PYC Therapeutics

29 AUGUST 2025

POLYCYSTIC KIDNEY DISEASE PROGRAM – PRESENTATION OF SAFETY DATA AT ANZSN

- **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 Dr. Aron Chakera will present the latest data from Part A of the ongoing Phase 1a/1b clinical trial evaluating the safety/tolerability profile of PYC-003 in a dose escalation study in healthy volunteers at the Australian and New Zealand Society of Nephrology (ANZSN) conference on 1 September 2025**

- **Highlights of Dr. Chakera's presentation of data from the three completed dose cohorts in Part A of the trial demonstrate a favourable emerging safety profile for PYC-003 throughout the expected human pharmacodynamic range[1], including:**
  - **No Treatment Emergent Serious Adverse Events;**
  - **No changes in serum electrolytes or creatinine[2]; and**
  - **No evidence of renal injury[3] following administration of PYC-003.**

- **A copy of Dr. Chakera's presentation is attached to this announcement**

PERTH, Australia and SAN FRANCISCO, California – 29 August 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 safety data from the three completed healthy volunteer cohorts in Part A of the combined Phase 1a/1b clinical trial will be presented by Dr. Aron Chakera at the Australian and New Zealand Society of Nephrology (ANZSN) meeting taking place in Perth, Western Australia between 30 August and 3 September 2025.

An overview of Parts A and B of the Phase 1a/1b study of PYC-003 is provided in *Figure 1*.

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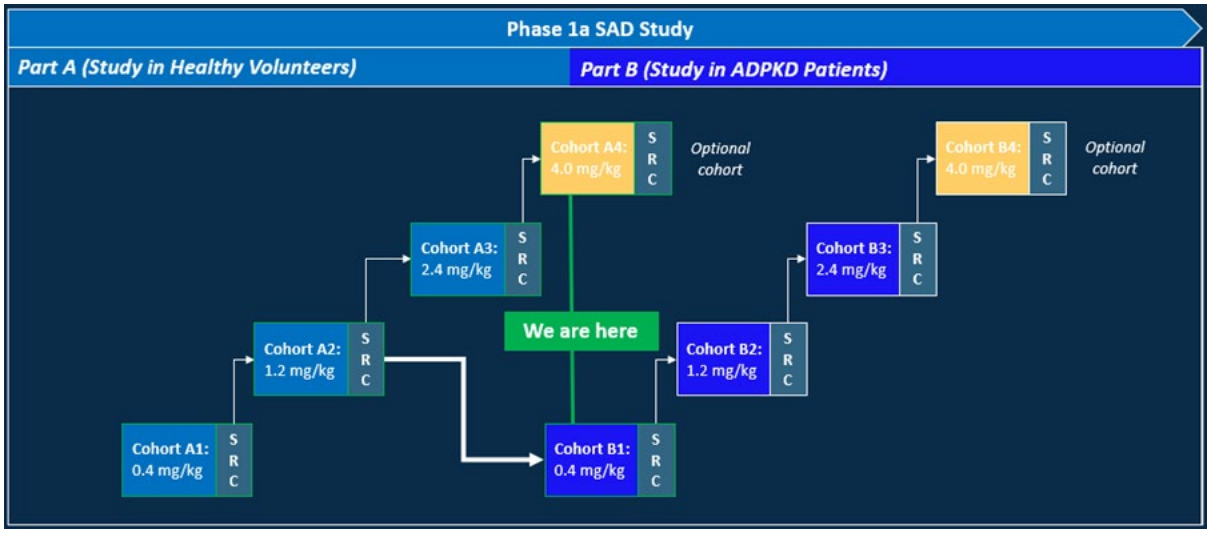
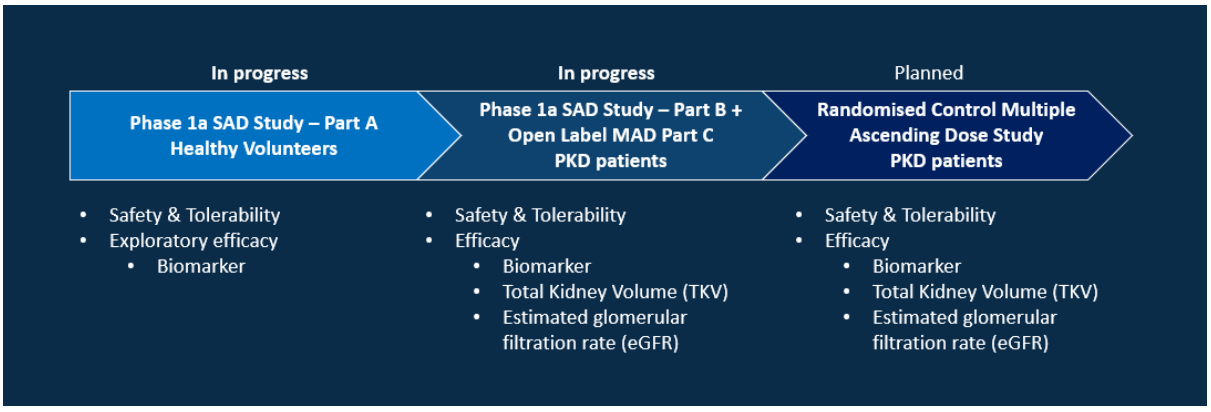
[1] See ASX announcement of 27 November 2024. Refer to slides 10 and 11 of the attached presentation for key safety data from the study.
[2] Outside of the reference range
[3] As assessed by biomarkers of renal injury including KIM-1 and NGAL

