antisense THERAPEUTICS

Investor Presentation

ASX:ANP | OTC:ATHJY

Gold Coast 2019 Investment SHOWCASE

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FORWARD LOOKING STATEMENTS

This presentation contains forward-looking statements regarding the Company's business & the therapeutic & commercial potential of its technologies & products in development. Any statement describing the Company's goals, expectations, intentions or beliefs is a forward-looking statement & should be considered an at-risk statement. Such statements are subject to certain risks & uncertainties, particularly those risks or uncertainties inherent in the process of developing technology & in the process of discovering, developing & commercializing drugs that can be proven to be safe & effective for use as human therapeutics, & in the endeavor of building a business around such products & 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.

ANTISENSE THERAPEUTICS OVERVIEW

Melbourne-based biopharmaceutical company **developing & commercialising antisense pharmaceuticals** for large unmet markets

Advanced stage product pipeline with positive Phase II clinical results delivered from two compounds (ATL1102 & ATL1103)

Substantial shareholders include renowned institutions in life sciences Australian Ethical Investment & Platinum Asset Management & biotech pioneer Leon Serry

Phase II clinical trial in Duchenne Muscular Dystrophy (DMD)* – ATL1102 trial at Royal Children's Hospital Melbourne, results expected Q4 CY2019

Establishing Early Access Program (EAP) for acromegaly – ATL1103

Plan to provide ATL1103 to acromegaly patients under an EAP in Europe

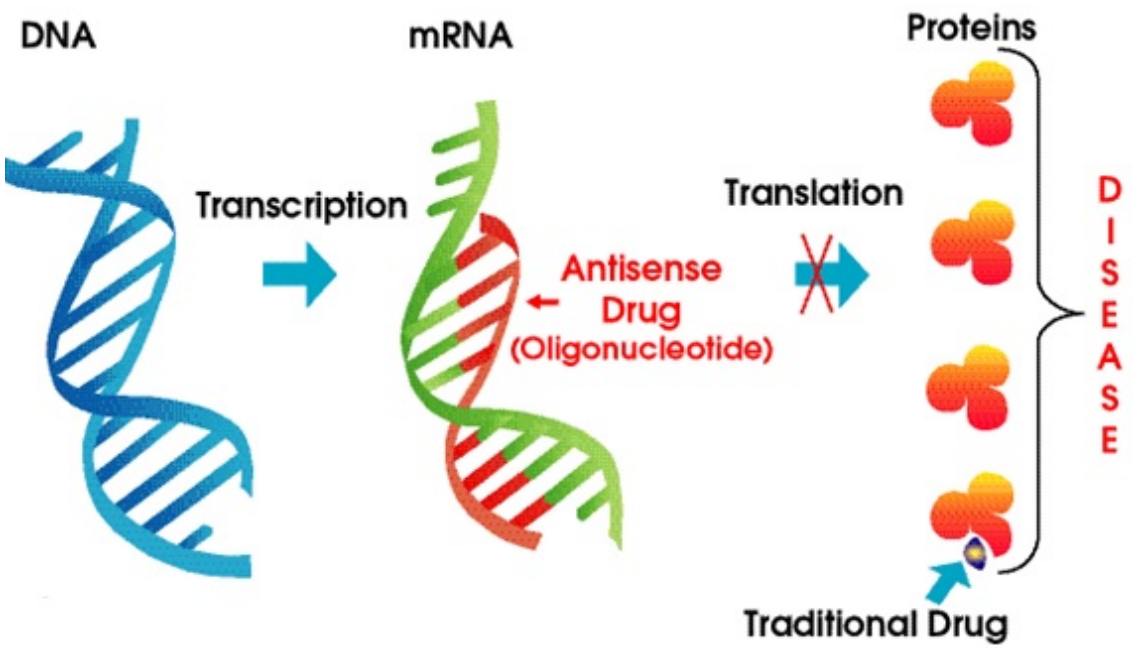
**DMD is one of the most common fatal genetic disorders caused by a mutation in the muscle dystrophin gene leading to severe progressive muscle loss & premature death in boys – high unmet medical need*

