PYC Therapeutics

Life-changing science

2026 Q2 Investor Webinar

May 2026

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Agenda for today

- Introduction to PYC
- Overview of the forward development plan for the company's pipeline programs
- Program-specific updates and immediate objectives
- Q&A

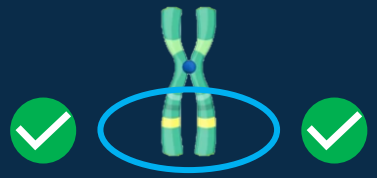
Sierra – living with Phelan-McDermid Syndrome[1]

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

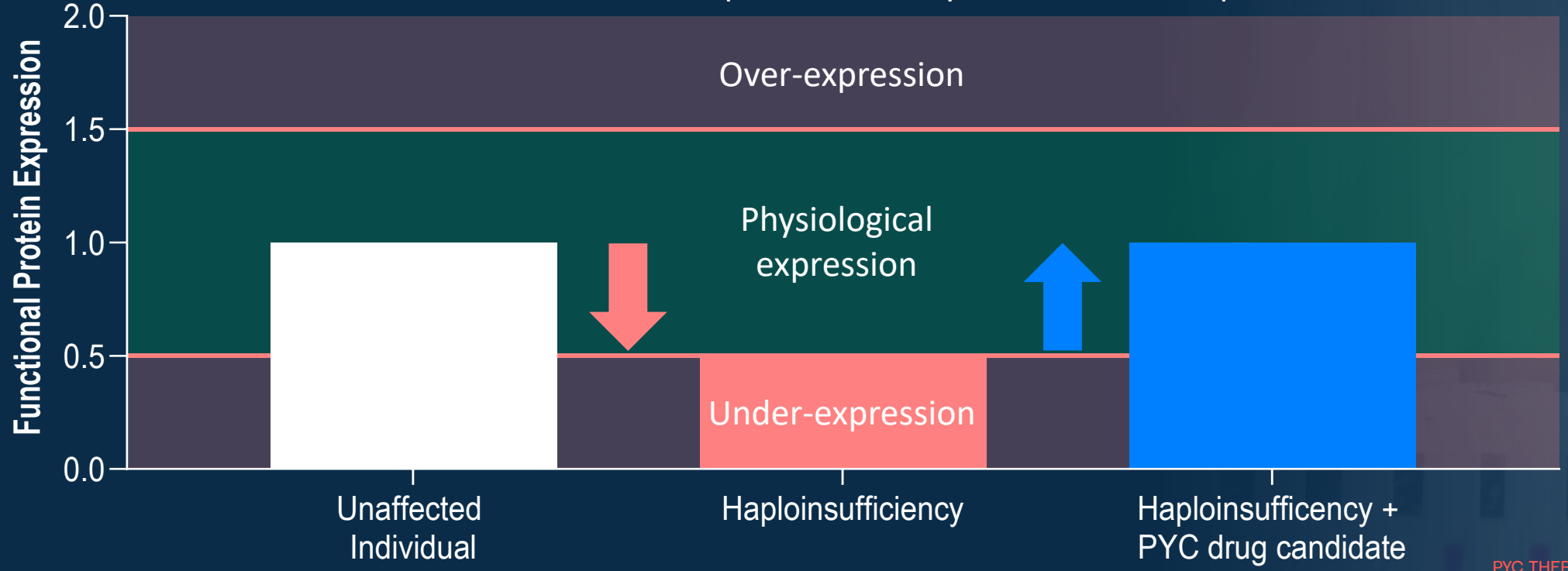
PYC designs RNA therapies to increase gene expression in diseases caused by haploinsufficiency



