Phylogica: Pivot to Platform

- BioShowcase Presentation
- By CSO Dr Robert Hayes
- January 2018

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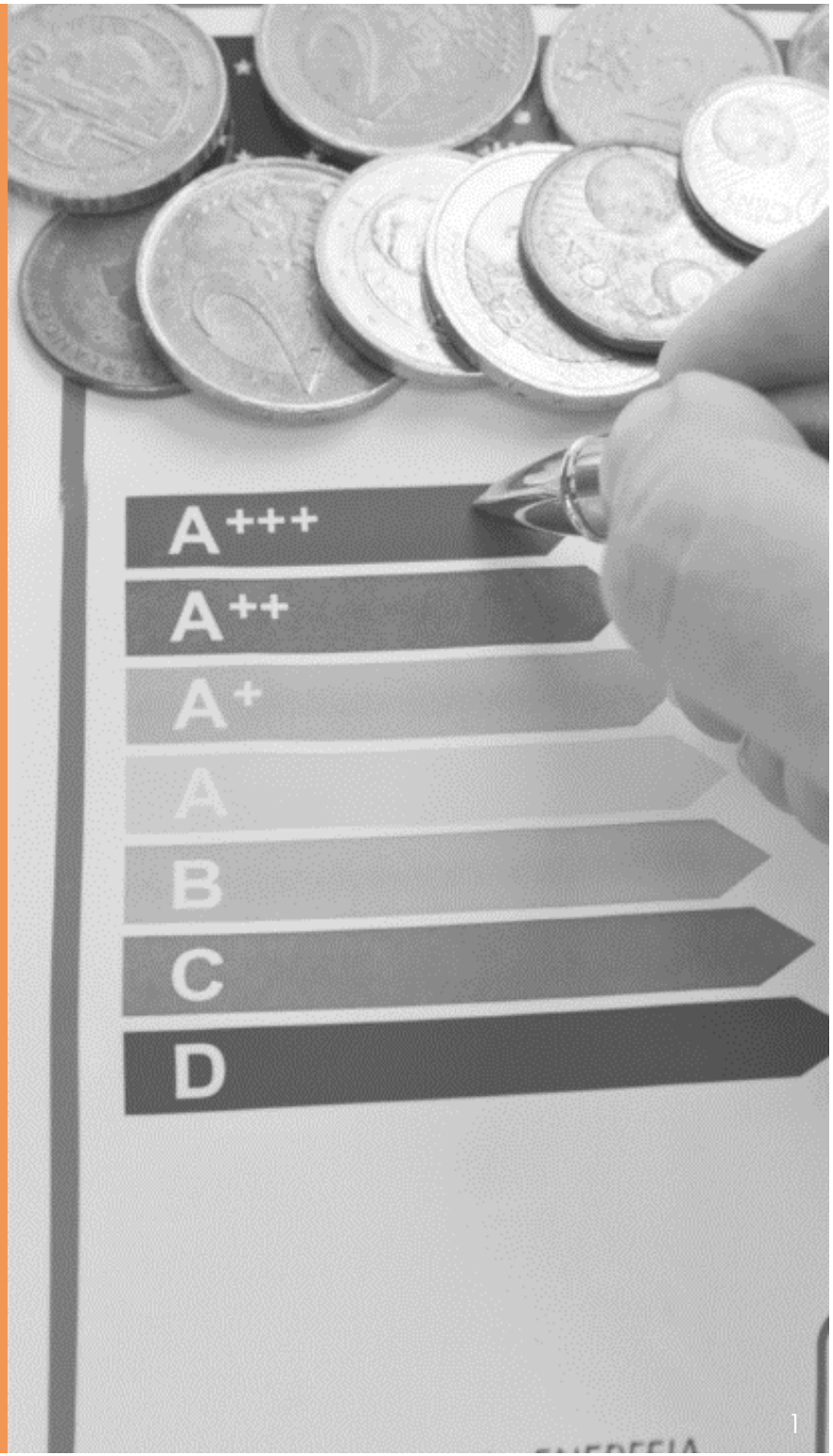


Pivot from developing drugs to commercialising the platform

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

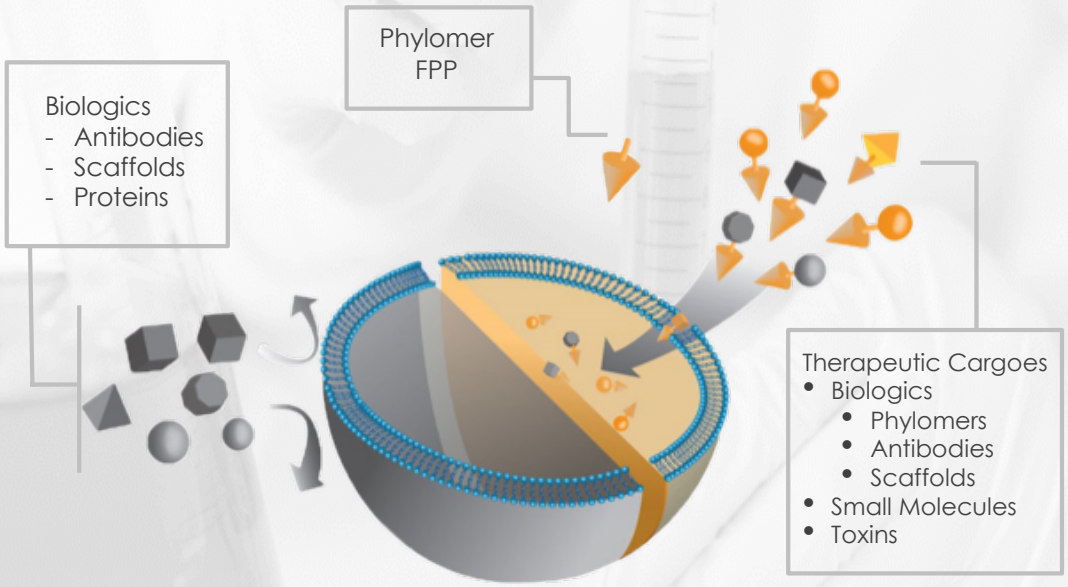
… huge potential market

- **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)

Significant constraints in existing drug discovery approaches

The problem?

