PYC THERAPEUTICS

Investor Presentation

June 2020

PYC Therapeutics: Mission Statement

PYC is part of the ‘precision medicine revolution’ targeting rare diseases…

…with a differentiated technology…

…a lead program treating a rare disease in the eye (a >US$1Bn p.a. market)…

…and a pipeline of further programs

Corporate Overview

PYC Corporate Snapshot (ASX: PYC)

Financial Information (18 June 2020, AUD)

Share price	**$0.09**
Number of shares	2,930M
Market Capitalisation	**$264M**
Cash (31-May-20)	$26M
Debt (31-May-20)	Nil
Enterprise Value	**$238M**

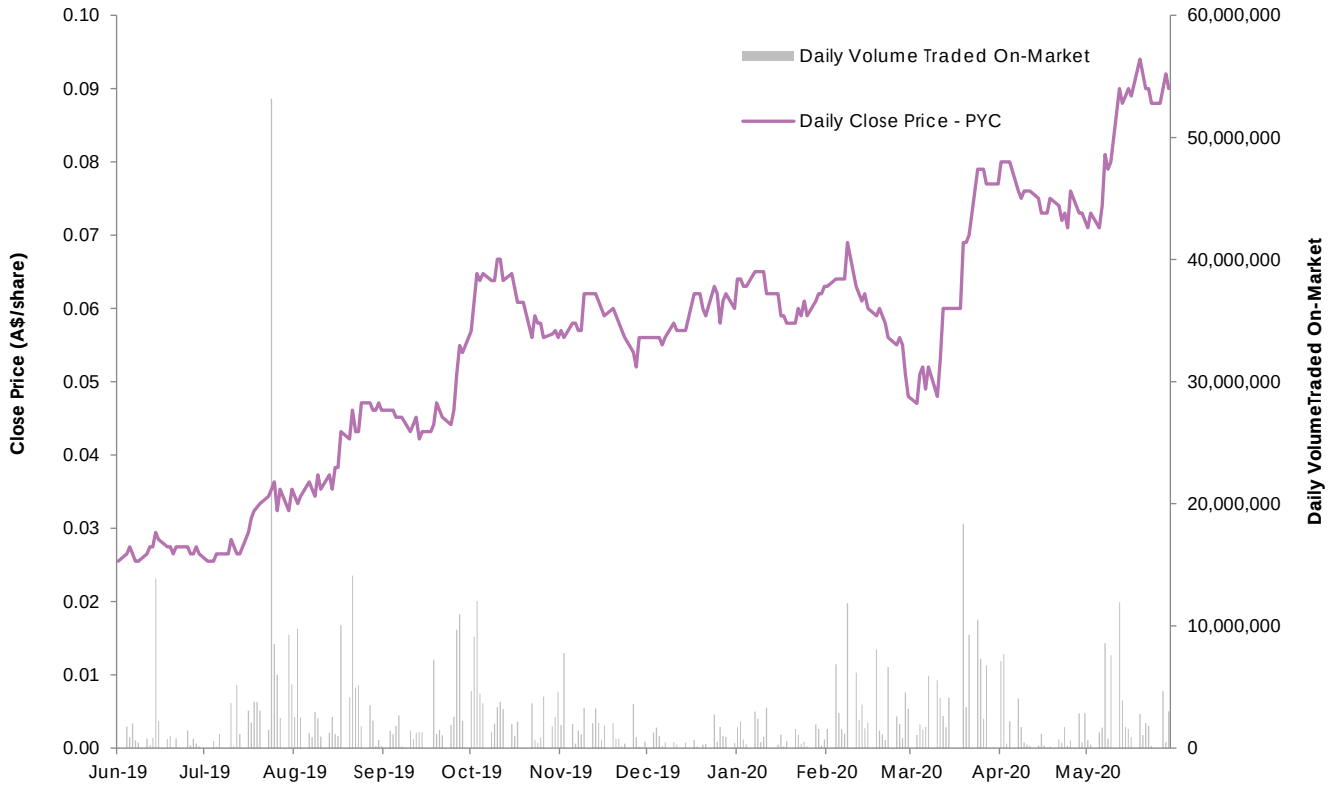
Board of Directors

- Alan Tribe – Chairman
- Doug Huey – Executive Director
- Dr Rohan Hockings – Executive Director
- Dr Bernard Hockings – Non-Executive Director

Top Shareholders (18 June 2020)

	%
Alan Tribe	30.1%
Sietsma Holdings	9.8%
Dr Bernard Hockings	9.0%
Anthony Barton	5.3%

Share Price Performance (12 months)



Source: IRESS

PYC has deep expertise in the management and advisory team

World-leading RNA, rare disease and clinical expertise + Commercial expertise to drive growth & value

Professor Sue Fletcher (PhD, BSc)

Chief of R&D (Perth)

Leading global expert in RNA therapeutics. Very well regarded for her role as co-inventor of Exondys-51 and Vyondys-53, both commercialised by Sarepta

Douglas Huey (MBA (Hons))

Executive Director & CEO (Boston)

Extensive experience across Strategy, Finance and Operations; previous partner at McKinsey & Co, where he led global multi-disciplinary teams.

Dr May Orfali (MD)

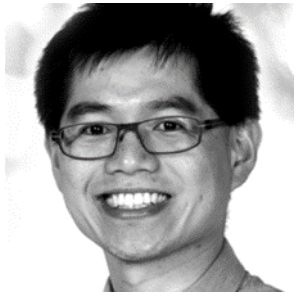
Chief Medical Officer (Boston)

20+ years experience in all aspects of clinical development, specialising in rare disease, including senior leadership roles within Pfizer's rare disease unit

Dr Rohan Hockings (MBBS (Hons), JD GDLP)

Executive Director & Chief Strategy Officer (Perth)

Experience across both clinical and commercial roles including Private Equity, Commercial Law, and Strategy, prior to joining PYC



Dr Fred Chen (MBBS (Hons), PhD, FRANZCO)

Ophthalmology Advisory Board (Perth)

Retinal clinician, co-inventor of VP-001 and leader of Ocular Tissue Engineering Laboratory at Lions Eye Institute

Kaggen Ausma (LLB, BEcons)

Chief Business Officer (Perth)

Previous roles in McKinsey & Co across Strategy, Commercial, VC and PE, and CLSA Asia-Pacific

