ASN KIDNEY WEEK • 22 OCTOBER 2026

# PYC-003 in ADPKD

## A peptide-oligonucleotide conjugate designed to increase PC1 expression

**Phase 1a/1b (PINACLE-1) Part B: single ascending dose in patients with autosomal dominant polycystic disease (ADPKD)**

Safety, tolerability and exploratory efficacy read-outs

**Jagadeesh Kurtkoti, MBBS, FRACP.**

Renal Medicine, South Coast Renal, Southport, Queensland, Australia

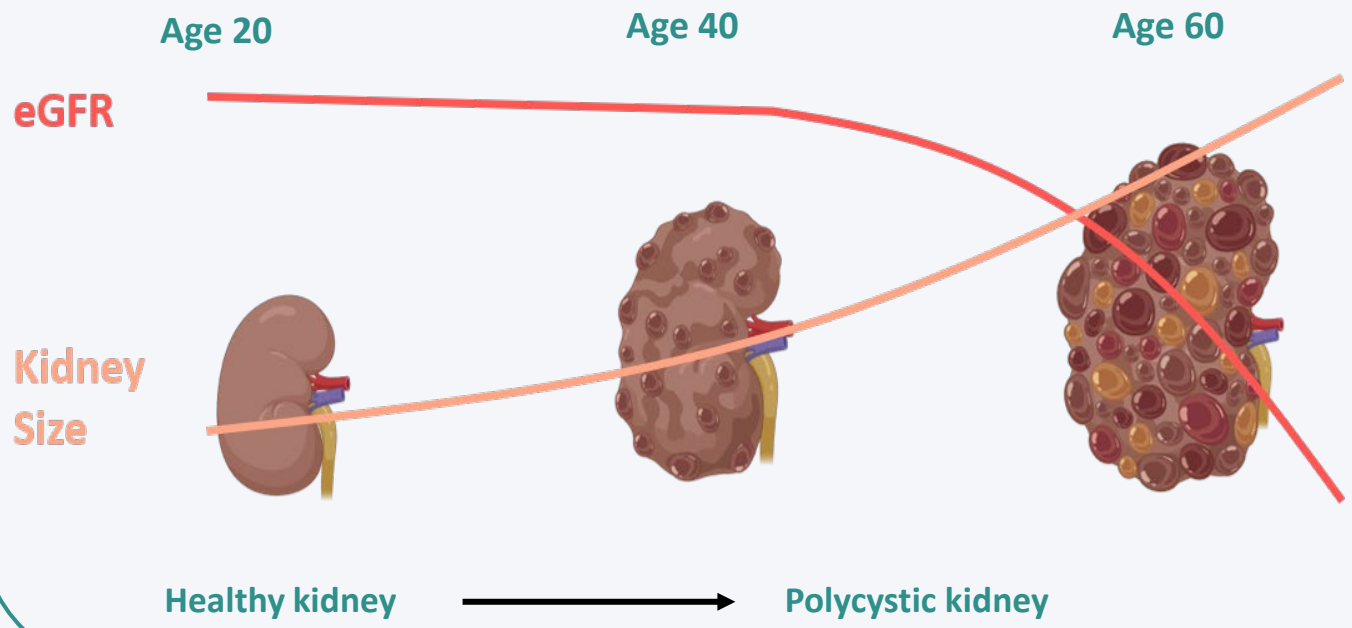
Abstract TH-OR060

# Disclosures

**No relevant financial relationships with ineligible companies.**

# ADPKD: a progressive disease with no disease-modifying therapy

**Progressive cyst growth enlarges the kidneys and reduces kidney function**




**1 in 1,000**

12.5 million people affected worldwide

**~80%**

*PKD1* mutation-driven PC1 deficiency is the main cause of ADPKD

**~50%**

progress to end-stage kidney disease by age 60

Images generated using BioRender.com.

