ASX Announcement

12 September 2022

Dosing commenced in DMD combination therapy study

- *mdx* mouse study to assess the potential clinical utility of ATL1102 in combination with dystrophin restoration agents in DMD
- Study results due Q4'CY22

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY], today announced that dosing has commenced in a muscular dystrophy (*mdx*) mouse model of DMD to assess the potential clinical utility of ATL1102 in combination with dystrophin restoration drugs (approved in the US for the treatment of DMD) to improve on therapeutic outcomes for patients with DMD.

Under the collaborative research agreement with the Murdoch Children's Research Institute's (MCRI), mice will be dosed with an antisense oligonucleotide designed to target CD49d (mouse equivalent of ATL1102) or control oligonucleotide or saline treatments in combination with a dystrophin restoration drug (morpholino oligonucleotide exon skipping drug of the same drug chemistry as the exon skipping treatments marketed in the US).

Antisense inhibition of CD49d has previously demonstrated activity in an *mdx* mouse model as a monotherapy, reducing CD49d+ immune cells and both the CD49d target in the muscle and muscle damage.

The combination study will assess the effects of antisense inhibition of CD49d in combination with a dystrophin restoration drug on markers of drug activity in the DMD *mdx* model including the potential of the combination to improve dystrophin expression levels beyond that achieved by the dystrophin restoration agent used alone, and thereby point to the potential utility of the combination treatment in the clinic.

This study is on track to be completed with results due Q4'CY22.

Sales of the dystrophin restoration drugs in the US for the 2nd Quarter of 2022 alone were in excess US$233 million[1]. Currently these drugs are used in combination with steroids and predominantly for the younger ambulant DMD population but are yet to demonstrate in controlled studies to be effective in further delaying loss of ambulation beyond the use of steroids alone, which underlines the exciting opportunity for a new combination therapy that can deliver improved outcomes for DMD patients.

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 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. ATL1102 has also shown to be very effective in reducing inflammatory brain lesions in patients with MS (Limmroth, V. et al Neurology, 2014; 83(20): 1780-1788) and recently delivered highly promising clinical results in patients with Duchenne muscular dystrophy (DMD) a rare and fatal muscle wasting disease where inflammation in the muscle leads to fibrosis and death of muscle tissue.

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.

About MCRI. The Murdoch Children's Research Institute (MCRI) is the largest child health research institute in Australia committed to making discoveries and developing treatments to improve child and adolescent health in Australia and around the world. They are pioneering new treatments, trialing better vaccines and improving ways of diagnosing and helping sick babies, children and adolescents. It is one of the only research institutes in Australia to offer genetic testing to find answers for families of children with previously undiagnosed conditions.

1 *Sarepta Therapeutics Second Quarter 2022 Financial Results & Recent Corporate Developments - 2 August 2022*
NS Pharma Viltepso US Quarterly Sales