PYC Therapeutics

Life-changing science

2026 Q1 investor update

February 2026

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Agenda for today

- A brief introduction to PYC
- Company highlights following the recent financing
- 24-month look-forward for the Company's pipeline assets
- Discussion of updated clinical development timelines
- Q&A

An introduction to PYC Therapeutics

Precision medicines	PYC is a drug discovery and development company focused on creating life-changing new therapies for patients who have genetic diseases and no treatment options available today
Disease-modifying	PYC's strategy is to use RNA therapeutics to increase gene expression in haploinsufficient diseases in tissues in which the delivery challenge has been overcome
Multiple assets	The Company has 3 clinical-stage assets that address the underlying cause of severe unmet medical needs
Immediate milestones	The Company will present human efficacy data for drug candidates with disease-modifying potential in 4 indications over the coming 24 months[1]

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

Highlights of PYC's drug development pipeline

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1

Disease-modifying drug candidates[1]

Each of PYC's pipeline programs address the root cause of the target disease

2

In areas of major unmet need

In a disease with no established standard of care and between $1 and $15 billion p.a. in market size[2]

3

With the highest probability of success

Up to 5x

With up to a 5x higher probability of success than the industry average[3]

4

Validated in patient-derived models

Quantitative rescue of the single gene insufficiency that causes the disease[4]

5

Generating human data in 2026/2027

Generating critical data this year - high-value human data readouts in major unmet patient needs[5]

1. Each of PYC's drug candidates are designed to target the root cause of the genetic deficit responsible for the relevant disease. Accurate as 24 February 2026. Subject to the risks and uncertainties outlined in this document and the Company's ASX disclosures of 2 February 2026
2. Utilising the prevalence for each indication outlined and referenced in the Company's ASX disclosures of 2 February 2026 and the median orphan drug price from 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. Based on the genetic validation of the target gene. See: King EA, Davis JW, Degner JF. Are drug targets with genetic support twice as likely to be approved? Revised estimates of the impact of genetic support for drug mechanisms on the probability of drug approval. PLoS Genet. 2019 Dec 12;15(12):e1008489. doi: 10.1371/journal.pgen.1008489.
3. PYC's drug candidates are capable of increasing target gene expression by up to 2-fold in patient-derived models (See detailed data supporting each drug candidate in the relevant ASX announcement or on the Company's website)
4. Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

PYC will generate human efficacy data for all 4 of these drug candidates over the coming 24 months[1]

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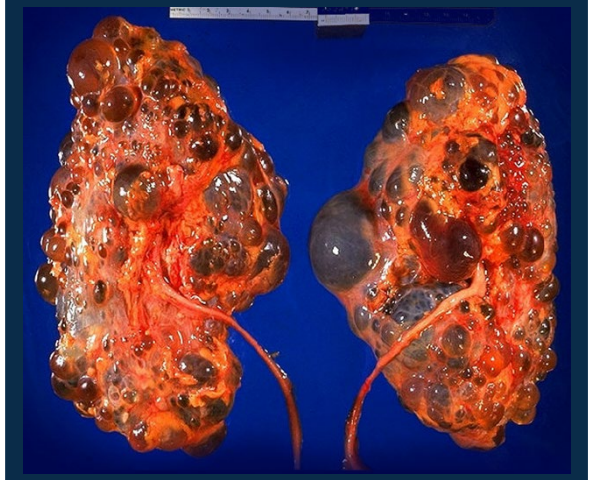
These data read-outs will highlight the potential of disease-modifying drug candidates in these genetically-defined diseases[1]

PYC-003 in ADPKD[2]



- Multi-dose safety and efficacy from ongoing study (NCT06714006)

