PYC Therapeutics

31 August 2026

POLYCYSTIC KIDNEY DISEASE – PRESENTATION OF CLINICAL SAFETY DATA

- **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 trials[1]**
- **PYC today announces that Dr. Aron Chakera will present the latest safety data from the ongoing Phase 1a/1b clinical trial evaluating the safety/tolerability profile of PYC-003 in healthy volunteers and PKD patients at the Australian and New Zealand Society of Nephrology (ANZSN) conference on 31 August 2026**
- **Highlights of Dr. Chakera's presentation of safety data from the completed single dose cohorts of the trial demonstrate a favourable emerging safety profile[2] for PYC-003 throughout the expected human pharmacodynamic range[3], including:**
  - **No Treatment Emergent Serious Adverse Events**
  - **No changes in serum electrolytes or creatinine[4];**
  - **No changes in liver function tests[5]; and**
  - **No evidence of renal injury[6] following administration of PYC-003**
- **A copy of Dr. Chakera's poster presentation is attached to this announcement**
- **Safety and efficacy data from the Phase 1a Single Ascending Dose (SAD) study[7] is expected to be presented in CY26 with data from the ongoing Phase 1b Multiple Ascending Dose (MAD) study and Open-Label Extension (OLE) expected to be presented in CY27[8]**

[1] Additional details on PYC's Phase 1 study of PYC-003 in ADPKD are available using the clinical trials identifier: NCT06714006
[2] Based on Safety Review Committee (SRC) review of day 28 post-dose data for patients enrolled in Part B of the trial
[3] Refer to the attached poster presentation for key safety data from the study
[4] Outside of the reference range
[5] As assessed by liver function tests (alanine aminotransferase and aspartate aminotransferase)
[6] As assessed by exploratory safety endpoints of renal injury including Kidney Injury Molecule-1 (KIM-1), Neutrophil Gelatinase-Associated Lipocalin (NGAL). As exploratory endpoints, these may not always form part of the Safety Review Committee (SRC) data review.
[7] See ASX announcements of 10 February 2025, 10 April 2025, 26 May 2025, 7 July 2025, 8 August 2025, 24 November 2025, 19 December 2025 and 27 February 2026 for further information on the Phase 1a trial
[8] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

