

## **PYC'S FOURTH DRUG CANDIDATE HAS DISEASE-MODIFYING POTENTIAL IN POLYCYSTIC KIDNEY DISEASE**

- PYC has developed a new drug candidate for the >5 million people worldwide<sup>1</sup> with Polycystic Kidney Disease (PKD)
- This drug candidate has **demonstrated efficacy in human models derived from the kidneys of patients with end-stage renal failure due to PKD**<sup>2</sup>
- PKD is a life-changing disease affecting 1 in every 1,000 people<sup>3</sup>
- Half of the patient population with PKD will require a kidney transplant by the age of 60 due to the absence of impactful treatment options in this disease<sup>4</sup>
- PKD represents an addressable market of **>US\$10 billion p.a.** and is an area of major commercial interest for the drug development industry<sup>5</sup>
- Pre-clinical models suggest that addressing the underlying cause of PKD (the way that PYC's drug candidate works) could **arrest** the course of the disease in humans, enabling damaged kidneys to **regenerate and restore function**<sup>6</sup>
- PYC plans to accelerate this drug candidate into human trials in ~12 months – pursuing a potential high-velocity path through clinical trials to market<sup>7</sup>

### **Investor Webinar Friday 17 November**

- PYC will host an investor call at 9am AWST/12pm AEDST on Friday 17 November to discuss these results – investors can register for the call here:

[https://us02web.zoom.us/webinar/register/WN\\_p2QQKKZ-TxOms2MOaUjjg](https://us02web.zoom.us/webinar/register/WN_p2QQKKZ-TxOms2MOaUjjg)

### **PERTH, Australia and SAN FRANCISCO, California – 13 November 2023**

PYC Therapeutics today announces the results of a study conducted in human 3-dimensional models derived from patients with end-stage renal failure due to Autosomal Dominant Polycystic Kidney Disease (PKD). The results demonstrate that an investigational drug candidate designed by PYC (known as PYC-003) to address this

<sup>1</sup> <https://www.niddk.nih.gov/health-information/kidney-disease/polycystic-kidney-disease/what-is-pkd>

<sup>2</sup> <https://www.crownbio.com/hubfs/WRCrownbio2021%20Assets/Resources/FactSheet/Crown-Bioscience-Factsheet-Cyst-Swelling-Assay-for-ADPKD.pdf>

<sup>3</sup> <https://www.mayoclinic.org/diseases-conditions/polycystic-kidney-disease/symptoms-causes/syc-20352820>

<sup>4</sup> Furlano M. Polycystic Kidney Disease. Medscape available at <https://emedicine.medscape.com/article/244907-overview?form=fp#a5>

<sup>5</sup> Based on the identified 160,000 patients with PKD in the US alone and median orphan drug pricing as per EvaluatePharma reports

<sup>6</sup> <https://medicine.yale.edu/news-article/adpkd-is-reversible-in-preclinical-models-finds-new-yale-study/>

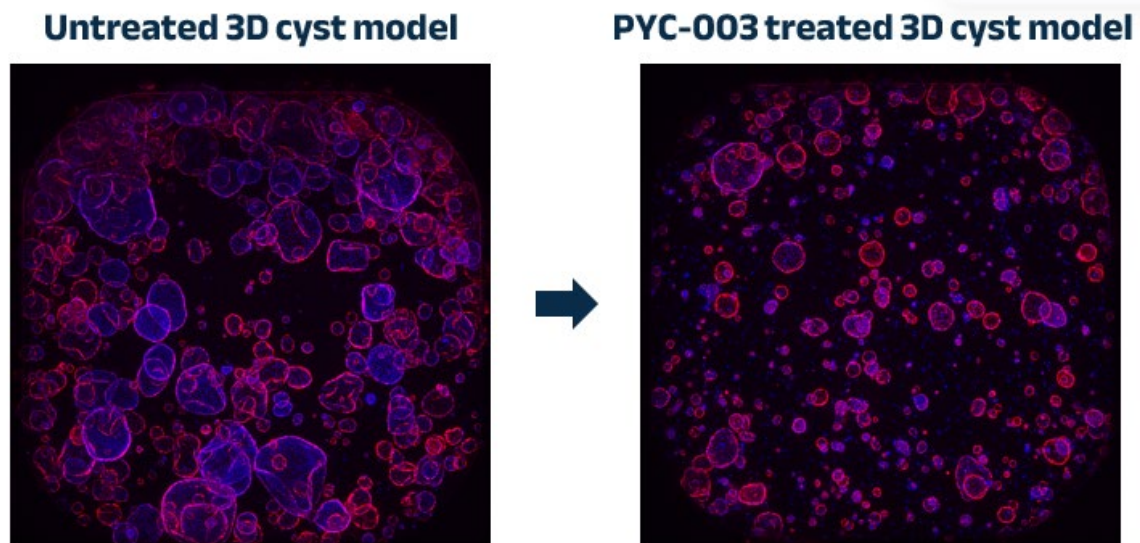
<sup>7</sup> <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval#:~:text=Mindful%20of%20the%20fact%20that,based%20on%20a%20surrogate%20endpoint.>

