PYC THERAPEUTICS

Successful Efficacy and Toxicity Results

Context

PYC recently announced a series of successful results for its lead drug program and RNA therapeutics platform:

- Successful Efficacy Result on Path to First in Human Studies (see ASX Announcement 1 April 2020)
- Successful Toxicity Results Confirm Safety Advantage (see ASX Announcement 8 April 2020)

This presentation contains detailed information related to the above recent announcements

PYC's successful efficacy readouts - Three primary messages

Patient impact

Our target market has thousands of patients burdened by a high unmet need with no other drugs in clinical development, estimated to be worth >USD 1 billion

Financial case

We have enough capital to fund our lead program to market, with a >50% probability of drug approval once we reach clinical trials

Scientific validation

Our drug has successfully treated its target disease in multiple models using cells derived from multiple patients

Patient impact: PYC's lead program targets a market with a significant unmet need

Prevalence

4,000-8,000 patients in the Western World with no available treatment

- Retinitis Pigmentosa affects 1 in 2,500 to 4,000 people
- 1.5-3% of Retinitis Pigmentosa is RP11

Impact/ Pricing

150-250k USD p.a.
8-10 years market exclusivity

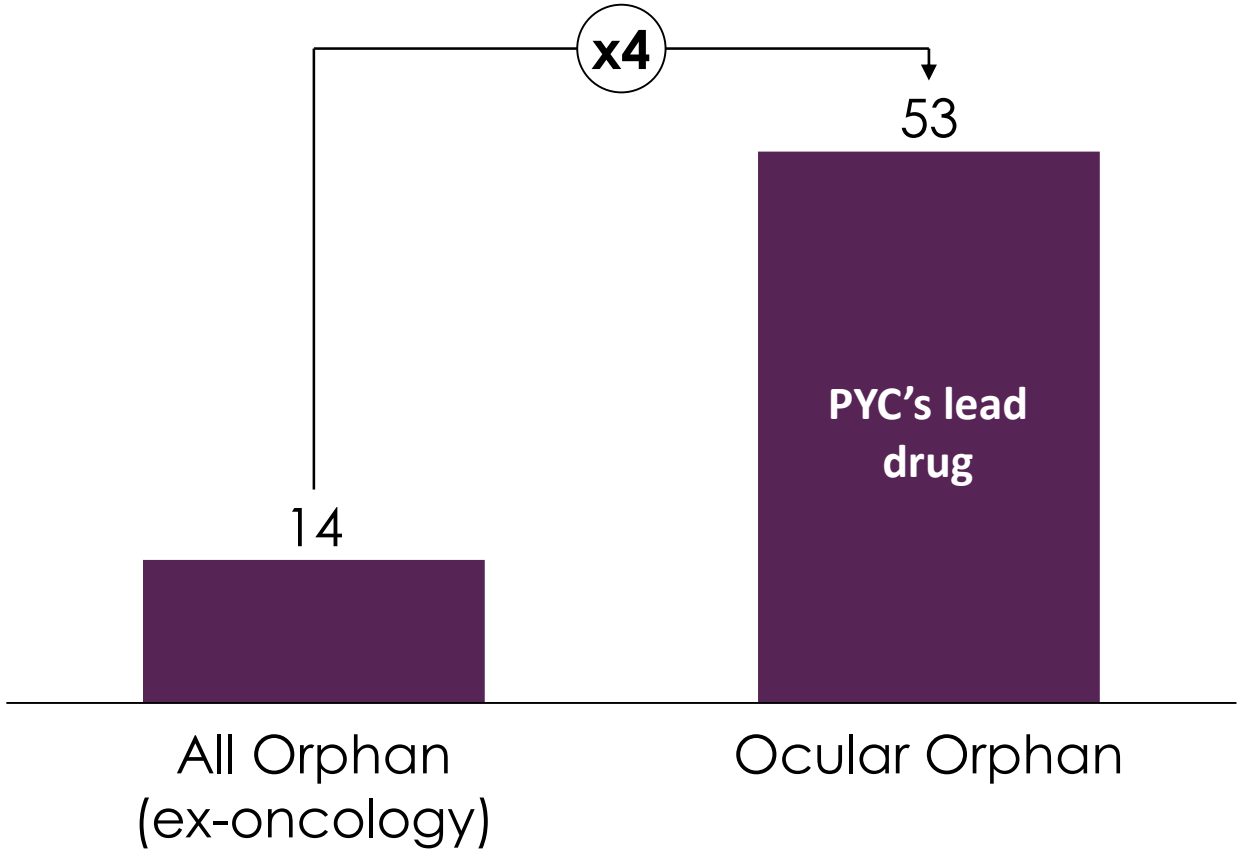
- Average orphan drug pricing of ~150k USD in US
- Luxturna for LCA-RPE65 (type of RP) priced at 450k USD per eye

Source: 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); EvaluatePharma 'Orphan drug Report 2019' (2019)

Financial case: The probability of reaching a market outcome is relatively high

RP11 represents a $1-2B market

Probability of success, Phase 1 to market, %



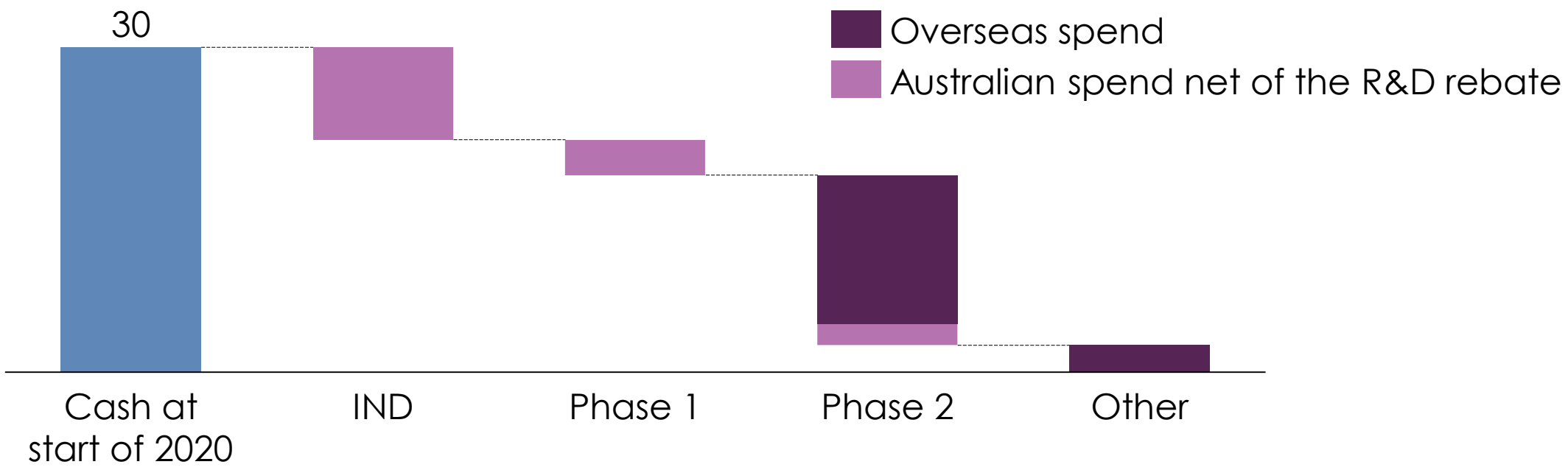
Source: Wong et al. 'Estimation of clinical trial success rates and related parameters', *Biostatistics*, 20 (2), 273-286 (2019)