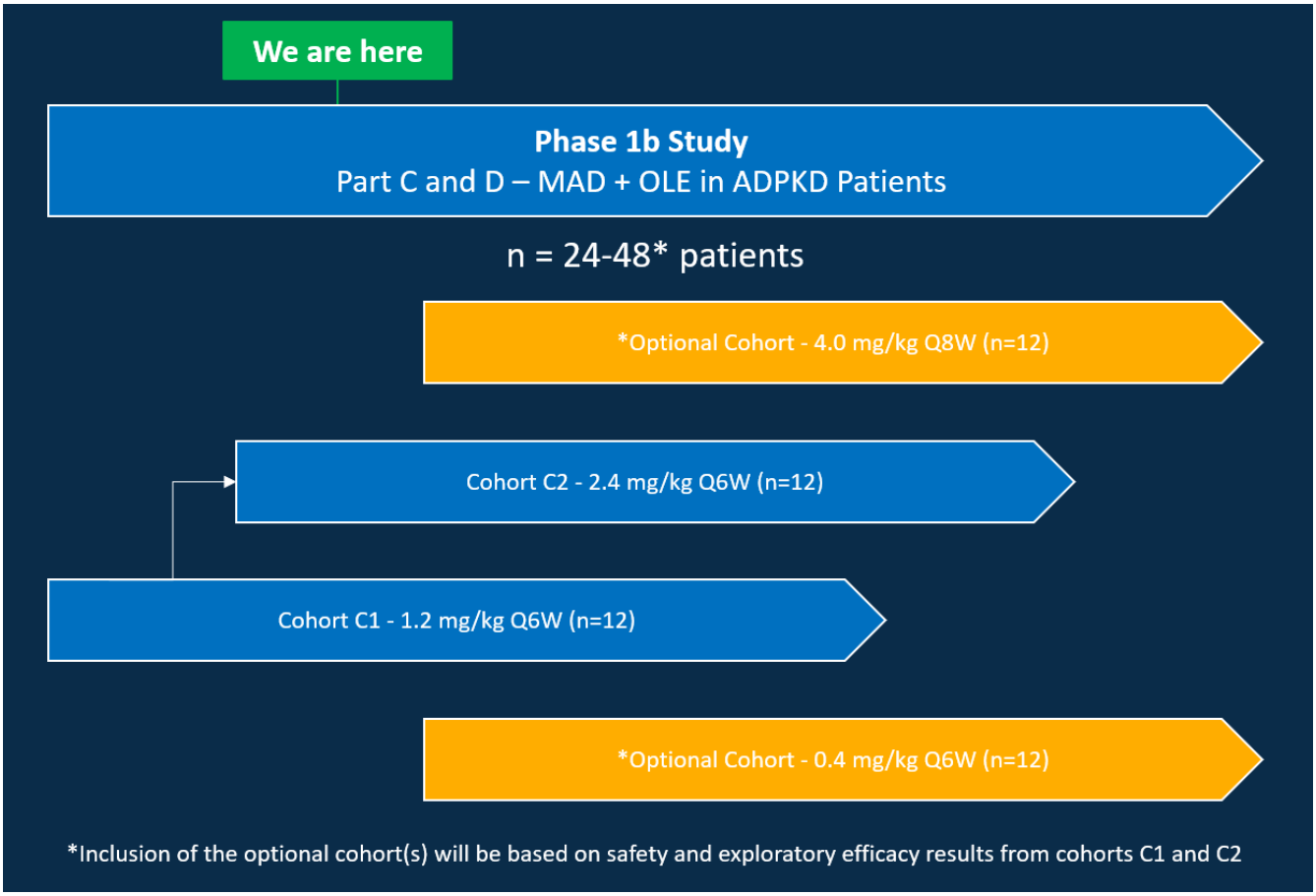
PERTH, Australia and SAN FRANCISCO, California – 31 August 2026

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 safety data from the ongoing Phase 1a/1b clinical trial evaluating the safety/tolerability profile of PYC-003 in healthy volunteers and PKD patients at the Australian and New Zealand Society of Nephrology (ANZSN) conference taking place in Brisbane, Queensland from 29 August 2026 to 2 September 2026.

An overview of the ongoing Phase 1b study of PYC-003 in PKD patients, comprising Part C (Multiple Ascending Dose (MAD)) and Part D (Open-Label Extension (OLE)) is shown below in Figure 1.

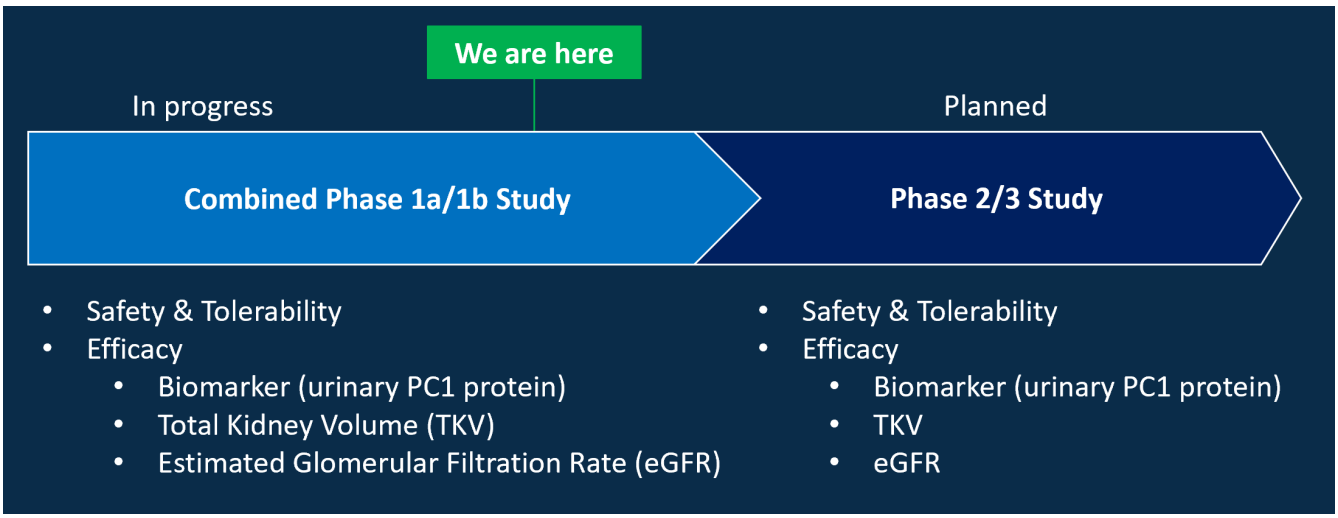
Figure 1. Phase 1b MAD + OLE study overview for PYC-003



