

CEO letter and operational update – 17 January 2019

We are here to address one of the biggest challenges in drug development

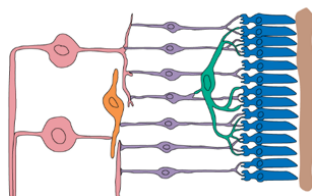


Effective delivery of large molecules across cell membranes is the rate-limiting step in the development of a novel class of highly effective therapeutics

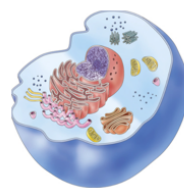
Phylogica's objective is to use our Cell Penetrating Peptide (CPP) platform to deliver a drug to its:



1. Target tissue;



2. Target cell within a tissue; and



3. Target location within the cell

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 on the inside of 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.

16 January 2019:

CEO letter highlights:

- The main **driver of valuation uplift for our platform technology is within reach** and results will be known in mid-2019 (*in vivo* therapeutic read-outs); and
- The **early indications of our prospects of success in these read-outs are encouraging**
 - a. Screening of our enriched peptide libraries has identified multiple potent 'second generation' Cell Penetrating Peptide (CPP) candidates; and
 - b. Translation of the performance of these CPPs from the test tube into animals will set us on the path to the clinic.

Dear Shareholder,

Two questions shape the long and difficult journey of drug discovery above all others:

- 1) Is the technology both effective and safe in animals; and
- 2) Is the technology both effective and safe in humans?

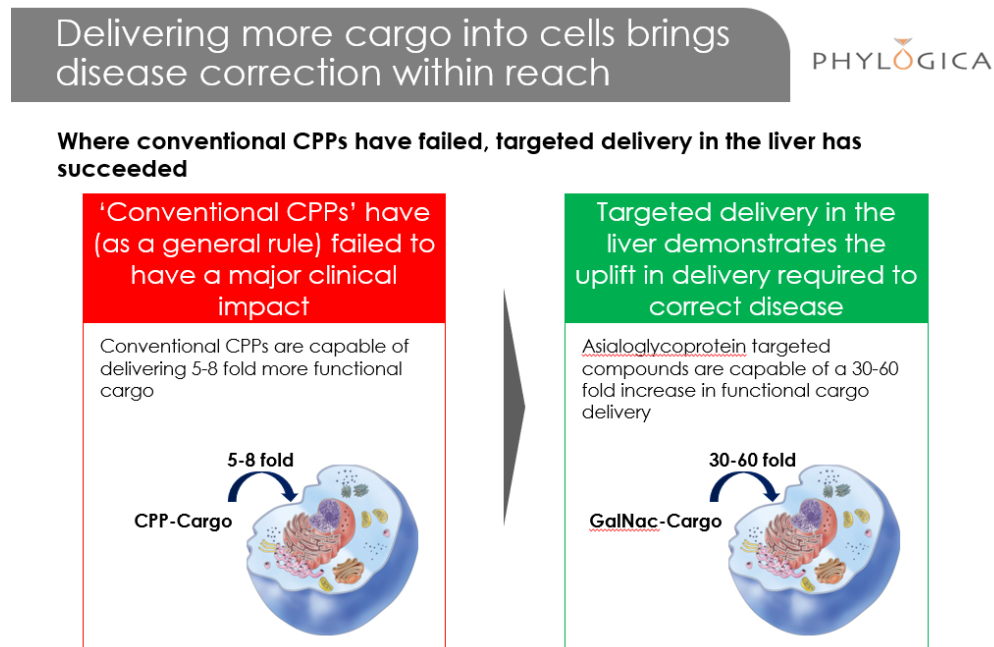
We begin 2019 within reach of the answer to the former - a major milestone for our Cell Penetrating Peptide (CPP) platform. This central question informs both the value of our technology and its progression into clinical (human) evaluation.

Success over the coming 12 months will see us initiate Investigational New Drug (IND)-enabling studies and leave us within reach of the clinic at the conclusion of 2019. We have the ability to leverage a successful answer to the first question through multiple programs across a range of diseases as we progress towards an answer to the second. A clinical phase intracellular delivery platform is a highly valuable asset.

What does 'success' look like?

