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Positive Results Achieved from Interim Analysis of ATL1103 Higher Dose Study

- IGF-I levels were reduced in all 3 patients
 - Normalisation of sIGF-I achieved in one patient
 - The other two patients experienced therapeutically relevant reductions
- No serious adverse events reported – ATL1103 was well tolerated at the doses tested
- Final results due Q4'2016
- Future clinical trials expected to test ATL1103 at doses beyond the highest dose tested

Antisense Therapeutics Limited ("ANP" or "the Company") is pleased to advise that positive results have been achieved from the interim analysis of data from its higher dose clinical trial of ATL1103 in patients with the growth hormone excess disorder, acromegaly.

The ATL1103 higher dose trial is an open-label study of the safety, tolerability, pharmacokinetics and efficacy [effect of ATL1103 on serum insulin-like growth factor I (sIGF-I) levels] in acromegaly patients. Eligible acromegaly patients who satisfied the entry criterion of sIGF-I levels more than 1.3 times the upper limit of normal were dosed with ATL1103 at 300 mg twice weekly, capped at a weekly dose of 6 mg/kg. In the previous ATL1103 trial, 200 mg twice weekly was the highest dose tested and there was no capping of the drug on a mg per kg basis (i.e. lighter body weight patients received up to 6.9mg/kg/week).

Two patients have completed 13 weeks of dosing and 2 months recovery. As the Company advised on 9 May 2016, the Principal Investigator Dr David Torpy requested that the 3rd patient continue dosing with ATL1103. After approval of a protocol amendment by the relevant ethics committee, the patient is currently being dosed in an extended dosing phase for an additional 12 weeks. An interim analysis was performed on data from all 3 patients after they had completed 13 weeks of dosing. The analysis included sIGF-I, adverse events, and laboratory test results collected to date with the results presented below confirming that the drug appears effective and safe at these higher doses tested.

Results of interim analysis

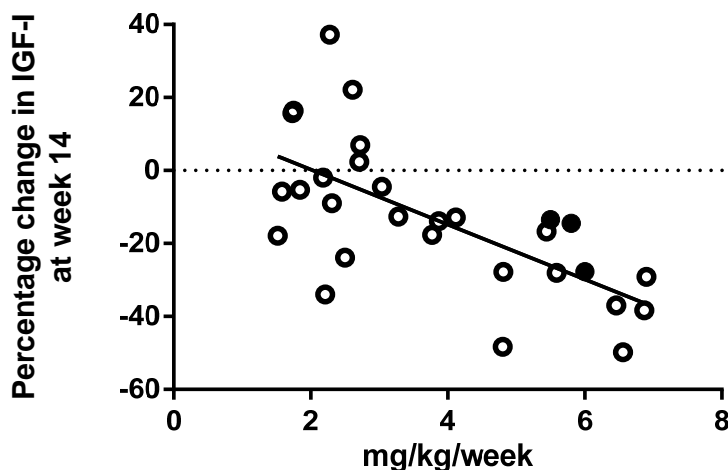
Efficacy

sIGF-I levels were reduced in all 3 patients by an average of 18.6% ($P = 0.06^*$) at week 14 (one week past the last dose which is the primary efficacy endpoint in the trial) and an average of 26.7% at week 13 being the last week of dosing ($P = 0.04^*$). Normalisation of sIGF-I was achieved in one patient who received the highest dose per kg of bodyweight (6 mg/kg). This is consistent with the previous Phase II study of ATL1103 where patients who received more drug per kg of bodyweight had greater reductions in their sIGF-I.

Reductions of sIGF-I to $< 1.3 \times \text{ULN}$ was achieved in the other two patients who had larger body weights (over 100kgs) and therefore received relatively lower doses of ATL1103 on a mg per kg basis (5.5 and 5.8 mg/kg/week) suggesting a therapeutic benefit in these 2 patients. These observations need to be qualified by the relatively small number of patients in the trial, however the statistical significance levels achieved give the Company confidence about the repeatability of the clinical findings that ATL1103 significantly reduces sIGF-I, the therapeutic goal for the treatment of acromegaly, in patients with the disease.

** As per protocol, Two-sided t-test, Ho: change from baseline = 0. Given that ATL1103 has consistently reduced sIGF-I levels in both animal and human studies, application of a one-sided t-test is justifiable, in which event the p-values for sIGF-I reductions at week 14 and week 13 would be $p=0.03$ and $p=0.02$ respectively.*

The graph below shows the percentage change in sIGF-I plotted against the dose of ATL1103 in mg/kg/week at week 14 of the study. The data is a combination of the IGF-I outcomes from the previous ATL1103 acromegaly study and the new data from the 3 patients in the current study. The new data (shown as filled in circles) is consistent with changes in sIGF-I levels seen in the previous Phase 2 acromegaly study. The data shows that higher dosing on a mg/kg/week basis produces greater sIGF-I reductions. In the previous study, dosing at ≥ 6.5 mg/kg/week achieved reductions in sIGF-I of $\sim 40\%$, with even further sIGF-I reductions predicted with longer dosing, meaning that a significant % of acromegalic patients would be expected to be successfully treated in longer term trials employing such dosing.



