PYC Therapeutics

27 March 2026

POLYCYSTIC KIDNEY DISEASE – PRESENTATION AT WORLD CONGRESS OF NEPHROLOGY

- **PYC is progressing a drug candidate (known as PYC-003) that addresses the underlying cause of Polycystic Kidney Disease (PKD) through clinical trials**
- **The Company today announces that it will present a poster on progress in the PYC-003 program at the World Congress of Nephrology (WCN) from 28 to 31 March in Yokohama, Japan**
- **A copy of the poster presentation is attached to this announcement**
- **Comprehensive safety and efficacy data from the ongoing Phase 1a Single Ascending Dose (SAD) study[1] in both healthy volunteers and PKD patients is expected to be presented in H2 CY26[2]**
- **PYC expects to initiate the Phase 1b Multiple Ascending Dose (MAD) study of PYC-003 in PKD patients in Q2 CY26 with safety and efficacy data from the MAD study expected to be presented in CY27[3]**

PERTH, Australia and SAN FRANCISCO, California – 27 March 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 it will present a poster update on progress in the PYC-003 drug development program at the World Congress of Nephrology (WCN) from 28 to 31 March in Yokohama, Japan.

A copy of the poster presentation is attached to this announcement.

[1] 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, 27 February 2026, 23 March 2026
[2] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
[3] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 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[4].

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.

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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[4] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

PINACLE-1: A Phase 1 Clinical Trial of PYC-003 for the Treatment of Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

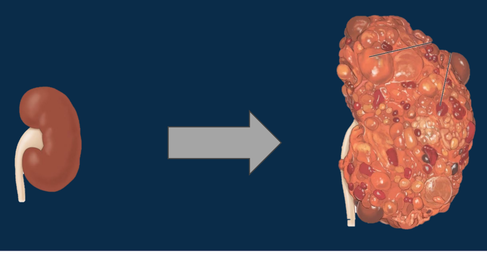
Anja Stirnweiss[1], Aron Chakera[1,2], Jessica Stevenson [1], Vanessa Neve[1], Genevieve Syn[1], Anna Mills[1], George Mitchell[1], Jan Hurst[1], Clarissa McDonagh[1], Bridget Flis[1], Maria Kerfoot[1], Adam Martin[1], Subrata Das[1], Sri Mudumba[1], Paula Cunningham[1]

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

ADPKD is an area of major unmet patient need

Autosomal Dominant Polycystic Kidney Disease is a highly prevalent, potentially lethal disorder

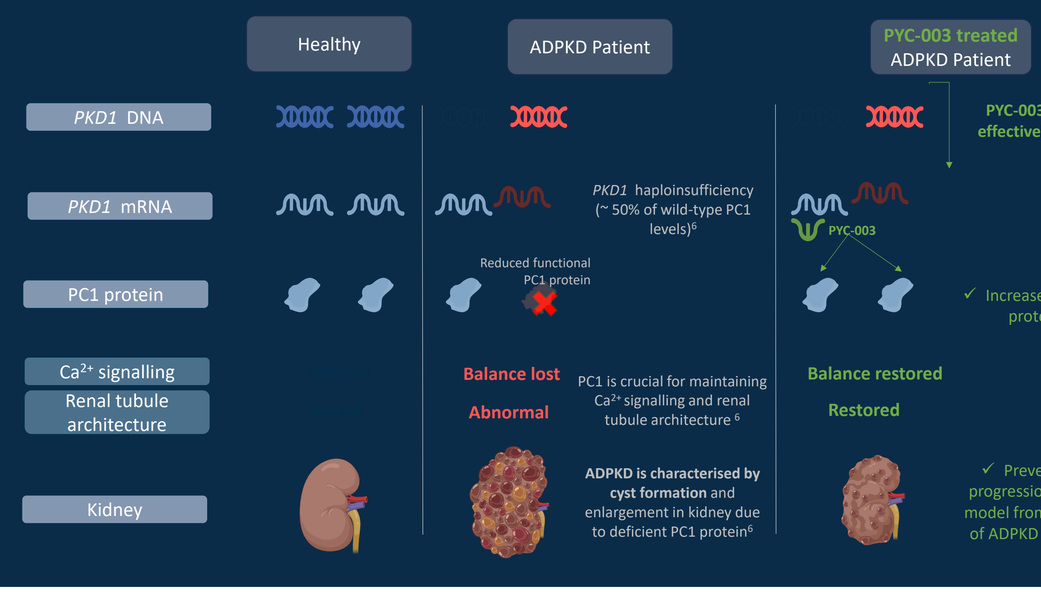
- Autosomal Dominant Polycystic Kidney Disease (ADPKD) affects ~1 in every 1,000 people, indicating over 12.5 million people are affected worldwide[1]
- ~80% of ADPKD patients have a mutation in one copy of the *PKD1* gene leading to insufficient Polycystin-1 (PC1) protein expression[2]
- Patients develop fluid filled cysts in the kidneys when PC1 functional activity falls below a critical level[3]
- These cysts grow over time, destroying the architecture and ultimately the function of the kidney
- Half of the patients progress to end-stage renal failure by the age of 60 and require a kidney transplant[4]
- Approximately 95% of patients with ADPKD have no treatment options available,[5] and there are no drugs that address the underlying cause of the disease