There are two copies of every gene in humans

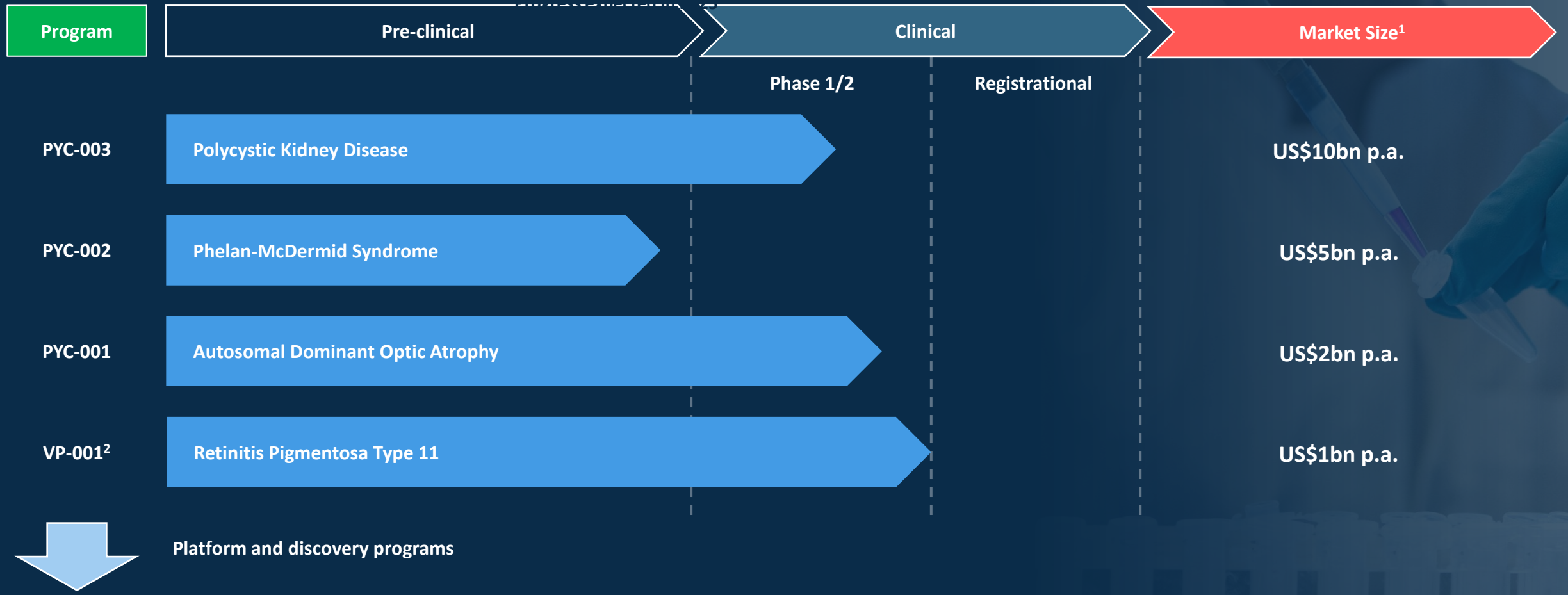
One copy of a gene is non-functional in a haploinsufficiency

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 built a pipeline of drug candidates with disease-modifying potential in large indications



1. Market size is projected by multiplying patient prevalence per indication by the median US orphan drug price of $200k p.a. (Althobaiti H, Seoane-Vazquez E, Brown LM, Fleming ML, Rodriguez-Monguio R. Disentangling the Cost of Orphan Drugs Marketed in the United States. Healthcare (Basel). 2023 Feb 13;11(4):558. See the 'Disease Prevalence References' section of the Company's 2025 Annual Report released to the ASX on 28 August 2025 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% of all other pipeline programs

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

Building Value: Registrational Strategy is Not Business Strategy

Most biotech CEOs figure out what it will take to get an idea to FDA or EMA approval and set out to do it. The thinking is you just fight hard enough, and you'll get there somehow. Eventually.

- Maybe its two Phase 3 studies that show that your new pain drug is effective.
- You run your way through Phase 1 and Phase 2 as quickly as possible to get to the Phase 3's.

This approach misses how the game is played. **It's not registration that you should focus on first. Rather, it's convincing investors to give you the money to get your drug to registration.** The FDA is not the customer you are trying to satisfy. It's the investor.