Financial case: PYC has the ability to fund its lead program to market

NOTE: DOES NOT REPRESENT A COMMITMENT ON BEHALF OF PYC

Timeline,
Months

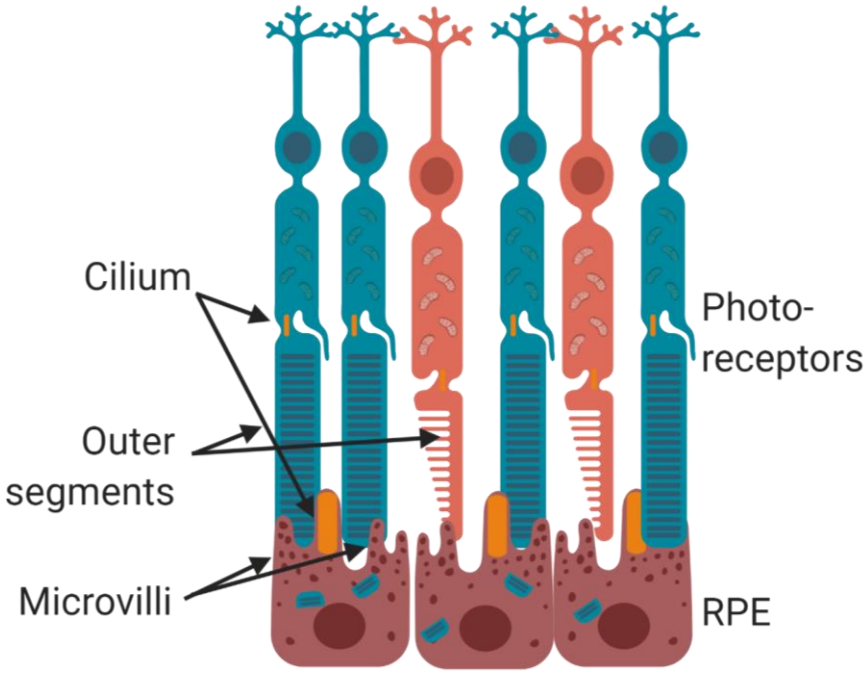
Potential cash disposition scenario,
AUD M



Source: Sertkaya et al., 'Key cost drivers of pharmaceutical clinical trials in the United States' *Clinical Trials* 13 (2016); Paul et al., 'How to improve R&D productivity: the pharmaceutical industry's grand challenge' Nat Rev Drug Disc, (2010)
Assumes Australia's R&D rebate remains unchanged

Scientific validation: PYC's drug has restored function in RP11-diseased cells across the two major assays

Structure of the Retina

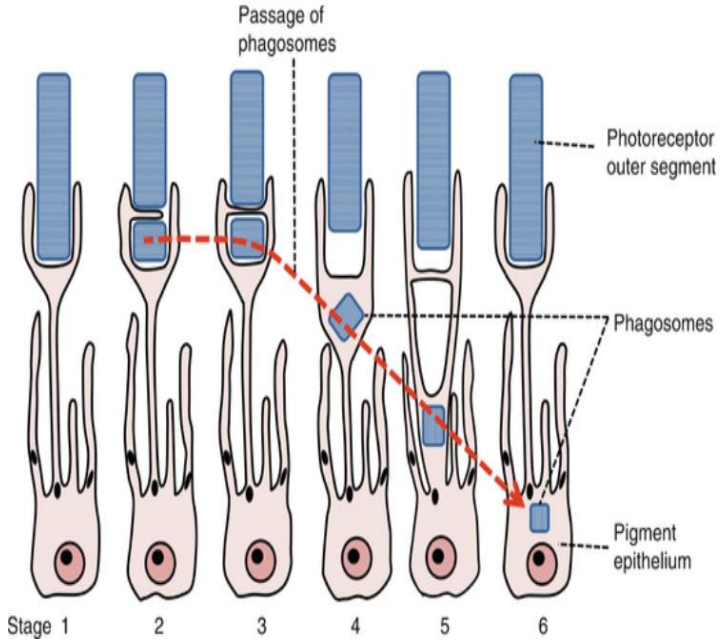


Impact of RP11

	Healthy	RP11	Impact of RP11	Restoration with PYC Drug
Cilia length			▪ Shorter 'stunted' connecting cilium in the photoreceptors	TBD
Phagocytosis			▪ Lower 'phagocytosis' of outer segments (lower ability of the RPE to dispose of the toxin)	✓
Cilia length			▪ Shorter and less frequent cilium on the RPE, showing poor RPE health	✓
Transepithelial resistance			▪ RPE cells are not tightly joined and become 'leaky', causing retinal degeneration	TBD
Microvilli health			▪ Short, less functional microvilli, which are the 'arms' that collect the outer segments during phagocytosis	TBD
Polarity			▪ RPE loses polarity – or simply the cell becomes 'disordered'	TBD

