PHYLOGICA

BREAKTHROUGH PEPTIDE THERAPEUTICS

ASX ANNOUNCEMENT

Flagship program – successful animal models

Delivering drug cargoes across cell membranes is the major challenge in the development of a revolutionary new class of drugs. Cell Penetrating Peptides (CPPs) can overcome this challenge and provide access to the 'undruggable genome' – the highest value drug targets that exist inside cells. Phylogica (ASX:PYC) owns the world's most structurally diverse peptide library and is using these libraries to identify a new generation of highly efficient CPPs.

12 March 2019:

Highlights:

1. Phylogica's 1st generation Cell Penetrating Peptides (CPPs) have successfully delivered an Anti-Sense Oligonucleotide (ASO) drug cargo into cells in multiple different tissue types in an animal model

2. The results prove that our CPPs can deliver an ASO into cells and achieve a functional outcome (exon skipping by the ASO) *in vivo*

3. These results pave the way for assessment of PYC's superior 2nd generation CPPs which will occur in Q2 2019

4. Successful outcomes with our 2nd generation CPPs will result in initiation of Investigational New Drug (IND)-enabling studies in preparation for clinical development of the Company's CPP platform

Background

In 2018, Phylogica prioritised 'building' our Cell Penetrating Peptide (CPP) platform in the context of an Anti-Sense Oligonucleotide (ASO) cargo because of the potency and precision of this class of molecule. ASOs represent a highly promising therapeutic class whose clinical application has been limited by their inability to reach their target inside cells. Our in-house efforts have been focused on demonstrating that our CPPs can deliver ASOs inside cells to reach their target and change the characteristics of those cells as a result.

We have now successfully demonstrated that our CPPs can achieve this objective across multiple tissue types in an animal. This addresses the major hurdle in the pre-clinical development of our platform.

Animal model details

Two of Phylogica's first generation CPPs were used to deliver a 'reporter' ASO via multiple routes of administration in a pilot animal model study:

- Systemic injection into the bloodstream; and
- Intra-vitreal injection in the eye

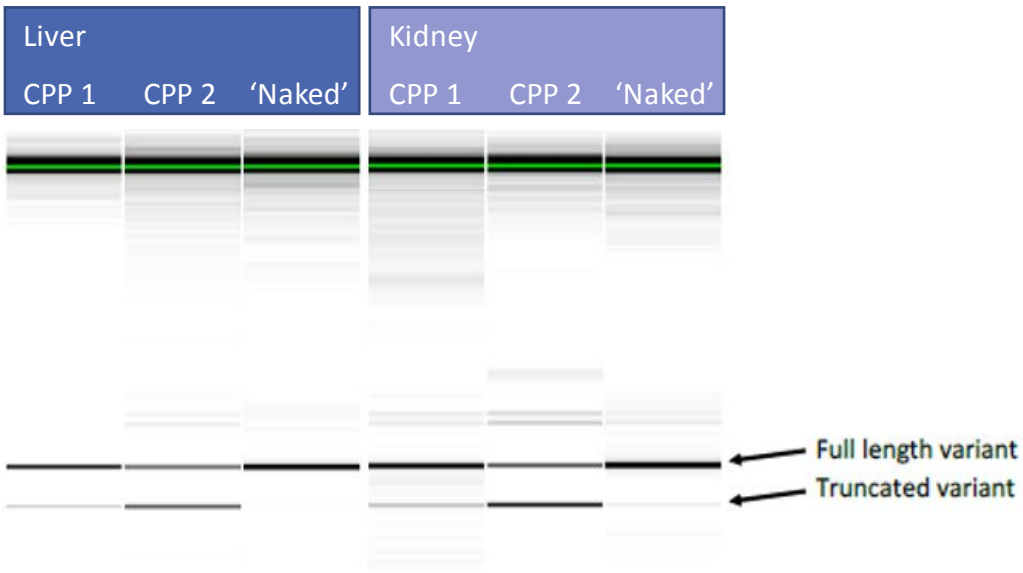
The reporter ASO, when effectively delivered to its target inside the cell, causes the production of a shortened version of a protein that is produced by all cells in the body (allowing evaluation across all types of tissue). The ratio of the mRNA coding for the shortened version of the protein (indicating successful exon skipping by the ASO in the cell's nucleus) to the mRNA coding for the full-length protein is then used as an objective measure of the functional efficacy of the CPP-ASO molecule.

All routes of administration demonstrated effective exon skipping in the target tissues harvested following administration. The systemic injection resulted in exon skipping in the eye, liver and kidney (with other tissues harvested yet to be processed). The intra-vitreal injections resulted in exon skipping in the anterior and posterior segment of the eye.

Technical Results

The results shown below in Figure 1 represent a read-out of two versions of mRNA transcripts from organ homogenates harvested 4 days after a single intravenous injection of 20mg/kg CPP-ASO. Successful delivery of the ASO by the CPP is reflected in an mRNA transcript for a shortened (truncated) version of the protein.

Figure 1.



'CPP 1' refers to Phylogica's original (first generation) lead CPP and 'CPP2' refers to a higher performing CPP also owned by Phylogica and also forming part of our first generation of CPPs. 'Naked' refers to the ASO cargo without a CPP facilitating intracellular delivery.

Put simply, the greater the amount of truncated variant and the lesser the amount of full-length variant present, the greater the effect of the CPP-ASO in the cells of the organ harvested.

A more detailed data pack on delivery within the eye as a target tissue will be provided in the future.

Implications

The results pave the way for evaluation of Phylogica's 'second generation' CPPs and optimised variants of these through the second quarter of 2019 in these same models. Successful outcomes here will set us on the path to the clinic. The extent of outperformance of our 'second generation' CPPs over our 'first generation' CPPs has been previously described (see ASX announcement of 17 January 2019).

Transition from the 'reporter' ASO described here to therapeutic ASOs is a rapid process with a high degree of reproducibility of result. These models are, therefore, a good indicator of our prospects of success in *in vivo* therapeutic models.

We are on track to demonstrate the unique advantages of our platform in the critical *in vivo* therapeutic setting and translating these results into where our platform is best applied clinically.

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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 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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