# PYC-003 addresses the root cause of ADPKD

## PYC-003 selectively blocks miR-17 binding to PKD1 mRNA, restoring PC1 expression

**UNAFFECTED INDIVIDUAL**

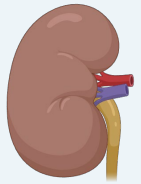
Two functional PKD1 mRNA transcripts

miR-17 suppresses PKD1 mRNA translation






Normal PC1 protein levels



Normal kidney

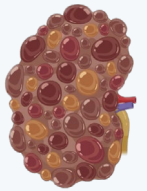
**ADPKD**

One functional PKD1 mRNA transcript





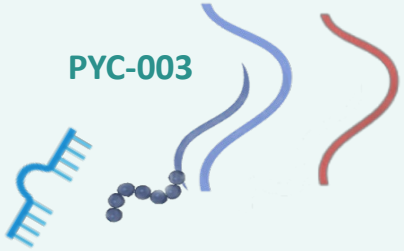
Reduced PC1 protein levels



Cyst growth and progressive dysfunction

**PYC-003 Treatment**

PYC-003 blocks miR-17 binding site on functional transcript

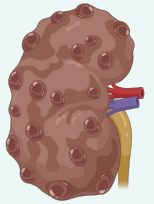



*Other miR-17 target mRNAs unaffected*

PKD1 mRNA protected



Increased PC1 protein levels



Slowed cyst growth, preserved function

# PYC-003 Global Phase 1a/1b Study (NCT06714006)

Placebo controlled SAD in healthy volunteers and open-label SAD/MAD in participants with ADPKD plus open-label extension

## Key ADPKD Eligibility Criteria

- Aged 18-65 years
- Genetic confirmation of ADPKD
- Mayo imaging classification (MIC) 1C, 1D, 1E
- eGFR ≥ 30 mL/min/1.73 $m^2$
- BMI ≥ 18.0 and ≤ 35.0 $kg/m^2$, weight ≥ 50 kg

## Key Endpoints

**Primary:** Safety and tolerability

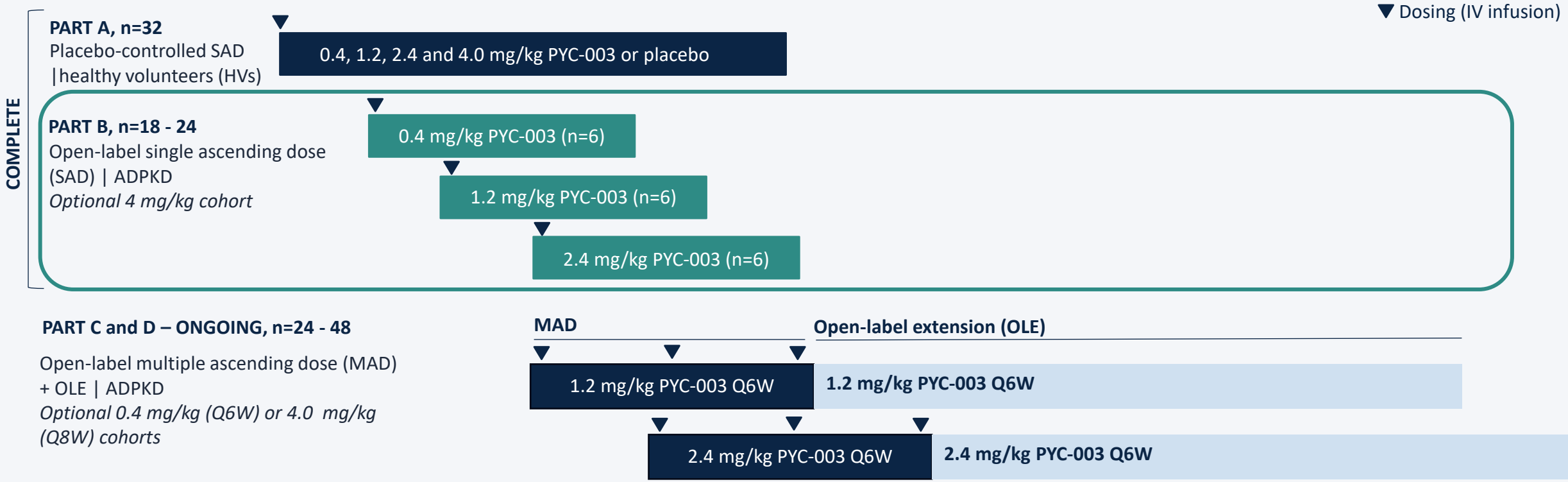
**Secondary and Exploratory:**

- Plasma and urinary PK
- PD biomarkers (uPC1), disease progression markers (total kidney volume (TKV), eGFR)

