

FIRST SUBJECT DOSED IN POLYCYSTIC KIDNEY DISEASE CLINICAL TRIAL

- **PYC is progressing a drug candidate (known as PYC-003) that addresses the underlying cause of Polycystic Kidney Disease (PKD)¹ through clinical trials for the millions of patients who suffer from this condition and who currently have no treatment options available**
- **The Company today announces that the first subject in the Phase 1a trial of PYC-003 has been dosed with the Company's investigational drug candidate**
- **If successful, PYC-003 has a potential high-velocity path to approval with a single combined registrational Phase 2/3 study expected to follow completion of the ongoing Phase 1a/1b trial²**

PERTH, Australia and SAN FRANCISCO, California – 10 April 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 the first subject in a Phase 1a Single Ascending Dose (SAD) study of PYC-003 in healthy volunteers has been dosed with the drug candidate.

The subject received a 0.4 mg/kg dose of PYC-003 intravenously. Seven additional healthy volunteers will receive either the drug candidate at the same dose or a placebo control over the coming weeks³. A meeting of the Safety Review Committee (SRC) overseeing this clinical trial will occur in June/July⁴ to review the 4-week follow-up data from all subjects in this cohort and an anticipated request to escalate dosing in cohort 2 of the SAD to 1.2 mg/kg⁵ (See Figure 1 for an overview of the clinical trial protocol in the SAD).

¹ PYC-003 addresses the underlying cause of autosomal dominant polycystic kidney disease caused by mutations in the *PKD1* gene

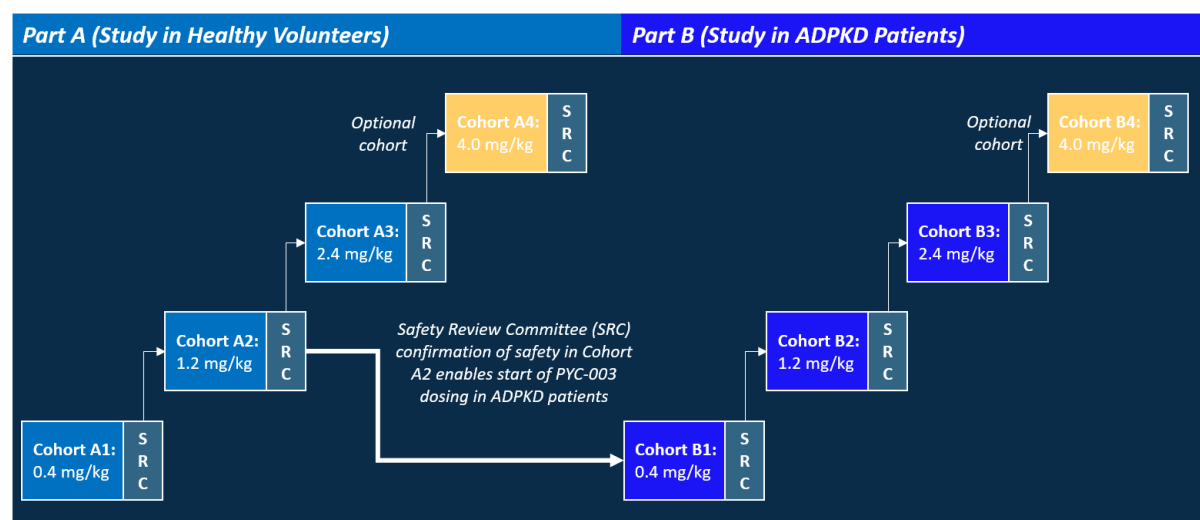
² Management expectation accurate as at 10 April 2025 and subject to the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025. See Figure 3 for more detail on the proposed clinical development plan for PYC-003

³ 6 subjects within the cohort will receive the active drug substance with 2 cohorts randomised to a placebo

⁴ The SRC will meet ~6 weeks after the last subject in the cohort has been dosed

⁵ Subject to confirmation of an acceptable safety/tolerability profile of PYC-003 in cohort 1

