PHYLOGICA

BREAKTHROUGH PEPTIDE THERAPEUTICS

26 May 2015

Phylogica Shareholder Update

- **Progress on key in-house breast cancer programs**
- **Collaboration with international breast cancer expert at Harry Perkins Institute**
- **Licensing deal with Cambridge University spin-off Phoremost**
- **Preliminary data confirms Phylogica's novel technology can treat drug resistant breast cancer cells and boost potency of existing cancer drugs**

Letter from the CEO

Dear Shareholders,

Your Company continues to make encouraging progress on its core scientific programs and is now focussing on the next development stage in animal models of cancer.

Underpinning our development strategy is a recently announced collaboration with a world-leading breast cancer expert and an important licensing agreement with a UK biotechnology company to screen our library of novel compounds to potentially develop other drugs.

Phylogica's Proprietary Breast Cancer Programs

Longstanding shareholders would be aware we have been testing our cell penetrating peptide (CPP) technology as a novel way to deliver the biologics drug candidate Omomyc directly into cancer cells, where it can target a previously inaccessible cancer 'master switch' known as MYC.

We have already demonstrated that our drug delivery process, in combination with Omomyc, can kill drug-resistant breast cancer cells in vitro and improve the efficacy of existing anti-cancer drugs.

Building on this, we have continued to advance our internal oncology programme aimed at generating Phylomer-based drugs against these high value cancer targets. These efforts represent an important step towards Phylogica developing its own lead drug oncology candidates.

Harry Perkins Collaboration

International breast cancer expert Adjunct Professor Pilar Blancafort from the prestigious Harry Perkins Institute in Western Australia has agreed to collaborate with Phylogica as the Company prepares to move into preclinical animal studies.

This is an important partnership, bringing impeccable scientific expertise to our investigations at a world-class research facility.

Under Professor Blancafort's guidance, key pilot studies of our CPP technology will be undertaken, designed to determine which of Phylogica's lead compounds will proceed to next stage preclinical animal model development.

We will update shareholders of progress in coming months, but in tandem, we will also be progressing several ongoing strategic collaborations with national and international groups (including the Harry Perkins) aimed at providing further independent validation of our technology.

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Phoremost

In another important development, Phylogica recently announced a new non-exclusive licensing agreement with Phoremost, a private UK-based biotechnology company.

Under the terms of the agreement, Phoremost will access Phylogica's extensive Phylomer libraries for phenotypic screening and small molecule drug discovery.

In return, Phylogica will acquire a 7.5% equity stake in Phoremost, which is progressing its own small molecule oncology program.

Shareholders should note this deal has been weighted to protect our commercial rights to all peptide-based therapeutics emanating from the collaboration – essentially preventing Phoremost from competing against our core business.

We also retain non-exclusive rights to the novel cancer targets and the Phylomer peptides identified via the Phoremost screening process, along with a first-right to negotiate exclusivity.

We are extremely satisfied with this arrangement as we believe it has potential to unlock significant value for Phylogica investors.

We remain open to engaging in other strategic partnerships aimed at unlocking further value from our proprietary Phylomer platform.

Response to Presentations at International Conferences

In May, Phylogica presented its exciting functional FPP validation data at two influential international conferences on peptides and protein therapeutics:

1. The IBC TIDES meeting in San Diego (http://www.ibclifesciences.com/TIDES/overview.xml) and

2. The Next Generation Protein Therapeutics Summit in San Francisco (http://www.ibclifesciences.com/ProteinSummit/agenda.xml). The response to both of these presentations was excellent resulting in 8 invitations to present to interested Pharma companies. These technical presentations are available from the Phylogica company website.

Finally

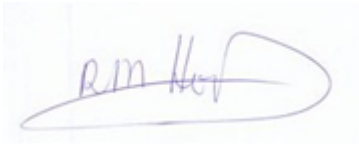
Finally, shareholders can be assured the Company's scientific programs are being strategically and methodically progressed.

We are now poised to enter a critical development phase, as we translate our technology into animal models of disease.

This data will enable us to define a clear path to preclinical development, which is where value creation can begin in earnest.

We thank you for your ongoing support.

Yours faithfully,



Dr Richard Hopkins
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Science Update

Progress Towards Fully Proprietary Phylomer-based Cancer Drugs

The Phylogica research team has focused on developing our own proprietary drugs against key oncology targets, including N-Myc and c-Myc. We have continued to make encouraging progress including:

- Selecting a panel of high-value cancer targets (including MYC)
- Successfully screening our Phylomer libraries against these targets generating hundreds of hits or binders
- Most recently, screening a pool of >100 MYC hits in appropriate cell-based biological assays to determine whether they are functionally active against MYC. I'm pleased to report that we've identified a panel of Phylomers able to inhibit MYC activity *in vitro* with a significant number showing equal or better activity that OmoMyc.

