ASX Announcement

13 February 2023

Limb Girdle Muscular Dystrophy R2 animal study commenced

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY | FSE:AWY] today announced the commencement of the second phase (chronic setting) of its program to study the effects of an antisense oligonucleotide (ASO) to CD49d (mouse equivalent of ATL1102) in a LGMDR2 animal model of dysferlin deficiency. Having previously successfully demonstrated drug activity (reducing target and immune cell RNA in muscle) in the first study in the dysferlin deficient animals[1], this follow-on chronic study will assess longer duration treatment effects on key disease progression endpoints including reduction in muscle adipose (fat) levels.

The study is being undertaken in collaboration with experts in genetic muscle disease at the Murdoch Children's Research Institute (MCRI) in Melbourne and the Jain Foundation in the USA. The Jain Foundation, a non-profit disease foundation established in the hopes of curing dysferlinopathy, is coordinating the worldwide efforts to find a treatment for dysferlinopathy[2]. Suitably aged mice with the dysferlin mutation and related disease progression characteristics have been sourced via the Jain Foundation for use in the study. In this blinded and controlled study, mice will be treated for four months with results to follow mid-2023.

LGMDR2 (also known as dysferlinopathy) is a rare genetic muscle disease that is caused by mutations in the dysferlin gene that leads to significant reduction or absence of dysferlin protein levels in muscle fibers. LGMDR2 is characterized by muscle inflammation, fibrosis, adiposity (fat) and progressive weakness in the hip and shoulder area (i.e. the limb girdle) proximal muscles (those closest to the center of the body) with loss of ambulation and upper limb function in adulthood. LGMDR2 affects ~ 1 in 125,000 people[3]. To date, no treatments have proven to be beneficial in slowing LGMDR2 disease progression.

The use of ATL1102 as a treatment for dysferlinopathy is covered in ANP's patent application PCTAU2020/050445 directed at modifying muscle performance by reducing muscle adiposity and provisional application 2021903024 that claims the use of ATL1102 to reduce thrombospondin-1 reported to be beneficial in treating the disease. As LGMDR2 is a rare disease, the Company expects to be eligible to apply for additional market exclusivity protection via Orphan Drug Designation in the US and Europe[4]. Such applications would be sought in the event of positive outcomes from this chronic study in the dysferlin deficient animal model.

Dr George Tachas Ph.D., Director, Drug Discovery and Patents at Antisense Therapeutics said "We are pleased to have commenced this chronic study into the effects of ASO to CD49d in the dysferlin deficient animal model and in turn to be continuing our key collaborations with the MCRI and the Jain Foundation. We look forward to the results of this follow-on study, which if positive could support advancement into a future clinical trial in patients with dysferlinopathy, a group in tremendous need of an effective therapy."

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 Limb Girdle Muscular Dystrophy R2 caused by the genetic loss of dysferlin

Limb-girdle muscular dystrophy (LGMD) is a group of rare muscular dystrophies primarily characterized by hip and shoulder (i.e. limb-girdle) proximal muscle weakness estimated to occur as a class in up to 6.9 in every 100,000 people[5]. Over 30 subtypes have been identified with different underlying genetic causes. Dysferlin loss occurs in the recessive genetic muscle disorder LGMDR2, formerly known as LGMD2B, and the related muscle disease Miyoshi myopathy dystrophy 1 (MMD1). Collectively these disorders caused by the loss of or reduced levels of dysferlin are called Dysferlinopathy. Dysferlinopathy (LGMDR2) prevalence is approximately ~ 1 per 125,000 people[3] or 2500 people in the US, or 18% of all LGMDs[5] with an estimated upper range for LGMDR2 of ~ 4000 people in the US.

In LGMDR2, the initial weakness is seen in the proximal muscles and in the case of MMD1 there is initially distal muscle weakness. However, natural history data on dysferlinopathy have shown that LGMDR2 and MMD1 are the same disease. Dysferlin is a transmembrane protein that has been shown to be involved in multiple cellular processes such as calcium regulation, membrane repair, and membrane trafficking. The absence of dysferlin in LGMDR2 is characterized by activated F4/80 macrophage and T cell inflammation and increase in fat replacing the muscle, where adipocytes replace dysferlin deficient muscle, as detected by MRI. This progressively reduces muscle strength, ability to walk, reduces upper limb function and quality of life[5]. There are currently no treatments for dysferlinopathy. The steroid drug deflazacort treatment failed in a 6 month patient study and made the disease worse. Deflazacort (1mg/kg) taken for a month, and every second day for 5 months reduced muscle strength, which reversed after cessation of steroid treatment[6]. There is an unmet need for effective therapies so that people with LGMDR2 can maintain ambulation, muscle strength and quality of life.

References

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