



antisense
THERAPEUTICS

(ASX: ANP)

Investor Presentation
May 2022

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 2021, which is available from the Company or at www.antisense.com.au.

Company Overview

- Antisense Therapeutics (ASX:ANP | US OTC: ATHJY | FSE: AWY)
 - Australian (Melbourne) based biopharmaceutical company developing and commercialising antisense pharmaceuticals for large unmet markets
- Market Capitalisation A\$64 million
- Cash reserves at Mar'22 A\$21.7m. No debt
- World-wide exclusive licenses to two clinically advanced drugs: ATL1102 and ATL1103 from **Ionis Pharmaceutical Inc** [(NASDAQ: IONS) Market cap US\$5B]
- Lead program ATL1102 for Duchenne muscular dystrophy (DMD)
 - Rare disease with high unmet medical need with no effective treatment for the more advanced (non-ambulant) sufferers
 - Positive Phase II trial data
 - Phase IIb/III pivotal trial to be initiated in Europe 2022
- Research underway to expand ATL1102's clinical application including in a new inflammatory muscle disease indication identified as initial focus (results due **2Q & 3Q'22**)

Board and Management Team

Highly experienced Board and Management with prior success in drug development and commercialisation

MR. MARK DIAMOND (Managing Director & CEO)

Mark Diamond has over 30 years experience in the pharmaceutical and biotechnology industry. Before joining Antisense Therapeutics Limited as MD and CEO in 2001, Mr. Diamond was employed in the US as Director, Project Planning/Business Development at Faulding Pharmaceuticals. Prior to this he held the positions of Senior Manager, Business Development and In-licensing within Faulding's European operation based in the UK and International Business Development Manager with Faulding in Australia.

DR. GEORGE TACHAS (Director of Drug Discovery & Patents)

Dr Tachas received his Ph.D from the University of Melbourne ('88) and a Diploma of Intellectual Property Law ('94). Dr Tachas Ph.D studies ('84-88) were in gene transfer, cloning and characterising of genes important in immunology at the Centre for Cancer and Transplantation, Uni. Melbourne. His post-doctoral studies were in molecular and cellular biology of vascular smooth muscle cells in cardiovascular disease as Head of Molecular Biology at the Cardiovascular Research Unit of Uni. Melbourne's Anatomy Department. Dr Tachas is inventor of using ATL1102 for the treatment of DMD.

MS. NUKET DESEM (Director of Clinical & Regulatory Affairs)

Ms Desem has over 25 years' experience in global regulatory affairs, clinical development and project management obtained through her roles within the pharmaceutical/ biotechnology industry, including senior positions in various biotech companies. Ms Desem was previously employed at Antisense Therapeutics (2004–2010) as the Company's Development Director where part of her responsibility was the management of ANP's clinical trial programs. Major achievements in this role included the successful conduct and completion of the Company's multinational Phase IIa clinical trial of ATL1102 for the treatment of Multiple Sclerosis.

DR. CHARMAINE GITTLESON (Chair)

Dr Gittleson is a senior executive with international experience as a pharmaceutical physician and enterprise leader in pharmaceutical drug development, governance and risk management gained during her 15-year tenure with global biotechnology company CSL Limited. At CSL, she had accountability for clinical research, medical safety, ethics for development, providing leadership across multiple therapeutic and rare disease areas.

DR. GARY PACE (Non-Executive Director)

Dr. Pace has more than 40 years of experience in the development and commercialization of advanced tech. in biotech., pharmaceuticals, and medical devices. In 2003 Dr. Pace was awarded a Centenary Medal by the Australian Government "for service to Australian society in research and development", and in 2011 was awarded Director of the Year (corporate governance) by the San Diego Directors Forum.

DR. GIL PRICE (Non-Executive Director)

Dr. Price is a clinical physician with a long-standing focus in drug development, adverse drug reactions, drug utilization and regulation. Dr. Price is an experienced biotech executive and entrepreneur with a depth of expertise across clinical asset investment strategy, evaluation, financing and execution. From 2007 to 2016, Dr. Price was a non-executive director of Sarepta Therapeutics, Inc., where he helped guide Sarepta's transition to become a multi-billion dollar company with the first approved drug for DMD (sales approaching US\$400M annually).

