PYC Therapeutics

Life-changing science

Investor Presentation

September 2026

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Agenda for today

- Introduction to PYC
- Review of organisational build-out
- Overview of the forward development plan for the company's pipeline programs
- Polycystic Kidney Disease program review and forward view of milestones
- Q&A

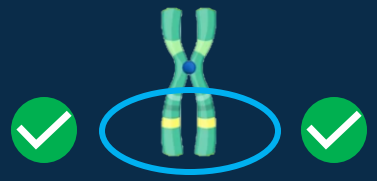
Sierra – living with Phelan-McDermid Syndrome[1]

PYC's mission is to create life-changing RNA therapies that address the root cause of diseases resulting from insufficient gene expression

The Company's work is dedicated to patients who currently have no treatment options available

1. PMS Foundation – Sierra's story

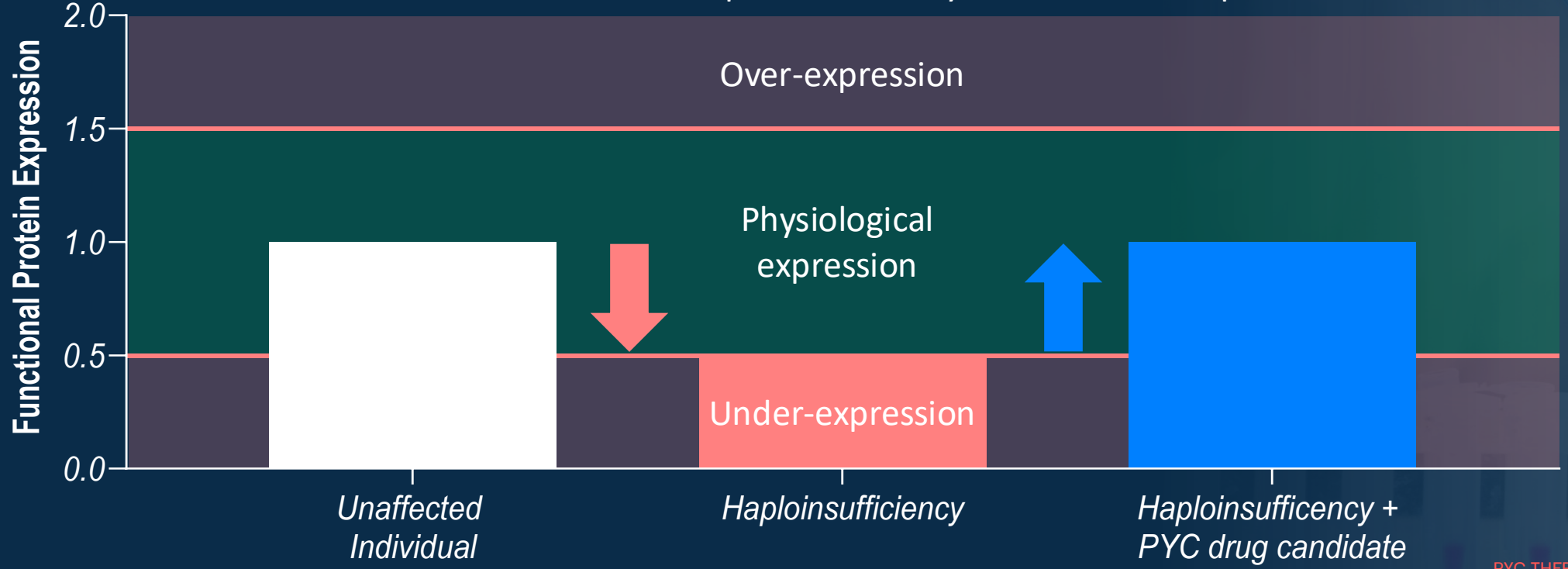
PYC designs RNA therapies to increase gene expression in diseases caused by haploinsufficiency



