ASX Announcement

2 October 2020

Statistically significant improvement in PUL2.0 with ATL1102 treatment in non-ambulant boys with DMD compared to a matched natural history control

- New ATL1102 data presented at the 25th International Annual Congress of the World Muscle Society
- ATL1102 treated patients showed a statistically significant mean improvement in Total PUL2.0 scores (assessment of muscle function) at 24 weeks compared to a matched natural history control
- A greater frequency of patients treated with ATL1102 showed improvement or maintenance of their Total PUL2.0 score relative to the natural history control group

Antisense Therapeutics Limited [ASX:ANP | US OTC:ATHJY] is pleased to report results presented at the 25th International Annual Congress of the World Muscle Society. PUL2.0 (Performance of Upper Limb Function) mean data from the ATL1102 Phase II trial was compared to a natural history control of matched non-ambulant boys on standard of care (corticosteroids) and showed a statistically significant improvement in Total PUL2.0 with a greater frequency of patients achieving an improvement or maintenance of their Total PUL2.0 scores relative to the matched natural history control group over 24 weeks.

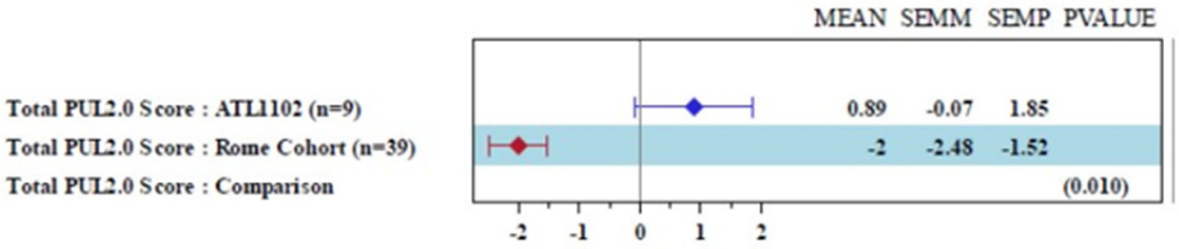
ATL1102 was recently assessed in an open label Phase II study in adolescent non-ambulant patients with DMD. In the Phase II study, nine patients, 12 to 18 years old [mean 14.9 (SD 2.1) years] were dosed with ATL1102 for 24 weeks (8 of 9 on corticosteroids) and assessed using PUL2.0. In a post study analysis, the mean PUL2.0 data from the ATL1102 treated patients was then compared with the 24-week PUL2.0 data of 39 assessments in 20 non-ambulant patients [mean age 15.61 (SD 2.02) years; 19 on corticosteroid] from a natural history database of DMD patients in Rome, Italy - the Rome cohort (RC). The RC were identified using the same inclusion criteria used to enrol patients in the ATL1102 Phase II study.

ATL1102 treated patients achieved statistically significant improvement in the mean Total PUL2.0 score of +0.89 (SD ±2.89) compared to -2.00 (SD ±3.018) in the matched RC control group (p=0.010) over 24 weeks. The RC data shows declines in PUL2.0 at 24 weeks consistent with declines reported in the published literature in non-ambulant patients over one and two years. The frequency of ATL1102 treated patients showing improvement or no change on the total PUL2.0 score was 78% compared to 33% in the RC group. This new external controlled comparative analysis is further evidence of a significant improvement in muscle function with the use of ATL1102 treatment as assessed by the Total PUL 2.0 test.

Importantly, there is general acceptance of the PUL2.0 assessment as the primary efficacy endpoint for registration studies in non-ambulant DMD patients. The significantly improved results of ATL1102 treatment on PUL2.0 when compared to a matched RC group together with its positive effects on multiple additional disease progression parameters, positions ATL1102 as an exciting prospect for the treatment of DMD patients, warranting its continued development and progress into a potentially pivotal Phase IIb trial in Europe. For further details on these new results please refer to the accompanying presentation.

