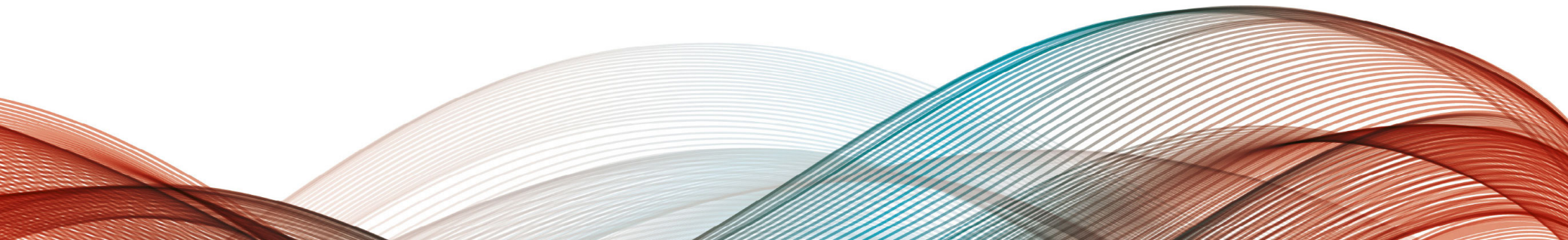
antisense THERAPEUTICS

AGM Presentation - November 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.

Corporate Snapshot

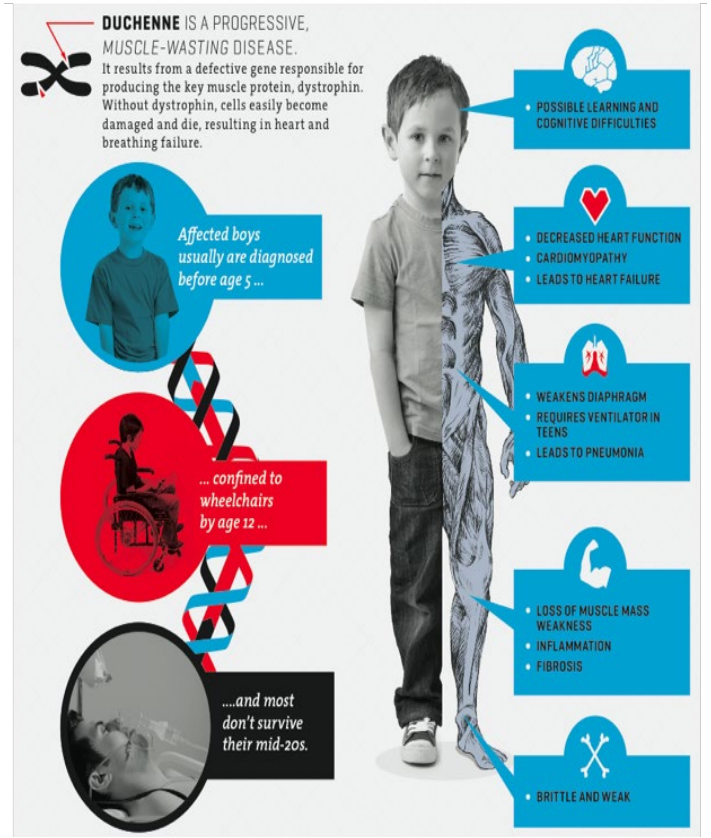
- ✓ Partnered with Ionis Pharmaceuticals (Nasdaq:IONS market capitalization: US$7 Billion), world leaders in antisense drug development and commercialisation, to develop RNA-targeted therapeutics
- ✓ Positive Phase 2 clinical results delivered from advanced stage product pipeline with two compounds (ATL1102 and ATL1103)
- ✓ Institutional raising completed in May 2018 for DMD trial, with Australian Ethical Investment & Platinum Asset Management entering the register as substantial shareholders
- ✓ **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*
- ✓ **Actively looking to expand product pipeline with the addition of complimentary new products/technologies**