PYC is dedicated to changing the lives of patients with rare genetic diseases – a unique opportunity in drug development

The need: Rare genetic diseases represent an urgent unmet patient need

- **~5,000** rare diseases with a genetic basis
- **> 95%** have no available treatment options
- **250 million** people affected worldwide
- **50%** of rare diseases affect children
- **30%** of these children will die before the age of 5 years

The opportunity: Developing drugs to address these needs has better odds of reaching patients

- **4 x** more likely to reach market from Phase 1 (45% likelihood for orphan non-oncology)
- **40%** reduction in clinical development timeline with opportunity to combine phases 2 and 3 and obtain accelerated approval
- **40%** lower cost of clinical evaluation with smaller patient numbers required
- **7 x** higher median pricing based on stronger reimbursement cases

Sources: www.thelancet.com/diabetes-endocrinology Vol 7 February 2019 Editorial 'Spotlight on rare diseases'; Paul SM, Mytelka DS, Dunwiddie CT, et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nat Rev Drug Discov. 2010;9(3):203-214. doi:10.1038/nrd3078; Hay et al., Nature Biotechnology, "Clinical Development Success Rates for Investigational Drugs", 2014; Jayasundara, K., Hollis, A., Krahn, M. et al. Estimating the clinical cost of drug development for orphan versus non-orphan drugs. Orphanet J Rare Dis 14, 12 (2019); EvaluatePharma Orphan Drug Report 2019

Our Approach & Progress to Date

PYC is part of the 'precision medicine revolution'

PYC THERAPEUTICS

RNA Therapeutics Examples

RNA-related small molecules

arrakis THERAPEUTICS

ribometrix

GOTHAM THERAPEUTICS

28

EXPANSION THERAPEUTICS

ACCENT THERAPEUTICS

SKYHAWK THERAPEUTICS

STORM THERAPEUTICS

Antisense Oligos

SAREPTA THERAPEUTICS

PYC THERAPEUTICS

IONIS

STOKE THERAPEUTICS

ProQR

siRNA

Alnylam PHARMACEUTICALS

Dicerna™

SILENCE THERAPEUTICS

AVIDITY BIOSCIENCES

mRNA

moderna

sylentis

RXi

BIONTECH

CUREVAC the RNA people®

DNA Therapeutics Examples

Gene Therapy

Spark THERAPEUTICS

nightstar THERAPEUTICS

bluebirdbio recode for life

SOLID BIOSCIENCES

CRISPR

editas MEDICINE

Intellia THERAPEUTICS

CRISPR THERAPEUTICS

What makes PYC different is the combination of our RNA drug design and intracellular drug delivery platforms

RNA drug design

PMO[1]

We design antisense oligos that can precisely treat genetic mutations…

- Precise control of protein expression
- No unwanted protein interactions
- Enhanced stability

Intracellular delivery

CPP

…and combine these drugs with our cell penetrating peptide technology…

- Enhanced delivery efficiency
- Enhanced toxicity performance

Therapeutic

CPP-PMO

…to create safe and effective therapies for genetic diseases

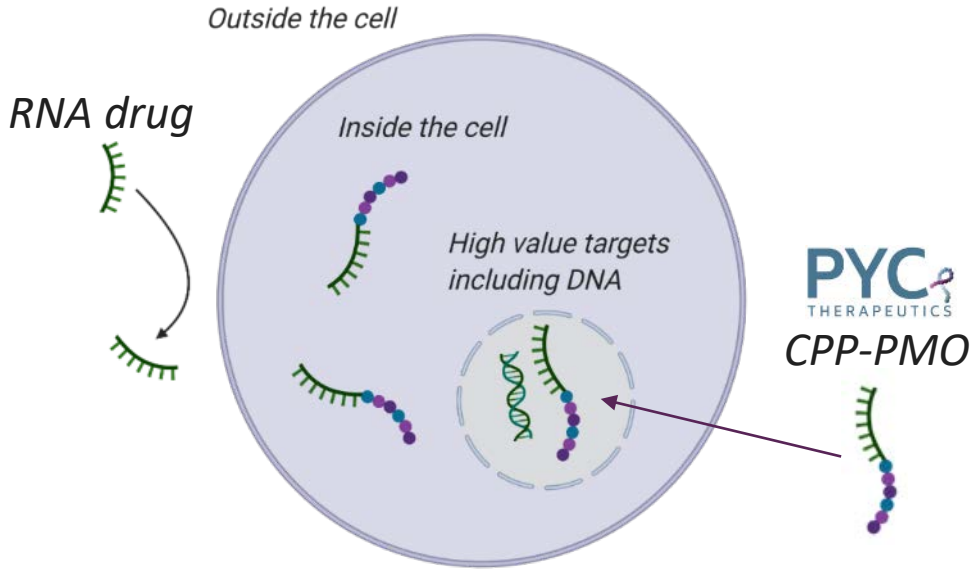
- Highly precise medicines that can be dosed at safe and effective levels

1 Phosphorodiamidate morpholino oligomers

PYC's drugs can access cells (and diseases) beyond the reach of competitive RNA technologies

The challenge for most RNA drugs

The cell membrane has evolved over hundreds of millions of years to keep foreign substances out

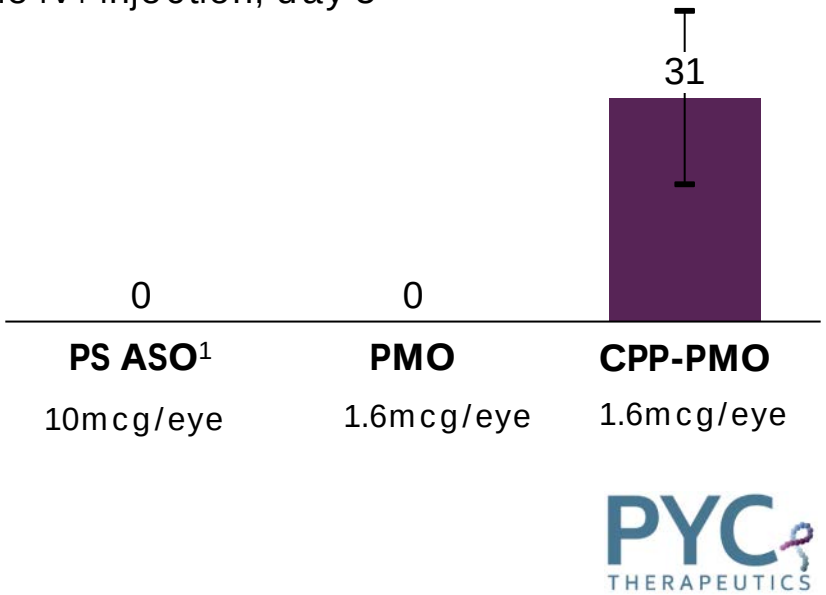


PYC's Cell Penetrating Peptides

PYC's proprietary Cell Penetrating Peptides (CPPs) can deliver drugs inside cells that are beyond the reach of competitive technologies

