ASX Announcement

14 December 2021

Positive PIP Decision from UK MHRA & ratification of PDCO opinion by EMA

- **Positive Decision received on UK PIP**
- **Positive PDCO decision ratified by EMA**
- **Phase IIb/III pivotal trial in Europe on track for proposed initiation in mid-2022**

Antisense Therapeutics Limited [ASX: ANP | US OTC: ATHJY | FSE: AWY] today announced that it has received a positive Decision from the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK on the UK Paediatric Investigation Plan (PIP) submission for the development of ATL1102 for Duchenne muscular dystrophy (DMD) (a separate PIP submission was made to the MHRA following the UK's withdrawal from the European Union). The UK is a key location for the conduct of the study and is the base of our Co-ordinating Principal Investigator, Professor Thomas Voit MD (Director of NIHR GOSH UCL Biomedical Research Centre, UK).

The measures outlined in the UK-PIP Decision are consistent with those adopted in the positive final Opinion on the Company's PIP for the development of ATL1102 for DMD provided by the Paediatric Committee (PDCO) of the European Medicines Agency (EMA) (ASX Announcement 1 November 2021). Subsequent to the reporting of this news, the Company has now received formal ratification by the EMA of this decision.

A PIP is a development plan that addresses the entire paediatric development program for ATL1102 in DMD (including future ambulant DMD patient studies) and is aimed at ensuring that the necessary data is obtained through studies in children (including the Phase IIb/III clinical trial of ATL1102 in non-ambulant DMD boys in Europe) that are run in accordance with the EMA and now the MHRA's expectations for future product approval. The Phase IIb/III clinical trial is a multicentre, randomised, double-blind, placebo-controlled study to determine the efficacy, safety and pharmacokinetic profile of ATL1102 in non-ambulatory participants with DMD with a follow-on open label extension trial.

The Company appointed Clinical Research Organisation (CRO) is finalising site evaluations via site inspections to select the sites (>30) in the United Kingdom, Netherlands, Germany, Italy, France, Belgium, Spain, Bulgaria and Turkey. Following completion of the evaluations and trial site selection, clinical trial agreements will be executed with all the trial sites and separate trial applications will be made to national competent authorities of all participating countries. Preparation of the requisite regulatory documentation to support ethics committee and competent authority clinical trial approvals is well advanced. ATL1102 clinical supplies for the trial are also being prepared for shipment to Europe for packaging and labelling into study medication kits, which would then undergo European Qualified Person (QP) release for clinical trial use. Following these activities patient recruitment would be expected to commence in mid-2022, as per the timelines noted in the 1 November 2021 investor presentation as lodged by the Company with the ASX.

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).

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.