12 July 2024

BIOSHARES BIOTECH SUMMIT PRESENTATION

PERTH, Australia and SAN FRANCISCO, California – 12 July 2024

PYC Therapeutics Limited (ASX:PYC) is pleased to provide a copy of the presentation that will be given by PYC's CEO, Dr Rohan Hockings, at the Bioshares Biotech Summit, 12 July 2024.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a clinical-stage biotechnology company creating a new generation of RNA therapies to change the lives of patients with genetic diseases. The Company utilises its proprietary drug delivery platform to enhance the potency of precision medicines within the rapidly growing and commercially proven RNA therapeutic class. PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**[1].

For more information, visit pyctx.com, or follow us on LinkedIn.

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Any forward-looking statements in this ASX announcement have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations, and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside the Company's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this ASX announcement include known and unknown risks. Because actual results could differ materially to assumptions made and the Company's current intentions, plans, expectations, and beliefs about the future, you are urged to view all forward-looking statements contained in this ASX announcement with caution. The Company undertakes no obligation to publicly update any forward-looking statement whether as a result of new information, future events or otherwise.

This ASX announcement should not be relied on as a recommendation or forecast by the Company. Nothing in this ASX announcement should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

This ASX announcement was approved and authorised for release by the CEO of PYC Therapeutics Limited

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[1] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

PYC Therapeutics

Life-changing science

Bioshares Biotech Summit

July 2024

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The purpose of this presentation is to provide an update of the business of PYC Therapeutics Limited (ASX:PYC) ['PYC']. These slides have been prepared as a presentation aid only and the information they contain may require further explanation and/or clarification. Accordingly, these slides and the information they contain should be read in conjunction with past and future announcements made by PYC Therapeutics and should not be relied upon as an independent source of information. Please contact PYC and/or refer to the Company's website for further information.

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Today's topics

- An introduction to PYC Therapeutics
- An outline of PYC's ambition – how 2024 will evolve into 2025
- How the pipeline was built around:
  - High propensity programs; with
  - A high-velocity path to market
- Why now is the critical time for the Company – illustrating the impact of 'clinical proof of concept' data through the RP11 program

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Company introduction

An introduction to PYC Therapeutics

- PYC is a clinical-stage drug discovery and development company with operations in Australia and the US

- The company is an emerging leader in the field of precision RNA therapies for patients with genetic diseases caused by haploinsufficiency in the eye, kidney and CNS

- PYC is developing four first-in-class drug candidates in areas of severe unmet need for the tens of millions of patients worldwide affected by these diseases:
  - Retinitis Pigmentosa type 11 (RP11)
  - Autosomal Dominant Optic Atrophy (ADOA)
  - Autosomal Dominant Polycystic Kidney Disease (ADPKD)
  - Phelan-McDermid Syndrome (PMS)

- PYC's novel therapeutics are based on a platform of oligonucleotides linked to guiding peptides - No viral vectors are used in the delivery technology

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The evolution of PYC's ambition through 2025

PYC is currently conducting 5 clinical trials in parallel

Indication	Trial	Early	Mid	Late
1) Retinitis Pigmentosa type 11	1) Natural History	*Ongoing*		
	2) SAD	→		
	3) MAD	→	→	
2) Autosomal Dominant Optic Atrophy	1) Natural History	*Ongoing*		
	2) SAD[1]	*Expected Q3 2024*		

SAD: Single Ascending Dose; MAD: Multiple Ascending Dose

1. Based on management's latest estimates accurate as at 4 July 2024 and subject to successful realisation of developmental milestones in each program as well as satisfaction of regulatory requirements and subject to all other risks customary to an early-clinical stage biotechnology company developing novel drug candidates

There is scope for this clinical pipeline to grow substantially in 2025[1]

