

## Achievement of major milestone – successful *in vivo* Cre delivery

*Phylogica (ASX:PYC) is the owner of a peptide library containing the extraordinary richness and diversity of nature. We are using these libraries to develop a drug delivery platform capable of reaching the highest value drug targets located inside cells. Our delivery platform enables drug cargoes to cross the cell membrane and directly reach their target.*

### 30 July 2018:

PYC is pleased to announce the successful achievement of a major technical milestone in the validation of its intracellular drug delivery platform.

#### Highlights:

- PYC has **successfully delivered the Cre enzyme (cargo) *in vivo*** into the nucleus of cells across **multiple types of tissue (lung, liver and kidney)** using our 'original' lead Cell Penetrating Peptide (CPP) (called 'CPP1');
- Our 'current' lead CPP ('CPP2') which is approximately twice as effective as CPP1 *in vitro* will soon be tested in the same animal model<sup>1</sup>; and
- Delivery of the Cre cargo *in vivo* represented the most significant technical challenge of the 'proof of concept' cargoes set in the strategic review in 2017 – the intracellular delivery platform has now been validated extensively *in vivo* and PYC has progressed to the therapeutic application of its technology (the development of new CPP-delivered drugs) and the progression of these candidates into the clinic.

#### *Background on the Cre cargo*

Cre is a well validated recombination enzyme that is widely used in biological research. In the current context, delivery of the enzyme will cause a colour change in cells when it is effectively delivered into the nucleus of the cell. Nuclear delivery of the Cre cargo removes a reporter gene for red fluorescent protein and 'switches on' a reporter for green fluorescent protein (changing the colour of the cell from red to green). The colour change shows which cells PYC's CPP has delivered the Cre cargo into.

#### *The result*

PYC tested the ability of our CPP1 joined to the Cre cargo ('CPP1-Cre') across two experiments involving a total of 24 mice (including controls). The statistical significance of the out-performance of the CPP conjugated cargo (CPP1-Cre) over the Cre cargo alone in reaching the nucleus was  $p < 0.0001$  (the strongest possible statistical result).

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<sup>1</sup> lead times for the synthesis of this improved CPP prevented it from being evaluated in parallel

### Significance of result

The *in vivo* delivery of this enzyme into multiple different tissue types is an important milestone for PYC because:

- i) Cre is a large cargo (the largest cargo PYC has delivered to date) – this result **expands the range of cargoes that PYC's delivery platform can be applied to;**
- ii) Cre has to be delivered into the nucleus of cells in order to be active – demonstrating that the CPP has delivered the cargo not just across the cell membrane and out of the endosome but also across the nuclear membrane (**proving that PYC's CPPs can reach different sub-cellular destinations**); and
- iii) The ability of the CPP to deliver Cre into multiple tissue types *in vivo* demonstrates the breadth of different disease indications that can be pursued using the CPP platform - **proving that PYC's CPPs can deliver cargoes into different tissue and cell types.**

Realisation of this milestone for PYC comes at a time of increasing interest both within the field of intracellular drug delivery generally and the use of CPPs specifically. Commenting on the disposition of Sarepta Therapeutics US\$1.1bn R&D budget recently Dr. Gunnar J Hanson (Senior Director of Research Chemistry) of Sarepta Therapeutics observed that Sarepta are '*investing a lot in these CPP conjugates*' and '*making a larger investment in this than just about anything and for good reason*'<sup>2</sup>.

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### About Phylogica

Phylogica Limited (ASX: PYC) is a biotech company focused on commercialising its intracellular drug delivery platform and screening its peptide libraries to identify drug cargoes for development against a wide range of disease targets. Phylogica controls access to the world's most structurally diverse source of peptides which have the ability to act as

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<sup>2</sup> Presentation at Sarepta Therapeutics Inc 2018 R&D Day entitled 'The Chemical Architecture of PPMO'

effective drug delivery agents and drug cargoes, penetrating cell walls to reach previously 'undruggable' targets across a range of disease types. Phylogica's platform of proprietary cell penetrating peptides has been validated across multiple animal models for the ability to deliver a diverse range of drug cargoes into cells. The company has collaborations with several pharmaceutical companies including Roche, Medimmune, Pfizer, Janssen and Genentech.

### **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 Phylogica'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 Phylogica'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. Phylogica 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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