



antisense

THERAPEUTICS

ASX:ANP | OTC:ATHJY

ANNUAL GENERAL MEETING 2019



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 2019, which is available from the Company or at www.antisense.com.au.



ANTISENSE THERAPEUTICS OVERVIEW



Australian, 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 Australian institutions in life sciences Australian Ethical Investment & Platinum Asset Management & Australian biotech pioneer Leon Serry



Phase II clinical trial in Duchenne Muscular Dystrophy (DMD)* – ATL1102 trial at Royal Children's Hospital Melbourne, Australia positive preliminary results reported

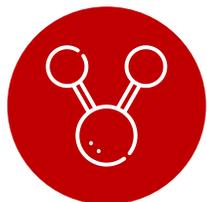


Potential for out-licensing of ATL1103 for acromegaly.
Preliminary interest from pharmaceutical companies

**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?



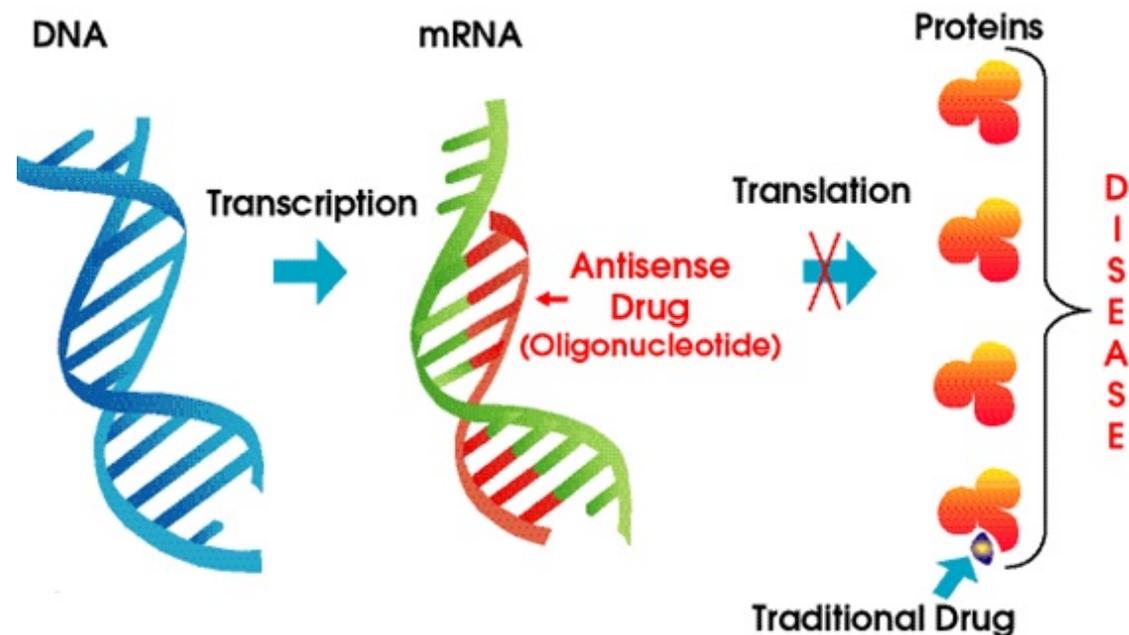
Antisense oligonucleotide drugs are small (12-25 nucleotides) DNA or RNA-like compounds that are chemically modified to create medicines



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



ANP is partnered with Ionis Pharmaceuticals (IONS: market capitalisation:US\$9 Billion), world leaders in antisense drug development & commercialisation





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, Australia*
- *Positive preliminary results reported*
- *Dosing completed in all 9 patients*

2

ATL1103 IN ACROMEGALY

- *Phase II clinical trial completed*
- *Potential for out-licensing to support and fund further clinical development*

