

ASX Announcement

14 December 2020

European Commission grants Orphan Drug Designation for ATL1102 in DMD

- **Orphan Drug Designation (ODD) granted by the Commission;**
- **Market exclusivity for 10 years upon regulatory approval;**
- **Additional 2 years of exclusivity on approval for pediatric use**

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJ | FSE:AWY], (the Company) is pleased to announce that it has received notification that the European Commission has adopted the decision relating to the designation of ATL1102 as an orphan medicinal product for Duchenne muscular dystrophy (DMD), under Regulation (EC) No 141/2000 of the European Parliament and of the Council.

Orphan drug designation was granted by the European Commission based on a positive opinion issued by the European Medicines Agency (EMA) Committee for Orphan Medicinal Products in November 2020. This follows the recent granting of both Orphan Drug Designation and Rare Pediatric Disease Designation for ATL1102 in DMD by the US Food and Drug Administration.

Orphan status in the EU brings development and marketing incentives, such as reduced fees on scientific advice and marketing authorisation application, and market exclusivity in Europe for 10 years upon regulatory approval of ATL1102 with an additional 2 years of exclusivity for its pediatric use in DMD. During that exclusivity period, neither the EU nor the Member States shall accept another marketing authorisation application for a similar medicinal product in the same therapeutic indication.

Mark Diamond, ANP's Managing Director and CEO said: "We are very pleased the EC has adopted the decision to designate ATL1102 for DMD as an Orphan Drug in the EU. We have now successfully achieved orphan drug designation in Europe and orphan drug and rare pediatric disease designations in the US, the world's major pharmaceutical markets. We expect that the incentives that come from such designations including marketing exclusivity periods will be of very significant commercial value should ATL1102 be successful in its progress through development and ultimately achieve marketing 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.