Developing Clinical Stage Programmes to Treat DMD and CDI

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## **Business Highlights**

Two mid-stage clinical development programs with opportunity to significantly advance current standard of care

#### Duchenne Muscular Dystrophy ('DMD')

- Novel utrophin modulation approach that we believe has the potential to treat 100% of DMD patients
- > Leadership position in utrophin modulation
- > Lead candidate advancing to Phase 2 proof of concept trial

#### C. difficile Infection ('CDI')

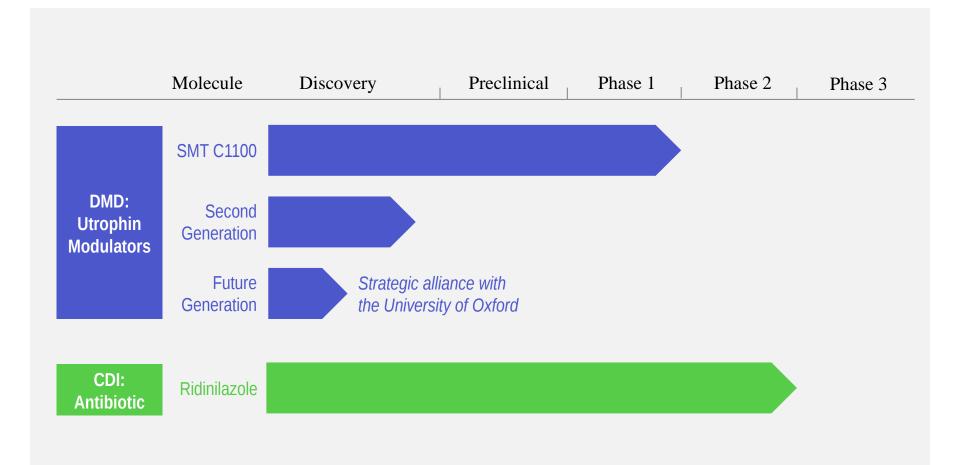
- > Novel class antibiotic, potential to treat initial infection and reduce recurrence
- > Achieved proof of concept in Phase 2 clinical trial that reported in late 2015







## Our Development Pipeline









## Duchenne Muscular Dystrophy Programme

Developing utrophin modulator therapies for the potential treatment of all DMD patients

## About Duchenne Muscular Dystrophy

DMD is one of the most common fatal genetic disorders diagnosed in children in the world

- > Progressive muscle wasting disorder life expectancy around late twenties
- > Eventual weakening of heart and respiratory system leads to death

Orphan disease with ~50,000 patients in developed world

X-linked genetic disease caused by mutations affecting the dystrophin gene

- > Predominantly affects males
- > 1/3 of DMD cases result from spontaneous mutations

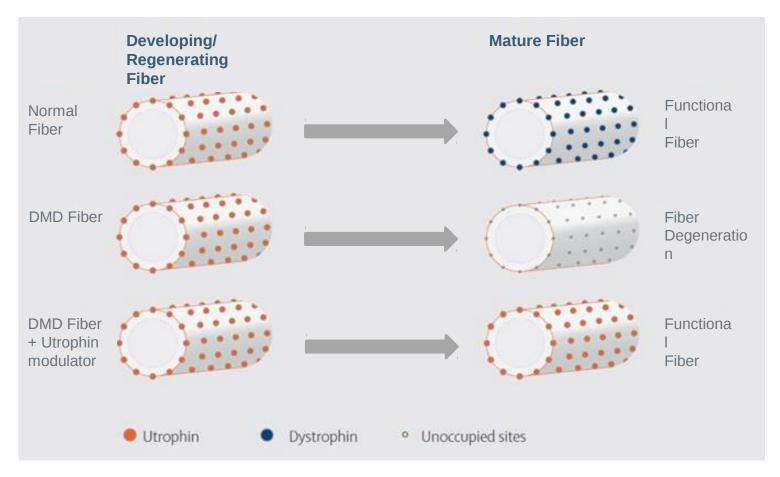


Picture courtesy of Parent Project Muscular Dystrophy



# Utrophin is Functionally Equivalent to Dystrophin in Developing and Repairing Muscle

> Modulation of utrophin protein has potential to compensate for lack of dystrophin





## Utrophin Modulation Programme: SMT C1100 Overview

**Molecule:** First-generation, orally administered small molecule utrophin modulator

#### Status:

- > Preclinical data show potential therapeutic benefit of SMT C1100
- > Well tolerated to date in Phase 1 clinical trials in healthy volunteers and patients
- > Orphan drug designation granted in US and Europe
- Strong IP: Granted composition of matter patent through 2029 in US, and 2027 in EU & Japan

#### Next steps:

> Regulatory and ethics approval in UK to commence Phase 2 proof of concept trial

>>> Next Milestone: Start of patient dosing in Phase 2 proof of concept trial Plan to report interim data periodically beginning H2 2016