## Regions

**Australia:** 10 sites
**New Zealand:** 1 site
**Hong Kong**: 1 site

## STUDY DESIGN



# Baseline characteristics were broadly comparable, with expected variability across small cohorts

| Characteristic | B1<br>n = 6 | B2<br>n = 6 | B3<br>n = 6 |
|---|---|---|---|
| **Age (years)** median (min/max) | 41 (33/46) | 44 (34/59) | 45 (31/56) |
| **Female** n (%) | 4 (67%) | 3 (50%) | 2 (33%) |
| **BMI at screening (kg/m²)** median (min/max) | 25 (21/27) | 28 (23/32) | 29 (22/31) |
| **eGFR at baseline (mL/min/1.73m²)** median (min/max) | 53 (42/106) | 74 (50/108) | 49 (30/90) |
| **TKV at baseline (mL)** median (min/max) | 1802 (1185/3808) | 1832 (923/4242) | 2204 (1317/3567) |
| **Mayo Imaging Classification** n (%) | | | |
| 1C | 1 (17%) | 3 (50%) | 3 (50%) |
| 1D | 4 (67%) | 3 (50%) | 2 (33%) |
| 1E | 1 (17%) | 0 (0%) | 1 (17%) |

*Descriptive baseline data only. No formal assessment of between-cohort balance was performed.*

# Single-dose PYC-003 was well tolerated

## No treatment-related serious adverse events or discontinuations

### SAFETY OVERSIGHT

- Safety evaluated through Day 28
- Independent safety review before each dose escalation
- No protocol-defined stopping rule triggered

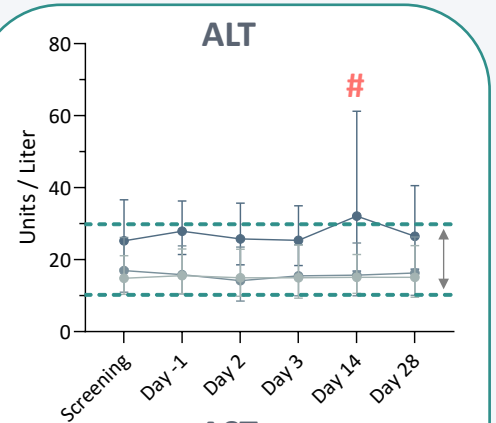
### Safety Outcomes for SAD Cohorts A (Healthy Volunteers) and B (ADPKD Participants)

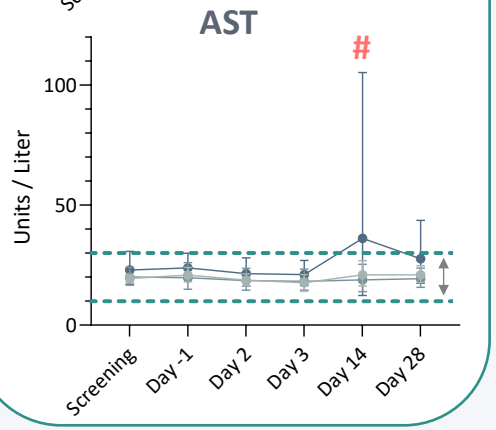
| | B1<br>0.4 mg/kg<br>n = 6 | B2<br>1.2 mg/kg<br>n = 6 | B3<br>2.4 mg/kg<br>n = 6 | Part A (HV)<br>n = 32 |
|---|---|---|---|---|
| Total TEAEs | 9 | 8 | 12 | 33 |
| Participants with ≥1 related TEAE | 0 | 1 | 1 | 3 |
| Total TESAEs | 1 | 0 | 0 | 0 |
| **Treatment-related TESAEs** | **0** | **0** | **0** | **0** |
| **TEAEs leading to discontinuation** | **0** | **0** | **0** | **0** |

- All AEs were mild to moderate
- The single SAE of mild transient amnesia in B1 was considered unrelated to study drug and has resolved

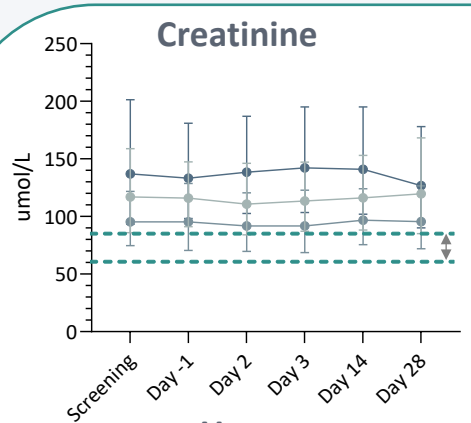
# No clinically meaningful treatment-related changes in hepatic, renal or electrolyte safety markers through Day 28