Drug discovery growth stagnating as biologics currently limited to extracellular targets (unable to enter cells)

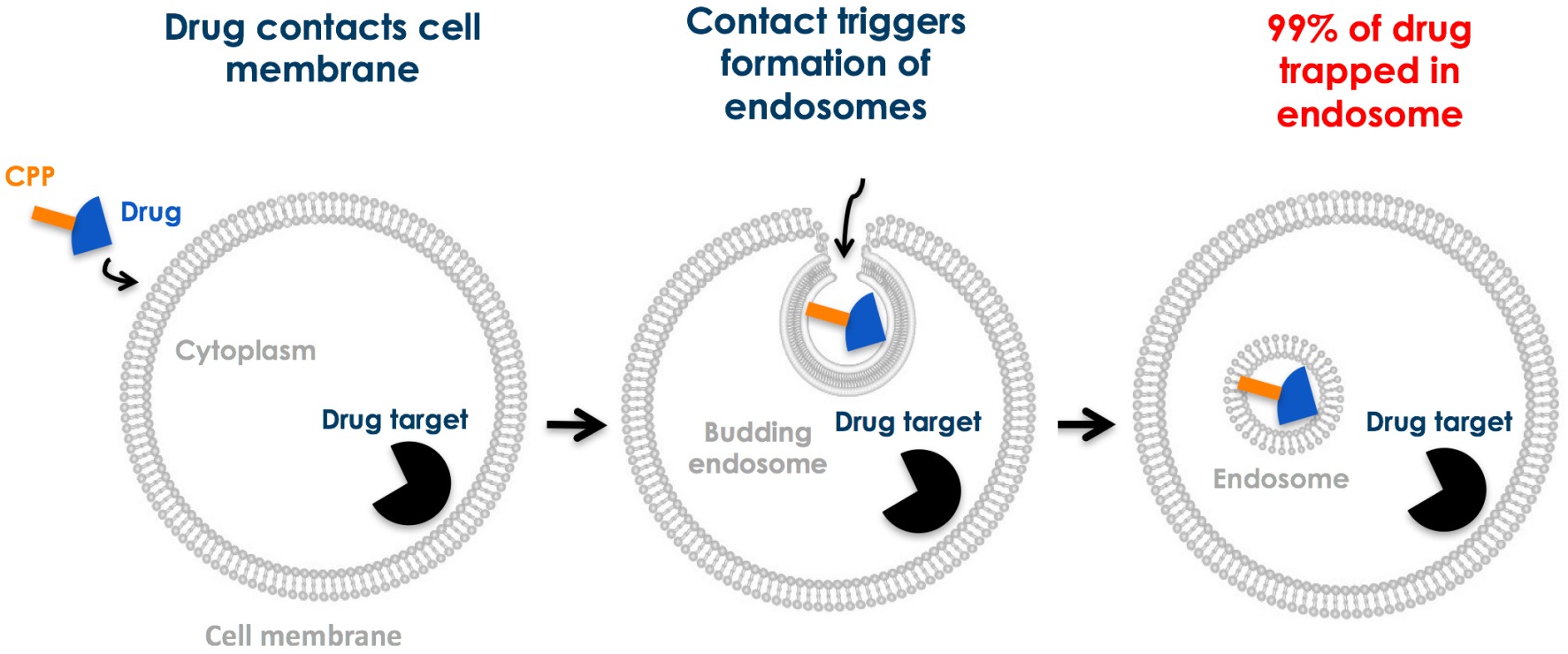


Our Functional Penetrating Peptides (FPPs) can deliver biologics into the cell

Our solution?

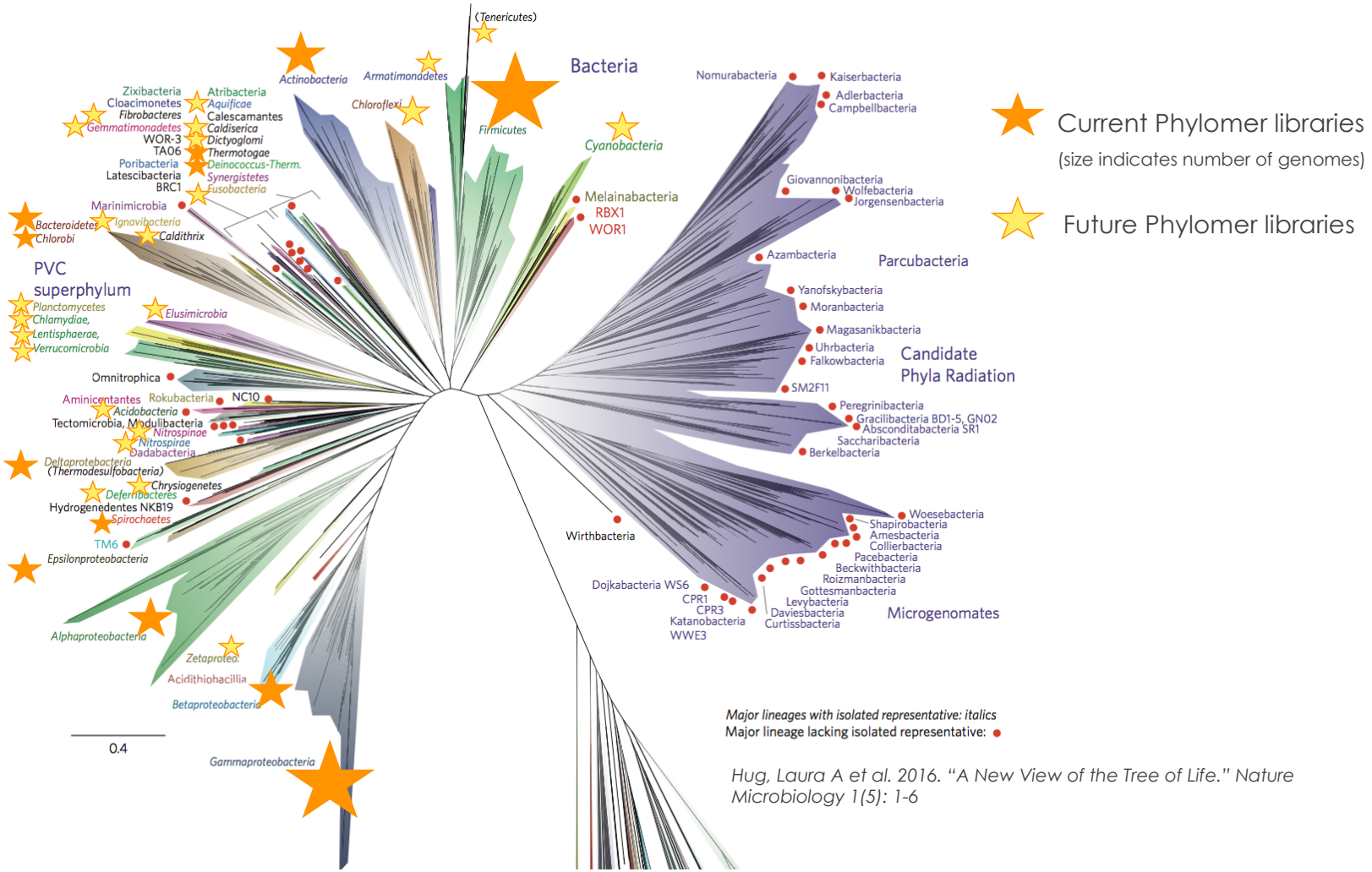
We can bring biologics into the cell, unlocking the potential of these powerful drugs by allowing them to reach intracellular targets

