ASX Announcement

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ATL1102 for DMD: Revised Clinical Development Plans accelerate reporting of unblinded data

- **Revised plan brings forward reporting of definitive unblinded data vs previous planned futility analysis**
- **Australian sites to be incorporated into the trial alongside key centres in Europe**
- **Trial anticipated to initiate Q42022**

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY] (ANP or Company) today announces that it intends to conduct a double-blind, placebo controlled six month dosing trial of ATL1102 followed by a six month open label phase (collectively the 'Phase IIb' trial) in non-ambulant boys with Duchenne's Muscular Dystrophy (DMD). The primary endpoint of PUL2.0 will be assessed after six months of treatment (versus 12 months in the Phase IIb/III study). This follows the Company's previous announcement on 13th July 2022 advising the re-evaluation of its clinical plans for ATL1102 in DMD to focus on the most effective deployment of existing cash reserves and to reduce upfront capital requirements.

The Phase IIb study aims to enrol and randomize 45 non-ambulant boys with DMD. Following the initial six-month regimen of either placebo, 25 mg or 50 mg once weekly, participants will be invited into a further six-month open label follow-up treatment period in which all boys will be on active treatment (25 or 50mg). This additional time period will be used to demonstrate longevity of response as well as collect additional safety data and facilitate streamlining and de-risking of a Phase III study, the most expensive phase of the drug's development (i.e., may reduce the number of dosing arms). It is the Company's view that if results from the Phase IIb proved to be highly successful, it would then engage with Regulatory Agencies in relation to obtaining an accelerated approval for the unmet medical need of non-ambulant DMD patients.

The Phase IIb trial design is modelled on the Phase IIb/III study outlined in Company's Paediatric Investigation Plan (PIP) (refer to following presentation for details on the Phase IIb trial design) and agreed by the European Medicines Agency (EMA) and The Medicines and Healthcare products Regulatory Agency (MHRA) in the UK. The Phase IIb/III clinical trial application submitted in Germany (BfArM) is undergoing evaluation. With the regulatory focus now directed to submission of the Phase IIb trial applications, no additional Phase IIb/III trial submissions are planned at this time.

The Company had previously announced that the next clinical milestone following Phase IIb/III trial initiation would have been a planned futility analysis after the first approximately 48 patients had completed their 6 months of dosing. This was to be a blinded analysis of the data by the Data Safety Monitoring Board and the outcome communicated as either a go or no-go decision to continue dosing as per protocol. No statistically analysed efficacy data would have been available at that time for reporting to the market. The revised trial design now to be conducted brings forward the definitive reporting of unblinded and statistically analysed trial data following the completion of the initial randomized blinded six-month dosing period. The Company believes that if successful, positive data from a controlled trial of ATL1102 in DMD patients could add substantial value to the program and, based on previous external feedback, garner serious partnering interest at an earlier point in the development program than previously anticipated.

The revised trial design has allowed for the opportunity to incorporate Australian sites alongside key trial centres in Europe. This provides the important benefit of continuity of working with Australian investigators who were involved in the conduct of the previous successful Phase II clinical trial of ATL1102 in DMD. The addition of Australian trial sites is expected to facilitate a significantly greater proportion of the trial costs as being eligible for the R&D tax incentive cash rebate, which should have a material impact on reducing the cash requirements for the conduct of the study.

The Company is able to leverage preparatory work undertaken for the Phase IIb/III trial including trial site and clinical investigator identification, selection and relationship development, clinical trial protocols and applications. The new strategy allows the Company to confirm drug efficacy through the rigor of the placebo-controlled trial design so as to allow for discussion with regulators for potential fast tracking into registration phase or potential accelerated approval, pending trial outcomes. The Company anticipates the first of the trial sites for the Phase IIb trial to be initiated in this calendar year. Based on current enrolment expectations, the last patient is projected to enter the trial in early 3Q'23 with the blinded phase of the trial to complete once the last patient has finished their six months of dosing. Reporting of the trial results would follow shortly thereafter.

These revised clinical plans have substantially reduced the Company's budgeted trial costs, and with the expected additional R&D tax incentive rebates, the Company now estimates that it can fund both the Company and the trial into 4Q'23. The Company will move forward with the study initiation as outlined above. There is an approximately mid-single digit A$m additional future cash requirement to get to the time point of the reporting of trial results and the Company will update the market upon confirmation of the amount of such additional future funding and how it will be sourced.

Dr Charmaine Gittleson, the Chair of Antisense Therapeutics said: "The Board, management and the Company's clinical advisors remain focused on bringing ATL1102 to the non-ambulant DMD population. We believe that the Phase IIb study provides a valuable and significant de-risking step toward achieving this outcome. It allows us to build upon past work and re-enter the clinic, within the current market's fiscal constraints, to obtain robust clinical outcome data that will either stand alone or form part of a broader regulatory submission. We believe this represents significant value to the DMD community and our shareholders."

