PYC Therapeutics

Life-changing science

Q2 Investor Update

June 2023

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Discussion topics – Q2 investor update

- Introduction to PYC Therapeutics
  - Vision
  - Strategy
  - Commercial framework
- Pipeline review
  - PYC's progress YTD 2023
  - Forward view for PYC in 2023
- Q&A

PYC Therapeutics

Life-changing science

PYC's vision

PYC discovers and develops RNA therapies to change the lives of patients with genetic diseases

PYC is progressing 3 first-in-class drug candidates with disease-modifying potential into the clinic within 18 months

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PYC IS HERE

1 From platform to program – making 'the drug'

2 Evolution to a clinical-stage multi-asset company

3 Scale into multiple clinical safety and efficacy read-outs

2023/24 Objectives

- **Establish human safety** of PYC's platform technology
- **3+ first-in-class and potentially disease modifying drugs** into the clinic, **each with >$1bn p.a. markets**
- **Enter the transactional window** for genetic medicines (Phase 1/2)

2019 → 2020 2021 → 2022 2023 → 2024

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PYC's strategy

PYC's RNA delivery platform overcomes the primary challenge for precision therapies – ensuring enough drug reaches its target

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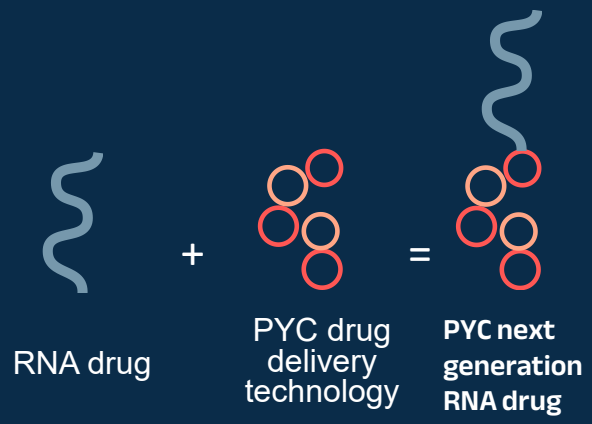
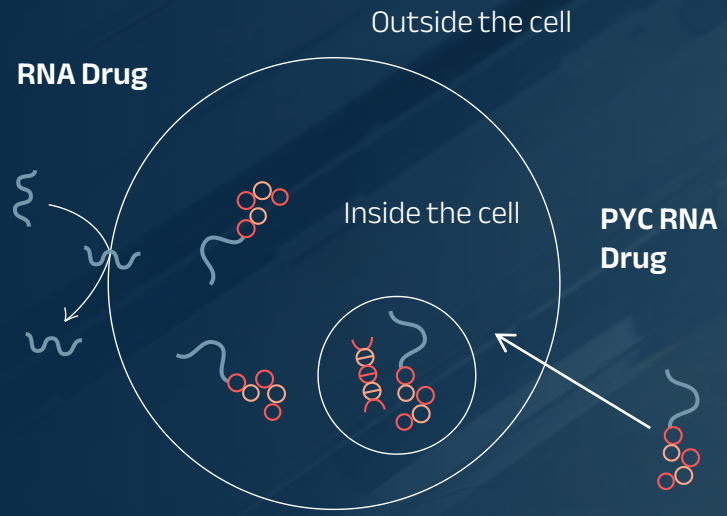
PYC combines existing RNA drug design technology with its proprietary drug delivery platform to create next generation RNA therapeutics



PYC's drug delivery platform is used to assist the RNA drug reach its target inside the cell



PYC is creating therapies for patients through a strategy anchored on four critical features

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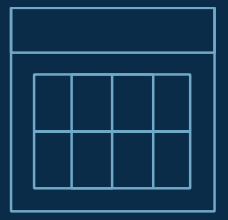
A HIGHER PROBABILITY OF SUCCESS

PYC focuses on monogenic indications. These have the highest likelihood of approval from the start of clinical trials to market of any indication*[1]



A FASTER PATH TO MARKET

The potential for approval following two clinical trials (not three) due to the absence of existing treatment options for patients with the targeted indications