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

ATL1102 in DMD	ATL1103 in acromegaly	ATL1102 in MS
• *Conducting Phase II clinical trial in Australia* • *Dosing commenced in August 2018*	• *Phase II clinical trial completed* • *Establishing Early Access Program in Europe*	• *Phase II clinical trial completed* • *Monitoring data from DMD trial to inform on future clinical development in MS*

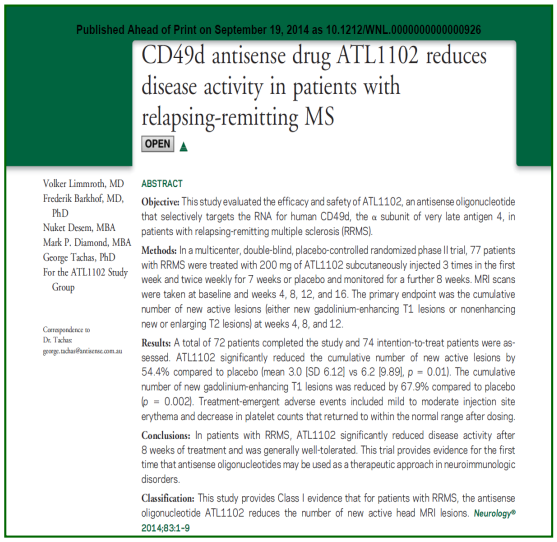
ATL1102 (targeting CD49d) for DMD

- 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



ATL1102 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



Published Ahead of Print on September 19, 2014 as 10.1212/WNL.0000000000000926

CD49d antisense drug ATL1102 reduces disease activity in patients with relapsing-remitting MS

OPEN

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ABSTRACT

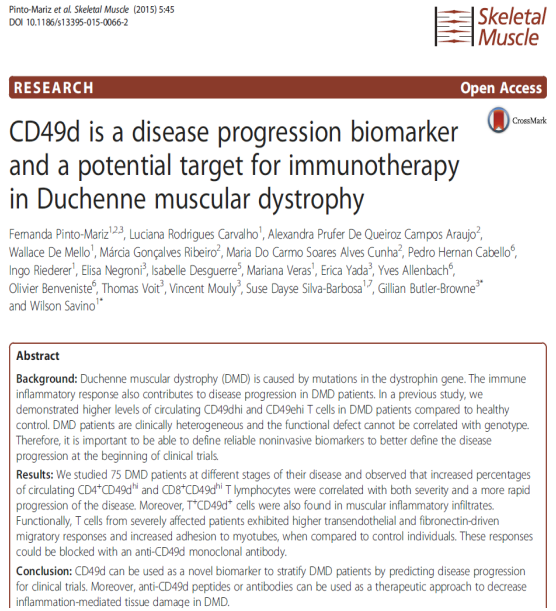
Objective: This study evaluated the efficacy and safety of ATL1102, an antisense oligonucleotide that selectively targets the RNA for human CD49d, the α subunit of very late antigen 4, in patients with relapsing-remitting multiple sclerosis (RRMS).

Methods: In a multicenter, double-blind, placebo-controlled randomized phase II trial, 77 patients with RRMS were treated with 200 mg of ATL1102 subcutaneously injected 3 times in the first week and twice weekly for 7 weeks or placebo and monitored for a further 8 weeks. MRI scans were taken at baseline and weeks 4, 8, 12, and 16. The primary endpoint was the cumulative number of new active lesions (either new gadolinium-enhancing T1 lesions or nonenhancing new or enlarging T2 lesions) at weeks 4, 8, and 12.

Results: A total of 72 patients completed the study and 74 intention-to-treat patients were assessed. ATL1102 significantly reduced the cumulative number of new active lesions by 54.4% compared to placebo (mean 3.0 [SD 6.12] vs 6.2 [9.89], $p = 0.01$). The cumulative number of new gadolinium-enhancing T1 lesions was reduced by 67.9% compared to placebo ($p = 0.002$). Treatment-emergent adverse events included mild to moderate injection site erythema and decrease in platelet counts that returned to within the normal range after dosing.