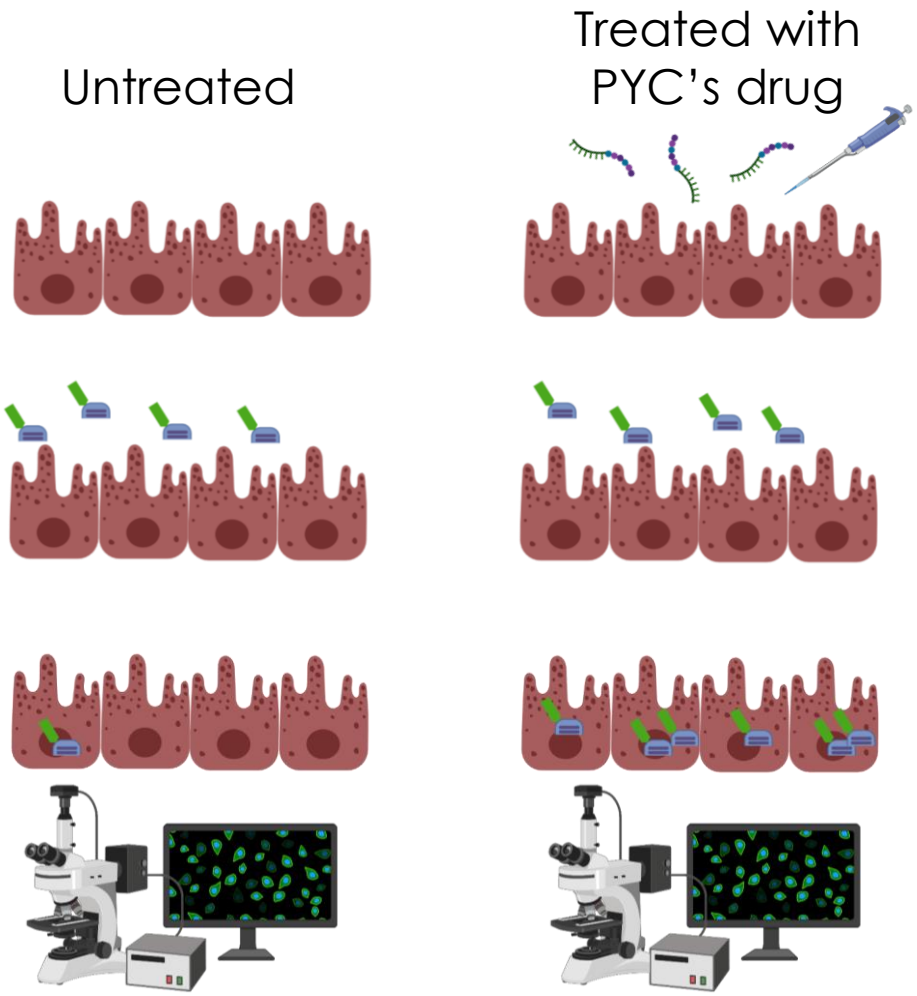
Scientific validation: What is phagocytosis, why does it matter, and how do we measure it?

What is phagocytosis and why does it matter?



If outer segments are not phagocytosed, they build up and can become toxic, impairing the 'visual cycle' (the chemical process that allows us to see)

How do we measure if PYC's drug improves phagocytosis?



Treatment group treated with PYC's drug (CPP-ASO)

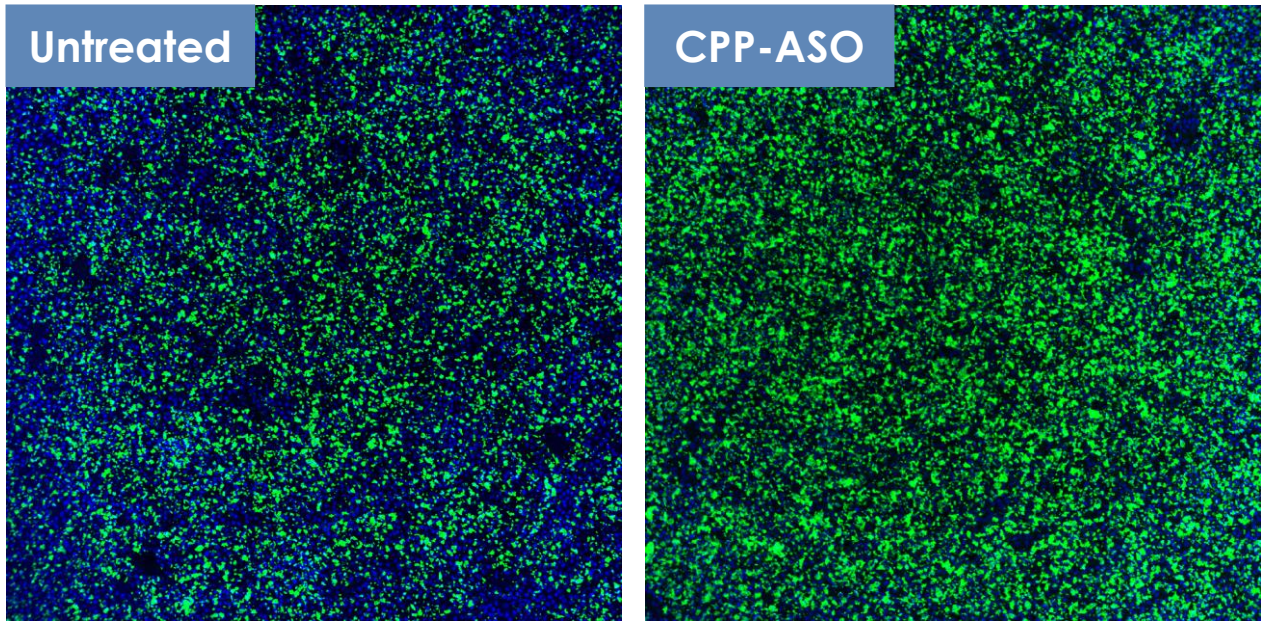
Fluorescently labelled outer segments (OS) added to both groups

Internalised fluorescent OS counted under microscope
More green = more phagocytosis

Scientific validation: PYC's drug has shown it can increase phagocytosis in RP11-diseased cells

Fig 1. Phagocytosis assay, 5μM 6hr timepoint

A)



NOTE: Green 'specks' are Phagocytosed outer-segments, with increased frequency of green indicating increased phagocytosis

B)

