ASX Announcement

22 June 2021

ATL1102 for DMD EMA PIP feedback and FDA regulatory progress

- Feedback received from EMA Paediatric Development Committee (PDCO) on PIP
- PDCO feedback in line with expectations
- FDA Fast Track Designation Request submitted
- To the extent possible, Company is taking the opportunity to harmonize EU and US development plans

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY], (the Company) today announced that it had received feedback on the Paediatric Investigation Plan (PIP) for the development of ATL1102 for Duchenne muscular dystrophy (DMD) from the Paediatric Committee (PDCO) of the European Medicines Agency (EMA). As part of its review of the PIP, PDCO provided feedback outlining additional information requirements on the Company's planned Phase IIb clinical trial in non-ambulant DMD boys. Overall, the feedback on the Phase IIb trial is in line with Company's expectations with the key features of the study protocol remaining as noted in the Company's PIP submission announcement of 25 February 2021.

As an interim step, prior to submission of the Phase IIb clinical trial application, ANP is now preparing responses to the PDCO information requirements. The Company anticipates finalising the trial design with PDCO later in Q3'CY21 ahead of submitting the clinical trial application for the Phase IIb trial of ATL1102 in non-ambulant DMD patients to be conducted in Europe shortly thereafter.

A paediatric investigation plan is a development plan aimed at ensuring that the necessary data is obtained through studies in children. Approval of the PIP is required to support the authorisation of a medicine for children in the European Union (EU). The PIP addresses the entire paediatric development program for ATL1102 in DMD (including potential ambulant DMD patient studies). ANP through its interactions with PDCO, is looking to ensure that its planned clinical studies will be run in accordance with PDCO expectations for future product approval.

Nuket Desem, Director, Clinical and Regulatory Affairs at Antisense Therapeutics said: "The EMA's PDCO feedback via the PIP Summary Report was constructive. We have appreciated the collaborative approach of the EMA to assist us in refining the study design for the proposed Phase IIb clinical trial in Europe. It's another important step towards bringing this new therapy to patients in the EU."

In parallel the Company continues to progress its interactions with the US Food and Drug Administration (FDA) and has recently submitted a FastTrack Designation Request (https://tinyurl.com/fwhemd95). Given the outcomes reported following ANP's recent Type C meeting with the FDA and the FDA's positive feedback on the design parameters for a US Phase IIb/III study, the Company continues to work with its expert US based regulatory advisors on appropriate next steps to advance the ATL1102 DMD program in the US.

While the Company's Phase IIb clinical trial protocol was initially developed to meet EMA's expectations, the recent feedback from the FDA has provided the Company the opportunity to streamline the regulatory processes in Europe and the US and to the extent possible harmonize the Company's overall global clinical development plans.

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. ATL1102 has also shown to be very effective in reducing inflammatory brain lesions in patients with MS (Limmroth, V. et al Neurology, 2014; 83(20): 1780-1788) and recently delivered highly promising clinical results in patients with Duchenne muscular dystrophy (DMD) a rare and fatal muscle wasting disease where inflammation in the muscle leads to fibrosis and death of muscle tissue.

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.