The percentage change in sIGF-I (from baseline levels) plotted against the dose of ATL1103. The data points from the higher dose study are shown in solid circles (doses 600 mg/week capped at 6 mg/kg/week). Data from patients dosed at 200mg and 400 mg/week in the previous acromegaly study shown as open circles. The regression slope for the dose-response correlation was calculated at -8.27 ($p = 0.0001$). The addition of the data points from the higher dose study has led to a slight change in slope for the dose response correlation to -7.52 ($P < 0.0001$).

Safety

ATL1103 appeared to be well-tolerated at the higher mg doses tested in the trial. No patient has withdrawn from the study and there have been no serious adverse events reported. To date, mild injection site reactions - ISRs (redness, bruising, swelling and itching) have been the most common adverse event reported, though these ISRs were of lesser severity and incidence when compared to the previous trial following the use of ISR mitigation strategies (e.g. icing of the injection site pre and post dosing and use of nanoneedles) recommended by Ionis Pharmaceuticals Inc. An elevated creatine kinase level has also been reported as adverse without apparent clinical sequelae.

Platelet reductions have been reported for the 3rd patient with the nadir 99,000 cells/microlitre (mild/grade 1 thrombocytopenia) at week 16. The ATL1103 dosing frequency was subsequently reduced to 300mg once weekly resulting in increased platelet counts which are reported to have since stabilised. As noted, this patient is continuing to be dosed in an extended dosing phase.

Mark Diamond, CEO of Antisense Therapeutics said; "These interim efficacy results are most encouraging and, importantly, consistent with our previous clinical trial results achieved with ATL1103. The positive safety profile demonstrated to date with ATL1103 suggests that the drug may be tolerated at doses above 600mg per week and future clinical trials would be expected to test ATL1103 at doses above this level, and potentially beyond the previous highest dose tested on a mg/kg/week basis of

6.9mg/kg/week, where even greater reductions in sIGF-I would be anticipated to potentially treat patients with larger body weights or those with more active disease”.

The 3rd patient is expected to complete the dosing extension phase at the end of the month and commence the two-month follow up period. The Company looks forward to reporting the final results of the study in Q4’2016.

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About ATL1103

ATL1103 is a second-generation antisense drug designed to block growth hormone receptor (GHR) expression thereby reducing levels of the hormone insulin-like growth factor-1 (IGF-1) in the blood and is a potential treatment for diseases associated with excessive growth hormone and IGF-1 action. These diseases include acromegaly, an abnormal growth disorder of organs, face, hands and feet, diabetic retinopathy, a common disease of the eye and a major cause of blindness, diabetic nephropathy, a common disease of the kidney and major cause of kidney failure, and some forms of cancer. Acromegalic patients have significantly higher blood IGF-1 levels than healthy individuals. Reduction of these levels to normal is accepted by clinical authorities as the primary marker of an effective drug treatment for the disease. GHR is a clinically validated target in the treatment of acromegaly. In the case of diabetic retinopathy, published clinical studies have shown that treatments producing a reduction in IGF-1 levels retarded the progression of the disease and improve vision in patients. Scientific papers have been published on the suppression of blood IGF-1 levels in mice (Tachas et al., 2006, J Endocrinol 189, 147-54) and inhibition of retinopathy in a mouse retinopathy model (Wilkinson-Berka et al., 2007, Molecular Vision 13, 1529- 38) using an antisense drug to inhibit the production of GHr. In a Phase I study in healthy subjects, ATL1103 demonstrated a preliminary indication of drug activity, including suppression of IGF-1 and the target GHR (via circulating growth hormone binding protein) levels. In a Phase II trial in acromegalic patients, ATL1103 met its primary efficacy endpoint by showing a statistically significant average reduction in sIGF-1 levels from baseline ($P < 0.0001$) at week 14 (one week past the last dose) at the twice weekly 200 mg dose tested. Antisense is currently undertaking a higher dose study in acromegaly patients (interim results reported as above).

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. ANP has 4 products in its development pipeline that it has in-licensed from Ionis Pharmaceuticals Inc., world leaders in antisense drug development and commercialisation - ATL1102 (injection) which 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 which in a Phase II clinical trial, successfully reduced blood IGF-I levels in patients with the growth disorder acromegaly, ATL1102 (inhaled) which is at the pre-clinical research stage as a potential treatment for asthma and ATL1101 a second-generation antisense drug at the pre-clinical stage being investigated as a potential treatment for cancer.