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

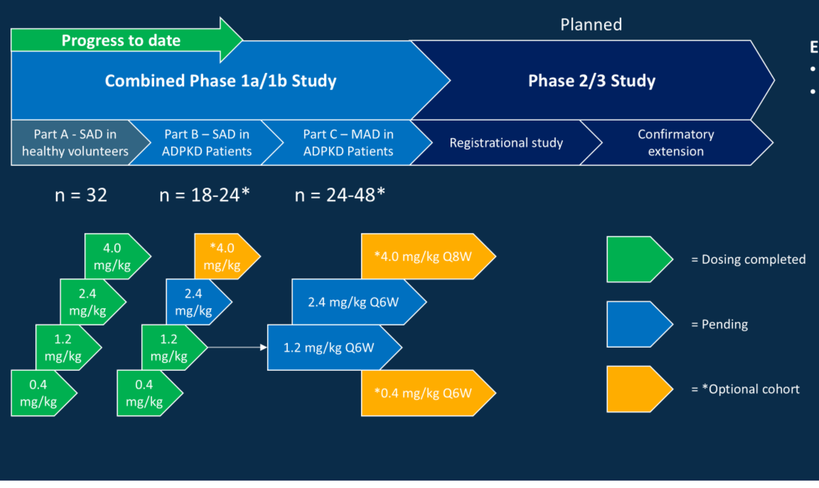
PYC-003 targets the deficient gene causing the disease and increases its expression

- PYC-003 specifically targets PKD1 to increase PC1 protein, thereby holding disease-modifying potential



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

- Key pre-screening criteria included an estimated glomerular filtration rate (eGFR) >30mL/min/1.73m2, Mayo imaging classification of C, D and E, and a genetically confirmed PKD1 mutation



Endpoints
- Safety & Tolerability
- Efficacy
  - Biomarker
  - Total Kidney Volume (TKV)
  - Estimated Glomerular Filtration Rate (eGFR)

PYC-003 was safe and well-tolerated at all doses assessed to date in healthy volunteers and ADPKD patients^

- No Treatment Emergent Serious Adverse Events
- No changes in serum or urinary electrolytes (creatinine, magnesium, potassium levels)

Healthy volunteers

Cohort A1 (0.4 mg/kg)

AE term	Comments
Headache	Not related
Viral illness	Not related
Headache	Unlikely related
Headache	Unlikely related

Cohort A2 (1.2 mg/kg)

AE term	Comments
Tinnitus	Possibly related
Upper back pain -muscle spasm	Not related
Hyperpigmentation from IPL	Not related
Simple headache	Not related
Upper respiratory tract infection	Not related
Headache	Not related
Bruise, right big toe	Not related
Abdominal cramps	Not related
Headache	Unlikely related
Erythema - venipuncture site	Not related

Cohort A3 (2.4 mg/kg)

AE term	Comments
Headache	Unlikely related
Headache	Not related
Diarrhea	Unlikely related

Cohort A4 (4.0 mg/kg)