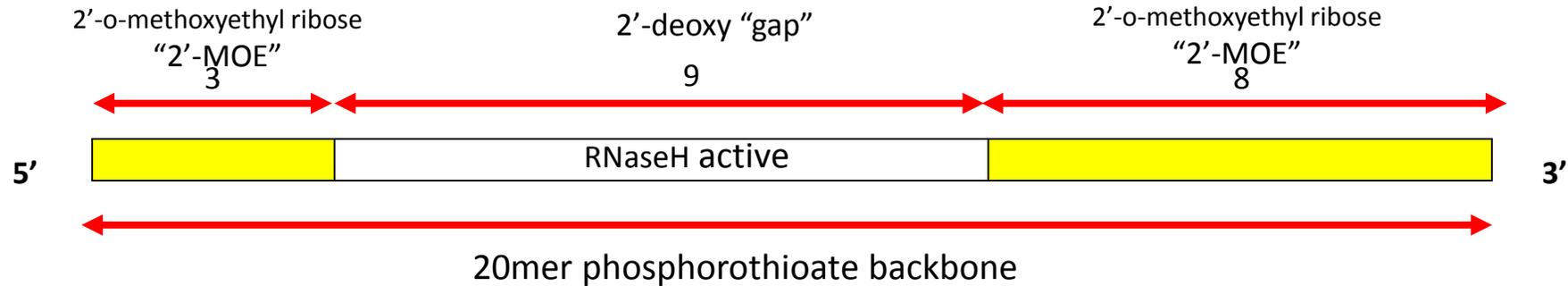
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ATL1102 IN MS

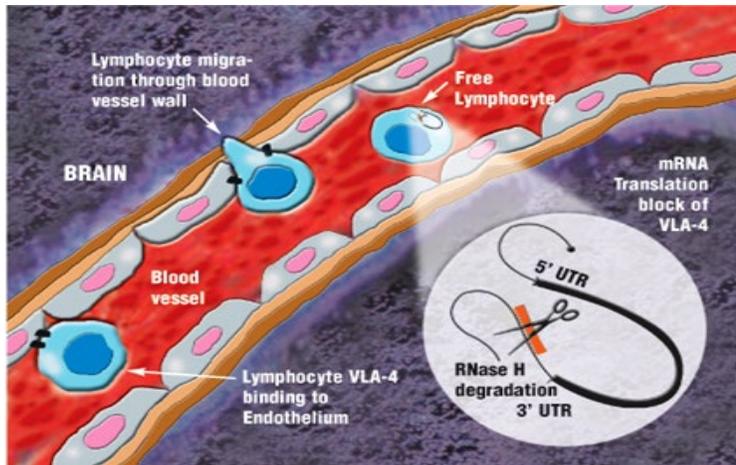
- *Phase II clinical trial completed*
- *Monitoring data from DMD trial to inform on future clinical development in MS*



ATL1102: DRUG, TARGET & ACTIVITY OVERVIEW



- ATL1102 is designed to inhibit CD49d expression on lymphocytes and thereby reduce their survival, activation and migration from the blood into sites of inflammation
- ATL1102 is an designed to inhibit CD49d expression on lymphocytes and thereby stop/restrict there migration from the blood into sites of inflammation (e.g. the CNS in Multiple Sclerosis patients as pictured below) to reduce or modulate the adverse inflammatory effects



WHAT IS DMD?

DUCHENNE IS A PROGRESSIVE, **MUSCLE-WASTING DISEASE.** It results from a defective gene responsible for producing the key muscle protein, dystrophin. Without dystrophin, cells easily become damaged and die, resulting in heart and breathing failure.

Affected boys usually are diagnosed before age 5 ...

... confined to wheelchairs by age 12 ...

....and most don't survive their mid-20s.

- POSSIBLE LEARNING AND COGNITIVE DIFFICULTIES
- DECREASED HEART FUNCTION
• CARDIOMYOPATHY
• LEADS TO HEART FAILURE
- WEAKENS DIAPHRAGM
• REQUIRES VENTILATOR IN TEENS
• LEADS TO PNEUMONIA
- LOSS OF MUSCLE MASS
• WEAKNESS
• INFLAMMATION
• FIBROSIS
- BRITTLE AND WEAK

