

POLYCYSTIC KIDNEY DISEASE PROGRAM – PRESENTATION OF DATA AT ASN CONFERENCE

- **PYC is a precision medicine company dedicated to changing the lives of patients with genetic diseases who have no treatment options available**
- **The Company is progressing a drug candidate (known as PYC-003) that addresses the underlying cause of Polycystic Kidney Disease (PKD) through clinical trials¹**
- **PYC today announces that it will present exploratory efficacy data from PKD patients who received a single-dose of PYC-003 in its ongoing Phase 1a/1b clinical studies at the upcoming American Society of Nephrology (ASN) conference in Denver, Colorado on 22 October 2026. The presentation includes quantification of:**
 - **Urinary PC1 protein levels (a marker of target engagement for PYC-003 in the kidney) demonstrating a 46% increase in patients treated with PYC-003 when compared to baseline (see Figure 1)²; and**
 - **Changes in Total Kidney Volume^{3,4} at 3 months after treatment with a single dose of PYC-003 compared to baseline (see Figure 2)⁵**
- **This encouraging exploratory efficacy data has been generated in a small number of patients over a short period of time and on endpoints that are variable by nature – it needs to be reproduced in repeat dose studies of PYC-003 in a larger number of PKD patients treated over a longer period of time before any conclusions regarding the likely impact of the drug candidate on the disease process can be drawn**
- **PYC expects to present data from its ongoing Phase 1b multiple dose study of PYC-003 in PKD patients and its associated Open-Label Extension study in CY27**

PERTH, Australia and SAN FRANCISCO, California – 7 October 2026

¹ Additional details on PYC's Phase 1 study of PYC-003 in ADPKD are available using the clinical trials identifier: NCT06714006

² Data presented is the geometric mean fold-change from baseline in urinary PC1 (uPC1) protein normalised to CD133 protein at Day 14. Data are shown for all patients with both baseline and Day 14 samples that passed quality control (QC) following a single dose of PYC-003 (1.2 mg/kg, n=3; 2.4 mg/kg, n=4). While both dose cohorts demonstrated a similar increase in uPC1:CD133 from baseline to Day 14, the small cohort sizes do not permit meaningful assessment of dose-dependent effects and data were therefore pooled for statistical analysis. Across the pooled cohorts, the geometric mean fold-change from baseline was 1.46 (95% CI: 1.11–1.92; paired t-test on log-transformed values, *p<0.05).

³ The anatomical surrogate of PKD disease progression designated as the registrational endpoint for an accelerated approval in PKD

⁴ <https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure>

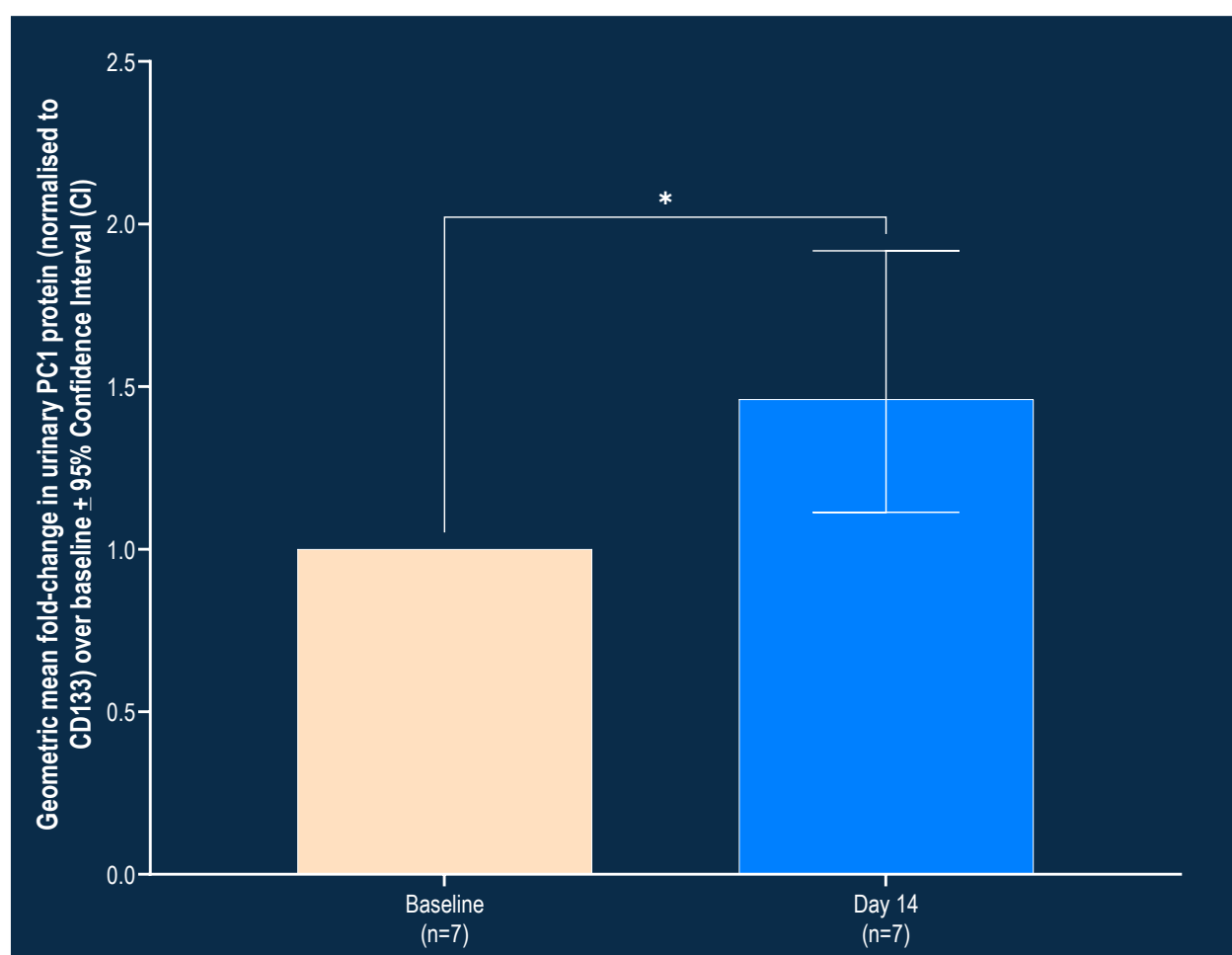
⁵ Data presented for all PKD patients enrolled in the Single Ascending Dose (SAD) study of PYC-003 with 3-month follow-up Total Kidney Volume (TKV) data (n=18) with 95% Confidence Intervals (CI) included.