There are two copies of every gene in humans

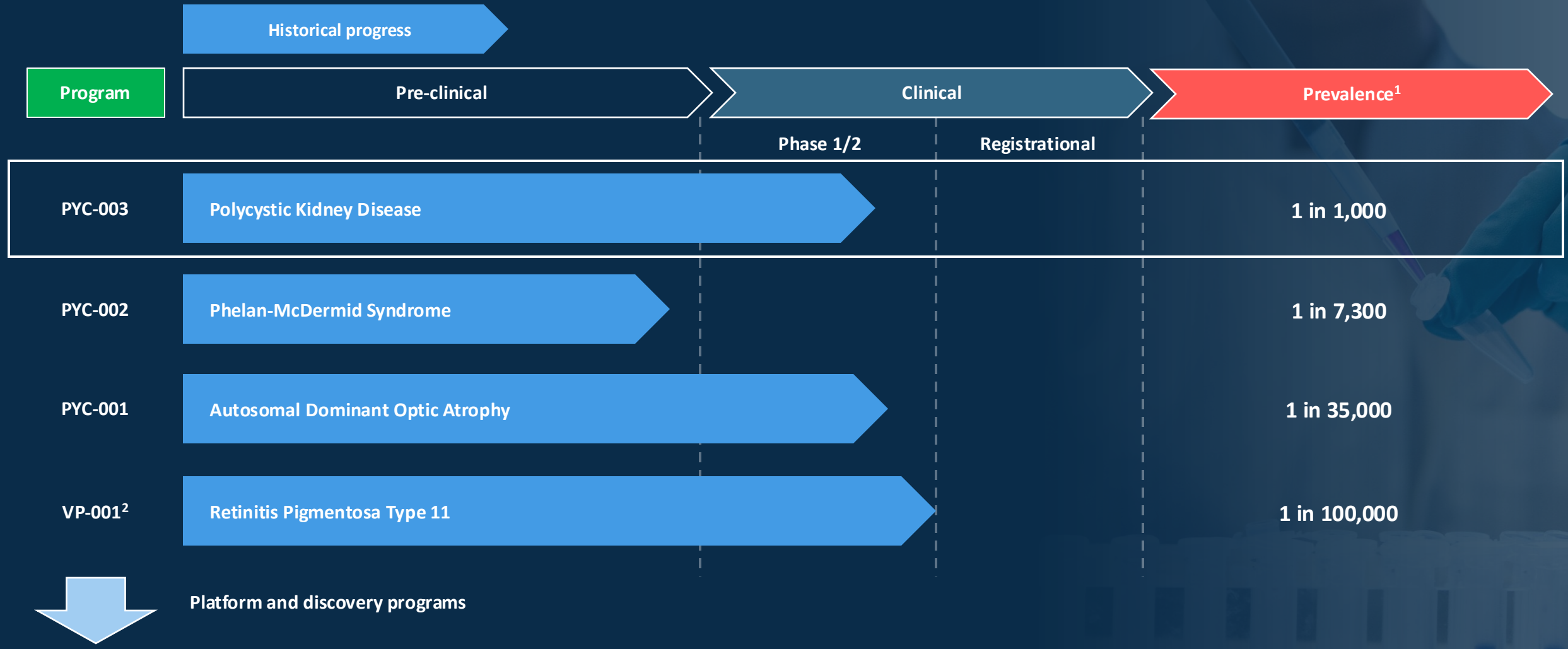
One copy of a gene is non-functional in a haploinsufficiency

PYC's drug candidates leverage the 'good' copy of the gene to restore expression[1]



1. Illustrative change in gene expression following administration of PYC's RNA therapy – detailed data for each drug development program in the Company's pipeline is available via the ASX platform and the Company's website.