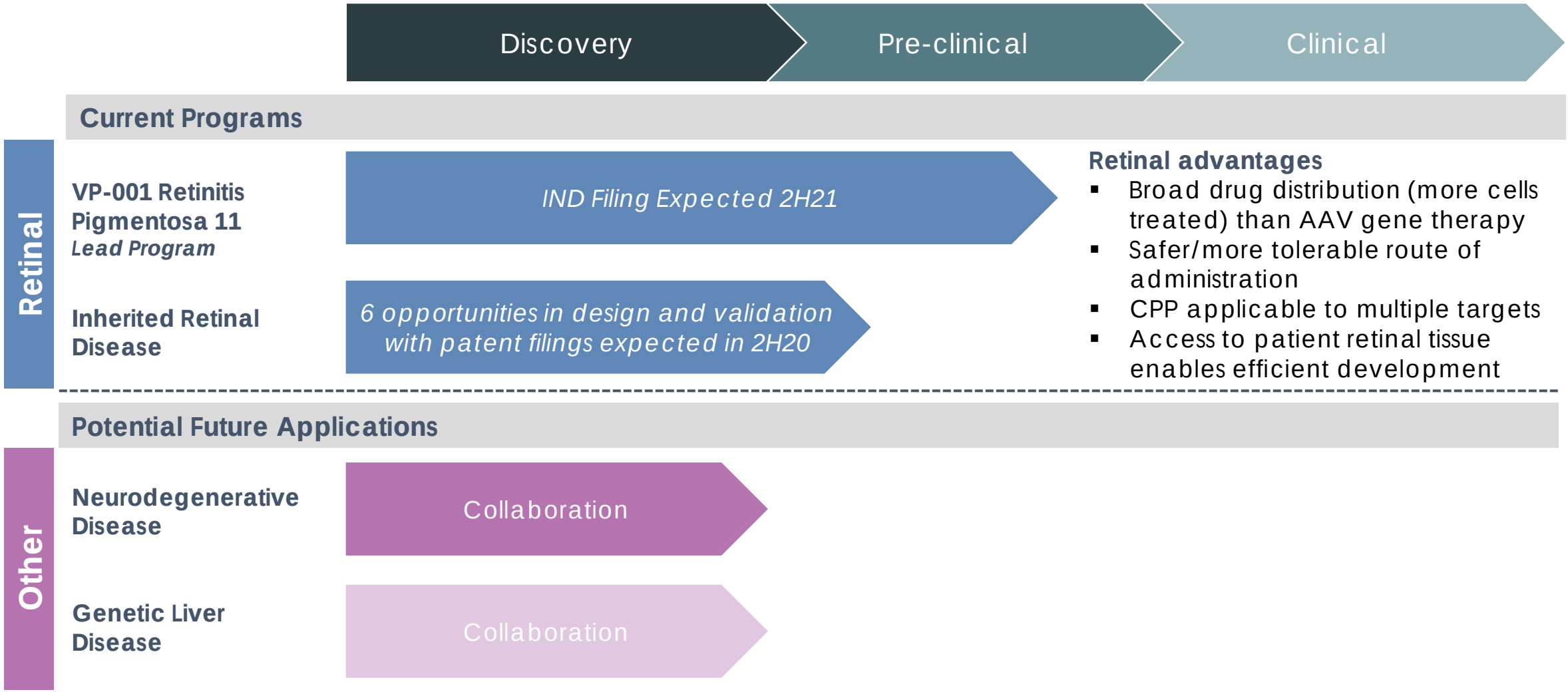
Exon skipping (%) in mouse Retinal Pigment Epithelium/Choroid

Single IVT injection, day 5



1 Phosphorothioate backbone antisense oligonucleotide

PYC is initially applying its CPP-PMO technology towards rare genetic eye diseases



Genetic eye diseases have a devastating impact on patients

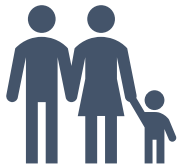
Losing eyesight can be frightening and overwhelming for patients, with major consequences on physical and mental health and overall quality of life

Genetic eye diseases like Retinitis Pigmentosa are progressive disorders

Patients begin to lose their vision typically as children, adolescents, and young adults

Many patients are legally blind by the age of 40

PYC's technology has several advantages over alternatives



Patient tolerability

PYC's drugs can be administered via intravitreal injection (a minimally invasive procedure), while other therapies often rely on sub-retinal injection (a highly invasive surgery) to reach their target cells

Control of gene expression

Retinal cells are more sensitive to gene over-expression, which increases the risks associated with AAV-gene therapy. Pan-retinal diseases like RP11 also require drug to be distributed throughout the retina which is beyond the reach of AAV-gene therapy

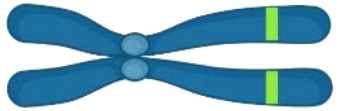
Accessibility to providers

RNA therapies administered via intravitreal injection are accessible to a broader set of Ophthalmologists and the reimbursement models are more attractive than DNA therapies

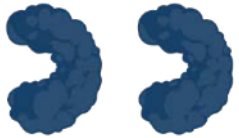
Our lead drug targets a down-regulator of the gene underlying Retinitis Pigmentosa Type 11 (RP11)

Healthy eye

We all have two copies of each gene in our chromosomes



Our body uses these genes to 'code' proteins in our cells



These proteins help our bodies function, including helping us to see

Eye with RP11

People with RP11 have only one healthy gene (and one mutated gene)

This leads to insufficient healthy protein being made by the cell (*haploinsufficiency*)

The lack of protein means the retinal cells in the eye don't function correctly and start to die – causing blindness

