**ASX ANNOUNCEMENT**

**9th October 2019**

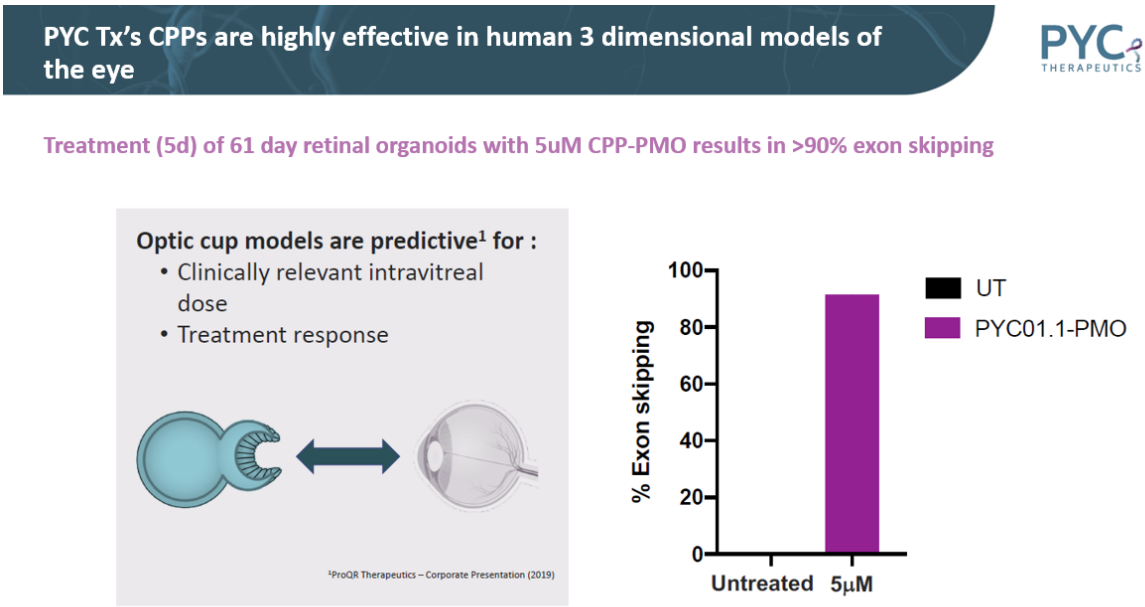
# Successful major milestone - human 'retina in a dish' models

HIGHLIGHTS

- PYC has successfully completed the first evaluation of its flagship drug program in a human 'retina in a dish' study and **achieved greater than 90% effectiveness after a single dose**
- A significant result which **materially increases the probability that PYC's flagship drug program will be successful in human studies**
- Potential to change the lives of patients in a **$1bn per annum target market** with no current treatment options

Phylogica Limited, trading as **PYC Therapeutics**, (**ASX: PYC**) ('The Company' or 'PYC'), a drug development company, has completed the first evaluation of its flagship drug program in a human 'retina in a dish' model and achieved greater than 90% effectiveness after a single dose[1].

Figure 1. Exon skipping achieved after a single dose of CPP-PMO in a 3D retinal organoid




[1] Effectiveness is measured as 'exon skipping' of our target gene, and 91% refers to 91% of the the gene's natural RNA as converted to our intended RNA

Realisation of this critical milestone demonstrates that PYC's lead drug program is highly effective in complex models of the human eye. PYC's flagship drug development program is a treatment for the leading cause of childhood blindness.

The study showed that the drug was effective in human 3-dimensional models of the eye, created from human stem cells, and was conducted at doses in-line with the Company's target human dosing regime. The result is the most meaningful outcome to date supporting the likely success of this program in upcoming human clinical trials.

PYC's Chief Executive Officer Dr Rohan Hockings said the successful study was an important milestone for the Company as it materially increased the probability that its flagship drug program would prove effective in human studies. The result complements earlier outcomes in animal models (see ASX announcement of 22 August 2019) and functional studies in human cells with the target disease (see ASX announcement of 6 August 2019).

"The Company is very excited by the result of this study given its implications for our objective of taking a treatment to market" Dr Hockings explained.

There are currently no treatment options for Retinitis Pigmentosa and PYC has the potential to change the lives of patients in a $1bn per annum target market.

This result is a product of PYC and the Lions Eye Institute's commercial collaboration for combining PYC's proprietary drug delivery technology (a Cell Penetrating Peptide or CPP) with a novel drug (known as an Anti-Sense Oligonucleotide or ASO) to create effective treatments for childhood blindness.