The Problem: drug cargoes are trapped in the endosomes



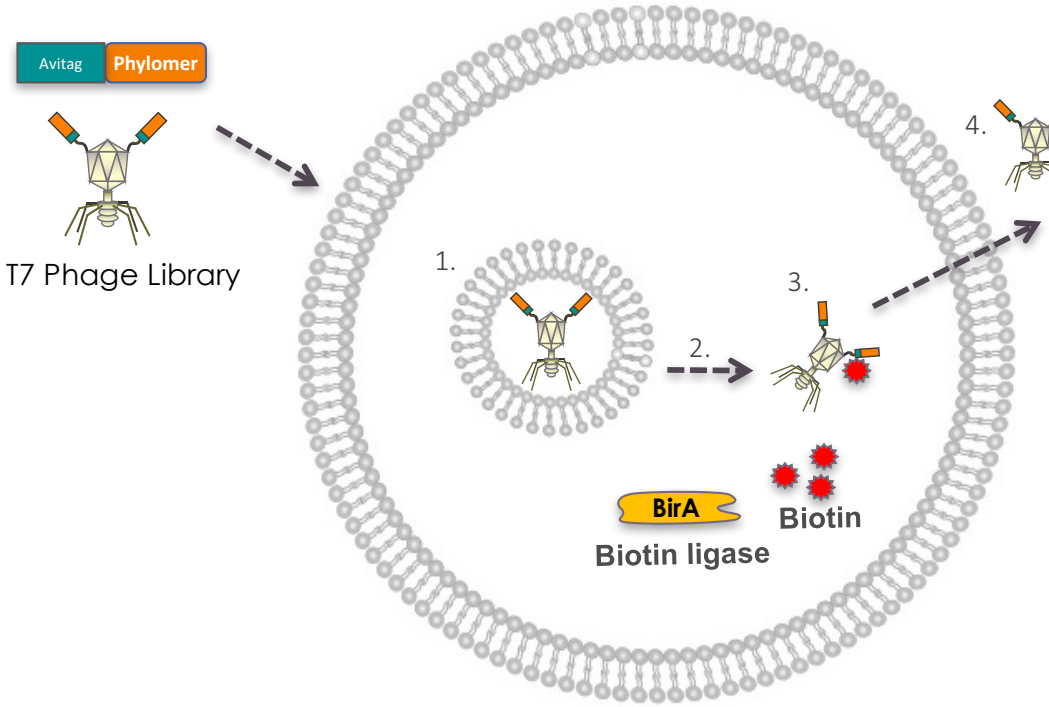
Conventional CPPs are often only active at concentrations of > 10 μM limiting feasible clinical applications (toxicity and high costs)

Harnessing the Microbiome for new Phylomer libraries



Hug, Laura A et al. 2016. "A New View of the Tree of Life." Nature Microbiology 1(5): 1-6

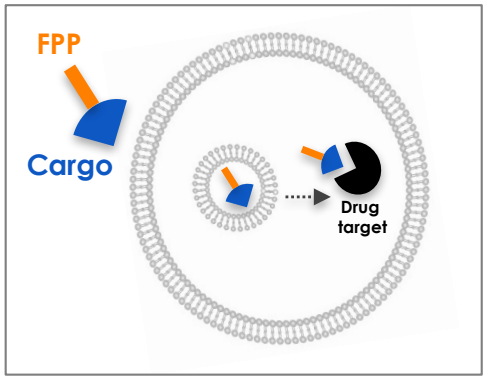
Our Solution: Phylogica's endosomal escape screen



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

FPP Bim Omomyc FPP

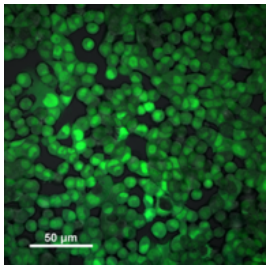
Cell Type

Cancer cell lines (Blood, breast, bone)

Dendritic cells

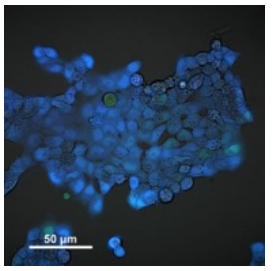
Liver and kidney cells

Muscle cells (leg, diaphragm, heart)