PYC has created a pipeline of clinical-stage drug candidates in areas of major unmet need

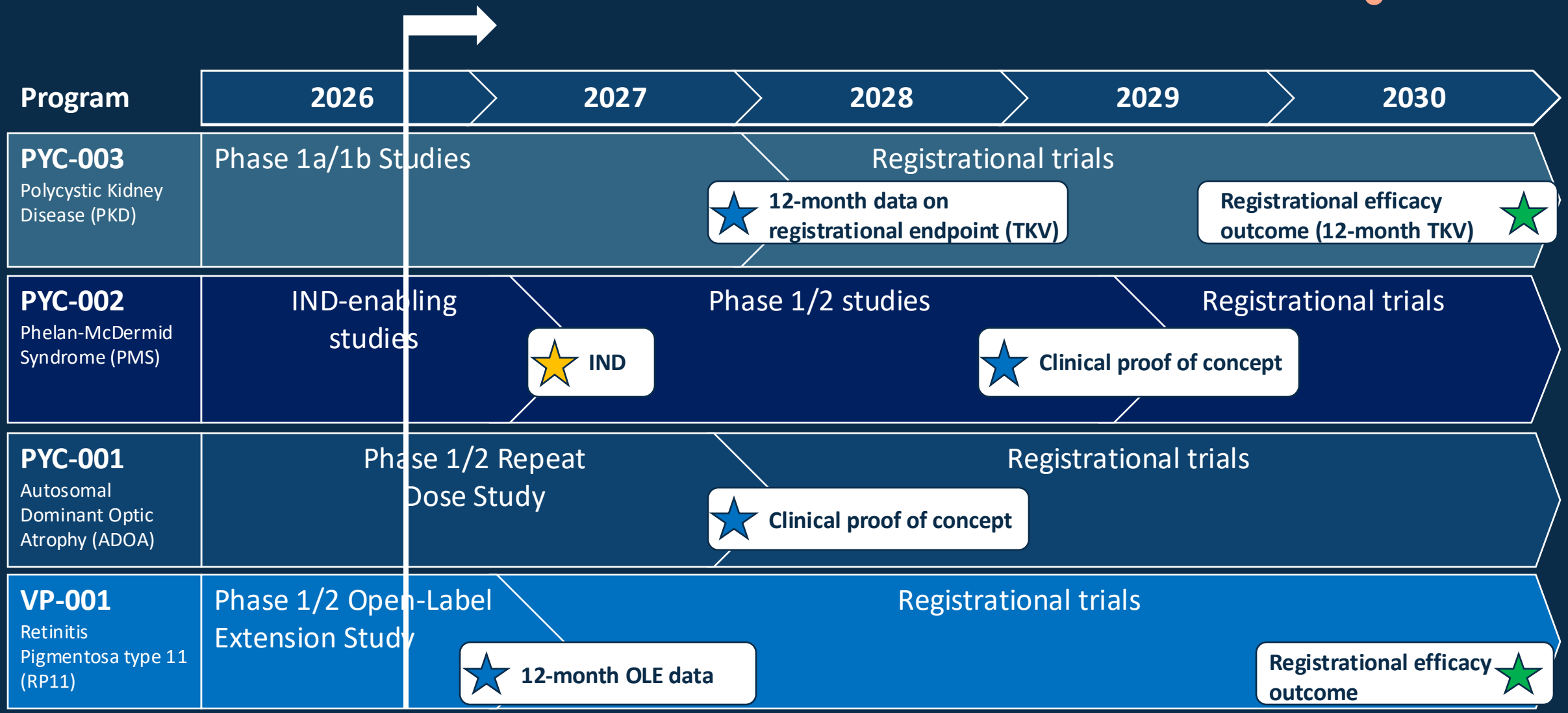


1. See disease prevalence references of the Company's 2026 Annual Report released to the ASX on 28 August 2026 for additional details on prevalence by indication
2. PYC owns 97.1% of VP-001 (2.9% ownership by Lions Eye Institute, Australia) and 100% ownership of all other pipeline programs

PYC continues its organisational build-out ahead of the progression into late-stage studies

- In Q2, the Company appointed a CFO and General Counsel/Co-Company Secretary
- In Q3, PYC has added a Chief Clinical Development Officer and Phelan-McDermid Syndrome Program Lead
- Near-term recruitment will focus on a Head of Regulatory Affairs and Ophthalmology Program Lead

PYC has multiple human safety and efficacy read-outs expected within the next 18 months[1]



1. Management forecast accurate as at the date of this announcement. Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026. Subject to change based on outcomes and strategic priorities.