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)⁶. PYC today announces that it will present exploratory efficacy data from PKD patients who have received a single dose of PYC-003 at the upcoming American Society of Nephrology conference. The data includes changes in:

- urinary PC1 (uPC1) protein levels - a marker of target engagement for PYC's investigational drug candidate in the kidney (see **Figure 1**); and
- Total Kidney Volume (TKV) - an anatomical surrogate biomarker of disease progression in PKD⁷ (see **Figure 2**).

Figure 1. Fold-change from baseline in urinary PC1 protein levels at Day 14 following a single dose of PYC-003⁸



PKD is caused by insufficient levels of PC1 protein in the kidneys⁹. Urinary PC1 is a pharmacodynamic biomarker of PC1 protein production. The observed increase in urinary PC1 protein levels following a single dose of PYC-003 is consistent with the proposed

⁶ For patients with PKD caused by a mutation in the *PKD1* gene

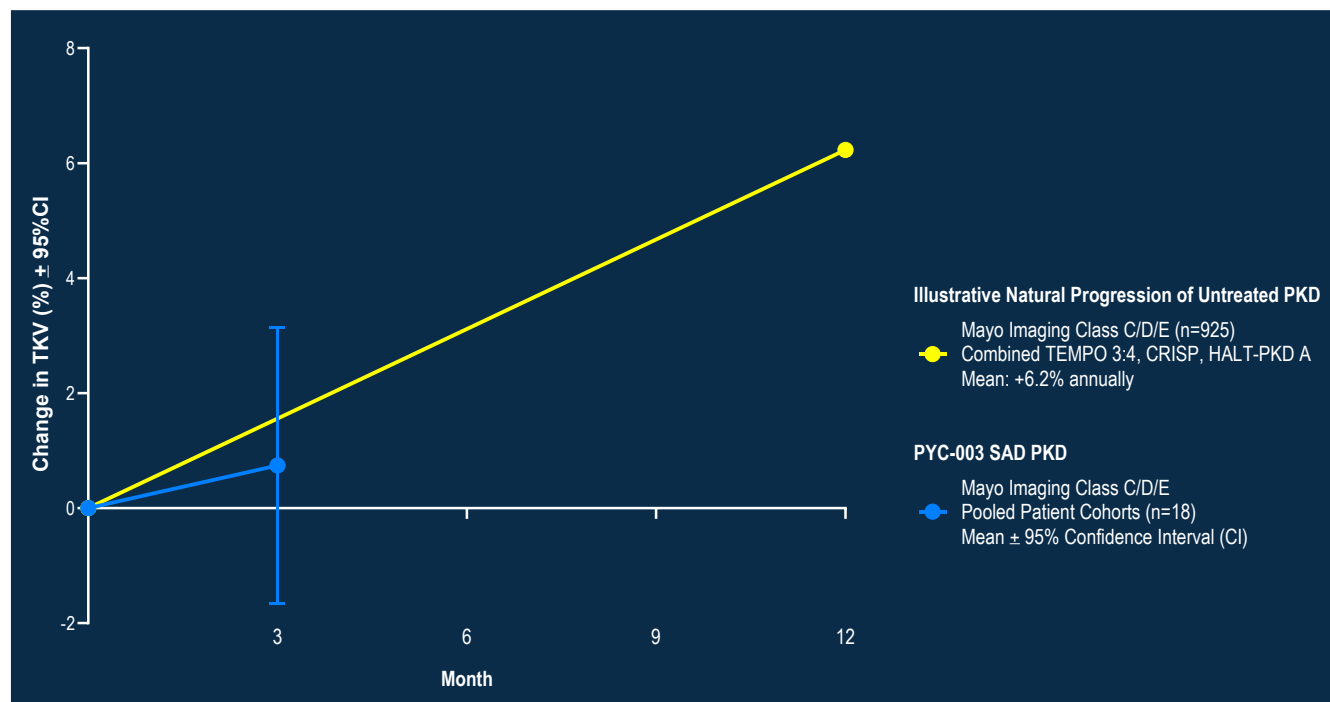
⁷ <https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure>

