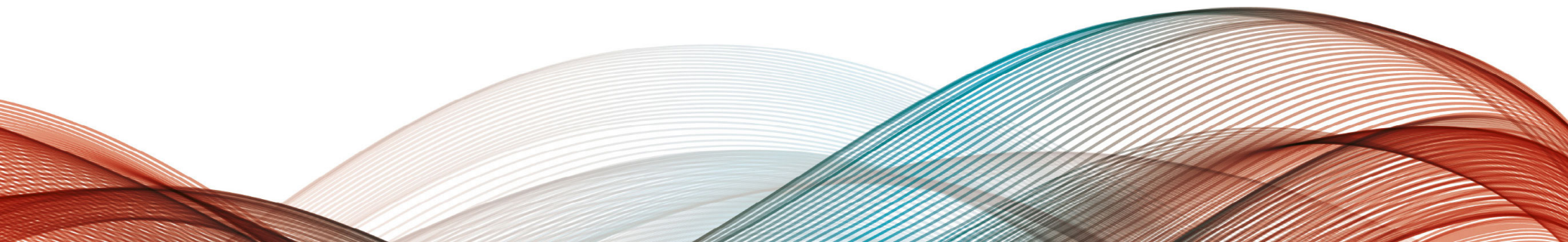




**Investor Presentation - October 2018**





## Forward Looking Statements

*This presentation contains forward-looking statements regarding the Company's business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing the Company's goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercializing drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this presentation. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the Antisense Therapeutics Limited Annual Report for the year ended 30 June 2018, copies of which are available from the Company or at [www.antisense.com.au](http://www.antisense.com.au).*

# Corporate Overview

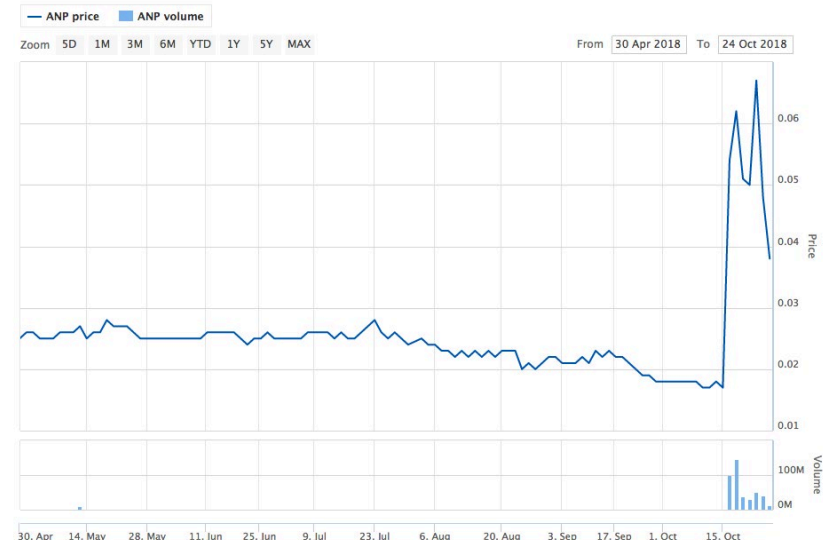
## Key Financials

Market Capitalization (@4.8c)	A\$18M
Shares on issue	371.6M
Share price (12 month)	\$0.017 - \$0.094
Cash as at 30 September 2018	\$3.4M

## Ownership Structure

- Substantial Shareholders
  - Australian Ethical Investment
  - Platinum Asset Management
- Top 40 holders – **55%**