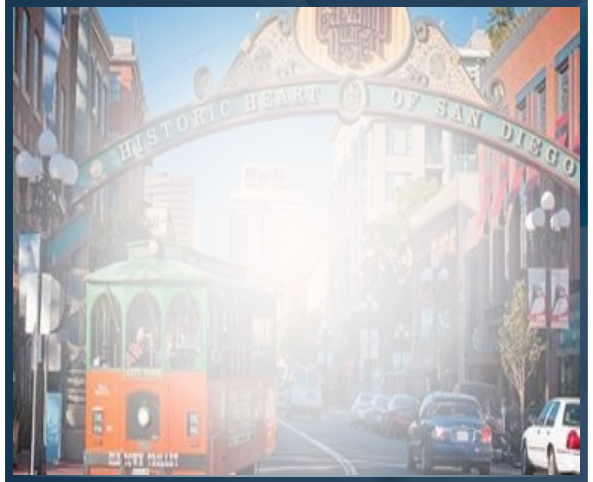
PYC-002 in PMS[3]

- Initiation of First-In-Human studies expected to commence in 2027 with early safety and efficacy readouts in H2 2027[1]

VP-001 in RP11[4]

- Efficacy data from P1/2 extension of the ongoing *DINGO* study (NCT06852963)

PYC-001 in ADOA[5]



- Efficacy data from ongoing P1/2 *MYRTLE* study (NCT06970106)

1. Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
2. Gross pathology of polycystic kidneys. CDC/Dr. Edwin P. Ewing, Jr.
3. PMS Foundation – Sierra's story
4. Representative vision loss experienced by an RP11 patient with moderate-advanced disease-progression
5. Representative vision loss experienced by an ADOA patient with moderate-advanced disease-progression

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Impact of the financing

February 2026

Company Highlights following completion of the Offer[1]

Successful completion of the capital raise will leave PYC:

- **Well resourced**: >$750m of cash on the balance sheet affording a funding runway through to CY2030[2];
- **With multiple assets**: Developing a diversified portfolio of assets that are in the M&A window (late-stage clinical development);
- **Near-term catalysts**: Multiple near-term human efficacy read-outs for drug candidates with disease-modifying potential in areas of major unmet patient need; and
- **Supported by a strong shareholder register**: made up of leading global specialist life science investors

1. Management forecast accurate as at the date of this announcement. Subject to full take-up of the Offer and the risks and uncertainties outlined in the Offer documentation
2. Management forecast accurate as at the date of this document