The objective of the ongoing Phase 1b MAD study is to determine the safety/tolerability profile and optimal dosing regimen of PYC-003 in a repeat dose setting ahead of a proposed transition to a registrational trial[9] (See Figure 2 for an overview of the proposed clinical development pathway for PYC-003[10]).

[9] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026 and alignment with relevant regulatory authorities
[10] Subject to confirmation with the relevant regulatory authorities

Figure 2. Proposed clinical development pathway for PYC-003[11]



Successful completion of the Phase 1b MAD study followed by alignment with relevant regulatory authorities will lead to initiation of a registrational combined Phase 2/3 trial aimed at supporting a New Drug Application for PYC-003 in PKD[12].

Next Steps

Data from PYC's Phase 1a Single Ascending Dose (SAD) study in PKD patients is expected to be presented in H2 CY26. Data from the ongoing Phase 1b MAD study and OLE is expected to be presented in CY27.

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[13].

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, 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

[11] Additional details on PYC's Phase 1 study of PYC-003 in ADPKD are available using the clinical trials identifier: NCT06714006
[12] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
[13] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

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

CONTACT US

Investor relations and media contact
investor@pyctx.com

A Phase 1 Study of PYC-003, a Peptide-Oligonucleotide Conjugate Designed to Increase PC1 Expression in Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Aron Chakera[1,2], Jessica Stevenson[1], Vanessa Neve[1], Genevieve Syn[1], Colette Moses[1], Clarissa McDonagh[1], Natali Vasilevski[1], Angelo Bautista[1], Jan Hurst[1], Sebastian Rauschert[1], Maria Kerfoot[1], Adam Martin[1], Subrata Das[1], George Mitchell[1], Anja Stirnweiss[1], Paula Cunningham[1]

[1] PYC Therapeutics, Perth, Australia [2] Sir Charles Gairdner Hospital, Perth, Australia

Disclosures: This study was sponsored by PYC Therapeutics. All authors are employees of PYC Therapeutics.

ADPKD is an area of major unmet patient need

ADPKD is a highly prevalent, potentially lethal single-gene disorder

- Autosomal Dominant Polycystic Kidney Disease (ADPKD) affects ~1 in every 1,000 people, indicating over 12.5 million people are affected worldwide [1]
- Approximately 95% of patients with ADPKD have no treatment options available,[2] and there are no drugs that address the underlying cause of the disease
- ~80% of ADPKD patients have a mutation in one copy of *PKD1* DNA leading to insufficient Polycystin-1 (PC1) protein [3]
- One non-functional *PKD1* allele leaves ~50% of wild-type PC1, and that shortfall drives loss of Ca^{2+} signaling, abnormal tubule architecture and patients develop fluid filled cysts in the kidneys [4,5]
- These cysts grow over time, destroying the architecture and ultimately the function of the kidney, with half of the patients progressing to end-stage renal failure by the age of 60 [6]