PYC's lead drug

Our drug knocks down a protein that down-regulates the RP11 target gene

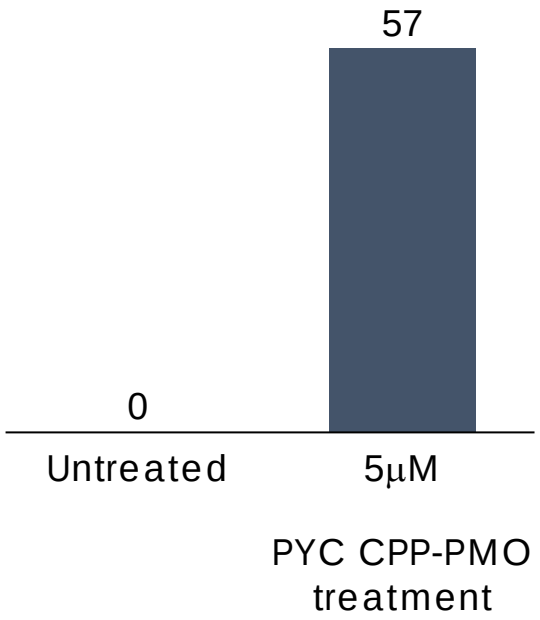
This increases the amount of protein from the healthy copy of the gene

The additional healthy protein restores the eye's ability to function properly and prevents further degeneration

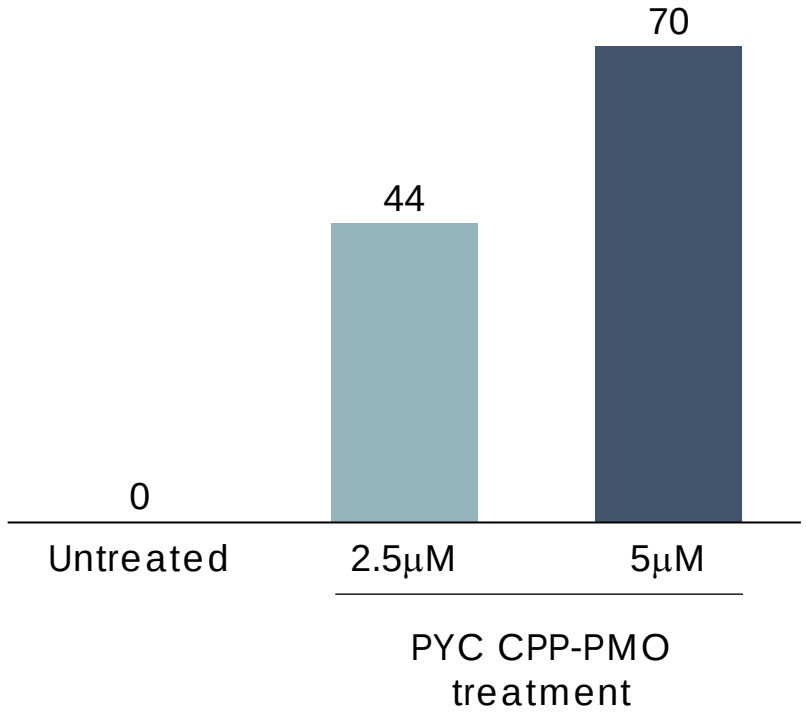
Proof of concept in multiple patient derived models

We have proven that our drug modulates target gene expression in multiple patient derived models...

Exon skipping, retinal organoid
Day 14, 2 treatments (n=2)



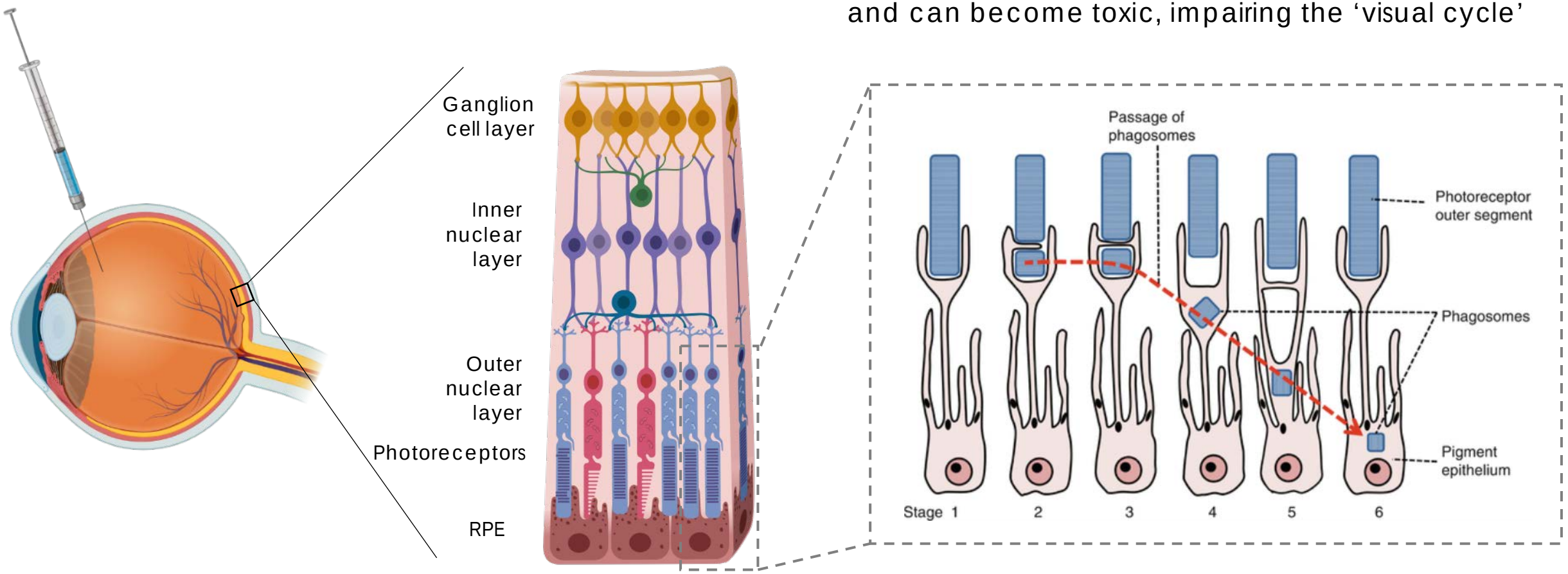
Exon skipping, Retinal Pigment Epithelial
Day 5, single treatment



