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Pivot from developing drugs to commercialising the platform

Value proposition: Enhance existing drugs to address a massive 250B USD (CAGR 10.6%) market

1. Bring drugs to the right place (i.e. to intracellular targets)
2. Enhance properties of drugs (i.e. improve therapeutic window)
3. Reduce discovery cycle time (by dramatically improving profile)
Our advantage is in using our assets as a platform to solve pharma problems

Phylogica has a unique selection of valuable assets …

- **Complex, rich Phylomer library** – provides tremendous value and flexibility in either target identification or drug discovery

- **Well validated platform** technology – *in vivo* work demonstrates delivery and Pharma deals with Genentech, MedImmune, Pfizer, Janssen Biotech, and Roche

- **Strong patent position** - international patents in place, latest endothelial cell structures granted in October

… huge potential market

- **Unmet need** – undruggable $250Bn growth market, intracellular hurdles across Pharma

- **Blue sky potential** - extensive Phylomer library to screen for diverse cargo classes and cell specificities

- **De-risked investment opportunity** - progressing 3 asset groups - intracellular delivery (delivery), biologic therapeutic solutions (delivery and cargo), and new drug discovery (screen for new targets)
Drug discovery growth stagnating as biologics currently limited to extracellular targets (unable to enter cells)

**The problem?**

Biologics
- Antibodies
- Scaffolds
- Proteins

**Our solution?**

We can bring biologics into the cell, unlocking the potential of these powerful drugs by allowing them to reach intracellular targets

**Our Functional Penetrating Peptides (FPPs)**
can deliver biologics into the cell
The Problem: drug cargoes are trapped in the endosomes

Conventional CPPs are often only active at concentrations of > 10 µM limiting feasible clinical applications (toxicity and high costs)
Harnessing the Microbiome for new Phylomer libraries

Our Solution: Phylogica’s endosomal escape screen

1. Phage is taken up by endosomes
2. FPP mediates phage release
3. Biotinylation of Avitag
4. Capture of biotinylated phage on Streptavidin beads

Our endosomal escape screen identifies FPPs that can escape the endosome allowing functional delivery of cargoes into the cytoplasm.
Phylogica’s FPPs allow functional delivery of therapeutic cargoes into the cytoplasm

**Cargoes**
- Peptides/proteins
- Enzymes
- Oligonucleotides
- Immunotoxins
- Bispecifics
- Enzymes
- Cell Type
- Cancer cell lines (Blood, breast, bone)
- Dendritic cells
- Liver and kidney cells
- Muscle cells (leg, diaphragm, heart)

Phylomer FPPs are **efficient, rapid and safe**

FPP-cargo

60 min
PYC has shown conclusively that FPPs work in animal models.

Inhibition of tumor growth in mouse cancer model

Restoring dystrophin levels by FPP mediated delivery of DMD PMO

Collaborator: Pilar Blancafort, Harry Perkins Institute

Collaborator: Sue Fletcher, Centre for Comparative Genomics
Efficient cytosolic delivery of proteins using a split β-lactamase complementation assay

Stably transfected mammalian cell

Only endosomal escape leads to β-lactamase complementation and signal development

CHO-CBLA cells incubated with 1746c27-NBLA (8 µM)

30 min

60 min

120 min
1746c27 has been significantly improved upon, and new variants are being validated in vitro.
Into 2018, PYC is validating a comprehensive matrix of FPPs - delivery of cargoes into different cell types

Hasegawa et al., 2013, Exp. Anim.62(4), 295-304
Phylogica’s collaboration with Cancer Immunology at the Telethon Kids Institute

- Phylogica co-located with the Telethon Kids Institute in Perth

- In 2015, Phylogica started collaborating with Jason Waithman, the head of TKI’s Cancer Immunology group, to investigate melanoma

- Skin cancer is a major problem in Australia:
  - 76,734 skin cancer cases treated in Western Australia in 2010 alone

- Cross-presenting Dendritic cells offer an attractive target for antigen delivery and the potential for peptide vaccines against a range of cancers