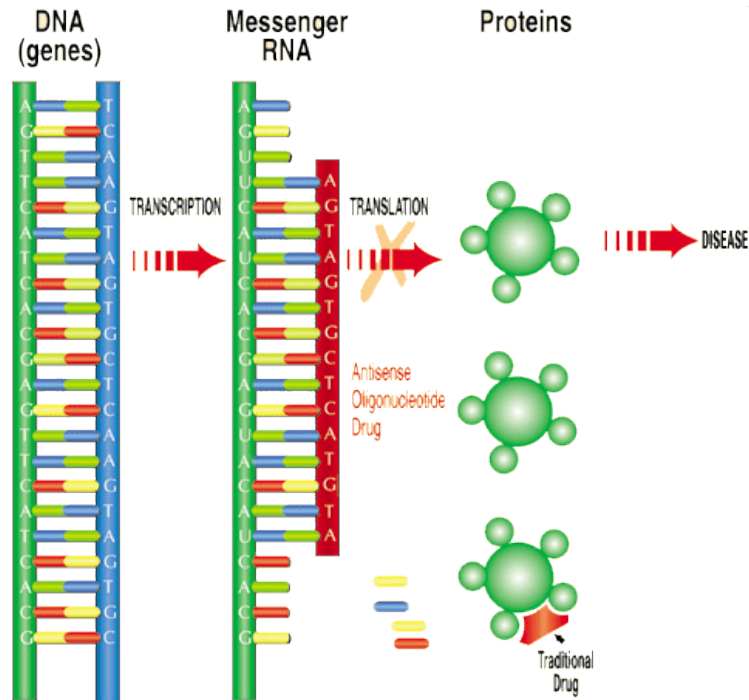
## ANP 6 month Trading History



# Corporate Snapshot

- ✓ Partnered with Ionis Pharmaceuticals (Nasdaq:IONS market capitalization: US\$6 Billion), world leaders in antisense drug development and commercialisation, to develop RNA-targeted therapeutics.
- ✓ Positive Phase 2 clinical results delivered from advanced stage product pipeline with two compounds (ATL1102 and ATL1103)
- ✓ **Dosing commenced in Phase II clinical trial in Duchenne Muscular Dystrophy (DMD) Program**
  - *DMD is one of the most common fatal genetic disorders caused by a mutation in the muscle dystrophin gene leading to severe progressive muscle loss and premature death in boys*
  - *High unmet medical need for new therapeutics targeting progressive destructive inflammation*
  - *Phase II clinical trial of ATL1102 in DMD patients being conducted at Royal Childrens Hospital, Melbourne in non-ambulatory DMD patients*
  - *Patient treatment commenced August 2018 for a six month dosing trial*
- ✓ **Establishing Early Access Program (EAP) for acromegaly**
  - *EAPs offer patients access to new non-registered drugs and companies can seek pricing reimbursement for drug supply in certain markets*
  - *Plan to provide ATL1103 to acromegaly patients under an EAP in Europe*

# Antisense – what is it and how does it work?



- *Antisense oligonucleotide drugs are small (12-25 nucleotides) DNA- or RNA-like compounds that are chemically modified to create medicines*
- *Antisense drugs prevent the production of proteins involved in disease processes by interrupting the translation phase of the protein production which results in a therapeutic benefit to patients*

- ***Advanced stage clinical pipeline***
- ***For diseases where there is a need for improved therapies***

### **ATL1102 in DMD**

- *Conducting Phase II clinical trial in Australia*
- *Dosing commenced in August 2018*

### **ATL1103 in acromegaly**

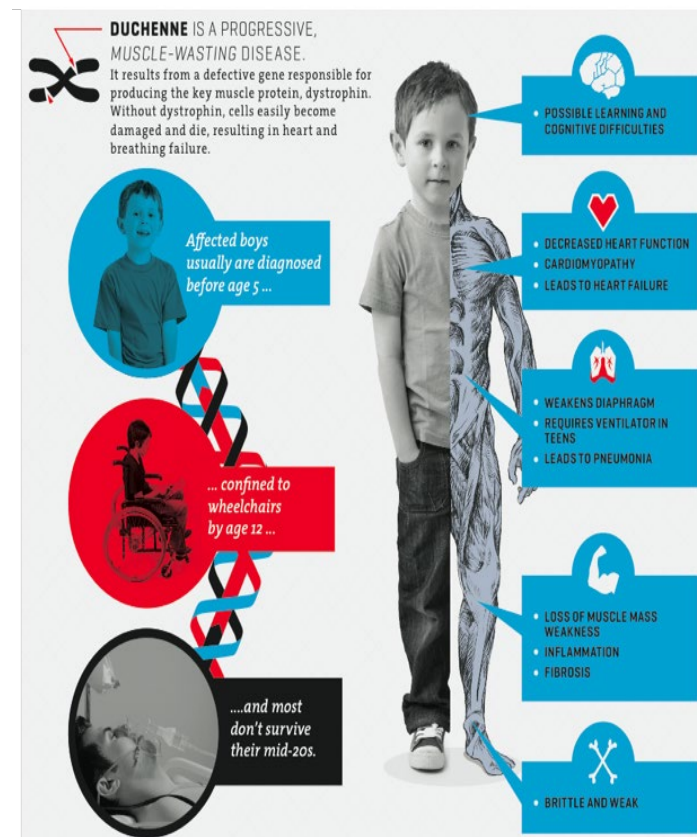
- *Phase II clinical trial completed*
- *Establishing Early Access Program in Europe*