Exon skipping in patient retinal organoid models (n=2 patients with RP11), with and without PYC's drug treatment. Organoids (4-6 organoids combined) were treated with 5μM of drug administered twice over a 14 day time period. Due to the successful delivery up to 71% of RNA molecules have been altered (skipped) by the PMO (n=1 sample per treatment)
Exon skipping in patient derived RPE model (n=1), with and without PYC's drug treatment. (n=2 per treatment)
See ASX Announcement 1 April 2020

RP11 patients experience lost functionality of Retinal Pigment Epithelial cells (RPE)

Structure of the Retina – target cells in the back of the eye (RPE)

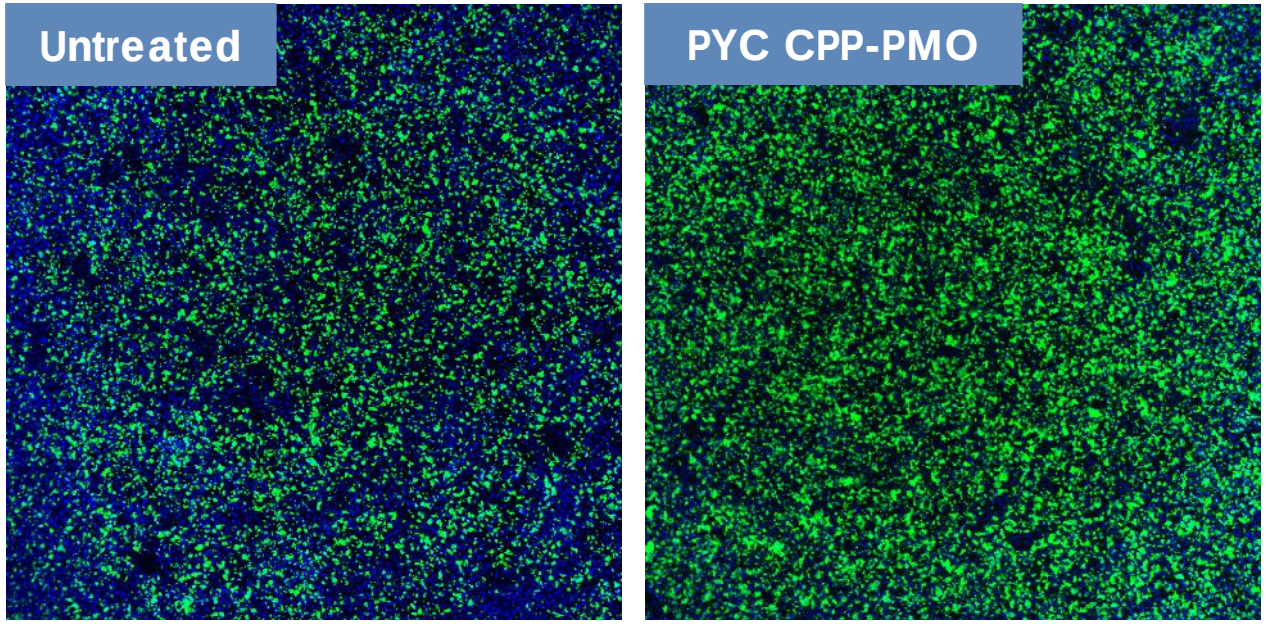


Phagocytosis – the 'self-repair' process where RPE cells 'clear away' debris from the photoreceptors. If outer segments are not phagocytosed, they build up and can become toxic, impairing the 'visual cycle'

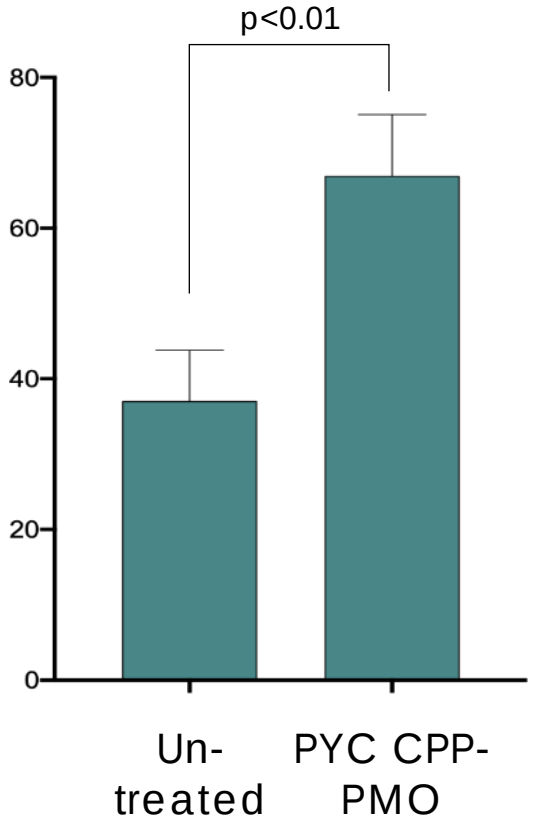
We have proven that our lead drug can restore RPE functionality in patient derived models

Phagocytosis assay, 5μM 6hr timepoint

A) Green 'specks' are Phagocytosed outer-segments (more green = improved functionality)



B) Intensity of phagocytosis per RPE cell



A) Phagocytosis in a patient with Retinitis Pigmentosa 11 with and without treatment with PYC's lead drug (more green = more phagocytosis). Photoreceptor outer segments have been labelled with a fluorescent green 'tag' and the ability of the RPE (nuclei stained in blue) to self- repair ('phagocytose') the green outer segments has been assessed. The cells treated with 5uM of PYC's drug demonstrate substantially greater ability to phagocytose the fluorescent green outer segments than the untreated cells. The Microscopic images taken 5 days post treatment at 10x magnification for both treated and untreated cells. These images are representative of a broader set of assays conducted across cells derived from multiple patients.