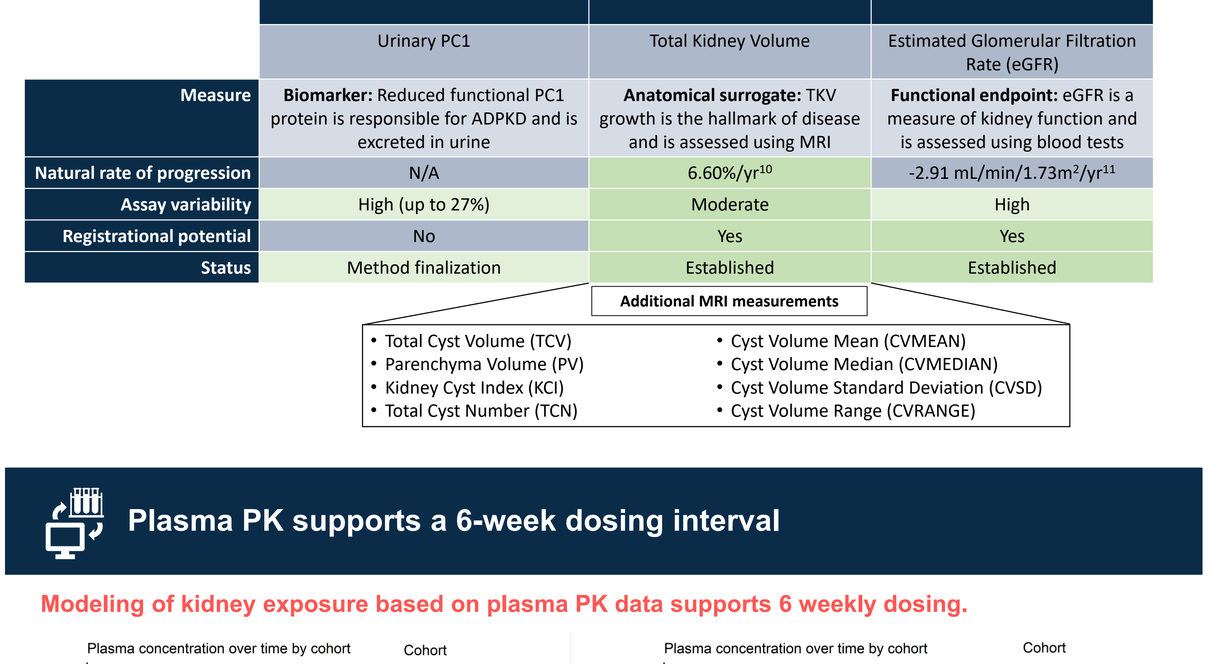
PYC-003 is designed to address the root cause of ADPKD

- PYC-003 is designed to address the underlying cause of PKD by increasing PC1 expression.
- PYC-003 increases PC1 protein levels and in a cyst model derived from ADPKD patient kidneys it prevents cyst progression
- PYC-003 has progressed from the Single Ascending Dose (SAD) protocol into the Multiple Ascending Dose (MAD) study
- PYC-003 demonstrates a favorable safety profile observed across all dose levels

Normal kidney[7] → **Polycystic kidney**

Clinical development overview for PYC-003

PYC-003 is currently progressing through a combined Phase 1a/1b clinical study in patients



Study objectives and endpoints

- **Primary:** Safety and tolerability
- **Secondary:** Plasma pharmacokinetics (PK)
- **Exploratory:** Pharmacodynamic biomarkers (uPC1), disease progression markers (TKV, eGFR), urinary PK, metabolites, and immunogenicity

Disease progression

	Urinary PC1	Total Kidney Volume	Estimated Glomerular Filtration Rate (eGFR)
Measure	**Biomarker:** Reduced functional PC1 protein is responsible for ADPKD and is excreted in urine	**Anatomical surrogate:** TKV growth is the hallmark of disease and is assessed using MRI	**Functional endpoint:** eGFR is a measure of kidney function and is assessed using blood tests
Natural rate of progression	N/A	6.60%/yr[10]	-2.91 mL/min/1.73m^2/yr[11]
Assay variability	High (up to 27%)	Moderate	High
Registrational potential	No	Yes	Yes
Status	Method finalization	Established	Established

Additional MRI measurements

- Total Cyst Volume (TCV)
- Parenchyma Volume (PV)
- Kidney Cyst Index (KCI)
- Total Cyst Number (TCN)
- Cyst Volume Mean (CVMEAN)
- Cyst Volume Median (CVMEDIAN)
- Cyst Volume Standard Deviation (CVSD)
- Cyst Volume Range (CVRANGE)