### **ATL1102 in MS**

- *Phase II clinical trial completed*
- *Monitoring data from DMD trial to inform on future clinical development in MS*

# ATL1102 (targeting CD49d) for DMD

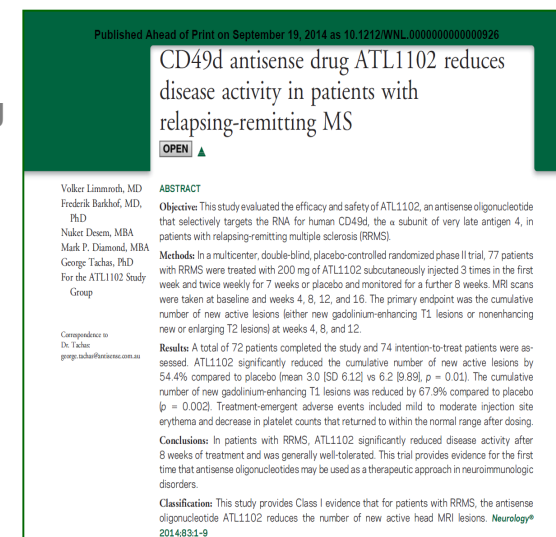
- Duchenne Muscular Dystrophy (DMD) is a devastating genetic muscular disease caused by loss of dystrophin with progressive muscle wasting and associated muscle injury leading to inflammation and fibrosis (100% mortality)
- Affects boys with an incidence of ~1 in 3,500 and prevalence of ~44,000 in US & EU
- Dystrophin restoration treatments recently approved – eteplirsen (Exondys 51: Sarepta Therapeutics) for the 13% of patients amenable to Exon 51 skipping
- Key challenge in management of DMD patients is to reduce the inflammation that exacerbates muscle fibre damage
- Corticosteroids (CS) **only** used to treat the inflammation in DMD but have insufficient efficacy and significant side effects e.g. weight gain, reduced bone density, and growth retardation
  - CS not as effective in patients with a greater no. of CD49d receptors on T cells





# Key drivers for moving ATL1102 into development for DMD

- Clear need for improved therapies to ameliorate DMD severity and delay disease progression
- **ATL1102, an antisense drug to CD49d, shown to be a highly active immunomodulatory drug** with potent effects on inflammatory processes in MS patients
  - 90% reduction in inflammatory brain lesions vs placebo [Limmroth V et al Neurology 2014]
  - Reduced CD49d on T and B cells, and T and B cell numbers by ~25 and 50% respectively
  - Pre-clinical and clinical data in MS has supported move directly into 6 month patient trial (effective leveraging of substantial investment and progress made to date in MS)
- **Pivotal scientific publication confirming CD49d as a potential target for DMD therapy**
  - DMD patients with greater no. of circulating T cells with high levels of CD49d (alpha chain of VLA-4) expression have both more severe and rapid progression of disease [Pinto-Mariz et al Skeletal Muscle 2015]
  - Ambulant patients on CS suggesting CS do not reduce CD49dhi expression on T cells
  - CS treatment does not modulate CD49d expression on T cells in MS
  - Non-ambulant DMD patients have greatest no. of CD49d high expressing T cells
- DMD is an orphan indication so will benefit from IP and development incentives
- Support of experts (refer Scientific Advisory Board)