Conclusions: In patients with RRMS, ATL1102 significantly reduced disease activity after 8 weeks of treatment and was generally well-tolerated. This trial provides evidence for the first time that antisense oligonucleotides may be used as a therapeutic approach in neuroimmunologic disorders.

Classification: This study provides Class I evidence that for patients with RRMS, the antisense oligonucleotide ATL1102 reduces the number of new active head MRI lesions. *Neurology®* 2014;83:1-9



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

Skeletal Muscle

RESEARCH Open Access

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

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

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 $CD4^+CD49d^{hi}$ and $CD8^+CD49d^{hi}$ T lymphocytes were correlated with both severity and a more rapid progression of the disease. Moreover, T^+CD49d^+ 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

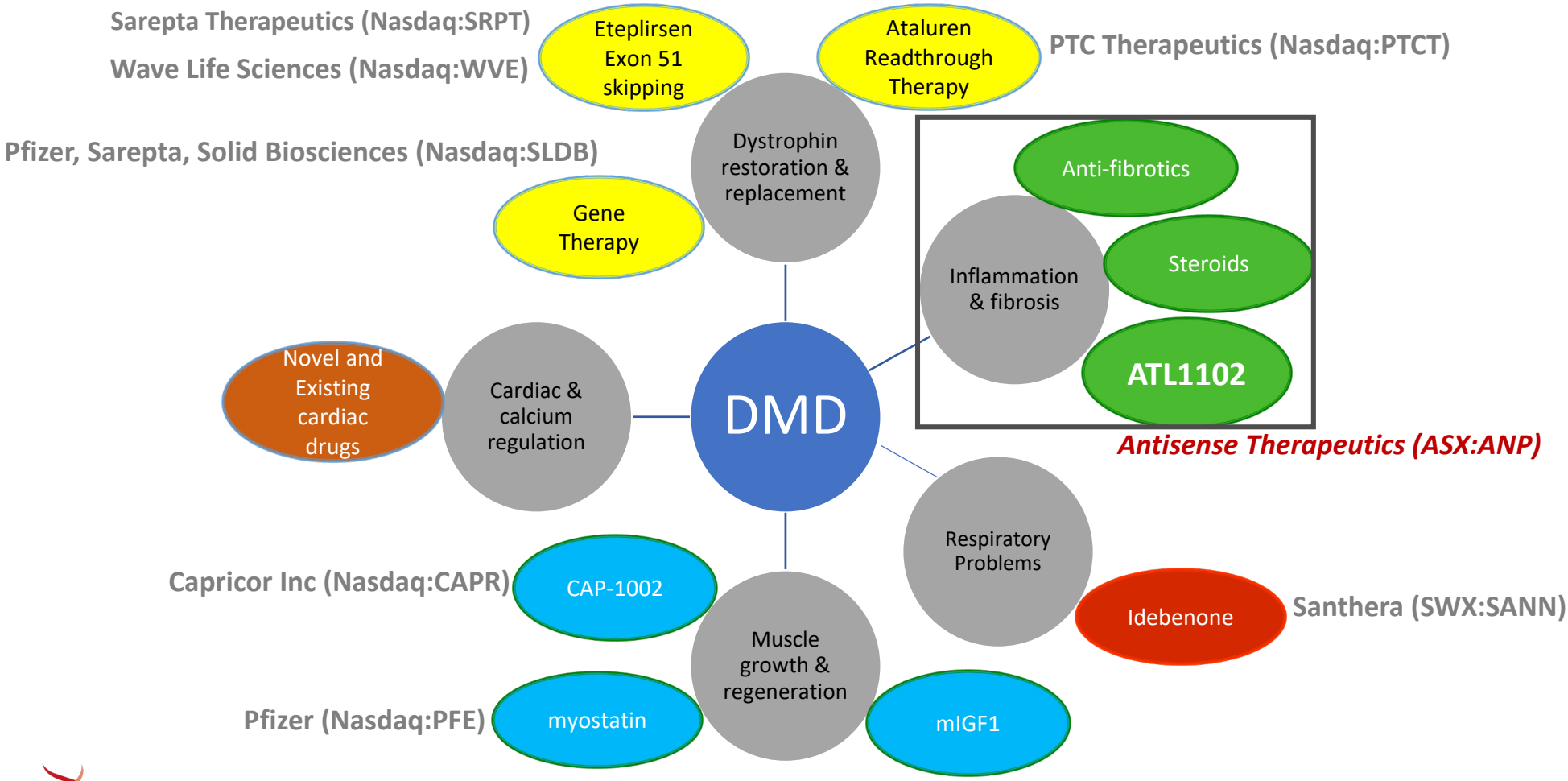
Director, Centre of Research in Myology, Sorbonne Universités, INSERM, Paris, France: Expert in inflammatory muscle disease

