PYC Therapeutics

10 February 2025

# APPROVAL TO COMMENCE HUMAN TRIALS IN POLYCYSTIC KIDNEY DISEASE

- **PYC is a genetic medicine company focused on the creation of precision therapies for patients with severe diseases and no treatment options available**
- **One of PYC's development programs is a drug candidate that addresses the underlying cause of Polycystic Kidney Disease (PKD) - a life-changing condition affecting more than 5 million people[1] globally**
- **PYC today announces that it has received regulatory approval to commence human trials of its drug candidate for PKD**
- **The Company will now commence clinical studies with initial human safety and efficacy data anticipated within 2025[2]**

**PERTH, Australia and SAN FRANCISCO, California – 10 February 2025**

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating precision therapies for patients with genetic diseases and no treatment options available. One of the Company's assets is an investigational drug candidate (known as PYC-003) that addresses the underlying cause of Autosomal Dominant Polycystic Kidney Disease (PKD)[3].

PYC today announces that it has received all required regulatory approvals to commence human trials of PYC-003. The Company will now proceed to initiate a Single Ascending Dose (SAD) study of this drug candidate in healthy volunteers (Part A) and PKD patients (Part B) (See Figure 1 for a schematic overview of the SAD study).

PKD is a life-changing disease characterised by multiple cysts forming throughout a patient's kidney that increase in size over time. The growth of the cysts destroys the architecture and ultimately function of the patient's kidney eventually leading to end-stage renal failure and the need for organ transplantation in the majority of patients by the age of 55. PKD affects ~1 in every 1,000 people and represents a major unmet need in medicine.

[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] Management forecast accurate as at 10 February 2025 and subject to the risks and uncertainties set out in the Company's ASX disclosures of 14 March 2024

[3] Caused by mutations in the *PKD1* gene

The progression of PYC-003 into human trials is supported by pre-clinical data generated in both animal and patient derived models[4]. PYC-003 has demonstrated high target tissue concentration at safe and well tolerated doses in Non-Human Primates[5] (NHPs). The efficacy of this drug candidate has been demonstrated:

- *Quantitatively* - in cells derived from kidneys (*in vitro*) and in animal models (*in vivo*); and
- *Phenotypically* - in human 3D kidney cyst models derived from patients with end-stage renal failure due to PKD.

**Study Overview**

The SAD study will involve subjects enrolled receiving a single intravenous infusion of PYC-003. The primary endpoint of the study will be Treatment Emergent Adverse Events (TE-AEs) and Treatment Emergent Serious Adverse Events (TE-SAEs). Enrolled subjects will also be monitored on a range of endpoints directed towards assessment of the efficacy of the drug candidate.

The study will be conducted across 4 sites located in Australia. Enrolled subjects will be aged between 18 and 60. The SAD study will be conducted in accordance with Good Clinical Practices (GCP) and the PYC-003 used in this study has been manufactured to according to Good Manufacturing Practice (GMP) standards.

Part A of the SAD study will be a double-blinded, placebo controlled format conducted in healthy volunteers and will consist of three cohorts who will receive 0.4 mg/kg, 1.2 mg/kg or 2.4 mg/kg of PYC-003 respectively. An optional fourth cohort will allow dose escalation to 4.0 mg/kg of PYC-003 if required. Each cohort in Part A will consist of 8 randomised subjects with 6 subjects to receive PYC-003 and 2 subjects to receive a placebo. A Safety Review Committee (SRC) will review the 4-week safety data for each cohort prior to escalation of dosing to the next level.

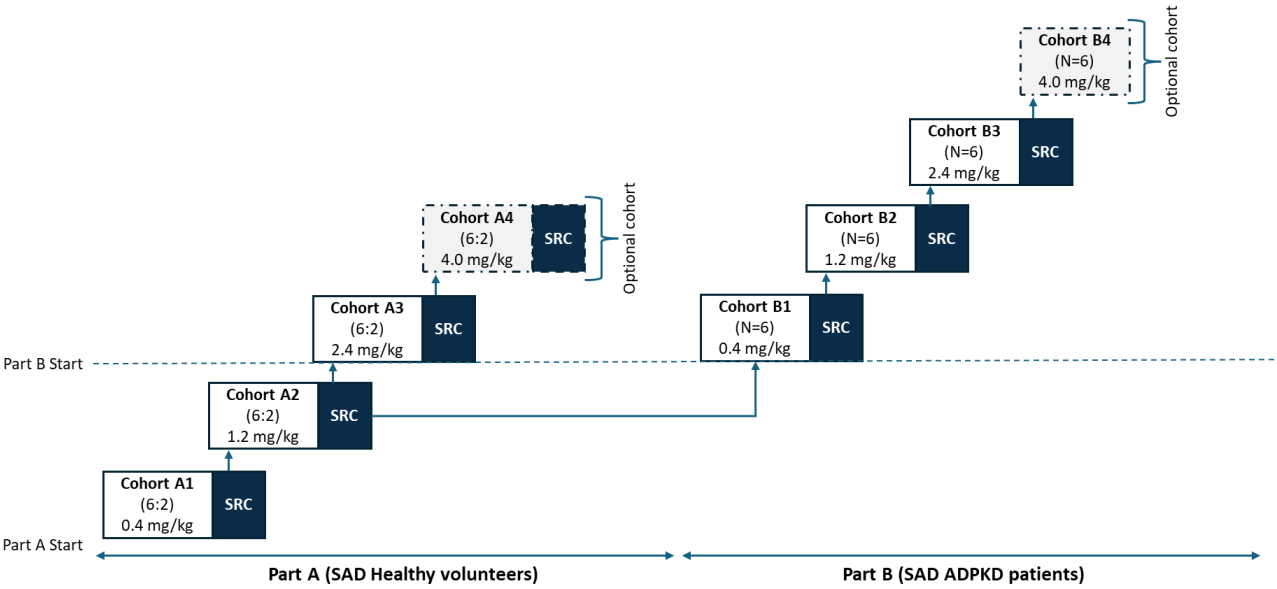
Part B of the SAD in PKD patients is expected to commence upon successful completion of the SRC review of cohort 2 in Part A of the study. Part B of the SAD will follow the design of Part A with 6 subjects per cohort and all subjects to receive PYC-003 under an open label format. All study participants will be monitored for 24-weeks following dosing.

