ASX Announcement

14 November 2022

ATL1102 toxicology study to support clinical program in the US

- Dosing expected to commence before the end of this calendar year
- Successful completion of the toxicology study is expected to be final step in lifting the partial clinical hold dosing restriction in the US
- Reporting of key study findings expected in 1H'24

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY] (ANP or Company) is pleased to announce that it has initiated the process with Contract Research Organisation (CRO) Pharmaron www.pharmaron.com to conduct a nine-month chronic monkey toxicology study to support the advancement of the ATL1102 program in the US for Duchenne muscular dystrophy (DMD) or any other clinical application of ATL1102.

Successful completion of the toxicology study is expected to be the final requisite step for the lifting of the partial clinical hold in the US that presently limits the dosing of ATL1102 to 25mg per week for 6 months. Lifting of the partial clinical hold would also allow ANP to apply for expedited program status with the US Food and Drug Administration (FDA) including Fast Track or potential Breakthrough Therapy designation.

As previously announced on 9th December 2021, interactions with the FDA had provided the Company with clarity on the requirement for the chronic monkey study. In the process, the Company submitted a protocol synopsis for the nine-month chronic monkey toxicology study to the FDA for their review and subsequently received FDA's feedback on the study design, which included the FDA's concurrence with the planned high dose level in the study.

There has been a well-documented long-term shortage of monkeys of the appropriate type and age available to the CROs for the conduct of such studies, leading to significant uncertainty on the possible future timing for an ANP study start. An opportunity recently presented to the Company whereby Pharmaron is able to run a study much earlier than anticipated following the cancellation of a similar study by one of Pharmaron's customers. To take advantage of this opportunity, ANP has taken on the husbandry and housing costs of the pre-allocated animals while completing the necessary arrangements with the CRO*. This enables Pharmaron to initiate the Company's chronic toxicology study with dosing of all animals to commence before the end of this calendar year with the reporting of key study findings expected in 1H'24, around the same time as six-month dosing results from the ATL1102 in DMD Phase IIb clinical study.

Dr Charmaine Gittleson, the Chair of Antisense Therapeutics said: "The commencement of a chronic toxicology study that aligns with FDA requirements is an important advancement for the ATL1102 program and a key value adding catalyst. Importantly it provides the Company the prospect of sharing with FDA a compelling data package encompassing the clinical results from the placebo controlled six-month study along with the outcome of the nine-month toxicology study. The Company expects that this investment in the chronic toxicology study should remove a key hurdle to lifting the partial clinical hold and in initiating clinical DMD studies under an IND and in turn provides more certainty on the path forward in the US. Furthermore, the alignment of the aforementioned toxicology and clinical data could provide an opportunity for more than one regulatory pathway to registration which would be discussed with FDA, and other regulators as relevant, at the appropriate time. The next calendar year is presenting as an exciting time for the Company and the DMD community as we commence these potentially transformative activities".

This announcement has been authorised for release by the Board.

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

*An agreement between the Company and Pharmaron to conduct the study has been executed and is effective immediately. It may be terminated by agreement, or according to common commercial termination provisions. The Company remains committed to the revised ATL1102 for DMD clinical plans as announced on 7 September 2022. The anticipated toxicology study costs (<US$2m) are well within the Company's current cash reserves.

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 q 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.