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Indication	Trial	Early	Mid	Late
1) Retinitis Pigmentosa type 11	1) Natural History	*Ongoing*		
	2) SAD	→		
	3) MAD	→	→	
	4) Pivotal	→	→	→
2) Autosomal Dominant Optic Atrophy	1) Natural History	*Ongoing*		
	2) SAD[1]	*Expected Q3 2024*		
	3) MAD	→	→	
	4) Pivotal	→	→	→
3) Blinding Eye Disease #3 e.g. Glaucoma	1) P2[2]	→	→	
4) Blinding Eye Disease #4 e.g. LHON	1) P2[2]	→	→	
5) Polycystic Kidney Disease	1) SAD	→		
6) Phelan-McDermid Syndrome	1) SAD	→		

SAD: Single Ascending Dose; MAD: Multiple Ascending Dose

1. Based on management's latest estimates accurate as at 4 July 2024 and subject to successful realisation of developmental milestones in each program as well as satisfaction of regulatory requirements and subject to all other risks customary to an early-clinical stage biotechnology company developing novel drug candidates
2. Subject to regulatory approval, PYC-001 can progress directly into a mid-stage (phase 2) trial in other blinding eye diseases where its mechanism of improving cellular bioenergetics holds potential for disease correction

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Building a pipeline (with a critical difference)

There are two elements embedded within PYC's pipeline that fundamentally change the probability of success in the clinic

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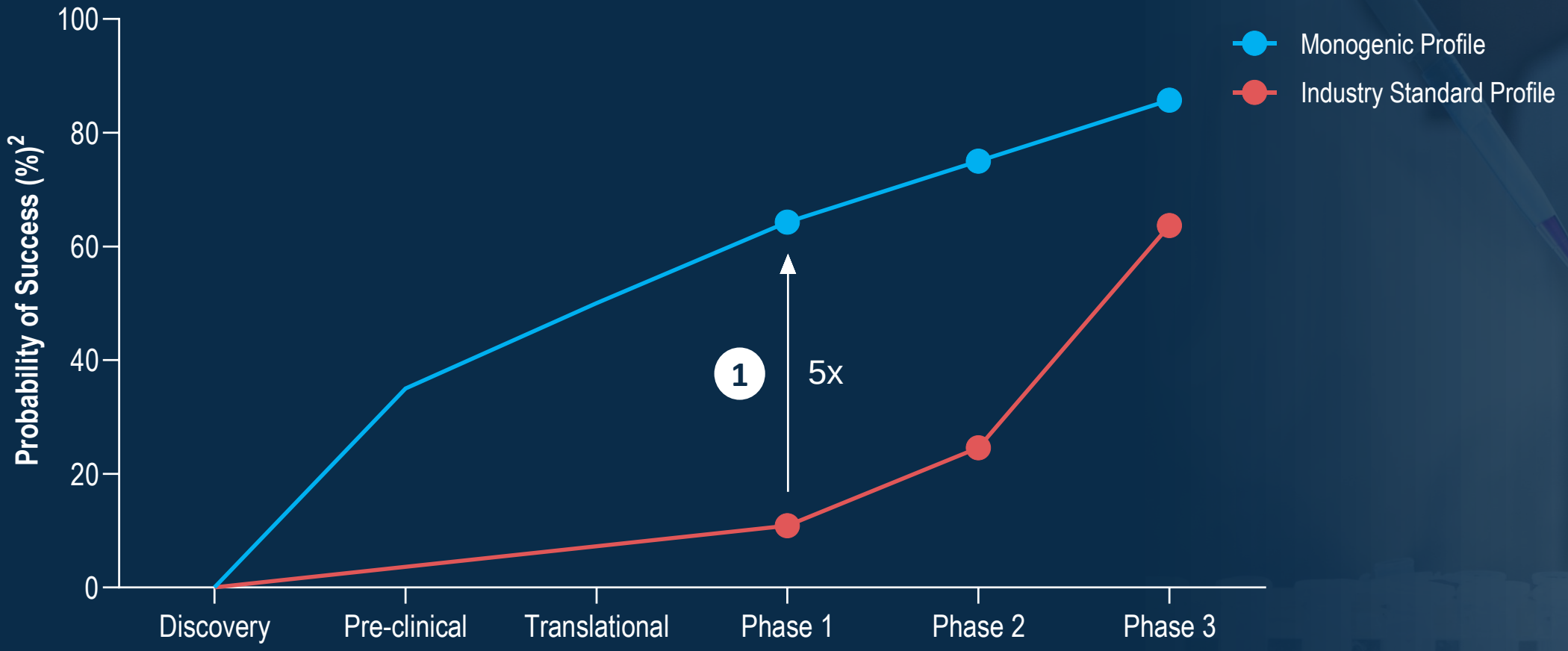
1. PYC pursues diseases caused by mutations in a single gene ('monogenic' diseases)