Antisense Corporate Overview

Share Price Performance

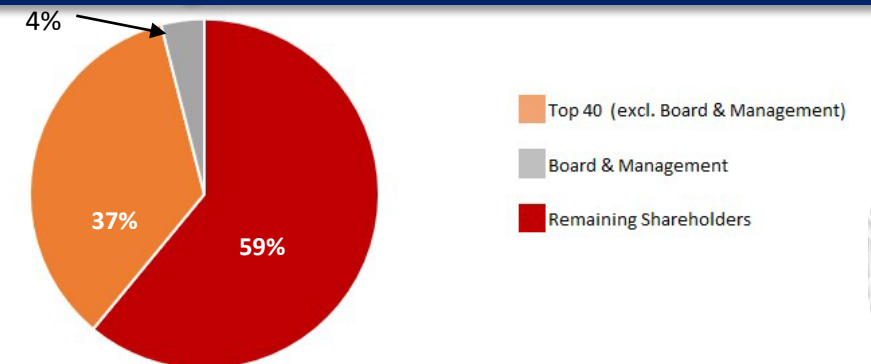


- **Analyst coverage** <https://www.antisense.com.au/broker-other-reports>
 - Shane Storey – Wilsons Equity Research
 - Dennis Hulme – Taylor Collison
 - Marc Sinatra – Corporate Connect
 - Ian Wilkie – Morgans
 - Mark Pachacz - Bioshares

Company Details

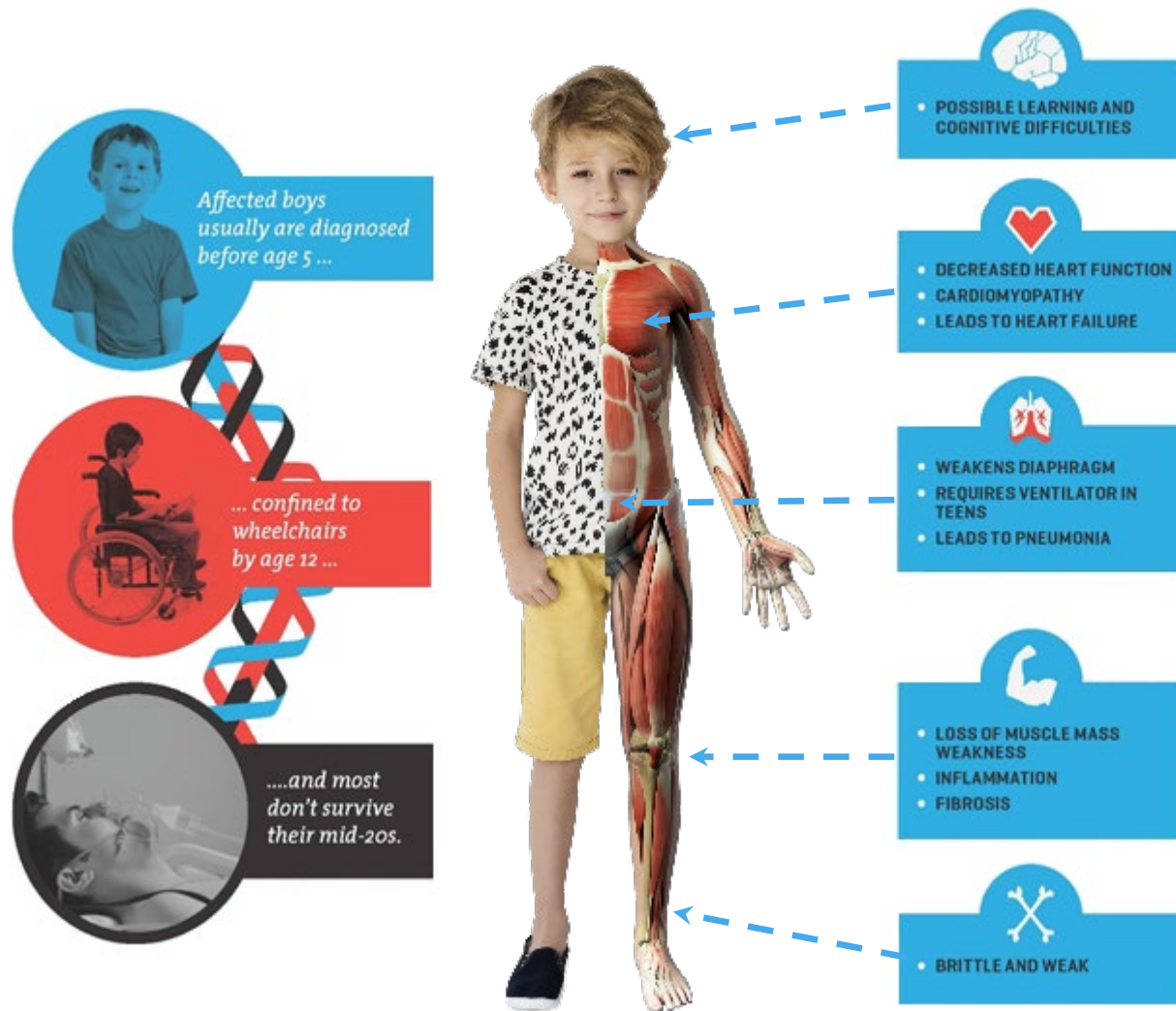
- Market Capitalisation @ \$0.096 = \$64M
- Ordinary fully paid shares on issue = 669M
- Cash at Mar'22 A\$21.7m
- Largest shareholder – **Platinum Asset Management (5.23%)**
- Top 40 Shareholders
 - Shares at 1 Jan '22 = 244M
 - Shares at 25 May' 22 = 249M

Current Register



What is DMD?