FPP-cargo

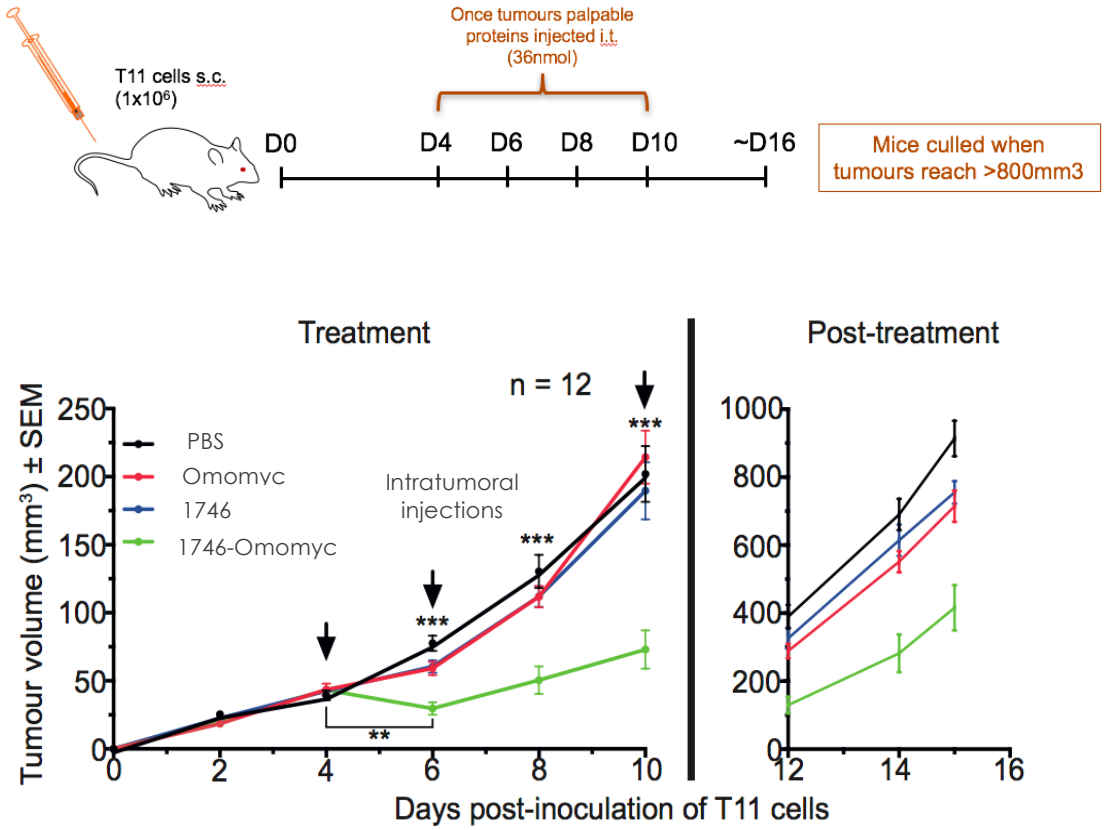
60 min



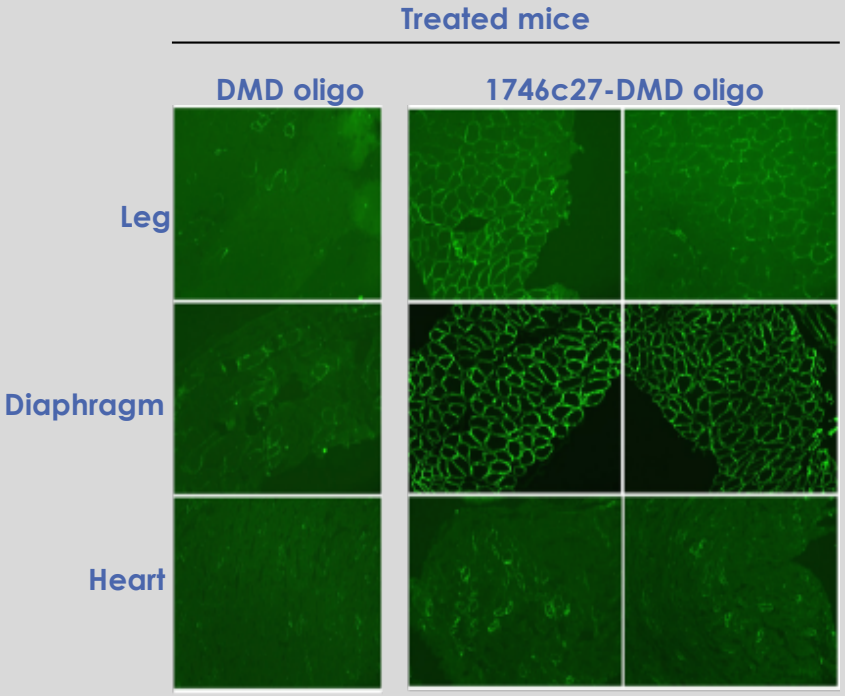
Phylomer FPPs are **efficient**, **rapid** and **safe**

PYC has shown conclusively that FPPs work in animal models

Inhibition of tumor growth in mouse cancer model



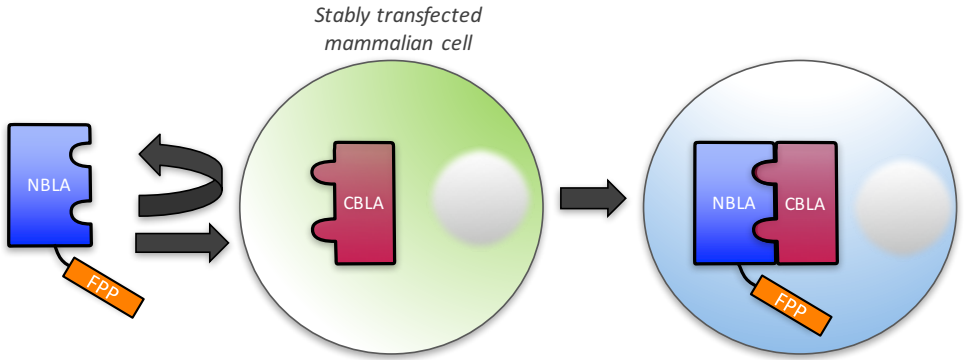
Restoring dystrophin levels by FPP mediated delivery of DMD PMO



Collaborator: Pilar Blancafort, Harry Perkins Institute

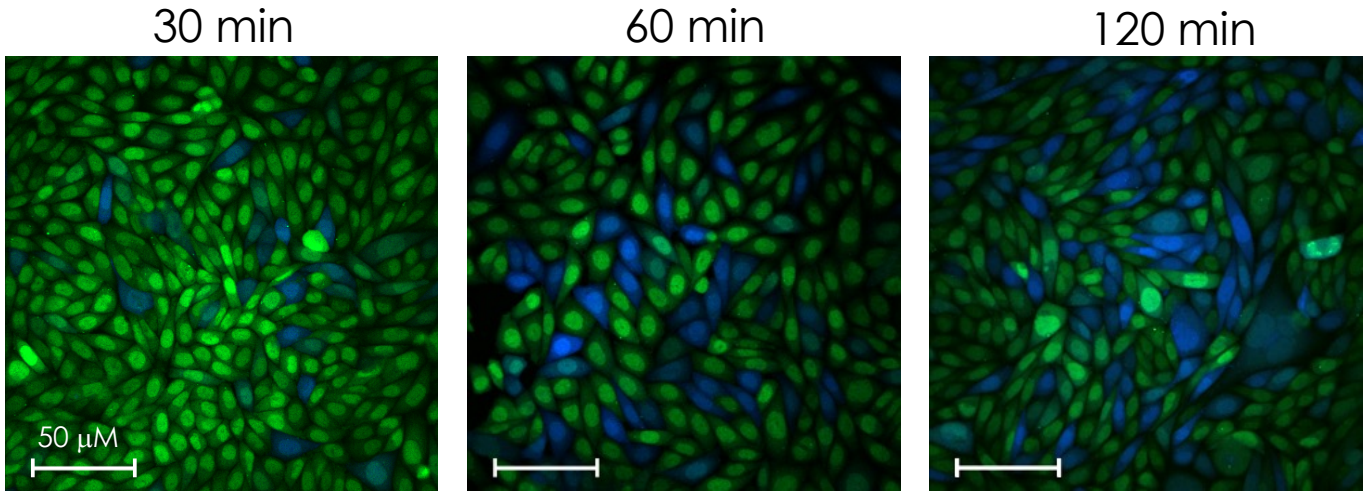
Collaborator: Sue Fletcher, Centre for Comparative Genomics

Efficient cytosolic delivery of proteins using a split β-lactamase complementation assay



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

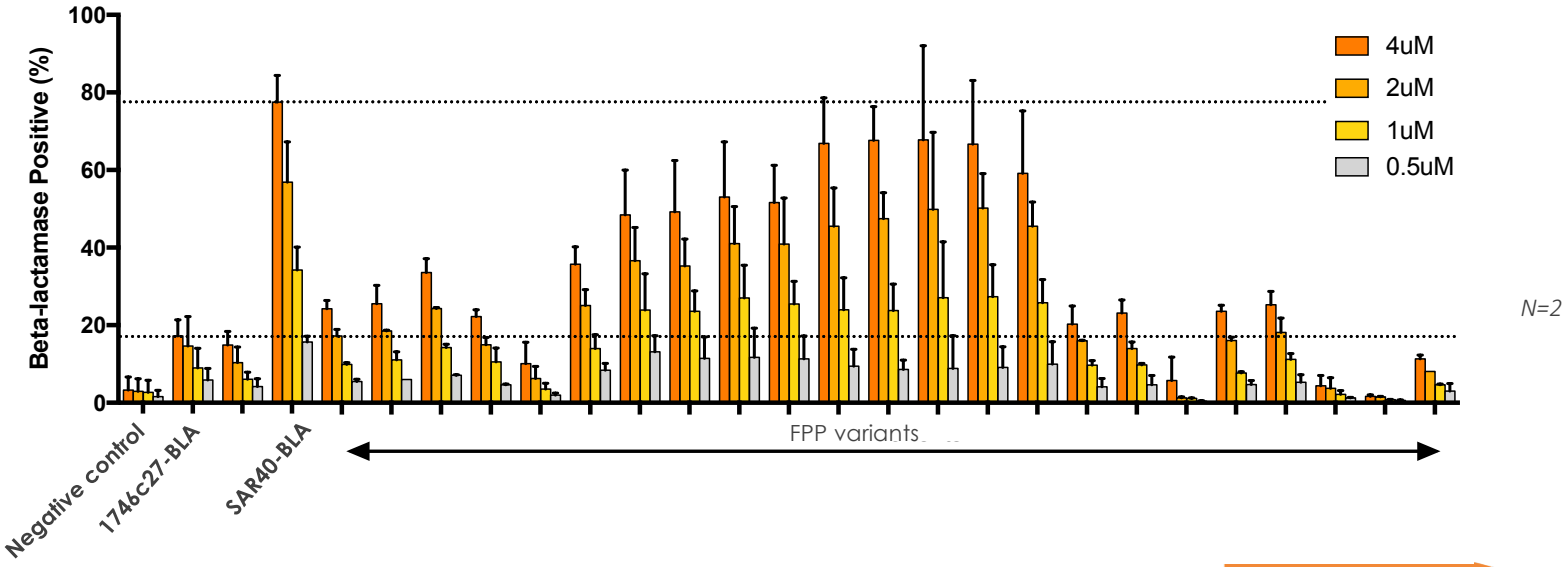
CHO-CBLA cells incubated with 1746c27-NBLA (8 μM)



