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ANP initiates ATL1102 Phase II clinical trial in Duchenne Muscular Dystrophy

Antisense Therapeutics ("ANP" or the "Company") is pleased to advise of the initiation of a Phase II clinical trial of its immunomodulatory therapy, ATL1102, in patients with Duchenne Muscular Dystrophy (DMD), an incurable muscle wasting disease of children, at the Royal Children's Hospital in Melbourne (RCH).

An initiation meeting with trial investigators, coordinators, clinical project managers, nurses and other key personnel involved in the study has been held at the trial site at the RCH and patient recruitment is now to proceed, led by the Principal Investigators Dr Ian Woodcock, a Neuromuscular Fellow at the RCH and Professor Monique Ryan, Director of the Neurology Department at RCH.

ATL1102 is to be used as a treatment for the inflammation that exacerbates muscle fibre damage, which is currently treated by using corticosteroids. Corticosteroids have a range of serious side effects when used at high doses for a prolonged period as required in DMD, and do not appear to be as effective in patients with a greater number of white blood cells that express high levels of CD49d receptors (ATL1102's biological target) on their surface. The trial will assess the safety and tolerability of ATL1102 and also its efficacy in terms of its effects on the blood and imaging markers of inflammation and muscle damage and other important markers of disease progression.

The ATL1102 trial is in non-ambulant boys aged between 10 years and 18 years with DMD. The development of ATL1102 in DMD is guided by a Scientific 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\$9bn). The Advisory Board is chaired by Mr William Goolsbee, a non-executive director of ANP and ex-Board Chairman of Sarepta Therapeutics.

"It is personally very gratifying to see our study successfully progressing in a disease area where I know there is a great need for better and safer treatments. What we want to do is to eliminate a substantial portion of continued muscle degeneration by ameliorating the damaging effects of the inflammation with the use of ATL1102 to help extend the period of mobility in the boys, and in particular the upper limb function of the wheel chair bound boys to be enrolled in our study," Mr Goolsbee said.

The DMD treatment is the same as that previously used by the Company in its successful Phase II trial in Multiple Sclerosis, which showed significant activity in reducing the number of newly formed inflammatory brain lesions.

Dosing of patients is expected to commence next month as anticipated based on enrolment and screening assumptions.

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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 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