



PHYLOGICA

**AGM**  
**25 November 2016**



## **PHYLOGICA PLATFORMS COMBINING TO PROGRESS COMMERCIALISATION**

Ms Stephanie Unwin

Chair

PHYLOGICA

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## 2016 A YEAR OF STRONG PROGRESS

### Further validation of our FPP intracellular delivery technology platform

- FPP-mediated delivery of protein cargoes is very rapid and efficient
- Quantified approximate concentration of the protein delivered into the cell
  - far superior concentrations (with a range of new cargoes) to those achievable with an extensively validated conventional cell penetrating peptide (TAT)

***FPP is consistently producing better results versus the gold standard***

# Identified Phylomers for use as the drug cargo itself

- Internal iMYC cancer program continues to build an impressive proof of concept data pack *on the way to formal preclinical development in the second half of 2017*
- Narrowed the number of proprietary iMYC candidates to five and the most suitable leads will be chosen for optimisation

# iMYC candidates

- Performing well on a number of measures
- No evidence of FPP-mediated toxicity
- Improvements in pharmacokinetics
- Evidence of activity in two independent animal models of cancer even when administered intravenously

# Building confidence in the iMYC program

- The iMYC program is our most advanced with entry into a formal pre-clinical program planned for H2 2017
- Phylogica is planning to achieve substantial increases in the potency of both its lead FPP and its lead iMYC before further multi-parameter optimisation of the conjugate begins

# Progress on Collaborations

- Since June we have signed three non-disclosure agreements with international pharmaceutical companies to discuss elements of Phylogica's technology portfolio.
- Genentech are due to make a decision regarding licensing/extension of novel antimicrobials research program in December 2016
- Phylogica's delivery technology (in the form of its FPPs) is being examined by multiple third parties (Academic, Biotech and Pharma) for the delivery of various proprietary drug cargoes

# Phylomer Platform

- The core intellectual property of Phylogica is our extensive library made up of protein fragments expressed from the genetic material of micro-organisms (Phylomers)
- For several years, our team of scientists, managers and advisers has been working hard to utilise our Phylomer library to discover more efficient peptides to deliver a range of biologics cargoes into the inside of cells



# Platform continued

- Phylogica has significantly expanded the landscape of druggable targets as well as enhancing the specificity and sensitivity of these drug-target interactions
- Searching through our extensive library to identify Phylomers that may be used as the drug cargo in conjunction with the Functional Penetrating Phylomers (FPPs) led to our iMYC program

# 2016 summary

- Shortlisted oncology drug candidates for lead optimisation
  - Potential for formal pre-clinical studies in second half of 2017
- FPP cell delivery system is showing excellent results and remains highly competitive
  - See the next presentation from Paul Watt, our Chief Scientific Advisor

***We thank all of our hard working scientific team and our loyal shareholders for their support, as Phylogica gets closer to reaching commercial outcomes from its exceptional Phylomer library***

