ASX Announcement

1 June 2021

US FDA Feedback on Type C Meeting for ATL1102 in the US

- Clarity on path forward for a Phase IIb/III including the potential exploration of higher doses
- Company to submit Fast Track Designation Request based on FDA feedback

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY], (the Company) today announced that further to the Type C guidance meeting with the US Food and Drug Administration (FDA) held on 19 April 2021, the Company has received the official minutes of the meeting in relation to further development of ATL1102 in Duchenne muscular dystrophy (DMD) in the US.

The feedback confirmed that the findings at 25mg/week in ANP's Phase II, open-label study conducted at Royal Children's Hospital in Melbourne, Australia are adequate to support larger studies. Provided appropriate safety-monitoring recommendations are adopted by ANP, FDA said it could consider the exploration of higher doses of ATL1102 beyond 25mg/week subject to adequate justification.

Importantly, the FDA noted that the proposed design of the Phase IIb/III study (as a single, randomized double blind, placebo-controlled study) and the primary endpoint (PUL2.0) appears acceptable. Secondary endpoints of muscle strength as assessed by MyoGrip, MyoPinch, and predicted forced vital capacity (FVC), also appear reasonable as was the 52-week study duration, non-ambulant patient population and number of subjects relative to statistical power assumptions. The FDA has suggested that ANP submit a study protocol with the features outlined above for their review.

With regard to the non-clinical requirements, the FDA expects the Company to conduct a nine-month monkey toxicology study to support the Phase IIb/III study. The agency stated, however, that because of the seriousness of the indication, ANP may initiate the 12-month Phase IIb/III human clinical study prior to submission of a nine-month toxicology study, provided that a draft study report is submitted before the duration of dosing in patients exceeds six months.

ANP is consulting with its US based regulatory advisors on the appropriate next steps and to fine-tune the Phase IIb/III study design and development plans for the US and will evaluate the cost and feasibility of the nine-month monkey study, which would also support other clinical applications of ATL1102 beyond DMD.

The Company also discussed potential expedited regulatory pathways with the FDA during the meeting, which the FDA thought reasonable. Based on this feedback, ANP plans to move forward with a Fast Track Designation Request (https://tinyurl.com/fwhemd95).

The Company continues to maintain its focus on the European Phase IIb study. ANP advises that a response from the European Medicines Agency's Paediatric Committee on its Paediatric Investigation Plan (PIP) is expected in the coming weeks and accordingly intends to provide a market update following its receipt.

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.