2. PYC validates its drug candidates in human target tissue *before* it progresses into clinical trials

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. Ashworth, K.E. et al. Inherited Retinal Diseases and Retinal Organoids as Preclinical Cell Models for Inherited Retinal Disease Research. Genes 2024, 15, 705. https://doi.org/10.3390/genes15060705

1. Monogenic drugs that enter human trials are 5x more likely to succeed[1]



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. Actual probability of success numbers begin with First-in-Human (Phase 1) as described by Alnylam in https://news.alnylam.com/rnai/articles/harnessing-human-genetics-power-next-wave-rnai-therapeutics

2. PYC validates all pipeline candidates in patient-derived models before it enters clinical development

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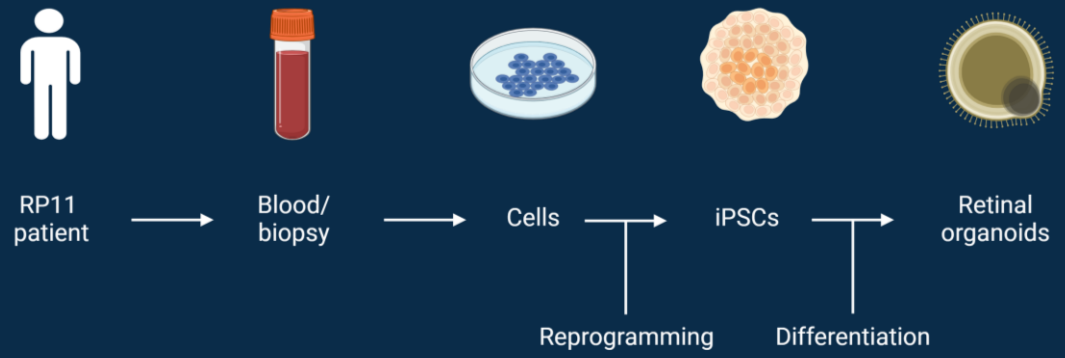
1. PYC can create a patient-derived retina



That enables it to determine whether its drug candidate can:

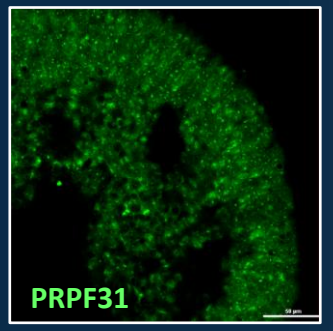
i. Address the underlying cause of the disease; and

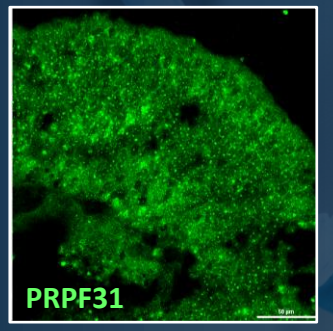
ii. Rescue the disease phenotype

Retinitis Pigmentosa type 11 (RP11) untreated

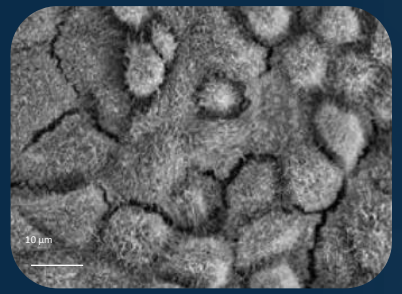
RP11 treated with VP-001

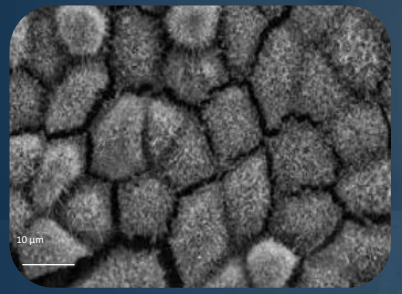
i.