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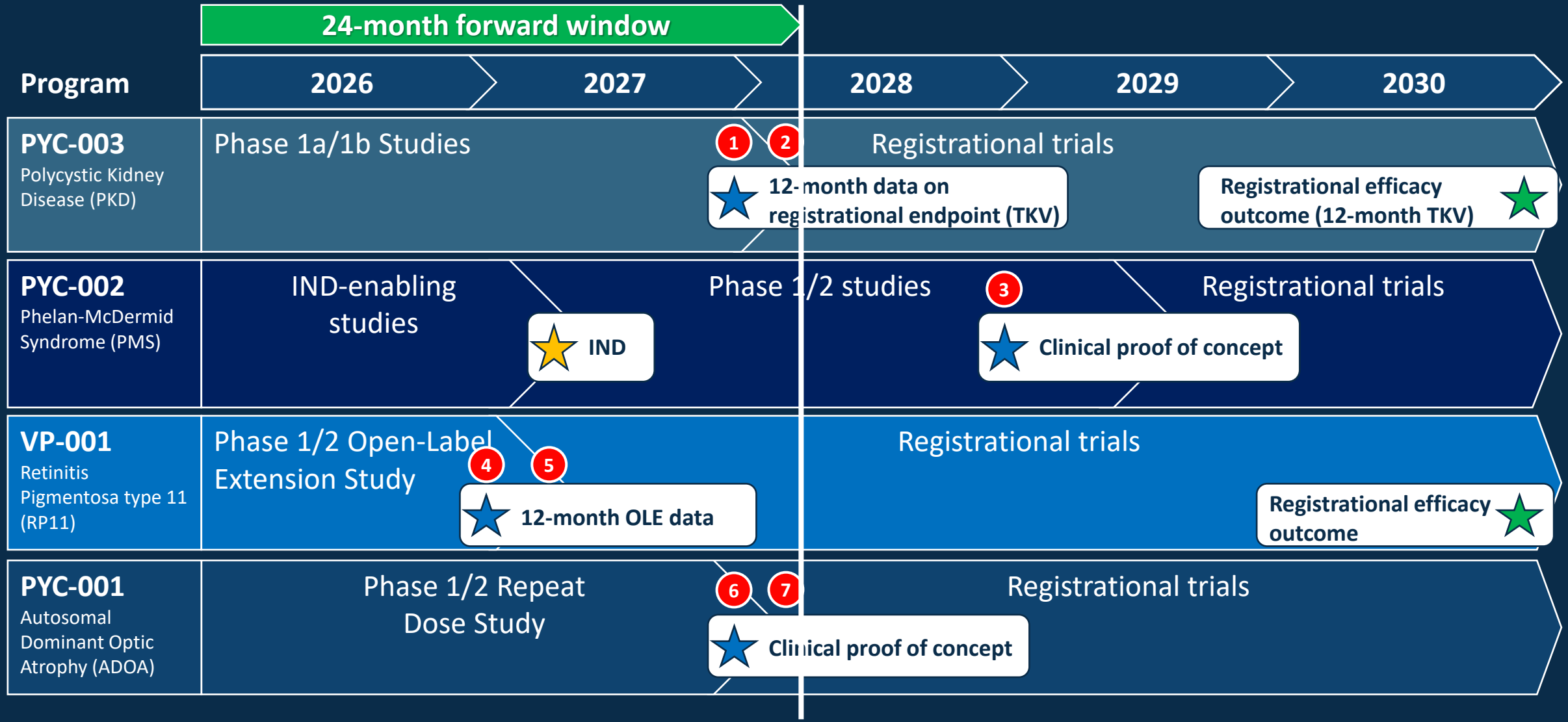
Forward view of program milestones

February 2026

PYC has multiple human efficacy read-outs expected within the next 24 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.

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]

Part A - SAD in healthy volunteers

Part B – SAD in ADPKD Patients

Part C – MAD in PKD Patients

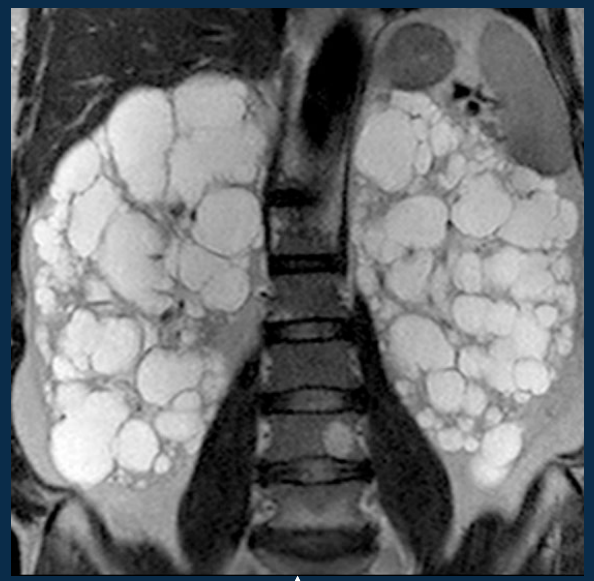
Phase 2/3 Study

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

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]