6 Month PUL2.0 mean changes: ATL1102 Phase II data compared to Rome Cohort Control

Forest Plot for the Mean Change (+/- SEM) in PUL2.0 Measures from Baseline to Month 6



Professor Eugenio Mercuri, Professor of Pediatric Neurology at the Catholic University, Rome, Italy said "ATL1102 treatment demonstrated a statistically significant improvement in the mean Total PUL2.0 score in non-ambulant boys with DMD when compared to our natural history Rome Cohort used as external controls. The level of improvement achieved is very positive and clinically relevant. As Total PUL2.0 is the key efficacy endpoint for seeking drug approval in non-ambulant patients with DMD, the comparative data further indicates ATL1102's promising potential to provide clinically meaningful benefits in the future treatment of non-ambulant DMD patients who have very limited treatment options".

Dr George Tachas, Antisense Therapeutics Director of Drug Discovery and Patents further noted "The level of improvement achieved in mean PUL2.0 over 6 months with ATL1102 treatment is to my knowledge yet to be seen with any other drugs in development for non-ambulant DMD boys. The comparison of the ATL1102 Phase II open label PUL2.0 data to a matched natural history external control elevates both the quality and clinical importance of our efficacy outcomes and we look forward to utilising this new comparative data in advancing the development of ATL1102 for DMD".

The Company will present on this new data at an investor webinar at 9AM (AEST) today | UK 12AM | US PDT 4:00PM, EDT 7.00PM (Thursday 1 October).

To access the webinar and for details of how to register online please follow this link:

https://us02web.zoom.us/webinar/register/WN_JPRXpRipQ2uzjHlFxRNqVA

This announcement has been authorised for release by the Board

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About Antisense Therapeutics Limited (ASX:ANP | US OTC:ATHJY) 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. ATL1102 has also shown to be very effective in reducing inflammatory brain lesions in a 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. The management of the inflammation associated with DMD is currently addressed via the use of corticosteroids, 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 inflammation associated 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 .

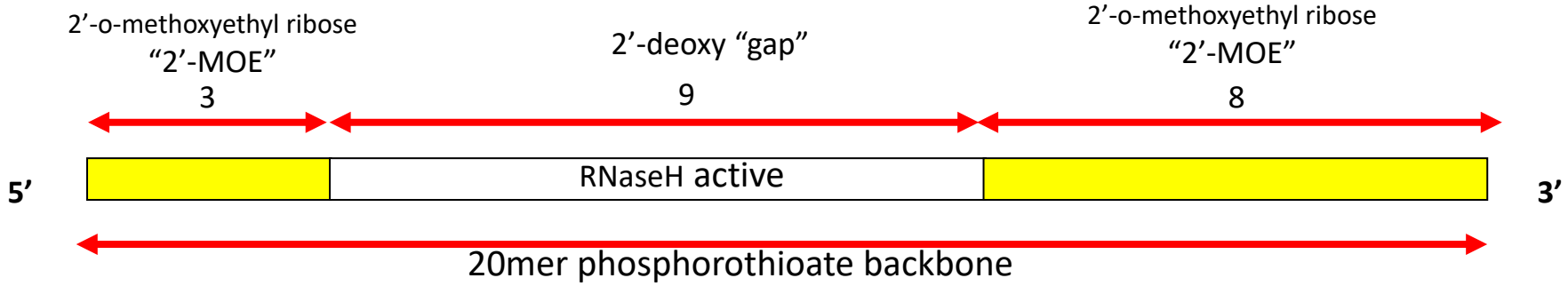
Pinto-Mariz F, Carvalho LR, Araújo AQC, *et al*. CD49d is a disease progression biomarker and a potential target for immunotherapy in Duchenne muscular dystrophy. *Skeletal Muscle* 2015, 5: 45-55.


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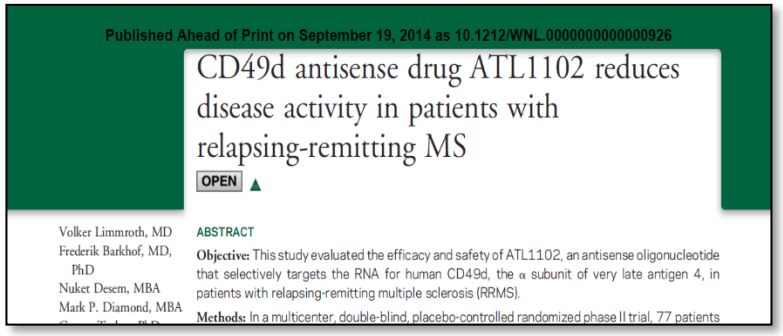
Forward Looking Statements

This presentation contains forward-looking statements regarding the Company's business & the therapeutic & commercial potential of its technologies & products in development. Any statement describing the Company's goals, expectations, intentions or beliefs is a forward-looking statement & should be considered an at-risk statement. Such statements are subject to certain risks & uncertainties, particularly those risks or uncertainties inherent in the process of developing technology & in the process of discovering, developing & commercializing drugs that can be proven to be safe & effective for use as human therapeutics, & in the endeavor of building a business around such products & services. Actual results could differ materially from those discussed in this presentation. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the Antisense Therapeutics Limited Financial Accounts for the year ended 30 June 2020, which is available from the Company or at www.antisense.com.au.