DMD is a rapidly progressing genetic disease resulting in low QOL and 100% mortality into patients' 30's



- 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 newborns¹ & prevalence of up to ~18,000 in US¹ and up to ~26,000 in EU²
- Key challenge in management of DMD patients is to reduce the inflammation and muscle fibre damage³
- Corticosteroids (CS) are the only therapy used to treat the inflammation in DMD⁴ but have insufficient efficacy⁵ & significant side effects including weight gain, reduced bone density & growth retardation³. CS not as effective in boys with a > number of T cells with high CD49d receptors⁶.
- ATL1102 is designed to inhibit CD49d expression on lymphocytes and is being developed as a treatment to reduce inflammation in DMD.

Source of Image Cure Duchenne

¹ McNeil et al, Muscle Nerve, 2010, 41(6): p. 740-5

² http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/orphans/2015/05/human_orphan_001571.jsp&mid=WC0b01ac058001d12b

³ Angelini and Peterle Acta Myologica 2012, XXXI: p. 9-15

⁴ Rosenberg et al, Science Translational Medicine 2015, 7, p.299

⁵ Miyatake et al Drug Design, Development & Therapy 2016, 10: p 2745-58

⁶ Pinto-Mariz et al Skeletal Muscle 2015, 5: p. 45-55

ATL1102 – Phase II Study Results

“Positive effects across multiple measures of muscle structure, function & strength”¹

Open label Phase II trial in nine non-ambulant (wheelchair bound) boys 10-18 years of age with DMD conducted over 24 weeks of dosing:

- Primary endpoint met with confirmation of drug’s safety and tolerability
- Strong effects on secondary endpoints on activity markers and disease progression
 - Improvement or stabilisation across different measures of motor function & strength
 - Activity on the targeted CD49d immune cells consistent with drug’s proposed mechanism of action
 - MRI data suggests stabilisation of percentage of fat in muscles and preservation of functional muscle mass
- International KOLs are supportive of Phase IIb plans

¹ *“The data certainly suggests an overall ‘stabilisation’ in disease progression at the very least which of itself is a very positive clinical outcome. MRI data confirms the positive changes at a muscular/cellular level and supports the observed physical stabilisation/ improvements in muscle strength and function.*

The consistency of positive clinically relevant effects of ATL1102 treatment across muscle measures of structure, strength and function are very pleasing and provide great encouragement for the treatment of non-ambulant patients with DMD.”

Professor Thomas Voit MD

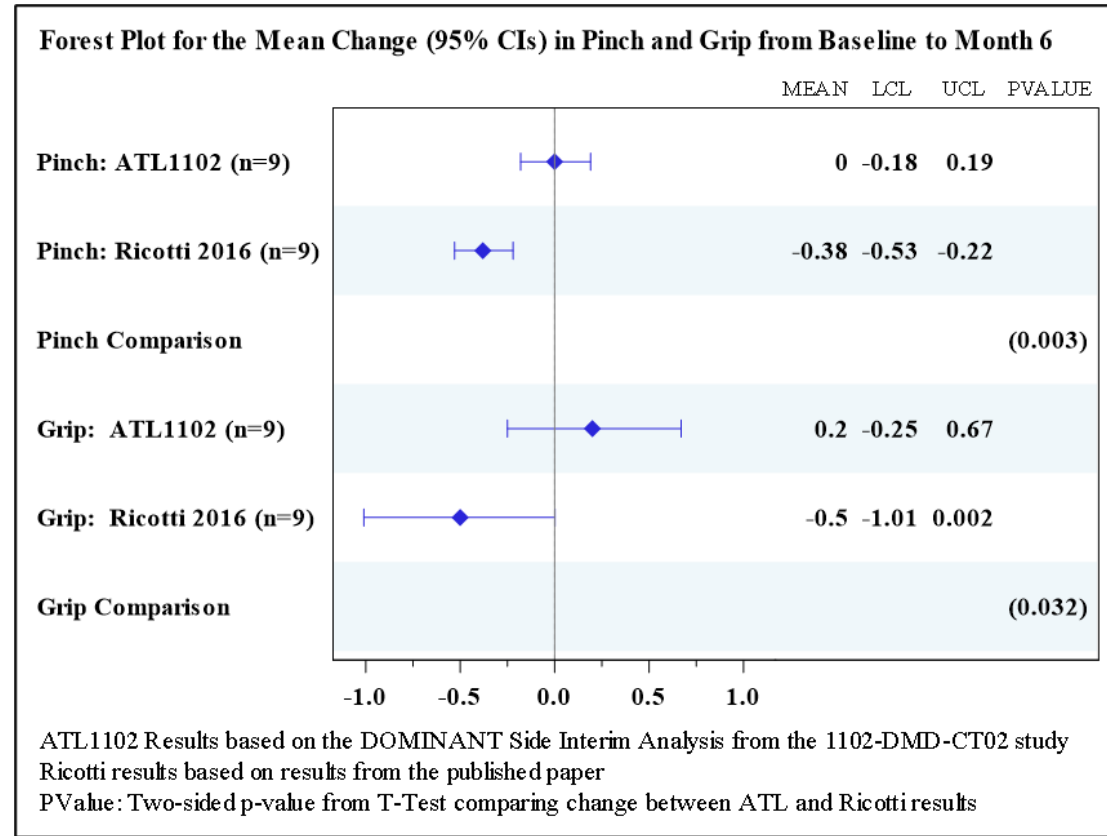
Director, NIHR GOSH Biomedical Research Centre, UK