PKD program deep dive

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Discussion topics

- An overview of the program – current progress
- An ‘outside in’ perspective – why safety is key
- The expected timeline for exploratory efficacy data
- What should we expect on these endpoints?

Overview of the clinical development pathway for PYC-003[1]

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Progress to date

Combined Phase 1a/1b Study[2]

Phase 2/3 Study

Part A - SAD in healthy volunteers

Part B – SAD in ADPKD Patients

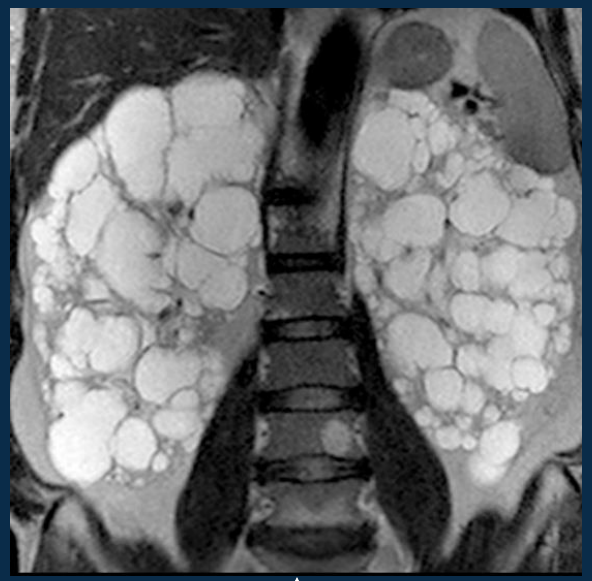
Part C and D – MAD + OLE in PKD Patients

Registrational study

Confirmatory extension

Commercialisation

Total Kidney Volume (TKV)
MRI[3]



PYC's immediate objective

12-month TKV read-out
Clinical proof of concept

New Drug Application (NDA)
12-month TKV readout[4]

Confirmatory
24-month eGFR readout

eGFR
Blood test

1. Subject to regulatory approval and the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
2. Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) studies in patients with PKD1 gene mutation associated autosomal dominant polycystic kidney disease (PKD)
3. Gradzik M, et al. Diagnostic Imaging of Autosomal Dominant Polycystic Kidney Disease. Pol J Radiol. 2016 Sep 17;81:441-453. doi: 10.12659/PJR.894482
4. FDA. Development and Approval Process | Drugs. 2022. https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approval-program - Accelerated approval allows for the earlier approval of drugs that treat serious conditions, and fill an unmet medical need based on a surrogate endpoint. There is an established accelerated approval path in PKD, which allows for Phase 3 trial to be conducted post approval. FDA has designated TKV as a reasonably likely surrogate endpoint (U.S. Food and Drug Administration, 2020) https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure

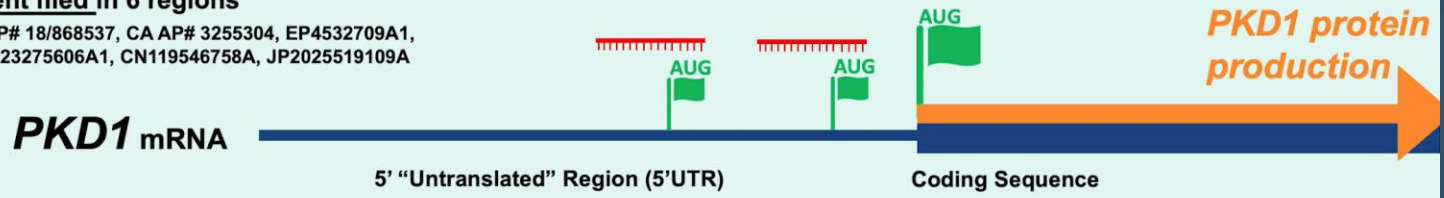
PKD1 protein translation is inefficient
due to upstream open reading frames (uORFs)