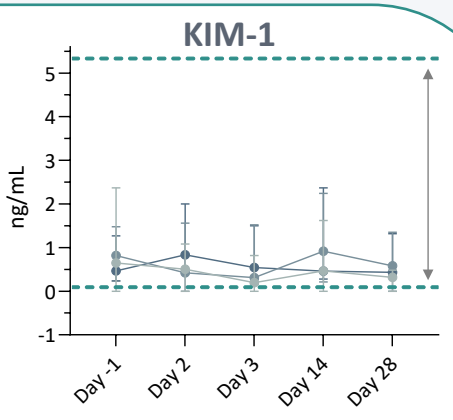
## HEPATIC

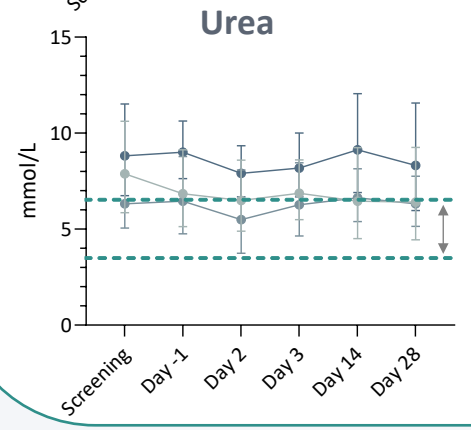


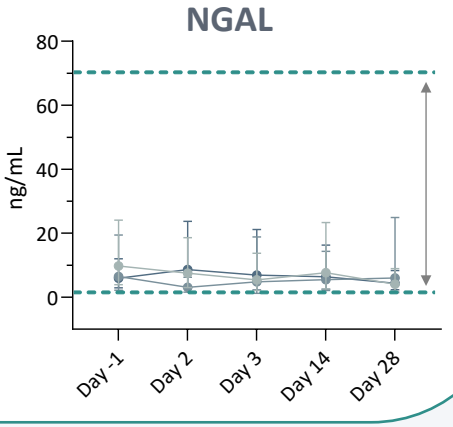




## RENAL / TUBULAR

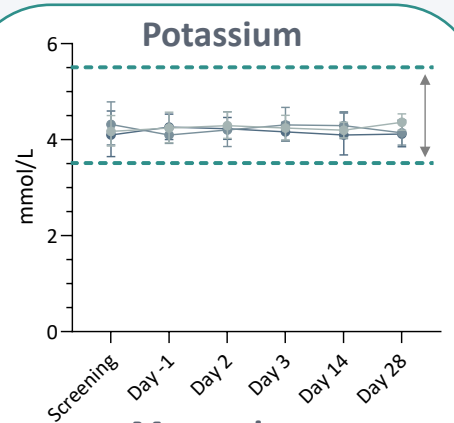


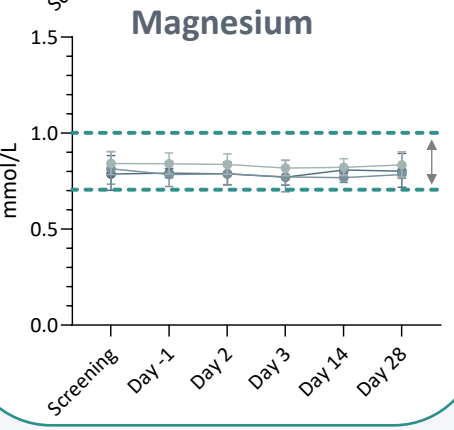




