ASX Announcement

4 April 2019

Phase II clinical trial in Duchenne Muscular Dystrophy – Update

- 7th patient enrolled into the trial
- Enrolment of final two patients is anticipated this month
- No Serious Adverse Events reported to date
- Accelerating development planning for next clinical trial of ATL1102 in DMD

Antisense Therapeutics ("ANP" or the "Company") is pleased to advise that seven patients are now enrolled in the nine patient Phase II clinical trial of its immunomodulatory therapy, ATL1102 for Duchenne Muscular Dystrophy (DMD).

One patient has completed dosing and the two month monitoring period. Five patients are in the treatment phase of the study with a seventh screened patient about to commence their dosing. No Serious Adverse Events have been reported to date. Subject to meeting the eligibility criteria, the final two patients are anticipated to be enrolled into the trial this month with dosing completion to follow in late September/early October 2019.

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 in Melbourne (RCH), which operates the largest clinic in the southern hemisphere treating children with DMD.

ATL1102 is an inhibitor of CD49d expression on certain immune cells (e.g. T cells). It has been reported in scientific literature* 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 and do not appear to be as effective in patients with a greater number T cells that express high levels of CD49d. Currently there are a limited number of anti-inflammatory drugs in clinical development for DMD and ATL1102 is the only CD49d targeting drug undergoing clinical trials in DMD patients in the world.

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 markers of inflammation, muscle damage and disease progression. The efficacy related endpoints will be assessed as changes from a patient's baseline (start of the trial) measurements to the same measurements at the completion of their dosing.

The extended dosing period (24 weeks) of this clinical trial may allow for ATL1102 to show an improvement in the clinical endpoints that are most relevant to DMD disease progression (e.g. the upper limb function of the boys). Previous published studies in non-ambulant DMD boys have reported that after six months there is a significant decline in such functional endpoints whether the patients are on corticosteroids or not.

The Company expects to report trial results shortly after the completion of dosing, it being the point at which the efficacy endpoints are assessed as noted previously, rather than post the end of the 2 month safety monitoring period.

Being an open label study, if meaningful interpretations can be made, there may be an opportunity for non-statistical study read-outs on preliminary data ahead of the completion of dosing in all patients, however this would require a sufficient number of patients to have completed their dosing.

As per ANP's ASX announcement of 13 March 2019, the Company has initiated a process focused on accelerating the development planning for ATL1102 which will include discussions with regulatory authorities, initially in Europe, on the design and conduct of the next clinical trial of ATL1102 (Phase IIb) in DMD and on the development path for product registration. This is based on advice received from international regulatory consultants that the existing preclinical and clinical data package generated on ATL1102 to date would support application for approval to conduct a Phase IIb clinical trial of the drug in DMD patients in Europe. This regulatory process will run in parallel with the running of the current study of ATL1102 thereby accelerating the development planning for ATL1102 in the DMD indication.

Mark Diamond, CEO of Antisense Therapeutics said. "We are very happy with the progress being made in the Phase II clinical trial of ATL1102 in DMD patients at the RCH. Clinical trials for rare diseases such as DMD are notoriously challenging to recruit for, so we are pleased that we are close to having full enrolment in our trial with relatively minor delay. With no serious adverse events reported to date, and our clinical trial database continuing to grow with data on the longer term patient exposure to ATL1102, we are excited about the impending occasion of the reporting of our results and in turn the prospect that ATL1102 may play an important future role in the treatment of DMD".

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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 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