ASX Announcement

9 December 2021

ATL1102 Toxicology Protocol submitted to US FDA

- ATL1102 toxicology protocol submitted to support extended clinical dosing in US studies
- FDA interactions on the development pathway for DMD to continue in parallel with the conduct of the Phase IIb/III trial in Europe
- Potential to receive highly valuable PRV, given EU trial timing and US Congress extension of PRV sunset provisions

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY], (the Company) today advised that it has submitted to the US Food and Drug Administration (FDA) the protocol synopsis for a nine-month chronic monkey toxicology study to support the dosing of patients with ATL1102 beyond six months in US for Duchenne Muscular Dystrophy (DMD) or any other clinical application of ATL1102. The Company is expecting to receive feedback from the FDA on the protocol in 1Q'22.

A Type C guidance meeting held with US FDA earlier in the year provided the Company with clarity on the requirement for the chronic monkey study and design of a Phase IIb/III trial for the US. Given the apparent high-level alignment between EMA and FDA on Phase IIb/III study requirements, the feedback from the FDA provides the Company with the opportunity to engage with the agency to streamline the regulatory processes and to the extent possible harmonize the Company's overall global clinical development plans.

The Company considers that it has potential optionality in its actions with FDA including to take the EU Phase IIb/III data to the FDA to be assessed as supportive data for a future marketing application or should the data warrant it, possibly an approval of ATL1102 for DMD without further trials.

FDA interactions to explore the optionality highlighted above are to continue in parallel with the conduct of Phase IIb/III pivotal trial in Europe. The timing of the initiation of the nine-month toxicology study will be dependent on these continued interactions with the agency.

An important consideration in the clinical and regulatory strategy outlined above is the news announced by ANP on 30 September 2020 that the US FDA had granted a Rare Pediatric Disease Designation to ATL1102 for the treatment of DMD. Should the Phase IIb/III pivotal trial in Europe be successful, the Company believes it could be in a position to receive a rare pediatric disease priority review voucher (PRV) if it obtains FDA approval for ATL1102 in the DMD indication (as the drug's first approval) before September 30, 2026 (being the extended sunset date of the RPD Priority Review Voucher Program approved by the US Congress). The Company may then choose to sell its PRV to use it as a source non-dilutive capital. From 2017 - 2021, sales of PRVs ranged between US$80 - $150 million.

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.