LIKELY RAPID UPTAKE IN MARKET

First-in-class drugs in rare diseases achieve rapid market penetration with a very short lead time to peak sales

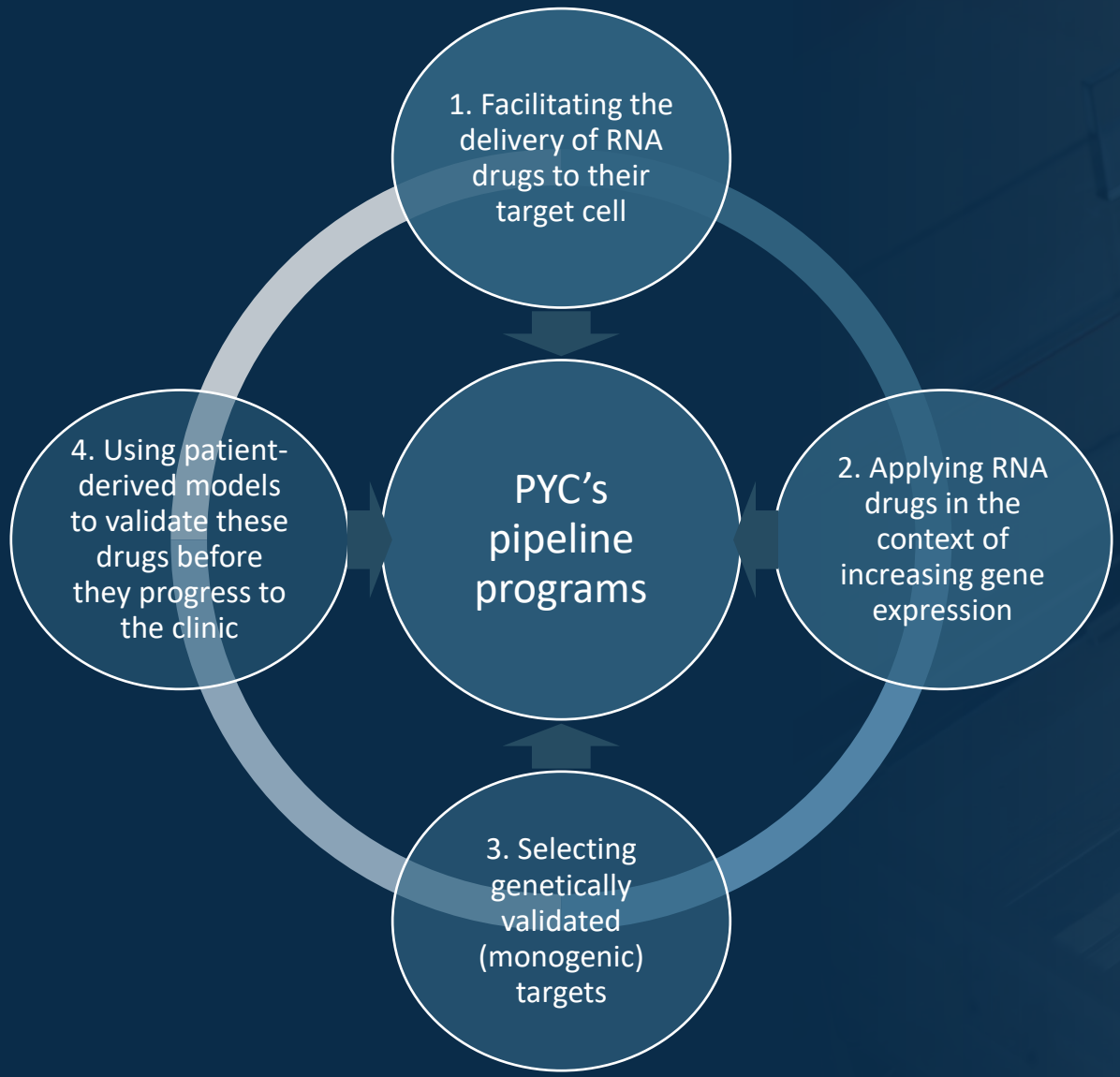
ORPHAN DRUG PRICING

Median list price of ~US$150,000[2] per patient per annum making for commercially attractive markets across the pipeline

*Monogenic indications compared to polygenic indications

1. Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank. doi: https://doi.org/10.1101/2020.11.02.20222232
2. EvaluatePharma. Orphan Drug Report. 2019.