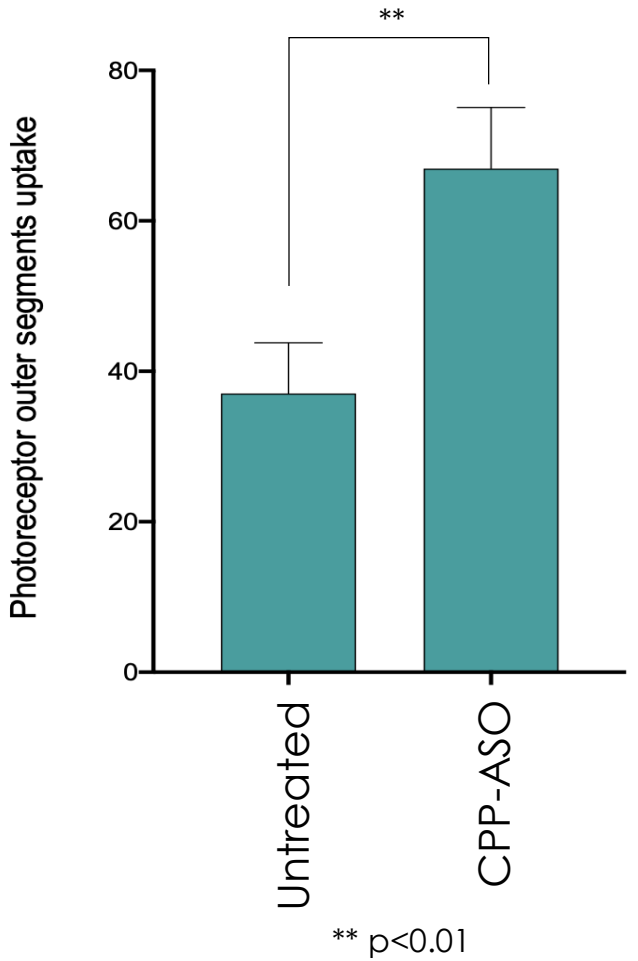
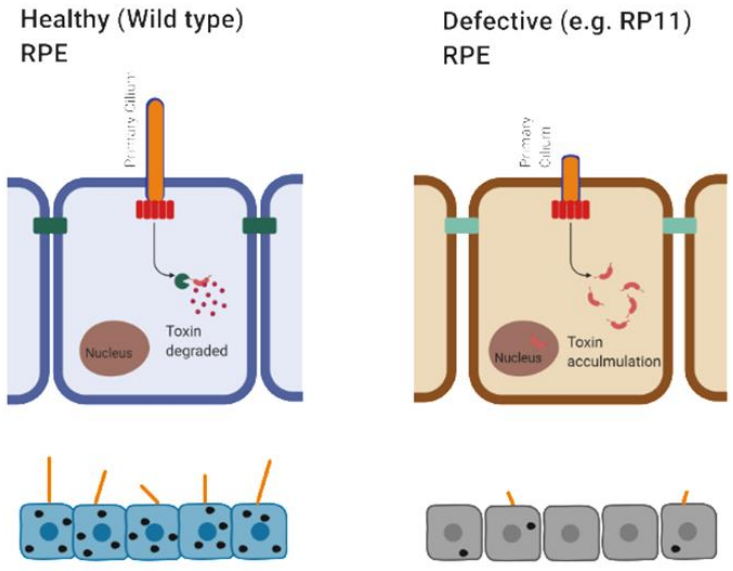


Fig 1. A) Phagocytosis in a patient with Retinitis Pigmentosa 11 with and without treatment with PYC's lead drug (more green = more phagocytosis). Photoreceptor outer segments have been labelled with a fluorescent green 'tag' and the ability of the RPE (nuclei stained in blue) to self- repair ('phagocytose') 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 5□M dose of drug (CPP-ASO, 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

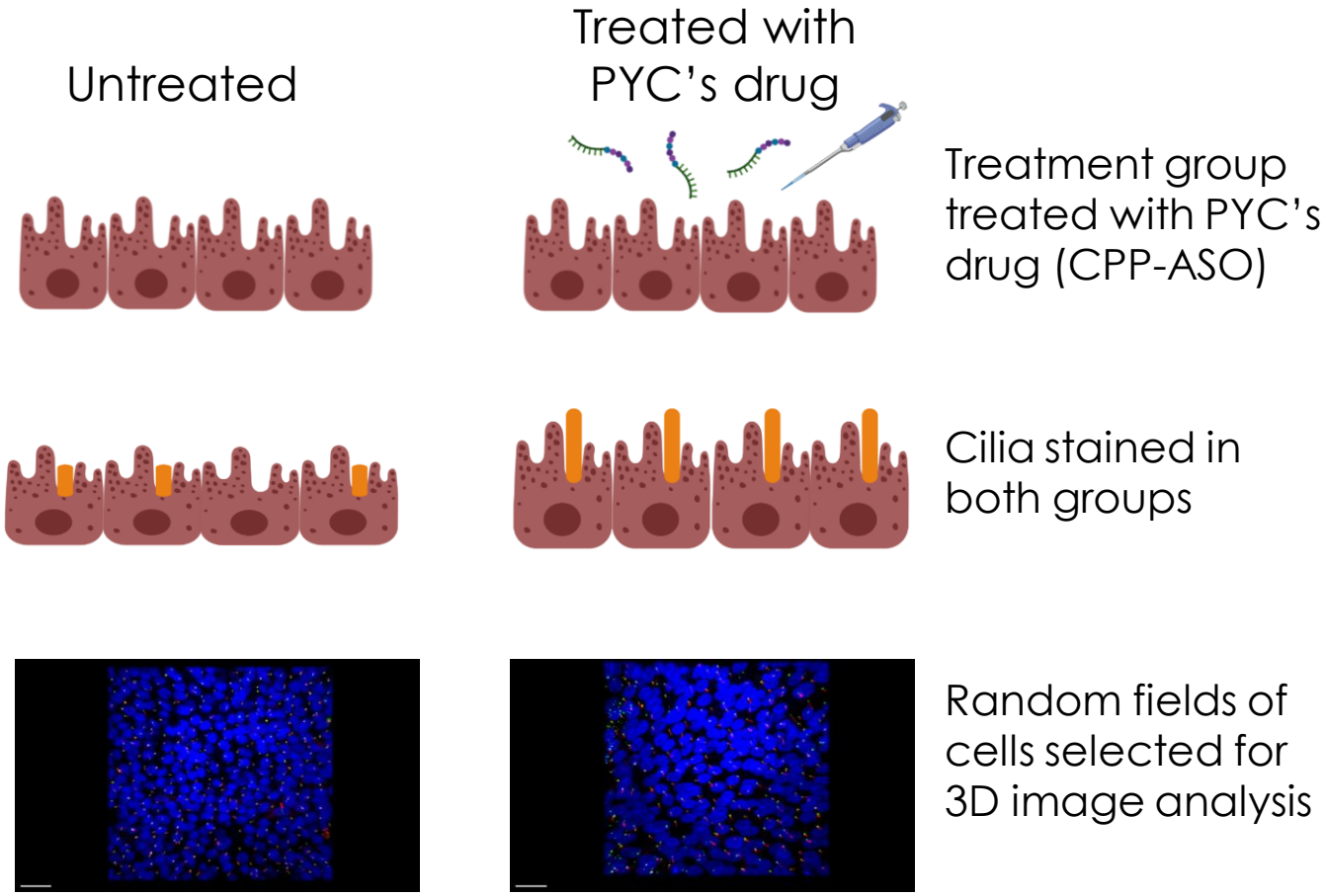
Scientific validation: What is cilia length, why does it matter, and how do we measure it?