1746c27 has been significantly improved upon, and new variants are being validated *in vitro*

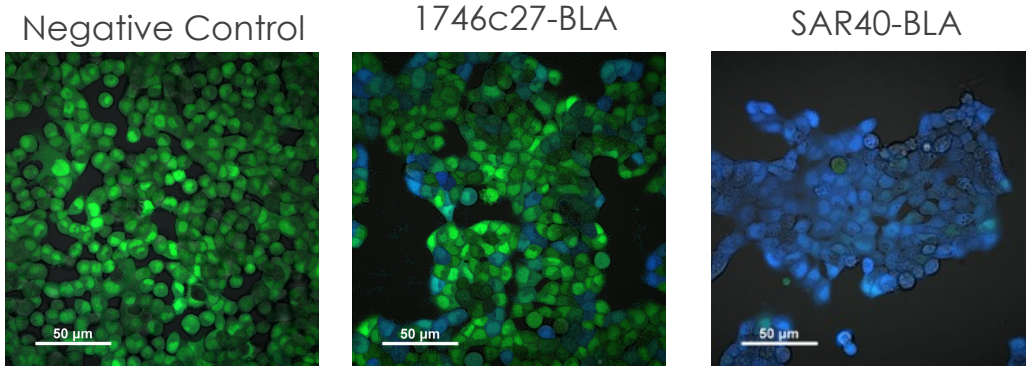
Flow cytometry

CHO-K1 cells
(1 h treatment)



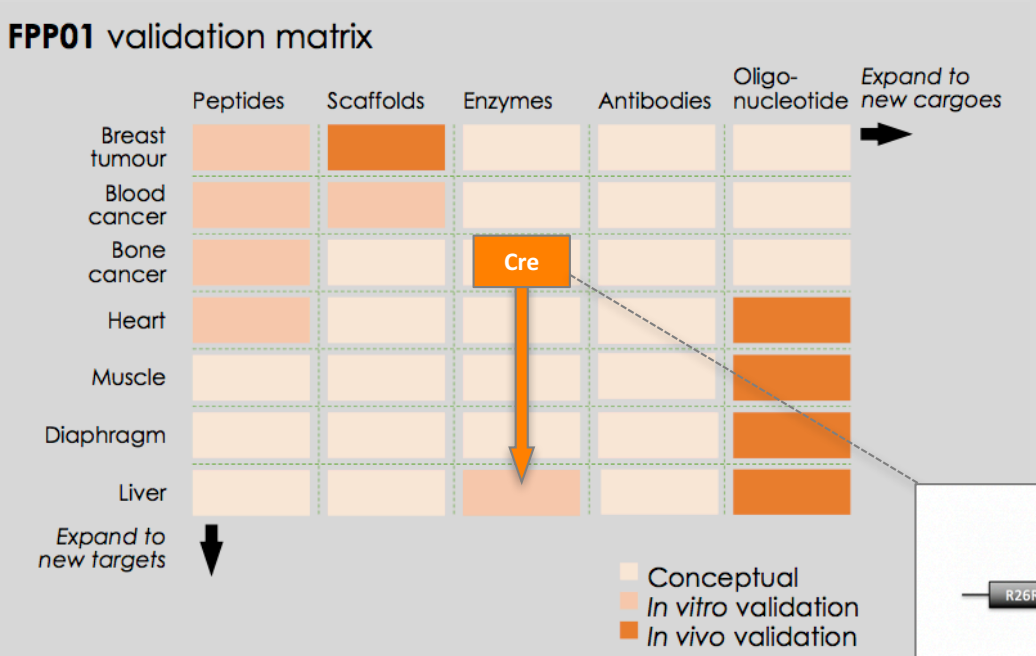
Confocal microscopy

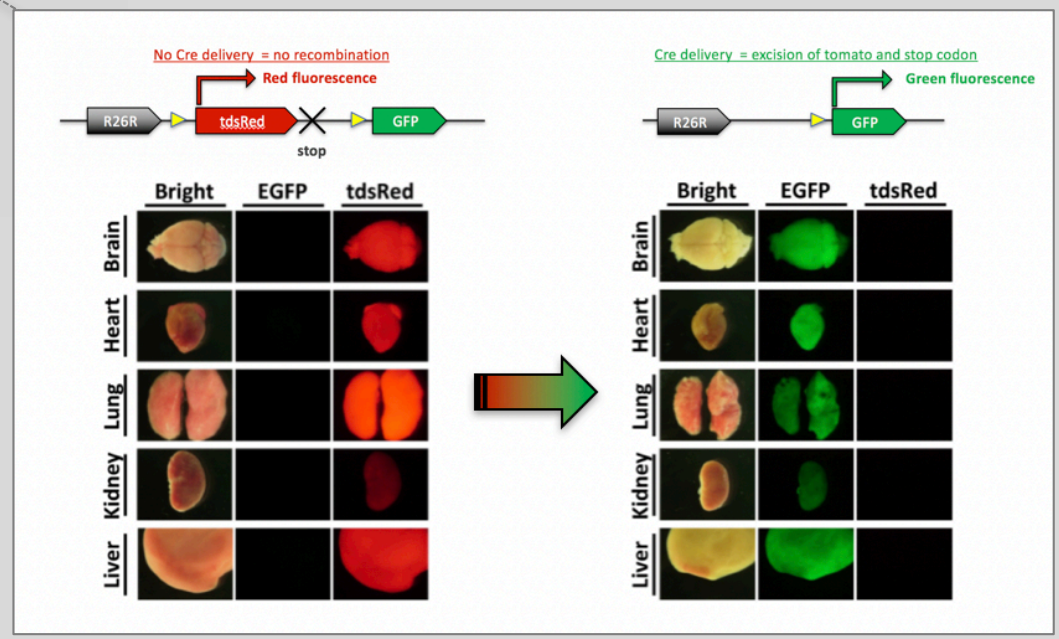
T47D cells
(4 µM, 1 h treatment)



Phylogica's FPP improvement program through rational design has demonstrated the ability to enhance potency with no increase in toxicity

Into 2018, PYC is validating a comprehensive matrix of FPPs - delivery of cargoes into different cell types