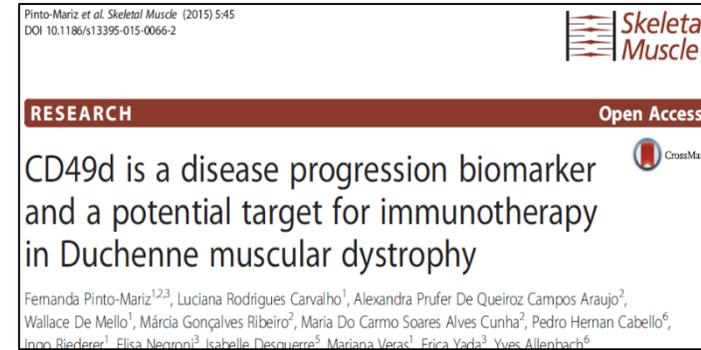
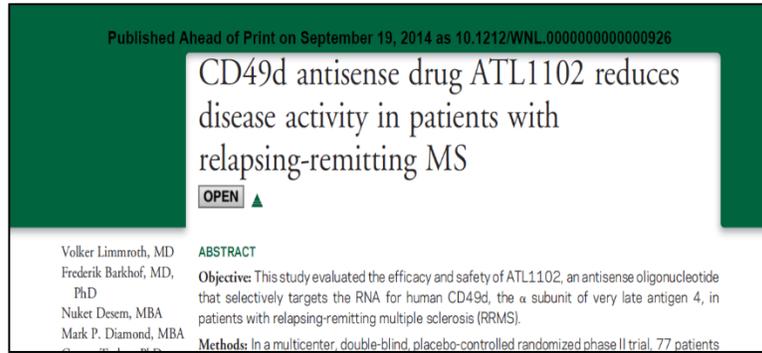
Source: CureDuchenne

- 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 only 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*



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)*

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*



ATL1102 PHASE II STUDY

- *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*

Study Title:

A Phase 2 open label study to determine the safety, efficacy and pharmacokinetic profile of weekly dosing of ATL1102 in patients with non-ambulatory Duchenne Muscular Dystrophy. (ACTRN12618000970246)

Primary objective:

To assess the safety and tolerability of 25 mg of ATL1102 administered once weekly (s.c. injection) for 24 weeks in non-ambulatory DMD participants

Secondary objectives:

To evaluate the

- lymphocyte-modulatory potential of ATL1102 in participants with DMD
- PK profile of ATL1102 in participants with DMD
- effects of ATL1102 on functional capacity in participants with DMD
- effects of ATL1102 on respiratory function in participants with DMD
- effects of ATL1102 on quality-of-life in participants with DMD

Design:

Single-centre, open-labelled study conducted at the Royal Children's Hospital (RCH), Melbourne, Australia

Sample size:

9 participants

Target population:

- participants diagnosed with DMD and have been non-ambulatory for at least 3 months
- 10 to 18 years of age
- body weight of more than 25 kg and less than or equal to 65 kg



ATL1102 PHASE II STUDY - SAFETY OVERVIEW

Preliminary Data Presented by Dr Ian Woodcock at Action Duchenne Conference Nov 2019 on first 7 boys to have completed dosing

An Independent Data and Safety Monitoring Board (DSMB) provides safety oversight for the study

- The DSMB consists of 3 paediatricians and a biostatistician, the DSMB is chaired by A/Professor Andrew Kornberg, MD
- The DSMB evaluate safety data on an ongoing basis and based upon the evaluation, issue formal recommendations for continuation/modification/discontinuation of the study to the sponsor
- Based on their review of the data to date, **the DSMB have no safety concerns**

ATL1102 appears to be generally well tolerated

- No Serious Adverse Events (SAEs) have been reported
- No participants have been withdrawn from the study for safety related reasons
- The most commonly reported TEAEs were injection site erythema (8 participants), skin discolouration (7 participants), injection site pain (5 participants) and injection site bruising (4 participants)



ATL1102 PHASE II STUDY

Overview of Efficacy Parameters - Preliminary Data

The Secondary Objectives of the study include evaluation of the following efficacy parameters:

- Lymphocyte-modulation potential to be determined by assessing number and percentages of lymphocytes, CD4+ and CD8+ T cells and, CD4+ CD49d and CD8+ CD49d T cells
 - *Early indications of an immunomodulatory effect have been observed where T-cell numbers (in particular those expressing the CD49d, the biological target of ATL1102) are trending downward during the 24-week treatment phase while returning to around starting levels post dosing*
- Effects of ATL1102 on functional capacity in participants with DMD
 - *Evaluation of muscle function via Performance of Upper Limb Test (PUL 2.0)*
 - *Evaluation of muscle strength via MyoGrip and MyoPinch assessments (using the Myoset System)*
- data presented on the following slide
- Effects of ATL1102 on respiratory function in participants with DMD
 - *Includes % predicted Peak Expiratory Flow (PEF) and % predicted Forced Expiratory Volume (FVC)*
- data presented on the following slide