ATL1102 Phase II Study Data *(Continued...)*

Efficacy Parameters – Muscle Strength (MyoGrip & MyoPinch)

Comparison of Phase II Study Data with published literature **showing statistically significant improvements**. *(Ricotti et. al. 2016)*

When ATL1102 Phase II study grip and pinch strength data is compared with published historical data as a control, **ATL1102 generated statistically significant improvements** in pinch strength, and grip strength.



Ricotti et. al 2016 . PLoS One, 11(9) e0162542 (are historical results from a Non – Ambulant cohort of 9 DMD patients all on CS for 6 months).

ATL1102 Phase II Study Data *(Continued...)*

Efficacy Parameters – Muscle Structure (MRI)

Mean Change (95% CI) Screening/Baseline to Week 24/ 6 Months				
MRI Parameter	N	ATL1102 Study Data	N	Published Data*
MRI CENTRAL READING				
<i>Fat Fraction (%)</i>				
Volar Muscle	9	-0.57 (-7.8, 6.7)	7	0.7 (-1.8, 3.3)
Dorsal Muscles [#]	9	-0.88 (-3.4, 1.7)	7	5.5 (2.7, 8.3)
ECRLB-Br	9	-0.12 (-6.4, 6.2)	7	6.1 (3.1, 9.2)
Average Fat Fraction	9	-0.52 (-5.6, 4.6)	7	3.9 (1.9, 5.7)
<i>Cross Sectional Muscle Area -total (mm²)</i>	9	22.33 (-36.8, 81.4)	7	42.1 (-47.0, 131.2)
<i>Remaining Muscle Area – total (mm²)</i>	9	13.9 (-72.6, 100.4)	7	-32.1 (-102.6, 38.1)
MRI PROXIMAL READING - Average Fat Fraction (%) [#]	9	-2.14 (-7.6, 3.3)	7	4.5 (2.7, 6.3)
MRI DISTAL READING - Average Fat Fraction (%)	7	-5.14 (-18.7, 8.4) [^]	7	2.2 (-0.05, 4.5)

*Ricotti et. al 2016. PLoS One, 11(9) e0162542 (results from Non – Ambulant cohort of 7 patients all but one on CS)

[^]Distal Reading is Average of Dorsal and Volar Muscle (ECRL-Br not measurable)

[#] T-Test analysis comparing the ATL1102 study data and the published data showed statistically significant differences for: MRI central reading mean change in percentage fat fraction from baseline to 6 months for the dorsal muscle group with a 2-sided p-value of 0.001. MRI proximal reading mean change in average fat fraction percentage with a 2- sided p-value of 0.018

Comparison of ATL1102 Phase II study data with data in published literature *(Ricotti et. al. 2016)*

“Based on the MRI data from the study, the observed stabilisation in the percentage fat fraction with ATL1102 treatment would not be expected in the natural course of disease in DMD even under corticosteroid treatment.

*Furthermore, the stabilisation of fat fraction percentage combined with the observed maintenance/increase of remaining muscle area is suggestive that ATL1102’s effect **could preserve the contractile muscle mass.**”*

Dr Valeria Ricotti MD,

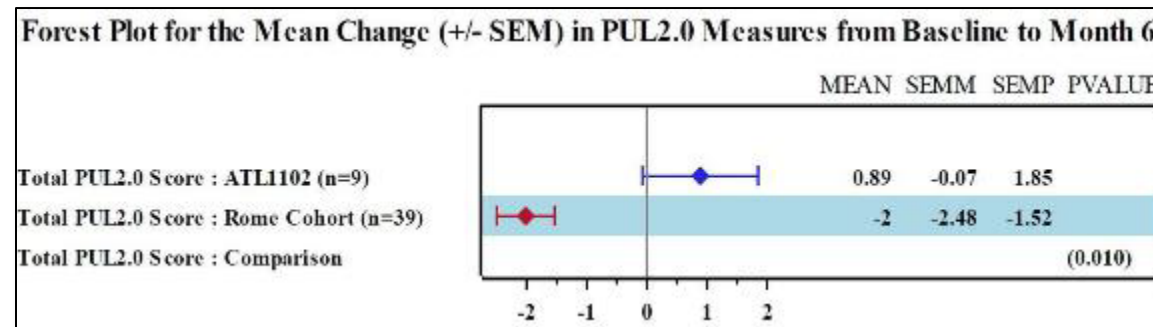
Researcher and Honorary Clinical Lecturer, Great Ormond Street
Institute of Child Health University College London, UK

