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ATL1102 for Stem Cell Mobilisation Trial Commencement

Antisense Therapeutics (ASX:ANP) is pleased to advise that it has commenced dosing in its Phase I Stem Cell Mobilisation (SCM) Human Proof of Concept trial of ATL1102, the Company's second generation antisense drug targeting the VLA-4 receptor. The trial will assess the safety, tolerability and effect of ATL1102 on the release of hematopoietic stem cells (CD34+) into the blood when dosed alone and in combination with an existing therapy (Granulocyte Colony Stimulating Factor (G-CSF)). The randomised, open label study of ATL1102 dosed over 5 days (given on day 1, 3 and 5) in 10 healthy volunteers is being conducted by leading Clinical Research Organisation, Nucleus Network at its clinical trial unit at the Alfred Hospital, Melbourne, Victoria. (The Study "Protocol Synopsis" following this announcement provides further information).

With the necessary screening, dosing and follow up of patients, ANP anticipates that results from the trial will be reported mid 2014.

The mobilisation (release) of these stem cells from the bone marrow into the blood is part of an important medical procedure used to improve outcomes for patients undergoing chemotherapy to treat certain cancers. The stem cells released into the blood are then collected and stored before high dose chemotherapy and then re-infused to replace those lost during chemotherapy in order to re-establish the immune system. The basis for using ATL1102 in the SCM indication is related to the role of VLA-4 in regulating the release of CD34+ stem cells from the bone marrow, with another drug that also targets VLA-4 having been shown to increase CD34+ stem cell release in humans. In a previous study in Multiple Sclerosis patients, ATL1102 demonstrated similar activity to that drug by increasing CD34+ levels in the blood.

Dr Jason Lickliter, Medical Director of Nucleus Network and Principal Investigator for the trial said "This human Phase I trial of ATL1102 is designed to evaluate whether ATL1102 can improve mobilization of CD34+ stem cells when used in combination with standard mobilisation therapy to levels that would make it clinically beneficial for use in the collection of stem cells for transplantation. There is an acknowledged clinical need for increasing mobilisation levels beyond those achieved by the current therapeutic approach, and so I am very pleased to be working with Antisense Therapeutics to assess the merits of ATL1102 in this important clinical setting."

Antisense Therapeutics Limited CEO and Managing Director Mark Diamond said "The stem cell mobilisation opportunity for ATL1102 while commercially attractive with, by our estimation, a market potential of several hundred million dollars per annum, also presents as an excellent return on investment proposition given costs are expected to be relatively low for developing the drug in this indication. We believe that positive outcomes from this trial will strongly enhance our drug's potential for this application and naturally we relish the opportunity to further develop a drug that can potentially provide better outcomes for cancer patients. We look forward to successfully conducting the study and to reporting results from this SCM trial which are anticipated mid-year."

Protocol Synopsis

Title	A Phase I, Randomised, Open Label Study to Assess the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Subcutaneous Doses of ATL1102 Alone and in Combination with G-CSF in Healthy Volunteers
Study Number	1102SCM-CT01
Study Design	Single-centre, open-label, randomised, parallel group study
Objectives	• To assess the safety and tolerability of subcutaneous doses of ATL1102 alone, and in combination with G-CSF in healthy volunteers • To assess the pharmacodynamics of ATL1102 alone, and in combination with G-CSF in healthy volunteers • To assess the pharmacokinetics of ATL1102 alone, and in combination with G-CSF in healthy volunteers
Endpoints	• Safety and tolerability of ATL1102 in combination with G-CSF • Pharmacokinetic profiles of ATL1102 • Pharmacodynamic measures including release of CD34+ haematopoietic stem cells and progenitor cells
Number of patients	It is planned that 10 patients will be randomised to one of 3 dosing groups for the study.
Key Patient Criteria	Healthy male volunteers between the ages of 18 and 50 years of age. BMI between 19 and 32 kg/m^2
Dosing	ATL1102 and G-CSF will be delivered as subcutaneous (s.c.) injections according to the following schedule: • Group A (n = 3) will receive Granulocyte-Colony Stimulating Factor (G-CSF; 10µg/kg/day) via s.c. administration on days 1, 2, 3, 4 and 5 • Group B (n = 3) will receive ATL1102 (400 mg/day) via via s.c. administration on days 1, 3 and 5 • Group C (n = 4) will receive G-CSF (10µg/kg/day) on days 1, 2, 3, 4 and 5 and ATL1102 (400 mg/day) on days 1, 3 and 5.
Per Patient Duration	Up to 28 days screening, one week dosing, one week follow up
Trial Location	Nucleus Network, Melbourne, VIC.
Principal Investigator	Dr Jason Lickiter
Trial Standard	GCP

About Stem Cell Mobilisation in Cancer treatment: stem cell mobilization and transplantation is a medical procedure used to improve clinical outcomes for patients undergoing chemotherapy to treat cancer. Some chemotherapy has toxic effects on bone marrow, so hematopoietic stem cells are collected from the blood of the patient – or from a donor's blood – before the patient receives chemotherapy. These collected stem cells are then stored and given back later to replace those lost during chemotherapy (engraftment). There are normally only a small number of stem cells in the blood, so stem cell mobilization agents are used to increase this number before stem cell collection from a donor or more typically from a patient. Granulocyte colony-stimulating factor (G-CSF) is the main agent used for hematopoietic stem cell mobilization. While G-CSF is successful in mobilizing hematopoietic stem cells, there is often the need for additional complimentary mobilizing therapies. The major product used in combination with G-CSF is Mozobil® however there is an opportunity to improve on the level of stem cell release achieved with G-CSF alone or in combination with Mozobil. At least 2 million CD34+ cells per kg are required for durable reconstitution of the immune system, however greater than 5 million CD34+ cells per kg, sourced in one or more collections, lead to improved engraftment and patient outcomes.

ATL1102 is a second generation antisense inhibitor of CD49d, a subunit of VLA-4 (Very Late Antigen-4). In inflammation, white blood cells (leukocytes) move out of the bloodstream into the inflamed tissue, for example, the Central Nervous System (CNS) in MS, and the lung airways in asthma. The inhibition of VLA-4 may prevent white blood cells from entering sites of inflammation, thereby slowing progression of the disease. VLA-4 is a clinically validated target in the treatment of MS. Antisense inhibition of VLA-4 has demonstrated positive effects in a number of animal models of inflammatory disease including MS with the MS animal data having been published in a peer reviewed scientific journal. ATL1102 was previously shown by Antisense Therapeutics to be highly effective in reducing MS lesions in a Phase IIa clinical trial in MS patients. The company has also lodged an International patent application on ATL1102 based on preliminary data in mice and humans supporting its' potential application as a stem cell mobilization agent for use in combination with G-CSF to improve the level of stem cell release achieved with G-CSF alone.

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 Isis 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 multiple sclerosis (MS), ATL1103 a second-generation antisense drug designed to block GHr production and thereby lower blood IGF-I levels and is in clinical development as a potential treatment for growth and other GH-IGF-I disorders, 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.

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