This is an encouraging outcome as it represents the penultimate stage-gate to confirming whether we can generate fully proprietary molecules. The last step will involve linking these hits to our own cell penetrating Phylomers and then deliverying them as drugs into cells to assess their level biological activity. We remain on-track to complete these studies over the 2-3 months

Harry Perkins Collaboration

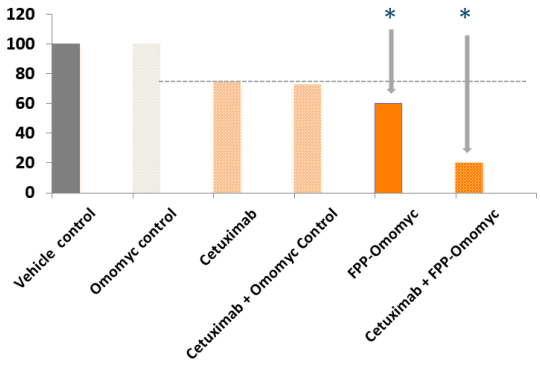
In collaboration with Perth-based Harry Perkins Institute, Phylogica has confirmed that its functional penetrating peptides (FPPs) linked to a biologic drug have escalated potency against particularly aggressive drug resistant breast cancer cells.

These preliminary results are part of an ongoing collaboration with the Harry Perkins Institute, aimed at providing independent validation of the Phylomer FPPs for delivery of intracellular biologics. FPPs derived from Phylomer libraries have previously been shown to be 37-160 times more efficient at intracellular delivery of biologic cargoes, including Omomyc – a potent inhibitor of one of the most sought after cancer targets known as MYC.

In collaboration with one of Australia's leading breast cancer experts, Adjunct Professor Pilar Blancafort at the Harry Perkins Institute in Perth Western Australia, Phylomer FFPs were used to deliver a panel of anti-cancer peptides and proteins. Professor Blancafort discovered intracellular delivery of FPPs fused to Omomyc was able to kill aggressive drug resistant breast cancer cells known as T11 with high potency. These breast cancer cells are known as 'triple negative' as they lack receptors for drugs such as Herceptin and Tamoxifen, which are often used to treat breast cancer.

In another significant finding, Professor Blancafort also observed that the FPP-Omomyc fusion worked co-operatively with existing anti-cancer drugs to significantly improve their activity *in vitro*. For example, when FPP 1746-Omomyc was added in combination with the FDA approved antibody drug Cetuximab, the effect on viability of the breast cancer cells was greater than either agent alone (see figure 1).

Fig. 1**: Effect of combining anti-tumour antibody and Phylomer FPP 1746-Omomyc on viability of triple negative breast cancer cells *grown in vitro***



Legend: 'Vehicle Control' contained only the buffer in which drugs were dissolved. 'Omomyc Control' containing the Omomyc cargo with no FPP intracellular delivery sequence, and the FPP-Omomyc test protein were each added at a concentration of (1μM), while the Cetuximab antibody was delivered at a concentration of (5μM), in all cases. The asterisk and arrows denote statistically significant decreases in viability, over the corresponding vehicle control.

The Y axis denotes percentage viability over the vehicle control.

A similar observation of drug synergy was observed for another FDA approved anti-cancer drug Docetaxel, where the addition of sub-micromolar doses of Phylomer FPP delivered cargoes allowed the dosage of the cancer drug Docetaxel to be reduced to only 50nM while still killing the cancer cells. This observation of *in vitro* drug synergy has particular clinical significance as Docetaxel is toxic at high doses, limiting its therapeutic application and usefulness for treatment of aggressive, resistant tumours.

Professor Pilar Blancafort commented*:* "The ability to combine drugs to treat breast cancer is particularly exciting as it lowers the likelihood of resistance, improves drug activity and potentially reduces chemotherapy side effects."

In a final pilot study the aggressive T11 breast cancer cells were used to generate tumours in an *in vivo* model of breast cancer. Once established, tumours were then injected with 30 nanomoles of the Phylomer FPP-Omomyc fusion every second day for seven days. A substantial reduction in tumour size was observed in tumours injected with FPP-Omomyc when compared to those injected with either Omomyc lacking the FPP or any added protein.

Recent examination of pathology specimens using microscopy revealed that tumours treated with the Phylomer/Omomyc fusion showed less evidence of cancer cell proliferation and more evidence of cancer cell death than those treated with the Omomyc or vehicle alone.

While this is a very encouraging outcome, this pilot study was undertaken using only a small number of tumours (three in each group) and needs to be repeated using larger groups to confirm its significance and determine the optimal dosing regimen.

Work is already underway to repeat this pilot with an expanded study and also to develop injectable formulations to be validated in appropriate animal models.