ATL1102 for DMD OVERVIEW



- ATL1102 is an antisense drug to CD49d (alpha chain of VLA-4) expressed on lymphocytes
- ATL1102 reduces inflammation in the CNS in Multiple Sclerosis patients,
- A scientific publication indicated CD49d is a progression and severity marker for DMD


Published Ahead of Print on September 19, 2014 as 10.1212/WNL.0000000000000926

CD49d antisense drug ATL1102 reduces disease activity in patients with relapsing-remitting MS

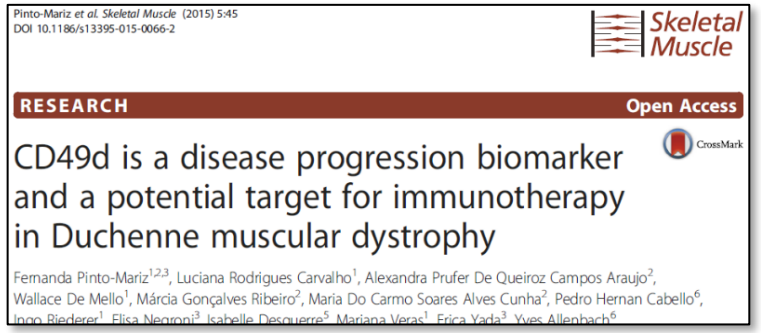
OPEN

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ABSTRACT

Objective: This study evaluated the efficacy and safety of ATL1102, an antisense oligonucleotide that selectively targets the RNA for human CD49d, the α subunit of very late antigen 4, in patients with relapsing-remitting multiple sclerosis (RRMS).

Methods: In a multicenter, double-blind, placebo-controlled randomized phase II trial, 77 patients


Pinto-Mariz *et al. Skeletal Muscle* (2015) 5:45
DOI 10.1186/s13395-015-0066-2

Skeletal Muscle

RESEARCH Open Access

CD49d is a disease progression biomarker and a potential target for immunotherapy in Duchenne muscular dystrophy

Fernanda Pinto-Mariz[1,2,3], Luciana Rodrigues Carvalho[1], Alexandra Prufer De Queiroz Campos Araujo[2], Wallace De Mello[1], Márcia Gonçalves Ribeiro[2], Maria Do Carmo Soares Alves Cunha[2], Pedro Hernan Cabello[6], Ingo Riederer[1], Elisa Negroni[3], Isabelle Desguerre[5], Mariana Veras[1], Erica Yada[3], Yves Allenbach[6]

- **A successful Phase II open label study with ATL1102 in 9 adolescent non-ambulant boys with DMD has been recently completed**

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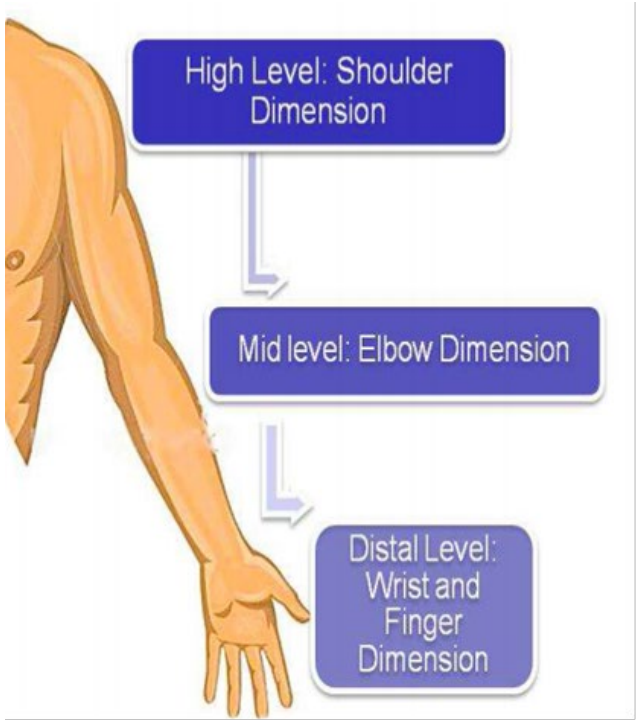
New Comparative Analysis with External Control