## Utrophin Modulation Programme: Pipeline Activities

#### Second generation utrophin modulators

- > Structurally related to SMT C1100 with more favourable pharmaceutical properties
- Positive preclinical efficacy data show increased utrophin expression, increased muscle stability and reduced fibre regeneration and necrosis

#### Future generation utrophin modulators

- > Research being undertaken in collaboration with research groups at the University of Oxford as part of an exclusive, multi-year strategic alliance
- > Alliance extended in 2015 until at least November 2019







## *C. difficile* Infection Programme

## Supported by wellcometrust

## CDI: A Major Healthcare Threat

*"This bacteria is an immediate public health threat that requires urgent and aggressive action"* 

US Department for Health and Human Services, 2013

Significant increase in global prevalence

> Between 450,000 and 700,000 cases of CDI in the US alone

Increasing severity

- > 14,000 deaths per year in the US according to CDC
- > Emergence of hypervirulent strains in US and Europe

High economic burden associated with the disease

> \$4.8B in annual acute care costs in the US



## Ridinilazole: A Selective Antibiotic for *C. difficile* Infection

**Molecule:** Novel class small molecule antibiotic, potent but highly selective for *C. difficile* bacterium

#### Status:

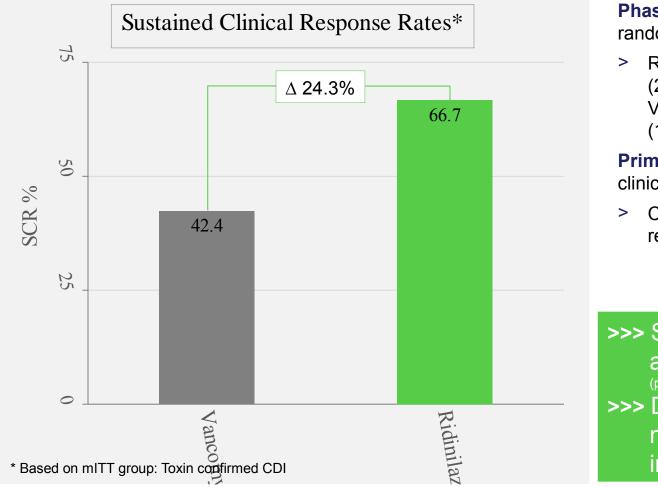
- > Phase 2 proof of concept trial reported statistical superiority over standard of care vancomycin in sustained clinical response
- > More detailed data to be published 1H 2016
- > QIDP status and Fast Track status granted
- > Strong IP: Granted and pending patents through 2029 in US, EU & Japan
- > Funding from Wellcome Trust supported development through Phase 2

#### >>> Next Step: Preparing to enter Phase 3 clinical trials



## Ridinilazole Displays Statistical Superiority Over Vancomycin in Phase 2 Trial





Phase 2 Trial: 100 patients randomized 1:1, 10 day dosing

 Ridinilazole (200mg, 2x daily), Vancomycin (125mg, 4x daily)

**Primary endpoint:** Sustained clinical response ('SCR')

 Cure at end of treatment, no recurrence 30 days later

 >> Statistical superiority achieved in SCR (pre-specified 90% confidence interval)
>> Driven by large numerical reduction in recurrence



## Phase 2 Data Support *in vitro* Selectivity Profile: Higher Preservation of Gut Microbiome

- > Potent *in vitro* bactericidal inhibition of *C. difficile* growth
- Superior preservation of gut microbiome with ridinilazole compared to current marketed treatments

Destarial Croups	Spectrum of Activity – MIC90 (µg/mL)				
Bacterial Groups	Ridinilazole†	Metronidazo	ole† Vancomycin†	Fidaxomicin†	
Clostridium difficile	0.25	2	4	0.5	
Bacteroides spp.		2	128		
Bifidobacterium spp.		128	1	0.125	
Lactobacillus spp.					
Eggerthella lenta		0.5	4	≤0.03	
Peptostreptococcus spp.	64	1	0.5	≤0.03	
Staphylococcus aureus		_	1	16	
Antibiotic effect Weak	Medium	Potent	Antimicrob. Agents Chemo Antimicrob. Agents Chemo		







### Financials

## **Summary Financials**

Key Items	Amount
AIM Price (Jan 27, 2016):	123.5p
AIM Shares O/S:	61.29M
Current Market Cap (Jan 27, 2016):	£76M
Cash Balance (Oct 31, 2015):	£22.2M
Debt:	£0





Symbol: SMMT



## **Future Clinical Milestones**

> Clinical milestones in both programs:

	Activities	Expected Date	
DMD	Phase 2 Proof of Concept trial initiation	Early 2016	
	Reporting of data from Phase 2 proof of concept trial	H2 2016 onwards	
CDI	Phase 2 Proof of Concept top-line Q4 2015	Q4 2015	~
	Phase 2 Proof of Concept additional data	H1 2016	







More Information:

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