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



Parts A and B of the SAD study will be followed by an Open-Label Multiple Ascending Dose (MAD) study facilitating repeat dosing and evaluation of the optimal dosing regimen of PYC-003. This study will be conducted alongside a Phase 1b randomised controlled trial 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[4]).

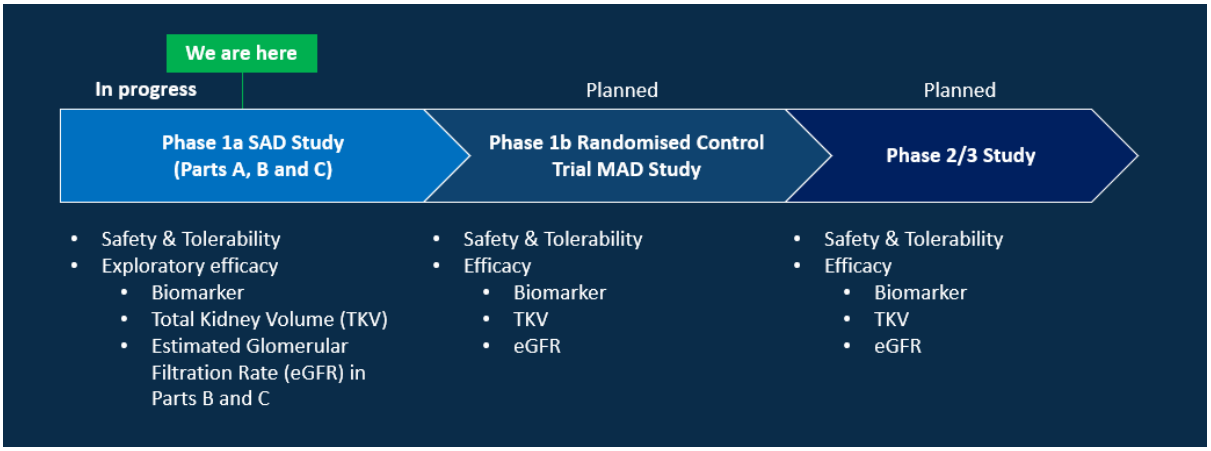
Figure 2. Integration of PYC's Phase 1a SAD (Parts A and B) with OLE MAD (Part C) and Phase 1b Randomised Control Trial (RCT) MAD studies



Successful completion of the Phase 1a/1b study described above will lead to initiation of a registrational combined Phase 2/3 trial aimed at supporting a New Drug Application for PYC-003 (See Figure 3[5]).