Objective was to compare the ATL1102 Phase II 24 week PUL2.0 mean change from baseline to a matched natural History Cohort Control

Performance of Upper Limb Module for DMD version 2.0 (PUL 2.0) is the primary endpoint for registration of treatments in non-ambulant children

Performance of Upper Limb Function PUL2.0

PUL2.0 Measures 3 Dimensions of upper limb function; the Shoulder, Elbow and Wrist-Hand



6 Items: Max score =12

9 Items: Max score =18

7 Items: Max score =14

TOTAL

PUL2.0 measures
22 main item activities important to non-ambulant patients for daily living and the Entry Item

Total PUL2.0 is generally accepted by regulators as the primary efficacy endpoint for registration of treatments in non-ambulant patients with DMD in placebo controlled studies

PUL2.0 also has 1 Entry Item: Max score = 6

Shows the Total PUL2.0 measure and the measures in the 3 dimensions and the Entry item

Methods

Rome Cohort Control Group

- Prof Mercuri, Dr Pane, and Dr Coratti, in Rome Italy maintain a natural history database of boys with DMD
- The inclusion criteria to enroll non-ambulant boys in the ATL1102 Phase II trial was used to identify 20 matched boys from their natural history database

Baseline Demographics

Rome Cohort Control Group compared to ATL1102 Phase II Participants

ROME COHORT (RC) Baseline

- 20 patients – 39 assessments at 24 weeks
- 37 assessments on steroids, 2 not on steroids
- Age at baseline Mean (SD):**15.6 (2.0)** *Range* 13-19
- Total PUL2.0 Mean (SD): **20.2(3.8)** Range (15-27)

ATL1102 COHORT Baseline

- 9 patients – 9 assessments at 24 weeks
- 8 assessments on steroids, 1 not on steroids
- Age at baseline Mean (SD):**14.9 (2.1)** *Range* 12-18
- Total PUL2.0 Mean (SD): **24.8(9.6)** Range (5-37)

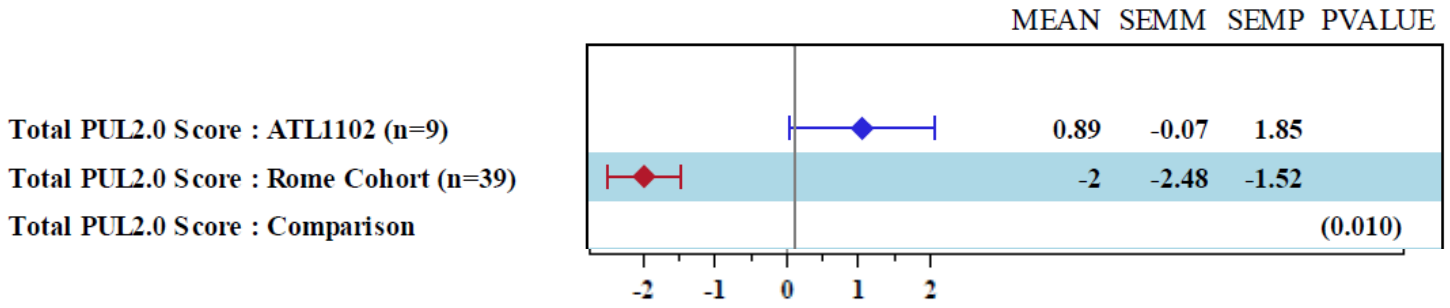
There was a similar age, high frequency of steroid use, and mean Total PUL2.0 score in the matched RC group compared to ATL1102 treated participants

Results

Rome Cohort Control Group compared to ATL1102 Phase II 24 week PUL2.0 mean changes