Pinto-Mariz et al. Skeletal Muscle (2015) 5:45  
DOI 10.1186/s13395-015-0066-2



## RESEARCH

## Open Access



## CD49d is a disease progression biomarker and a potential target for immunotherapy in Duchenne muscular dystrophy

Fernanda Pinto-Mariz<sup>1,2,3</sup>, Luciana Rodrigues Carvalho<sup>1</sup>, Alexandra Prufier De Queiroz Campos Araujo<sup>2</sup>, Wallace De Mello<sup>1</sup>, Márcia Gonçalves Ribeiro<sup>2</sup>, Maria Do Carmo Soares Alves Cunha<sup>2</sup>, Pedro Hernan Cabello<sup>4</sup>, Ingo Riederer<sup>1</sup>, Elisa Negroni<sup>5</sup>, Isabelle Desguerre<sup>6</sup>, Mariana Veras<sup>1</sup>, Erica Yada<sup>7</sup>, Yves Allenbach<sup>8</sup>, Olivier Benveniste<sup>8</sup>, Thomas Voit<sup>1</sup>, Vincent Mouly<sup>3</sup>, Suse Dayse Silva-Barbosa<sup>1,2</sup>, Gillian Butler-Browne<sup>3\*</sup> and Wilson Savino<sup>1\*</sup>

### Abstract

**Background:** Duchenne muscular dystrophy (DMD) is caused by mutations in the dystrophin gene. The immune inflammatory response also contributes to disease progression in DMD patients. In a previous study, we demonstrated higher levels of circulating CD49dhi and CD49ehi T cells in DMD patients compared to healthy control. DMD patients are clinically heterogeneous and the functional defect cannot be correlated with genotype. Therefore, it is important to be able to define reliable noninvasive biomarkers to better define the disease progression at the beginning of clinical trials.

**Results:** We studied 75 DMD patients at different stages of their disease and observed that increased percentages of circulating CD4<sup>+</sup>CD49d<sup>hi</sup> and CD8<sup>+</sup>CD49d<sup>hi</sup> T lymphocytes were correlated with both severity and a more rapid progression of the disease. Moreover, T<sup>H</sup>CD49d<sup>hi</sup> cells were also found in muscular inflammatory infiltrates. Functionally, T cells from severely affected patients exhibited higher transendothelial and fibronectin-driven migratory responses and increased adhesion to myotubes, when compared to control individuals. These responses could be blocked with an anti-CD49d monoclonal antibody.

**Conclusion:** CD49d can be used as a novel biomarker to stratify DMD patients by predicting disease progression for clinical trials. Moreover, anti-CD49d peptides or antibodies can be used as a therapeutic approach to decrease inflammation-mediated tissue damage in DMD.



# ATL1102 for DMD – Scientific Advisory Board

## Dr. Ian Woodcock MD (Principal-Investigator)

*Royal Childrens Hospital (RCH) Neuromuscular Fellow, Melbourne Australia*



## Professor Monique Ryan MD (Co- Investigator)

*Director Neurology Department, Head of Royal Children's Hospital, Neuromuscular Clinic RCH, MCRI, Melbourne Australia*



## Professor Steve Wilton Ph.D

*Western Australian Neuroscience Research Institute (NRI), Foundation Chair in Molecular Therapy at Murdoch University, Perth, Western Australia: Patent holder on target sequence of Sarepta's drug eteplirsen and all additional exon-skipping (Splice Switching Oligimer) drugs*



## Professor Sue Fletcher, PhD

*Principal Research Fellow, NRI Murdoch University, Perth, Western Australia: Patent holder on target sequence of Sarepta's drug eteplirsen and all additional exon-skipping drugs*



## Dr. Gillian Butler-Browne, PhD

*Director, Centre of Research in Myology, Sorbonne Universités, INSERM, Paris, France: Expert in inflammatory muscle disease*



## Mr William Goolsbee (SAB Chairman)

*Antisense Therapeutics Ltd, non-executive director: Chairman, Sarepta Therapeutics, 2010-2014, Developers of eteplirsen for the treatment of DMD*



# DMD Program Status – Phase II clinical trial

- ANP conducting an open label Phase II trial in DMD patients at the Royal Childrens Hospital (RCH) Melbourne
  - *Study in n=9 non-ambulant (wheel chair bound) boys 10 to 18 years of age with DMD*
  - *Will assess ATL1102's safety and tolerability and its effects on the inflammation that contributes to disease progression in DMD over 24 weeks of dosing at 25mg/week*
  - *Study is a safety and tolerability investigation while also looking to show a difference in serum biomarkers of inflammation and muscle damage and to detect a difference at 6 months in key clinical endpoints (e.g. the upper limb function of the boys)*
- **ATL1102 is the only CD49d targeting drug in clinical development for DMD**
- Trial costs eligible for R&D tax incentive refund
- Dosing commenced in August 2018
- Patient enrolment and dosing completion projected for mid 2019 with results to follow
- Open label study - possibility for earlier study read outs