## ELECTROLYTES

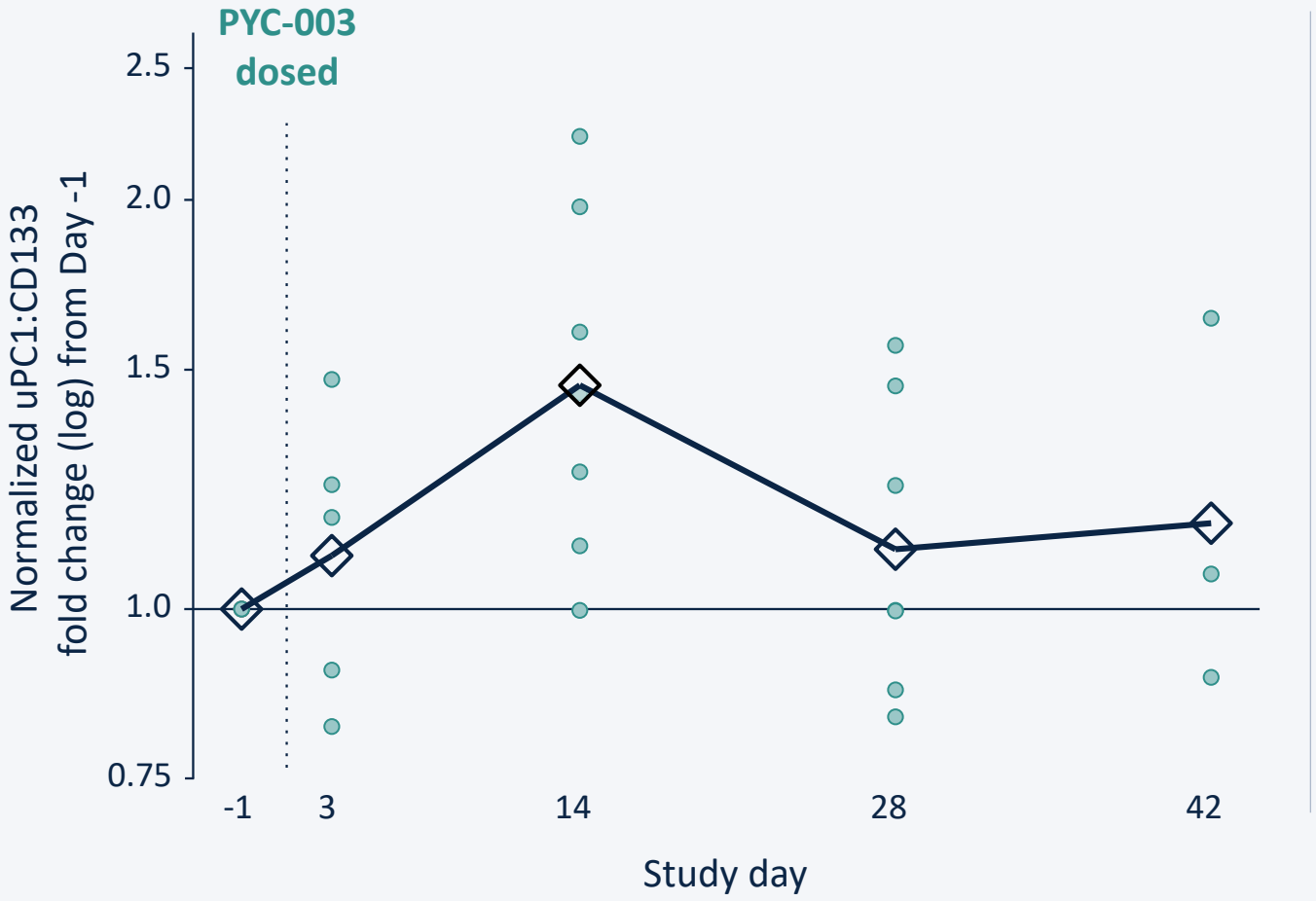



B1 (0.4 mg/kg) B2 (1.2 mg/kg) B3 (2.4 mg/kg) Reference range

*# The Day 14 elevation in one B3 participant occurred with flu-like symptoms and was assessed as unrelated to study treatment.*