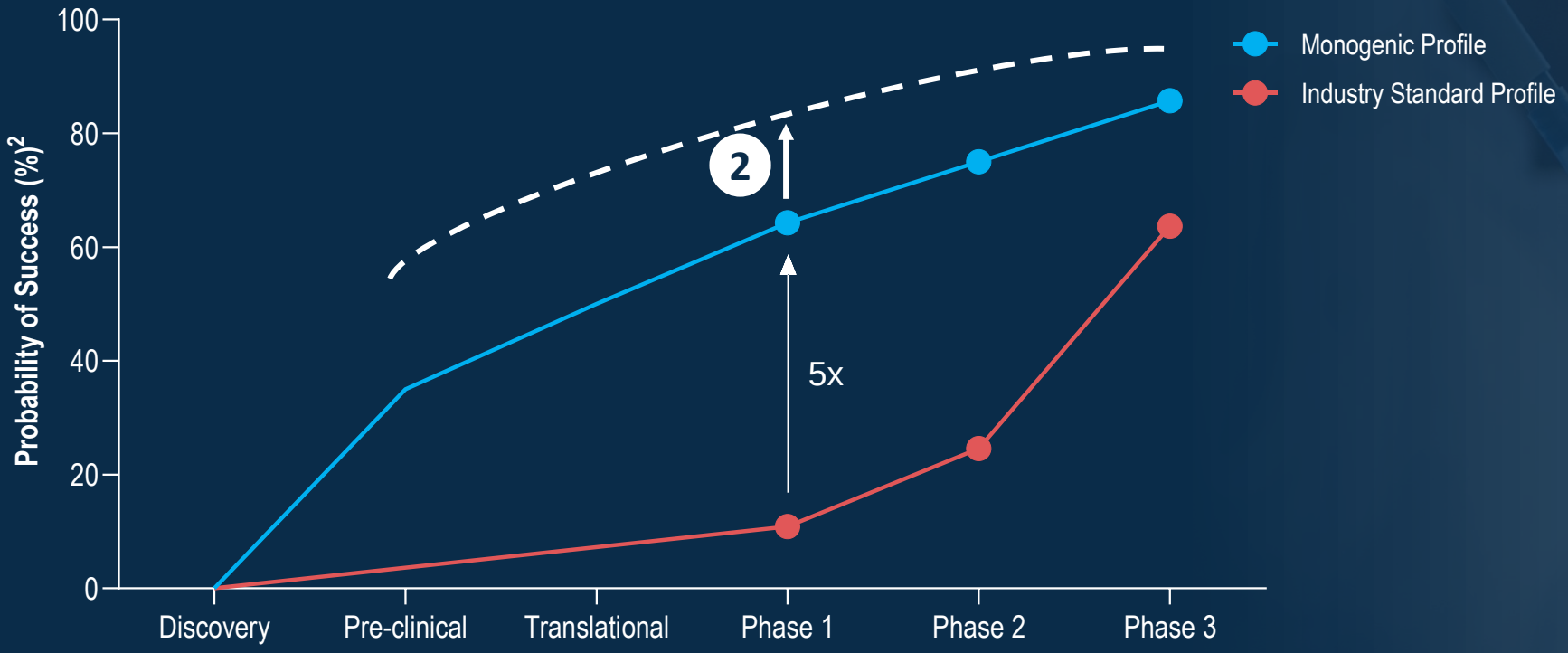
ii.