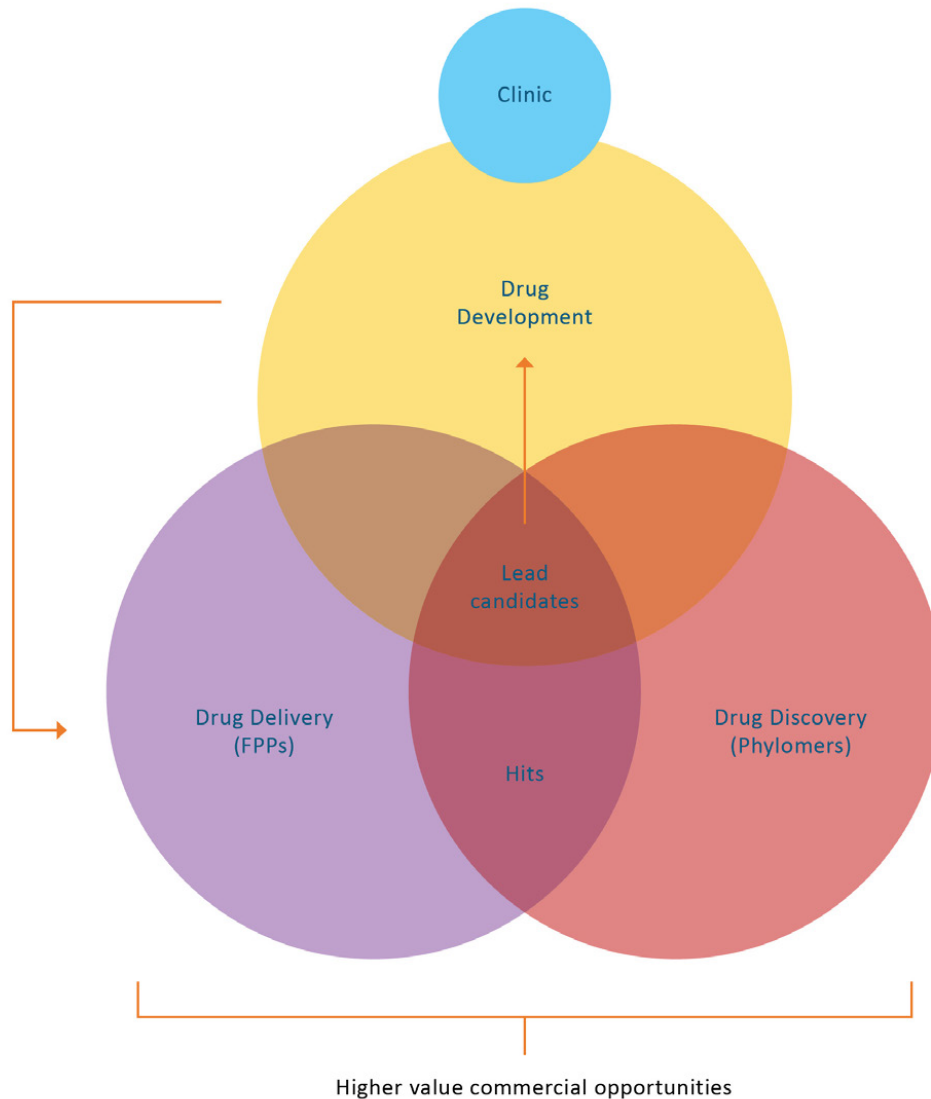


# Technology Overview and Update

Adjunct Professor Paul Watt

Chief Scientific Advisor

# Phylogica Value Creation Engines

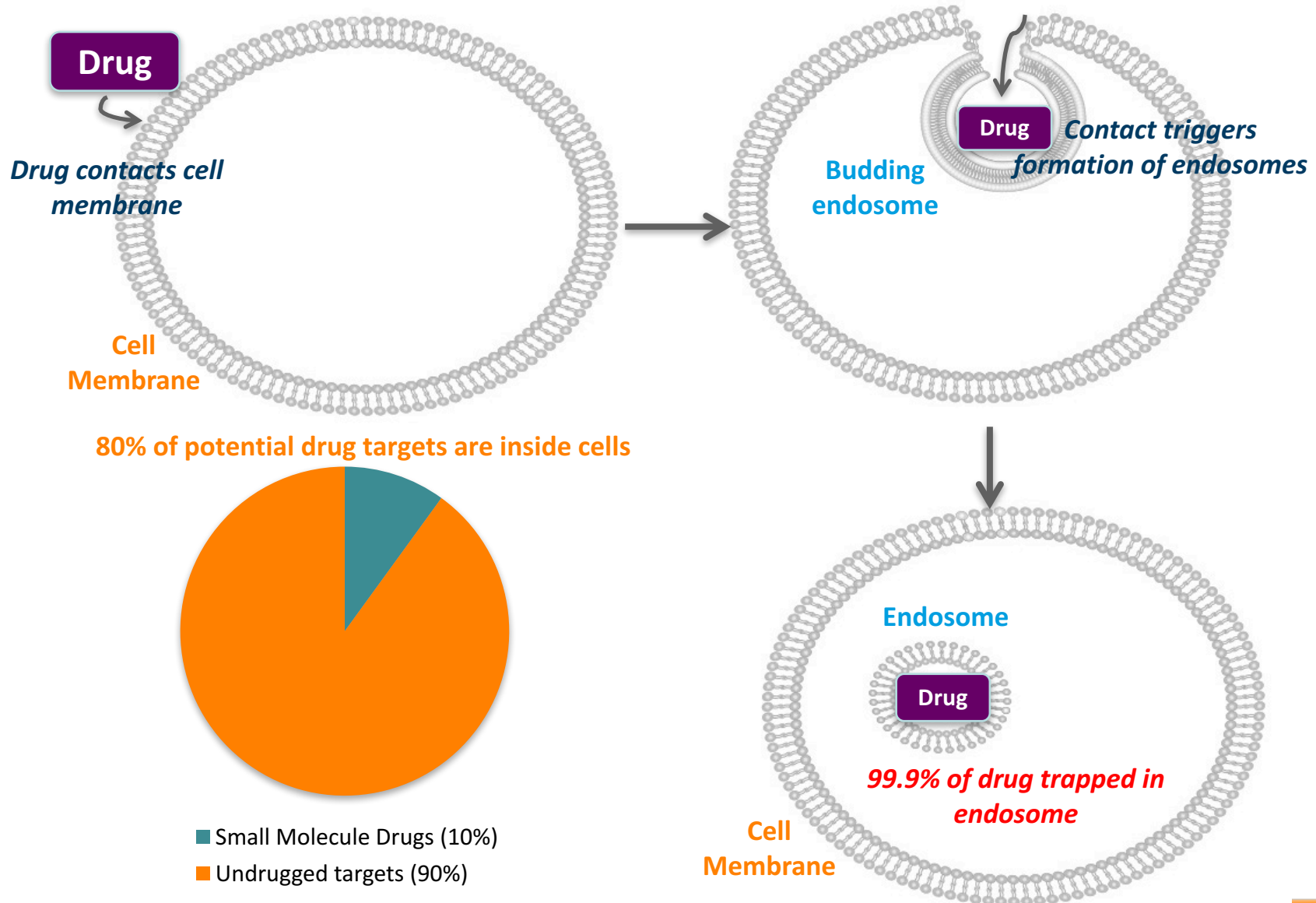


- **Discovery (Phylomers)**
- **Delivery (FPPs)**
