



PYC
Therapeutics

Life-changing science

Polycystic Kidney Disease Program

Investor webinar

November 2024



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Executive Summary

- On 27 November 2024, PYC released its pre-clinical data pack in support of PYC-003 – a first-in-class RNA conjugate for the treatment of Autosomal Dominant Polycystic Kidney Disease (PKD) due to mutations in the *PKD1* gene¹
- In December 2024, PYC will make the regulatory submission required to progress PYC-003 into First In Human (FIH) studies²
- Today's objectives are to progress the discussion to an evaluation of:
 - Why PYC-003's disease-modifying mechanism of action is uniquely suited to addressing PKD; and
 - The extent of *PKD1* gene upregulation required to have a meaningful impact on disease progression in PKD patients

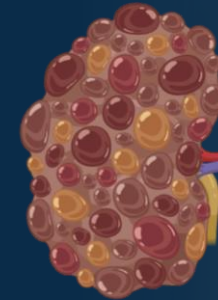
There is an urgent need to create treatment options for the PKD patient community

Polycystic Kidney Disease

Healthy adult kidney



Polycystic kidney



High prevalence

PKD affects **1 in every 1,000** people meaning **>5 million people worldwide** have the disease^{1,2}

Life-changing

Half of all PKD 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** in PKD

Targeting the root cause of PKD (insufficient PC1 protein expression) may be the only therapeutic option in this disease



“It remains possible that multiple pathways that are directly regulated by the polycystins concur in the prevention of cyst formation and may need to be concomitantly targeted.

Thus, re-expressing the polycystins might ultimately remain the best — or possibly the only — way to revert the disorder”¹

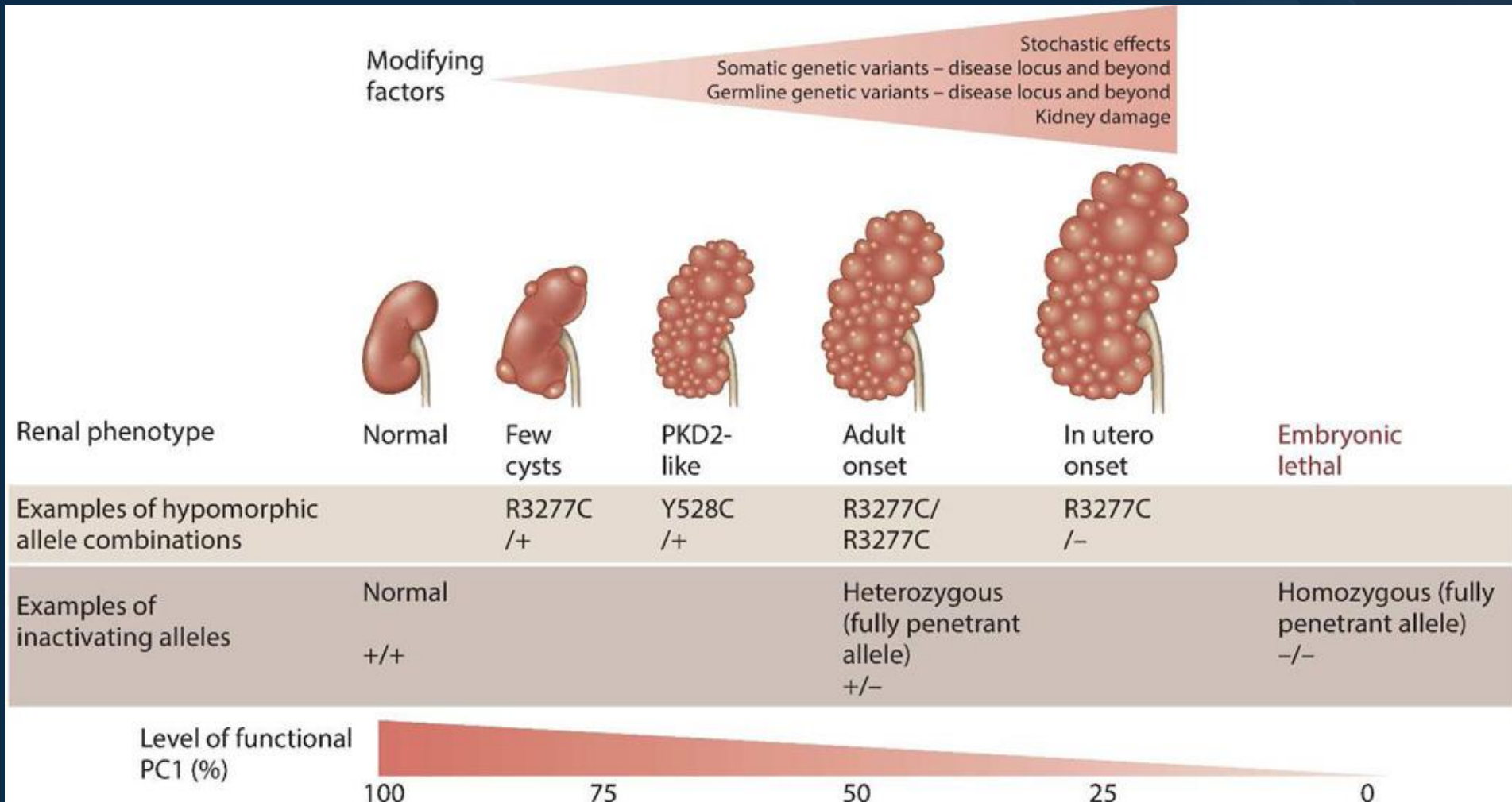
The *PKD1* gene in isolation drives polycystic kidney disease¹