YALE VENTURES

Novel ASO Therapy

Patent filed in 6 regions

US AP# 18/868537, CA AP# 3255304, EP4532709A1, AU2023275606A1, CN119546758A, JP2025519109A



Yale

Yale Life Sciences
PITCHFEST

Source: Yale Ventures. PKD1 uORF-blocking ASOs as therapy for ADPKD
Available from: https://vimeo.com/1153969046 0:37 to 2:45

Modelled peak target tissue concentration is similar after single and repeat dosing[1]

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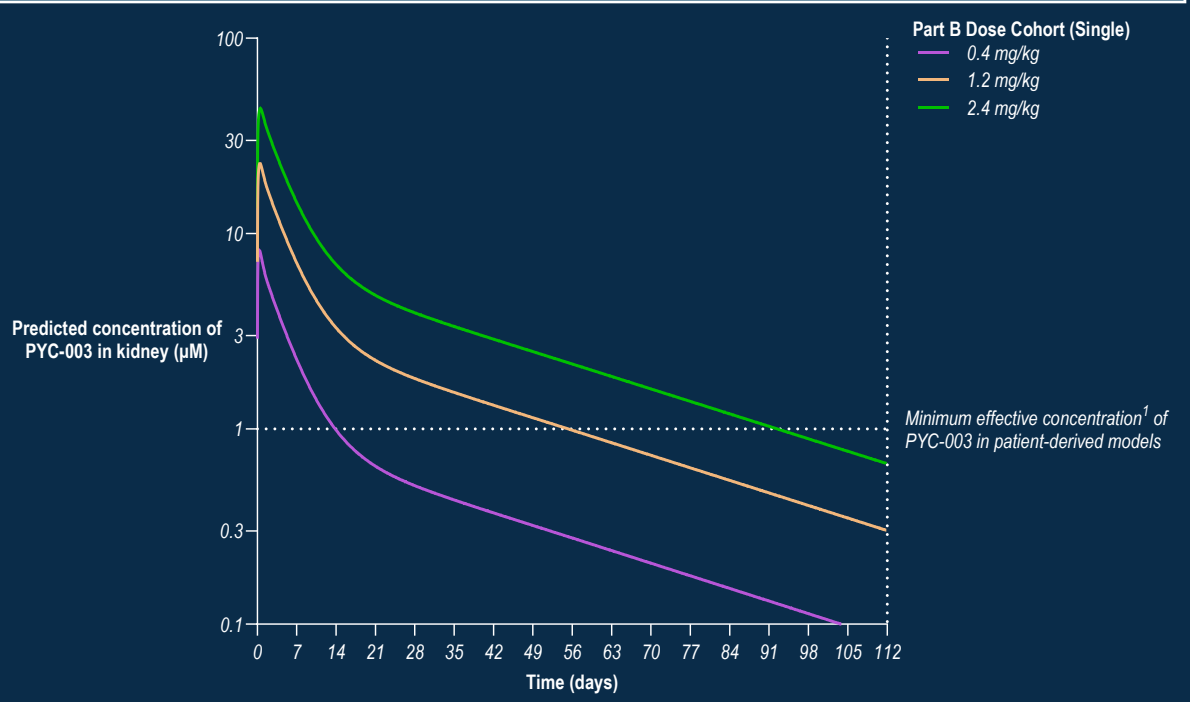
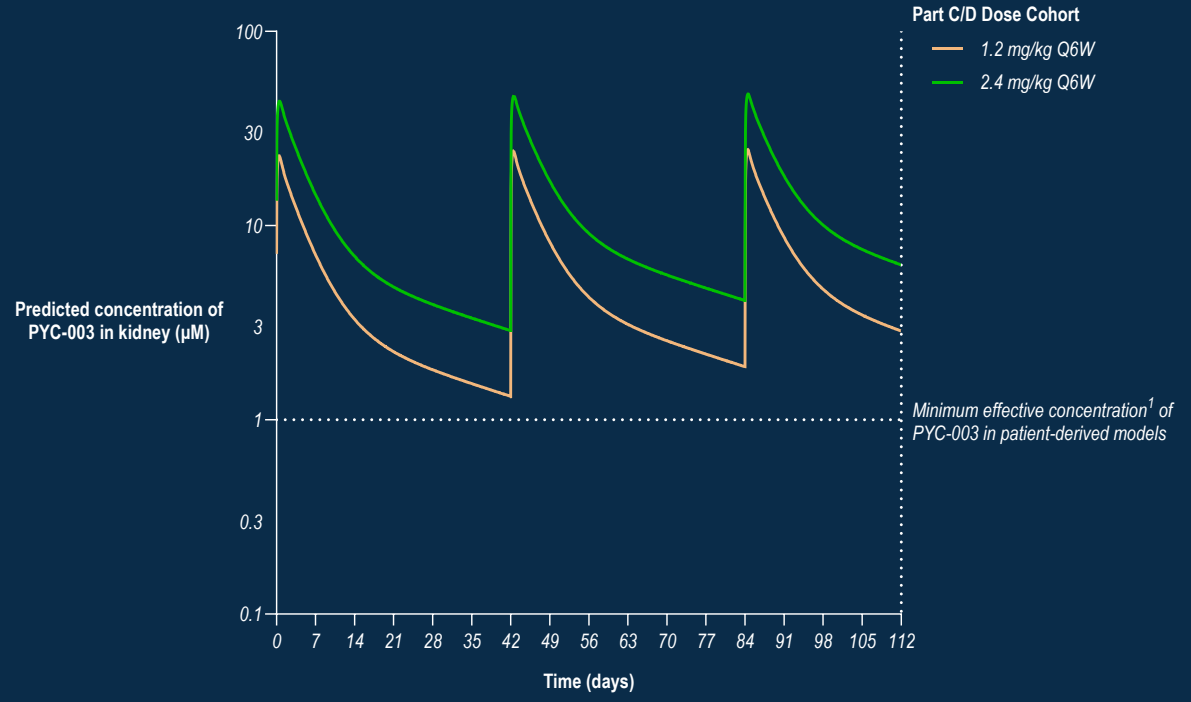
SAD