The primary endpoint of the study will be Treatment Emergent Adverse Events (TE-AEs) and Treatment Emergent Serious Adverse Events (TE-SAEs). The study will also collect data on exploratory endpoints directed towards efficacy of the drug candidate including urinary biomarkers. Patients in Part B of the study will undergo Magnetic Resonance Imaging (MRI) for analysis of biometric markers including, but not limited to, height-adjusted Total Kidney Volume (hTKV), Total Cyst Number (TCN) and Cyst Parenchyma Surface Area (CPSA).

This SAD study forms the basis of the clinical trial pathway aligned with the US Food and Drug Administration during a pre-Investigational New Drug (pre-IND) meeting that occurred in 2024. Dosing of patients in this study is expected to be completed in ~12 months with a budgeted cost of A$10 million.

[4] See ASX announcement 27 November 2024
[5] See ASX announcement 27 November 2024

**Figure 1.** Schematic overview of the SAD study




## About PYC-003 – a first-in-class drug candidate with disease-modifying potential in PKD

PKD affects ~1 in every 1,000 people. The disease is characterised by large numbers of cysts forming in patient kidneys. These cysts increase in size over time and ultimately destroy the kidney tissue resulting in renal failure with the majority of PKD patients requiring a kidney transplant[6].

Approximately 95% of patients with PKD have no treatment options available to them today[7]. As a result of this major unmet need, the US Food and Drug Administration has outlined a pathway for a New Drug Application to be submitted in PKD following a Phase 2 clinical trial based on a surrogate endpoint[8].

PKD represents an estimated >US$10 billion p.a. market[9]. PYC-003 holds potential for both first-in-class and best-in-class status in this indication[10] due to its highly specific mechanism of action that targets the underlying cause of the disease.

## 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.

[6] Cloutier M, et al. The societal economic burden of autosomal dominant polycystic kidney disease in the United States. BMC Health Serv Res. 2020;20(1):126.
[7] Dong K, Zhang C, Tian X, Coman D, Hyder F, Ma M, Somlo S. Renal plasticity revealed through reversal of polycystic kidney disease in mice. Nat Genet. 2021 Dec;53(12):1649-1663. doi: 10.1038/s41588-021-00946-4. Epub 2021 Oct 11. PMID: 34635846; PMCID: PMC9278957.
[8] See ASX announcement 13 November 2023
[9] Based on prevalence of the indication of 1 in 1,000 as per the PKD Foundation and median orphan drug pricing of US$160k p.a. as per EvaluatePharma
[10] Refer ASX Announcement 17 November 2023

PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**[11].

**PYC's drug development programs**

**Retinitis Pigmentosa type 11**

- A blinding eye disease of childhood affecting 1 in every 100,000 people[12]
- Currently progressing through phase 1/2 clinical trials with preparation under way for a potentially registrational trial to commence in 2025[13]

**Autosomal Dominant Optic Atrophy**

- A blinding eye disease of childhood affecting 1 in every 35,000 people[14]
- Currently progressing through phase 1/2 clinical trials with human safety and efficacy read-outs anticipated in 2025[15]

**Autosomal Dominant Polycystic Kidney Disease**

- A chronic kidney disease affecting 1 in every 1,000 people[16] that leads to renal failure and the need for organ transplantation in the majority of patients
- Currently progressing through phase 1a/1b clinical trials with human safety and efficacy data anticipated throughout 2025 and 2026[17]

**Phelan McDermid Syndrome**

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[18]
- PYC will initiate Investigational New Drug (IND)-enabling studies in 2025 to facilitate progression into human trials in 2026

For more information, visit pyctx.com, or follow us on LinkedIn and Twitter.

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

[12] Sullivan L, et al. Genomic rearrangements of the PRPF31 gene account for 2.5% of autosomal dominant retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2006;47(10):4579-88

[13] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

[14] Yu-Wai-Man, P. et al. The Prevalence and Natural History of Dominant Optic Atrophy Due to OPA1 Mutations Ophthalmology. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038

[15] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

[16] 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.

[17] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

[18] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/

*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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