ANTISENSE – WHAT IS IT & 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

Antisense Therapeutics is partnered with Ionis Pharmaceuticals (market capitalisation:US$9 Billion), world leaders in antisense drug development & commercialisation, to develop RNA-targeted therapeutics



IONIS PHARMACEUTICALS

ANTISENSE THERAPEUTICS ADVANCED STAGE CLINICAL PIPELINE

Targeting diseases where there is a need for improved therapies

1

ATL1102 IN DMD

- *Conducting Phase II clinical trial at Royal Children's Hospital in Melbourne*
- *Trial is fully enrolled, results expected Q4 CY2019*

2

ATL1103 IN ACROMEGALY

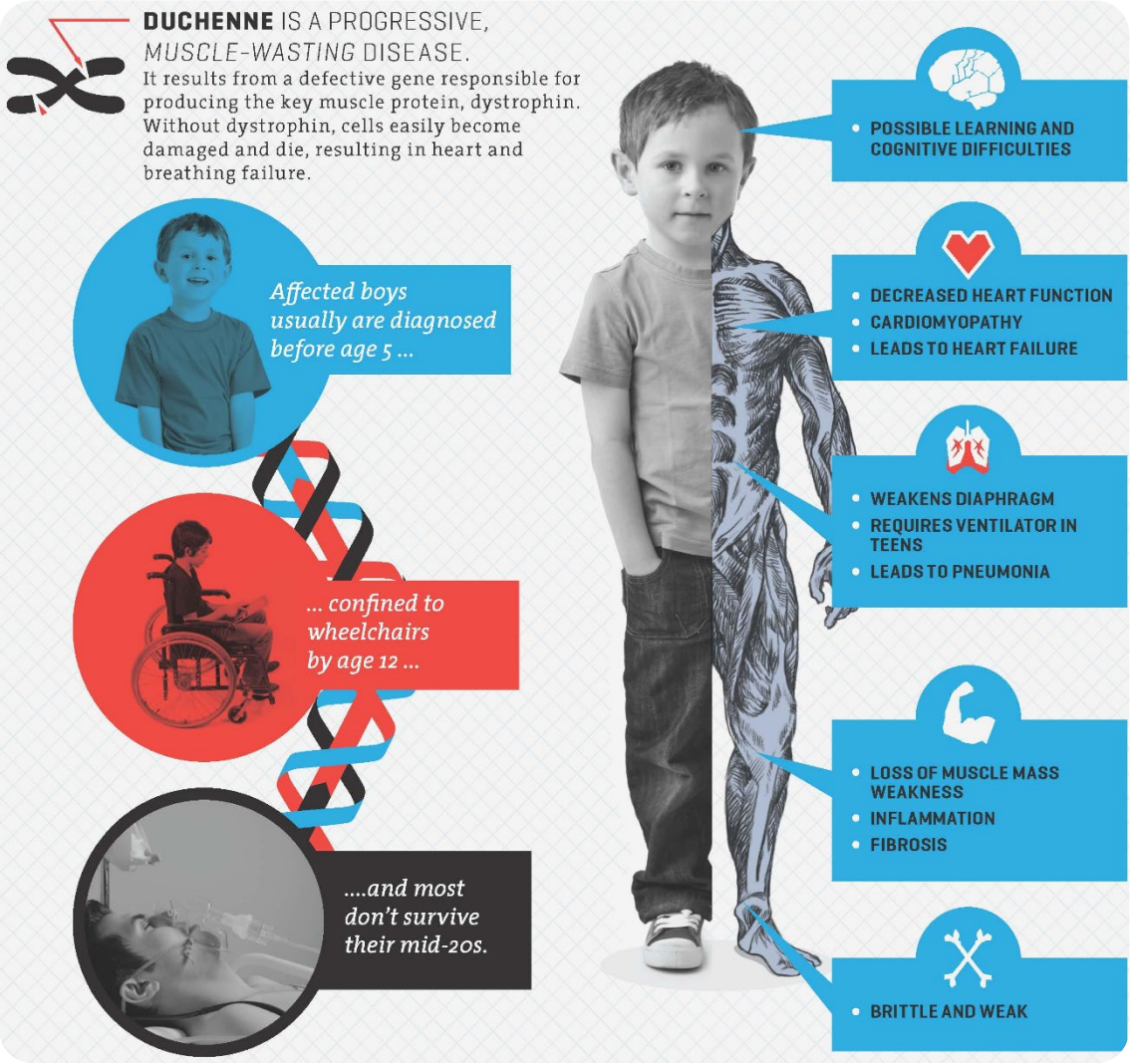
- *Phase II clinical trial completed*
- *To establish an Early Access Program in Europe*