ATL1102 Phase II Study Data *(Continued...)*

Efficacy Parameters – Performance of Upper Limb Function (PUL2.0)

- ATL1102 data presented at the 25th International Annual Congress of the World Muscle Society in 2020
- ATL1102 treated patients demonstrated a statistically significant improvement in the mean (SD) PUL2.0 scores for the 24 week treatment compared to external control (Rome Cohort)

ATL1102 Shows Statistically Significant Improvement vs Natural History Control in PUL 2.0 the registration endpoint for treatments in non-ambulant DMD



*“The level of improvement achieved **is very positive** and clinically relevant. As Total PUL2.0 is the key efficacy endpoint for seeking drug approval in non-ambulant patients with DMD, the comparative data further indicates **ATL1102’s promising potential** to provide clinically meaningful benefits in the future treatment of non-ambulant DMD patients who have very limited treatment options.”*

Professor Eugenio Mercuri,
Professor of Pediatric Neurology at the Catholic University, Rome, Italy

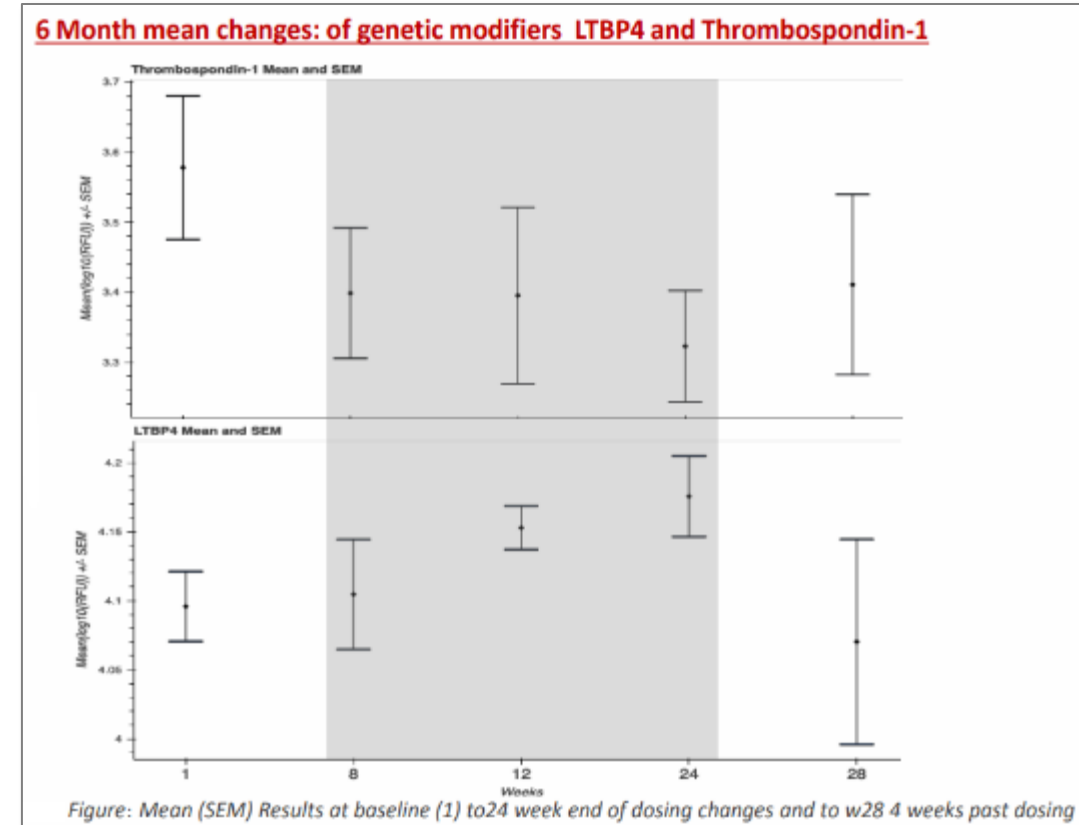
ATL1102 Research

Statistically significant modulation in two DMD disease modifier proteins supports potential of ATL1102 in ambulant DMD and fibrotic conditions

ATL1102 data presented at the 26th International Annual Congress of the World Muscle Society in 2021

- **Statistically significant mean** modulation at 24 weeks compared to baseline in Thrombospondin1 (TSP-1) **(-49%)*** and Latent TGF-beta-binding protein 4 (LTBP4) **(20.7%)*** levels, two proteins that modify the rate of loss of ambulation in DMD.
- **Positive effects** on LTBP4 and TSP-1 positions ATL1102 as an exciting prospect for the treatment of both non-ambulant and ambulant patients with DMD and the treatment of other muscle and fibrotic conditions.
- **New Provisional Patent** application filed covering this new data and applications of ATL1102 in new potential disease settings including diabetic, respiratory and age-related diseases.
- **Increase at 24 weeks** in plasma VCAM-1 supportive of the ATL1102 mechanism of action of reducing CD49d on the surface of cells to which soluble VCAM-1 **(18.0%)*** is bound, and in CXCL16 **(29.9%)*** which **can promote muscle regeneration**.

