ASX Announcement

26 April 2023

ATL1102 Phase IIb DMD trial - Bulgarian approval received with UK and Australian approval process advancing

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY] (ANP or Company) today announced that it has received both regulatory authority and ethics committee approval to conduct its double-blind, placebo controlled Phase IIb trial of ATL1102 in non-ambulant boys with Duchenne muscular dystrophy (DMD) in Bulgaria. Requisite contracts have also been executed with the Bulgarian trial site allowing for immediate site set up.

The Bulgarian approval follows similar approval received in Turkey in February this year.

UK & Australia approvals progress

As advised in December last year[1] the Company had submitted a Clinical Trial Application (CTA) for approval to conduct the Phase IIb trial in UK, Bulgaria and Turkey and that approvals would come through in a staggered manner.

The MHRA (UK regulatory authority) has evaluated the CTA and the Company has recently received their review questions. Ethics Committee (EC) feedback has also been received and the Company will submit a response to the EC together with the responses to the MHRA questions and the Company will communicate further upon receiving their anticipated approvals.

The Company also expects to conduct the trial at sites in Australia. After undergoing the Ethics assessment, the Company has received requests for clarification and is preparing a response. Once EC approval is received the Company will make a submission to the Therapeutic Goods Administration, Australia (TGA) via the Clinical Trial Notification scheme and upon the TGA's acknowledgement, be positioned to initiate Australian trial sites.

As noted in the Company's Quarterly Activities report[2], progress is being made in Turkey with both clinical trial sites having completed site initiation procedures and advancing to site activation, following which patient screening and enrolment can commence. The Company is grateful to the Turkish sites and all vendors for their efforts in achieving these milestones, despite the recent natural disaster of the February 2023 earthquake.

Antisense Therapeutics Board Chair Dr. Charmaine Gittleson said: "Tremendous effort has gone into the implementation of the substantially revised clinical development strategy as advised by the Company just over six months ago[3]. The revised approach necessitated modifications to the trial protocol and regulatory submission documents, which in turn impacted the many supporting elements of the clinical trial. In addition, identification of new countries, study investigators, and trial sites was necessary and bespoke trial applications had to be submitted into each of the selected countries. We have only been able to achieve all these aspects, within this timeframe, through the dedication and hard work of our internal team and good collaboration with the trial sites, Parexel and other vendors. We are pleased then to see the validation of our Clinical and Regulatory team's perseverance via the CTA acceptance and approvals now coming though from the regulatory authorities and gratified to be on the doorstep of launching this clinical trial and bringing this much needed therapy to the DMD community."

This announcement has been authorised for release by the Board.

1 ASX Announcement - 19th December 2022
2. Quarterly Activities Report - 17 April 2023
3. ASX Announcement - 7 September 2022

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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 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). ATL1102 is the only drug targeting CD49d in clinical development for DMD.

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 and with current treatment typically limited to only the second or third decade of life. The management of the inflammatory damage to muscle associated with DMD is currently addressed via the use of corticosteroids prednisolone and deflazacort which delay disease progression prolonging ambulation by a median 2 to 3 years (Shieh et al, 2018) and reduce loss of upper limb function as measured by performance of upper limb function (PUL) scores, (Pane et al, 2018), an objective measurement of function. Corticosteroids are, however, acknowledged as providing insufficient efficacy and are associated with significant side effects including bone loss that require monitoring, management, and treatment (Ward et al 2018). As a consequence, there is an acknowledged high need for new therapeutic approaches for the treatment of the immune mediated inflammation associated muscle damage in 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.

Shieh et al, Deflazacort versus prednisone/prednisolone for maintaining motor function and delaying loss of ambulation: A post HOC analysis from the ACT DMD trial. Muscle Nerve. 2018 Nov; 58(5): 639–645. Muscle & Nerve November 2018 639

Pane M, Coratti G, Brogna C, Mazzone ES, Mayhew A, Fanelli L, Mercuri E et al. (2018) Upper limb function in Duchenne muscular dystrophy: 24 month longitudinal data. PLoS ONE 13(6): e0199223. https://doi.org/10.1371/journal. pone.0199223

Ward L.M, Hadjiyannakis, S, McMillan, HJ, Noritz, G, and Weber, DR, Bone Health and Osteoporosis Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics. 2018 October; 142(Suppl 2): S34–S42. doi:10.1542/peds.2018-0333E.