3

ATL1102 IN MS

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

WHAT IS DMD?

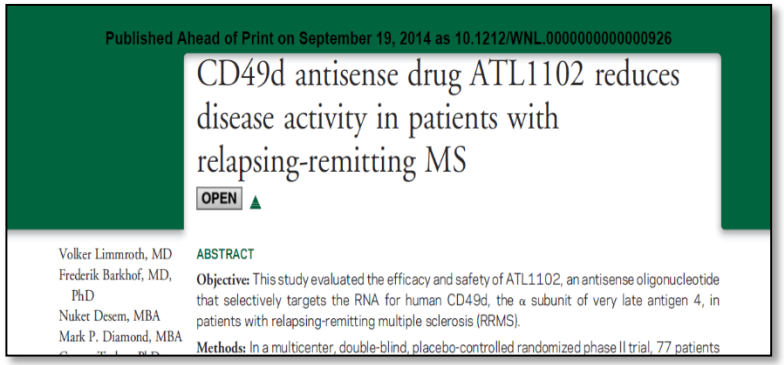


Source: CureDuchenne

- Duchenne Muscular Dystrophy (DMD) is a devastating genetic muscular disease caused by loss of dystrophin with progressive muscle wasting & associated muscle injury leading to inflammation & fibrosis (100% mortality)
- Affects boys with an incidence of ~1 in 3,500 & 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) are the <u>only</u> therapy used to treat the inflammation in DMD but have insufficient efficacy & significant side effects including weight gain, reduced bone density & growth retardation. CS not as effective in patients with a greater number of CD49d receptors on T cells.

WHY ATL1102 for DMD?

- Improved therapies are needed to ameliorate DMD severity & delay disease progression
- DMD is an orphan indication so can benefit from IP & 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

Volker Limmroth, MD
Frederik Barkhof, MD, PhD
Nuket Desem, MBA
Mark P. Diamond, MBA

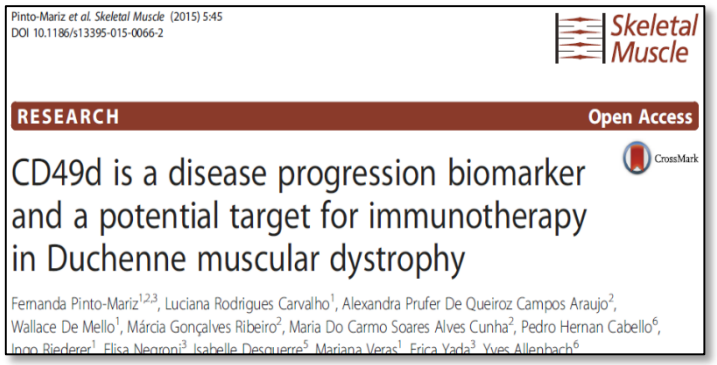
ABSTRACT

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

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 & B cells, and T & B cell numbers by ~25 & 50% respectively*
- *Pre-clinical & clinical data in MS has supported move directly into the six-month DMD patient trial (effective leveraging of substantial investment & progress made to date in MS)*


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

Skeletal Muscle

RESEARCH Open Access

CrossMark

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]

Pivotal scientific publication confirming CD49d as a potential target for DMD therapy

- *DMD patients with greater number of circulating T cells with high levels of CD49d (alpha chain of VLA-4) expression have both more severe & 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 number of CD49d high expressing T cells*

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ATL1102 DMD PHASE II CLINICAL TRIAL