1. Refer ASX Announcements 7 October 2020, 16 December 2020 and 6 May 2024. Representative illustration of patient-derived models (Created with Biorender)

Validation of PYC's drug candidates in patient-derived models further enhances their probability of success in the clinic



"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 which can be expensive and time-consuming"

Mattias Lutolf, Roche Institute of Human Biology[1]

1. Endpoints News. Roche doubles down on organoids, human model systems with new research institute - https://endpts.com/roche-launches-institute-of-human-biology-in-search-of-predictive-models/
2. Actual probability of success numbers begin with First-in-Human (Phase 1) as described by Alnylam in https://news.alnylam.com/rnai/articles/harnessing-human-genetics-power-next-wave-rnai-therapeutics. The extent of the enhanced probability of success associated with validation in patient derived models is conceptual and has not been (and is not intended to be) quantified in this representation

PYC's strategy sees it developing best-in-class assets with a high probability of success in the clinic

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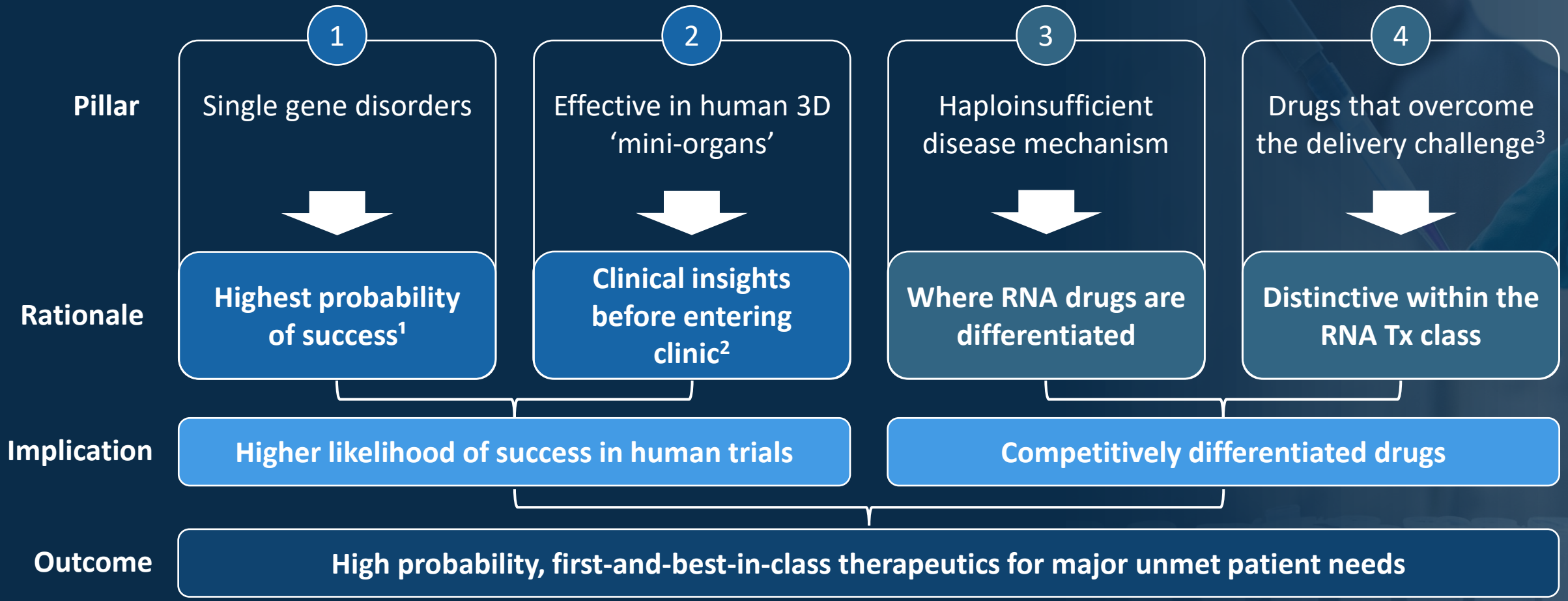

1. Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank. doi: https://doi.org/10.1101/2020.11.02.20222232
2. https://endpts.com/roche-launches-institute-of-human-biology-in-search-of-predictive-models/
3. Refer ASX announcement 3 October 2022 for PYC OTS Poster Presentation