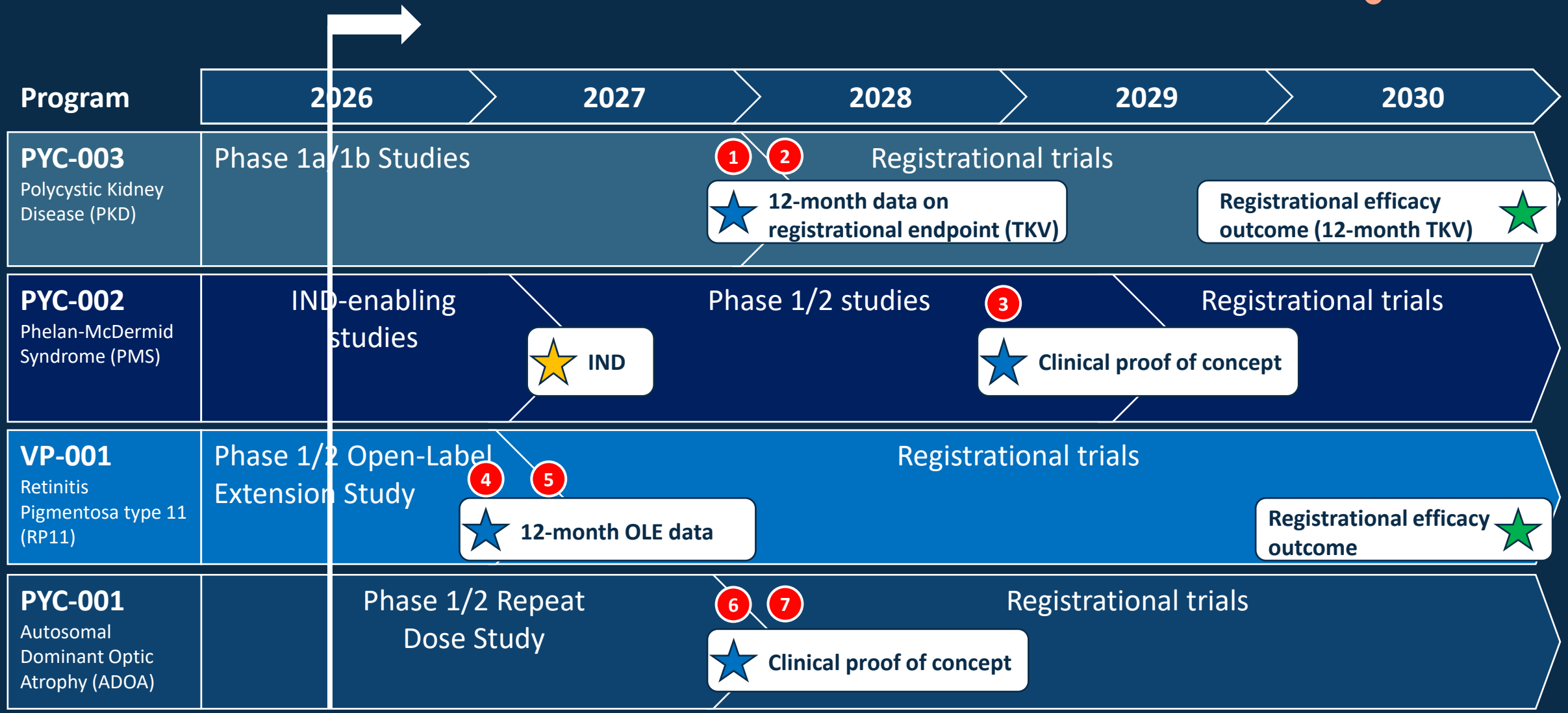
- What you want to do is run the study that allows you to fund the program to registration.
  - The only time to run Phase 3 studies is when you know they are going to work.
  - Losing tens of millions of dollars in Phase 3 is an unforgivable mistake. You waste money that could have been used to serve patients otherwise.
- That is, you need data out of your early clinical study that convinces that you have an active drug candidate:
  - You need to get investors excited about the potential of the project with data.
  - If you do it right, investors will give you a mandate to go forward and take your drug to the market.
- More or less, investors follow Bayes' Theorem:
  - Given a dataset what is the probability of FDA approval?
  - If the probability is high and your market is big, your valuation will be high. If your valuation is high, you can raise all the money you need. You can run registrational Phase 3 studies all day.
- **Basically, early drug development is a *business* exercise; not a *clinical* exercise. Biotech access to resources is highly constrained and must be earned through displaying strong efficacy datasets to the market.**

A common biotech mistake is failing to design strategies that allow a company to fund itself to registration.