[4] Subject to confirmation with the relevant regulatory authorities
[5] Subject to confirmation with the relevant regulatory authorities

Figure 3. Proposed clinical development pathway for PYC-003



Next Steps

The primary objective of the ongoing Phase 1a/1b study is to evaluate the safety/tolerability profile of PYC-003 with a secondary objective to evaluate the efficacy of the drug candidate in PKD patients.

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 [6].

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.

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

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 CEO of PYC Therapeutics Limited

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

Dr Aron Chakera

September 2025

Disclaimer

The purpose of this presentation is to provide an update of the business of PYC Therapeutics Limited (ASX:PYC) ['PYC']. These slides have been prepared as a presentation aid only and the information they contain may require further explanation and/or clarification. Accordingly, these slides and the information they contain should be read in conjunction with past and future announcements made by PYC Therapeutics and should not be relied upon as an independent source of information. Please contact PYC and/or refer to the Company's website for further information.

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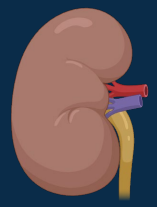
Objectives for today

- Introduce you to the clinical development pathway for PYC-003 – the first investigational drug candidate to address the root cause of Polycystic Kidney Disease (PKD)
    - PYC-003 is an RNA therapy that increases Polycystin 1 (PC1) protein expression and rescues the cystic phenotype in pre-clinical models of PKD
    - This drug candidate has now progressed into a combined Phase 1a/1b clinical trial and has:
        - A favourable emerging safety/tolerability profile in Healthy Volunteers; and
        - Is now being administered to PKD patients in a Single Ascending Dose (SAD) study
    - Disease-modifying drugs hold unique potential in PKD and the ongoing SAD and upcoming Multiple Ascending Dose (MAD) studies of PYC-003 will seek to demonstrate the impact of this approach in PKD patients for the first time

ADPKD is an area of major unmet need due to its high prevalence and devastating consequences

Polycystic Kidney Disease

Healthy adult kidney



Polycystic kidney

High prevalence

ADPKD affects **1 in every 1,000** people meaning **>5 million people worldwide** have the disease[1,2]

Life-changing

Half of all ADPKD patients will **require a kidney transplant** by the age of 60 due to **end-stage renal failure**[3]

Limited treatment options

There are **no drugs available** that address the underlying cause of the disease and there is an **urgent need for treatments with disease-modifying potential**

1. Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [Updated 2022 Sep 29]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews. Seattle (WA): University of Washington, Seattle; 1993-2023.
2. Willey et al. Analysis of Nationwide Data to Determine the Incidence and Diagnosed Prevalence of Autosomal Dominant Polycystic Kidney Disease in the USA: 2013-2015. Kidney Dis (Basel). 2019;5(2):107-17.
3. Cloutier et al. The societal economic burden of autosomal dominant polycystic kidney disease in the United States. BMC Health Serv Res. 2020;20(1):126.

PYC-003 is the first drug candidate that directly addresses the root cause of ADPKD to have advanced into human trials

PYC-003

- PYC-003 is an antisense oligonucleotide conjugated to a delivery peptide which is administered via intravenous infusion
- The oligonucleotide stabilises *PKD1* at the mRNA level and enhances translation – increasing expression of the missing PC1 protein

Efficacy

- PYC-003 increases PC1 expression *in vitro* and rescues the cystic phenotype in a 3D cyst assay derived from patients with advanced polycystic kidney disease