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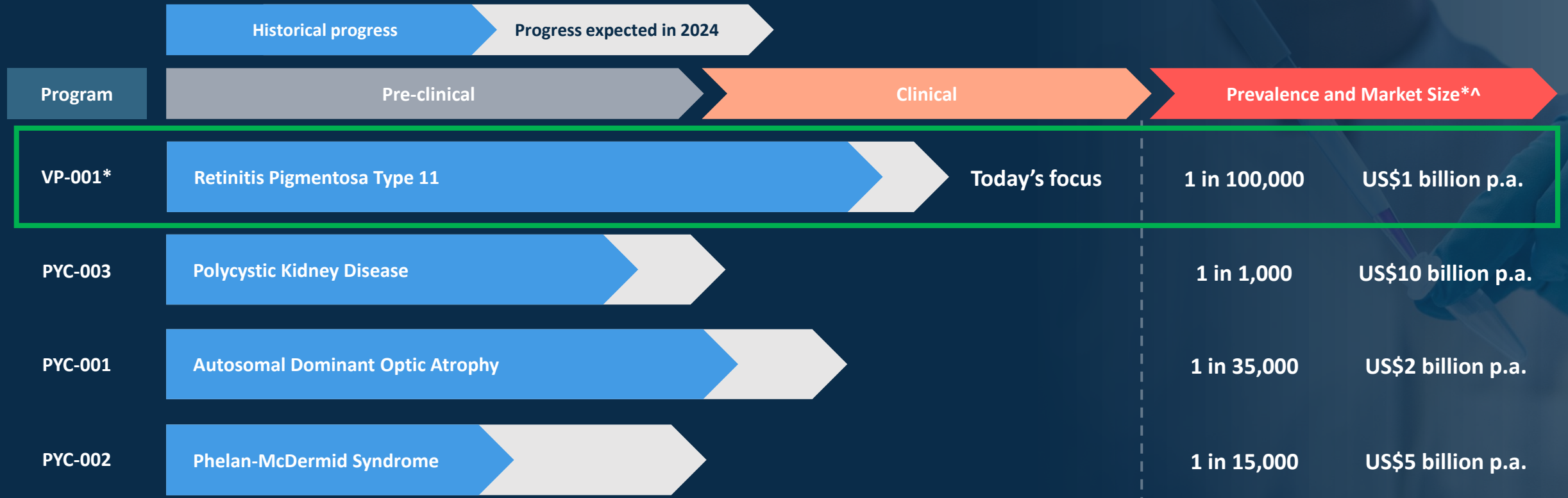
RP11 – illustrating the potential for patient impact

In focus: PYC has progressed the first drug candidate for patients with a blinding eye disease into human trials



- PYC 96.2% ownership of VP-001 (3.8% ownership by Lions Eye Institute, Australia) and 100% ownership of all other pipeline programs
- Based on management's latest estimates accurate as at 4 July 2024 and subject to successful realisation of developmental milestones in each program as well as satisfaction of regulatory requirements and subject to all other risks customary to an early-clinical stage biotechnology company developing novel drug candidates

*Prevalence: disease global prevalence estimates, individual references can be found at end of presentation

^ Market size is projected by multiplying patient prevalence per indication by the median orphan drug price of $150k p.a. EvaluatePharma. Orphan Drug Report. 2019.

The integration of the data generated to date sets a strong platform leading into PYC's human efficacy read-outs

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Pre-clinical

RP11 Patient-derived models

Safety and efficacy[1]

Non-human primate

Safety and high drug concentration in tissue[2]

Clinical

RP11 Patient

Safety[3]

RP11 Patient

Early efficacy[4]

RP11 Patient

Clinical proof of concept

PYC will generate human efficacy data across two concurrent clinical trials in its RP11 program in H2 2024[5]

1. See ASX announcement of 7 October 2020, 16 December 2020 and 6 May 2024
2. See ASX announcement of 10 May 2022 and 7 November 2022
3. See ASX announcement of 1 July 2024
4. See ASX announcement of 6 May 2024
5. Based on management's latest estimates accurate as at 4 July 2024 and subject to successful realisation of developmental milestones in each program as well as satisfaction of regulatory requirements and subject to all other risks customary to an early-clinical stage biotechnology company developing novel drug candidates