What is cilia length and why does it matter?



Shortened cilia are indicative of poor cellular health and are likely to be related to the reduced functionality of cells in patients with RP11

How do we measure if PYC's drug improves cilia length?



Scientific validation: PYC's drug has shown it can increase cilia length in RP11-diseased cells (RPE)

Fig 2. Cilia frequency and length assay, 5μM at 5 days Penetrant patient

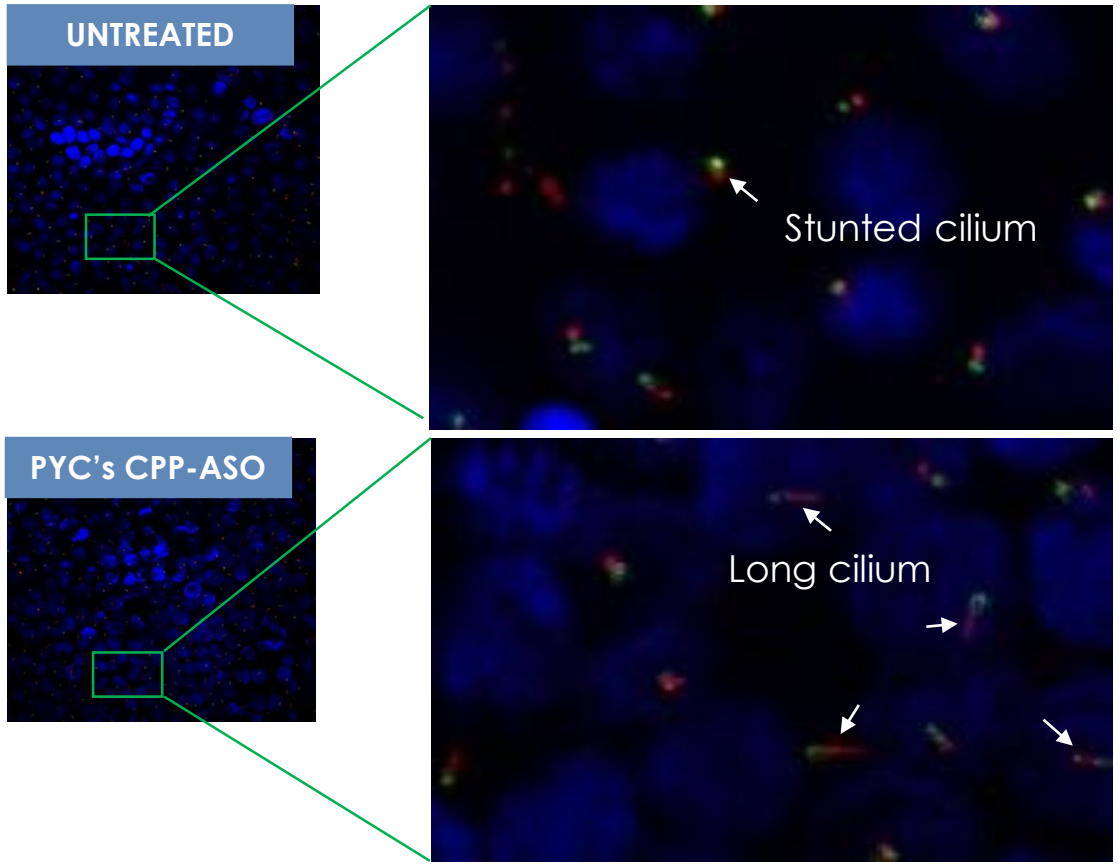
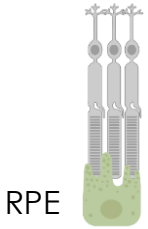
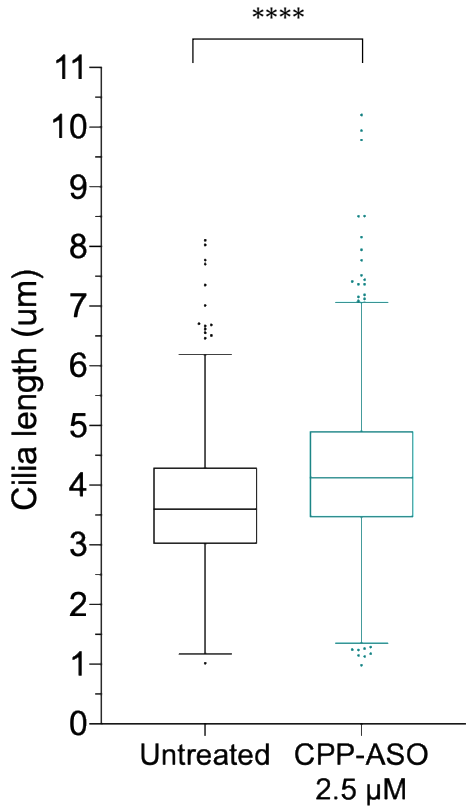


Fig 3. Cilia frequency and length assay, 2.5μM at 5 days, Non-penetrant patient





**** p<0.0001

Fig 2. RPE cilia length in cells derived from an individual with a RP11 mutation, with and without PYC's drug treatment 5 days after a single 5μM drug treatment. The magnified images below represent a higher resolution on the section of the upper image represented in the white box. In the magnified images, the basal bodies of the cells (seen in red in Figure 4) have been stained in green and the cilia have been stained in red. Arrows in the treatment group illustrate the increase in the cilia length observed when compared to the untreated group.
Fig 3. RPE cilia length in cells from an individual with a RP11 mutation, with and without PYC's drug treatment 5 days after a single 2.5μM drug treatment. Treatment with PYC's significant increase in cilia length which is indicative for a improvement of functionality (p<0.0001, two-tailed unpaired t-test). The length (in mycrometers) of at least 1000 cilia has been measured across five image fields per sample.