OPEN LABEL PHASE II TRIAL IN DMD PATIENTS AT THE ROYAL CHILDREN'S HOSPITAL (RCH) MELBOURNE

- *Study in nine non-ambulant (wheelchair bound) boys 10-18 years of age with DMD*
- *Will assess ATL1102's safety & tolerability as well as its effects on the inflammation that contributes to disease progression in DMD – conducted over 24 weeks of dosing at 25 mg/week*
- *Study is a safety & tolerability investigation while also looking to show a difference in serum biomarkers of inflammation & muscle damage & to detect a difference at 6 months in key clinical endpoints (e.g. the upper limb function and strength of the patients)*

Dr Ian R Woodcock
Neuromuscular Fellow,
RCH, Melbourne Australia

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

- Trial being led by RCH Head of Neuromuscular Clinic Professor Monique Ryan & RCH Neuromuscular Fellow Dr Ian Woodcock
- Neuromuscular clinic at RCH the largest in the Southern Hemisphere for treating boys with DMD
- No serious adverse events reported from the trial to date
- Trial is fully enrolled, results expected in Q4 CY2019
- As an open label study there is the possibility for earlier study read outs on preliminary data in a sufficient number of patients

PHASE IIB CLINICAL TRIAL

1. Accelerating development planning for ATL1102 in seeking path to product registration
2. Advice received from regulatory consultants that, based on existing ATL1102 preclinical & clinical data, ANP could seek approval in Europe for a Phase IIb clinical trial
3. Discussions to be held with authorities (in Europe initially) for the design & conduct of the next clinical trial of ATL1102
4. This regulatory process is to run in parallel with the Phase II trial at RCH in Melbourne, thereby accelerating development

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ATL1102 FOR DMD – SCIENTIFIC ADVISORY BOARD

Dr Ian Woodcock MD (Principal Investigator)
Royal Children's Hospital (RCH) Neuromuscular Fellow, Melbourne Australia

Professor Sue Fletcher PhD
Principal Research Fellow, NRI Murdoch University, Perth, Western Australia: Patent holder on target sequence of Sarepta's drug eteplirsen & additional exon-skipping drugs

Professor Monique Ryan MD (Co- Investigator)
Director Neurology Department, Head of Royal Children's Hospital, Neuromuscular Clinic
RCH, MCRI, Melbourne Australia

Dr Gillian Butler-Browne PhD
Director, Centre of Research in Myology, Sorbonne Universités, INSERM, Paris, France: Expert in inflammatory muscle disease, author of CD49d Skeletal Muscle 2015 research paper

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 & additional exon-skipping drugs

Mr William Goolsbee (SAB Chairman)
Antisense Therapeutics Ltd, non-executive director: Chairman, Sarepta Therapeutics, 2010-2014, Developers of eteplirsen for the treatment of DMD

The Royal Children's Hospital Melbourne

MURDOCH UNIVERSITY PERTH, WESTERN AUSTRALIA

UNIVERSITÉ PARIS SORBONNE PARIS IV

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TREATMENT DEVELOPMENT FOCUSING ACROSS ALL INTERVENTION POINTS

Prospect for these therapies to be complementary rather than competitive

DMD	INTERVENTION POINTS	TREATMENT	PROVIDERS
	INFLAMMATION & FIBROSIS	ANTI-FIBROTICS	
		STEROIDS	
		ATL1102	antisense THERAPEUTICS
	CARDIAC & CALCIUM REGULATION	NOVEL & EXISTING CARDIAC DRUGS	
	DYSTROPHIN RESTORATION & REPLACEMENT	GENE THERAPY	*Pfizer, Sarepta, Solid Biosciences (Nasdaq:SLDB)*
		ETEPLIRSEN EXON 51 SKIPPING	*Sarepta Therapeutics (Nasdaq:SRPT)* *Wave Life Sciences (Nasdaq:WVE)*
		ATALUREN READTHROUGH THERAPY	*PTC Therapeutics (Nasdaq:PTCT)*
	RESPIRATORY PROBLEMS	IDEBENONE	*Santhera (SWX:SANN)*
	MUSCLE GROWTH & REGENERATION	CAP-1002	*Capricor Inc (Nasdaq:CAPR)*
		MYOSTATIN	*Pfizer (Nasdaq:PFE)*
		MIGF1	

frontiers in Genetics

MINI REVIEW
published: 10 April 2018
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Combined Therapies for Duchenne Muscular Dystrophy to Optimize Treatment Efficacy