⁸ Data presented is the geometric mean fold-change from baseline in urinary PC1 (uPC1) protein normalised to CD133 protein at Day 14. Data are shown for all patients with both baseline and Day 14 samples that passed quality control (QC) following a single dose of PYC-003 (1.2 mg/kg, n=3; 2.4 mg/kg, n=4). While both dose cohorts demonstrated a similar increase in uPC1:CD133 from baseline to Day 14, the small cohort sizes do not permit meaningful assessment of dose-dependent effects and data were therefore pooled for statistical analysis. Across the pooled cohorts, the geometric mean fold-change from baseline was 1.46 (95% CI: 1.11–1.92; paired t-test on log-transformed values, *p<0.05).

⁹ In the majority of PKD patients who have a loss of function mutation in one copy of the *PKD1* gene

mechanism of action of the drug candidate which is designed to increase PC1 protein levels¹⁰ and address the disease process at its root cause.

Figure 2. Change from baseline¹¹ in Total Kidney Volume (TKV) at 3 months following a single dose of PYC-003¹²



Total Kidney Volume (TKV) is an accepted surrogate marker of disease progression in PKD¹³. The exploratory findings presented here show changes from baseline in TKV at 3 months following a single dose of PYC-003 (blue line in **Figure 2**). Also shown for context is the estimated historical rate of TKV progression in the absence of treatment (yellow line in **Figure 2**)¹⁴. The trajectory of PKD in the absence of treatment has been established by combining the relevant patients of TEMPO 3:4, CRISP and HALT-PKD A trials illustrating the natural progression of untreated PKD. These trials were open to patients with PKD due to mutations in any gene¹⁴, whereas PYC's clinical trials evaluating PYC-003 in PKD patients enrol only patients with a mutation in the *PKD1* gene¹⁵. Patients with a *PKD1* mutation progress faster toward end-stage kidney disease (and are consequently expected to have accelerated rates of TKV growth over time) than patients with mutations in other genes that cause PKD^{16,17}.

Confirmation in ongoing repeat-dose studies will be required to determine whether these findings across both urinary PC1 protein levels and TKV changes are reproducible.

¹⁰ in patients with PKD caused by mutations in the *PKD1* gene

¹¹ Baseline MRI must occur within the 28 days preceding treatment

¹² Data presented for all PKD patients enrolled in the Single Ascending Dose (SAD) study of PYC-003 with 3-month follow-up Total Kidney Volume (TKV) data (n=18) with 95% Confidence Intervals (CI) included.

¹³ <https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure>

¹⁴ The weighted mean annual % change in TKV is presented for patients with Mayo Imaging Class C/D/E from these trials. See Table 2 of Perrone RD, et al. The STAGED-PKD 2-stage adaptive study with a patient enrichment strategy and treatment effect modeling for improved study design efficiency in patients with ADPKD. *Kidney Med.* 2022;4(10):100538. doi:10.1016/j.xkme.2022.100538. The data in this table combines natural disease progression observed in the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP; NCT01039987) study with the placebo arm of the HALT Progression of Polycystic Kidney Disease Study A (HALT-PKD A; NCT00283686) trials to provide mean annual % change in TKV for each Mayo Imaging Class of patients illustrating the natural progression of untreated PKD. See Table 2 of Irazabal MV, et al. Prognostic enrichment design in clinical trials for autosomal dominant polycystic kidney disease: the TEMPO 3:4 clinical trial. *Kidney Int Rep.* 2016;1(4):213-220. doi:10.1016/j.ekir.2016.08.001. The data in this table provides mean annual % change in TKV for each Mayo Imaging Class of patients and the placebo-arms can be used to illustrate natural progression of untreated PKD.