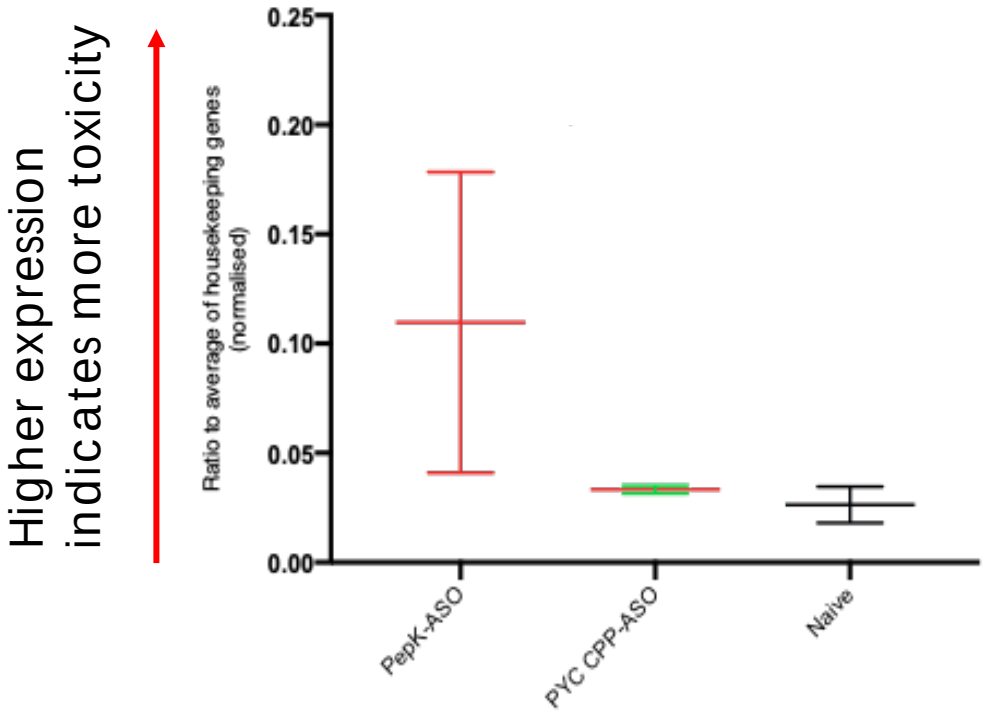
B) Comparison of the level of phagocytosis in RPE cells (signal intensity of green florescent 'tag' per cell actively phagocytosing) derived from a patient with RP11, with and without treatment with PYC's drug. Within 5 days, a single 5μM dose of drug (CPP-PMO, 2 samples) increased the phagocytosis ability of the diseased RPE cells by more than 1.5-fold (p=0.0083, two-tailed unpaired t-test) compared to untreated cells (4 samples).

See ASX Announcement 1 April 2020

PYC's lead drug is competitively differentiated in achieving this functional correction without causing toxicity in the retina

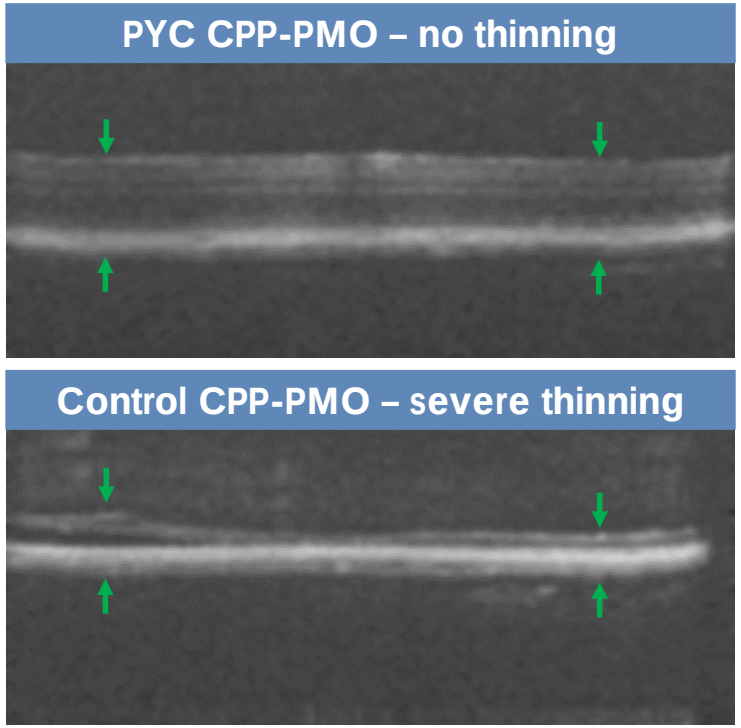
Retinal stress marker expression in mice

Day 5 post single 1.6μg IVT injection



Retinal thinning in mice

Day 21 post IVT injection OCT imaging



Toxicity determined by treating mouse retinas with 1.6 micrograms of an Antisense Oligonucleotide (ASO) delivered by each peptide and then measuring retinal stress based on levels of Glial Fibrillary Acidic Protein (GFAP). GFAP levels have been measured after retinal harvesting from mice at day 5 post intravitreal injection and normalised to a pool of 'house-keeping' genes. Notes i) PepK – a third-party delivery peptide that serves as the current benchmark for delivery peptides in clinical development (Red, n=6); ii) PYC's delivery peptide (Green, n=2); and iii) a control group which received no treatment (Black, n=3). One-way ANOVA p values – PepK:naïve 0.1379; PYC CPP:naïve 0.9892