- **Development (iMYCs)**

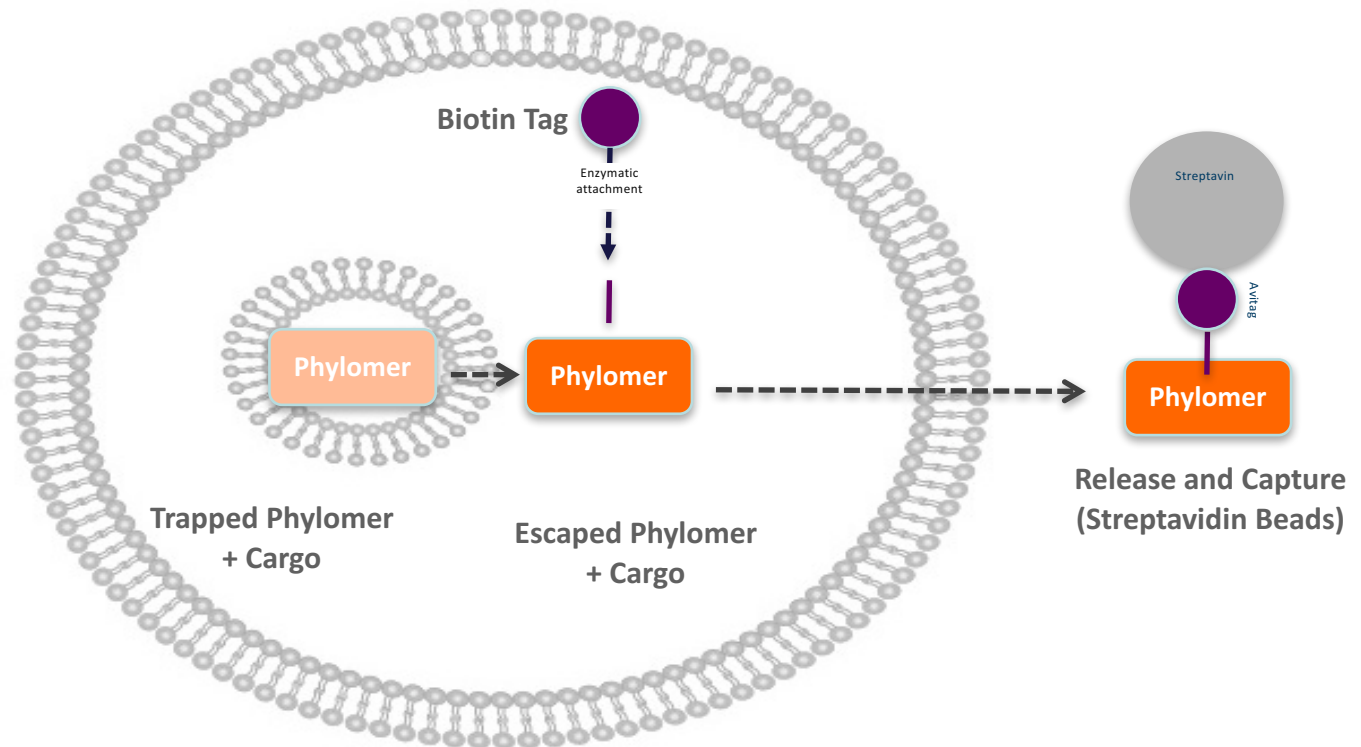
**DELIVERY:**

**Functional Penetrating Phylomers “FPPs”**

# Biologics drugs are trapped within endosomes and thus their therapeutic effects are constrained

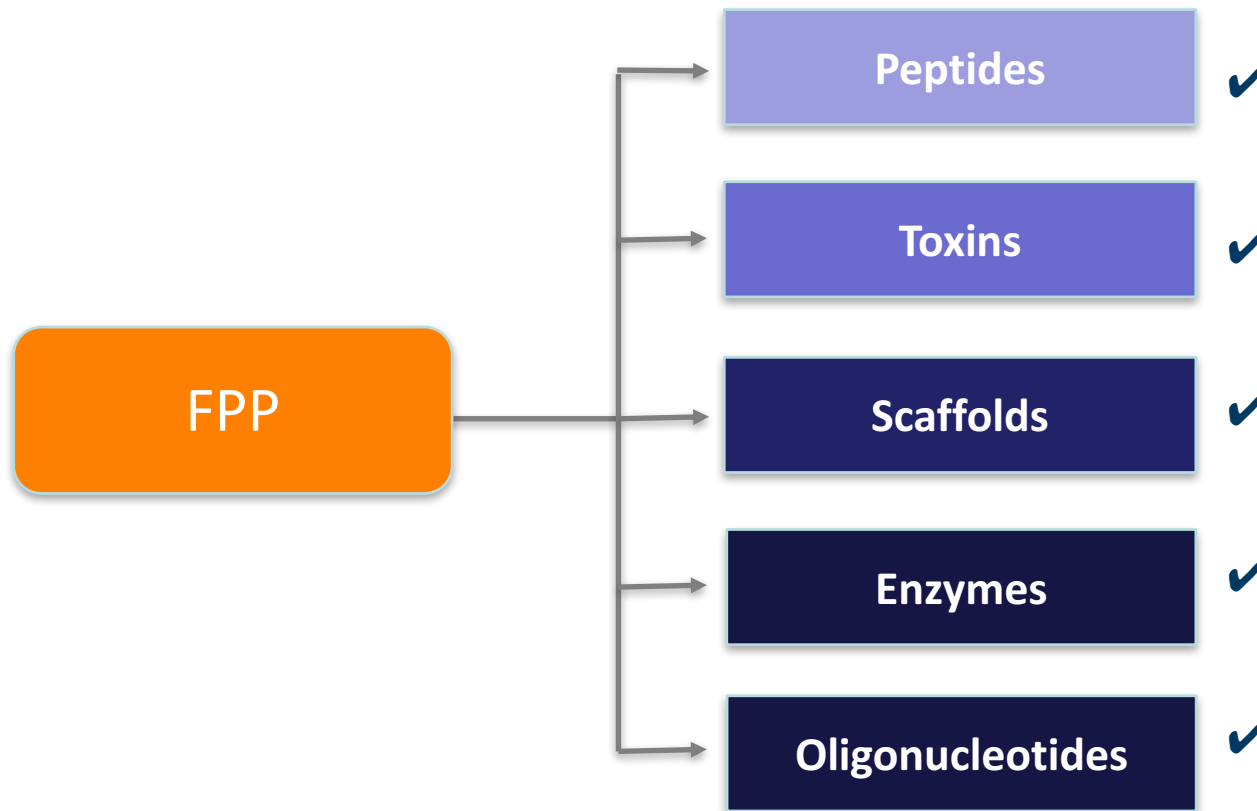


# PYC's Endosomal Escape Trap Assay identifies Phylomers that can liberate cargoes OUT of endosome



- Rare Phylomers identified that can deliver cargoes into cells and then liberate cargoes from the endosome are called 'FPPs'

