ASX Announcement

1 March 2022

Poster Presentation at 2022 MDA Clinical & Scientific Conference

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY] today announced that new data on ATL1102 in DMD is to be presented in a poster presentation at the Muscular Dystrophy Association (MDA) Clinical & Scientific Conference, being held in Nashville, TN, USA 13–16 March 2022 (US CDT).

The e-poster presentation titled: **"ATL1102 treatment in non-ambulant boys with DMD modulates plasma proteins with roles in TGF-beta mediated fibrosis, and cartilage and bone physiology"** G. Tachas; C. Mueller; R.K DeLisle; I.R Woodcock; M.M Ryan; A. Padhye; N. Desem; will be a virtual presentation by Dr George Tachas, Antisense Therapeutics Director of Drug Discovery and Patents, conducted during the dedicated poster session times of 6:00 PM - 8:00 PM (CDT) 13–15 March 2022.

The ATL1102 poster presentation abstract is now available on-line, https://mdaconference.org/node/1703 and follows this announcement.

The MDA conference is the largest of its kind in highlighting unprecedented research advancements and clinical achievements in neuromuscular diseases (NMD). For exhibitors and sponsors, it offers unique opportunities for unparalleled engagement with world leaders and ground-breaking innovators in NMDs in both an in-person and virtual environment. The conference will explore all aspects of pre-clinical, translational, and clinical research and care across neuromuscular diseases to support the development of better care and treatments.

This announcement has been authorised for release by the CEO.

For more information please contact:

Antisense Therapeutics
Mark Diamond
Managing Director
+61 (0)3 9827 8999
www.antisense.com.au

Investment Enquiries
Gennadi Koutchin
XEC Partners
gkoutchin@xecpartners.com.au
1300 932 037

US/European IR & Media
Laine Yonker/Joe Green
Edison Investor Relations
lyonker@edisongroup.com
+1 646-653-7035

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 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, 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 the immune mediated inflammation associated muscle damage 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.

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

ATL1102 treatment in non-ambulant boys with DMD modulates plasma proteins with roles in TGF-beta mediated fibrosis, and cartilage and bone physiology

Tachas[1] G, Mueller[2] C, DeLisle[4] R.K, Woodcock[3] I, Ryan[3] M.M, Padhye A[1], and Desem[1] N.

1. Antisense Therapeutics Limited, Melbourne, Victoria, 3142, Australia. www.antisense.com.au
2. Boulder Bioconsulting, Inc., Boulder, Colorado, 80303, USA . https://boulderbioconsulting.com/
3. Murdoch Children's Research Institute, Melbourne, 3052, Australia, https://www.mcri.edu.au/
4. SomaLogic, Inc., 2945 Wilderness Pl. Boulder, Colorado 80301, USA. www.somalogic.com

ATL1102, an antisense drug to CD49d, the alpha chain of VLA-4, has been evaluated in a Phase II study in nine non-ambulant patients with Duchenne muscular dystrophy (DMD) at the Murdoch Children's Research Institute. All patients (12 to 18 years of age) were dosed with ATL1102 once weekly at 25mg s.c. for 24 weeks. Eight of the patients were on standard of care corticosteroid treatment. ATL1102 was shown to be safe, and modulated CD49d+ lymphocytes, and stabilized upper limb muscle function, strength, and fat fraction.

Post-hoc analysis of plasma from the study assessed ATL1102's effects on proteomics as measured by the SomaScan® assay, a large scale, aptamer-based assay, using normalized relative fluorescence units (nRFU). Parametric mixed effect longitudinal analysis was conducted to determine the average percent change over time, p-value and Benjaminin-Hochberg false discovery rate (FDR) adjusted p-value.

At 24 weeks, statistically significant mean decreases of Thrombospondin-1 (-49.3%) and increases of LTBP4 (20.7%), BMP5 (46.2%) and BMP6 (34.4%) were observed compared to baseline levels (FDR p-value <0.0005). Compared to a healthy adult control, nRFU baseline levels of LTBP4, BMP5 and BMP6 were below average, and ATL1102 treatment modulated each to nearer the external control mean.

ATL1102 increase of LTBP4, which sequesters TGF-beta, and ATL1102 decrease of Thrombospondin-1, which activates TGF-beta, suggest potential for reduced TGF-beta associated fibrosis.

ATL1102 increases of BMP5 and BMP6, ligands of the TGF-beta superfamily of proteins, with a role in cartilage and bone formation, suggest a potential for improved bone density. Serum BMP6 levels are reportedly associated with improved elbow flexion in DMD patients.

The effects on these proteins and others detected relevant to immune response, muscle and bone physiology may have a role in the observed ATL1102 function and strength stabilization and MRI benefits in the non-ambulant patients in the Phase II DMD study.