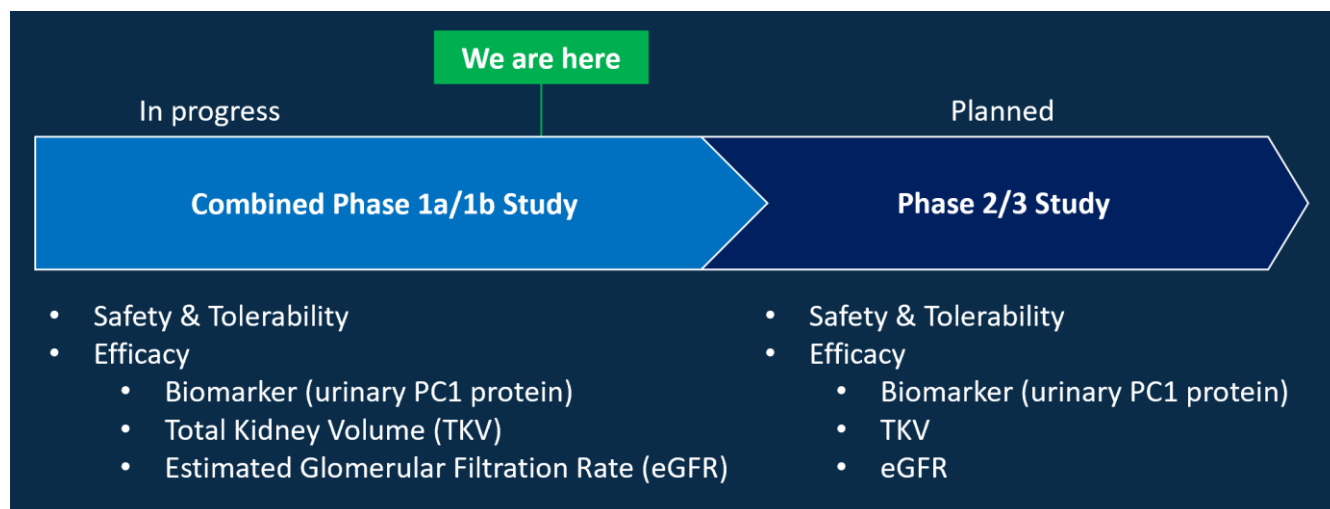
¹⁵ PYC is currently evaluating PYC-003 in *PKD1* patients only

¹⁶ Cornec-Le Gall E, et al. The PROPKD Score A New Algorithm to Predict Renal Survival in Autosomal Dominant Polycystic Kidney Disease. *J Am Soc Nephrol.* 2016 Mar;27((3)):942-51. doi: 10.1681/ASN.2015010016.

¹⁷ Cornec-Le Gall E, et al. Type of PKD1 mutation influences renal outcome in ADPKD. *J Am Soc Nephrol.* 2013;24((6)):1006-13. doi: 10.1681/ASN.2012070650.

PYC is currently progressing PYC-003 through a Phase 1b Multiple Ascending Dose (MAD) and Open Label Extension (OLE) study (see Figure 3 for an overview of the proposed clinical development pathway for the investigational drug candidate¹⁸).

Figure 3. Proposed clinical development pathway for PYC-003¹⁹



Further progression in these ongoing studies is expected to be accompanied by alignment with relevant regulatory authorities on the initiation of a registrational combined Phase 2/3 trial aimed at supporting a New Drug Application for PYC-003 in PKD²⁰.

Next Steps

PYC will present the exploratory efficacy data following a single dose of PYC-003 described here at the ASN conference in October. Data from PYC's repeat dose studies of PYC-003 (the Phase 1b MAD study and OLE) is expected to be presented in CY27²¹.

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 development²².

For more information, visit pyctx.com, or follow us on [LinkedIn](#).

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,

¹⁸ Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

¹⁹ Additional details on PYC's Phase 1 study of PYC-003 in PKD are available using the clinical trials identifier: NCT06714006

²⁰ Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

²¹ Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

²² Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank <https://doi.org/10.1101/2020.11.02.2022232>

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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