Delivery

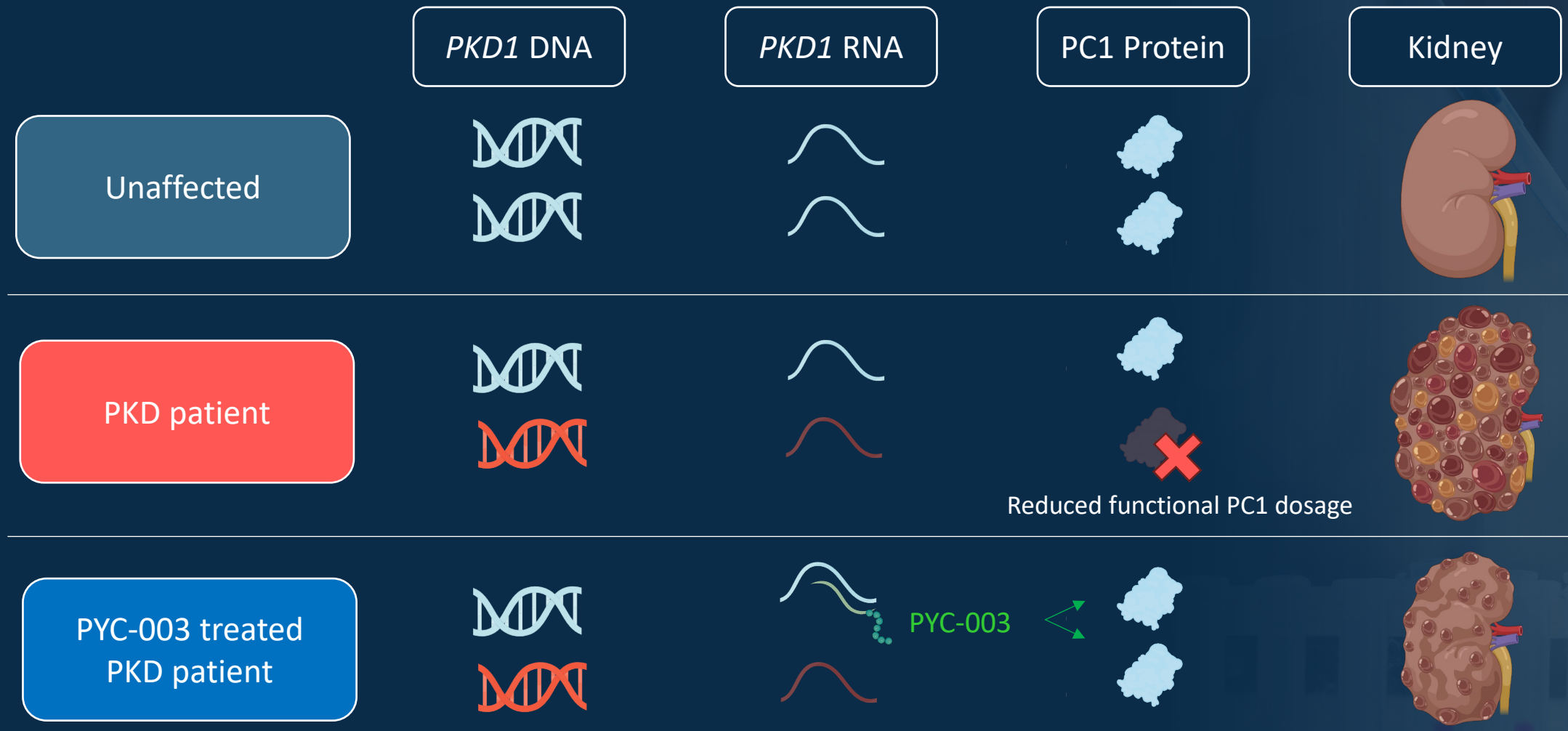
- PYC distributes primarily to the two key organs affected in PKD – the kidney and the liver
- Within the kidney, PYC-003 is taken up by Renal Tubular Epithelial Cells including the cyst-lining cells in animal models of PKD

Safety

- PYC-003 achieves target tissue concentrations at safe and well tolerated doses *in vivo* that exceed the pharmacodynamic range *in vitro* and *ex vivo*