Phoremost Agreement

In April Phylogica announced a licensing agreement with Phoremost, a private biotechnology company based in the UK. Under the agreement, Phylogica grants to Phoremost a world-wide, non-exclusive license to use certain Phylomer libraries solely for phenotypic screening. Their aim is to screen for novel targets involved in diseases, such as cancer, and then to develop small molecule drugs against these targets.

What is Phenotypic screening?

Phenotypic screening is used in drug discovery to identify compounds, such as small molecules, peptides or RNAi, that alter the appearance or behaviour (phenotype) of a cell or organism in a desired manner. For example, a common phenotypic screen in cancer might involve a search for drugs able to cause death or cell differentiation – considered highly desirable properties for a cancer drug. Notably a high proportion of drugs that have come to market were discovered using phenotypic screening approaches.

Why is Phoremost interested in the Phylomer libraries for phenotypic screening?

The high structural diversity offered by the Phylomer libraries makes them very powerful tools to efficiently probe the entire intracellular landscape for novel targets involved in disease. To achieve this, Phylomer libraries will be screened for the ability to modulate the activity of intracellular targets in a manner that generates the desired phenotype (eg cell death in the case of a cancer screen).

Once a Phylomer has been shown to generate a phenotype of interest the next step is to determine what targets it binds to inside the cell. These are known as target identification screens and they take advantage of another important feature of the Phylomer peptides. Here the Phylomers are used as hooks to 'fish-out' the appropriate target from the soup of proteins found inside the cell.

Once the targets have been captured and identified, Phylomers can then be used to map the binding interface on the target protein. This

information is critical for Phoremost to initiate programs aimed at developing small molecule drugs against these targets. Importantly, this same information can also be used by Phylogica to launch peptide-based therapeutics programs.

So Phenotypic screens yield three important outcomes:

- Information about novel targets involved in disease = High Commercial Value
- Phylomer peptides validated for the ability to inhibit novel drug targets
- High resolution information on target binding interfaces that help inform the process of drug design, including the design of small molecule drugs.

What does Phylogica gain from the Phoremost agreement?

The agreement has been weighted to ensure that a number of benefits flow back to Phylogica including:

- Access to non-dilutive funds (potentially millions of pounds) to drive platform development.
- A 7.5% equity stake in Phoremost – which is progressing its own small molecule oncology program.
- Rights to enter non-exclusive agreements with other parties although the number of these agreements is capped during the 18 month preference period.
- Commercial rights for all peptide-based therapeutics that prevents Phoremost from competing against our core business.
- Non-exclusive rights to the novel cancer targets and the Phylomer peptides identified from the Phoremost screens, along with a first-right to negotiate exclusivity.
- An opportunity to replenish Phylogica's own oncology pipeline with novel targets and functionally validated Phylomers.

PhoreMost's CEO, Dr Chris Torrance, co-founded and commercialised Horizon Discovery. This pioneering phenotypic screening company recently floated on the London Stock Exchange and is currently valued at about £150 million. Horizon has developed powerful screening tools based on a technique called RNAi (i=inhibition) that disables specific genes.

About Phylogica

Phylogica Limited (ASX: PYC) is a biotechnology company based in Perth, Australia with a world-class drug discovery platform harnessing the rich biodiversity of nature to discover novel peptide therapeutics from the most structurally diverse libraries available. The Company listed on the ASX in 2005 as a spin out from the Telethon Kids Institute (Perth, Australia) and the Fox Chase Cancer Centre (Philadelphia, USA). The Company's drug discovery platform is based on its proprietary Phylomer® libraries containing over 400 billion unique natural peptides, which have been optimised by evolutionary selection to adopt stable drug-like structures. Phylogica offers fully integrated drug discovery services to the pharmaceutical industry utilising its Phylomer® libraries and proprietary screening technologies in exchange for licence fees, milestones and royalties. Partners from discovery alliances within the last 5 years include Roche, MedImmune, Pfizer, Janssen, Cubist Pharmaceuticals and Genentech.

About Phylomer® Peptides

Phylomer peptides are derived from biodiverse natural sequences, which have been selected by evolution to form stable structures. These bind tightly and specifically to disease associated target proteins, both inside and outside cells. Suitable targets for blockade by Phylomers include protein interactions that promote multiple diseases, such as infectious diseases, cancer, autoimmunity and heart disease. Phylomer peptides can have drug-like properties, including specificity, potency and thermal stability, and can be produced by synthetic or recombinant manufacturing processes. Phylomer peptides are also readily formulated for administration by a number of means, including parenteral or intranasal delivery approaches. Current Phylomer libraries comprise more than 400 billion distinct sequences derived from thousands of protein structure families encoded by biodiverse genomes, representing the most structurally diverse peptide libraries available. Phylomer peptides have also been demonstrated to have world-class cell penetrating ability, enabling them to deliver protein cargoes with unprecedented efficiency.

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