Dose	% of AUC above minimum effective concentration[1] at Month 4
0.4 mg/kg	~40%
1.2 mg/kg	~70%
2.4 mg/kg	~90%

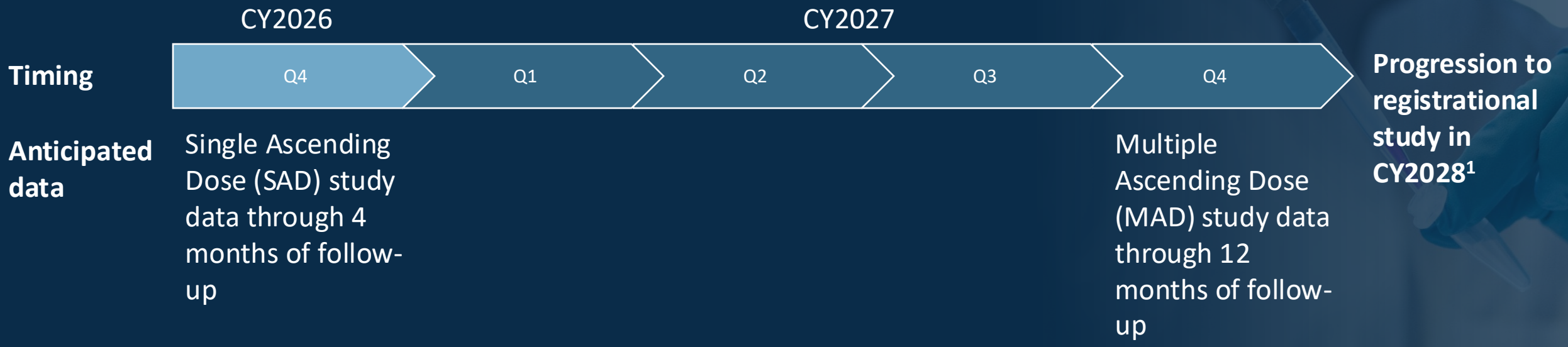
MAD



Dose	% of AUC above minimum effective concentration[1] at Month 4
1.2 mg/kg Q6W	100%
2.4 mg/kg Q6W	100%

