16 June 2017

Positive effects seen with ATL1102 on Multiple Sclerosis "Black Hole" brain lesions

Antisense Therapeutics ("ANP" or the "Company") reports today that a post hoc analysis of brain lesion data from the Phase II study of the ATL1102 in patients with Multiple Sclerosis (MS) [*Limmroth et al 2014 Neurology*] has shown that ATL1102 significantly reduces the number of active MS lesions that convert to "Black Holes", areas of axonal (nerve fiber) loss or permanent tissue damage. The positive effect of ATL1102 on black holes suggests that along with its action in reducing the number of inflammatory lesions, ATL1102 may also be potentially neuroprotective in protecting the axons in the lesion from degeneration.

ATL1102 is an antisense inhibitor of CD49d, a subunit of VLA-4 (Very Late Antigen-4). In a Phase II study of ATL1102 in RRMS patients, ATL1102 met its primary endpoint in reducing the cumulative number of new active MS lesions by 54% vs placebo[1].

A post hoc analysis of the Magnetic Resonance Imaging data from the Phase II study was conducted to assess the effect of ATL1102 on the conversion of the remaining active lesions to T1 black holes (BH). The analysis showed that there was a significant reduction in active lesions at weeks 8 and 12 converting to BH at week 16 in the ATL1102 treated patients (13.2%) compared to patients on placebo (27.6%), with the odds of converting to BH in the placebo arm 2.51 times the odds of converting in the treatment arm (p= 0.0376).

An inhouse review of published data on the effect of registered MS disease modifying agents on BH[2-5] suggests the effects observed with ATL1102 in reducing active lesions converting to BH appear relatively rapid (seen with only 8 weeks of dosing) and potent.

The post hoc analysis was conducted by Dr Frederik Barkhof, Professor of Neuroradiology, Department of Radiology and Nuclear Medicine, VU University Medical Centre, Amsterdam, and co-author on the Limmroth et al Neurology publication.

Prof Barkhof said of the results; "Assessing the effect of MS treatments to prevent lesions evolving into so-called "Black Holes" is a relatively new manner to determine neuroprotection in MS. Reducing black holes signifies preservation of brain tissue and the slowing of MS disease progression. The positive effects observed with ATL1102 on black holes are encouraging and suggestive of ATL1102's potential neuroprotective effects, which could be very important, particularly when contemplating the drug's potential as a treatment for progressive forms of MS".

The Company has filed a provisional patent application incorporating this new data while an abstract of the results is to be submitted for presentation at an MS scientific meeting this year.

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[1] Limmroth, et al. *Neurology*, 2014, 83(20): 1780-1788
[2] Bastianello et al. *BMC Neurology,* 2011;11:125
[3] Zivadinov et al. *J Neurol* 2015, 262:648–653
[4] Barkhof et al. *Neurology* 2010,74;1033-1040
[5] Brex et al. *Neurology* 2001;57, 2185-2190

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. Its mission is to create, develop and commercialise second generation antisense pharmaceuticals for large unmet markets. The products in ANP's development pipeline are in-licensed from Ionis Pharmaceuticals Inc., world leaders in antisense drug development and commercialisation. ATL1102 (injection) has successfully completed a Phase II efficacy and safety trial, significantly reducing the number of brain lesions in patients with relapsing-remitting multiple sclerosis (RRMS). ATL1103 drug designed to block GHr production successfully reduced blood IGF-I levels in Phase II clinical trials in patients with the growth disorder acromegaly.

About Multiple Sclerosis (**MS**) MS is a life-long, chronic disease that progressively destroys the central nervous system (CNS). It affects approximately 400,000 people in North America and more than 2 million worldwide. It is a disease that affects more women than men, with onset typically occurring between 20 and 40 years of age. Symptoms of MS may include vision problems, loss of balance, numbness, difficulty walking and paralysis. In Australia MS affects over 20,000 people. **Relapsing-Remitting MS (RR-MS):** People with this type of MS experience clearly defined attacks of worsening neurologic function. These attacks—which are called relapse or exacerbations —are followed by partial or complete recovery periods (remissions), during which no disease progression occurs. Approximately 85% of people are initially diagnosed with relapsing-remitting MS. **Secondary-Progressive MS** (**SP-MS)** occurs when after an initial period of relapsing-remitting MS, many people develop a secondary-progressive disease course in which the disease worsens more steadily, with or without occasional flare-ups, minor recoveries (remissions), or plateaus. Before the disease-modifying medications became available, approximately 50% of people with relapsing-remitting MS developed this form of the disease within 10 years. The market for drugs treating RR-MS has been valued at more than USD$20 billion. There are limited treatment options for SP-MS patients. The market potential for SP-MS treatments has been estimated at US$7billion.

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 RR-MS patients. The ATL1102 Phase IIa clinical data has been published in the medical Journal ***Neurology*** (Limmroth, V. et al Neurology, 2014; 83(20): 1780-1788).