“These observations collectively point to PKD1 as the primary, if not the sole, factor governing cyst onset and growth”¹

PYC-003 acts directly on the functional *PKD1* transcript to upregulate PC1 protein expression



How much PC1 protein will be sufficient to make a meaningful impact on disease progression?

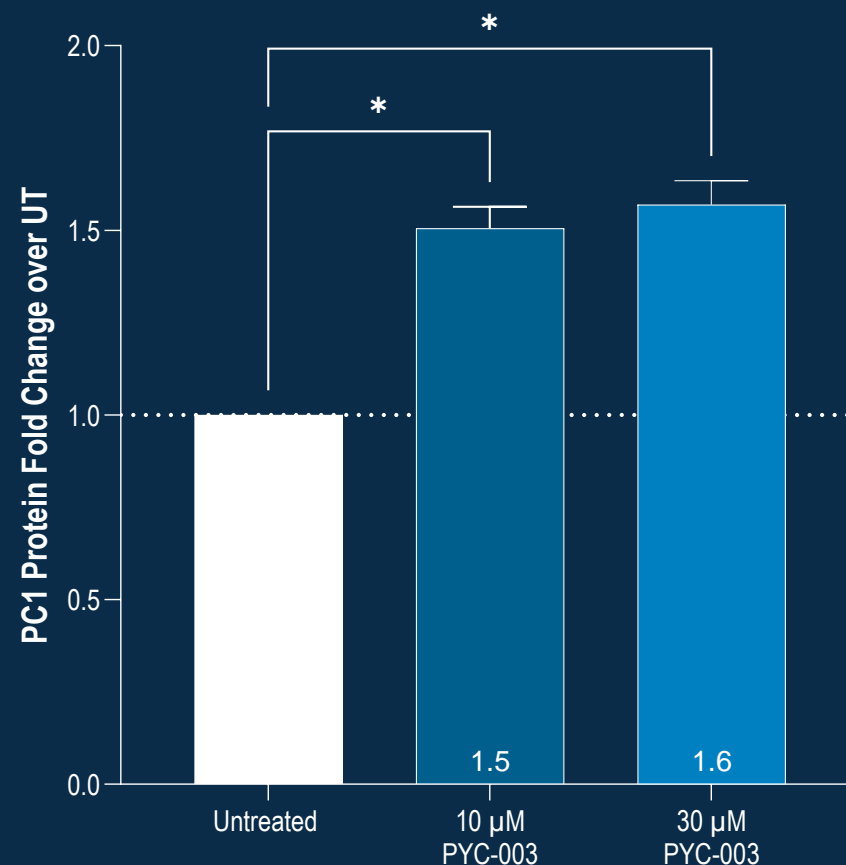


PYC-003 increases PC1 protein levels by >1.5-fold¹



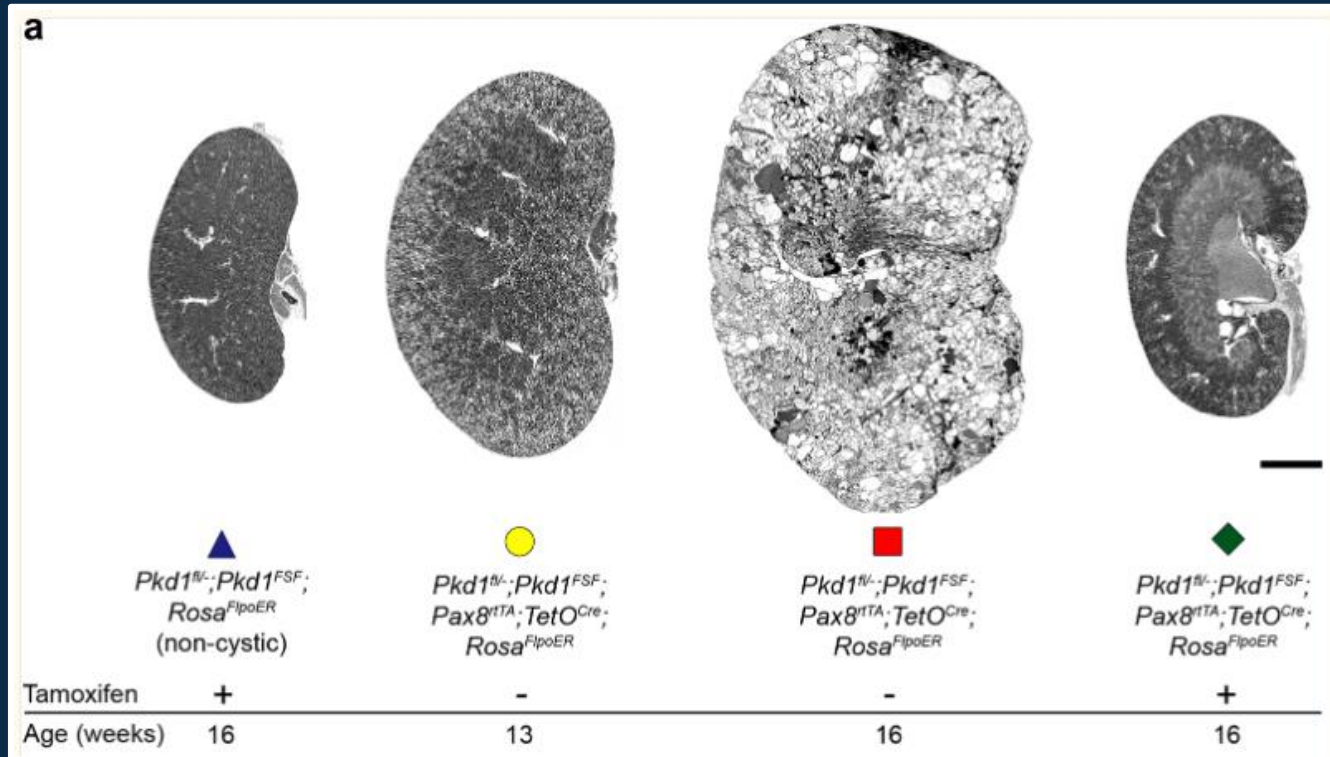
PYC-003 addresses the root cause of PKD in human kidney cells²

PYC-003 increases levels of PC1 protein (the missing protein that causes PKD) in a human kidney cell line