AE term	Comments
Bilateral tinnitus	Possibly related
Left ACF bruising	Not related
Left ACF pain	Not related
Dry mouth	Not related
Oliguria	Not related
Upper respiratory tract infection	Not related
Contact dermatitis left antecubital fossa	Not related
Contact dermatitis secondary to IVC dressing	Not related
Headache	Not related
Postural lightheadedness	Unlikely related
Tinnitus	Possibly related
ECG dot dermatitis	Not related
Headache	Not related

ADPKD patients

Cohort B1 (0.4 mg/kg)

AE term	Comments
Dog bite	Not related
Headache	Not related
Dermatitis from IV dressing	Not related
Dermatitis from IV dressing	Not related
Diarrhoea	Not related
Transient amnesia	Not related
Headache	Not related
Nausea	Not related
Sacroiliitis	Not related

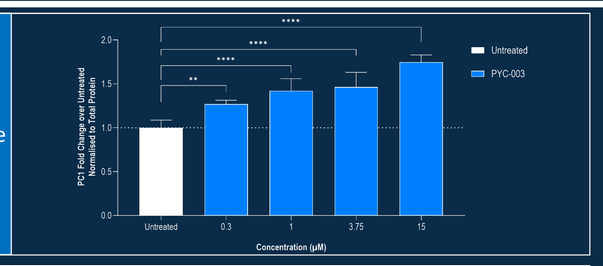
Cohort B2 (1.2 mg/kg)

AE term	Comments
Headache	Not related
Cervical pain	Not related
Erythema on V3 and V4 ECG dot placement	Not related
Right antecubital fossa cannula site bruise	Not related
Headache	Unlikely
Left hand swelling	Unlikely
Renal cyst rupture	Unlikely
Rash – left quad	Possible

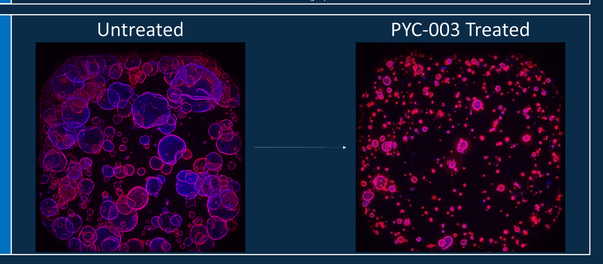
^ AEs taken from day 28 data taken from SRC

Efficacy and biodistribution in ADPKD models alongside PK/PD modelling suggest PYC-003 will reach therapeutic human kidney exposure with safe & infrequent doses

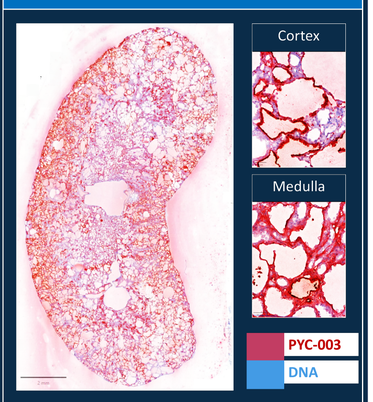
Pre-clinical efficacy: Increased target gene expression^