4 powerful forces are converging around PYC's programs that enhance their prospects of success in clinical development



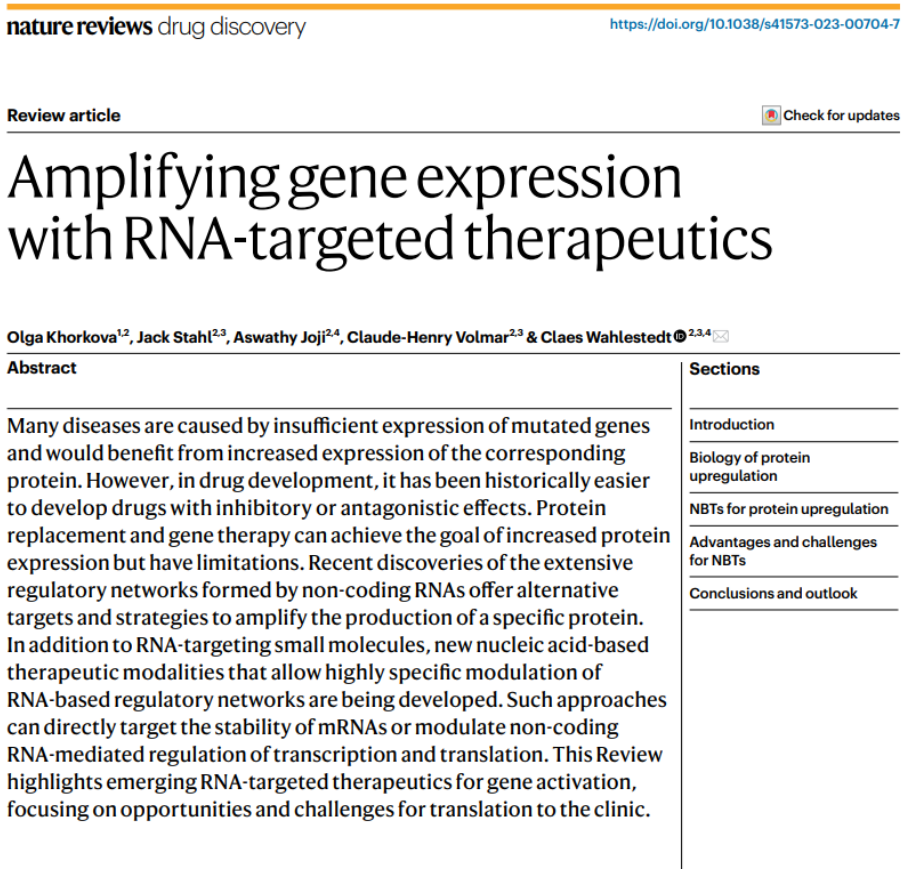
1. Facilitating the delivery of RNA drugs to their target cell substantially enhances the prospect of disease-correction

"My view of the next 20 years is that we are going to a see a remarkable expansion of gene, cell, gene editing and RNA-based strategies in medicine that emerge across a broad swath of disease. And I think, ***most importantly, we are going to open delivery for some of these genetic medicines beyond the current restricted tissues and cells****."*

John Maraganore, former CEO Alnylam

Interview with Stifel/Torreya

2. The specific application of RNA drugs to increase gene expression is gaining increased appreciation



nature reviews drug discovery

https://doi.org/10.1038/s41573-023-00704-7

Review article

Check for updates

Amplifying gene expression with RNA-targeted therapeutics

Olga Khorkova[1,2], Jack Stahl[2,3], Aswathy Joji[2,4], Claude-Henry Volmar[2,3] & Claes Wahlestedt[2,3,4]