disease at its root cause is effective. These 3D patient-derived cyst models represent the 'gold-standard' pre-clinical assay for evaluating drug candidates in this indication<sup>8</sup>.

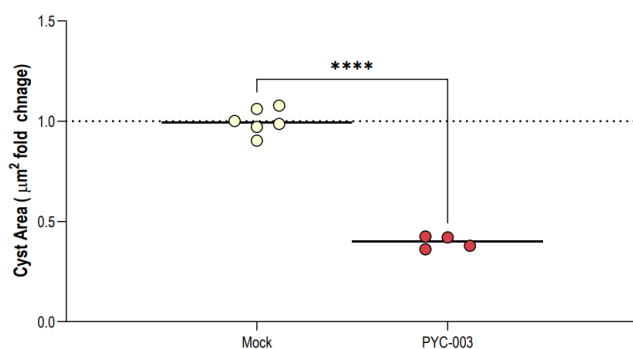
PYC-003 is the fourth program in the Company's development pipeline – joining three other first-in-class RNA drug candidates with disease-modifying potential currently progressing into or through human trials.

### PYC-003 is effective in models derived from PKD patients

**Figure 1.** Reduction in cyst size and frequency following treatment with PYC's drug candidate (PYC-003) in a human 3D model generated using tissue collected directly from the kidneys of PKD patients<sup>9</sup>. The assay shows larger cysts (stained with blue and red) in the untreated 3D model when compared to the PYC-003 treated 3D model.



**Figure 2.** Quantification of the reduction in cyst area in the PYC-003 treated 3D cyst model when compared to the untreated control (5% H2O treatment labelled 'Mock')<sup>10</sup>.



<sup>8</sup> [https://journals.lww.com/kidney360/fulltext/2023/08000/experimental\\_models\\_of\\_polycystic\\_kidney\\_disease\\_23.aspx](https://journals.lww.com/kidney360/fulltext/2023/08000/experimental_models_of_polycystic_kidney_disease_23.aspx)

<sup>9</sup> Images are captured 7 days after treatment with the drug candidate in the Crown Biosciences 3D cyst assay. See:

<https://www.crownbio.com/hubfs/WRCrownbio2021%20Assets/Resources/FactSheet/Crown-Bioscience-Factsheet-Cyst-Swelling-Assay-for-ADPKD.pdf> for more detail

<sup>10</sup> One biological replicate with four technical replicates presented as mean + standard deviation with \*\*\*\* representing a p value of <0.0001 using student's t-test.

## Next steps

PYC plans to accelerate PYC-003 into human trials following these results. An Investigational New Drug (IND) application to the US Food and Drug Administration (FDA) to enable the commencement of human trials for this drug candidate is planned for H2 2024.

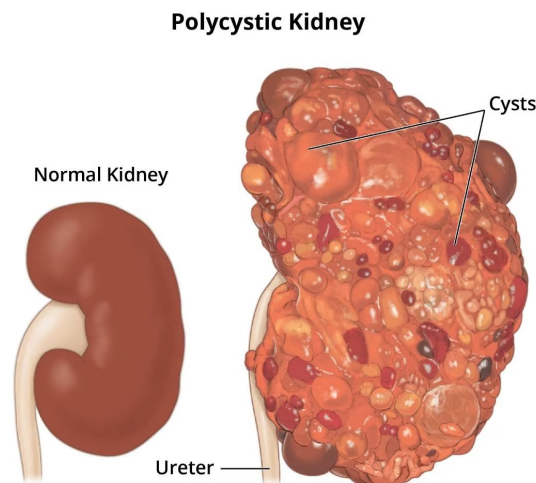
PYC-003 is expected to have an accelerated pathway through human trials due to the extent of the unmet patient need in PKD. A New Drug Application in support of this candidate could be submitted following two clinical trials rather than the conventional three<sup>11</sup>.