Pre-clinical efficacy: Reduced cyst volume#

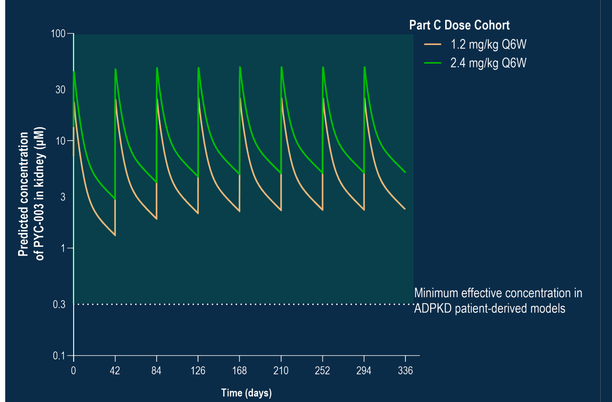


Distribution to cyst-lining cells in ADPKD mouse model (*Pkd1*-KO)$

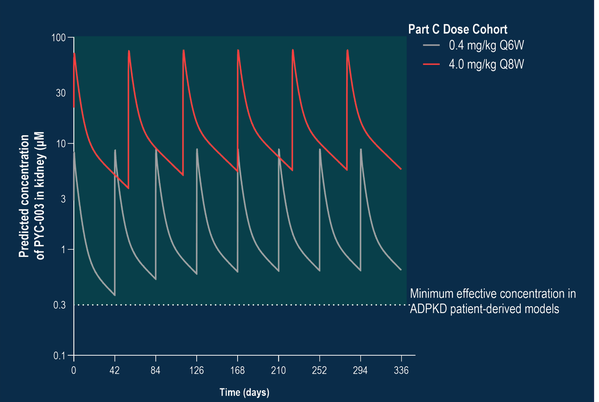


^ PC1 full length protein fold-change over untreated (normalised to total protein) assessed at day 7 following treatment with PYC-003. Data presented as mean+SD. The data shows a statistically significant (one-way ANOVA vs untreated **p<0.01, ****p<0.0001) difference between treatment groups and the untreated control. Assessed in iPSC-PTL (iPSC-proximal tubular like) cells derived from an ADPKD patient with *PKD1* mutation.
# In a patient-derived 3D cyst assay - Refer to ASX Announcement of 13 November 2023
$ Distribution of PYC-003 to cystic kidney in PKD1 knockout (KO) model of PKD. Images captured Day 3 post-dose single 10 mg/kg dose of the drug candidate and measured by miRNAscope

Confirmed dose intervals for repeat dose study



Optional dose intervals for repeat dose study



^ Dose cohorts proposed for Part C (repeat dose study) are safe and well-tolerated in healthy volunteers as single doses and are predicted to consistently exceed the current minimum effective concentration of PYC-003 in ADPKD patient-derived models.

Three endpoints (uPC1, TKV, and eGFR) will be used to evaluate PYC-003 in the repeat-dose study in ADPKD patients

	Urinary PC1	Total Kidney Volume	Estimated Glomerular Filtration Rate (eGFR)
	Disease progression →		
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^	-2.91 mL/min/1.73m^2/yr#
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)

^ Average TKV growth rate of 6.60%/yr for Mayo Classification C, D and E - from STAGED-PKD trial
# Average eGFR rate of decline of -2.91 mL/min/1.73m^2/yr for Mayo Classification C, D and E - from STAGED-PKD trial

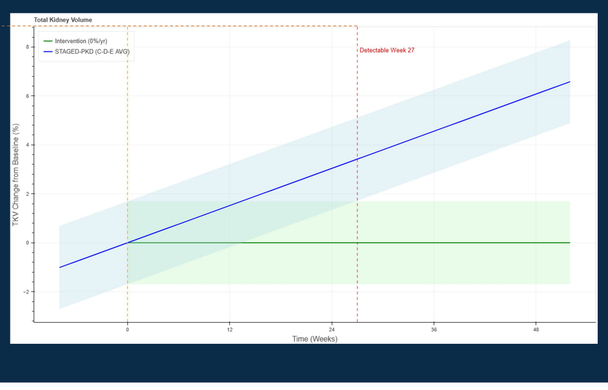
>6 months of data is required for meaningful insight on TKV growth

This is to allow for signal detection above the 'noise' of the data set, driven by:

- Variability observed on this endpoint in natural history studies;
  - Small group size (total n=24, n=12 per cohort); and
  - Natural variability associated with MRI measurements

Assumption: a treatment that arrests TKV growth

A treatment that halts disease progression in ADPKD will show significant divergence from published placebo control progression (STAGED-PKD) after **~27 weeks**



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[3] Ferreira, F. M., et al. (2015). https://doi.org/10.15586/codon.pkd.2015.ch7
[4] Cloutier, M., et al. (2020). https://pubmed.ncbi.nlm.nih.gov/32070341/
[5] Otsuka's JYNARQUE® (tolvaptan) was approved in 2018 for ADPKD with a black box warning for serious liver injury.

Disclaimer: Clinical development plan is subject to confirmation with relevant regulatory authorities and may change