Abstract

Many diseases are caused by insufficient expression of mutated genes and would benefit from increased expression of the corresponding protein. However, in drug development, it has been historically easier to develop drugs with inhibitory or antagonistic effects. Protein replacement and gene therapy can achieve the goal of increased protein expression but have limitations. Recent discoveries of the extensive regulatory networks formed by non-coding RNAs offer alternative targets and strategies to amplify the production of a specific protein. In addition to RNA-targeting small molecules, new nucleic acid-based therapeutic modalities that allow highly specific modulation of RNA-based regulatory networks are being developed. Such approaches can directly target the stability of mRNAs or modulate non-coding RNA-mediated regulation of transcription and translation. This Review highlights emerging RNA-targeted therapeutics for gene activation, focusing on opportunities and challenges for translation to the clinic.

Sections

HEALTH & DISEASE

Hope for haploinsufficiency diseases

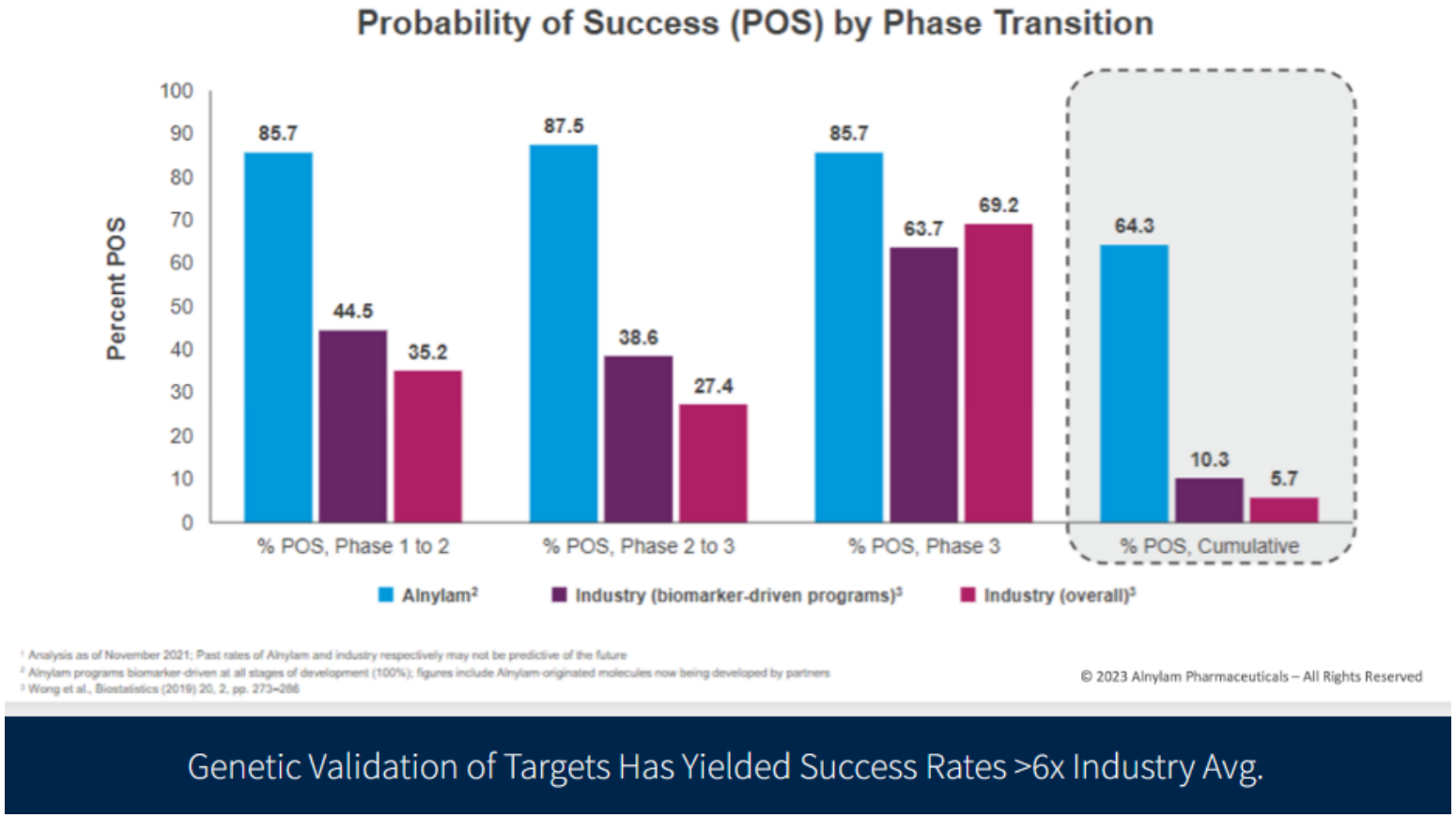
Genetic conditions like Dravet syndrome, which causes severe childhood epilepsy, are hard to tackle with traditional gene therapy. New approaches in the works include using antisense therapy to boost mRNA splicing.