A webinar will be held at 12.30pm to overview the announcement and for associated Q&A time permitting https://us02web.zoom.us/webinar/register/WN_53u2na0zSVqUnsmcEWraMw

This announcement has been authorised for release by the Board.

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About Antisense Therapeutics Limited [ASX: ANP | US OTC: ATHJY | FSE: AWY] is an Australian publicly listed biotechnology company, developing and commercializing antisense pharmaceuticals for large unmet markets in rare diseases. The products are in-licensed from Ionis Pharmaceuticals Inc. (NASDAQ: IONS), an established leader in antisense drug development. The Company is developing ATL1102, an antisense inhibitor of the CD49d receptor, for Duchenne muscular dystrophy (DMD) patients and recently reported highly promising Phase II trial results. ATL1102 has also successfully completed a Phase II efficacy and safety trial, significantly reducing the number of brain lesions in patients with relapsing-remitting multiple sclerosis (RRMS). The Company

has a second drug, ATL1103 designed to block GHr production that successfully reduced blood IGF-I levels in Phase II clinical trials in patients with the growth disorder acromegaly.

About ATL1102 ATL1102 is an antisense inhibitor of CD49d, a subunit of VLA-4 (Very Late Antigen-4). Antisense inhibition of VLA-4 expression has demonstrated activity in a number of animal models of inflammatory disease including asthma and MS with the MS animal data having been published in a peer reviewed scientific journal. ATL1102 was shown to be highly effective in reducing MS lesions in a Phase IIa clinical trial in patients with RR-MS. The ATL1102 Phase IIa clinical data has been published in the medical Journal ***Neurology*** (Limmroth, V. et al Neurology, 2014; 83(20): 1780-1788). ATL1102 is the only drug targeting CD49d in clinical development for DMD.

About DMD Duchenne Muscular Dystrophy (DMD) is an X-linked disease that affects 1 in 3600 to 6000 live male births (Bushby *et al*, 2010). DMD occurs as a result of mutations in the dystrophin gene which causes a substantial reduction in or absence of the dystrophin protein. Children with DMD have dystrophin deficient muscles and are susceptible to contraction induced injury to muscle that triggers the immune system which exacerbates muscle damage as summarized in a publication co-authored by the Director of the FDA CDER (Rosenberg et al, 2015). Ongoing deterioration in muscle strength affects lower limbs leading to impaired mobility, and also affects upper limbs, leading to further loss of function and self-care ability. The need for wheelchair use can occur in early teenage years for patients on corticosteroids with a mean age of 13, with respiratory, cardiac, cognitive dysfunction also emerging. Patients with a greater number of immune T cells expressing high levels of CD49d have more severe and progressive disease and are non-ambulant by the age of 10 despite being on corticosteroid treatment (Pinto Mariz et al, 2015). With no intervention, the mean age of life is approximately 19 years and with current treatment typically limited to only the second or third decade of life. The management of the inflammatory damage to muscle associated with DMD is currently addressed via the use of corticosteroids prednisolone and deflazacort which delay disease progression prolonging ambulation by a median 2 to 3 years (Shieh et al, 2018) and reduce loss of upper limb function as measured by performance of upper limb function (PUL) scores, (Pane et al, 2018), an objective measurement of function. Corticosteroids are, however, acknowledged as providing insufficient efficacy and are associated with significant side effects including bone loss that require monitoring, management, and treatment (Ward et al 2018). As a consequence, there is an acknowledged high need for new therapeutic approaches for the treatment of the immune mediated inflammation associated muscle damage in DMD.

Rosenberg AS, Puig M, Nagaraju K, et al. Immune-mediated pathology in Duchenne muscular dystrophy. Sci Transl Med 2015, 7: 299rv4.

Bushby et al for the DMD Care Consideration Working Group/ Diagnosis and management of Duchenne muscular dystrophy, part 1 Lancet Neurol. 2010 Jan;9(1):77-93 and part 2 Lancet Neurol. 2010 Feb;9(2):177-89 .

Pinto-Mariz F, Carvalho LR, Araújo AQC, et al. CD49d is a disease progression biomarker and a potential target for immunotherapy in Duchenne muscular dystrophy. Skeletal Muscle 2015, 5: 45-55.

Shieh et al, Deflazacort versus prednisone/prednisolone for maintaining motor function and delaying loss of ambulation: A post HOC analysis from the ACT DMD trial. Muscle Nerve. 2018 Nov; 58(5): 639–645. Muscle & Nerve November 2018 639

Pane M, Coratti G, Brogna C, Mazzone ES, Mayhew A, Fanelli L, Mercuri E et al. (2018) Upper limb function in Duchenne muscular dystrophy: 24 month longitudinal data. PLoS ONE 13(6): e0199223. https://doi.org/10.1371/journal. pone.0199223

Ward L.M, Hadjiyannakis, S, McMillan, HJ, Noritz, G, and Weber, DR, Bone Health and Osteoporosis Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics. 2018 October; 142(Suppl 2): S34–S42. doi:10.1542/peds.2018-0333E.