For our delivery platform to be successful, we need to achieve a ~30-60 times increase in cargo delivery (relative to the 'naked' drug cargo). This uplift in the amount of cargo delivered represents the threshold required to correct a disease process occurring within that cell. Figure 1 demonstrates the difference between delivery approaches that have not met absolute disease correction thresholds ('conventional CPPs' on the left-hand side) with those that have (targeted delivery on the right-hand side).

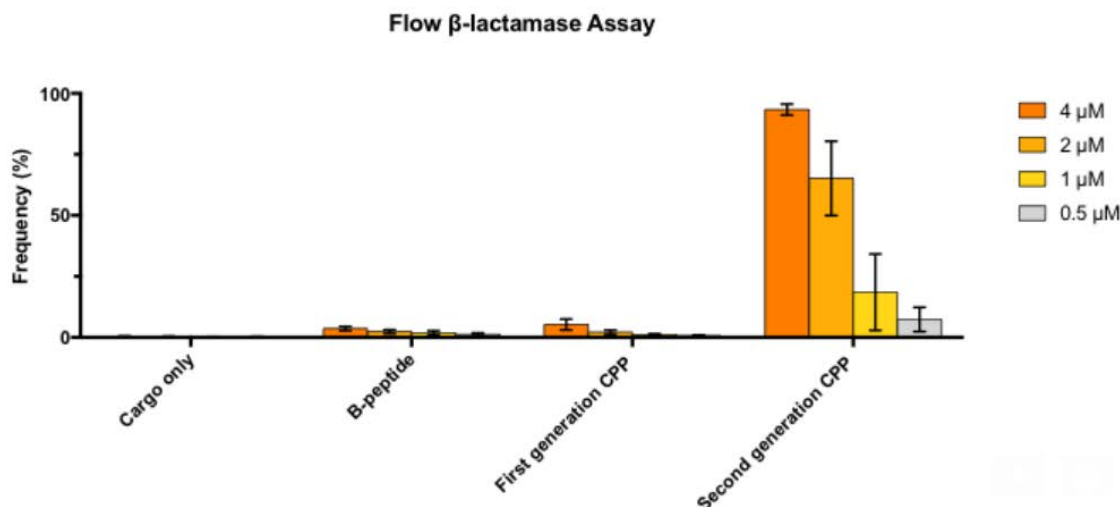
Figure 1



Are we likely to achieve success?

We are well on the way to achieving this objective. We are greatly encouraged by the *in vitro* (test tube) performance of our 'second generation' CPPs which include candidates capable of delivering 25-150 times as much cargo into a target cell when compared to the cargo alone. Figure 2 below demonstrates the extent of outperformance of our 'second generation' CPPs over our 'first generation' lead CPP and the B-peptide as an example of 'conventional CPPs'.

Figure 2.



The recently announced results from an evaluation of our peptide vaccine in an animal model of Herpes Simplex Virus (see ASX announcement of 6 December 2018) provide further encouragement for our prospects in these critical upcoming studies. Those results demonstrate a clear correlation between the performance of the CPP in the test tube and the outcomes of the animal model. Given the extent of the outperformance of our second generation CPPs *in vitro*, this bodes well for our imminent therapeutic *in vivo* read-outs.

Importantly, the 'second generation' CPP seen in Figure 2 is very attractive in terms of its 'drug-like' properties (toxicity, manufacturability etc.) indicating an improved probability of success in navigating the IND approval process in the event that therapeutic *in vivo* efficacy is established.

Next steps

1H2019 represents an opportunity to show that our 'second generation' CPPs yield meaningful *in vivo* read-outs, demonstrating our ability to correct human disease processes in animal models of that disease. Success in these models will propel our platform into the clinic.

Read-outs will be delivered across the three cargo classes highlighted for prioritisation in the annual report (see ASX announcement of 15 October 2018 for more detail). In addition to the milestones described above for our priority 'in-house' cargo classes, we will also pursue partnerships with leading global commercial and academic groups to advance a range of alternative cargo classes in 2019. These partnerships will allow us to progress work in three additional classes of cargo (scaffolds, protein degradation and small interfering RNA) through to

'proof-of-concept' milestones without impacting on our internal focus of pushing towards clinical evaluation of our 'in-house' pipeline.

I look forward to providing you with updates on our progress throughout the journey ahead.

Kind regards,

Dr. Rohan Hockings

Phylogica CEO

ENDS

For further information, please contact:



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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