# Phylomer FPPs can deliver a diverse range of biologics cargoes into cells





# Phylomer FPPs can deliver a diverse range of biologics cargoes into cells - continued

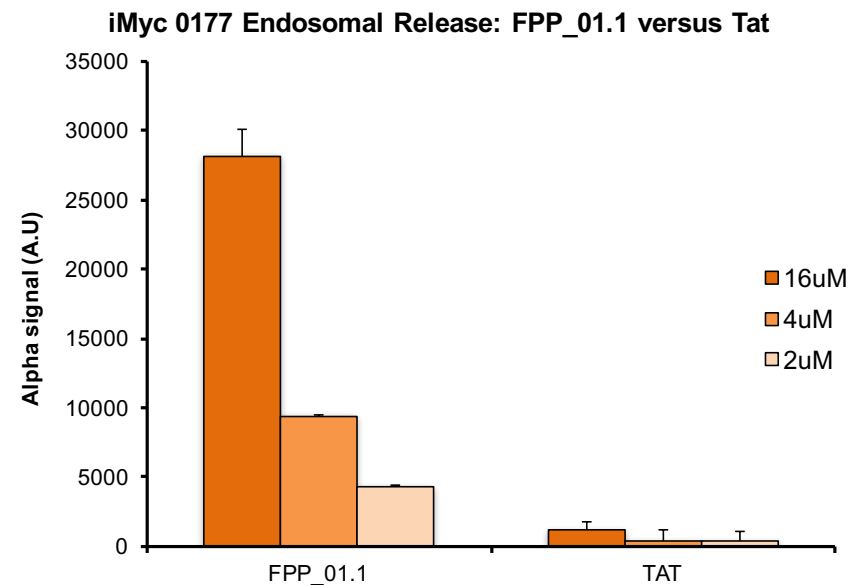
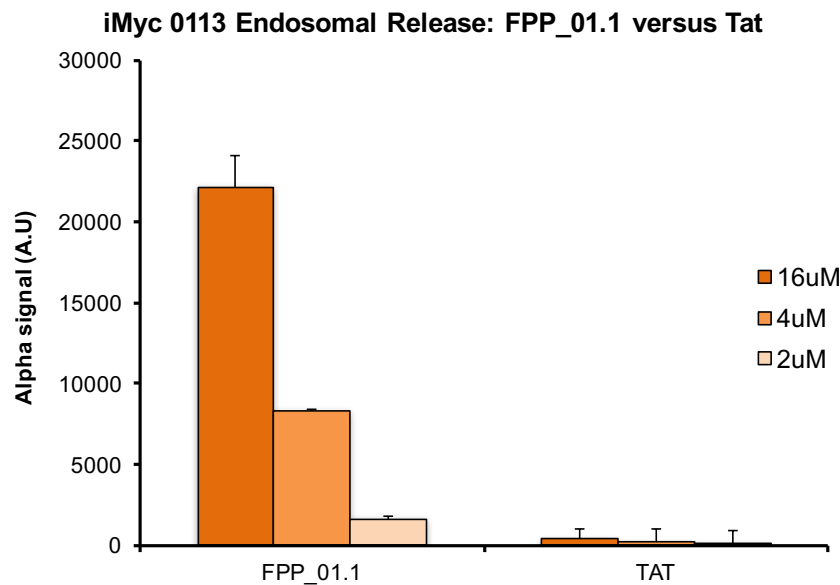
- Examples of cargoes delivered with FPP01 or its derivatives
- FPP versatile enough to deliver multiple cargoes with diverse size and charges

Cargo Class	Cargo	Size/Charge	IC50*	**MED
Toxin / large protein	Bouganin	28-50kDa, pI 7.8 (different constructs)	20nM	ND
Small protein scaffold	Omomyc	11kDa, pI 9.6	700nM-5μM	ND
Enzymatic protein	$\beta$ -lactamase	42 KDa, pI 5.5	ND	ND
Large disordered protein	PAS	50kDa MW, 600kDa equiv. hydrodynamic radius, pI 5.9	ND	5μM
Peptide	Apoptotic (PAP)	17aa, pI 10.7	1.7μM	1.25μM
	PPI inhibitor (DPML $\alpha$ )	15aa, pI 8.26	8μM	
	Split protein complementation (S11 of GFP)	30aa, pI 6.75	ND	
	Bcl-2 family inhibitory peptides – 26aa	26aa, pI 6.28	1.6μM	
Bispecifics	Bcl-2 inhibitory peptide + Omomyc scaffold	37kDa, pI 8.02	190nM	156nM
Oligonucleotides	Exon-skipping Morpholinos	24 base pairs, neutral	ND	50nM