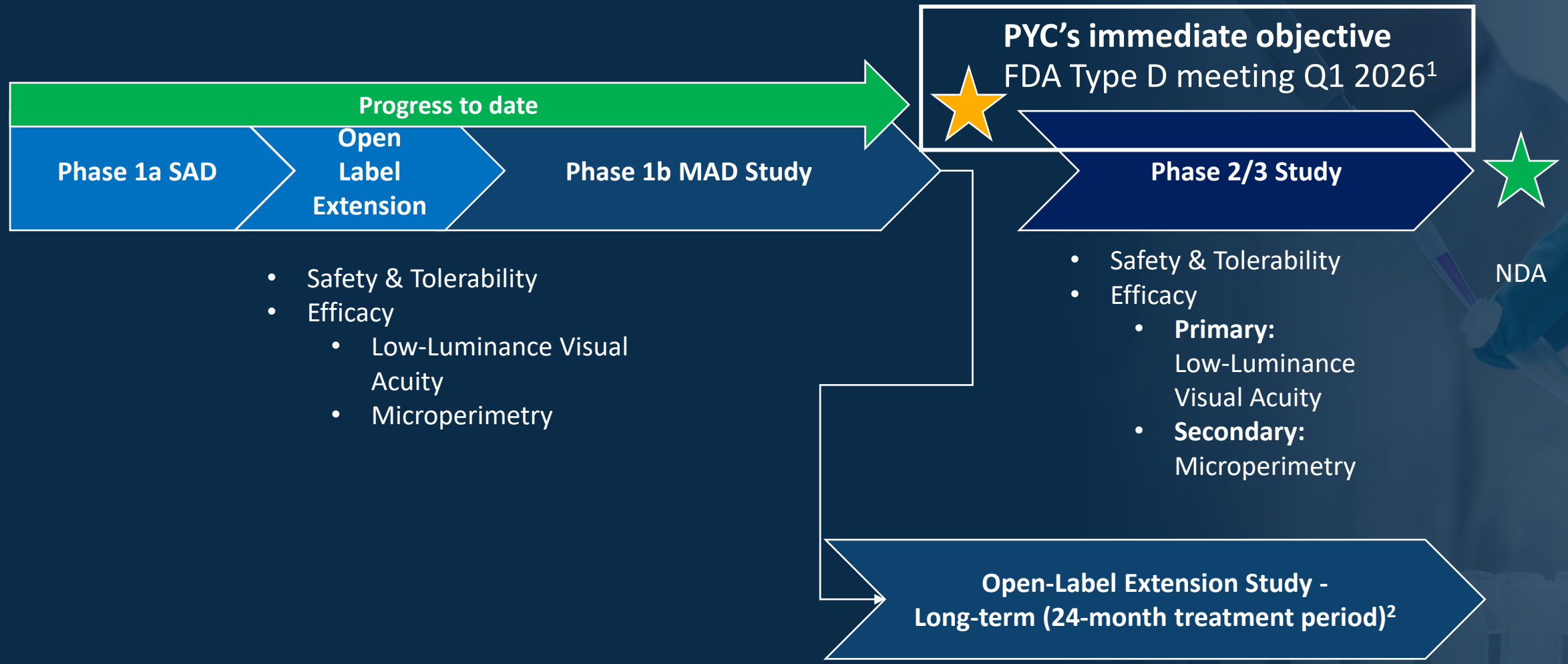
Established pathway

NDA

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

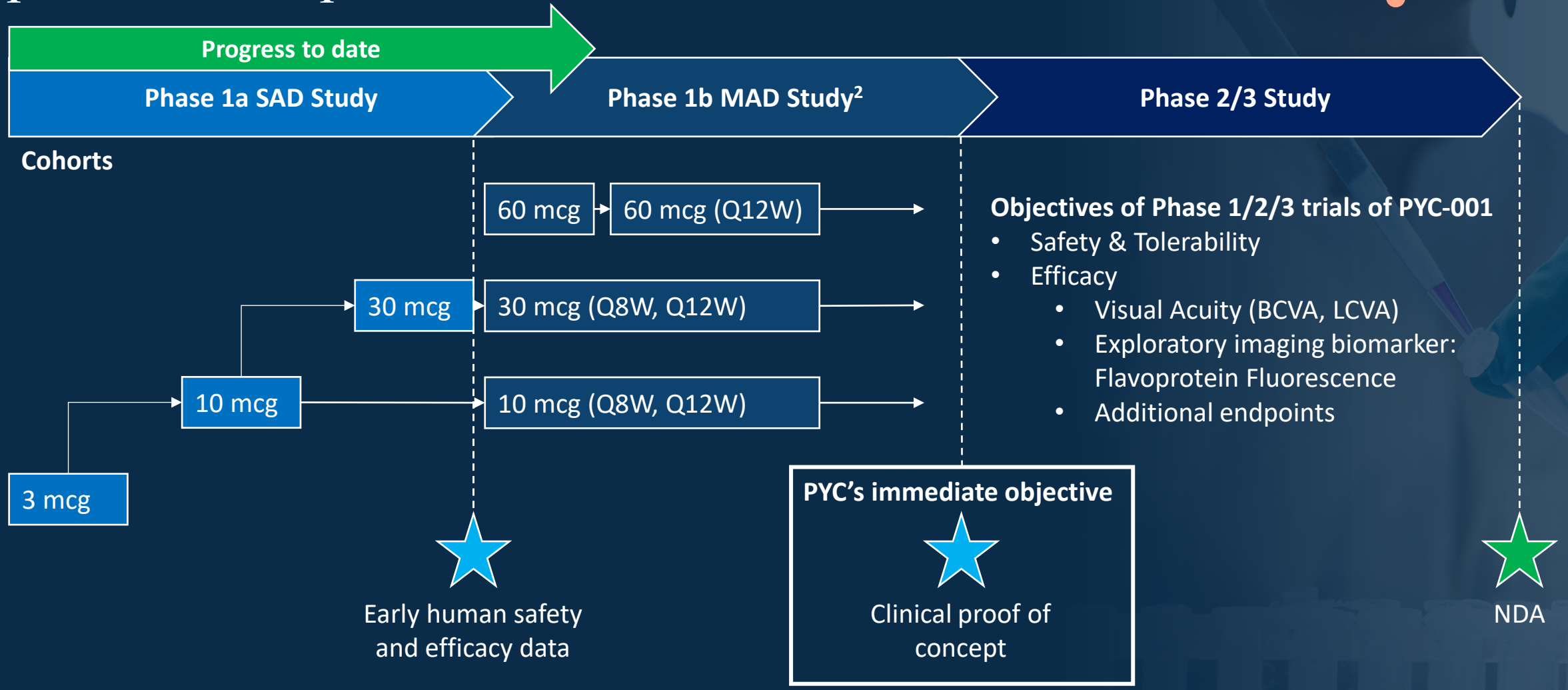
1. For phosphorothioate oligonucleotides delivered via an intrathecal route of administration in diseases of neurons in the Central Nervous System (CNS) - Refer to ASX Announcement of 13 October 2025 for more detail
2. Jafar-Nejad P, et al. The atlas of RNase H antisense oligonucleotide distribution 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

PYC's immediate objective is to align on the pathway to an NDA in RP11



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)

PYC's immediate objective in ADOA 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

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Updates to program timelines

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PYC is on track to advance all 4 of its drug candidates into registrational trials[1]

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Cash runway following completion of the Offer extended to CY2030[1]

Program	2026	2027	2028	2029	2030
PYC-003 Polycystic Kidney Disease (PKD)	Phase 1a/1b Studies		1 2 Registrational trials ★ 12-month data on registrational endpoint (TKV)		Registrational efficacy outcome (12-month TKV) ★
PYC-002 Phelan-McDermid Syndrome (PMS)	IND-enabling studies	★ IND	Phase 1/2 studies 3	★ Clinical proof of concept	Registrational trials
VP-001 Retinitis Pigmentosa type 11 (RP11)	Phase 1/2 Open-Label Extension Study	4 5 ★ 12-month OLE data		Registrational trials	Registrational efficacy outcome ★
PYC-001 Autosomal Dominant Optic Atrophy (ADOA)	Phase 1/2 Repeat Dose Study		6 7 ★ Clinical proof of concept	Registrational trials	

1. Management forecast accurate as at the date of this announcement. Subject to successful completion of the Offer and the risks and uncertainties outlined in the Offer documentation. Subject to change based on outcomes and strategic priorities.

RP11 example: How do the dynamic variables PYC is measuring influence projected development timelines?