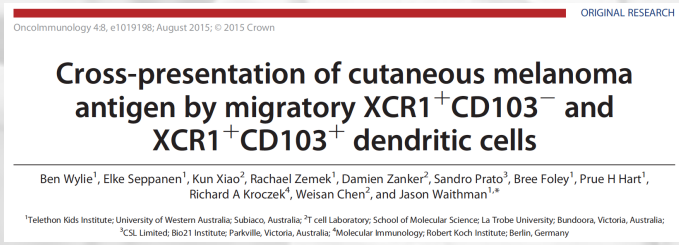




Hasegawa et al, 2013, *Exp. Anim.62(4), 295-304*

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



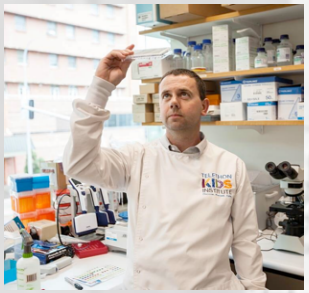
ORIGINAL RESEARCH

OncoImmunology 4:8, e1019198; August 2015; © 2015 Crown

Cross-presentation of cutaneous melanoma antigen by migratory XCR1^{+}CD103^{-} and XCR1^{+}CD103^{+} dendritic cells

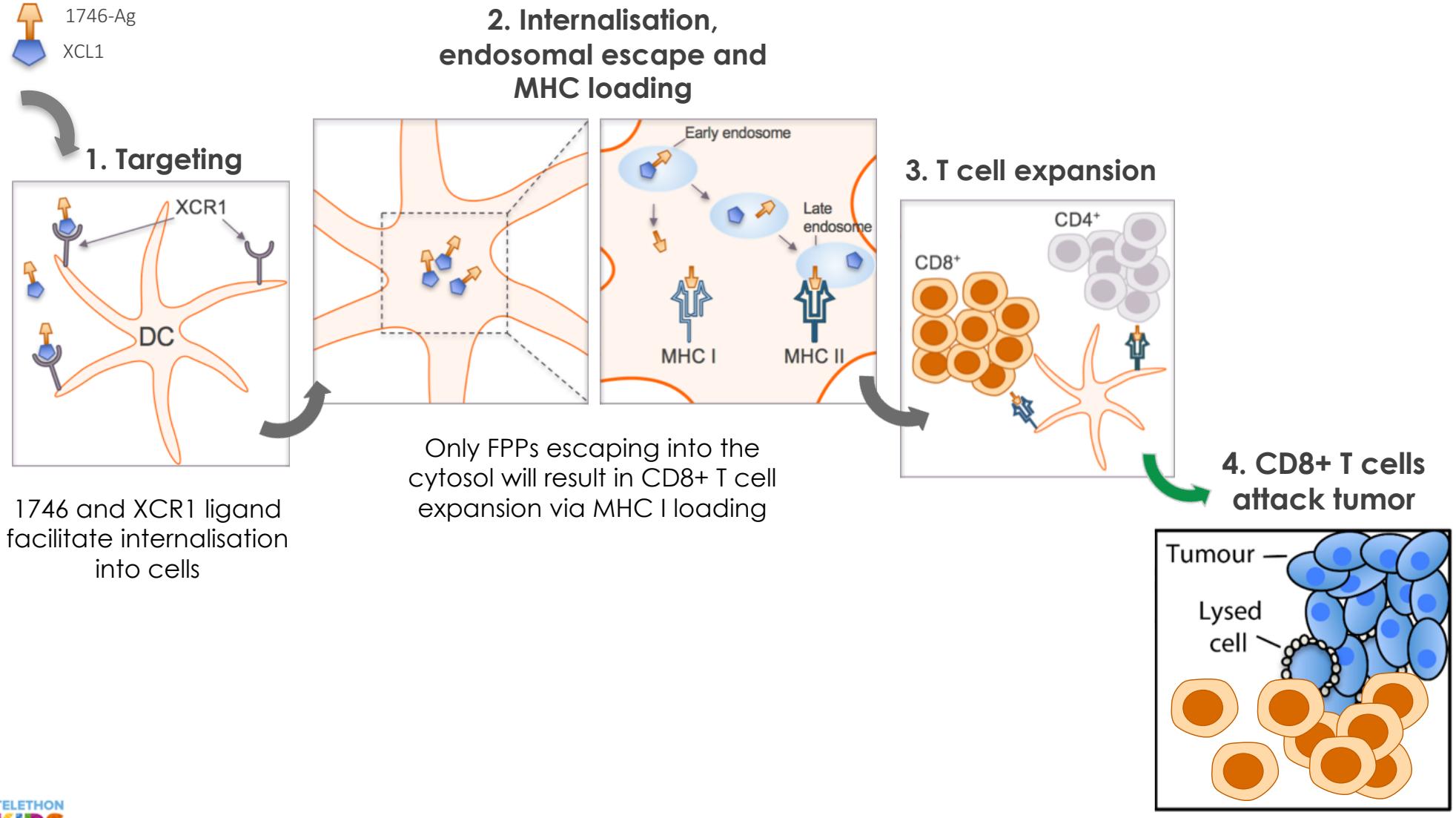
Ben Wylie[1], Elke Seppanen[1], Kun Xiao[2], Rachael Zemek[1], Damien Zanker[2], Sandro Prato[3], Bree Foley[1], Prue H Hart[1], Richard A Kroczek[4], Weisan Chen[2], and Jason Waithman[1,*]

[1]Telethon Kids Institute; University of Western Australia; Subiaco, Australia; [2]T cell Laboratory; School of Molecular Science; La Trobe University; Bundoora, Victoria, Australia; [3]CSL Limited; Bio21 Institute; Parkville, Victoria, Australia; [4]Molecular Immunology; Robert Koch Institute; Berlin, Germany

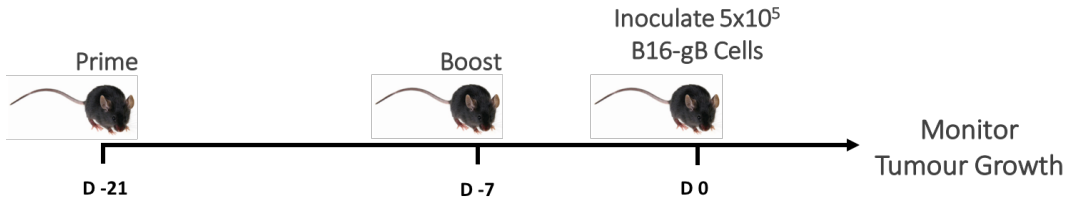


Jason Waithman, Telethon Kids Institute (left) & Shane Stone, Phylogica

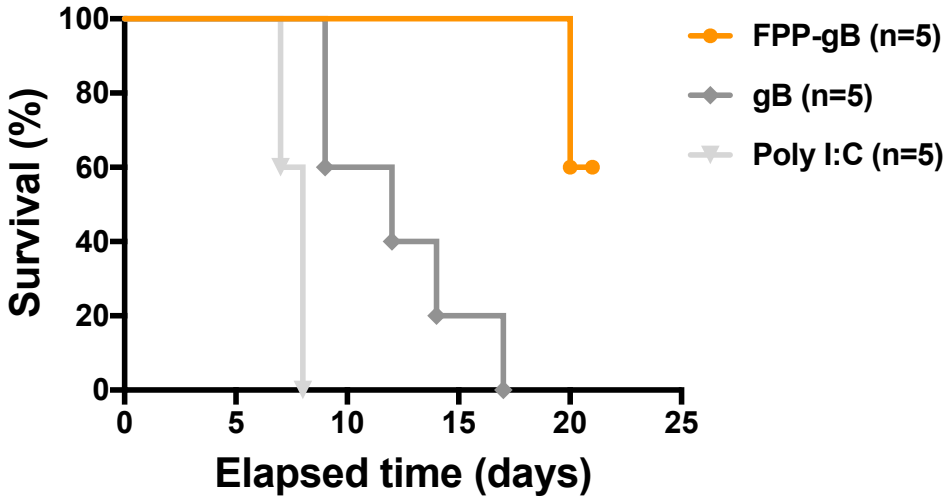
FPP efficiently targets cross presenting dendritic cells (DCs) for an effective peptide vaccine



