ASX Announcement

26 May 2021

Manufacture of ATL1102 clinical supplies for Phase IIb trial in DMD

- Manufacture of ATL1102 active pharmaceutical ingredient (API) batch completed
- Formulation into injectable product for use in the Phase IIb trial completed
- Drug Product testing underway for release for use in clinical trials

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY], (the Company) is pleased to provide the following progress update on the manufacture of clinical supplies for its planned Phase IIb clinical trial of ATL1102 in non-ambulant Duchenne (DMD) patients.

The manufacture of ATL1102 active pharmaceutical ingredient (API) for the Phase IIb trial was undertaken in North America by Nitto Denko Avecia (Avecia) a contract manufacturing organization (CMO) with over 27 years of experience in oligonucleotide (antisense) development and production. Avecia has supported the commercial launch of oligonucleotide products since 2004 and offers complete continuity of supply up to multiple kilograms per batch with its large scale and commercial capabilities in support of advanced clinical trials and subsequent commercial supply.

Upon completion of the manufacture of this batch of API by Avecia last month, the material was then shipped to Contract, Parenteral (injectable) Drug Product Manufacturer Pyramid Laboratories in Costa Messa, Southern California and formulated into injectable product for use in the Phase IIb trial. This formulated injectable product (Drug Product or DP) is currently undergoing finished product release testing for clinical use, with results anticipated later next month.

Mark Diamond CEO of Antisense Therapeutics said: "We are very pleased with how the manufacture of clinical supplies for our planned Phase IIb trial of ATL1102 has proceeded particularly given the challenges that have presented to all CMO's during the global covid pandemic. We are indeed fortunate to be partnered with such high quality CMOs that have a deep experience with antisense drugs and both of which we have been working with for over 15 years and that can support manufacture all the way through to commercial sale of product".

This announcement has been authorised for release by the CEO.

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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.

About Nitto Avecia Nitto Avecia is the largest oligonucleotide manufacturer in the world and continues to play an integral role in advancing the oligo therapeutic market. With over 20 years of experience and over 1,000 sequences manufactured, we fulfill our client's needs for pre-clinical, clinical, and launched products. With production capacity in FDA- audited facilities near Boston, MA, and Cincinnati, OH, we produce a novel class of active pharmaceutical ingredients (APIs) -- oligonucleotides -- used by pharmaceutical and biotechnology companies to develop drug treatments for a variety of health indications. In addition to our pre-clinical and CGMP oligo manufacturing capability, we leverage our wealth of expertise to offer a portfolio of services that includes Analytical Development, Process Development, and Quality Control testing. Contact us @ www.avecia.com