# Single-dose PYC-003 showed a directional increase in urinary PC1, an exploratory read-out of renal PC1 expression




◇ Geometric mean, combined dose groups

● Individual values

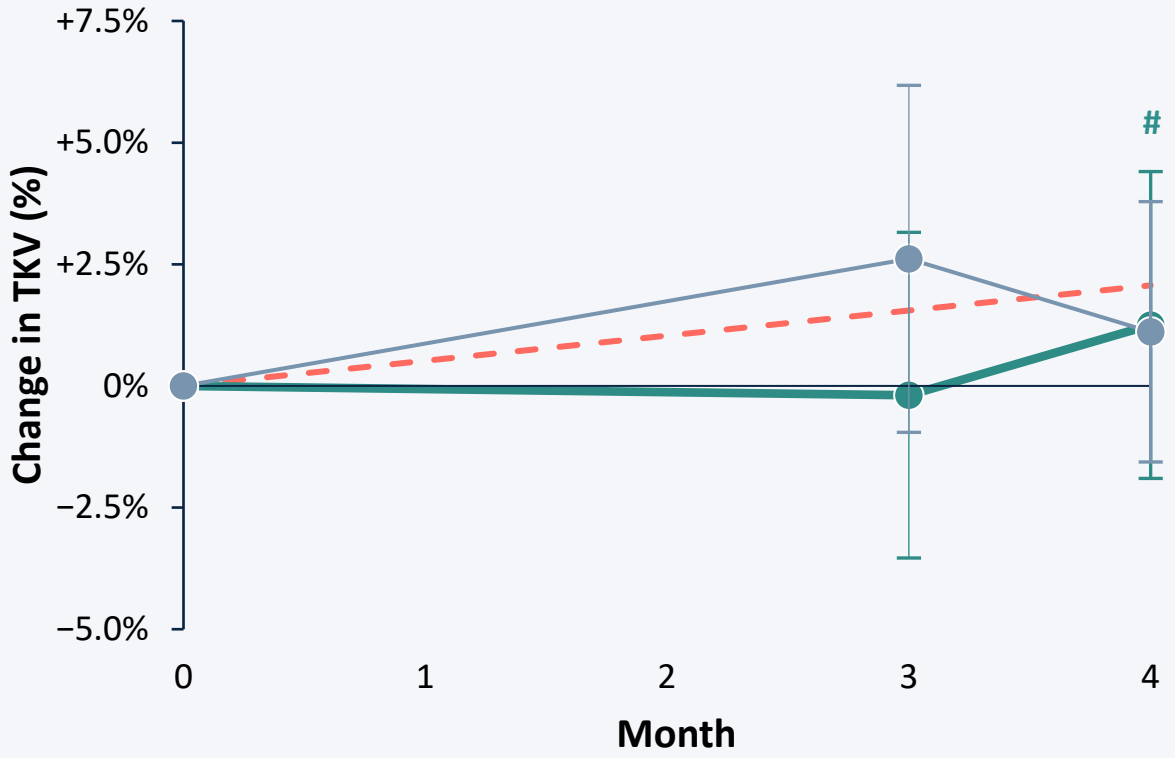
**Participants (n) by scheduled visit**

| Study day | 1.2 mg/kg | 2.4 mg/kg | Combined |
|---|---|---|---|
| **-1** | 3 | 5 | **8** |
| **3** | 2 | 3 | **5** |
| **14** | 3 | 4 | **7** |
| **28** | 3 | 4 | **7** |
| **42** | 2 | 1 | **3** |

*Earlier SAD cohorts' samples were collected under different conditions and are not included; 1.2 mg/kg data are from samples collected after a first dose in MAD.*

# Early TKV change after a single dose is directionally encouraging but requires confirmation in repeat-dose cohorts

## Mean TKV change: B1 and pooled B2/B3




**Illustrative Natural Progression of Untreated PKD (n = 925)**

Mayo Imaging Class C/D/E
Combined TEMPO 3:4, CRISP, HALT-PKD A)
**Mean: +6.2% annually**

**PYC-003 SAD PKD (B1 n=6, B2/B3 n=12 at M3; n=11 at M4)[#]**

Mayo Imaging Class C/D/E
Pooled B2/B3 (doses taken forward to MAD)
B1 (only assessed in SAD)
**Mean ± 95% Confidence Interval**
**[#] 4-month data pending for one B3 patient**

***PYC-003:*** *B2/B3 pooled (n=12 at Month 3; n=11 at Month 4) and B1 separately (n=6 at both visits); mean ± 95% CI.*
***Illustrative Natural Progression of Untreated PKD:*** *weighted mean annual % change in TKV from CRISP natural history, HALT-PKD A placebo (Perrone RD, et al. Kidney Med. 2022) and TEMPO 3:4 placebo (Irazabal MV, et al. Kidney Int Rep. 2016) illustrating the natural progression of untreated PKD.*

# Conclusions: Part B  single-dose PYC-003

1. **Safe and well tolerated:** no treatment-related serious adverse events or discontinuations

2. **No safety biomarker signal:** no evidence of renal or liver injury, and no clinically meaningful treatment-related changes through Day 28

3. **Target engagement:** directional increase of exosomal PC1, an exploratory read-out of renal PC1 expression

4. **Early TKV:** directionally encouraging, but requires confirmation in repeat-dose cohorts

**Next: repeat-dose MAD and OLE studies are ongoing, with data expected in 2027**

# Acknowledgements


**PARTICIPANTS AND FAMILIES**

We thank the participants who volunteered for this study, and their families and carers for their support.

**INVESTIGATORS AND SITE TEAMS**

We thank the investigators, study coordinators, and the nursing, pharmacy, imaging and laboratory staff at all participating sites, as well as referring nephrologists and PKD Australia for their support.






*This study was sponsored by PYC Therapeutics.*