Overview of Inclusion/Exclusion Criteria Part B/C

Inclusion criteria

- Male or female aged **18 to 65 years** (inclusive at the time of informed consent
- ADPKD diagnosis as confirmed by the presence of genetic mutations associated with ADPKD, including, but not limited to, the **presence of *PKD1* mutation**
- **Class 1C, 1D or 1E per Mayo Imaging Classification** System for Predicting Kidney Outcomes in ADPKD[8]
- (Estimated glomerular filtration rates **(eGFR) ≥ 30 mL/min/1.73m^2** via the CKD EP1 2021 calculation[9]
- 18 ≤ BMI ≤ 35 kg/m2 and weight ≥ 50 kg

Exclusion criteria

- **Presence of potentially confounding genetic mutations** including, but not limited to, the presence of *PKD2*, *HNF1B*, *GANAB*, *IFT140* and/or *DNAJB 11* mutations
- **Use of (or anticipated use of) Tolvaptan and/or metformin administration within 30 days** prior to the first administration of IP until study completion
- Has only 1 kidney or has a kidney transplant
- Abnormal ECG findings at Screening, Day -1 or pre-dose that are considered by the PI or designee to be clinically significant
- **History of borderline to low blood magnesium and potassium levels** and/or Screening or Day -1 blood magnesium level < 0.7 mmol/L and potassium levels < 3.5 mmol/L

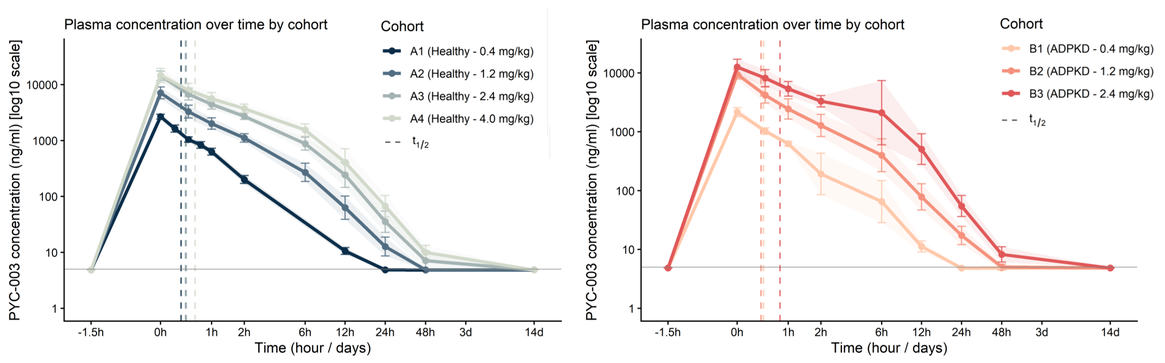
No treatment-related serious adverse events across all completed cohorts

Single doses of PYC-003 were safe and well-tolerated in Healthy volunteers and PKD patients

	Healthy volunteers				ADPKD patients		
	A1 (0.4 mg/kg) N = 8	A2 (1.2 mg/kg) N = 8	A3 (2.4 mg/kg) N = 8	A4 (4.0 mg/kg) N = 8	B1 (0.4 mg/kg) N = 6	B2 (1.2 mg/kg) N = 6	B3 (2.4 mg/kg) N = 6
Number of any Treatment Emergent Adverse Events (TEAEs)	4	11	5	13	9	8	12
Participants with at least one treatment related TEAEs*	0	1	0	2	0	1	1
Number of any Treatment Emergent Serious Adverse Events (TESAEs)	0	0	0	0	1	0	0
Number of any Treatment Related TESAEs	0	0	0	0	0	0	0
Any TEAEs leading to discontinuation	0	0	0	0	0	0	0