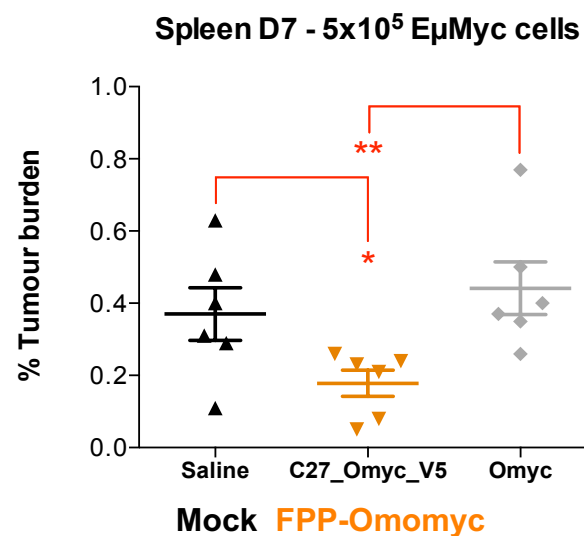
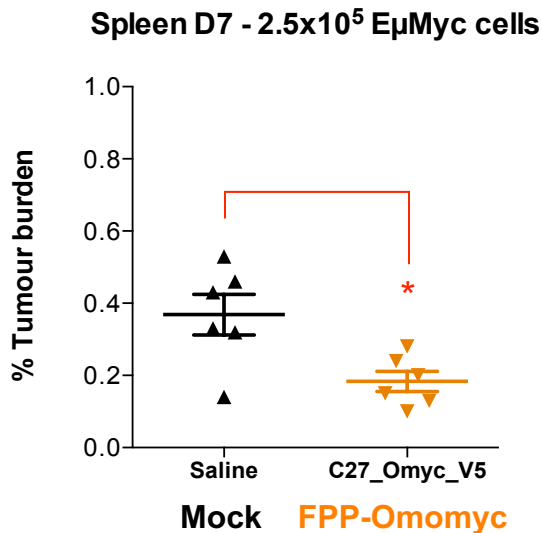
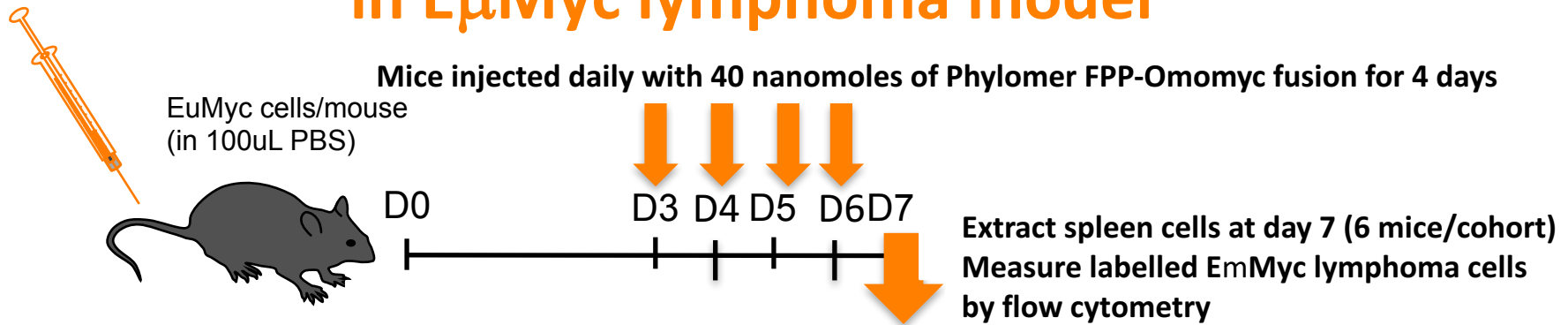
# Further evidence for superior delivery of FPP vs. TAT: quantified delivery of larger (iMyc) cargoes

- Two distinct FPP-iMyc fusion proteins applied to mammalian cells for 60min
- Assay that specifically quantifies the efficiency of cell entry & escape of iMyc from the endosome to the cytoplasm
- **FPPs again show vastly superior uptake and endosomal escape compared to the conventional CPP TAT, particularly at lower concentrations**

*FPP conjugates of iMyc cargoes (0113 and 0177) show greater endosomal release than equivalent Tat conjugates at all concentrations tested*



# Evidence of efficacy following *intravenous* delivery in EμMyc lymphoma model



- 4 daily\* injections of FPP-Omomyc reduced growth of lymphoma cells in spleen
- Also saw a reduction in lymphoma cells in the bone marrow with FPP-Omomyc injections
- FPP-Omomyc demonstrates efficacy following IV injection, prior to any optimisation