See ASX Announcement 1 April 2020

Scientific Validation: PYC's drug successfully reaches and performs its intended function on its target gene

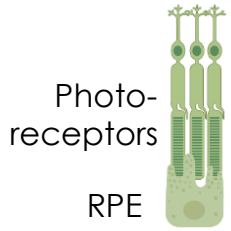


Fig 4. Exon skipping, retinal organoid
Day 14, 2 treatments

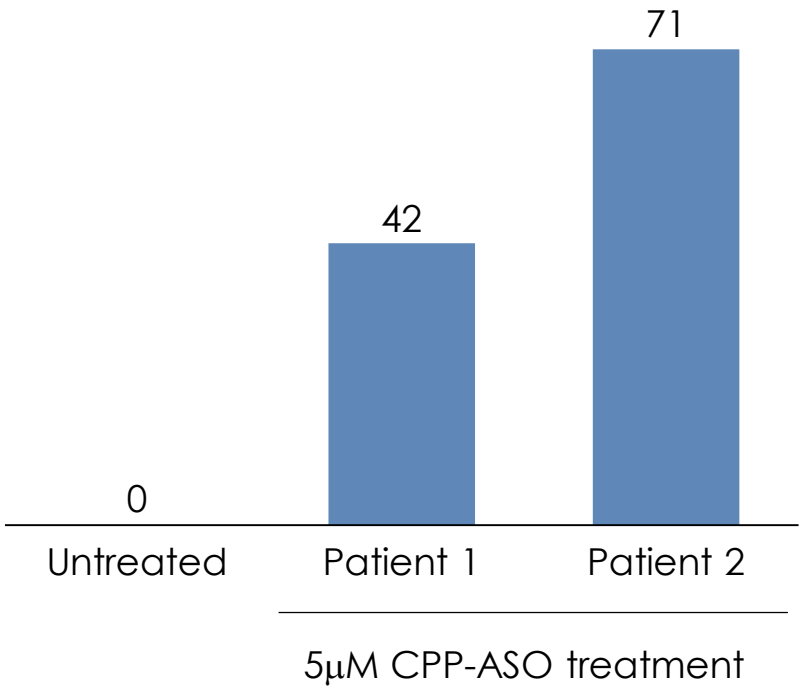


Fig 5. Exon skipping, RPE
Day 5, single treatment

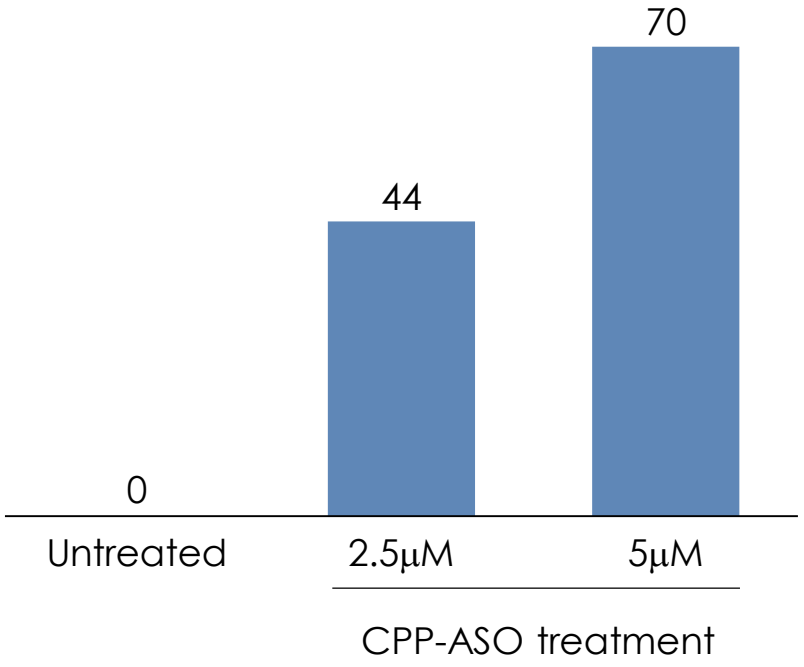
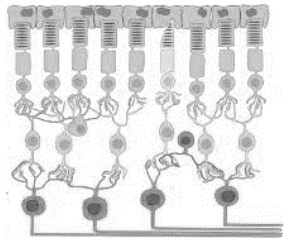
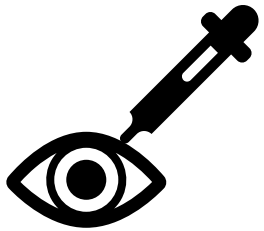


Fig 4. Exon skipping in patient 'retina in a dish' models (n=2 patients with RP11), with and without PYC's drug treatment. Organoids (4-6 organoids combined) were treated with 5μM of drug administered twice over a 14 day time period. Due to the successful delivery up to 71% of RNA molecules have been altered (skipped) by the ASO (n=1 sample per treatment)
Fig 5. 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