In progress validation - FPP peptide vaccine retards tumor growth



- 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:

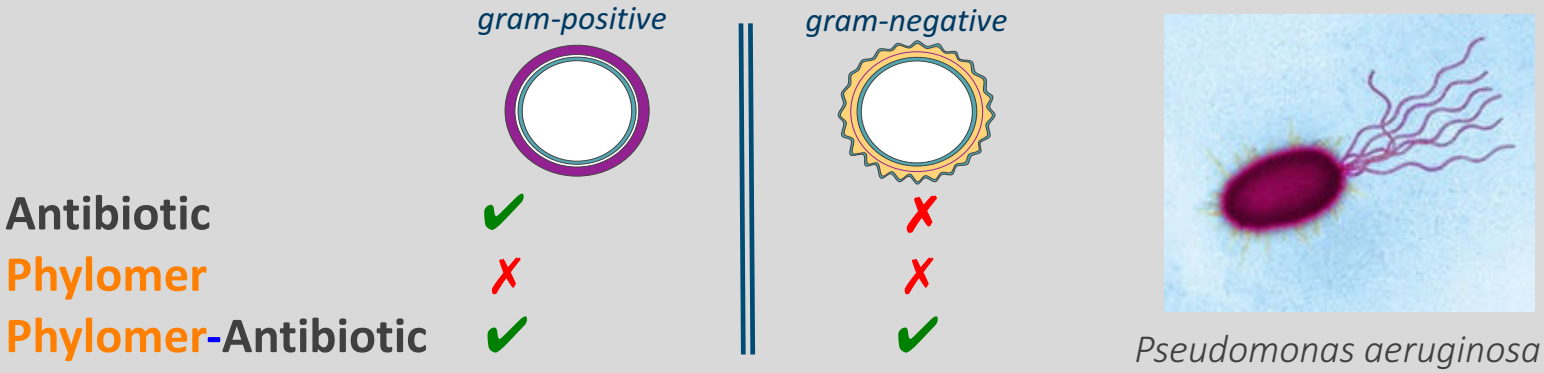
- Primes tumor specific CD8+ T-cells
- FPP containing peptide vaccine retards tumour growth greater than non-FPP control
- FPP-peptide vaccines have the potential to synergize with existing immunotherapies

Collaborator: Jason Waithman, Telethon Kids Institute

(Refer ASX release dated 8 January 2018)

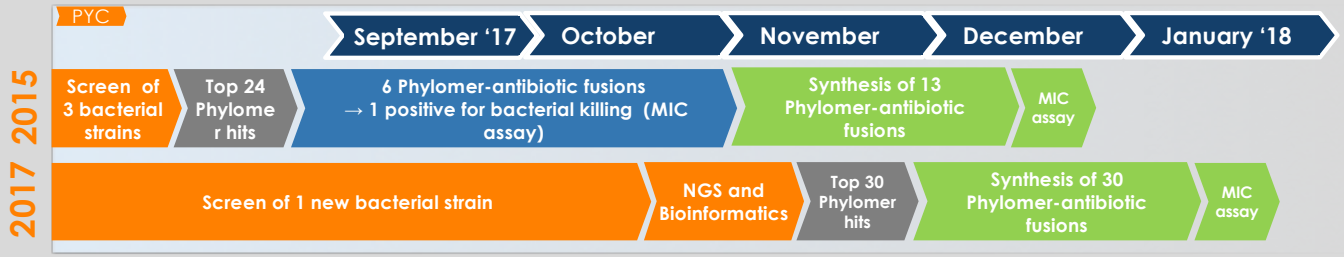
Partnering strategy: Genentech work continues to be successful

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



Pseudomonas aeruginosa

increased antimicrobial range



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

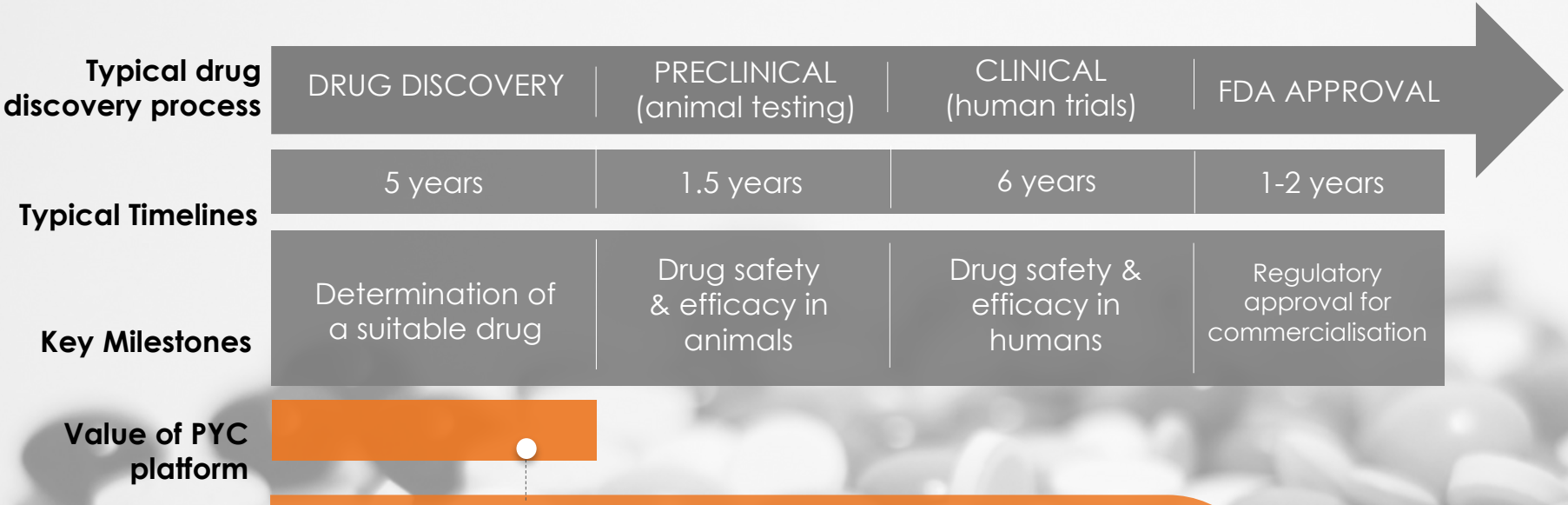
"*Cell specific delivery of siRNA by FPPs would open a universe of therapeutic opportunities*"

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

Phylogica shortens Pharma discovery phase



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

Proving the value proposition of our platform

1

- Deliver ***in vivo*** functional validation
- Demonstrate the **improvement potential** of existing FPPs
- **Enrich and validate** our library