* (False Discovery Rate: p -value < 0.0005)



The positive effects shown on the above proteins strengthen ATL1102's profile in the treatment of both non ambulant and ambulant DMD patients while positioning it as an exciting prospective therapeutic approach in other muscle and fibrotic conditions.

DMD Development Landscape

Limited emerging competition in non-ambulant space

ATL1102 is a well-positioned differentiator from other products in development for treatment of DMD

INTERVENTION MECHANISMS	ASSET	SPONSORS
INFLAMMATION & FIBROSIS	ATL1102	antisense THERAPEUTICS
	STERIODS Emflaza, VBP15	PTC, Santhera
	ANTI-FIBROTICS pamrevlumab	FibroGen
CARDIAC & CALCIUM REGULATION	CARDIAC DRUGS Ifetroban	Cumberland Pharma
	CALCIUM BALANCE Rimeporide	EspeRare Foundation
DYSTROPHIN REPLACEMENT & RESTORATION	GENE THERAPY	Pfizer/Sarepta
	EXON 51 /EXON 53/EXON 45 SKIPPING	Sarepta Therapeutics
	Ataluren READTHROUGH THERAPY	Nippon Shinyaku PTC Therapeutics
RESPIRATORY CELL ENERGY	A0364	Astellas Pharma
MUSCLE GROWTH & REGENERATION	CAP-1002 (intravenous cell therapy)	Capricor Inc
	Givinostat	Italfarmaco

- ATL1102 has a novel MOA to reduce inflammation in DMD patients
 - Anti-inflammatory steroids, dystrophin restoration technologies and gene therapies are being tested in predominantly ambulant patients
 - ATL1102's novel mechanism in targeting CD49d suggests potential for drug to be used in combination with steroid anti-inflammatory agents
- ATL1102 has potential to be synergistic with other projects in development reducing competitive pressure of other potential product launches
- ATL1102 has a mechanism that appears effective across all genetic subtypes of DMD - a key differentiator among the exon skipping therapies which increases the addressable patient pool

Significant Market Opportunity

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

ANTI-INFLAMMATORY

The market[^] size is expected global anti-inflammatory reach

US\$191B by 2027

(Fortune Business Insights)

[^]MS, Rheumatoid Arthritis, Asthma, Sinusitis Respiratory, IBD

DMD THERAPIES

The global DMD drug market estimated to reach

US\$4B by 2023 and

US\$10B by 2030

(Kamet Research)

CORTICOSTEROIDS

The global steroid market is forecast to attain value of

US\$17 Billion in 2025

(QY Research)

- Rare disease company **Sarepta Therapeutics Inc.** (NASDAQ: SRPT) (Mkt Cap **US\$6B**) 2021 DMD Sales Revenue was > **US\$700M**
- Cost of current DMD therapies: Deflazacort (Emflaza) - CS approved in US only - avg cost ~**US\$93K¹** per patient per year
 - Exondys 51 (exon-skipping/dystrophin restoration agent) avg cost in US ~**US\$750K¹** per patient per year
 - Ataluren (Translarna) - stop codon skipping/dystrophin restoration) cost in EU ~**US\$320K¹** per patient per year

Assuming:

\$200K per annum with 50% of boys non ambulant at any one time

ATL1102 has a **US\$4B** market opportunity for DMD in US/EU

³ DelveInsight - Duchenne Muscular Dystrophy (DMD) Market Insight, Epidemiology, and Market Forecast—2030 (August 2021)

Note: Antisense's modelling is indicative and illustrative only and is not a forecast or projection of actual pricing of ATL1102 or the Company's ability to penetrate the depicted markets. A number of variable factors that will impact upon and influence actual pricing, market penetration and revenue and neither detailed and/or independent price modelling or audit has been undertaken.

