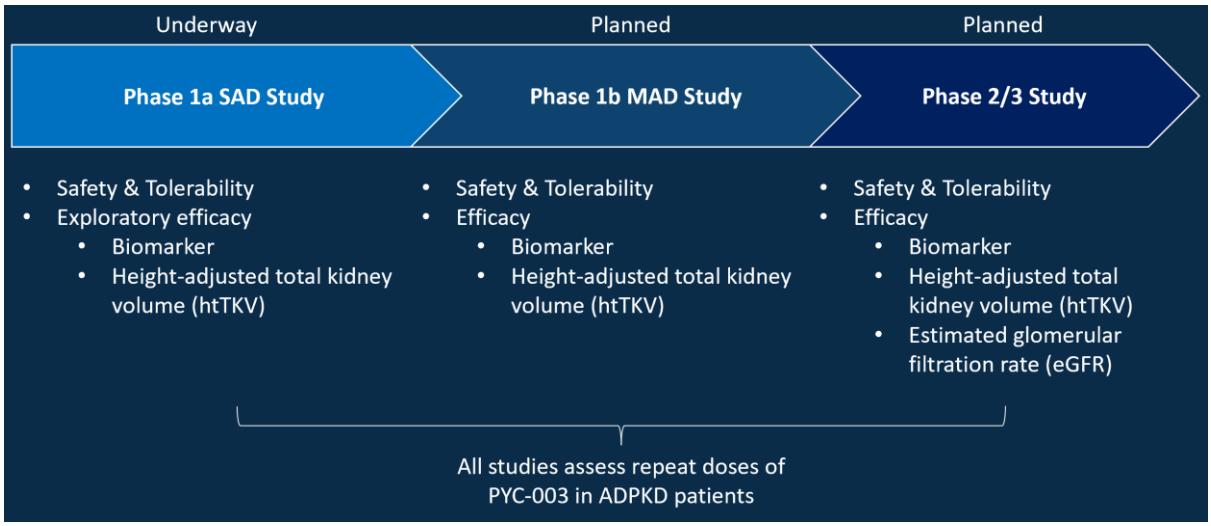
Figure 2. Integration of PYC's planned Phase 1a SAD (with OLE) and MAD studies



Successful completion of the Phase 1a/1b study described above will lead to initiation of a registrational combined Phase 2/3 trial aimed at supporting a New Drug Application for PYC-003 (See Figure 3)[5].

[4] See ASX announcement of 10 April 2025 for further details
[5] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025

Figure 3. Proposed clinical development pathway for PYC-003[6]



Next steps

The primary objective of the ongoing Phase 1a SAD study is to evaluate the safety/tolerability profile of PYC-003 with a secondary objective to evaluate the efficacy of the drug candidate when the study moves into PKD patients in H2 2025.

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**[7].

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.

[6] Subject to confirmation with the relevant regulatory authorities

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

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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