PHYLOGICA

Operational Update

21 December, 2016

Dear Shareholders,

In establishing Phylogica as a leading intracellular delivery company, we are pleased to report significant progress has been made over the last quarter in the areas of:

i) intracellular delivery technology – further advances in our FPP intracellular delivery platform which we believe is best in class with demonstrable, significant endosomal escape and outperformance over other delivery technologies such as TAT.

ii) Internal oncology program – refined our shortlist of proprietary iMYC cargoes aimed at the high-value intracellular cancer target Myc to 5 high quality candidates for optimisation, and completed our proof of concept toxicity experiments.

iii) commercialisation – a number of presentations to interested pharma and biotechnology companies were made during the quarter to discuss current and future collaborations.

We have also been very pleased to recently announce that Genentech has extended its exclusivity period for the Research Collaboration and License Agreement to discover novel antibiotics utilizing Phylogica's Phylomer® drug discovery platform, including our proprietary cell penetrating peptide discovery technology, resulting in a US$2m milestone payment.

1. Progress on FPP platform development

Our work this quarter has further supported our FPP (Functional Penetrating Phylomer) intracellular delivery platform as being superior to other delivery technologies. Key attributes of our platform include:

- Enables endosomal escape
  - Endosomal escape is a critical feature required for efficient intracellular delivery, which other intracellular delivery platforms have not demonstrated to our knowledge to this extent, and helps establish our FPPs as best-in-class.
- Compatible with a wide range of cargoes
  - Our FPPs are able to deliver cargoes from as small as oligonucleotides and siRNA to as large as enzymes – which greatly expands the range of therapies for which FPPs can be used to deliver and the diseases that can be treated.
- Outperforms other intracellular delivery technologies in delivering more efficiently to the cytoplasm
  - Our delivery of cargoes to the cytoplasm outperforms the current gold standard of intracellular delivery technology known as TAT.
- Functional in multiple cell types
  - FPP-delivered cargoes can function in various cell types rather than being restricted to only cell types such as liver cells or transformed cancer cells. This provides significant scope for expanding the range of treatable targets.

- Preliminary evidence of intravenous *in vivo* efficacy(with Omomyc cargo)
  - Evidence of *in vivo* activity in two distinct animal models following intravenous administration.
- Promising initial safety signals
  - Our *in vitro* experiments show little evidence of toxicity. This is supported by preliminary evidence from *in vivo* experiments, both of our own and with collaborators, with no evidence of toxicity of FPP-only controls.

Externally, we continue our commercialisation discussions and presentations with individual pharma companies, with several recent face-to-face meetings in US and Europe. The discussions are for both established opportunities under evaluation and to initiate new ones to assess the FPP delivery platform with various types of proprietary pharma cargoes in multiple disease areas.

2. Progress on the i-MYC cancer program

Our proof of concept (POC) data pack is almost complete, with significant work undertaken in the last quarter. Formal preclinical development is still targeted to commence during the second half of 2017. Table 1 summarises the elements of the program, with relevant updates as follows:

- iMYC Phylomer cargo candidate selection
  - 5 candidates with high quality features have been selected for optimisation, with early stages of the optimisation process now underway.
- Data pack and optimisation progress
  - Potency:
    - Affinity maturation and other approaches have commenced as part of the early optimisation process, in order to achieve further increases in potency.
  - Toxicity:
    - Additional experiments have again showed no evidence of toxicity, completing this key element of the proof-of-concept data pack.
  - Pharmacokinetics (PK):
    - Well-established optimization approaches are being assessed to enhance PK and we are confident that we can achieve the objectives of PK and biodistribution as we progress through the optimization process.
  - Selectivity:
    - For selectivity, having established proof of concept we are now continuing to generate further supporting data using transcriptional analysis of a signature of Myc target genes.