1. The predicted human kidney concentration is modelled on the observed Non-Human Primate plasma:kidney PK data and the observed human plasma PK data
2. The Minimum Effective Concentration (MEC) in patient-derived models is ~300nM, however, the MEC has been set at 1uM for the purposes of this modelling to predict the duration of exposure above a 1.2-fold increase in PC1 expression

Expected timelines for the Phase 1b exploratory efficacy data[1]



1. Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

Fast-progressing patients have been prioritised for the MAD study to maximise potential for early signal detection

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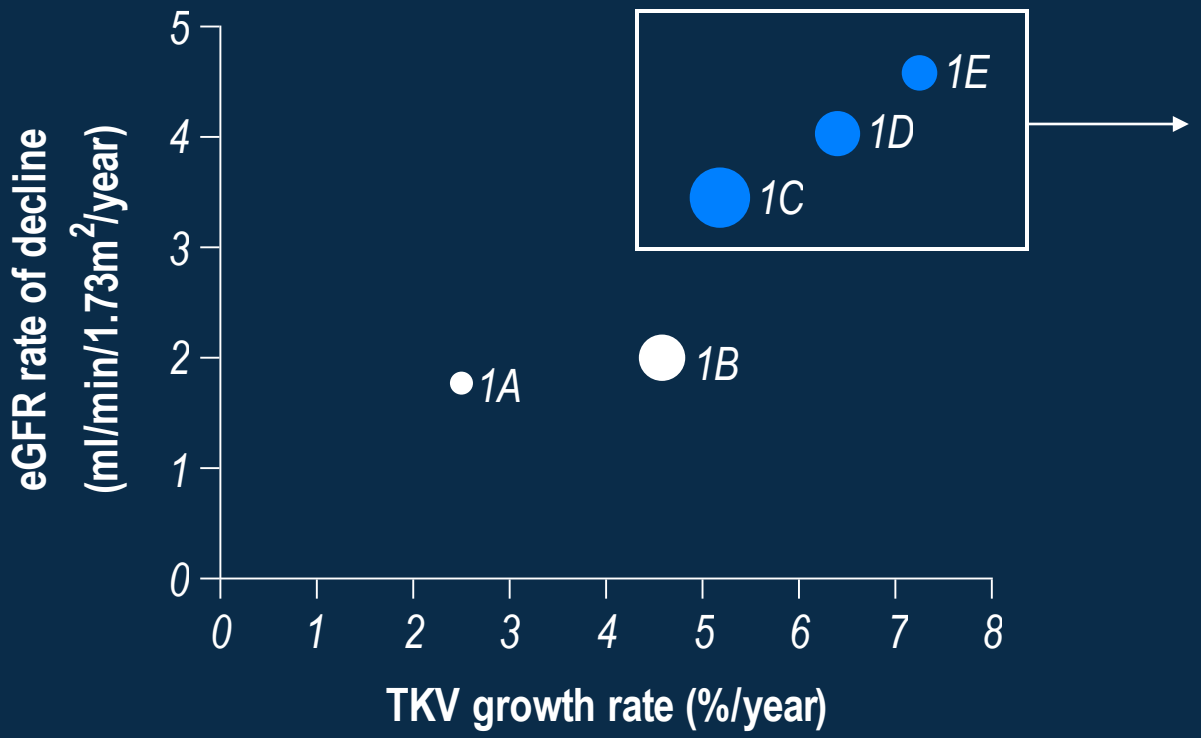
Observed annual rate of change on TKV and eGFR by Mayo Class[1]



Patients in Mayo Class 1C to 1E are expected to show >5% growth in Total Kidney Volume (TKV) per year

This maximizes the potential for detecting an early treatment effect with PYC-003