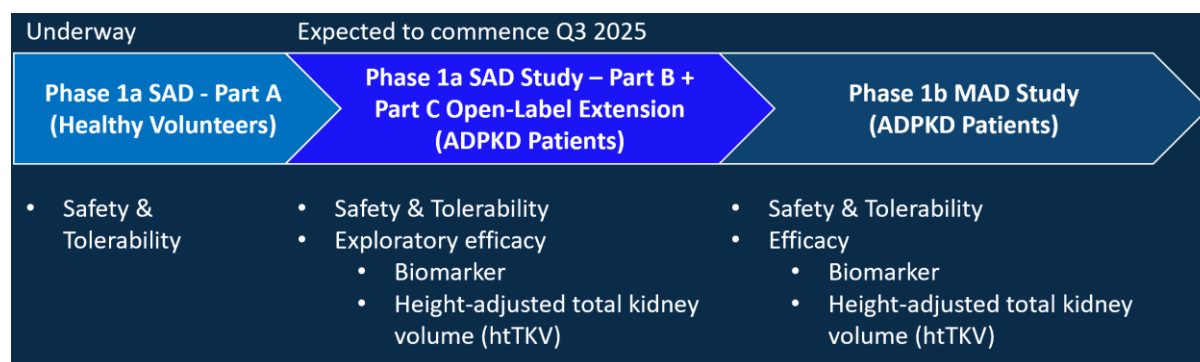
Figure 1. Phase 1a SAD study overview for PYC-003



Part B of this Phase 1a study will evaluate the safety/tolerability and efficacy profile of PYC-003 in patients with PKD – this part of the trial is expected to commence in Q3 2025⁶.

Parts A and B of the SAD 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) study 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 and Figure 3 for an overview of how this combines with the proposed registrational study⁷).

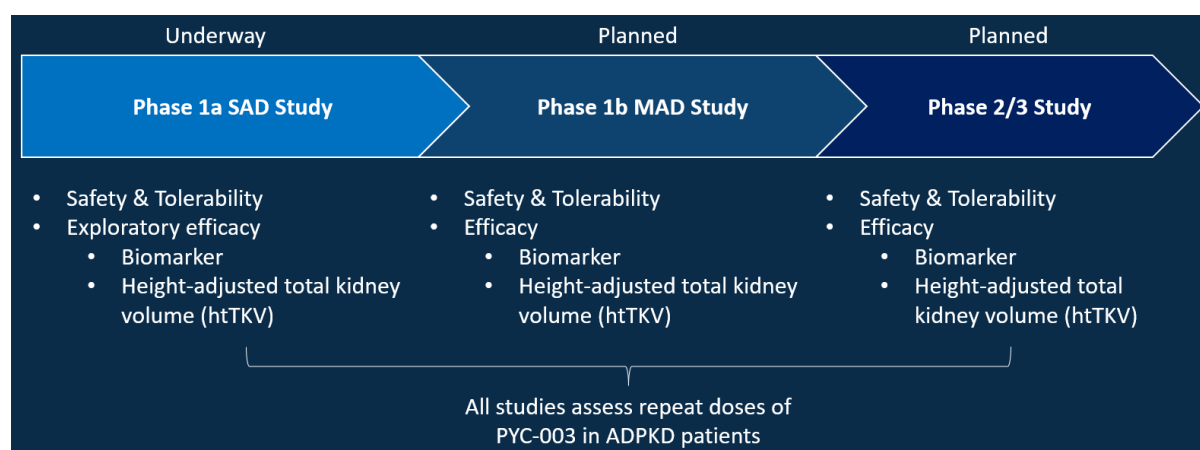
Figure 2. Integration of PYC’s planned Phase 1a SAD Parts A, B and C with the Phase 1b MAD study



⁶ Subject to the risks and uncertainties outlined in the Company’s ASX disclosures of 17 February 2025

⁷ 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-003⁸



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 2H 2025.

PYC will continue to update shareholders on progress within this high-velocity clinical development program on each of the milestones outlined in this announcement.

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**⁹.

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.

⁸ Subject to confirmation with the relevant regulatory authorities

⁹ Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank
<https://doi.org/10.1101/2020.11.02.2022232>

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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