PKD is a monogenic disease (meaning that it is caused by a mutation in a single gene). Drugs targeting monogenic diseases have the highest likelihood of demonstrating efficacy in clinical trials<sup>12</sup> and lower probability of off-target safety issues.

## PKD represents a major global health challenge

PKD affects 1 in every 1,000 people across the globe. There are currently no drugs available that address the underlying cause of the disease and approximately 50% of PKD patients will progress to end-stage renal failure by the age of 60. PKD is characterised by the formation of multiple fluid filled cysts throughout the kidney and, to a lesser extent, other organs. Progression of the cyst frequency and volume over time ultimately leads to destruction of the internal architecture and function of the kidney.

**Figure 3.** An illustration of the impact of PKD on the kidney<sup>13</sup>. The increase in size and abnormal appearance of the kidney in PKD is driven by the cyst formation and swelling that characterises the disease and compromises kidney function.



## PYC has solved the 'other' critical dimension in PKD – the 'delivery challenge'

The data demonstrating that PYC-003 is effective in 3D patient-derived cyst models complements existing data from animal models highlighting the ability of this drug candidate to reach the cells affected in PKD<sup>14</sup>. PYC's drug delivery platform has already

<sup>11</sup> <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval#:~:text=Mindful%20of%20the%20fact%20that,based%20on%20a%20surrogate%20endpoint.>

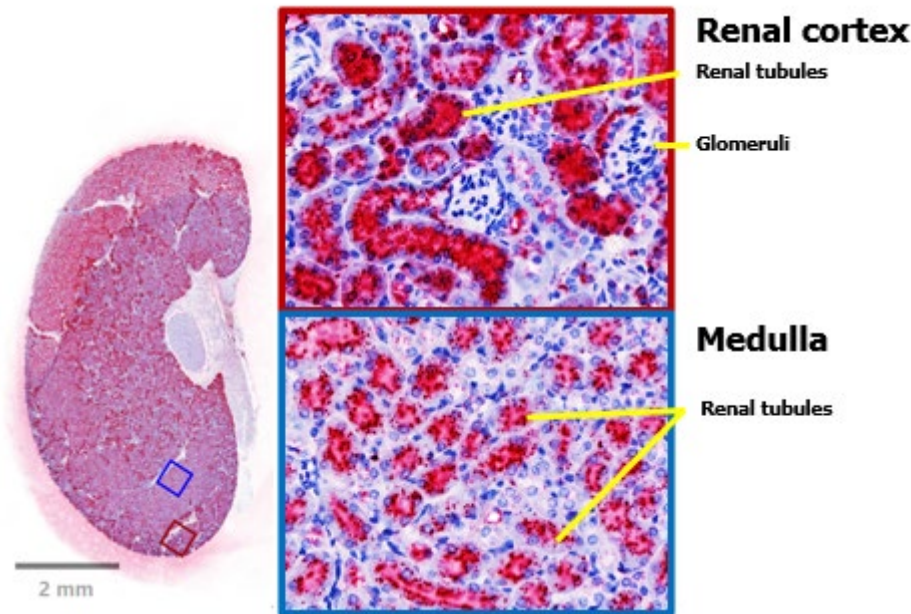
<sup>12</sup> Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank <https://doi.org/10.1101/2020.11.02.20222232>

<sup>13</sup> <https://www.niddk.nih.gov/health-information/kidney-disease/polycystic-kidney-disease/what-is-pkd>

<sup>14</sup> Using a PKD therapeutic designed specifically for the mouse *PKD1* gene

demonstrated the ability to deliver an RNA therapy to the target cells affected by the disease *in vivo* in high concentration (see Figure 4).

**Figure 4.** Cross section of a mouse kidney 3 days after a single 10mg/kg intravenous dose of the mouse equivalent of PYC-003 demonstrating high concentration of PYC's RNA drug candidate (illustrated with pink dots by miRNAscope) within the target organ.



## Investor Call

PYC will host an investor call on Friday 17 November at 9am AWST/12pm AEDST to explain the PKD program in detail. Investors can register for this call at the following link:

[https://us02web.zoom.us/webinar/register/WN\\_p2QQKKZ-TxOms2MOaUjig](https://us02web.zoom.us/webinar/register/WN_p2QQKKZ-TxOms2MOaUjig)

## 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**<sup>15</sup>.

The Company was the first to progress a drug candidate for a blinding eye disease of childhood into human trials and is now progressing multiple 'fast-follower' programs into the clinic. For more information, visit [pyctx.com](http://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*

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*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 CEO of PYC Therapeutics Limited*

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