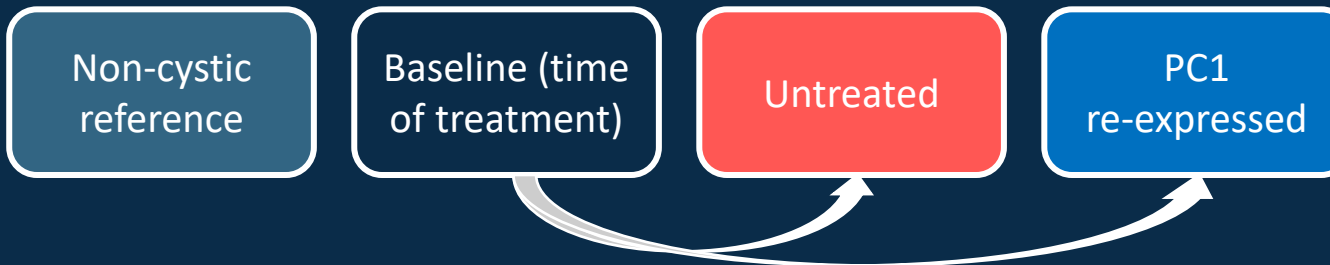


1. Refer ASX Announcement 17 November 2023
2. PC1 full length protein fold-change over untreated (normalised to total protein) assessed at day 3 following treatment with either 10 µM or 30 µM PYC-003. Data presented mean+S.D (n=2 for protein). The data show a statistically significant (Dunnett's post-hoc test, *p<0.05) difference between treatment groups. Assessed in HEK293 cells.

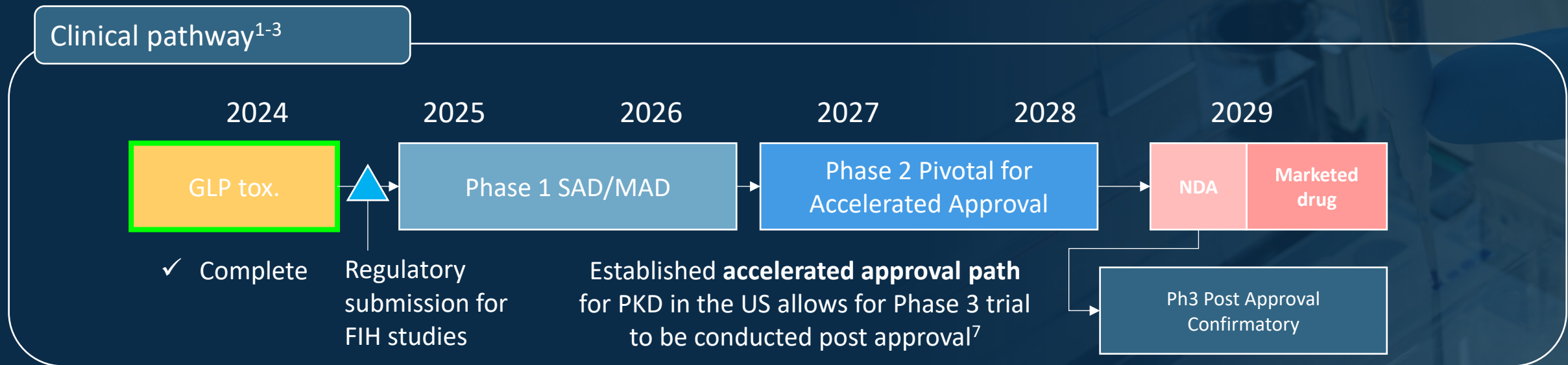
The potential of disease-modifying approaches in PKD are foreshadowed by the results of animal models



“Even if one could have hypothesized that re-expressing PKD genes would slow disease progression, **the rapidity and completeness of the reversal are astonishing** and are likely indicative of a unique and previously **unappreciated regenerative potential of the kidney**”²



PYC-003 will progress to human trials in 2025¹



FDA special designations

Potentially accelerating path to market:

1. **Fast Track - Potential**
2. **Orphan Drug Designation – Potential**

1. Clinical trial plan is subject to confirmation and depends on multiple factors, including the duration of action of the therapeutic candidate and regulatory approval. Management forecast as of 27 November 2024.
2. Refer ASX announcement 13 November 2023 and 17 November 2023
3. Accelerated approval allows for the earlier approval of drugs that treat serious conditions, and fill an unmet medical need based on a surrogate endpoint. FDA has designated TKV as a reasonably likely surrogate endpoint.
<https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure>

PYC-003 for Polycystic Kidney Disease (PKD)

Q&A