Most simply chase the registration without contemplating what investors need to see first.

1. Stifel: Building value in biotech 26 February 2024

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.

The Company has arrived at the ‘turning of the cards’

Commandment #8 - “I’m from Missouri… show me data”.

As he says, “the coinage of the realm is data” so spare the hand-waving talk, wordy powerpoints, and show the data, “gleamed both at the bench but also occasionally in hard-nosed reviews with experts”. He’s definitely one of those hard-nosed experts now. I share Phil’s appreciation of the great Edwards Deming quote: “In god we trust, all others must bring data”.

1. Phil Needleman's Ten Commandments of Drug R&D - LifeSciVCLifeSciVC

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PKD program

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PYC's immediate objective in PKD is to demonstrate clinical proof of concept on the registrational endpoint

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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

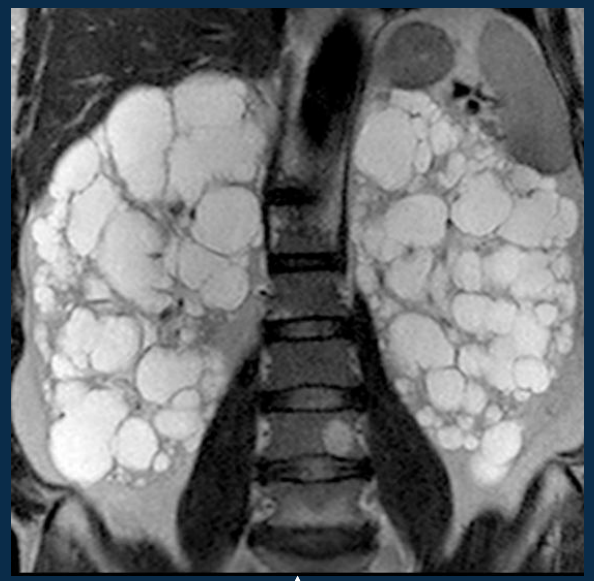
Part C – MAD in PKD Patients

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

Confirmatory
24-month eGFR readout

eGFR
Blood test

1. 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
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

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PMS program

May 2026

The Company's PMS program is preparing to enter the clinic

Commandment #7 - "Find the shortest route to heaven".

In discovery, don't spend years doing every preclinical pharmacology model – do a few, not half-a-dozen or more – and then with confidence sprint quickly to the drug's PoC in patients. In the clinic, if you need to focus on a limited-use first, go for it and get approved with a narrow label fast, even over the cries of your commercial colleagues. Get to heaven and you can figure out the rest later.

1. Phil Needleman's Ten Commandments of Drug R&D - LifeSciVCLifeSciVC

PYC's immediate objective in PMS is to complete GLP toxicology studies enabling 'first in human' trials to commence

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Progress to date

Pre-clinical studies → **GLP. PK and Toxicology Studies** → **Clinical Trials**

For this combination of:

- Chemistry: 2'MOE PS[3]
- Administration: intrathecal
- Target cell: neurons

Clinical validation of this modality via the same route of administration has been established in other CNS diseases[1,2]

PYC-002 is effective in PMS patient-derived models *in vitro* and has fully-integrated PK/PD and safety data *in vivo*[1]

Established pathway

NDA

The pattern of RNA therapeutic distribution and activity in the CNS of preclinical species translates to the human CNS[2]