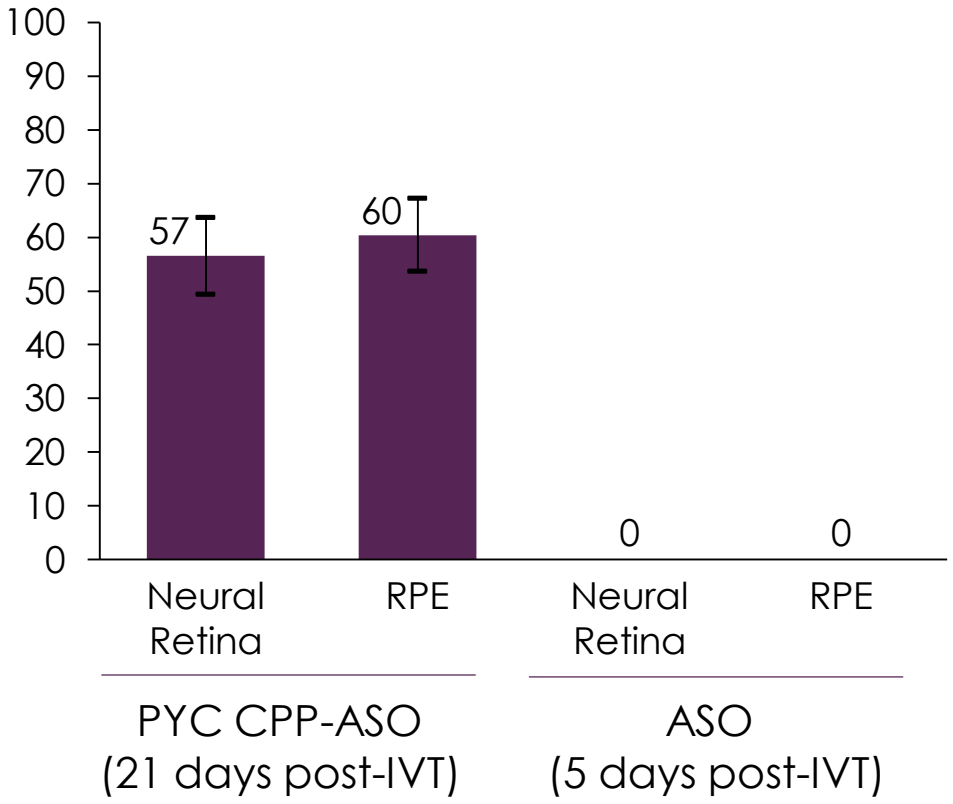
Successful efficacy results in context of *in vivo* results to date

	Captured in previous pages		Captured in following pages		
Milestone	**Human cells**	**3D 'retina in a dish' models**	**Animal models**	**Humans**	**Patient impact and Revenue**
					
PYC's lead drug program…	Has **reversed the target disease** in human cells	Has proven to be **highly effective in 3D models of human retinas** (made from human stem cells)	Is **effective in animals** and has a **safety advantage**	Will prove effective in **clinical trials**?	Will create the **first treatment** for children with a form of Retinitis Pigmentosa and **capture a $1bn p.a. market**?
Outcome	✓	✓	✓	?	?

PYC's drug shows functional and durable effects in animals

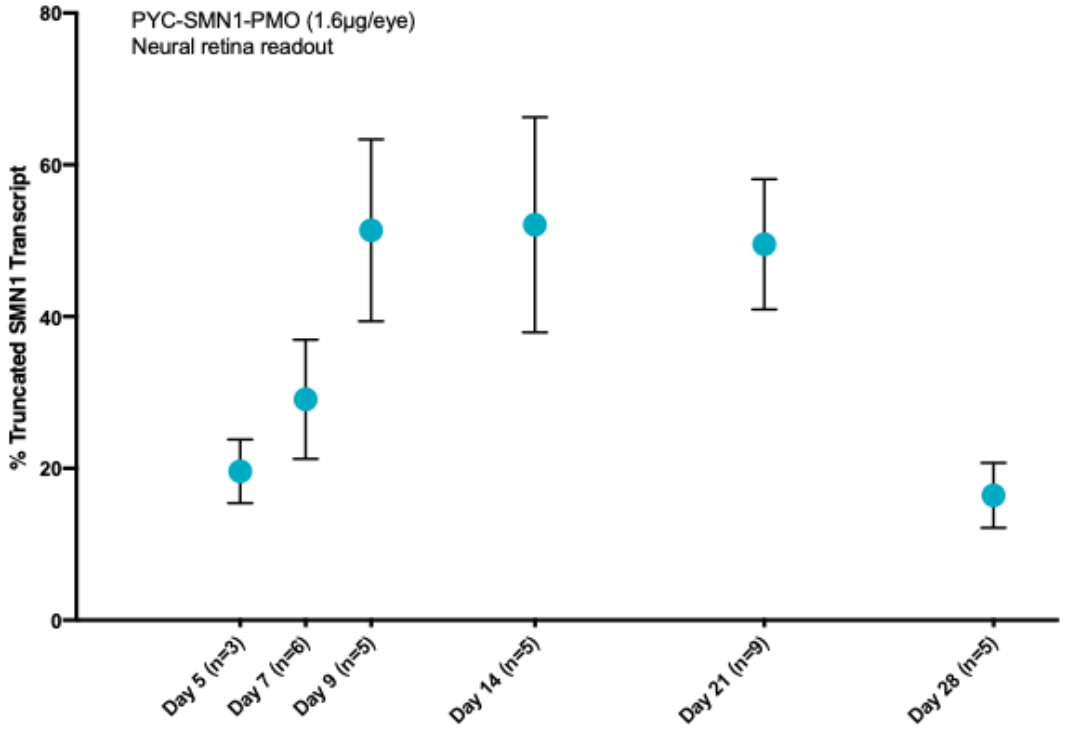
Efficient and functional ASO delivery to target retinal cells *in vivo*