ATL1102 PHASE II STUDY

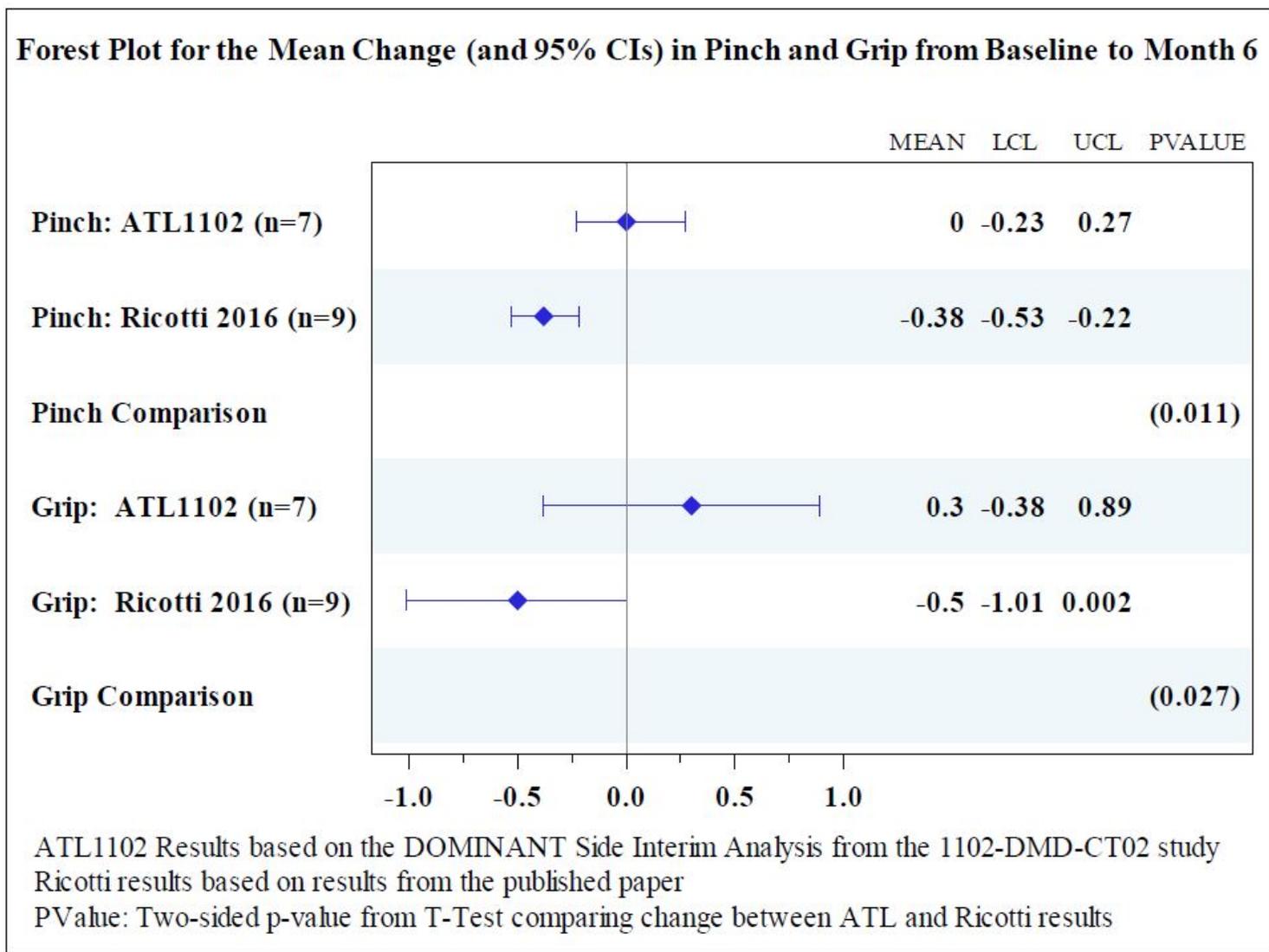
Overview of Efficacy Parameters - Preliminary Data