ATL1102 for DMD Clinical Development EU

EU Phase IIb/III Clinical Trial

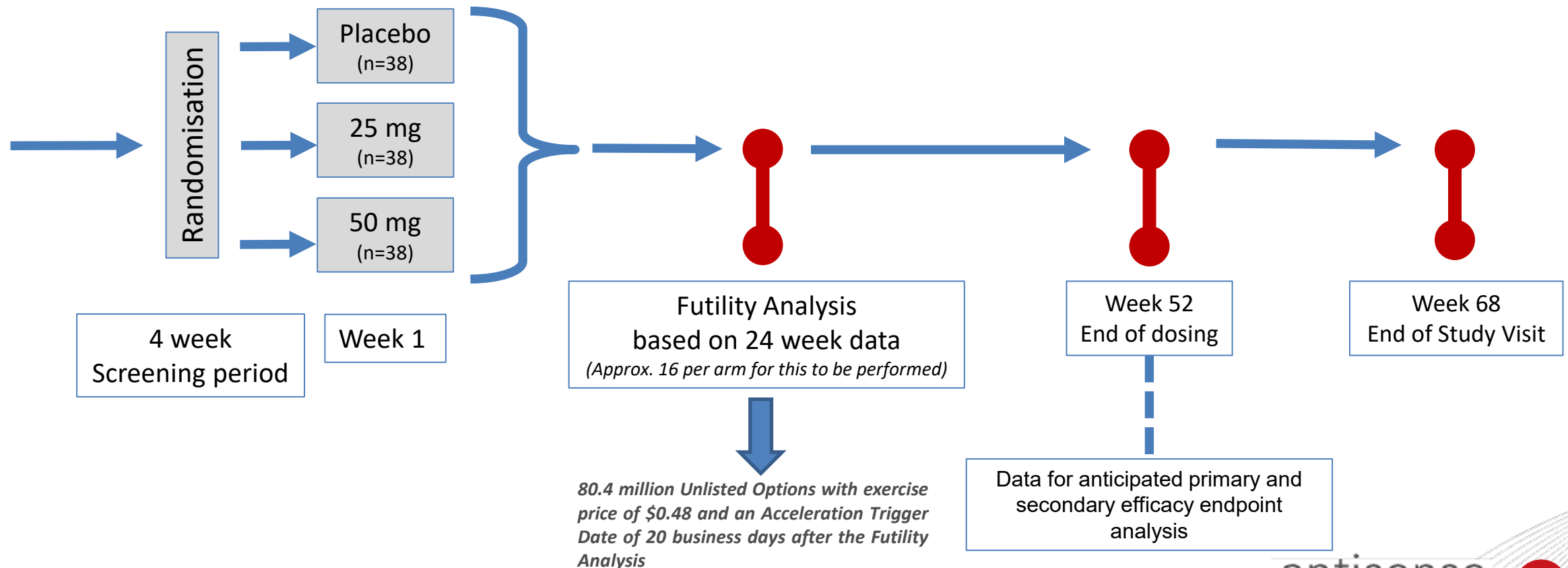
- ANP will conduct a multi-centre, randomised, double-blind placebo-controlled Phase IIb/III study of ATL1102 in non-ambulant patients dosed with ATL1102 for 12 months at two dose levels as a potentially pivotal (approvable) trial with a follow-on open label extension phase.
- ANP has received a positive opinion for its ATL1102 Phase IIb/III Paediatric Investigational Plan (**PIP**) from EMA Paediatric Committee (**PDCO**) and Medicines and Healthcare products Regulatory Agency (MHRA) in the UK
- Professor Thomas Voit MD (Director of NIHR GOSH UCL Biomedical Research Centre, UK) will be the Coordinating Principal Investigator of the trial
- ANP has appointed globally renowned Clinical Research Organisation (CRO) Parexel to conduct and manage the Phase IIb/III study
- Site evaluations completed. Site selection close to finalization for sites (>30) in 9 countries
- Clinical trial agreements being executed with all trial sites and submission of the clinical trial application to be made to each of the national regulatory authorities
- Trial approvals expected to come through on a rolling basis depending on ethics and reg approval requirements of the individual authorities



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EU Phase IIb/III Study Program

A multicentre, randomised, double-blind, placebo-controlled study to assess the efficacy, safety, and pharmacokinetic profile of two dose levels of ATL1102 to be conducted in 108 (114 randomised) DMD non-ambulant participants in ~9 countries across >30 trial sites with an open label extension phase