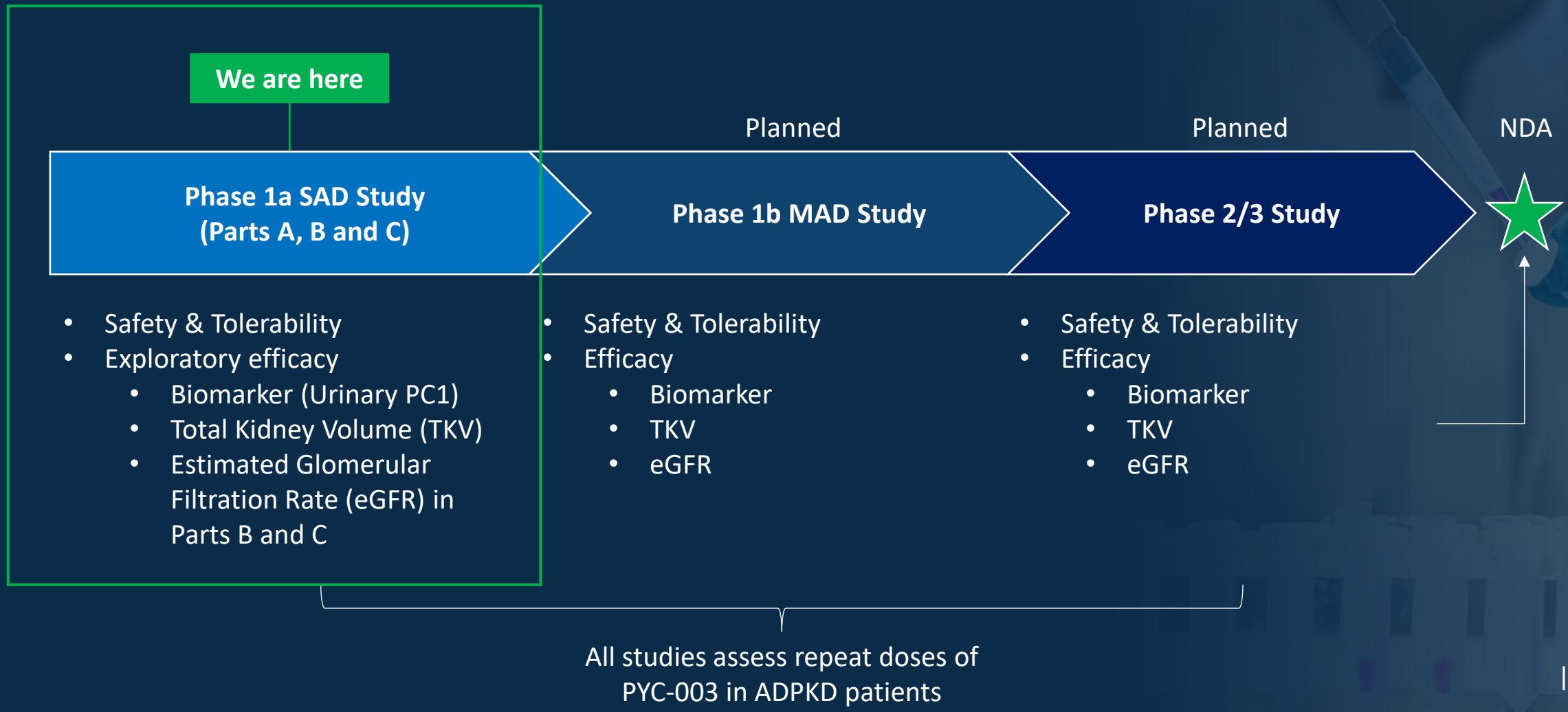
For more details see poster #74

PYC-003 is an RNA therapy with disease-modifying potential for ADPKD patients



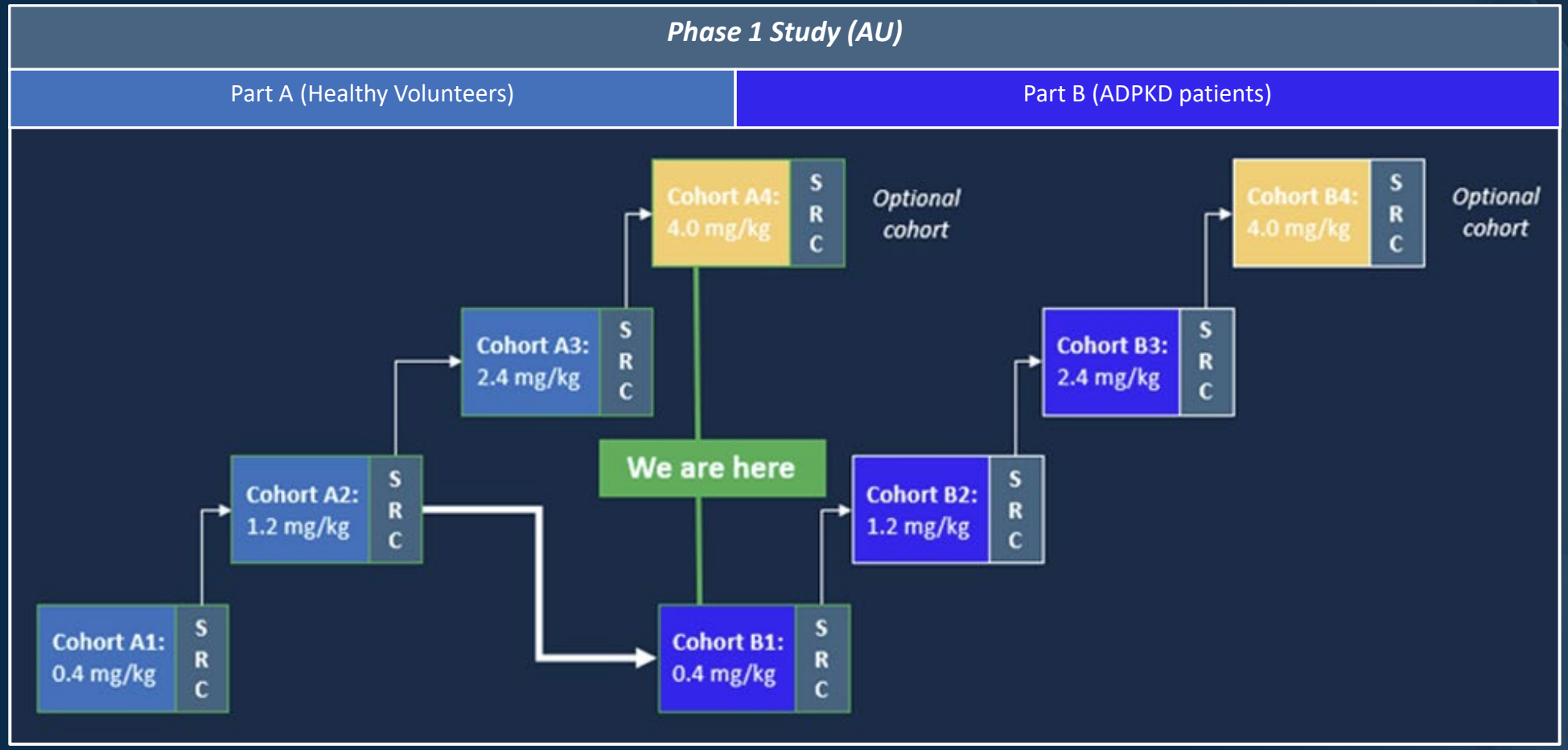
Created using BioRender

PYC-003 has a high-velocity path to a New Drug Application



PYC-003-CL-001: Phase 1 Study to Evaluate the Safety and Tolerability of Intravenously Administered PYC-003

- Phase 1 Parts A and B are ongoing and an amendment to add Part C (MAD) study is in preparation



Part B key eligibility criteria are:

Inclusion criteria

- Male or female aged 18 to 60 years (inclusive) at the time of informed consent.
- ADPKD diagnosis based on Ravine Pei diagnosis criteria (Pei et al. 2009)
- 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 (Irazabal et al. 2015)
- Estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m2 via the CKD EPI 2021 calculation (Inker et al. 2021)
- BMI ≥ 18.0 and ≤ 32.0 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

PYC-003 was safe and well-tolerated at doses up to 2.4 mg/kg in Healthy Volunteers

- **No Treatment Emergent Serious Adverse Events**
- **No changes in serum or urinary electrolytes (creatinine, magnesium, potassium levels)**
- **No evidence of renal injury following administration of PYC-003**

Cohort 1 (0.4 mg/kg)