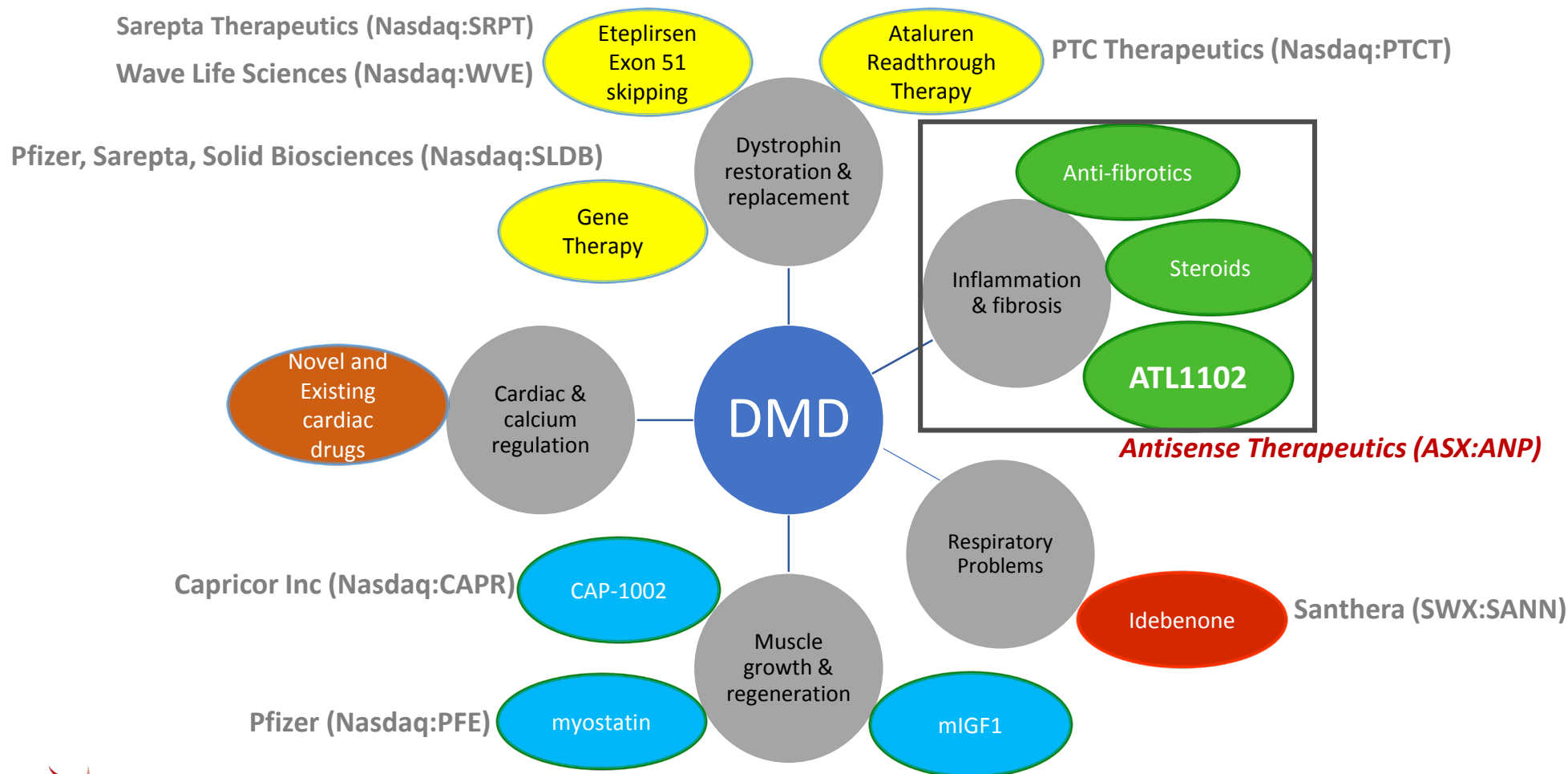
**Dr Ian R Woodcock**  
Neuromuscular Fellow, RCH,  
Melbourne Australia



