

## CEO Update – 9th July 2018

Phylogica (ASX:PYC) is the owner of a peptide library containing the extraordinary richness and diversity of nature and is using these libraries to develop a delivery platform capable of reaching the highest value drug targets located inside cells.

**9 July 2018:** Phylogica is pleased to provide the following operational update and CEO letter to the market.

### Operational update:

- Experimental timelines are on track to assess the ability of our 'original' lead Cell Penetrating Peptide (CPP) to **deliver the Cre cargo into the nucleus of cells in multiple tissues in a live animal (*in vivo* model) in July<sup>1</sup>** - a significant technical milestone in the validation of our platform;
- We have already **commenced high throughput (at scale) screening** of our re-populated libraries to identify additional CPPs – leveraging the richness of our libraries to build a true intracellular delivery platform; and
- Our 'base case' (no revenue) **cash runway extends into CY2019<sup>2</sup>** on current expenditure projections – if revenue is generated through commercial arrangements with parties seeking access to Phylogica's technology this will supplement current cash runway forecasts.

### CEO letter highlights:

1. The macro trend within the Pharmaceutical industry towards the pursuit of intracellular targets is encouraging – **there is a large and rapidly growing target market for our technology;**
2. Within the field of intracellular drug delivery, the benefits of CPPs are increasingly being recognised – **we are in the right place at the right time;** and
3. Phylogica has a real near-term opportunity to demonstrate a competitive advantage by showing head to head outperformance of the current delivery approach for cargoes of interest – **we have a clear path to platform validation.**

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<sup>1</sup> This represents the most substantial challenge of the 'proof of concept' cargoes described in the ASX announcement of 4 December 2017 'Phylogica Strategic Update – Pivot to Platform' and builds on the *in vitro* proof of concept for this cargo announced to the ASX on 2 March 2018 'Cre Enzyme Delivery Provides Validation & Strategic Value' – the delivery challenge is greatest for this cargo because it has to be delivered not only across the cell membrane but also into the nucleus of the cell in order to have its effect

<sup>2</sup> An R&D cash rebate is expected to be received in Q1 of the 2019 Financial Year

Dear Shareholder,

I am writing to share my perspective on recent progress within Phylogica and our current outlook.

My primary observation since joining the company in April this year is that we have the right strategy in place and are well positioned in a large and growing market. It has also become apparent to me that there is an opportunity to improve the communication around (and therefore understanding of) the Company's activities and its underlying technology.

PYC's core asset is the most structurally diverse drug library known today (containing hundreds of billions of peptides derived from Nature). This library can be used in many ways. PYC has chosen to use its libraries to identify Cell Penetrating Peptides (CPPs). These CPPs are able to cross the cell membrane and reach the inside of cells where the highest value drug targets exist. This is a rare and valuable attribute for a peptide because it opens up the possibility that the CPP can deliver a drug cargo inside the cell to reach a high value target which would otherwise be inaccessible to the drug cargo.

Many of the organisms in our library are known to have the ability to cross the cell membrane making the library a fertile hunting ground for CPPs. PYC's technology has the potential to deliver many different types of drug cargoes inside the cell to their target.

As knowledge of PYC's work in this area becomes more widespread within the pharmaceutical industry, strong interest has been generated from companies that have developed drug cargoes and who are looking for an effective delivery platform. The further we advance the platform towards the clinic, the less risk for the counter-party licensing the technology and the more advantageous the commercial terms to Phylogica of a licensing agreement.

Right now, work continues on two fronts:

**Technical:**

- Continued evaluation of existing CPPs to determine their effectiveness in penetrating cells (intracellular delivery); and
- Scanning the vast (and recently expanded) library for even better performing CPPs.

**Commercial:**

- Holding discussions with interested pharmaceutical and biotechnology companies who have developed drugs that need a more effective delivery platform (specific cargoes).

**1. Intracellular drug delivery is gaining momentum**

Dr. Jay Bradner, Head of the Novartis Institute of Biomedical Research, recently identified charting a 'new path to intractable protein targets'<sup>3</sup> as one of the highest value applications of biotechnology investment. Phylogica's central purpose is to provide access to the 80% of drug targets that exist inside cells which are also known as 'undruggable' targets. The quest for greater sensitivity and specificity (better drugs with fewer side effects) requires larger molecules

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<sup>3</sup> <https://www.fiercebiotech.com/biotech/novartis-jay-bradner-bemoans-redundant-investment-biotech-sector-some-cancer-r-d>

with the ability to bind these complex targets to have access to the intracellular space where they reside. Phylogica is not a 'fast follower', 'narrow differentiator' or part of the 'distracting hype'<sup>4</sup> – we are seeking to make a fundamental change to the therapeutic landscape.

