

Operational Update

ASX Announcement

11 July 2017

Perth, Australia

Dear Shareholders,

We are pleased to have made strong progress during the June quarter operationally as well as significant progress in our drug development program, with highlights including:

- Stephanie Unwin appointed Chief Executive Officer, providing significant senior executive and commercial experience to the strategic direction of Phylogica.
- Dr Robert Hayes appointed Chief Scientific Officer, bringing extensive experience in biotechnology research and drug development to the commercialisation of Phylogica candidates.
- Dr Rick Kendall appointed Non-Executive Director, offering valuable experience in pharmaceutical research and oncology drug development.
- Successful fundraising of \$5m to enhance the pre-clinical validation of Phylogica intracellular delivery technology and proprietary drug cargoes.
- Identification of new Phylomer FPPs with improved ability to deliver a range of biologics inside cells, expansion of the potency of Phylomer FPPs, and extension of in vivo half-life of our FPP cargo conjugates. We have completed several in vivo studies that demonstrate that we can significantly extend the half-lives of Phylomer FPPs using protein engineering. Encouragingly these engineered Phylomer FPPs are not trapped in one tissue or location in the animal model, such as the liver or the kidney, but are distributed throughout the body. All of these constitute key milestones in the development of a robust delivery technology that will allow us to deliver biologics targeted towards intracellular therapeutic targets.
- Further progress with iMyc lead optimisation to improve their potency, identification of biomarker signature to track on-target effect of iMyc leads, and confirmation of potent activity of iMyCs across a wide range of blood cancer cell lines.

A more detailed overview of Phylogica's cancer drug discovery program is included as an appendix to this announcement, discussing FPP platform development, new intellectual property around FPP leads, progress on the i-MYC cancer program, and external collaborations.

Conference call

Shareholders are invited to join a conference held at 10.30am AEST / 8.30am AWST on Wednesday 12 July, hosted by recently appointed CEO, Stephanie Unwin and CSO, Dr Robert Hayes, to discuss activity during the quarter, followed by Q&A with participants. To pre-register for the call, with diary note automatically sent to your calendar, [click here](#).

Conference code: **603 086**

Dial in numbers:

Australia Toll Free:	1 800 558 698
Australia (Alternate)	+61 2 9007 3187

New Zealand Toll Free: 0800 453 055
 Hong Kong: 800 966 806
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Update on Phylogica's Drug Development Program

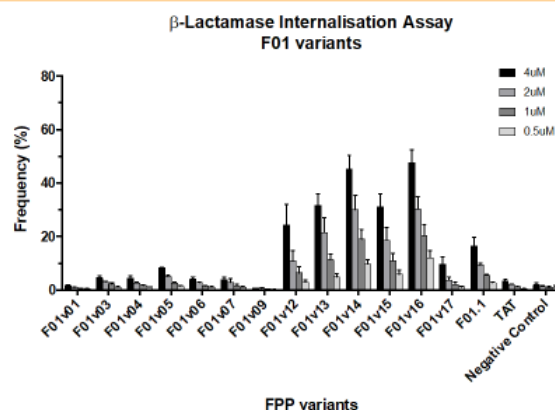
Progress on FPP platform development

The focus of the Phylogica team during the second quarter of 2017 has been on expanding the number of Phylomer FPPs we have available, and the enhancing the potency of those FPPs. The number of FPPs that we have available to deliver a cargo inside of a cell is important, because every cargo has its own unique properties meaning that some FPPs will work better with some cargoes than others.

Identification of new FPPs

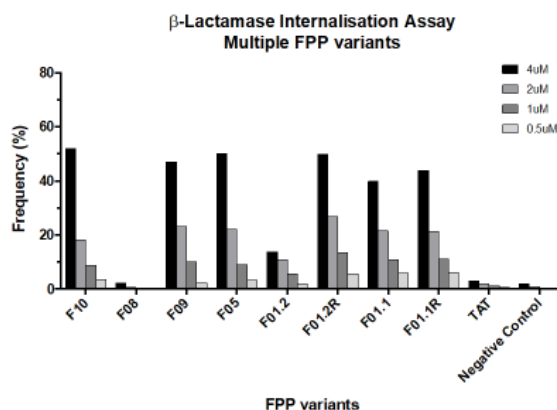
We have established sensitive and robust in-house assays to allow for the screening of hundreds of synthetic variants of FPPs. Using these assays, we have identified novel candidates which show excellent ability to cross the cell membrane and escape the endosome. We are now evaluating 13 of the 47 additional prospective variants for the delivery of a range of cargoes, as well as establishing a toxicity profile for each prospective FPP.

The β -Lactamase internalisation assay is a measure of cargo delivery efficiency



- F01v12, F01v13, F01v14 and F01v16 deliver β -Lactamase more efficiently than the primary F01.1 and TAT
- The β -Lactamase internalisation assay is a better measure of cargo delivery efficiency than the NF-internalisation assay

The β -Lactamase internalisation assay has identified FPPs equal to or better than F01.1



- F10, F09, F05, F01.2R and F01.1R deliver β -Lactamase more efficiently than the primary F01.1 and TAT
- These 5 Phylomer FPPs are promising candidates for enhanced cell delivery of iMycs

Increased potency of FPPs

We have seen significant improvements in the potency of our FPPs in the early stages of our lead optimisation process. These potency improvements (observed across multiple FPP families) provide an early and encouraging indication, with the potential to achieve a significant improvement in the efficacy of our FPP-cargo conjugates when we re-enter animal models of disease late this year/early next.