By Elie Dolgin | 04.13.2023

Khorkova, O., Stahl, J., Joji, A. et al. Amplifying gene expression with RNA-targeted therapeutics. Nat Rev Drug Discov (2023). https://doi.org/10.1038/s41573-023-00704-7

Knowable Magazine. Elie Dolgin – Hope for haploinsufficiency diseases. April 2023

3. Genetic validation of the target remains the single most important consideration informing success in the clinic



Like Alnylam, PYC pursues drug targets with the highest degree of genetic validation

4. The use of patient-derived models provides an early insight into efficacy of the drug candidate in the clinic

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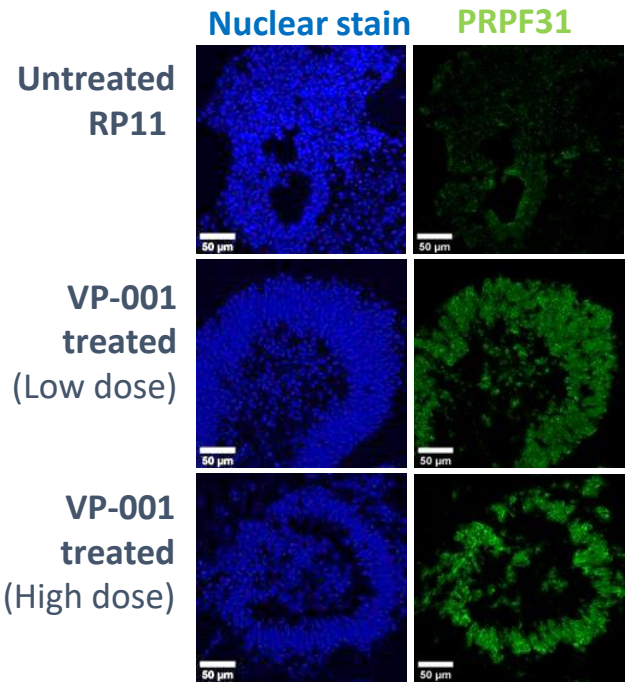
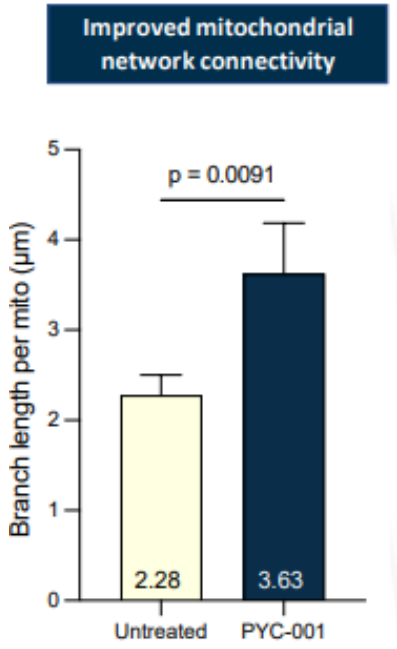
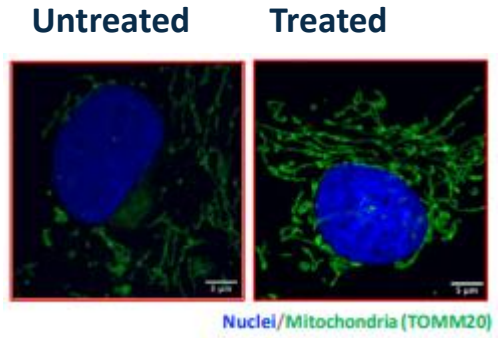
Program #1 (RP11) patient-organoid



