PYC Therapeutics

19 December 2025

POLYCYSTIC KIDNEY DISEASE CLINICAL TRIAL – SAFETY OUTCOMES IN PART A

- **PYC is progressing a drug candidate (known as PYC-003) that addresses the underlying cause of Polycystic Kidney Disease (PKD) through clinical trials**

- **The path to market for PYC-003 is expected to consist of:**
  - **a Phase 1a/1b study (that is currently ongoing); followed by**
  - **a single registrational combined Phase 2/3 study directed towards supporting a New Drug Application (NDA)[1]**

- **The Safety Review Committee (SRC) governing the Phase 1a/1b study has confirmed that single doses of PYC-003 up to and including 4 mg/kg in healthy volunteers were considered to be safe and well tolerated[2]**

- **PYC has commenced dosing PKD patients in cohort 2 (1.2 mg/kg of PYC-003) in Part B of this study and is now preparing for the initiation of repeat dosing in PKD patients in Part C of the study in H1 2026[3]**

PERTH, Australia and SAN FRANCISCO, California – 19 December 2025

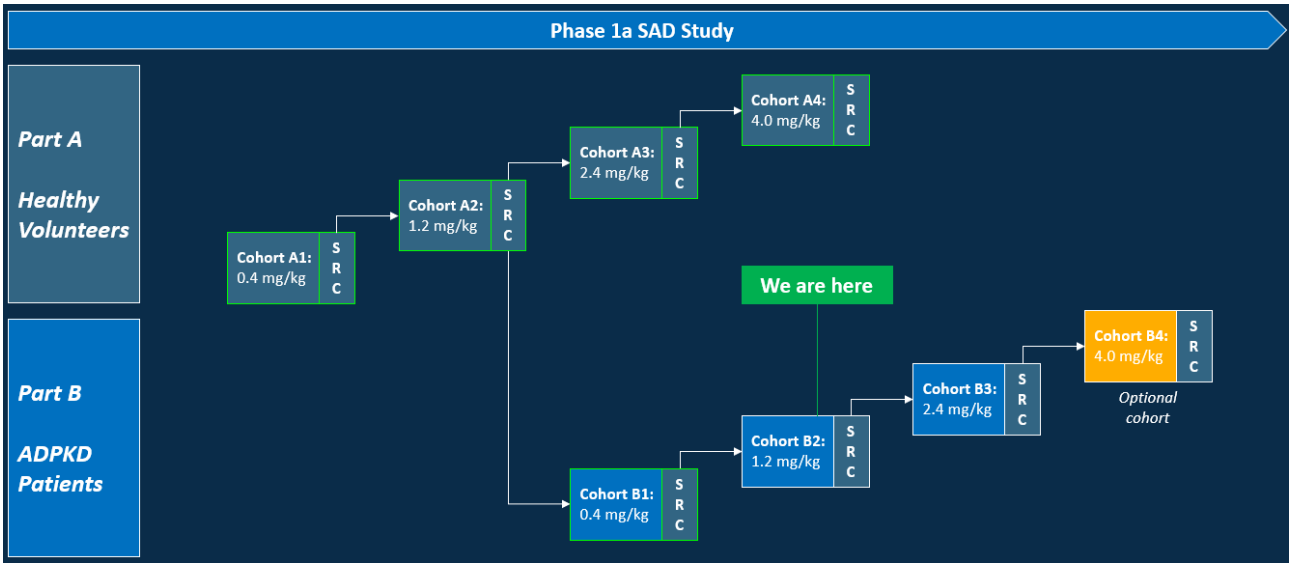
PYC Therapeutics Limited (ASX:PYC) (PYC or the Company) is a precision medicine Company dedicated to changing the lives of patients with genetic diseases who have no treatment options available.

The Company currently has three clinical-stage drug development programs including a drug candidate (known as PYC-003) that addresses the underlying cause of autosomal dominant Polycystic Kidney Disease (PKD). PYC today announces that the Safety Review Committee (SRC) governing the Single Ascending Dose (SAD) clinical trial of PYC-003 has reviewed the 4-week safety data from all 4 cohorts of healthy volunteers enrolled in part A of this study. The SRC has confirmed that there were no Treatment-Emergent Serious Adverse Events in any subject dosed in Part A of the study and that PYC-003 was safe and well-tolerated up to and including doses of 4 mg/kg[4].

[1] Management forecast accurate as at the date of this announcement and subject to regulatory approval and the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025. See Figure 3 for more detail. The US Food and Drug Administration has previously accepted a proposed single pivotal study for Regulus Therapeutics' Farabursen in autosomal dominant PKD.
[2] There were no Treatment-Emergent Serious Adverse Events (TE-SAEs) in any subject dosed in Part A of the Phase 1a/1b study through a minimum of 4-weeks of follow-up post dosing with the drug candidate
[3] Subject to successful completion of Part B and all necessary human ethics and regulatory approvals
[4] Through a minimum of 4-weeks of follow up (cohort 4)

