Positive preliminary results from ATL1102 for DMD Phase II trial

- Data Safety Monitoring Board recommends continuation of the trial with no safety concerns
- Preliminary data from 6 month dosing is indicative of positive drug effect at dose tested

Antisense Therapeutics ("ANP" or the "Company") is pleased to advise that a review of the preliminary data from the 6 patients who have completed their 24 weeks of dosing in the Phase II clinical trial of ANP's immunomodulatory therapy, ATL1102 for Duchenne Muscular Dystrophy (DMD) therapy, is indicative of a positive drug effect of ATL1102 at the dose tested both at an immunomodulatory (i.e. effects on relevant immune cells) and disease progression (i.e. effects on muscle strength and function) levels.

ATL1102 is an inhibitor of CD49d expression on certain immune cells (e.g. T cells). It has been reported that patients with DMD who have a greater number of T cells with high levels of CD49d on their surface have more severe and rapid disease progression. ATL1102 is being developed as a novel treatment for the inflammation that exacerbates muscle fibre damage in DMD patients, currently treated with corticosteroids. Corticosteroids have a range of serious side effects when used for a prolonged period as required in DMD.

The primary endpoints of the trial relate to the safety and tolerability of ATL1102 with the efficacy of ATL1102 in DMD assessed in terms of its effects on disease processes and progression. With respect to the safety related trial data, no Serious Adverse Events have been reported to date. The Data Safety Monitoring Board have recently evaluated the safety data and have recommended continuation of the trial with no safety concerns. It is important to note that this is the first occasion ATL1102 has been dosed for an extended duration (6 months) in this patient population of non-ambulant DMD patients and so the Company expects such safety observations will be important support for the proposed longer dosing in a Phase IIb trial.

With reference to the safety profile, Dr Ian Woodcock, Paediatric Neurologist and Honorary Fellow at The Murdoch Children's Research Institute, Melbourne and the Principle Investigator of the ATL1102 Phase II DMD trial said, "Based on a preliminary review of the DMD trial data from the first six patients, the safety profile of ATL1102 appears satisfactory with no serious adverse events being reported during the trial so far. It has been great to be able to include the boys with Duchenne Muscular Dystrophy who are no longer ambulant in a clinical trial and the participants have enjoyed being able to take part".

In regard to the trial's secondary endpoints that assess drug activity/efficacy, the Company is highly encouraged that the data to date is indicative of drug effect, particularly considering the small number of patients evaluated and that the progress of the final three patients (due to complete dosing in November) appears consistent with this view that the drug is showing activity.

Early indications of an immunomodulatory effect are underpinned via observations that certain immune cell numbers (in particular those expressing the CD49d, the biological target of ATL1102) are trending downward during the treatment phase while returning to around starting levels post dosing.

As an indicator of ATL1102's suggestive positive effects on disease progression (being the type of endpoints required for future product registration) in the current trial, ANP has previously referenced the Ricotti et al 2016 publication that evaluated disease progression in non-ambulant boys over a 6 month period, where a significant mean reduction in upper body muscle strength of the subjects was observed. By comparison, the data on the first 6 patients completing dosing in the ATL1102 trial, shows a distinct improvement in these strength parameters over the losses noted in the Ricotti publication (refer Appendix A).

The results appear highly supportive of the Company's plans for a Phase IIb clinical trial of ATL1102 in DMD with these plans to be reviewed with three European regulatory authorities at Scientific Advice meetings with the first meeting commencing next month. All three meetings have now been confirmed.

The Company is encouraged by the initial feedback it received from discussions with internationally recognized DMD experts, who are actively involved in developing new therapies for DMD in Europe and with whom the Company is consulting in regard to the ongoing development of ATL1102 and the Phase IIb clinical trial. The Company is further analyzing the preliminary trial data to confirm the level and rate of response to therapy within the trial to date. This response to ATL1102 treatment is to be determined with reference to expected outcomes from patients at a similar stage of disease progression (i.e. years since ambulation), age and loss of upper limb function and strength. This ongoing experts' analysis and their views on response to ATL1102 treatment is key to contextualizing the specific trial data being generated.

The preliminary data including any further analyzed data is planned to be presented by Dr Woodcock at the Action Duchenne Conference in the UK on 15 - 16 November 2019.

Mark Diamond, CEO of Antisense Therapeutics said: "Given that there is currently no effective treatment for non-ambulant DMD patients, we are particularly encouraged by the preliminary data from the first six patients in this trial, which suggests a positive drug effect and may also demonstrate a meaningful slowing of disease progression compared to what might otherwise have been expected. We expect this preliminary data to assist us in our planned regulatory interactions on the design and conduct of the Phase IIb clinical trial that should allow examination of dosages of 25mg and higher to determine the optimal dosage".