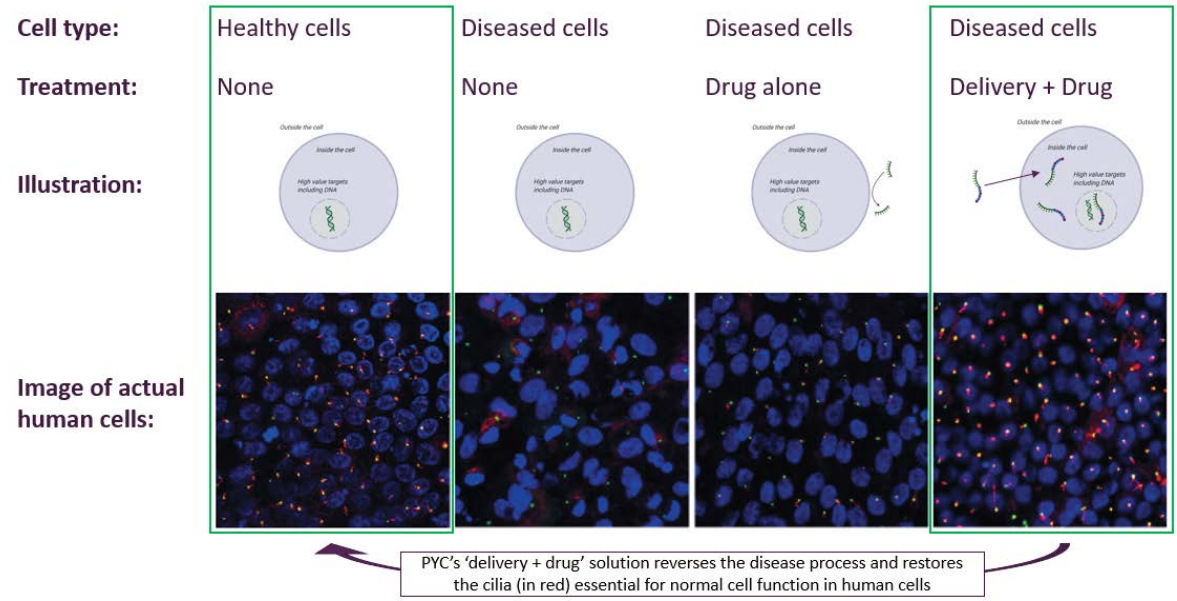
PYC's flagship drug program for treating Retinitis Pigmentosa has now shown:

- highly effective delivery *in vivo* (in animals) with sustained duration of effect[2];
- the ability to reverse the disease process in human cells (see Figure 2 below) and also ASX announcement of 6 August 2019);
- highly effective outcomes in complex models of the human eye in this 'retina in a dish' study; and
- a favourable proof of concept toxicity profile[3].

[2] See ASX announcement 'Successful Time-Course Studies in Animals' 25/09/2019

[3] See ASX announcement 'Animal Models - 400% Outperformance of Gold Standard' 23/07/2019

Figure 2. Explains how PYC's lead program achieves this reversal of the disease process




The difference between PYC's previous human cellular readout (seen in Figure 2) and today's successful 'retina in a dish' results is that the human cellular readout shows only the target cells relevant to the Retinitis Pigmentosa disease process in isolation. The 'retina in a dish' model is a 3 dimensional model of the human eye with multiple cellular layers that 'recapitulates organ architecture with remarkable fidelity'[4]. The success of the drug in the context of the complexity of this 3D model that closely resembles the human eye is very encouraging for upcoming clinical (human) studies.

PYC's next major milestone is to seek validation of the 'retina in a dish' results across multiple patients with different genetic mutations in the same 'retina in a dish' models. This will enable PYC to commence Investigational New Drug (IND) enabling studies (including large animal toxicology studies) before progressing into human clinical trials.

**ENDS**

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*About the 'retina in a dish'*

*The human 'retina in a dish' is a revolutionary technology in drug discovery, enabling PYC access to a pre-clinical model rarely available to drug development companies. It involves taking living patient material (a skin sample) and transforming those cells into our target retinal cells to provide an effective 'patient retina in a dish' (ie. 'grow' another version of their retina). Combined with in vivo animal studies, 'retina in a dish' studies provide PYC a significant*

[4] Disease modelling in human organoids, Madeline A. Lancaster, Meritxell Huch, Disease Models & Mechanisms 2019 12: dmm039347 doi: 10.1242/dmm.039347 Published 29 July 2019

*advantage in understanding the probability of success for our lead drug program in clinical studies. These models have already been used in support of FDA approved clinical studies and have led to highly successful results[5]. Lions Eye Institute, PYC's collaborator on its lead drug program, is a world leader in optic drugs through its Ocular Tissue Engineering Laboratory led by Fred K. Chen.*

### *About Retinitis Pigmentosa*

*Retinitis Pigmentosa is a rare, severe genetic disease, affecting 4,000-8,000 people in the western world. A genetic mutation causes the retina of the eye to degrade with age, causing initial night-blindness, then tunnel vision, and finally, for many patients, complete blindness. There are currently no drugs for the genetic defect that causes our target indication of Retinitis Pigmentosa.*

### *About PYC Therapeutics*

*Phylogica Limited trading as 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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[5] ProQR Announces Positive Interim Results from Phase 1/2 Clinical Trial of QR-110 in LCA10 Patients, and Plans to Start a Phase 2/3 Pivotal Trial, 5th September 2018 ( see proqr.com for full press release)