PROPERTIES	POC FEASIBILITY SIGNAL (2H 2016)	STATUS OF POC	OPTIMAL LEAD CANDIDATE (2H 2017)
In-vitro Potency	Demonstration of low micromolar potencies	✓	Demonstration of nanomolar potencies
Selectivity	Evidence for modulation of downstream targets and initial binding kinetics	✓	Confirmed inhibition of MYC and downstream targets, detailed binding kinetics, solved target/ligand structure
Toxicity	Evidence of maintenance of viability for FPP vs FPP-cargo at micromolar concentrations in-vitro	✓	Preclinical tox pack in-vivo. (rodents, non GMP)
Serum Stability	>40% stability after 12 hrs in static serum	✓	>80% stability after 12 hrs in static serum
PK Profile	Evidence of delivery to target tissue and acceptable level of renal clearance	progressing	>4 hrs serum half life in mice/ rats
Efficacy in Animal Models	Confirmed activity in animal model of disease (following IV injection)	✓	Confirmed activity in disease-relevant animal models (following IV injection)
Scalable production/ formulation	Recombinant expression at adequate yields and good solubility for animal studies	✓	Recombinant expression at adequate yields and good solubility for scaling-up to further animal and then human studies

Table 1: POC Data Pack Milestones

3. Progress on other external collaborations and discussions

- Genentech – Antimicrobial collaboration exclusivity extension with US$2m milestone payment
  - We have announced earlier this month the excellent news that Phylogica will received a $US2m milestone payment from Genentech to extend its exclusivity period for the Research Collaboration and License Agreement to discover novel antibiotics utilizing Phylogica's Phylomer® drug discovery platform, including our proprietary cell penetrating peptide discovery technology.
  - This is an exciting collaboration to develop novel antibiotics to treat bacterial infections including antimicrobial-resistant infection, an area of critical unmet need, which has received increased attention this year from the World Health Organisation and the UN.
- Murdoch University – Oligonucleotide delivery collaboration progressing
  - We have seen further encouraging progress in our collaboration with Murdoch University on oligonucleotide delivery. A round of intravenous animal model experiments has shown preliminary signs of efficacy, and importantly, lack of toxicity, in delivery of exon-skipping oligonucleotides in models of both Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA) to muscles in a range of locations (including cardiac, diaphragm and tibia). Excitingly, we have seen

evidence for increased levels of the dystrophin protein following treatment with FPP-delivered exon-skipping oligonucleotides.

- Olivia Newton John Cancer Research Institute (ONJCRI) collaboration – NHMRC grant awarded
  - In November we announced the receipt of a ~$750,000 grant by our collaborator Doug Fairlie at ONJCRI to support a 4 year project entitled "Dual targeting of Myc and apoptosis pathways for improved blood cancer treatment outcomes". A small part of these funds will help subsidise the cost of synthesis of our peptide and protein constructs, but most importantly the funding allows research to progress on further validating our FPP platform and iMYCs in the area of blood cancers such as leukaemia and lymphoma.
- University of Queensland (UQ) collaboration progressing
  - In our ARC grant-funded collaboration with the Institute for Molecular Biosciences at UQ, we have confirmed high hit rates from new synthetic phylomer libraries against several target classes. This collaboration is on track for the validating of prototype arrays of Phylomers for use in universal diagnostics.

Also our collaboration with Dana Farber has continued with work on both our STAT5 and YB1 proprietary oncology cargoes advancing; and our phenotypic screening collaboration with Phoremost continues.

In addition, since the end of September, we've signed a further non-disclosure agreement with an international pharmaceutical company to discuss elements of Phylogica's technology portfolio. This brings the total of additional NDAs signed since the end of March to 5 which, although early stage, indicate an increasing interest in Phylogica's progress.

As we move into 2017, we are proud of the progress we have made over the last 12 months and are excited to be further advancing our intracellular delivery technology, our innovative cancer program and our discovery platform. With the work completed over the last calendar year, Phylogica is now firmly established as a leading intracellular delivery platform outperforming all other known delivery platforms. We look forward to updating you through 2017, as the iMYC cancer program approaches formal preclinical development in the second half of the year, and as we see further internal and external validation of our FPP intracellular delivery platform.

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Chair
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