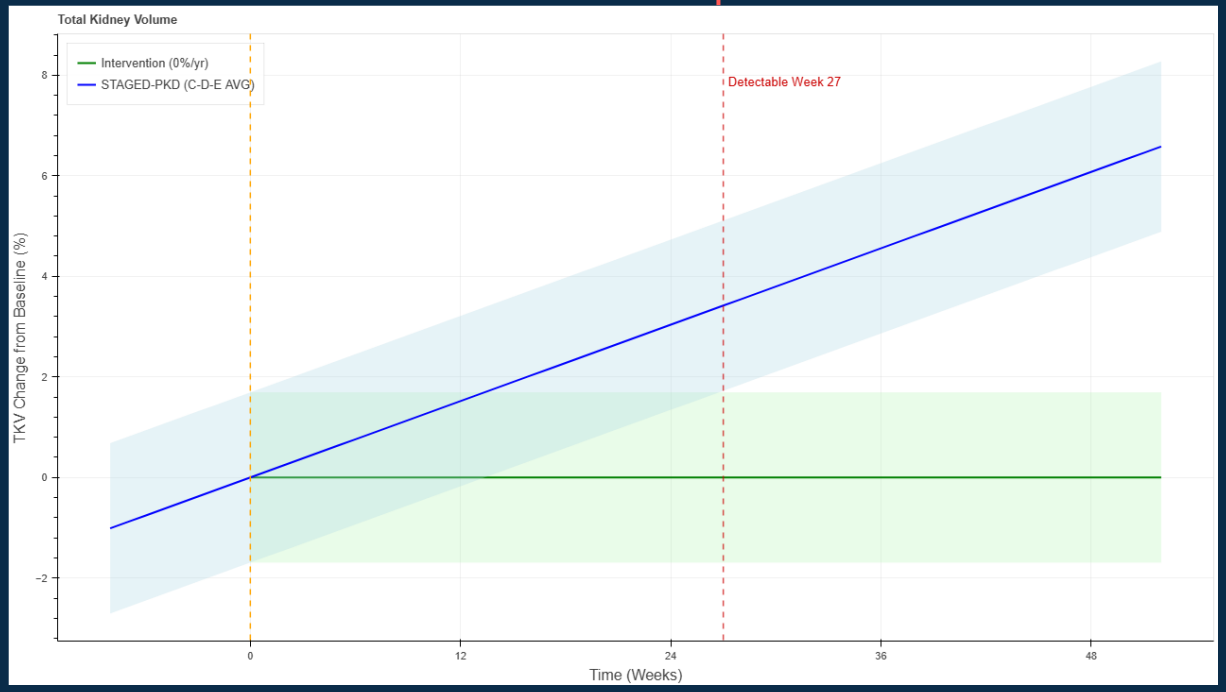
1. Bais et al. 2024. Validation of the Mayo Imaging Classification System for Predicting Kidney Outcomes in ADPKD. Mar 2024. Population (n) for each Mayo Class (1A = 34, 1B = 138, 1C = 234, 1D = 131 and 1E = 81)

≥6 months of data is required for meaningful insight on TKV following treatment with PYC-003[1]

This is to allow for signal detection above the 'noise' of the data set, driven by:

- Variability observed on this endpoint in natural history studies;
- Small group size (total n=24, n=12 per cohort); and
- Natural variability associated with MRI measurements.

Assumption: arrest of TKV growth



A treatment that halts disease progression in ADPKD will show significant divergence from published placebo control progression (STAGED-PKD) after **~27 weeks**

Combines both 1.2 mg/kg and 2.4 mg/kg and assumes equal efficacy for both (n=24)

1. With an input assumption that both 1.2 mg/kg and 2.4 mg/kg are effective doses

PYC is focused on delivering near-term human Proof of Concept (PoC) read-outs for its pipeline of drug candidates

Commandment #10 - "The world belongs to finishers"

Finishing requires focus: pick a few things and deliver on them. In drug discovery, it's always easier to "turn over new rocks than to concentrate your attention and resources to meet expectations and deadlines". While it's exciting to push new discoveries, it takes "discipline, management, people skills, encouragement, toughness to finish" and bring a drug through to PoC and eventually to market.

1. Phil Needleman's ten commandments of drug development – courtesy of Bruce Booth at LifeSciVC

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Q&A

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