# FPPs – What we have now established

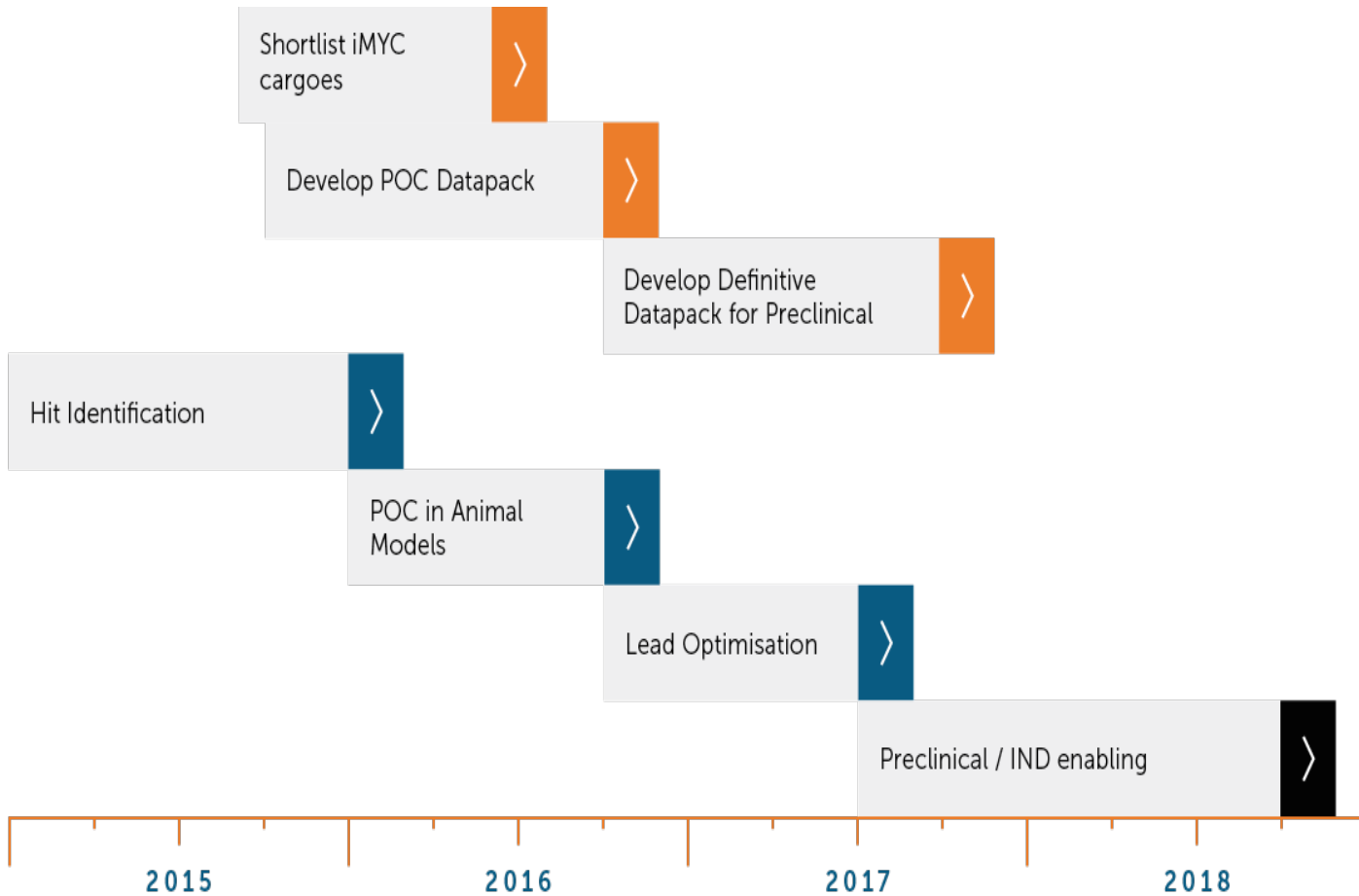
- Enables endosomal escape
- Compatible with wide range of cargoes
- Outperforms other intracellular delivery technologies
- Functional in multiple cell types
- Viable manufacturing and strong IP Position
- Better understanding of mechanism of action
- Preliminary evidence of *in vivo* efficacy
- Promising initial safety signals