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

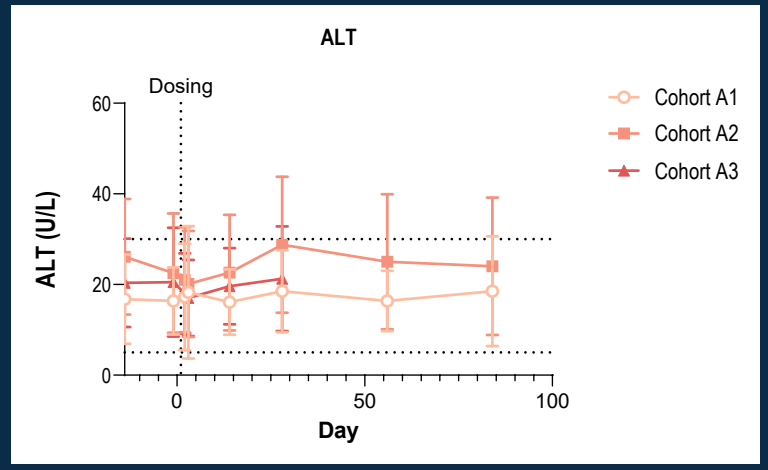
Cohort 2 (1.2 mg/kg)

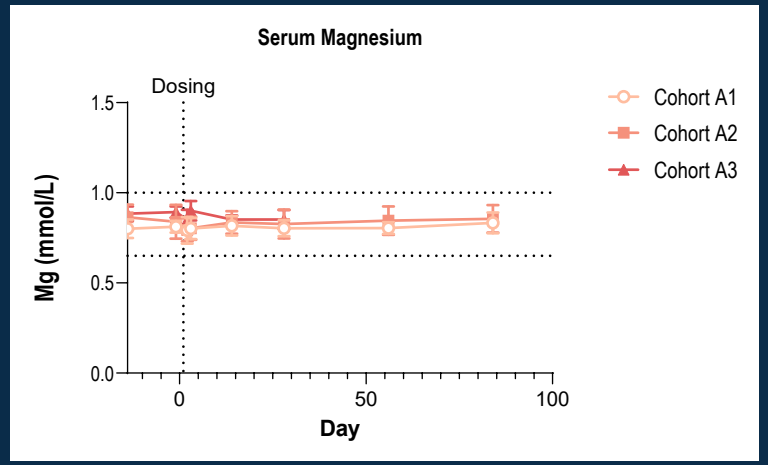
AE term	Comments
Tinnitus	Possibly related
Upper back pain-Muscle Spasm	Not related
Hyperpigmentation from IPL	Not related
Simple headache	Not related
Upper respiratory tract infection	Not related
Headache	Not related
Bruise, right big toe	Not related
Abdominal cramps	Not related
Headache	Unlikely related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

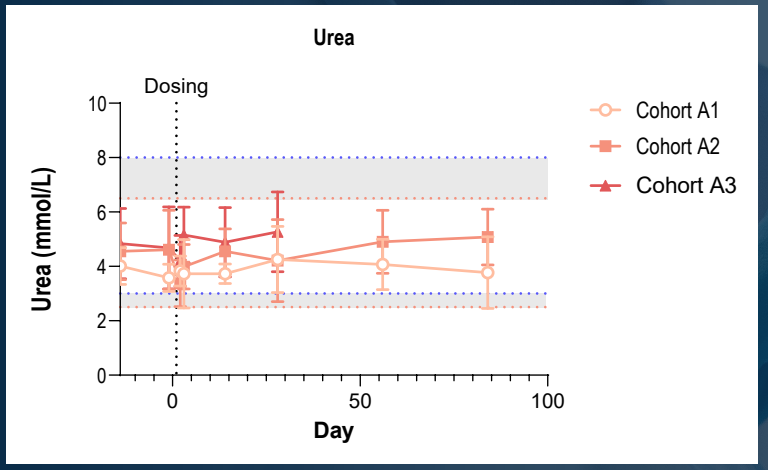
Cohort 3 (2.4 mg/kg)