Mr William Goolsbee (SAB Chairman)

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

Treatment development focuses across all DMD Intervention points

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



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 to be conducted in n=9 non-ambulant 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)*
- Dosing commenced in August 2018 with 3 patients currently being dosed and 2 additional patients confirmed for screening before end of the year
- No serious adverse events reported from the trial to date
- Patient enrolment in line for dosing completion in 3Q'2019 with results to follow
- Open label study = possibility for earlier study read outs on preliminary data in a sufficient number of patients



Dr Ian R Woodcock
Neuromuscular Fellow, RCH, Melbourne Australia

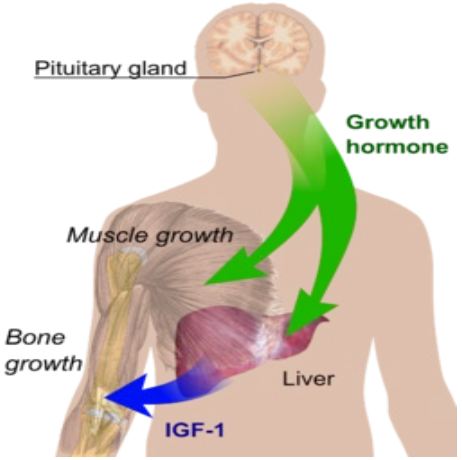


Prof. Monique Ryan
Head of Neuromuscular Clinic RCH, Melbourne Australia
Consultant Neurologist

ATL1103 for Acromegaly

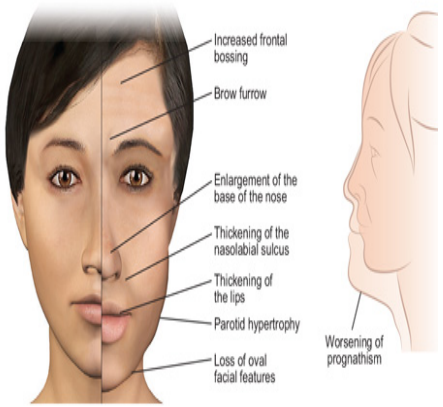
Acromegaly

- 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 approx. 10 patients for 1 year. Possible for ANP to manufacture additional material to facilitate further demand under EAP*
  - *Potential for income generation - current average cost for 2nd line acromegaly treatment in Europe is approximately A$80K per patient per annum*
  - *Labelled and packaged in the UK, ATL1103 drug product is to be shipped to myTomorrows in the Netherlands for EAP distribution subject to myTomorrows clearance for importation*
  - *Additional (to what has been required to support clinical trial usage) product data and documentation has had to be, and is being generated in order for the ATL1103 drug product to be supplied in accordance with the required regulatory and quality standards for use in the EAP. ANP is working closely with myTomorrow's in order that this process may be finalized and product released by myTomorrow's asap for use in the 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
- ✓ ATL1102 Phase II clinical trial in Duchenne Muscular Dystrophy
  - *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*
  - *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*
- ✓ Actively looking to expand product pipeline with the addition of complimentary products/technologies

Corporate Overview

Key Financials	
Market Capitalisation (@3.8c)	A$14M
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 – **54%**

ANP 12 month Trading History