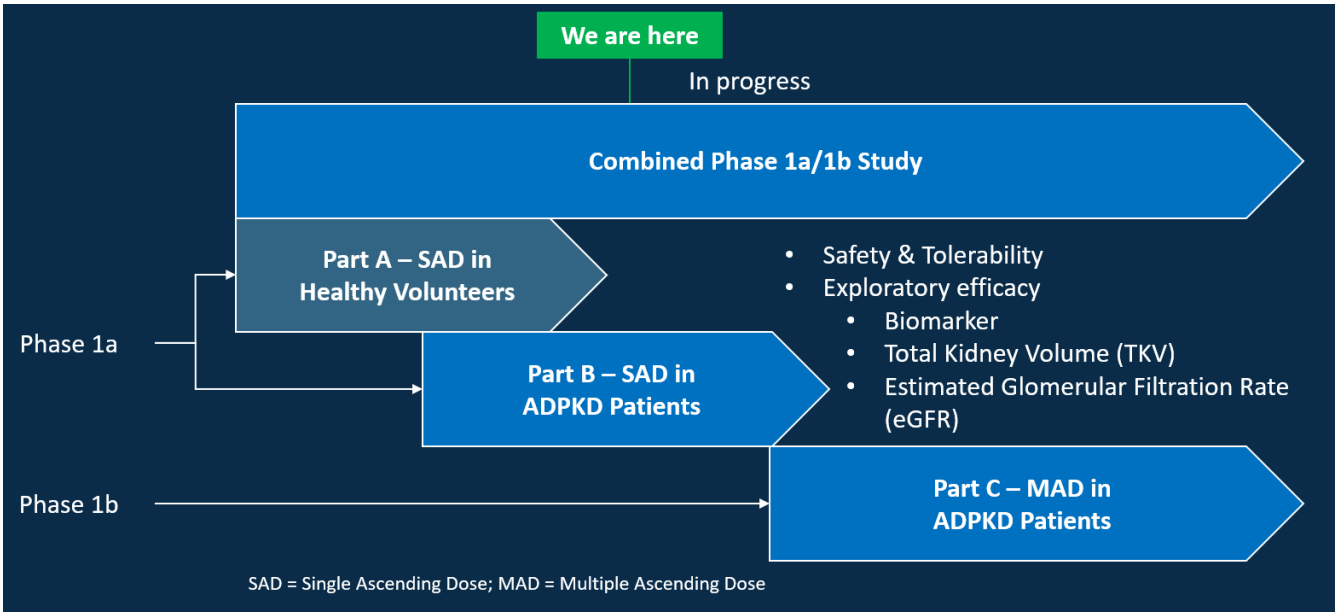
PYC does not currently intend on escalating dosing in healthy volunteers further because the predicted range of pharmacological activity for PYC-003 in PKD patients is below 4 mg/kg[5].

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



Part B of the SAD study will be followed by an open-label repeat dose study designed to evaluate the safety/tolerability and optimal dosing regimen 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[6]).

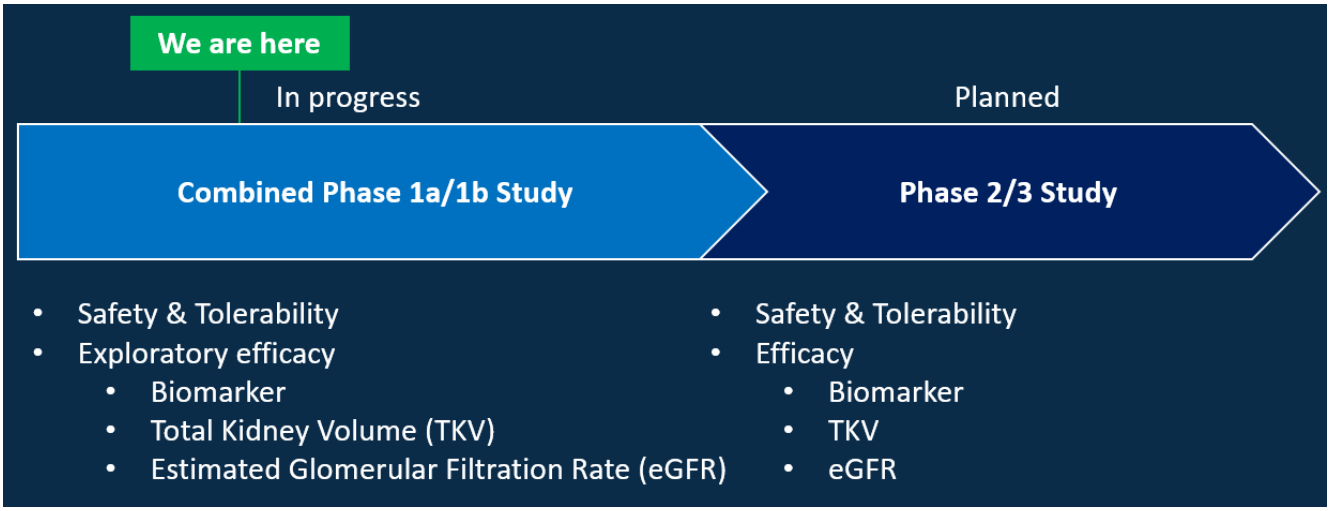
Figure 2. Integration of PYC's Phase 1a SAD (Parts A and B) with repeat dose (Part C) studies



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[7]).

[5] See footnote 2 and subject to confirmation of pharmacokinetic/pharmacodynamic modelling based on additional data expected from part B of the 1a/1b study
[6] Subject to confirmation with the relevant regulatory authorities
[7] Subject to confirmation with the relevant regulatory authorities

Figure 3. Proposed clinical development pathway for PYC-003



Next Steps

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

PYC will continue to update shareholders on progress in the ongoing Phase 1a/1b study with repeat dose safety and efficacy data expected in 2026.

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 [8].

For more information, visit pyctx.com, or follow us on LinkedIn and X.

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.

[8] 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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