	Change from Baseline to Week 24						
Patient No.	PUL 2.0	MyoGrip (dom) (Kg)	MyoGrip (dom) (% Pred)	MyoPinch (dom) (Kg)	MyoPinch (dom) (% Pred)	% Predicted FVC	% Predicted PEF
01-001	+2	-0.63	-4.49	0.03	-0.62	-3.20	6.30
01-002	+2	0.22	0.49	-0.02	-0.29	-14.8	-17.3
01-003	0	0.68	1.02	-0.40	-6.59	-9.10	8.70
01-004	+2	1.09	1.01	0.37	2.99	0.80	7.20
01-006	-3	-0.27	-0.60	0.07	0.94	-6.50	6.90
01-008	+7	1.00	1.11	0.30	2.77	-7.70	-18.2
10-009	0	-0.33	-3.75	-0.22	-4.97	-9.10	-4.30
01-010							
01-011							
Mean Change (95% CI):	1.4 (-1.39, 4.25)	0.3 (-0.38, 0.89)	-0.7 (-2.95, 1.47)	0.0 (-0.23, 0.27)	-0.8 (-4.23, 2.58)	-7.09 (-11.6,-2.53)	-1.53 (-12.5, 9.46)



ATL1102 Phase II Study

Efficacy Parameters – Comparison to Published Data for Myoet Assessments



* Ricotti et. al 2016 . PLoS One, 11(9) e0162542 historical results from 8 Non – Ambulant patients on CS for 6month



ATL1102 PHASE II STUDY

Summary of Safety and Efficacy Parameters - Preliminary Data

- ATL1102 appears to be generally safe and well tolerated in non-ambulant boys with DMD
 - No Serious Adverse Events (SAEs) have been reported
 - The DSMB, responsible for safety oversight of the study, have no safety concerns
 - To date the most commonly reported TEAEs were injection site erythema (8 participants), skin discolouration (7 participants), injection site pain (5 participants) and injection site bruising (4 participants)
- ATL1102, a novel antisense drug being developed for the treatment of inflammation that exacerbates muscle fibre damage in DMD, appears to be demonstrating positive effects on disease progression parameters
 - Data from the first 7 participants completing dosing shows an apparent improvement in muscle strength based on the change from baseline after 24 weeks of dosing with ATL1102 as assessed by MyoGrip and MyoPinch compared to the loss of muscle strength reported in the literature in similar patient populations
 - The preliminary data is also suggestive of an improvement in muscle function as assessed by the Performance of Upper Limb Test (PUL 2.0), where the majority of participants have demonstrated either improvements or no change in their PUL 2.0 scores from baseline after 24 weeks of dosing with ATL1102
- Promising preliminary results support continued development of ATL1102 for the treatment of DMD



ATL1102 PHASE II STUDY

Reporting of data from all 9 subjects post completion of dosing

- All 9 participants have completed their 6 months of dosing
- The trial is continuing with patients in the 2 month monitoring phase or follow up period of the trial
- The Last Participant Last Visit (in follow up period) for the study will be beginning of Jan 2020
- Results from the completion of dosing in all patients remain on track to be reported before the end of the year
- Data is to be reviewed by the Board during their AGM associated visit and expected to be reported soon thereafter