Gonzalo Cordova[1], Elisa Negroni[1], Claudio Cabello-Verrugio[2,3], Vincent Mouly[1] and Capucine Trollet[1]*

[1] Sorbonne Université, Institut National de la Santé et de la Recherche Médicale, Association Institut de Myologie, Centre de Recherche en Myologie, UMRS974, Paris, France, [2] Laboratorio de Patologías Musculares, Fragilidad y Envejecimiento, Departamento de Ciencias Biológicas, Facultad de Ciencias Biológicas, Universidad Andres Bello, Santiago, Chile, [3] Millennium Institute on Immunology and Immunotherapy, Santiago, Chile

Duchene Muscular Dystrophy (DMD) is the most frequent muscular dystrophy and one of the most severe due to the absence of the dystrophin protein. Typical pathological features include muscle weakness, muscle wasting, degeneration, and inflammation. At advanced stages DMD muscles present exacerbated extracellular matrix and fat accumulation. Recent progress in therapeutic approaches has allowed new strategies to be investigated, including pharmacological, gene-based and cell-based therapies. Gene and cell-based therapies are still limited by poor targeting and low efficiency in fibrotic dystrophic muscle, therefore it is increasingly evident that future treatments will have to include "combined therapies" to reach maximal efficiency. The scope of this mini-review is to provide an overview of the current literature on such combined therapies for DMD. By "combined therapies" we mean those that include both a therapy to correct the genetic defect and an additional one to address one of the secondary pathological features of the disease. In this mini-review, we will not provide a comprehensive view of the literature on therapies for DMD, since many such reviews already exist, but we will focus on the characteristics, efficiency, and potential of such combined therapeutic strategies that have been described so far for DMD.

MARKET CONSIDERATIONS FOR ATL1102

ATL1102 - anti-inflammatory and immune modulating agent with potential for multiple clinical applications

ANTI-INFLAMATORY

*Anti-Inflammatory Therapeutics Market^ is expected to garner **US$106.1 billion** by 2020*

(Allied Market Research)

^MS, Arthritis, Psoriasis, Respiratory, IBD

CORTICOSTEROIDS

*The global steroid market is forecast to attain the value of **US$17 Billion** by the end of 2025*

(QV Research)

DMD THERAPIES

*The global DMD drug market is expected to reach over **US$4 Billion** by 2023*

(Grand View Research)

- Corticosteroids are the only marketed therapy to treat the inflammatory damage associated with dystrophin loss in DMD
- Prevalence of DMD in EU and US est. 44,000 with most ambulant and ~2/3 of non-ambulant patients on corticosteroids*
- DMD cost of therapy considerations

  Deflazacort (Emflaza) is a CS approved in US only - average annual cost estimated US$65K per patient per annum

  Exondys 51 (dystrophin restoration agent) cost in the US is US$300K per patient per year

* Cowan L et al BMC Neurology (2019), 1-10

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VALUE CREATION POTENTIAL OF ATL1102 FOR DMD

- Approval based on the surrogate endpoint of dystrophin increase in skeletal muscle observed in some Exondys 51-treated patients
- Sarepta market capitalisation has grown from ~US$60m prior to FDA approval of Exondys 51 (July 2012) to today's ~US$9 billion
- Exondys 51 – despite being first FDA approved treatment for DMD is only useful in 13% of boys with the exon 51 mutation
- Inflammation (the target of ATL1102 in DMD) contributes to disease progression in all DMD patients