ATL1102 for DMD Clinical Development US

US Regulatory Plans

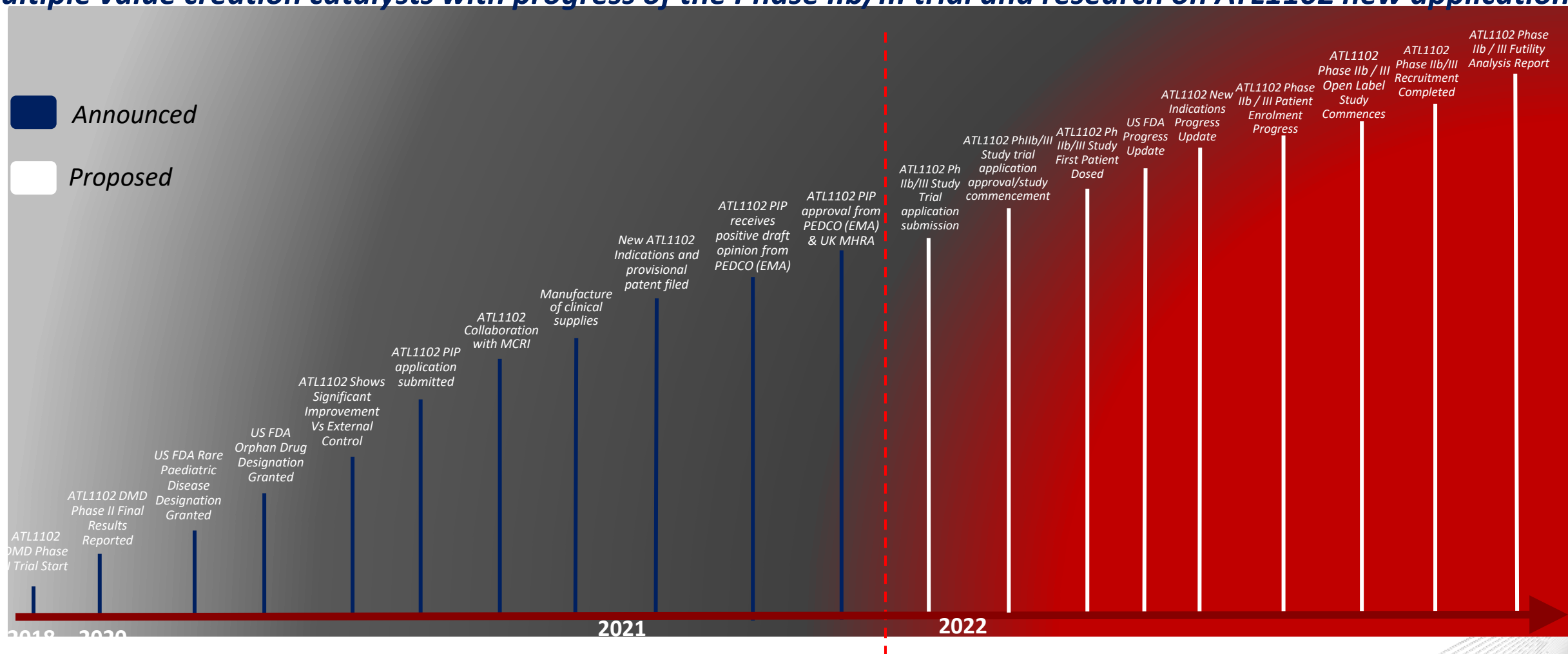
- FDA require a nine-month chronic monkey toxicology study of ATL1102 to support the dosing of patients beyond six months in US.
 - FDA have provided feedback on the protocol synopsis including their concurrence with the proposed high dose. Timing of the initiation of the nine-month toxicology study dependent on the progress of the EU Phase IIb/II study and continued interactions with the FDA (refer below)
- Apparent high-level alignment between EMA and FDA on Phase IIb/III study requirements provides opportunity for ANP to engage with the FDA to streamline the regulatory processes
 - ANP considers that it has potential optionality in its actions with FDA including to take the EU Phase IIb/III data to the FDA to be assessed as supportive data for a future marketing application or should the data warrant it, possibly an approval of ATL1102 for DMD without further trials
 - FDA interactions to explore the optionality highlighted above are to continue in parallel with the conduct of Phase IIb/III pivotal trial in Europe
- Potential for ANP to receive a rare pediatric disease priority review voucher (PRV) if it obtains FDA approval for ATL1102 in the DMD indication (as the drug's first approval) before Sep 30, 2026. ANP may choose to sell its PRV. From 2017 - 2021, sales of PRVs ranged between US\$80 - \$150 million.

ATL1102 New Indications

- Focus on advancing ATL1102 for DMD towards commercialisation whilst expanding the clinical application of ATL1102 beyond DMD
 - capitalising on the extensive data package generated on ATL1102 to deepen the product pipeline to add further value for shareholders and to diversify possible indication risk
- Several inflammatory muscle disease indications (like DMD) have been identified as initial focus
 - to leverage established core competencies (rare disease experience, scientific partnerships and collaborations e.g. MCRI, KoL's etc)
 - commercially attractive space (like DMD) with limited competition, premium pricing, and orphan drug development incentives
 - opportunity to generate valuable IP from animal studies to underpin development/commercialisation (including supporting future orphan drug designation applications)
 - potential for ANP to move rapidly into the clinic based on positive animal data or out-license
- Collaboration with Murdoch Children's Research Institute (MCRI) the largest child health research institute in Australia
 - Study 1 – combination study with the dystrophin restoration drugs in *mdx* (DMD) mouse model **(Results anticipated Q3'CY22)**
 - Study 2 - another animal model of muscle disease **(Results from 1st Phase anticipated in 2Q'CY22 and from 2nd Phase in 2H'CY22)**
- Collaboration to study the neurological aspects of Long COVID-19 (Long Neuro COVID-19) with US based researchers led by Dr Igor Koralnik at the Northwestern Medicine Neuro-COVID clinic in Chicago **(First results anticipated mid-2022)**

Major Achievements and Upcoming Key Activities

Multiple value creation catalysts with progress of the Phase IIb/III trial and research on ATL1102 new applications





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