PHASE IIB CLINICAL TRIAL

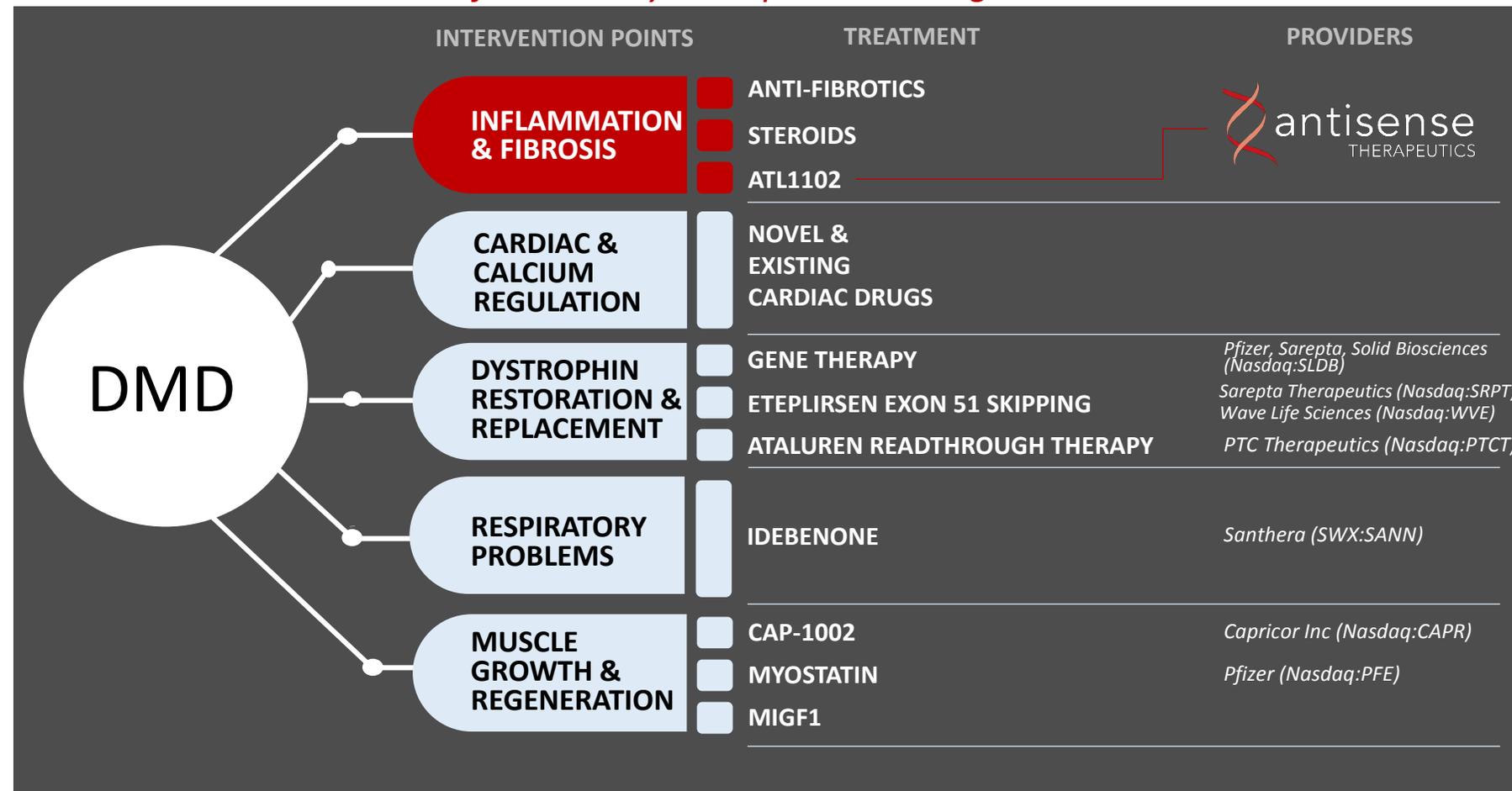
- Scientific Advice (SA) meetings held with three European regulatory authorities
- SA meetings focussed on the Phase Iib trial design, dose escalation plans, applicability of the study end-points and the study duration. ANP expects to receive written responses month following each meeting
- General acceptance by the agencies on the trial efficacy endpoints (Pul2, Myoset), safety monitoring plan, dosing duration (1 year) and the use of higher doses
- Clarification provided by the agencies that the above could be a path forward to an approval on positive Phase Iib results
- Next step is to follow up development plan with the European Medicines Agency (EMA) and subsequent to the finalisation of the results from the current Phase II trial, engage with the Food and Drug Administration (FDA) on development plans for the US



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

TREATMENT DEVELOPMENT FOCUSING ACROSS ALL INTERVENTION POINTS

- Prospect for these therapies to be complementary rather than competitive
- Other anti-inflammatory therapies are being tested in ambulant children



Combined Therapies for Duchenne Muscular Dystrophy to Optimize Treatment Efficacy

Gonzalo Cordova¹, Elisa Negroni¹, Claudio Cabello-Verrugio^{2,3}, Vincent Mouly¹ 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, UMR5974, Paris, France, ² Laboratorio de Patologías Musculares, Fragilidad y Envajamiento, Departamento de Ciencias Biológicas, Facultad de Ciencias Biológicas, Universidad Andrés Bello, Santiago, Chile, ³ Millennium Institute on Immunology and Immunotherapy, Santiago, Chile

Duchenne 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.