Fig 6a. Exon skipping in mice retinas
1.6µg IVT injection



Durable Effect reduced dosing frequency

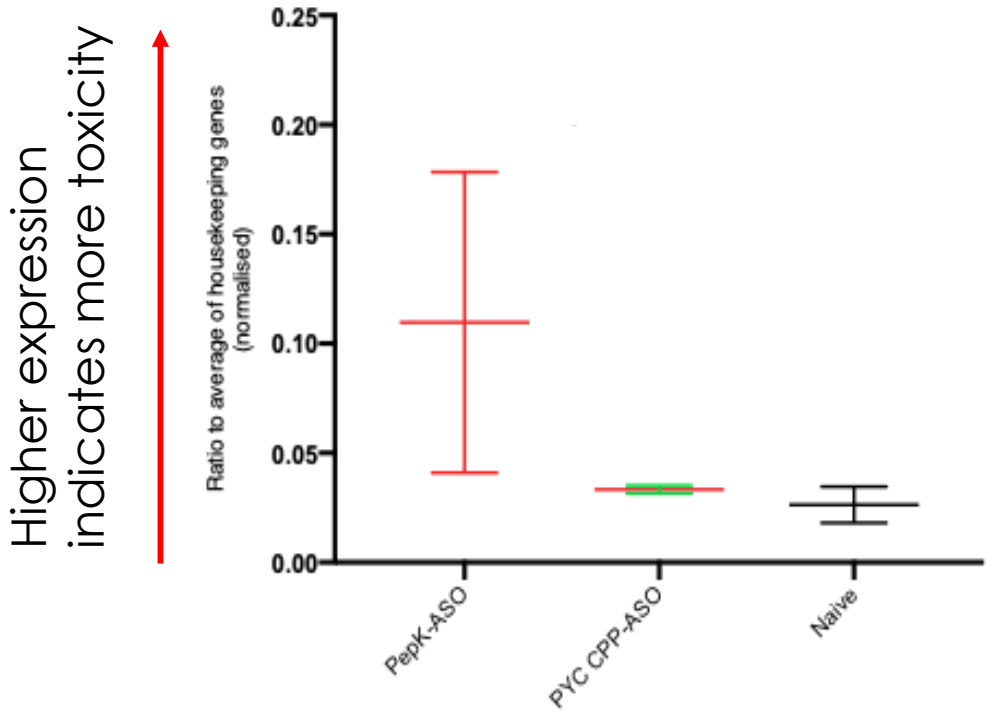
Fig 6b. Exon skipping in mice retinas
1.6µg IVT injection



See ASX Announcements 3 September 2019 and 25 September 2019

PYC's drug also shows minimal local toxicity *in vivo*, highly important in the sensitive retina

Fig 7. Retinal stress marker expression in mice
Day 5 post single 1.6µg IVT injection



- **The safe delivery of drugs to the retina is critically important for ophthalmic (eye) therapeutics**
  - The retina is a highly sensitive organ
  - The retina is a difficult organ to fully penetrate, to ensure effective delivery of a drug

"The intravitreal delivery of drugs to the retina should be primarily evaluated in terms of toxicity issues"[1]

Fig 7. 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

1 Rodrigues, et al, 'CHAPTER 15 - Retina and ocular toxicity to ocular application of drugs' (2010)

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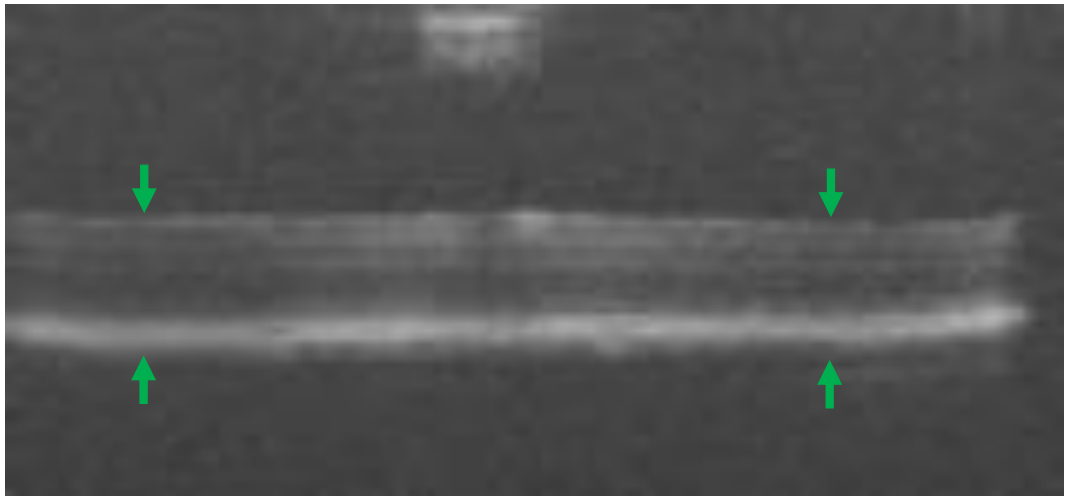
Retinal cells are sensitive – the safety profile of PYC's CPP is a major competitive advantage

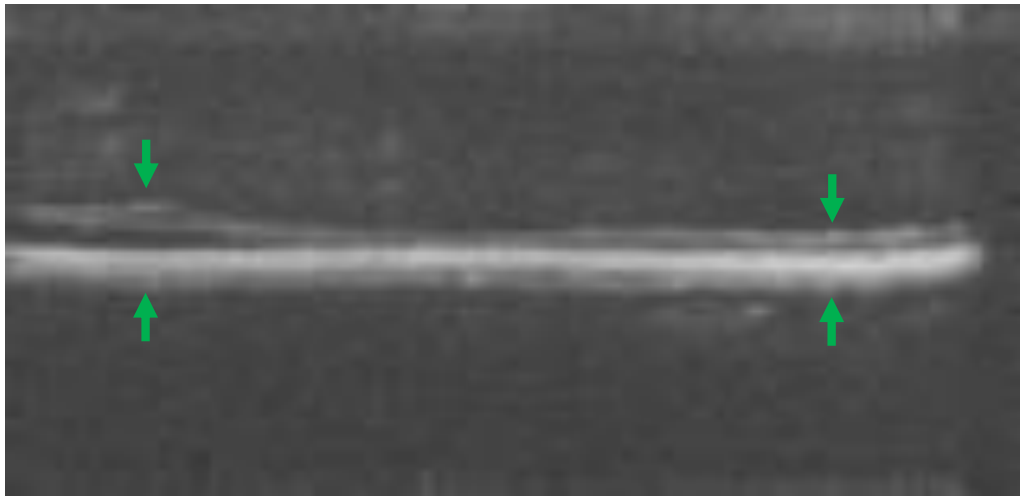
Fig 8. OCT imaging from mice at day 21 post IVT injection (n=1)

PYC lead CPP



No evidence of retinal thinning

PYC control CPP



Evidence of severe retinal thinning

GFAP over vehicle	**1.4x**	**CPP with elevated GFAP**

See ASX Announcement 8 April 2020

ENDS For further information, please contact:

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

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a drug development company solving a major challenge in the development of a revolutionary new class of drugs – delivering large drugs into cells. Cell Penetrating Peptides (CPPs) can overcome 'the delivery challenge' and provide access for a wide range of potent and precise drug 'cargoes' to the 'undruggable genome' – the highest value drug targets that exist inside cells. PYC Therapeutics is using its CPP platform to develop a pipeline of novel therapies with an initial focus on inherited retinal diseases.

Forward looking statements

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.

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