Plasma PK supports a 6-week dosing interval

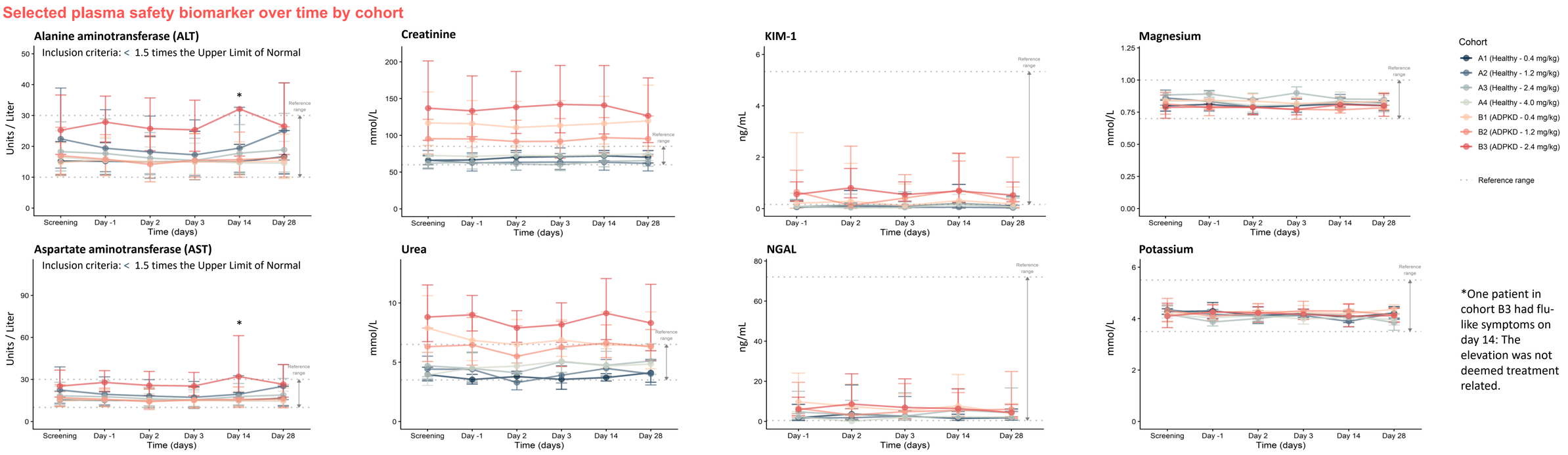
Modeling of kidney exposure based on plasma PK data supports 6 weekly dosing.



Data was generated from n=6 participants for cohort A and n=4-6 participants for cohort B. Points represent the geometric mean with error bars extending the 95% CI

No PYC-003-related effects were observed across key safety biomarkers.

Selected plasma safety biomarker over time by cohort



*One patient in cohort B3 had flu-like symptoms on day 14: The elevation was not deemed treatment related.

Data was generated from n=8 for cohort A and n = 6 for cohort B, with exceptions on Day 2 (AST n=5 for B1; KIM, NGAL n=7 for A3, n=5 for B2), Day 3 (KIM, NGAL n=5 for B2), Day 14 (KIM, NGAL n=5 for B3) and Day 28 (n=7 for A3 and n=5 for B3). Points represent the geometric mean with error bars extending the 95% CI

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6. Cloutier, M., et al. (2020). BMC Health Services Research, 20(1), 126.
7. Adapted from MacAskill CJ et al. (2026). Pediatr Radiol, PMID: 42517885, CC BY 4.0. Cropped and intensity-matched. Different subject, age and acquisition to the ADPKD image; illustrative only.
8. Irazabal, M. V., et al. (2015). Journal of the American Society of Nephrology, 26(1), 160-172.
9. Inker LA, et al. (2021). N Engl J Med. 2021;385:1737-1749.
10. Average TKV growth rate of 6.60%/yr for Mayo Classification C, D and E - from STAGED-PKD trial
11. Average eGFR rate of decline of -2.91 mL/min/1.73m2/yr for Mayo Classification C, D and E - from STAGED-PKD trial

Clinical development plan is subject to confirmation with relevant regulatory authorities and may change. Subject to the risks and uncertainties outlined in PYC Therapeutics ASX disclosures of 2 February 2026.

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