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ATL1103 Higher Dose Study

- Higher dose clinical study of ATL1103 in acromegaly patients now closed with clinical study report in preparation
- All 3 patients received a therapeutic benefit from the drug with 2 of the 3 patients achieving the goal of sIGF-I normalisation
- sIGF-I levels normalised in 3rd patient who completed an extended (26 weeks) dosing period
- ATL1103 was well tolerated at the doses tested

Antisense Therapeutics Limited ("ANP or "the Company") is pleased to advise that the higher dose clinical trial of ATL1103 in acromegaly patients is closed. The last patient's last clinic visit was on 29th September 2016. The final data is being compiled and a clinical study report is in preparation.

The higher dose study was an open-label study of the safety, tolerability, pharmacokinetics and efficacy in acromegaly patients. The primary efficacy endpoint of the trial was the reduction of serum Insulin like Growth Factor I (sIGF-I) levels in acromegaly patients as they have significantly higher levels than healthy individuals and sIGF-I normalisation is accepted by authorities as the therapeutic goal for the treatment of acromegaly.

Three patients were enrolled in the study and dosed with ATL1103 at 300 mg twice weekly (2 patients), capped at a weekly dose of 6 mg/kg (1 patient). All 3 patients were dosed for 13 weeks, with one patient at the request of the Principal Investigator receiving an extended dosing period of an additional 12 weeks. There was a follow-up period of 2 months for all patients.

Positive results of an interim analysis of the data from the study were reported by the Company on 27th July 2016. At that time two patients had completed the study and one patient was still being dosed in the extended dosing period. The interim analysis confirmed that the drug appeared effective and safe at the doses tested with normalisation of IGF-I in one patient and therapeutically relevant reductions in two patients.

Now that the 3rd patient has completed the study the Company can confirm that the patient's IGF-I level was normalised during the extended dosing period. Maximal suppression of IGF-I in that patient was 44% from baseline at week 26 (vs 33% at week 13). This is higher than the mean reduction reported in the interim analysis (26.7% at week 13 and 18.6% at week 14) and is consistent with ATL1103 dose modelling predictions that greater effects are achievable with longer ATL1103 dosing regimens.

As reported previously, the dosing frequency was reduced in this patient to 300 mg once weekly during the extending dosing due to mild/grade 1 thrombocytopenia (low platelet counts). Platelet counts stabilised at this reduced dosing frequency, and returned to normal levels during the follow-up period. As reported above, IGF-I levels normalised during the extended dosing period despite this reduction in dosing frequency.

There were no new significant adverse safety findings beyond those reported on 27 July 2016. ATL1103 appeared to be well-tolerated at the higher mg doses tested in the trial. No patient withdrew from the study and there have been no serious adverse events reported.

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Mark Diamond, CEO of Antisense Therapeutics said; "While it was a small study, it is most pleasing to report on the very encouraging efficacy and safety profile of ATL1103 demonstrated in this higher dose trial. All 3 patients received a therapeutic benefit from the drug and 2 of the 3 patients achieved the goal of sIGF-I normalisation including the patient administered with ATL1103 for an extended dosing period of 6 months whose disease had not been controlled on their prior acromegaly medications. The clinical experience gained from this trial will be important in the continued development and commercialisation of ATL1103 for acromegaly".

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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 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.