**Further validation of FPP Platform is generating increased external interest**

# iMYC Program

*(FPP combined with iMYC cargo)*

# iMYC Program Development Timelines



\*N/B Indicative estimates only

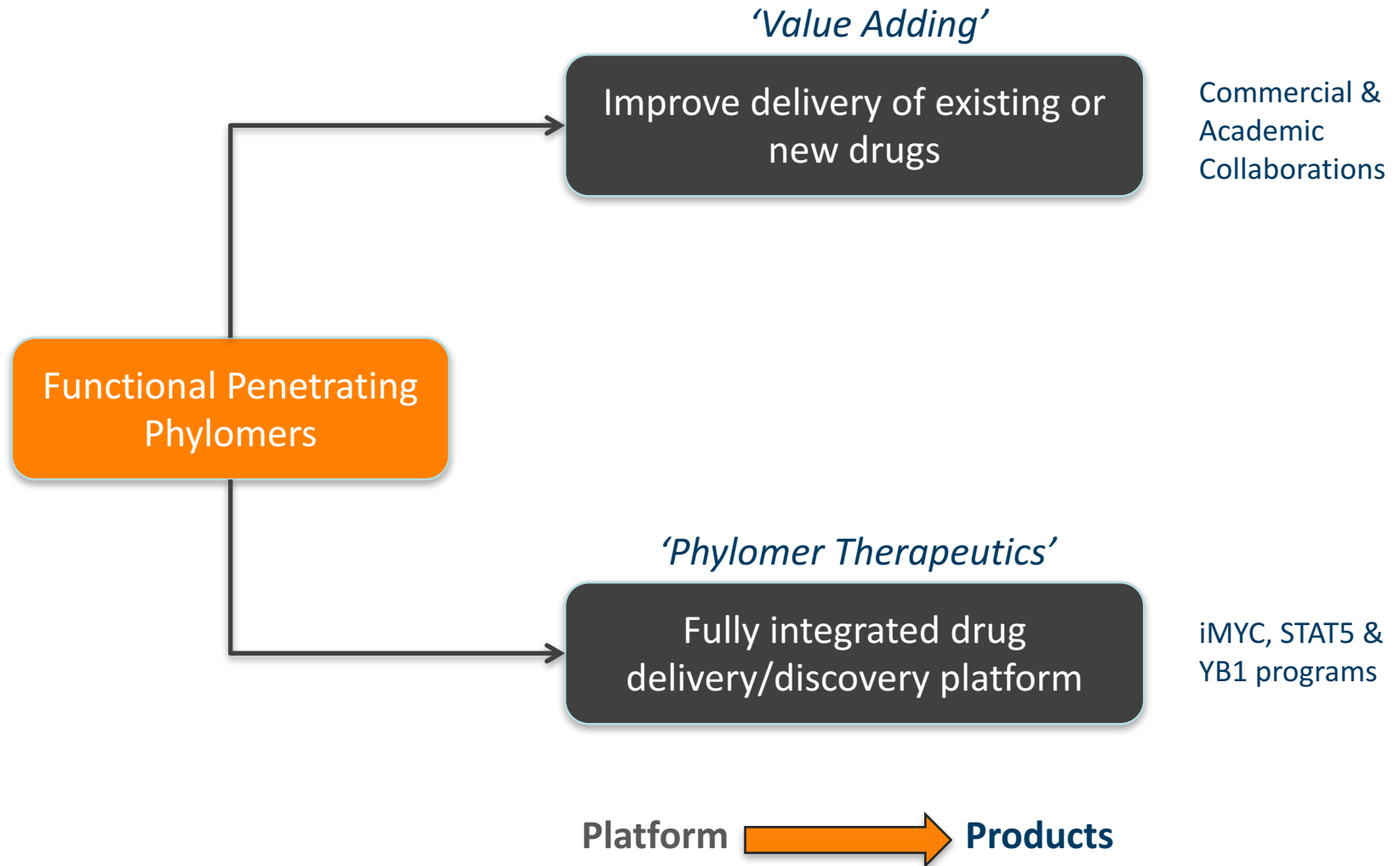
# Good progress with proof-of-concept discovery program

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

# SUMMARY



# Multiple commercialisation opportunities for FPPs



# Commercialisation Progress

- Academic and Commercial Collaborations progressing
  - Murdoch University – Oligonucleotides for Muscular Dystrophy
  - ONJCRI (formerly Ludwig Institute) – Myc and Bcl2/Mcl1 Bispecifics
  - Genentech – Next generation Antimicrobials
  - >5 active other (confidential) collaborations
  - 5 new NDAs with Pharma/Biotech signed since end of Q1, 2016
- iMYC program
  - Early engagement underway with pharma/biotech
  - On track for formal preclinical in 2H17 – next value milestone
- Phylomer Libraries
  - Phoremest target and small molecule discovery alliance
  - Potential to generate novel targets and new chemistry

# Thanks to our talented R&D team for their hard work and to our shareholders for support

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