PYC Therapeutics

22 April 2024

POLYCYSTIC KIDNEY DISEASE DRUG CANDIDATE PROGRESSING TO HUMAN TRIALS

- **PYC has completed dose range finding studies for its Polycystic Kidney Disease (PKD) drug candidate in Non-Human Primates (NHPs)**
- **The study results support progression of this drug candidate into human trials with:**
    - **all doses assessed determined to be safe and well-tolerated; and**
    - **high concentrations of the drug present in the kidney highlighting the impact of PYC's proprietary drug delivery technology**
- **This outstanding *in vivo* profile complements the *ex vivo* efficacy profile already established for this drug candidate in patient derived models of PKD[1]**
- **PYC is now preparing to advance the drug candidate into human trials**
    - **Good Laboratory Practice toxicology studies will commence in Q3 2024**
    - **A regulatory submission will be made in Q4 2024[2] to enable human trials to commence**
    - **Human safety and efficacy data will be available in 2025[3]**
- **Successful clinical trials could lead to a potential commercial launch of this drug candidate following a phase 2 clinical trial[4] for the 1 in every 1,000 people who suffer from PKD[5]**

PERTH, Australia and SAN FRANCISCO, California – 22 April 2024

PYC Therapeutics Limited (ASX:PYC) (**PYC** or the **Company**) today announces the successful completion of Dose Range Finding (DRF) studies of its investigational drug candidate known as PYC-003 in Non-Human Primates (NHPs). This drug candidate has

[1] See ASX announcement of 13 November 2023
[2] Subject to successful Good Laboratory practice toxicology and other pre-clinical study outcomes
[3] Subject to successful completion of the Investigational New Drug enabling studies scheduled for 2024, receipt of regulatory approval to commence human trials and successful progression through early clinical studies
[4] The US Food and Drug Administration has designated Total Kidney Volume as a surrogate endpoint and anticipates that this surrogate endpoint could be appropriate for use as a primary efficacy clinical trial endpoint for drug or biologic approval - see https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure
[5] Willey C, 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)

been designed for the 1 in every 1,000 people who suffer from Autosomal Dominant Polycystic Kidney Disease (PKD)[6] who have no treatment options available to them today[7]. PYC-003 was found to be safe and well tolerated at all doses assessed in the non-Good Laboratory Practice (non-GLP) NHP DRF studies (See Table 1). Importantly, these studies also demonstrated high concentrations of the drug candidate in the target tissue (kidney) at these safe and well tolerated doses (See Table 2). These results support progression of this drug candidate into human trials in a market worth >US$10 billion p.a.[8].

PYC's CEO, Dr. Rohan Hockings, commented on these study outcomes:

"*These are very encouraging results. We anticipate that the therapeutic dose of PYC-003 in humans is around one-tenth of the highest dose administered in these studies based on the data that we have generated to date.*

If we can repeat these NHP results in the upcoming GLP toxicology studies, we expect to have a very substantial safety margin for PYC-003. This raises the possibility of observing an efficacy signal very early on in clinical development as we expect even the lower doses administered in the planned Single Ascending Dose study could be within the therapeutic range in patients with PKD."

Background on Polycystic Kidney Disease (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 as a consequence of the disease[9].

Approximately 95% of patients with PKD have no treatment options available to them today[10]. 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[11].

PKD represents an estimated US$10 billion p.a. market[12]. PYC-003 holds potential for both first-in-class and best-in-class status in this indication[13] due to its highly specific mechanism of action that targets the underlying cause of the disease.

Study Results

Table 1. Non-GLP DRF study outcomes for PYC-003 in NHPs. Study animals were monitored for 28 days following a single intravenous administration of PYC-003 at the relevant dose. Potential adverse events were monitored for via in-life observations and biochemical markers through regular blood testing. All major organs were analysed for histopathological changes upon completion of the in-life study period. No Treatment Related Adverse Events were reported in any of the study animals or control group at any of the doses administered.

[6] Harris PC, Torres VF. Polycystic Kidney Disease, Autosomal Dominant. 2007 [Updated 2022]. (https://www.ncbi.nlm.nih.gov/books/NBK532934/)
[7] Otsuka's JYNARQUE® (tolvaptan) was approved in 2018 for the treatment of ADPKD with a black box warning – "for risk of serious liver injury". Approximately 95% of ADPKD patients cannot take or tolerate JYNARQUE® (tolvaptan) and hence have no treatment options available today. (Gansevoort RT, et al. Recommendations for the use of tolvaptan in autosomal dominant polycystic kidney disease: a position statement on behalf of the ERA-EDTA Working Groups on Inherited Kidney Disorders and European Renal Best Practice. Nephrology Dialysis Transplantation. 2016;31(3):337-48)
[8] Market size is projected by multiplying patient prevalence (See: Willey C, 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) in commercially accessible geographies by the median orphan drug pricing of $150k p.a. (Evaluate Pharma. Orphan Drug Report. 2019).
[9] 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.
[10] See footnote 5
[11] See footnote 3
[12] See footnote 2
[13] Refer ASX Announcement 17 November 2023

Cohort	Number of animals in cohort	Treatment group	Treatment Related Adverse Events (occurrence/number of animals)	Outcome (Tolerated/Not tolerated)
1	2	Vehicle control	0/2	Tolerated
2	2	3 mg/kg PYC-003	0/2	Tolerated
3	2	10 mg/kg PYC-003	0/2	Tolerated
4	2	30 mg/kg PYC-003	0/2	Tolerated

Table 2. Non-GLP DRF study biodistribution outcomes for PYC-003 in NHPs. Drug concentration in NHP target tissue (kidney) following a single intravenous administration of PYC-003.

Cohort	Number of animals in cohort	Dose of PYC-003	Concentration in kidney at Day 3	Concentration in kidney at Day 28
2	n=3 at Day 3 n=4 at Day 28	3 mg/kg	13,500 ng/g	250 ng/g
3	n=2	10 mg/kg	Not assessed	3,600 ng/g
4	n=2	30 mg/kg	Not assessed	Above the upper limit of quantitation of the assay

Next Steps

PYC is now preparing to conduct Good Laboratory Practice (GLP) toxicology studies for PYC-003. These studies are required to enable First In Human (FIH) trials of this drug candidate to commence. PYC remains on track to realise its objective of filing a regulatory submission in support of FIH studies in Q4 2024. If successful, PYC expects to have initial human data across both safety and efficacy dimensions available in 2025[14].

This announcement was approved for release by the Board of PYC Therapeutics Limited.

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

[14] See footnote 1

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**[15].

The Company was the first to progress a drug candidate for a blinding eye disease of childhood (Retinitis Pigmentosa type 11) into human trials. The Company is progressing a second drug program targeting a blinding eye disease (Autosomal Dominant Optic Atrophy) and a third program targeting Polycystic Kidney Disease which are anticipated to commence human trials in mid-2024 and early 2025 respectively.

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 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.

CONTACTS:

INVESTORS and MEDIA
info@pyctx.com

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