Program #2 (ADOA) patient-derived model





"We need to understand as early as possible **whether a drug candidate is safe and works in patients**, not wait to find out in clinical trials"

Roche

Endpoints news 'Roche launches institute of human biology in search of predictive models'
See ASX announcements of 19 April 2023 and 2 May 2023

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Commercial implications

Each of the programs in PYC's pipeline is directed towards a $1 billion+ addressable market[1]

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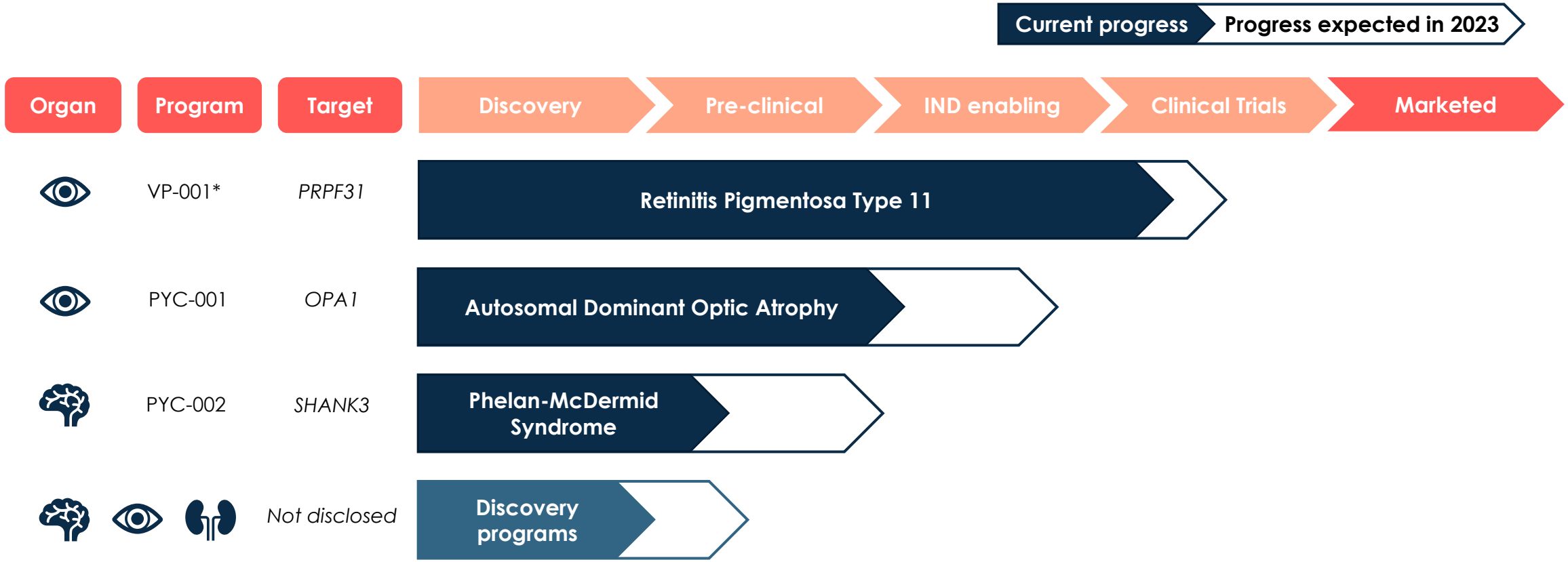

PYC's technology is a scalable platform with broad potential application across many different disease indications