PYC is translating these outcomes into patients now

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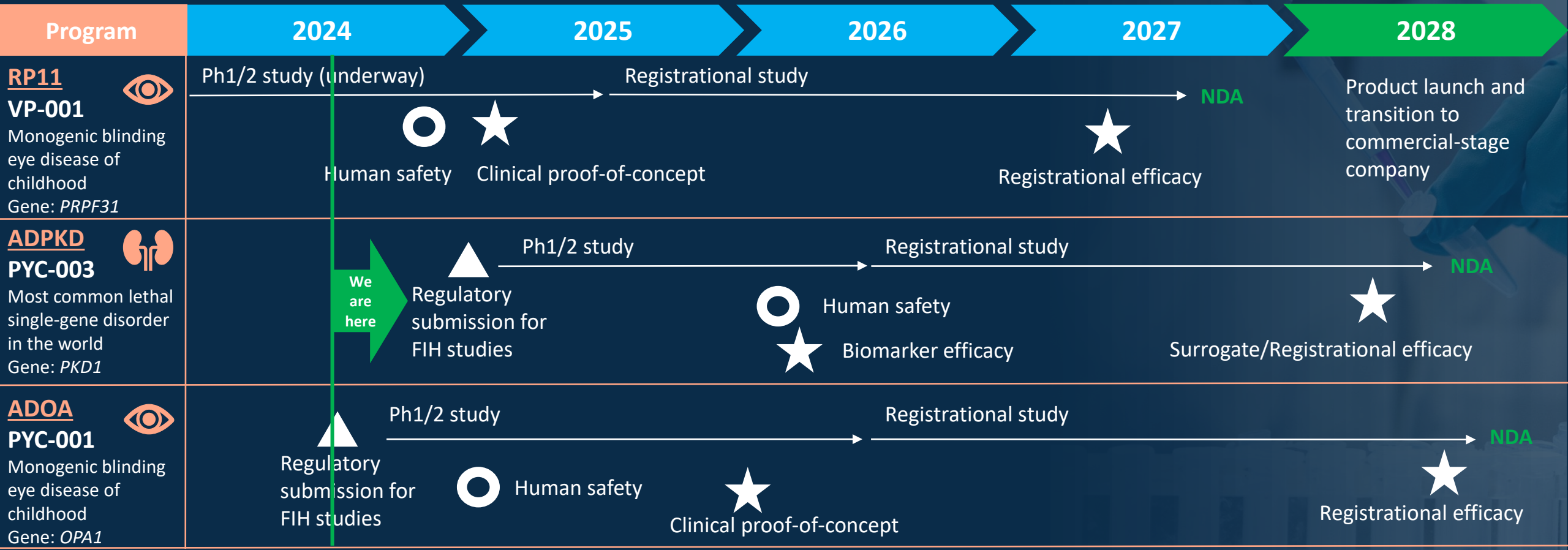
PYC's path to market is staged with human data read-outs for first-in-class drugs with disease-modifying potential[1]



1. Based on management forecasts as at 4 July 2024 and subject to the risks set out in the company's ASX disclosures of 14 March 2024

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References

Prevalence references

Program	References for prevalence estimate
Retinitis Pigmentosa type 11	• Daiger S, et al. 'Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa' Cold Spring Harb. Perspect. Med. 2014;5 • Ellingford J, et al. 'Molecular findings from 537 individuals with inherited retinal disease' J Med Genet. 2016;53, 761-776 • Sullivan L, et al. Genomic rearrangements of the PRPF31 gene account for 2.5% of autosomal dominant retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2006;47(10):4579-88 • Sullivan L, et al. Prevalence of Mutations in eyeGENE Probands with a diagnosis of autosomal dominant retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2013;54(9):6255-61 • Rose A, and Bhattacharya S. Variant haploinsufficiency and phenotypic non-penetrance in PRPF31-associated retinitis pigmentosa. Clin Genet, 2016;90: 118-126.
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Phelan-McDermid Syndrome	• Cochoy DM, et al. Phenotypic and functional analysis of SHANK3 stop mutations identified in individuals with ASD and/or ID. Mol. Autism. 2015;6(23) doi: 10.1186/s13229-015-0020-5 2. • Zeidan J, et al. Global prevalence of autism: A systematic review update. Autism Research. 2022;1–13. doi: 10.1002/aur.2696 3. • https://pmsf.org/about-pms/