Pharmaceutical and large biotechnology companies are increasingly attracted to these intracellular targets with entire fields (eg. gene editing, gene therapy etc.) directed towards delivering large cargoes into cells. The pace of development within the delivery field has not matched that of the cargoes, leaving the substantial investment that has been made in cargo development at risk of finding an effective delivery solution. The need for an effective intracellular delivery modality is growing rapidly.

## 2. CPPs have an important role to play in this delivery challenge

Multiple different delivery technologies for large cargoes exist – the value of intracellular drug targets informs the many different efforts in train, which include technologies such as:

- i) Adeno-Associated Viruses (AAVs);
- ii) Electroporation;
- iii) Lipid based delivery systems; and
- iv) CPPs amongst others.

Each of these delivery technologies has their own benefits and drawbacks. The recent investment by Sarepta Therapeutics in a pipeline of PMO therapies all joined to their CPP (known as PPMO or peptide-PMO therapies and within the class of cargoes known as 'ASO's – Anti-Sense Oligonucleotides) is testament to the increasing preference for CPP based delivery vehicles in certain settings. The lead therapy in this pipeline is currently in Phase1/2A human clinical trials and has led to the observation that 'we will see more CPP-ASO candidates move towards clinical drug development'<sup>5</sup>. The opportunity for Phylogica is to clearly demonstrate the competitive advantage of our CPPs in this context.

## 3. Demonstrating the competitive advantage of Phylogica's CPPs

On 1 June 2018 we held the first formal review of our platform with our newly appointed Scientific Advisory Board. It was clear from this discussion that Phylogica has a near-term opportunity to improve the commercial attractiveness of our platform by showing that we can deliver a cargo class of interest into a target cell of interest more efficiently than the relevant competitive technology. The outcome of these comparative studies and progression into clinical evaluation are the two primary drivers of platform validation and therefore the value of the company's assets. Realisation of this competitive assessment requires selection of a cargo since joining the CPP to a cargo has the ability to change the properties of both elements of the 'conjugate' (CPP and cargo).

The extension of our 2017 strategic review is to now move from 'proof of concept' to therapeutic cargoes and to:

- i) obtain a competitive read-out with the existing delivery modality for that cargo class to show greater efficacy (more cargo delivered) and/or lower toxicity; and to do so
- ii) in primary cells (*ex vivo*) or in a relevant *in vivo* setting.

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<sup>4</sup> <https://www.fiercebiotech.com/biotech/novartis-jay-bradner-bemoans-redundant-investment-biotech-sector-some-cancer-r-d>

<sup>5</sup> <https://pdfs.semanticscholar.org/2005/98e92ff961ea33a8ee6a307c631cedc1f190.pdf>

Successful delivery of the Cre cargo in the animal experiments planned for this month will represent a major milestone as it will enable the transition from 'proof of concept' (platform validating) to therapeutic drug cargoes (cargoes that are disease relevant). The company will shortly be updating shareholders on the extension of this strategy and, specifically, the cargo classes that will form the focus of the company's attention as we look to advance towards the clinic.

Our focus as an organisation is on achieving recognition of the value of our assets through:

- i) identifying new CPPs from our screening efforts that are differentiated from competitors by:
  - a. efficiency (quantity of cargo delivered at a non-toxic dose)
  - b. specificity for a target cell of interest
  - c. properties of the CPP (enabling cargoes of different properties to be delivered); and
- ii) demonstrating the competitive advantage of our CPPs for particular therapeutic cargoes in the context of the relevant therapeutic setting (model of disease).

In summary, Phylogica is at an exciting point in its development with multiple platform validating milestones within our reach. We are in the right space at the right time - intracellular drug delivery is at the forefront of modern medicine and is rapidly gaining traction and interest from both Pharma and large Biotech customers. I am excited about what the company can accomplish in the next 12 months and look forward to sharing updates with you as we execute on our plan.

Kind regards,

Rohan Hockings

Phylogica CEO

**ENDS**

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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.

This ASX announcement should not be relied on as a recommendation or forecast by Phylogica. Nothing in this ASX announcement should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

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