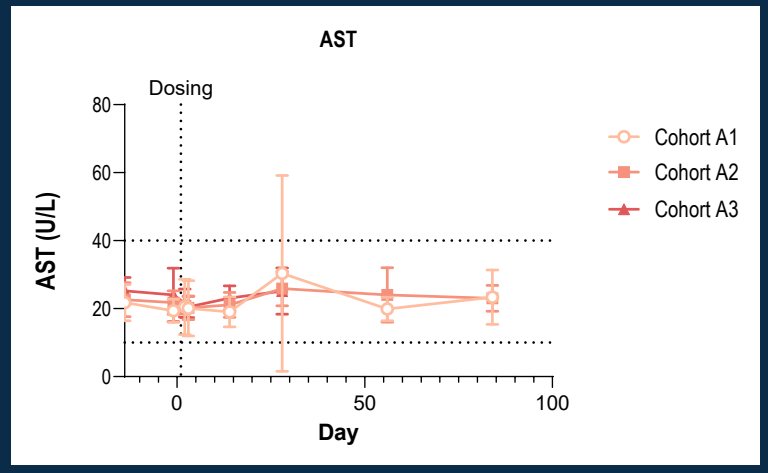
AE term	Comments
Headache	Unlikely related
Headache	Not related
Diarrhea	Unlikely related

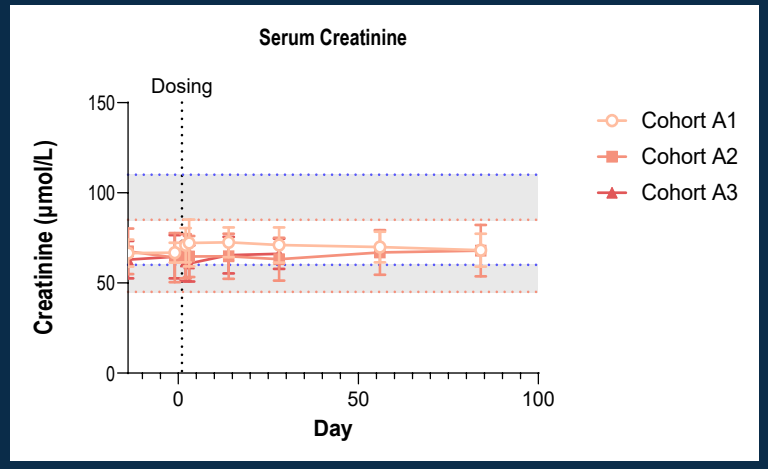
No changes in blood chemistry or increases in kidney markers were seen in HVs dosed up to 2.4 mg/kg

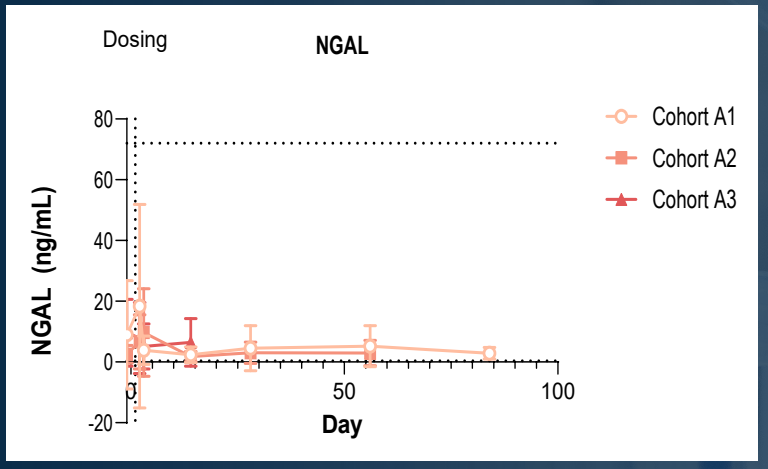












The ongoing Phase 1a/1b studies are currently active across 5 sites with 2 more pending activation

Activation pending:

- Sunshine Hospital in collaboration with Doherty Clinical Trials
- Concord Hospital

To learn more about this clinical trial visit clinicaltrials.gov, email pkd@pyctx.com or scan the QR code