ATL1102's novel mechanism in targeting CD49d suggests potential for drug to be used in combination with other treatments including anti-inflammatory agents

MARKET CONSIDERATIONS FOR ATL1102

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

ANTI-INFLAMMATORY

*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

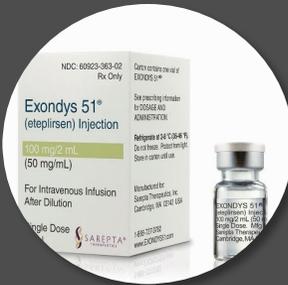
Deflazacort (Emflaza) is a CS approved in US only - average annual cost estimated > US\$80K per patient per annum

Exondys 51 (dystrophin restoration agent) cost in the US is > US\$400K per patient per annum

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

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 (July 2012) to \$3 billion on FDA approval of Exondys 51- today ~US\$6.5 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
 - 2nd quarter 2019 total net revenue for Exondys 51 – US\$94.7 million
 - 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





DMD & INDUSTRY CONFERENCES

Meetings ANP may present at and or attend include:

DMD related scientific conferences

- SOS ACTT Duchenne Conference in Melbourne, Australia, March 2020
- Muscular Dystrophy Association (MDA) conference in Orlando, Florida US, March 2020
- American Academy of Neurology (AAN) in Toronto, Canada, April-May 2020
- PPMD conference, Arizona, US, June 2020
- World Muscle Society Congress Halifax, Canada, Sept/October 2020
- Action Duchenne Conference November in the United Kingdom (2020 tbd)
- TREAT-NMD Conference in Leiden, Netherlands (2020 tbd)

Industry investor/partnering meetings

- Bio Partnering J.P. Morgan annual conference in San Francisco, US, 13-16 January 2020
- Europe Spring conference in Paris, France, March 2020
- Bio Asia-Tokyo, Japan, March 2020
- Bio International Convention conference San Diego, US, June 2020
- Bio-Europe Conference in Munich, Germany, October 2020



ATL1102 for OTHER AUTOIMMUNE – INFLAMMATORY DISEASES

- *ATL1102 targets CD49d+ immune cells involved in disease processes*
- *CD49d is a clinically validated target in multiple disease indications and a potential superior target in other autoimmune inflammatory disease*
- *Pipeline development focus*
- CD49d is clinically validated in Multiple Sclerosis and Crohns disease where antibody drugs to CD49d are used
- There are several orphan indications (like DMD) where CD49d expression is important in disease processes, and where CD49d appears to be a superior target
- ANP could move directly into clinical studies based on existing preclinical and clinical data
- Grant funding opportunities exist for such projects
- ATL1102 drug product is available for studies
- ANP to progress in indications where there are ATL1102 platform (antisense) and target (CD49d) based advantages
- **Further details to be advised once appropriate Intellectual Property protection is in place**



ANPOB LISTED OPTIONS & CAPITAL MANAGEMENT UPDATE

- ANPOB options monies received to date (>\$650K) plus commitments to exercise from holders including Key Management Personnel will take total to in excess of \$1million
- Further option exercise anticipated ahead of option expiry on 19 December 2019
- R&D tax credit of \$559K received
- Based on above, ANP will be funded into 2H'20 calendar year including costs associated with European regulatory interactions to prepare the application for the Phase IIb DMD trial
- Additionally a non-discounted funding facility has been Board approved to provide supplementary capital at Company's discretion
 - Stock to be issued within available placement capacity
 - At a price and volume set by the Company
 - No obligation on ANP to utilize
 - To be accessed if and when required



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 \$0.08)	A\$34M
Shares on issue	423.6M
52-week high/low	\$0.145 - \$0.023
Options (ANPOB, \$0.08 exp. 19/12/19)	64.3M
Cash as at 30 September 2019	\$2M

OWNERSHIP STRUCTURE

Top 40 holders	54.27%
Substantial Shareholders	
• Australian Ethical Investment	16.04%
• Platinum Asset Management	6.27%
• Leon Serry	6.15%





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 with multiple clinical applications**



Highly regarded Australian institutional shareholders - Australian Ethical Investment & Platinum Asset Management



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

- Trial is fully enrolled and all patients have completed dosing
- Positive preliminary results reported from first 7 patients having completed dosing
- Phase IIb trial design and approval process running in parallel to potentially accelerate 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



ATL1103 (atesidorsen) for acromegaly

- Potential for partnering to further develop the compound



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