- Key synergy - Phylogica’s FPPs deliver cargoes to the cytoplasm allowing MHC-I processing, thus CD8+ expansion

Jason Waithman, Telethon Kids Institute (left) & Shane Stone, Phylogica
FPP efficiently targets cross presenting dendritic cells (DCs) for an effective peptide vaccine

1. Targeting

1746 and XCR1 ligand facilitate internalisation into cells

2. Internalisation, endosomal escape and MHC loading

Only FPPs escaping into the cytosol will result in CD8+ T cell expansion via MHC I loading

3. T cell expansion

4. CD8+ T cells attack tumor
Subcutaneous B16 melanoma model engineered to express glycoprotein B (gB) from Herpes Simplex Virus

Peptide vaccine contains a well characterized CD8+ T cell gB peptide epitope with and without FPP

Our FPP peptide vaccine approach:

- Primes tumor specific CD8+ T-cells
- FPP containing peptide vaccine retards tumor growth greater than non-FPP control
- FPP-peptide vaccines have the potential to synergize with existing immunotherapies

In progress validation - FPP peptide vaccine retards tumor growth

Collaborator: Jason Waithman, Telethon Kids Institute

(Refer ASX release dated 8 January 2018)
Partnering strategy: Genentech work continues to be successful

- Isolating Phylomers that can help kill gram-negative bacteria (multi-drug resistant “super bugs”)
- Evaluation period end of CY 2019

Antibiotic

Phylomer

Phylomer-Antibiotic

increased antimicrobial range

Pseudomonas aeruginosa
Building on the success of the past, turning towards the future of FPPs

**Building Therapeutics Logically**

- Identify FPPs that work well in different cell types and tissues
- Select best FPPs for each cargo
- Provide the tools that will allow us to optimize our customer’s drugs

**New Technologies**

- HTP automation to rapidly discover the best molecules in our new libraries
- Working with some of the best chemists in USA and Asia to use FPPs for siRNA delivery
  
  “Cell specific delivery of siRNA by FPPs would open a universe of therapeutic opportunities”
  
  Pharma Exec

- Collaboration with alternative scaffold company under discussion
  
  - Small, super stable, antibody-like proteins, that bind to therapeutic targets with excellent affinity
  - Easy to rapidly identify those that inactivate proteins involved in disease
### Typical drug discovery process

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug Discovery</strong></td>
<td>5 years</td>
</tr>
<tr>
<td><strong>Preclinical</strong> (animal testing)</td>
<td>1.5 years</td>
</tr>
<tr>
<td><strong>Clinical</strong> (human trials)</td>
<td>6 years</td>
</tr>
<tr>
<td><strong>FDA Approval</strong></td>
<td>1-2 years</td>
</tr>
</tbody>
</table>

### Typical Timelines

- Determination of a suitable drug
- Drug safety & efficacy in animals
- Drug safety & efficacy in humans
- Regulatory approval for commercialisation

### Key Milestones

- **Value of PYC platform**
  - Highly attractive for Pharma customers
    - Significantly improve the profile of customer drugs
    - Massively shorten the discovery phase
    - Customers reach their value inflection points faster
To achieve PYC – the Platform: we need to be laser focused on 3 goals

1. **Proving the value proposition of our platform**
   - Deliver *in vivo* functional validation
   - Demonstrate the *improvement potential* of existing FPPs
   - Enrich and validate our library

2. **Transforming our operations to achieve scale**
   - Reduce discovery and validation *cycle times* with automation
   - Engage *world class CROs* to drive scale

3. **Turbocharging our commercial engine**
   - Close multiple deals across therapeutic areas
   - Grow *existing collaborations*
   - Focus on how Phylogica’s technology *solves critical problems*

**Outcome:**
A validated, sought after platform that helps Pharma customers create better drugs for patients and unlocks significant, sustainable cash flow for Phylogica
Thank you

For more information contact
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roberth@phylogica.com