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About Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical company, developing and commercialising antisense pharmaceuticals for large unmet markets. The products are in-licensed from Ionis Pharmaceuticals Inc. (NASDAQ:IONS), world leaders in antisense drug development and commercialisation. ATL1102 (injection) has successfully completed a Phase II efficacy and safety trial, significantly reducing the number of brain lesions in patients with relapsing-remitting multiple sclerosis (RRMS). ATL1103 drug designed to block GHr production successfully reduced blood IGF-I levels in Phase II clinical trials in patients with the growth disorder acromegaly. The Company is conducting a Phase II clinical trial of ATL1102 in DMD patients at the Royal Childrens Hospital, Melbourne.

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 RR-MS patients. The ATL1102 Phase IIa clinical data has been published in the medical Journal ***Neurology*** (Limmroth, V. et al Neurology, 2014; 83(20): 1780-1788).

About ATL1102 DMD Trial The Company is undertaking a clinical trial of ATL1102 in patients with Duchenne Muscular Dystrophy. The open label six-month dosing trial of ATL1102 in nine non-ambulant patients with DMD aged between 10 and 18 years is being conducted at the neuromuscular centre of the Royal Children's Hospital (RCH) which operates the largest clinic in the southern hemisphere treating children with DMD. The primary endpoints of the trial relate to the safety and tolerability of ATL1102. The efficacy of ATL1102 will also be assessed in terms of its effects on disease processes and progression (e.g. the upper limb strength and function of the boys). Further details on the trial are available here on the Australia and New Zealand Clinical Trials Registry.

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 wheelchair bound 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. The management of the inflammation associated with DMD is currently addressed via the use of corticosteroids, however they are acknowledged as providing insufficient efficacy and are associated with significant side effects. As a consequence, there is an acknowledged high need for new therapeutic approaches for the treatment of inflammation associated with DMD.

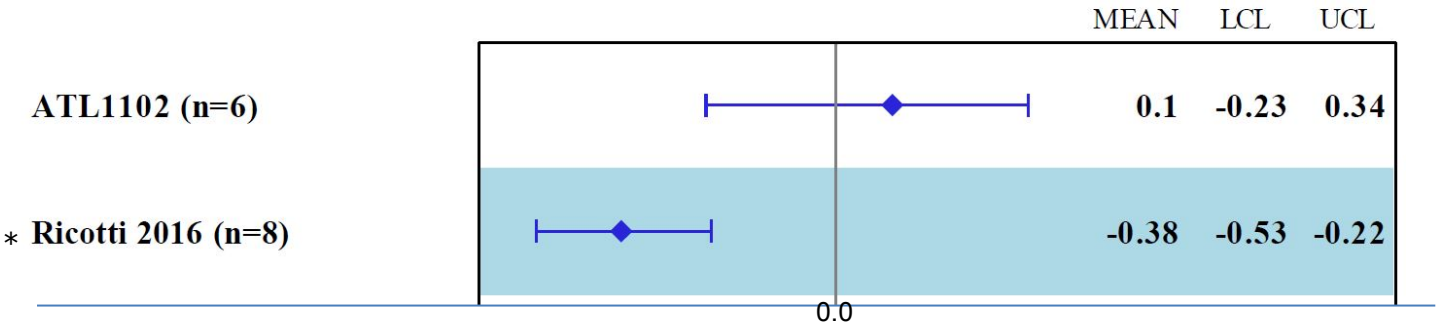
Rosenberg AS, Puig M, Nagaraju K, *et al*. Immune-mediated pathology in Duchenne muscular dystrophy. *Sci Transl Med* 2015, 7: 299rv4.

Busby 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 .

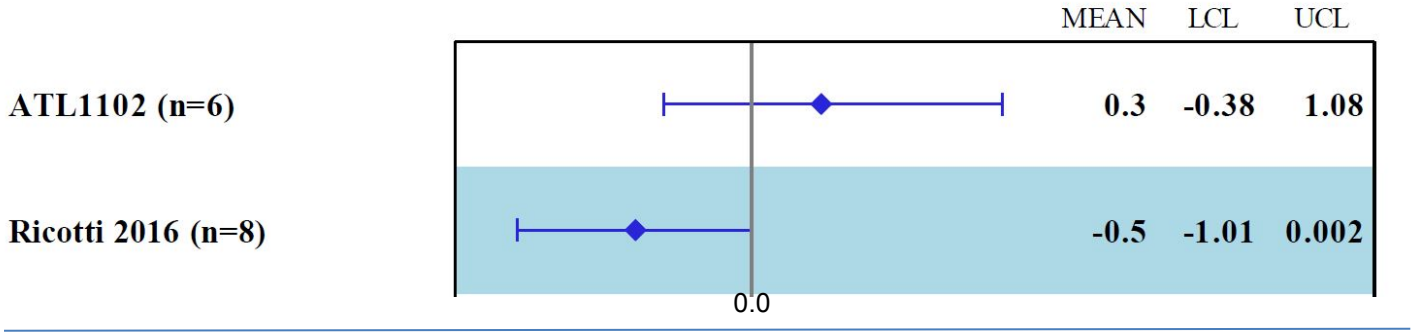
Pinto-Mariz F, Carvalho LR, Araújo AQC, *et al*. CD49d is a disease progression biomarker and a potential target for immunotherapy in Duchenne muscular dystrophy. *Skeletal Muscle* 2015, 5: 45-55