1. For phosphorothioate oligonucleotides delivered via an intrathecal route of administration in diseases of neurons in the Central Nervous System (CNS) - Refer to ASX Announcement of 13 October 2025 for more detail
2. Jafar-Nejad P, et al. The atlas of RNase H antisense oligonucleotide distribution and activity in the CNS of rodents and non-human primates following central administration. Nucleic Acids Res. 2021 Jan 25;49(2):657-673. doi: 10.1093/nar/gkaa1235.
3. Phosphorothioate (PS) chemistry 2'MethOxy Ethyl (MOE) oligonculeotides

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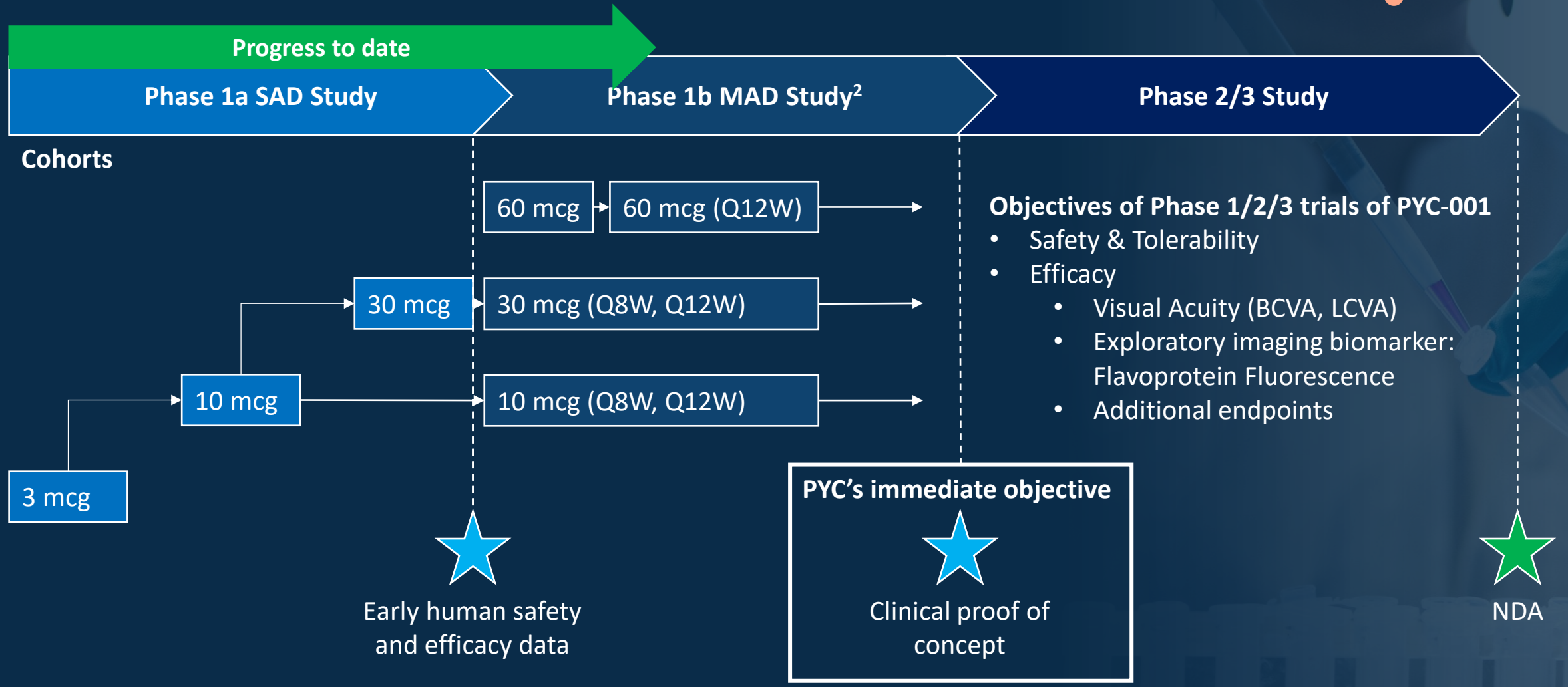
Ophthalmology programs