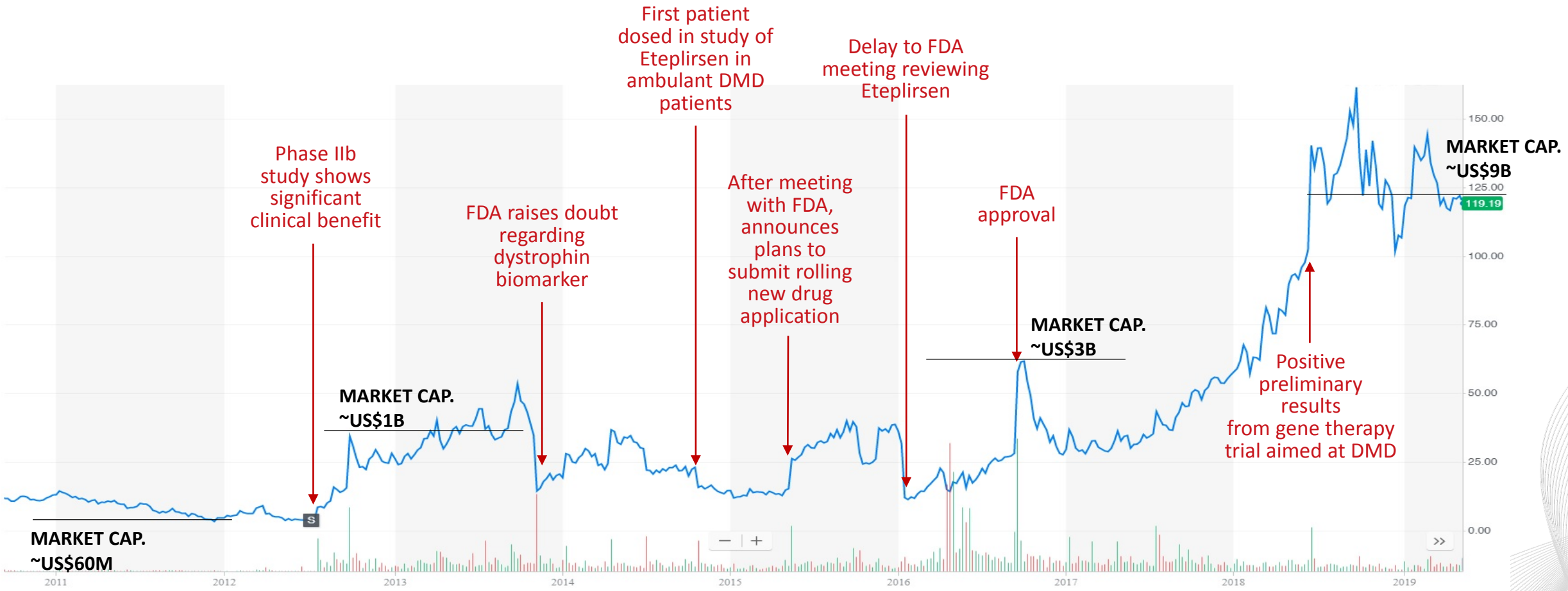
- Cost per patient of Exondys 51 is US$300K/year
- 4th quarter 2018 total net revenue for Exondys 51 – US$84.4 million
- Exondys 51 inventor Professor Steve Wilton (Murdoch University, Perth) is a member of the Antisense Therapeutics Scientific Advisory Board
- Mr William Goolsbee, ex Chairman of Sarepta, is a non-executive director of Antisense Therapeutics

EXONDYS 51 (DEVELOPED BY SAREPTA) APPROVED BY THE FDA IN LATE 2016 UNDER THE ACCELERATED APPROVAL PATHWAY

SAREPTA THERAPEUTICS

VALUE CREATION POTENTIAL OF ATL1102 FOR DMD

Sarepta Therapeutics & its approved DMD drug Eteplirsen



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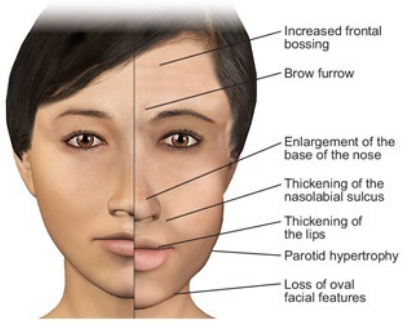
ATL1103 FOR ACROMEGALY