- ATL1102 treated patients demonstrated a statistically significant improvement in the mean (SD) scores for the 24 week treatment compared to baseline data with
  - Total PUL2.0 of +0.89 (2.89) compared to -2.00 (3.018) in the RC group (n=20, 39), (p=0.010)
- The Forest Plot below shows the results of the statistical analysis comparing the ATL1102 Phase II mean PUL2.0 data at 24 weeks from baseline compared to the RC Group

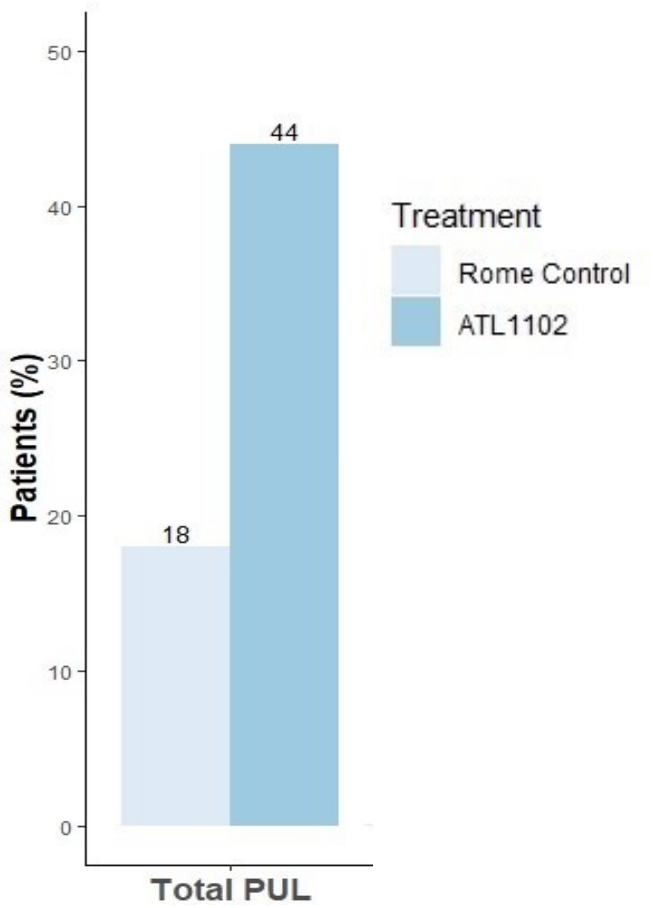
Forest Plot for the Mean Change (+/- SEM) in PUL2.0 Measures from Baseline to Month 6



Results

6 Month PUL2.0 % Patient Responders: ATL1102 Phase II data compared to the Rome Cohort Control Group

- *Results of the % patient responders in ATL1102 Phase II PUL2.0 24 week changes compared to RC*



- The Figure shows 44% (4 of 9 patients) treated with ATL1102 in the Phase II trial had an improvement in the Total PUL2.0 score at 24 weeks compared to 18% in the RC group.
- These 4 ATL1102 treated patients all had a clinically meaningful improvement in the Total PUL2.0 score of at least +2 whereas 3/39 assessments in the RC group achieved a Total PUL2.0 scores of +2 (data on file).

The frequency of ATL1102 treated patients showing improvement or no change in the total PUL2.0 score was 78% (7 of 9 patients) compared to 33% in the RC Group

Conclusions

- ATL1102 Phase II trial PUL 2.0 data when compared to the matched RC control group, shows ATL1102 treated patients with a statistically significant improvement in mean Total PUL2.0 score of muscle function and a greater frequency of patients with improvement or maintenance of their Total PUL2.0 relative to the matched RC control group.
- This external control comparative analysis shows:

  ATL1102 treated patients achieved statistically significant improvement in the mean Total PUL2.0 score of +0.89 (SD 2.89) compared to -2.00 (SD 3.018) in the matched RC control group (p=0.010) over 24 weeks.

- Such as significant gain in Total PUL2.0 in 6 months is to our knowledge yet to be reported with other drugs in non ambulant DMD, a patient group who have very limited treatment options.
- There is general acceptance for the Performance of Upper Limb Function PUL2.0 as the primary efficacy endpoint for registration studies in non-ambulant DMD patients.
- The significantly improved results of ATL1102 treatment on PUL2.0 when compared to a matched RC control group together with its positive effects on multiple additional disease progression parameters, positions ATL1102 as an exciting prospect for the treatment of DMD patients, warranting its continued development in non-ambulant patients



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