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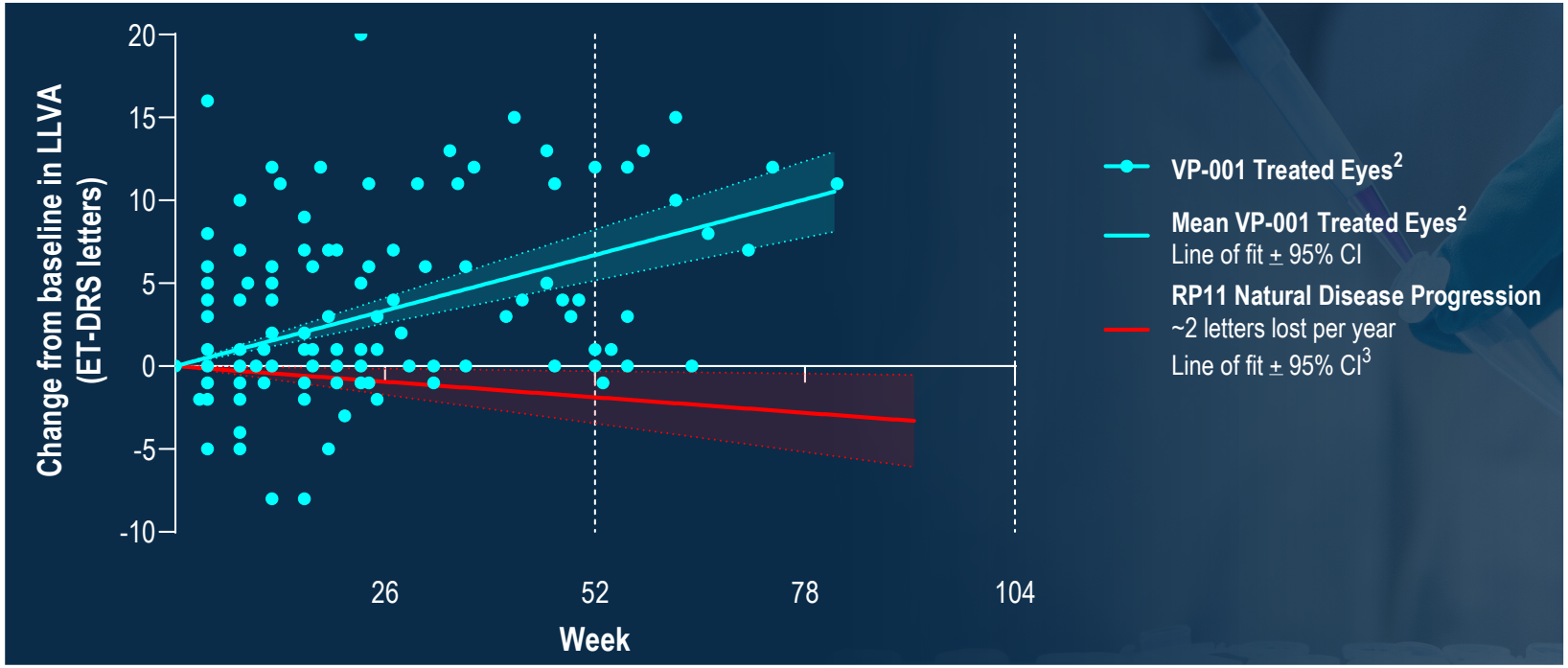
Human safety[1]:
RP11 patients

- No Treatment Related-Serious Adverse events observed in any subject dosed with VP-001 to date[1]
- Treatment-Emergent Adverse Events (TE-AEs) were mostly mild, and procedure related[1]
- No TE-AEs leading to discontinuation of treatment

Human efficacy:
Change in Low-Luminance Visual Acuity (LLVA) in RP11 patients[2,3]



Improvements in visual acuity are consistent with patient-reported outcomes of improved vision and quality of life after treatment with VP-001[4]