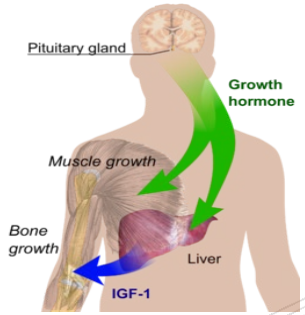
ACROMEGALY

- Abnormal enlargement of organs & bones of the face, feet & hands
- Due to a benign tumor of the pituitary gland causing excess growth hormone & Insulin-like Growth Factor 1 (sIGF-I) leading to diabetes, hypertension, & cancer (increased mortality rate up to 2.7x normal)
- Affects ~85 per million in the US & 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, reducing serum IGF-I
- Normalising sIGF-I is the treatment goal in acromegaly
- ATL1103 has suppressed sIGF-I in all animal & 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*)
- **Orphan drug designation in US & Europe**, lower cost of therapy, improved safety profile, more convenient dosing & administration





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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 & 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 Antisense Therapeutics will seek reimbursement for drug supply costs

- *Antisense Therapeutics has sufficient supplies of ATL1103 drug product for approx. 10 patients for one year. Possible for Antisense Therapeutics 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 & 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 & documentation has had to be, & is being generated in order for the ATL1103 drug product to be supplied in accordance with the required regulatory & quality standards for use in the EAP. Antisense Therapeutics is working closely with myTomorrows in order that this process may be finalised & product imported & released by myTomorrows for use in the EAP*

BOARD OF DIRECTORS

Mr Robert W Moses

Independent Non-Executive Chairman

Formerly Corporate Vice President of CSL Limited. Mr. Moses draws on more than 40 years' experience in the pharmaceutical/ biotechnology industry.

Mr Mark Diamond

Managing Director & Chief Executive Officer

Over 30 years' experience in the pharmaceutical & biotechnology industry. Formerly Director, Project Planning/Business Development at Faulding Pharmaceuticals in the USA, Senior Bus Dev Manager within Faulding's European operation & International Business Development Manager with Faulding in Australia.

Dr Graham Mitchell

Independent Non-Executive Chairman

Joint Chief Scientist for the Victorian Government Department of Environment & Primary Industries. Formerly Director of Research in the R&D Division of CSL Limited.

Dr Gary Pace

Independent Non-Executive Director

Dr Pace has more than 40 years' international experience in the development & commercialisation in biotechnology/ pharmaceuticals industries. Long-term board level experience with both multi-billion & small cap companies.

