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Approval received for Phase II trial of ATL1102 in Duchenne Muscular Dystrophy

Antisense Therapeutics ("ANP" or the "Company") is pleased to advise that the Company has received approval from the Royal Children's Hospital (RCH), Melbourne Human Research Ethics Committee, to undertake a Phase II clinical trial of its immunomodulatory therapy, ATL1102, in patients with Duchenne Muscular Dystrophy (DMD), an incurable muscle wasting disease of children. The trial is on track for commencement in Q2'18 and will be conducted at the RCH neuromuscular centre, which operates the largest clinic in the southern hemisphere treating children with DMD.

The study is a single dose investigation of 25mg of ATL1102 administered weekly in wheel chair bound boys with DMD who are 10 to 18 years of age and weigh between 25 to 60kg. The primary goal of the study is to establish ATL1102's safety and tolerability in this DMD patient population at the dose being investigated. The potential efficacy of ATL1102 will also be assessed via ATL1102's effects on important blood and imaging (MRI) markers of inflammation and muscle damage associated with DMD. Notably, the extended (6 month) dosing period of this clinical trial may also allow for ATL1102 to show an improvement in key clinical endpoints that are relevant to DMD disease progression (e.g. the upper limb function of the boys) and that are of the type that would be required for future product registration.

The Principal Investigators for the trial are Dr Ian Woodcock, a Neuromuscular Fellow at the RCH and Professor Monique Ryan, Director of the Neurology Department at RCH. The clinical development of ATL1102 trial in boys with DMD is to be directed by an Advisory Board of international experts in the field including inventors of the FDA approved antisense drug, eteplirsen, used to increase muscle dystrophin in DMD patients and marketed by Sarepta Therapeutics (NASDAQ:SRPT, US$4bn). The Advisory Board is chaired by Mr William Goolsbee, a non-executive director of ANP and ex-Chairman of Sarepta Therapeutics.

Further details are provided in the study synopsis below.

Principal Investigator Dr Woodcock said: "Duchenne Muscular Dystrophy is a common, debilitating and ultimately terminal degenerative condition causing muscle inflammation and wasting. There is a dire need for more effective therapies than those we have already. The approach of using ATL1102 to inhibit CD49d+ T cells to treat this inflammation is consistent with observations of international researchers and published studies. Every day I see the pain and suffering that patients with DMD and their families go through and I am highly motivated to help in the development of new drugs and therapies that will benefit these children".

Mark Diamond, CEO of Antisense Therapeutics said: "We are very pleased to have received approval for our Phase II study in DMD patients. DMD is a rare disease with high unmet medical need, and so we are keen to establish ATL1102's effectiveness in treating children with this devastating condition".

An update on the previously advised capital raising plans is expected to be provided shortly.

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Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. Its mission is to create, develop and commercialise second generation antisense pharmaceuticals for large unmet markets. The products in ANP's development pipeline are in-licensed from Ionis Pharmaceuticals Inc., 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.

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 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 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 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 with a mean age of 13, with respiratory, cardiac, cognitive dysfunction also emerging. Patients with immune T cells expressing high levels of CD49d have more severe and progressive disease and are wheelchair bound by the age of 10 (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. https://mdaustralia.org.au/.

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

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

Protocol Synopsis

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 (wheel chair bound) Duchenne Muscular Dystrophy.
Study Number	1102-DMD-CT02
Study Design	Single-centre, open-label, single arm study
Endpoints	Primary objective: • To assess the safety and tolerability of ATL1102 in patients with Duchenne Muscular Dystrophy (DMD) Secondary objectives: • To evaluate the efficacy of ATL1102 in patients with DMD • To investigate the immunomodulatory effects of ATL1102 in patients with DMD • To evaluate the pharmacokinetic profile of ATL1102 in patients with DMD Exploratory objectives: • To further evaluate the pharmacodynamic effects of ATL1102 in patients with DMD
Number of patients	Approx. 10 participants with DMD are to be enrolled.
Key Patient Criteria	Male patients with DMD between 10 and 18 years of age weighing from 25 to 60kg
Dosing	Subcutaneous administration of ATL1102 at 25 mg/week (0.42 – 1mg/kg depending on body weight) once per week for 24 weeks
Per Patient Duration	Up to 28 days screening, 24 weeks dosing, eight weeks follow up
Trial Location	Royal Children's Hospital, Melbourne, VIC.
Principal Investigator(s)	Dr Ian Woodcock and Professor Monique Ryan
Trial Standard	GCP