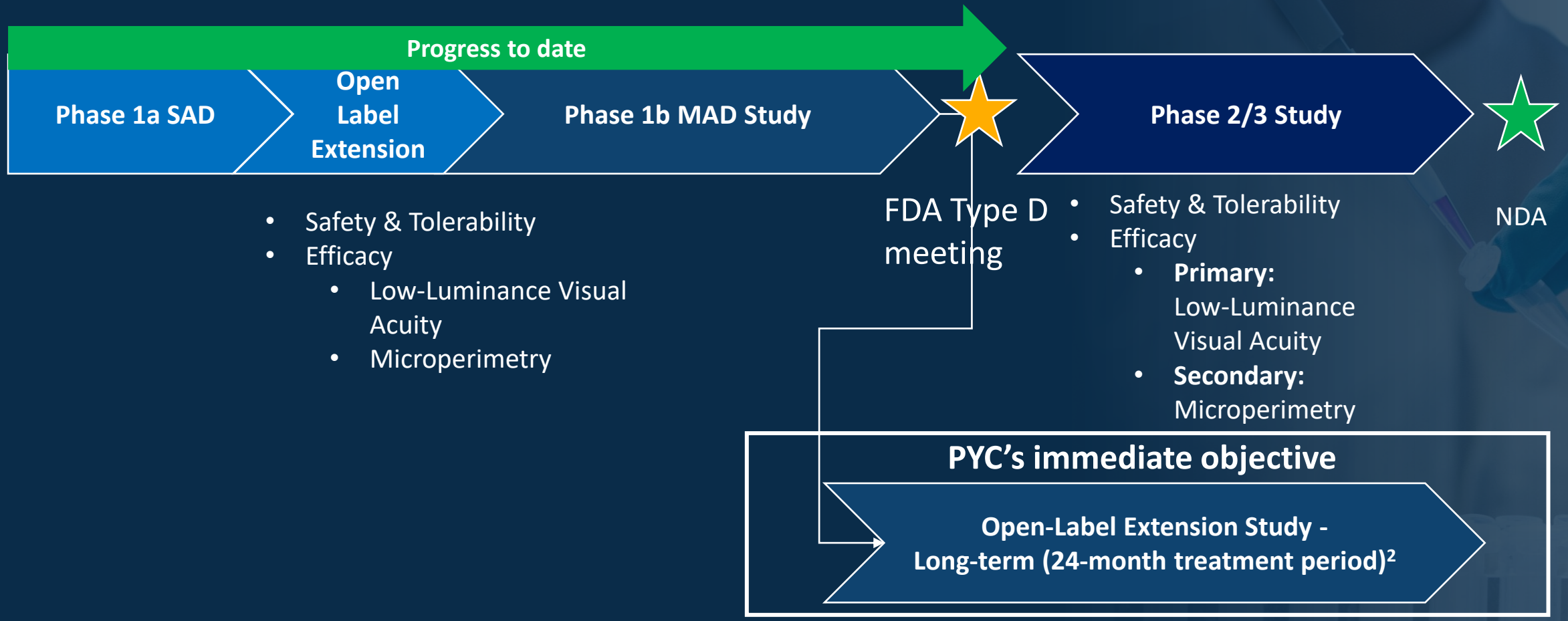
May 2026

PYC's immediate objective in the ADOA program is to demonstrate 'clinical proof of concept'



1. 'Clinical proof of concept' in this context means initial evidence that a new drug or treatment is likely to be effective and safe in humans
2. PYC may engage with regulatory authorities to discuss the potential for an open-label extension of the 'Phase 1b MAD study' to provide data for longer-term dosing of PYC-001 in ADOA patients ahead of initiating registrational trials

PYC's immediate objective in the RP11 program is to define the path to an NDA



1. Subject to the risks and uncertainties outlined in this document and the Company's ASX disclosures of 17 February 2025 (See: PYC Equity Raising Presentation Appendix A' specifically) and 2025 Annual Report (See ASX announcement of 28 August 2025)
2. Subject to regulatory approval and the risks and uncertainties outlined in this document and the Company's ASX disclosures of 17 February 2025 (See: PYC Equity Raising Presentation Appendix A' specifically) and 2025 Annual Report (See ASX announcement of 28 August 2025)

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Q&A

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