**Prof. Monique Ryan**  
Head of Neuromuscular Clinic  
RCH, Melbourne Australia  
Consultant Neurologist

# Treatment development focuses across all DMD Intervention points

- *Prospect for therapies to be complementary rather than competitive*



# Recently Initiated Therapeutic Product Trials in DMD

- **Limited number of anti inflammatory drugs in development**
- MNK-1411 below, CAT-1004, VBP15 have completed Phase II and target NF Kappa B, which is thought to be the MoA of the CS drugs that **do not modulate CD49d expression**

Date Commenced	Company	Technology	Therapy ID	Phase	Pathological Process
Apr-18	Pfizer	Gene therapy	PF-06939926	Phase Ib	Dystrophin production
Apr-18	Capricor Inc	Cardiosphere-derived cell therapy	CAP-1002	Phase II	Cellular re-generation
<b>Mar-18</b>	<b>Mallinckrodt</b>	<b>Synthetic melanocortin receptor agonist</b>	<b>MNK-1411</b>	<b>Phase II</b>	<b>Anti-inflammatory</b>
Dec-17	Sarepta	Oligomer	SRP-5051	Phase I/IIa	Dystrophin production
Dec-17	Solid Biosciences	Vector-mediated gene transfer	SGT-001	Phase I/IIa	Dystrophin production
Nov-17	Wave Life Sciences	Exon skipping (Exon 51)	WVE-210201	Phase I	Dystrophin production
Oct-17	Italfarmaco	Histone deacetylase inhibitor	Givinostat	Phase II/III	Anti-fibrotic
Jul-17	PTC Therapeutics	Oxadiazole small molecule, unknown MoA	Ataluren	Phase III	Dystrophin production

Source: Bioshares - 27 April 2018, Edition 740

# Value Creation Potential of ATL1102 for DMD - Sarepta Therapeutics

- Prior to the approval of Exondys 51, Sarepta had a market capitalisation ( m / c ) of ~US\$60m (July 2012)
- Exondys 51 was approved by the FDA in late 2016 under the accelerated approval pathway based on the surrogate endpoint of dystrophin increase in skeletal muscle observed in some Exondys 51-treated patients
- Following FDA approval of Exondys 51 Sarepta's m/c increased to US\$3.3Billion (current m/c US\$8Billion)
- Exondys 51 is the first FDA approved treatment for DMD - **only useful in 13% of boys** with the exon 51 mutation, where as **inflammation contributes to disease progression in all DMD patients**
- Cost per patient of Exondys 51 is US\$300K/year
- 3rd Qtr 2018 total net revenue for Exondys 51 was US\$78.5 million
- **Notably, Mr William Goolsbee, ex Chairman of Sarepta, is a non-executive director of ANP and Exondys 51 inventor, Professor Steve Wilton (Murdoch University, Perth) is a member of the Scientific Advisory Board**

## Relevant transactions in DMD



### 2018 Is the Year for Making Strategic Alliances in DMD

Publication Date: March 2018

*'...In **2017, \$2.2B was issued in capital raising deals involving DMD pipeline drugs**, and two-thirds of these deals were equity offerings. This suggests that companies were focusing on raising funds and investing in DMD research, which is likely to lead to further collaborative transactions in the coming years.*

*There was **very high investment activity in 2017**. Therefore, it is likely that these high value capital raisings will continue into 2018, but **will switch to favour DMD strategic alliances by the end of 2018 and into 2019**. As such, a big strategic alliance deal for DMD drugs is anticipated for later this year.'*