Mr William Goolsbee

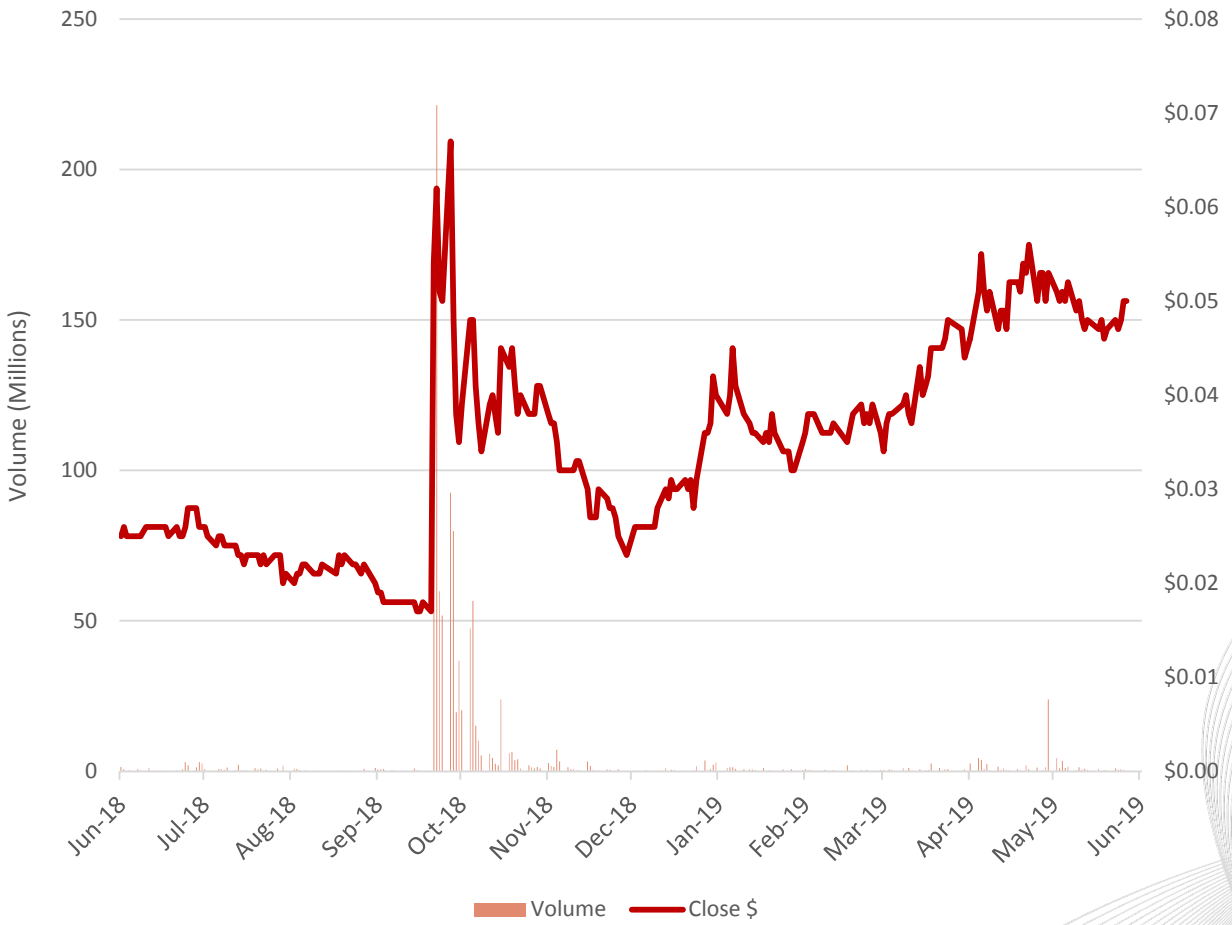
Independent Non-Executive Director

Founder, Chairman & CEO of Horizon Medical Inc. 1987 – 2002 until acquisition by UBS Private Equity. Founding Director then Chairman of ImmunoTherapy Corporation until acquisition by AVI Biopharma, Inc. (now Sarepta Therapeutics). Former Chairman of privately held BMG Pharma LLC & Metrodora Therapeutics.

CORPORATE OVERVIEW

KEY FINANCIALS	
Market Capitalisation (at $0.047)	A$20M
Shares on issue	420.1M
52-week high/low	$0.094 - $0.017
Options (ANPOB, $0.08 exp. 19/12/19)	68.7m
Cash as at 31 March 2019	$3.67M

OWNERSHIP STRUCTURE	
Top 40 holders	$58.7%
Substantial Shareholders	
• *Australian Ethical Investment*	*19.96%*
• *Platinum Asset Management*	*8.57%*
• *Leon Serry*	*6.15%*



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ANTISENSE THERAPEUTICS SUMMARY & VALUE DRIVERS

Advanced stage product pipeline – **two compounds with positive Phase II clinical results published in high quality peer reviewed scientific journals**

Highly regarded substantial shareholders – have increased their holdings

Phase II clinical trial in Duchenne Muscular Dystrophy (DMD) – ATL1102

- Trial is fully enrolled, results expected Q4 CY2019
- Phase IIb trial design and approval process to run in parallel, accelerating development of ATL1102
- Drug potentially complementary to other DMD programs e.g. Sarepta Therapeutics
- Significantly 'underserved market' with comparable company benchmarks demonstrating substantial value creation potential

Establishing Early Access Program (EAP) for acromegaly – ATL1103

- Plan to provide ATL1103 to acromegaly patients under an EAP in Europe
- Potential for income generation & partnering to further develop the compound

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