ASX Announcement

31 August 2020

ANP submits EMA Orphan Drug designation application for ATL1102 in DMD

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY], (the Company) is pleased to announce that it has submitted its application for Orphan Drug designation of the Company's drug ATL1102 for treatment of Duchenne muscular dystrophy (DMD) to the European Medicines Agency (EMA) Committee for Orphan Medicinal Products.

This follows the Company's Orphan Drug designation application for ATL1102 in DMD to the US FDA earlier this month.

Mark Diamond, ANP's Managing Director and CEO said: "This is an important regulatory step in supporting our clinical development and commercialisation plans for ATL1102 in Europe. The EMA looks to support the development of medicines that address the unmet medical needs of patients and may grant a conditional marketing authorisation for medicines aimed at treating, preventing or diagnosing seriously debilitating or life-threatening diseases. This includes medicines for orphan indications."

The designation is given to medicinal compounds meant to treat rare conditions that are life-threatening or chronically debilitating and where the treatment provides a significant benefit to those affected by the condition or no satisfactory treatment is available. Orphan status brings development and marketing incentives, such as reduced fees, scientific advice and market exclusivity for 10 years upon regulatory approval.

This announcement has been authorised for release by the Board.

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About Antisense Therapeutics Limited (ASX:ANP | US OTC:ATHJY) 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).

About ATL1102 DMD Trial The Phase II clinical trial of ATL1102 in patients with Duchenne Muscular Dystrophy was an open label six-month dosing trial of ATL1102 administered SC at 25mg per week in nine non-ambulant patients with DMD aged between 10 and 18 years. The trial was conducted at the neuromuscular centre of the Royal Children's Hospital (RCH) in Melbourne, Australia. The primary endpoints of the trial related to the safety and tolerability of ATL1102. The efficacy of ATL1102 was also assessed in terms of its effects on disease processes and progression (e.g. the upper limb strength and function of the boys). Given the exploratory nature of this first trial in boys with DMD, it was not powered to see a statistical difference on these disease progression endpoints, which would be expected in future longer-term clinical studies in a larger number of patients. However, highly encouraging positive trends across multiple parameters have been reported in this Phase II clinical trial. 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 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. 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.

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.