

## Successful competitive drug evaluation in animals

### Highlights

- PYC owns a drug delivery technology that can carry drug cargoes across the cell membrane to the highest value targets on the inside of cells
- PYC has compared an Anti-Sense Oligonucleotide ('ASO') drug delivered both with and without our technology. The results show that:
  - The ASO drug delivered **with** PYC's technology **is** effective at a dose of less than 1 microgram per eye; and
  - The ASO drug **without** PYC's delivery technology **is not** effective at a dose of 10 micrograms per eye (**a 10x higher dose**).
- This result from an animal model proves that **drugs incorporating PYC's delivery technology are effective at substantially lower doses**
  - This is a major advantage for correcting diseases and avoiding toxic side-effects and an encouraging indicator of clinical success
  - This demonstrates the benefit of PYC's delivery technology for a rapidly growing class of drugs. A single ASO drug, SPINRAZA, has established a A\$2.7B market globally<sup>1</sup>

**3 September 2019:** Phylogica Limited trading as PYC Therapeutics (ASX: PYC) 'The Company' or 'PYC' has successfully completed a competitive evaluation of a drug that includes our delivery technology compared to a 'naked' Anti-Sense Oligonucleotide (ASO) that does not. The drug that includes our delivery technology is effective at a dose of less than 1 microgram per eye in a mouse and the drug that does not include our delivery technology is not effective at either 1 microgram or 10 micrograms per eye. The results show that PYC's delivery platform can make ASOs into potent drugs at doses that are otherwise ineffective – meaning better drugs with fewer side effects.

Delivering more drug to the target in a non-toxic manner is the rate-limiting step in the burgeoning field of RNA therapeutics<sup>2</sup> – an emerging field in which ASOs are a leading class of drug across a range of diseases. This data provides the central piece of pre-clinical evidence that our delivery platform is capable of achieving outcomes that competitive technologies alone cannot.

The increase in effectiveness observed in these models (see Figure 1 below) complements the decreased toxicity associated with the type of ASO that PYC has prioritised for clinical

<sup>1</sup> Biogen's last 12 month (3Q18-2Q19) SPINRAZA revenue (SEC filings 10K & 10Q), converted AUD:USD at 0.715

<sup>2</sup> Delivery is key: lessons learnt from developing splice-switching antisense therapies, Virginia Arechavala-Gomez. EMBO Molecular Medicine

development known as a 'morpholino' or 'PMO' when compared to the phosphorothioate or 'PS' backbone used by a majority of our peers in ASO drug development. This decreased toxicity was elegantly demonstrated at the cellular level by our collaborators at the Centre for Molecular Medicine and Innovative Therapeutics (CMMIT) at Murdoch University recently (see Figure 2).

The improved effectiveness of the drug that incorporates PYC's delivery technology along with the decreased toxicity of these molecules gives our approach to RNA therapeutics a dual advantage in the critical 'therapeutic index' of a drug (the ability to effectively treat a patient without causing toxic side effects).

#### Technical results

#### Measure of drug efficacy, % exon skipping in mice at day 5 post single intravitreal administration

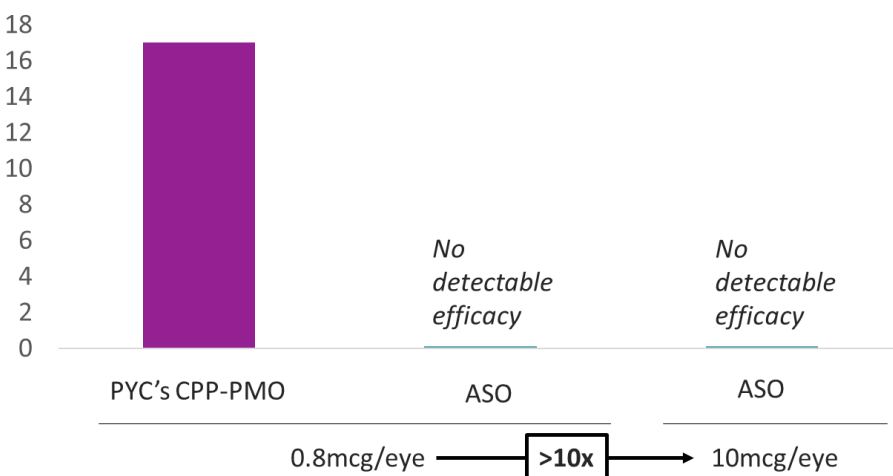


Figure 1. A 'naked' ASO with a phosphorothioate 'PS' backbone chemistry compared to an ASO with a morpholino 'PMO' backbone chemistry conjugated to PYC's CPP known as a CPP-PMO at 0.8 micrograms per rodent eye at day 5 post injection. The result from the retinal pigment epithelium/choroid layer of the eye demonstrates no efficacy of the 'naked' PS ASO at 0.8 micrograms per eye<sup>3</sup> nor the escalated dose of 10 micrograms per eye for the PS backbone ASO whereas the CPP-PMO demonstrates substantial efficacy at the lower 0.8 microgram dose.

<sup>3</sup> Note: a 'naked' PMO backbone ASO was also tested at 0.8 micrograms per eye with no detectable efficacy

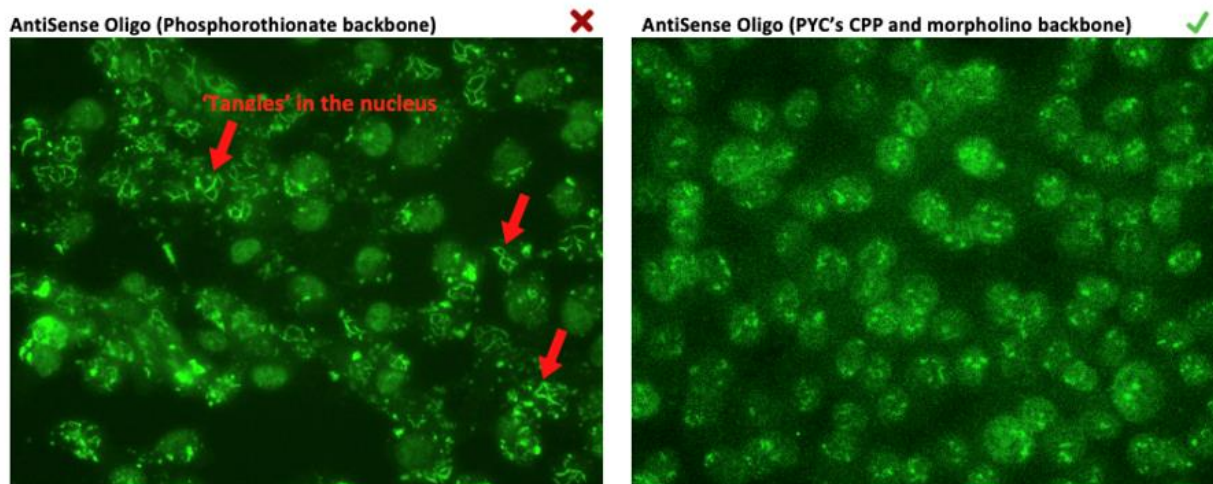


Figure 2. Nuclear protein staining demonstrating 'tangles' in the nucleus of retinal pigment epithelium tissue culture cells treated with PS backbone chemistry ASO. These abnormal structures have been associated with cell stress. No evidence of such tangles can be found in the CPP-PMO treated cells.

**ENDS**

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**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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