Transforming our operations to achieve scale

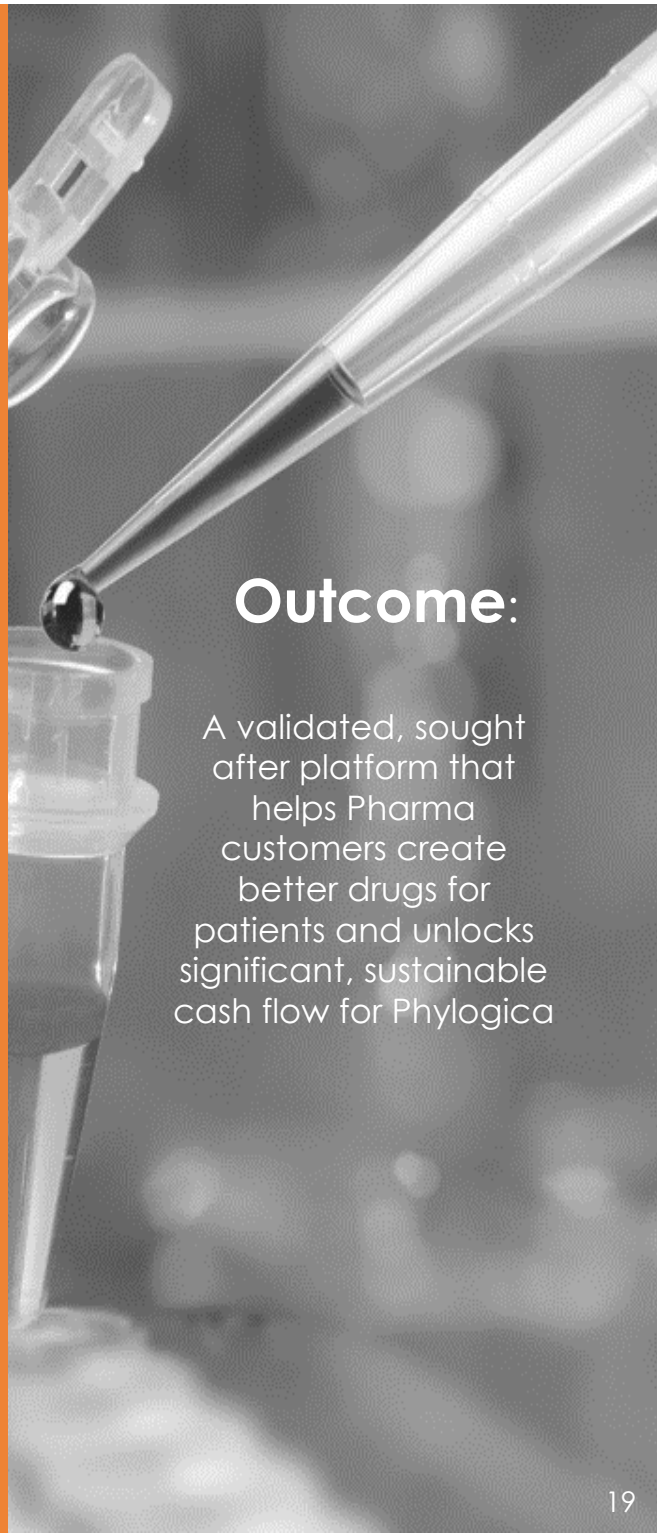
2

- **Reduce** discovery and validation **cycle times with automation**
- Engage **world class CROs** to drive scale

Turbocharging our commercial engine

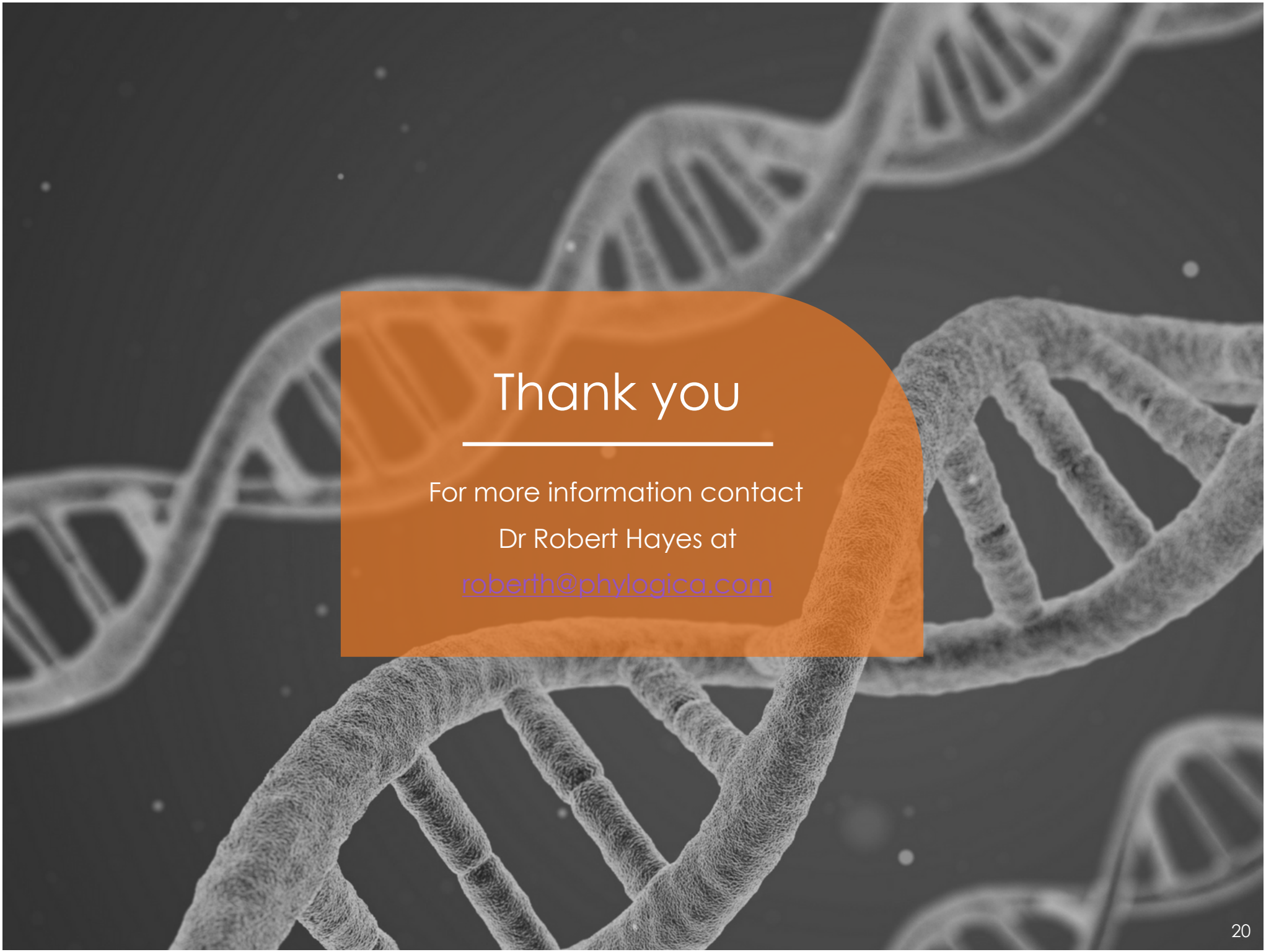
3

- **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

Dr Robert Hayes at

roberth@phylogica.com