See ASX Announcement 8 April 2020

Path to Market & Next Steps

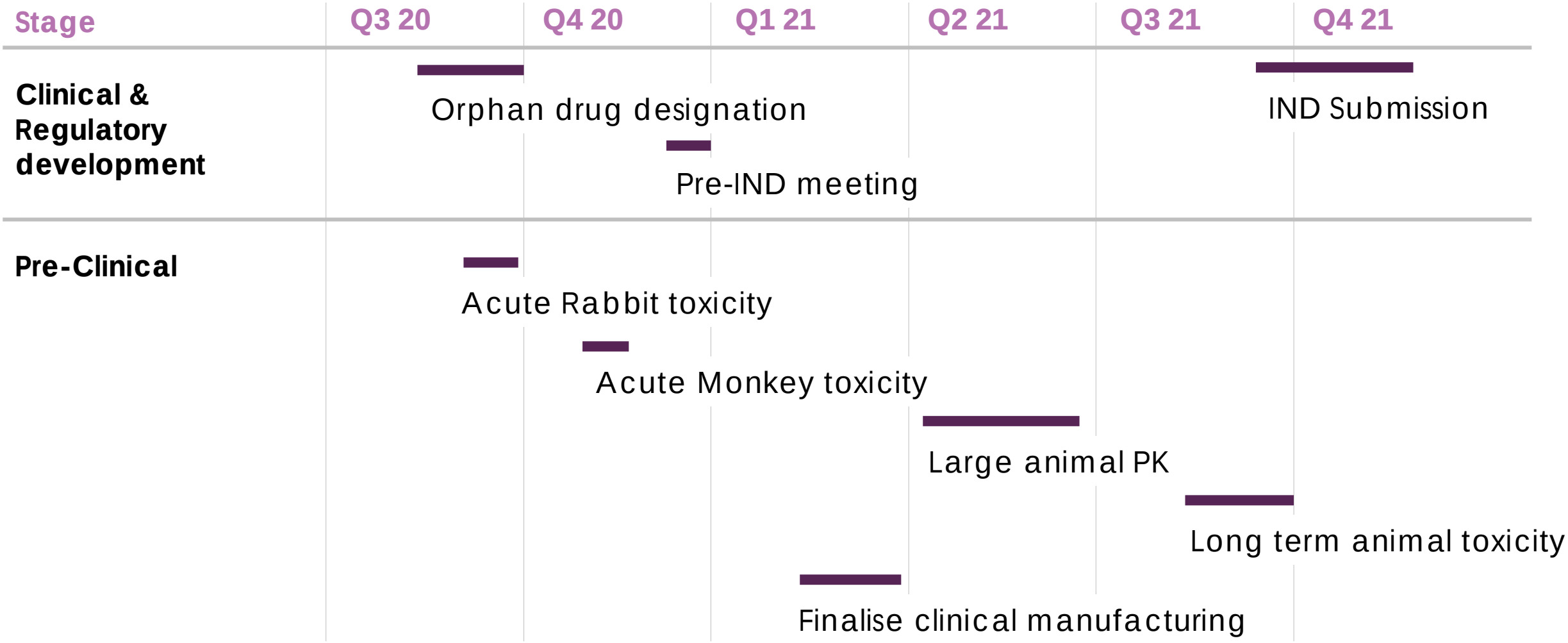
The path to market for our lead drug has several major advantages over conventional clinical development pathways

Stage	IND-enabling	Phase 1	Phase 2/3	Approval
Timeline	18 months	15 months	18 months	6 months

Advantage	Rationale
✓ **Higher probability of success**	• Precision medicines have a much higher probability of success than traditional drugs (45% ph1 to market) • Validation of VP-001 in patient-derived cell models
✓ **Shorter time to market**	• Only a single pivotal trial will likely be required • Faster turnaround of regulatory decisions for high unmet need. FDA regulatory pathways for rare drugs include: Orphan drug designation, Fast track designation, Accelerated approval, Priority review, Priority review ticket
✓ **Lower cost and reduced COVID exposure**	• Smaller patient numbers in clinical trials • Low impact of COVID in Australia (phase 1 location) • 43% reduction in cost through Australian R&D tax rebate

All numbers and timelines are estimates and are applicable to change and revision

Upcoming development milestones for VP-001



Addressable Market for our Lead Drug

Retinitis Pigmentosa (RP) prevalence proportion of people in the population with RP	1 in 2,500-4,000[1]
Proportion of RP that is autosomal dominant (adRP) Inherited in a dominant pattern	30-40%[1]
Proportion of adRP that is RP11 Patients is a disease causing mutation in PRPF31	8-10%[1]
Reimbursable RP11 patients Number of patients in the US, EU, and Japan	4,000-8,000 patients
Median Rare Disease drug price Annual reimbursed cost for a rare disease drug	US$250,000 p.a.[2]
Total addressable market Margins assumed at 90% due to low COGs[3]	**US$1-2bn p.a.**

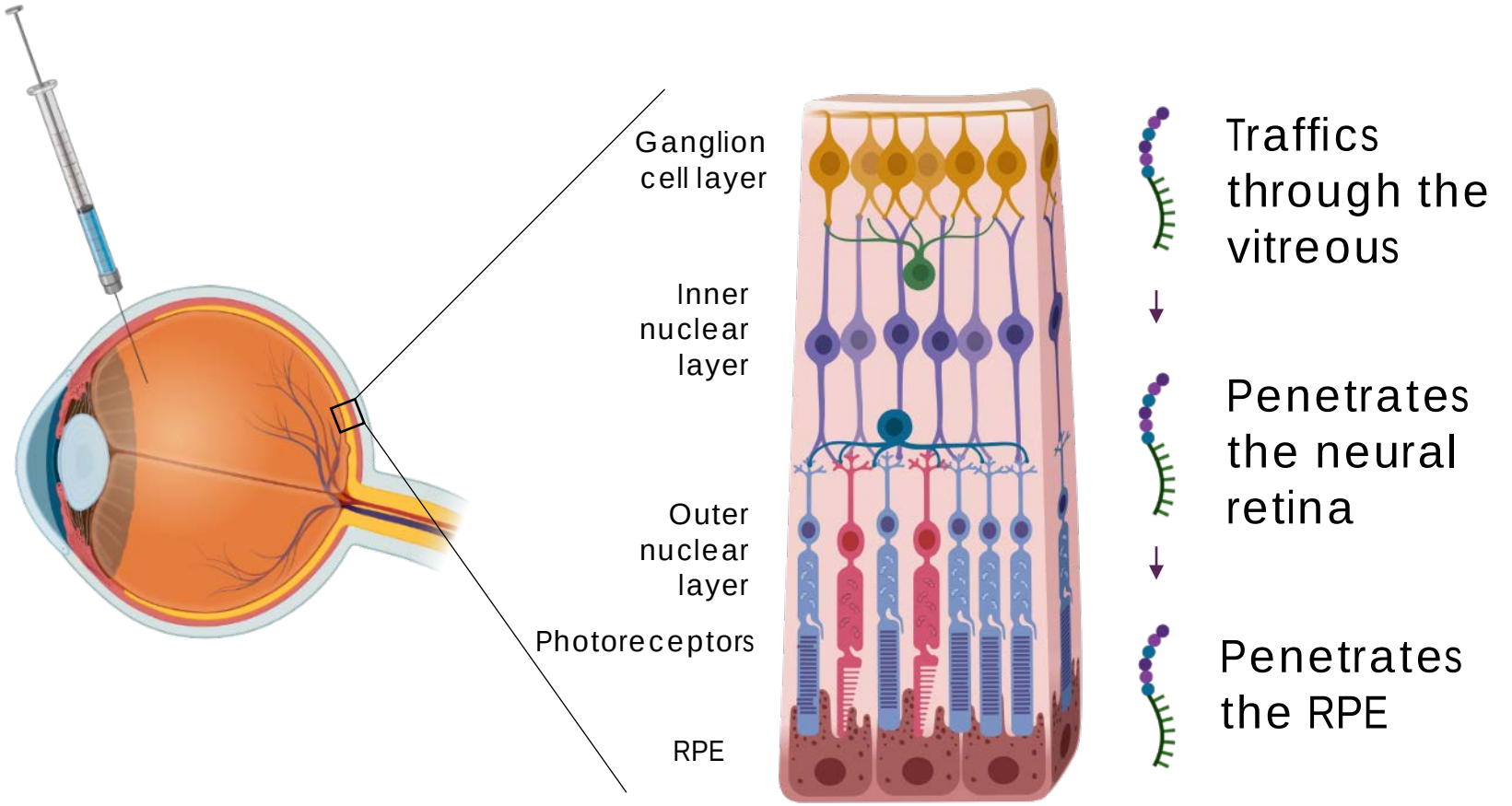
No competitors in market or in clinical development