1. See ASX announcement of 14 November 2025
2. Accurate as at 14 November 2025
3. Analysis of all data available for the treated eyes of patients who received 30 mcg or more of VP-001 in PYC's Platypus and Wallaby studies. Line of fit of data collected from RP11 patients enrolled in PYC's Natural History Study followed for at least 52 weeks (n=16 eyes)
4. See ASX announcement of 2 May 2025

PYC is working to define signal within highly variable ('noisy') data sets

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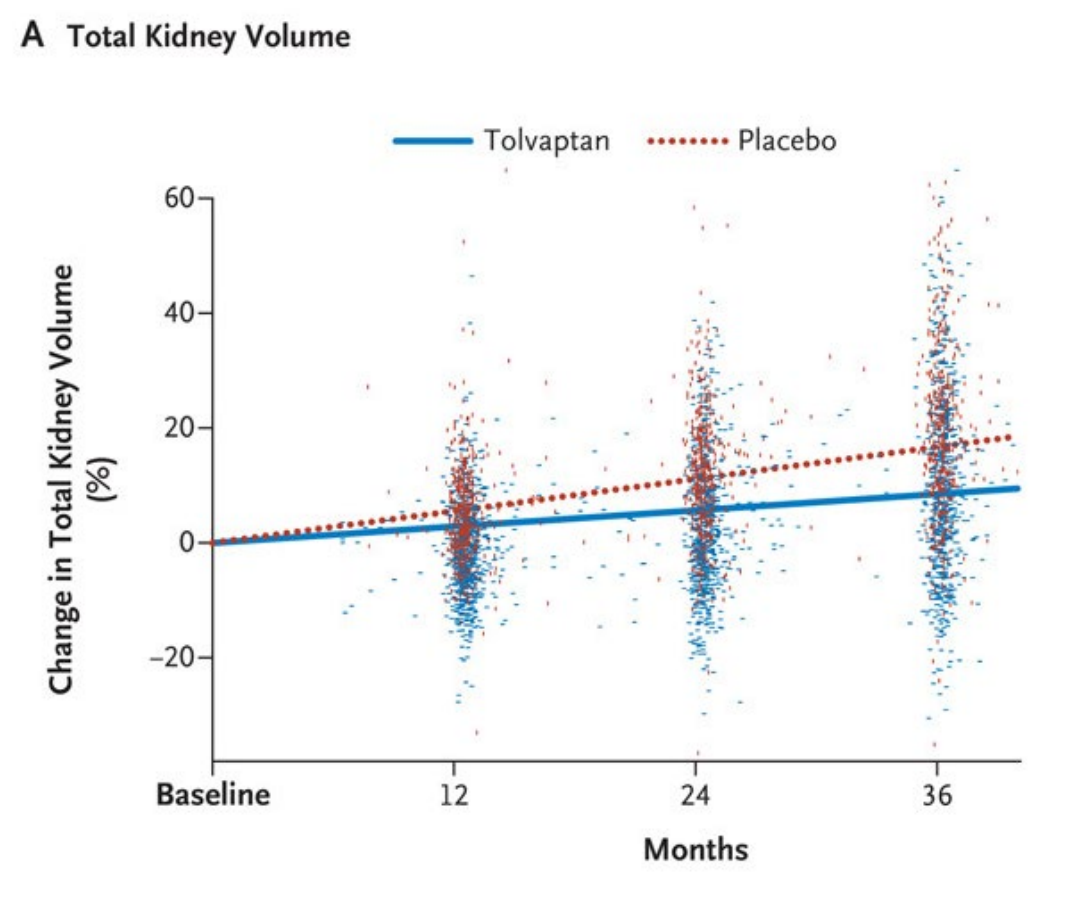
Effect of Tolvaptan on the Annual Change in Total Kidney Volume (TKV)



The TKV data from ~12 months of drug exposure onwards is likely to be more informative in PYC's upcoming phase 1b study in PKD

1. Vicente E. Torres, et al., "Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease," NEJM, December 20, 2012.

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Q&A

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