

13 July 2022

ATL1102 for DMD Clinical Trial Application Submitted in Europe

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY] (ANP or Company) is pleased to advise that it has submitted its first clinical trial application (CTA) for the Phase IIb/III clinical trial of ATL1102 in non-ambulant patients with Duchenne muscular dystrophy (DMD) to the Federal Institute for Drugs and Medical Devices in Germany (BfArM) for their evaluation and subsequent approval of the application.

This is a significant milestone for ANP encapsulating an extensive effort by the Company in establishing an agreed clinical and regulatory pathway with the European Medicines Agency and in preparing the comprehensive documentation package required by the regulators for trial approval. The Company is continuing to work with its Clinical Research Organisation partner, Parexel, in advancing the regulatory process for the program in Europe and will continue to provide updates on material progress.

In parallel the Company has been extensively evaluating its clinical plans for ATL1102 in DMD with the focus on deploying its existing cash reserves in the most effective manner, to reduce upfront capital requirements and extend its cash runway. The Company believes this capital management focus, including the review of financing requirements and options for sourcing future funding (as and when required), to be prudent given the present challenging market conditions.

The Company remains committed to its DMD program and to initiating the next clinical trial of ATL1102 in DMD as soon as possible to advance its clinical development for the benefit of the patients with DMD and the broader Duchenne community.

The Company expects to provide a more detailed program update in the coming weeks once the planning in line with the expectations noted above is sufficiently affirmed.

This announcement has been authorised for release by the Board.

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About Antisense Therapeutics Limited [ASX: ANP | US OTC: ATHJY | FSE: AWY] 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). ATL1102 is the only drug targeting CD49d in clinical development for DMD.

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 and with current treatment typically limited to only the second or third decade of life. The management of the inflammatory damage to muscle associated with DMD is currently addressed via the use of corticosteroids prednisolone and deflazacort which delay disease progression prolonging ambulation by a median 2 to 3 years (Shieh et al, 2018) and reduce loss of upper limb function as measured by performance of upper limb function (PUL) scores, (Pane et al, 2018), an objective measurement of function. Corticosteroids are, however, acknowledged as providing insufficient efficacy and are associated with significant side effects including bone loss that require monitoring, management, and treatment (Ward et al 2018). As a consequence, there is an acknowledged high need for new therapeutic approaches for the treatment of the immune mediated inflammation associated muscle damage in 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.

Shieh et al, Deflazacort versus prednisone/prednisolone for maintaining motor function and delaying loss of ambulation: A post HOC analysis from the ACT DMD trial. Muscle Nerve. 2018 Nov; 58(5): 639–645. Muscle & Nerve November 2018 639

Pane M, Coratti G, Brogna C, Mazzone ES, Mayhew A, Fanelli L, Mercuri E et al. (2018) Upper limb function in Duchenne muscular dystrophy: 24 month longitudinal data. PLoS ONE 13(6): e0199223. <https://doi.org/10.1371/journal.pone.0199223>

Ward L.M, Hadjiyannakis, S, McMillan, HJ, Noritz, G, and Weber, DR, Bone Health and Osteoporosis Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics. 2018 October; 142(Suppl 2): S34–S42. doi:10.1542/peds.2018-0333E.