1 Daiger et al. 'Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa' Cold Spring Harb. Perspect. Med. 5 (2014); Ellingford et al. 'Molecular findings from 537 individuals with inherited retinal disease' J Med Genet 53, 761-776 (2016);
2 Based on Luxturna pricing over 4 years (450k USD per eye). Luxturna is a gene therapy for treatment of a rare inherited retinal disease, approved in 2017, marketed by Spark Therapeutics.
3 Sarepta Therapeutics' marketed Exondys 51 for a DMD subpopulation has margins which exceed 90% for a systemically delivered drug (much more product per dose)

Other Applications for PYC's Drug Delivery Technology

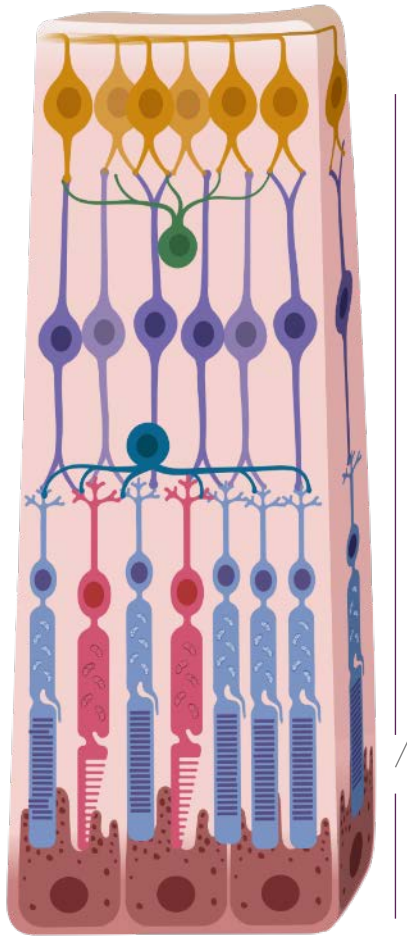
PYC's delivery technology

- ✓ **Penetration** – reaches the deepest layer of cells within the retina – the RPE
- ✓ **Distribution** – achieves a broad distribution throughout the entire retina – a major competitive advantage over gene therapy
- ✓ **Validation** – demonstrated safety and efficacy across: 1) human primary cells, 2) 3D organoid models of the eye, and 3) animal models



Advancing our lead program into the clinic will validate our drug delivery platform for retinal disease

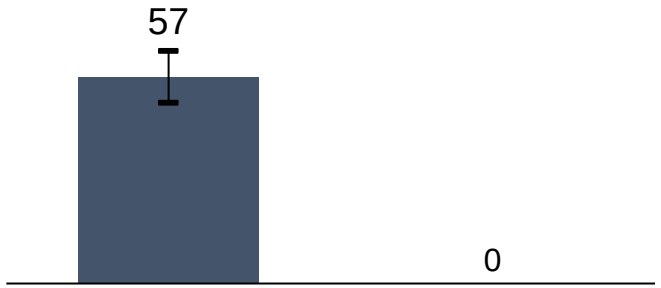
The Retina is a high value target

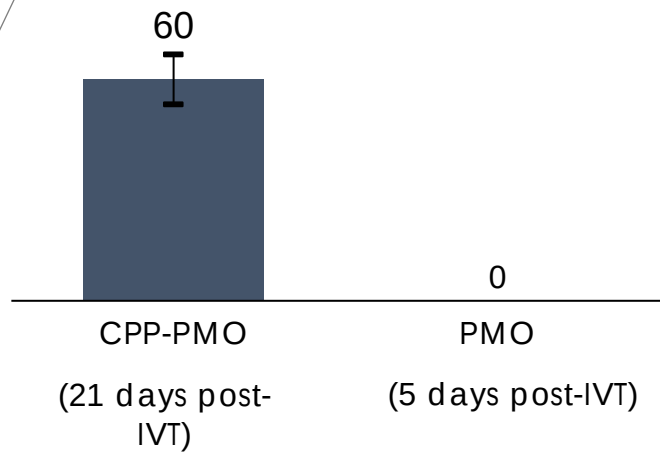


Proven Delivery in the Eye

1.6ug IVT injection in mice

% truncated SMN1 transcript





Develop Further Applications

Diseases primarily affecting the Photoreceptors

- Usher Syndrome
- Rhodopsin RP (most prevalent adRP in the US)
- >10 commercially viable Inherited Retinal Diseases

Diseases primarily affecting the RPE

- Wet age-related macular degeneration (wAMD)
- Dry age-related macular degeneration (dAMD)
- Diabetic retinopathy
- >5 commercial Inherited Retinal Diseases

Upcoming milestones

Progressing Our Lead Drug (VP-001 for Retinitis Pigmentosa 11)

- Acute animal toxicity data – 2H 2020
- Orphan drug designation for VP-001 for RP11 – 2H 2020
- Clinical manufacturing studies – 1H 2021
- Large animal PK data – 1H 2021
- Large animal long term toxicity data – 2H 2021
- Commencing human trials – 2H 2021

Bolstering Our Retinal Application Pipeline

- Filing of provisional patents for Retinal targets 2 & 3 – 2H 2020

Accelerating Growth of PYC

- Expansion of management team – mid-2020
- Scaling up our US-based presence – mid-2020
- Identify potential CNS delivery molecule – 1H 2021

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