APPENDIX A

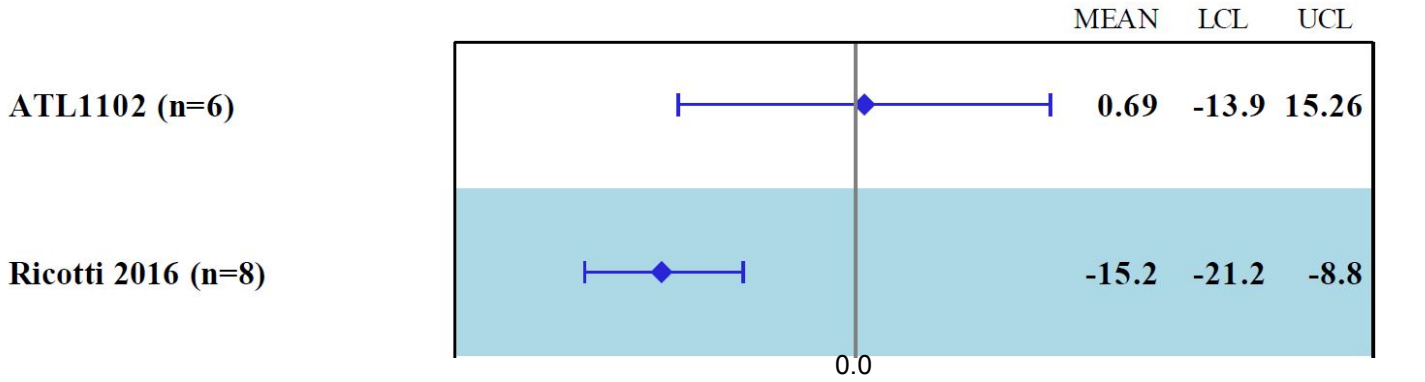
Forest Plot for the Mean Change (and 95% CIs) from Baseline Pinch to Month 6



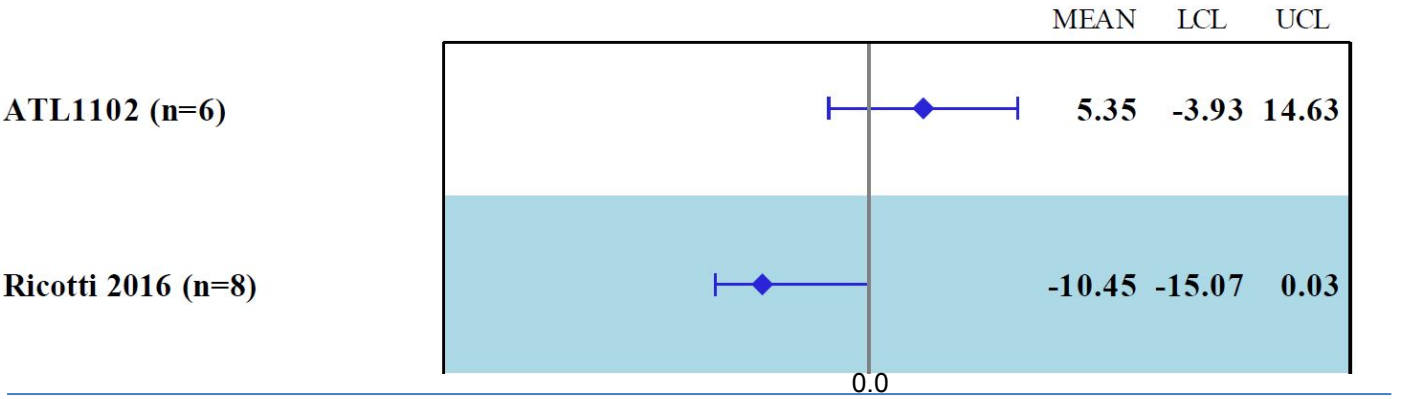
Forest Plot for the Mean Change (and 95% CIs) from Baseline Grip to Month 6



Forest Plot for the Mean Percent Change (and 95% CIs) from Baseline Pinch to Month 6



Forest Plot for the Mean Percent Change (and 95% CIs) from Baseline Grip to Month 6



* Ricotti V, Evans MRB, Sinclair CDJ, ButlerJW, Ridout DA, Hogrel J-Y, et al. (2016) Upper, Limb Evaluation in Duchenne Muscular Dystrophy: Fat-Water Quantification by MRI, Muscle Force and Function Define Endpoints for Clinical Trials. PLoS ONE 11(9): e0162542. doi:10.1371/journal.pone.0162542.