1 Assumes median orphan drug pricing applicable to each drug candidate (EvaluatePharma Orphan Drug Report 2019) and prevalence based on Sullivan, L et al. Genomic rearrangements of the PRPF31 gene account for 3% of autosomal dominant retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2006;47(10):4579-88 and Han, J., Li, Y., You, Y. et al. Autosomal dominant optic atrophy caused by six novel pathogenic OPA1 variants and genotype–phenotype correlation analysis. BMC Ophthalmol 22, 322 (2022) and Phelan McDermid Syndrome Patient Foundation

* PYC 95.2% ownership of VP-001 (4.8% ownership by Lions Eye Institute, Australia) and 100% ownership of all other pipeline programs

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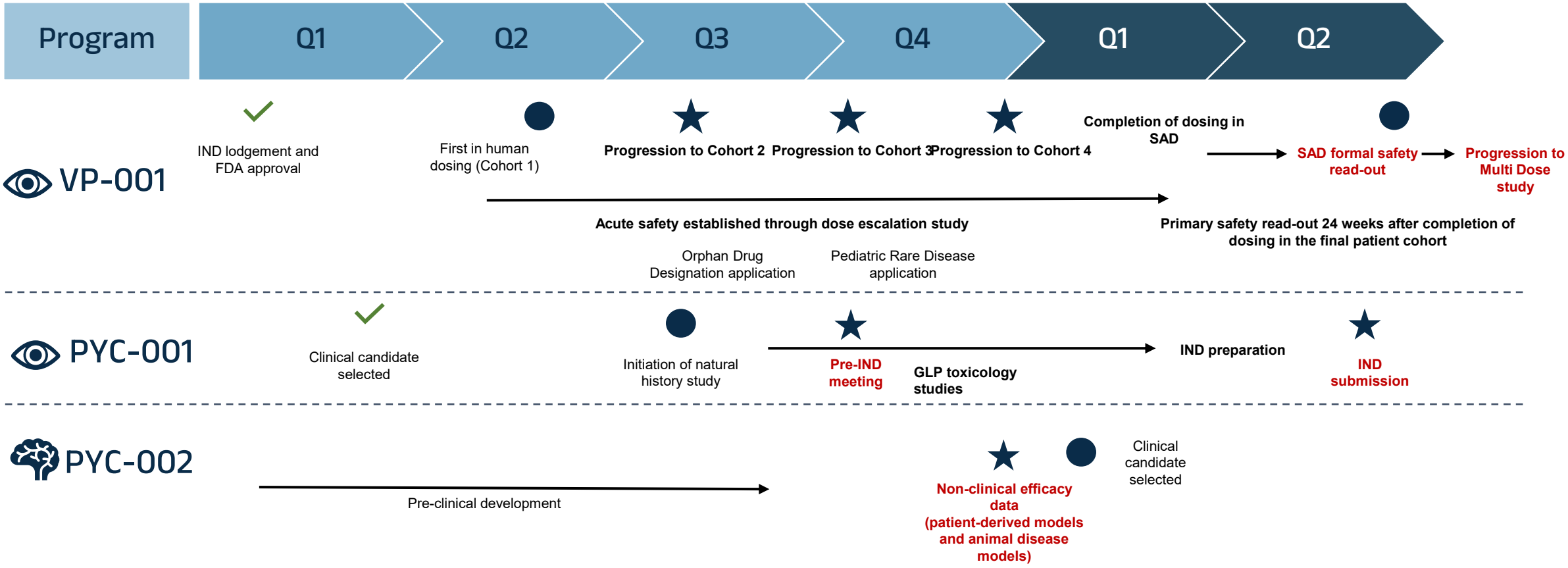
Program deep-dives (progress and anticipated milestones)

PYC has mapped out the path to progression of 3 first-in-class drugs with disease-modifying potential into the clinic

Human safety data to be generated across 2023 in VP-001 program, with PYC-001 expected to enter the clinic in 2024



Anticipated milestones are projections based on latest company perspective on drug development plans as at May 2023

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Q&A