These optimisation results have been achieved through:

- modifying the length of FPPs to identify their functional sequence/structure; and
- creating genetic variants of the identified FPPs

We have achieved potency improvements of up to 5-fold through this early optimisation work and will continue to pursue complementary improvement approaches before finalising our lead Phylomer FPPs later this year.

We have also demonstrated for the first time, using sophisticated bioinformatics analysis, that FPP sequences cluster into a distinct class when compared to conventional cell penetrating peptides including TAT, R9 and penetratin. The identification of the attributes that distinguish Phylogica's FPPs from conventional cell penetrating peptides provides an early insight into the critical question of why Phylogica's FPPs achieve a far superior efficiency of intracellular delivery, when compared to historical attempts to address this critical issue in drug discovery. This analysis will enable us to optimise our FPPs in a 'rational' rather than a 'random' manner, using machine learning drug discovery approaches.

Pharmacokinetic Optimization

In a further positive development, we have conducted initial *in vivo* toxicity assays on our lead FPP, and have seen no evidence of toxicity across a range of liver and kidney toxicity biomarkers. We have also begun to look at half-life extension technologies that are compatible with Phylogica FPPs and their cargoes. The criteria at this stage are: (1) that we see a meaningful increase in half-life in mice; (2), the efficacy of the cargo isn't significantly affected; (3) that we see good biodistribution; (4) that the half-life technologies we use are compatible with

modern manufacturing techniques; (5) if we need to licence a half-life technology, it would likely be on reasonable terms.

Based on the early data, we can confidently say that we can extend the half-life of a FPP-cargo constructs using two or three different half-life technologies. In the next few months we will use larger animals (e.g. rats) because the half-lives obtained from these can be scaled to humans with more confidence. Interestingly, the different half-life extension technologies provided different biodistribution patterns, and by varying dosing regimens, doses magnitude and routes of administration, we will be able to optimize both dose and route of administration in our preclinical large animal work.

Capturing new intellectual property around FPP leads

Phylogica is in the fortunate position of being able to 're-start the clock' on its intellectual property portfolio as the company's IP estate matures. This is possible since the methods patents that were obtained for the process of creating the Phylomer libraries continue to be complemented with new 'composition of matter' patents around the specific lead FPPs and cargoes that we have identified.

Phylogica's patent attorneys are currently in the process of drafting a new patent application to capture IP around variants of two of our lead Phylomer FPP families. This filing which is scheduled for this July, will allow Phylogica to publicise details around its exciting findings in high impact publications that we are currently preparing as well as at international conferences. We expect this exposure of our science will help build interest in our technology from prospective alliance partners in the pharmaceutical industry through the independent validation of peer reviewed publication. Phylogica is also planning to further the refresh of our IP estate with a patent filing scheduled for H1 2018 around optimized variants of the iMyc sequences.

Progress on the i-MYC cancer program

- *Progressing our iMyc lead optimisation to improve their potency*

Phylogica has initiated the lead optimisation phase of this program having identified several iMyCs with suitable properties across a range of assays. We are pursuing parallel approaches for optimisation of these iMyc leads by affinity maturation - both a structure based design approach and a random mutagenesis approach, working with international contract research organisations who have extensive experience in these activities.

- *Identification of a biomarker signature to track the specific on target effect of iMyc leads*

Pharmacodynamics (PD) measures the effect of a drug on biological responses in an animal. Since Myc is a transcription factor the most direct means of monitoring specific effects of Myc inhibitors is to monitor their effect on Myc-dependent target genes. These effects should be dose responsive. We have identified a specific and robust signature of dose responsive Myc target genes to monitor PD responses to iMyc inhibitors. We are now complementing the PD studies with investigations to determine the detailed mechanism of action of our iMyc inhibitors.

- *Confirming potent activity of iMyCs across a wide range of blood cancer cell lines*

In addition to a wide range of breast cancer cell lines, we have now confirmed that iMycs also show potent activity in a wide range of human blood cancer cells, including multiple myeloma, acute promyelocytic leukaemia (APL), acute myelocytic leukaemia (AML), and plasmacytoma. We are extending this panel to include additional Myc-dependent cancers to establish the versatility of our iMyc inhibitors which will ultimately inform the breadth of application of our FPP-iMyc conjugate across different forms of cancer.

External collaborations

As previously reported, Phylogica has collaborations with Genentech and Professor Sir David Lane the Chief Scientist of A*Star, Singapore. Although we are unable to provide details of these collaborations due to confidentiality constraints, both are active and proceeding well. We have begun new screens for our partner Genentech, which are already yielding encouraging results around the previously reported expansion of our antimicrobial collaboration.

The efficacy of Phylogica's FPPs are also gaining increased recognition among key academic opinion leaders. For example, collaborators in Professor David Lane's laboratory have shown that Phylogica's FPPs are able to enhance the delivery of their peptides more effectively than other CPP approaches they've tried.

This encouraging technical progress complements the recent announcement regarding appointment of our Executive team and extension of our cash runway. We look forward to updating you on further developments as we approach the critical in vivo evaluation of our two lead assets (FPP and iMyc) in animal models later this year/early in 2018.

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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