ASX Announcement

12 August 2021

ANP Updates on US Regulatory Plans for ATL1102 in DMD

- Revised clinical trial protocol to be submitted to support lifting of the partial clinical hold
- Fast Track Designation request to be resubmitted once partial hold is lifted

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY], (the Company) wishes to advise the following in relation to its US regulatory plans for ATL1102 in Duchenne muscular dystrophy (DMD).

Given the outcomes reported following ANP's Type C meeting with the FDA and the FDA's positive feedback on the design parameters for a US Phase IIb/III study (refer Company's 1 June 2021 ASX announcement), the Company has continued to work with its expert US based regulatory advisors on appropriate next steps to advance the ATL1102 DMD program in the US. Accordingly, and as suggested by the FDA in their Type C meeting feedback, the Company submitted a Fast Track Designation (FTD) request for ATL1102 in DMD. In the FTD the Company has conveyed its intent to submit a revised clinical study protocol, with design features as discussed with the FDA including higher and longer dosing. ANP also expects to submit the protocol synopsis for a nine-month chronic monkey toxicology study to support the dosing of patients beyond 6 months.

An important development in clarifying the regulatory path for the Company in the USA has been the recent feedback received from the FDA on the Company's request for FTD. The FDA has clarified that prior to FTD being granted, the regulatory process for lifting the ATL1102 Investigational New Drug (IND) partial clinical hold that presently limits the dosing of ATL1102 to 25mg per week for 6 months in the US must be completed. Specifically, this involves including the requisite documentation (updated clinical and toxicology protocols) in a resubmission as suggested by the FDA. The Company has been working with its advisors on the revised study protocols for submission of its complete response to the partial hold and will continue to update the market on material progress in its US regulatory planning.

The agency noted in their response to the Company that, 'DMD is certainly a serious condition, and it appears that ATL1102 may have the potential to demonstrate an effect on a serious aspect of the condition and provide benefit over currently approved therapies…however…We cannot determine whether the overall development plan will enable you to obtain the data necessary to evaluate whether your product meets this unmet medical need because your IND is currently on partial hold' and that ..'We recommend that you send a new request for Fast Track designation after the partial hold issues are resolved.'

Antisense Therapeutics Ltd Chair Dr Charmaine Gittleson said, 'We are pleased the FDA shares our view that DMD is a serious condition for which ATL1102 may have benefit and that FDA is working with us in navigating through the technical regulatory requirements. A lifting of the partial hold would facilitate the IND becoming active and potentially allow for patients in the USA access to ATL1102 through a clinical program as well as clear the path for FDA consideration of the FTD submission.'

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.