*..Lisa Marris, GlobalData Common Content Databases Associate Analyst*



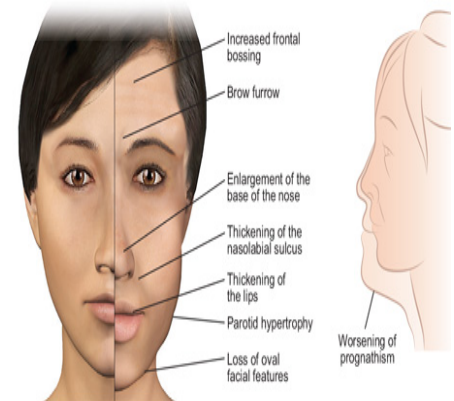
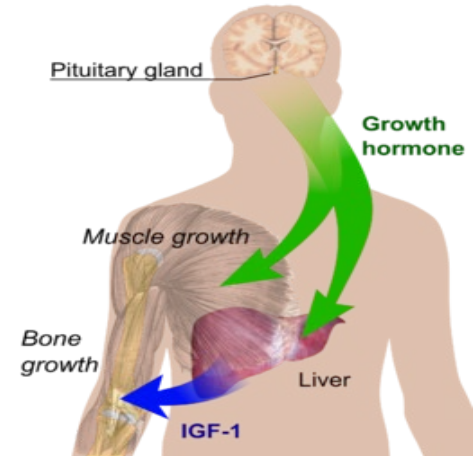
# ATL1103 for Acromegaly

## Acromegaly

- Abnormal enlargement of organs and bones of the face, feet and hands
- Due to a benign tumor of the pituitary gland causing excess Growth Hormone and Insulin-like Growth Factor 1 (sIGF-I) leading to diabetes, hypertension, and cancer (increased mortality rate up to 2.7x normal)
- Affects ~85 per million in the US and Europe (~85,000 adults): Orphan disease = incentives to develop
- Global sales for acromegaly drug treatment ~ \$1B/annum

## ATL1103

- ATL1103 (generic name – atesidorsen) reduces expression of GHr in the liver & blocks GH action on the liver, which reduces serum IGF-I
- **Normalising sIGF-I is the treatment goal in acromegaly**
- **ATL1103 has suppressed sIGF-I in all animal and human studies undertaken to date**
- Successful Phase II clinical trial with results published in peer reviewed journal (*Trainer PJ et al., Eur. J. Endocrinology, 2018*)
- **ATL1103 – Orphan drug designation in US & Europe**, lower cost of therapy, improved safety profile, more convenient dosing and administration



# Acromegaly Program Status – Early Access Program

- Early Access Program (EAP)
  - *Provide eligible patients with access to investigational medicines for unmet medical needs within the scope of the existing early access legislation*
  - *Provided in response to physician requests where other treatments have been unsuccessful and no alternative or appropriate treatment options are available to these patients*
- Agreement with myTomorrows to provide ATL1103 under an EAP in Europe in countries where ANP will seek reimbursement for drug supply costs
  - *ANP has sufficient supplies of ATL1103 drug product for 10 patients for 1 year*
  - *Labelled and packaged in the UK, drug product is ready to be shipped to myTomorrows warehouse in the Netherlands for EAP distribution subject to myTomorrows clearance for importation*
  - *Potential for income generation - current average cost for 2nd line acromegaly treatment in Europe is approximately A\$80K per patient per annum.*
  - *Possible for ANP to manufacture additional material to facilitate further demand under EAP*



myTomorrows



# ANP summary and near term value drivers

- ✓ Advanced stage product pipeline - two compounds with positive Phase II clinical results published in high quality peer reviewed scientific journals
- ✓ \$5m institutional raising @ \$0.024 completed in May 2018 for current DMD trial, with Australian Ethical Investment & Platinum Asset Management entering the register as substantial shareholders
- ✓ Dosing underway with potential for early study readouts in 2019 given open label trial status
- ✓ Drug potentially complementary to other DMD programs including those from Sarepta Therapeutics
- ✓ ATL1102 Phase II clinical trial in Duchenne Muscular Dystrophy
  - *Significantly 'underserved market' with comparable company benchmarks (Sarepta Therapeutics) demonstrating significant value creation potential*
  - *Scientific advisory board of internationally renowned experts with both DMD and related drug commercialisation experience in the space to guide development*
- ✓ ATL1103 Early Access Program (EAP)
  - *Allow biopharmaceutical companies to provide eligible patients with access to investigational medicines for unmet medical needs within the scope of the existing early access legislation*
  - *Potential to i. further stimulate Key Opinion Leader interest and support within a major pharmaceutical (Europe) market, ii. produce additional safety data (without associated clinical trial costs), iii. generate income and iv. facilitate partnering interest for the continued development of the drug*