ANTISENSE THERAPEUTICS

12 March 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Antisense Therapeutics Limited: Investor Update – March 2004

Please find attached Antisense Therapeutics Limited's Investor Update.

Yours sincerely

Mark Diamond
Managing Director

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INVESTOR update

ANTISENSE THERAPEUTICS

March 2004

Dear Shareholder

Welcome to another update on the progress of Antisense Therapeutics' key development projects.

We are pleased to provide this update summarising several recent positive developments.

In summary, our lead projects continue to maintain momentum and are progressing to plan, while I am also very excited about our recent decision to move forward with a new compound.

We appreciate your continued support, and I look forward to bringing you further good news in the future.

Regards

Mark Diamond
Chief Executive Officer

1. Recent Highlights

- ATL1102 for MS - Phase I human clinical trials commenced in August 2003 and have progressed rapidly with both single and multiple dosing schedules now complete. There are favourable preliminary indications from the data that have been collected and analysed.

- ATL1101 for Psoriasis - The manufacture of the active pharmaceutical ingredient for the Psoriasis 'proof-of-concept' study is now complete. The precursory animal toxicology studies are scheduled to commence in mid-2004 following successful formulation.

- ATL1103 for Growth Hormone disorders – The Company announced that it is developing a new compound designed to block Growth Hormone receptor (GHr) expression. Successful testing undertaken in mice indicates it has potential as a treatment for growth and sight disorders.

- The early filing with the US Food and Drug Administration (FDA) by US biotech company BioGen Idec and its partner Elan of a marketing application for their MS antibody drug Antegren™ provides Antisense Therapeutics with greater confidence in the likely success of ATL1102. Both Antegren and ATL1102 target the VLA-4 protein, which is considered to be involved in the progression of MS.

- The company released its half-yearly financial results for the six-month period to 31 December 2003, reporting a loss of $1,626,940 (2002: $3,882,283). Cash reserves currently stand at $15 million following successful capital raisings during the period.

2. Project Review

ATL1102 for Multiple Sclerosis

ATL1102 is designed to block the synthesis of an immune system component or protein called VLA-4 that is known to play a part in both the onset and progression of multiple sclerosis ('MS').

In August 2003, Antisense Therapeutics commenced Phase I human clinical trials of ATL1102 at the Charterhouse Clinical Research Unit in London.

The aims of these Phase I trials are to obtain information on the pharmacokinetic[1] behaviour of ATL1102 in humans and to assess the safety and tolerability of increasing dose levels of ATL1102 injected as single and multiple doses. Fifty-four healthy volunteers have participated in the placebo-controlled, randomised, double-blind study.

The study has progressed rapidly, having completed both single and multiple dosing schedules.

Laboratory investigations of the biological samples collected during the trial are currently taking place.

Some preliminary data from these clinical trials were presented at the Australian Neuroscience Society Scientific Conference in Melbourne on 30 January 2004. As reported by the Company at this time, preliminary indications from the data collected and analysed so far are favourable in terms of both safety and pharmacokinetics.

Full and final results are expected to be reported mid year.

At present, study designs for the Phase IIa clinical trial are being discussed with potential clinical trialists and contract organisations.

Once final reports are received for the Phase I trial and the results are assessed as satisfactory, the Company will make an application for the Phase IIa patient trial.

Regulatory agency approval and commencement of the Phase IIa trial are targeted for the second half of 2004.

ATL1101 for Psoriasis

ATL1101 is designed to block the synthesis of the IGF-1 receptor, a protein involved in the regulation of cell growth in psoriasis. The psoriasis project is supported by a Commonwealth Government R&D Start grant of AUD1.1 million.

In July 2003, the company announced its plans to undertake a 'proof of concept' study, which will accelerate the testing of ATL1101 in humans suffering from psoriasis. In this study - also referred to as the small plaque assay (SPA) - a relatively small quantity of ATL1101 will be applied to areas of psoriatic skin on a limited number of patients. The SPA is designed to carefully monitor and also restrict the extent of patients' exposure to the test compound.

This human study is to commence once supplies of drug product are manufactured and the required precursory animal toxicology program is performed. The manufacture of the active

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[1] "Pharmacokinetics" is how the drug distributes in the body over time after administration, helpful in deciding dosing frequency in future studies.

pharmaceutical ingredient and the analytical work has been completed and the formulation of injectable and cream presentations of ATL1101 is currently underway.

Looking forward, the animal toxicology studies for ATL1101 are scheduled to commence in mid-2004, following completion of the formulation activities. Subject to receiving the relevant approvals to conduct the study, the human 'proof of concept' study is expected to begin in the second half of 2004.

ATL1103 for Growth and Sight disorders

Following successful animal testing, Antisense Therapeutics is moving forward on a new compound codenamed ATL1103. ATL1103 is an antisense inhibitor designed to block Growth Hormone receptor (GHr) expression.

The results from animal testing confirm its potential as a treatment for diseases associated with excessive growth hormone action.

These include acromegaly (abnormal growth of organs, face, hands and feet) and two other diseases known to be major causes of blindness - diabetic retinopthy and wet age-related macular degeneration (AMD).

ATL1103 was tested on mice at the University of Queensland by Professor Michael Waters, who is internationally recognised for his research on GHr and associated disorders. The study results are comparable to those achieved by pegvisomant - the latest drug to be approved in Europe and the US for the treatment of acromegaly - in an equivalent animal model.

The animal study results for ATL1103 are being presented by Antisense Therapeutics to an International GH-IGF Symposium in Cairns on 20 April 2004.

ATL1103 may have important clinical advantages over octreotide - which is the most widely used treatment for acromegaly - and pegvisomant, including more convenient route of administration and less frequent dosing.

Sales of the newer drug, pegvisomant, are projected to reach US$500 million per annum, which indicates both the size of the market and the potential for ATL1103.

There are no pharmaceutical therapeutics approved for the treatment of diabetic retinopathy. There are also no standard and effective therapies for most AMD patients.

The market potential for effective medicines to treat these diseases is estimated at several billion dollars.

Further details regarding ATL1103 and sight and growth disorders is contained in the 24 February 2004 ASX announcement enclosed with this investor update.

3. Market Developments

An endorsement for Antisense Therapeutics' MS compound

US Biotech company BioGen Idec and its partner Elan announced that they are planning to file their Multiple Sclerosis drug, Antegren™, with the US Food and Drug Administration (FDA).

This announcement follows the completion by Biogen/Elan of the first year of their two-year Phase III studies of Antegren™ in MS patients. Whilst the results have not been released, early

discussions with the FDA have been interpreted by commentators as a positive indication of the likelihood of success of the drug in the clinic.

Both BioGen Idec (market cap: US$19 billion) and Elan (market cap: €5 billion) have enjoyed significant increases in their respective share prices on the release of their news (Biogen's share price has increased by 33 per cent and Elan's by 89 per cent to 4 March 2004).

So, how does this impact on Antisense Therapeutics and, more particularly, the development of its own MS drug, ATL1102?

Both Antegren™ and Antisense Therapeutics' MS compound ATL1102 block the VLA-4 protein, which is considered to be responsible for the progression of MS (refer 17 June 2002 Investor Update 'The Rationale for VLA-4 as a Target Treatment for MS' which can be found at www.antisense.com.au).

ATL1102 is a second generation antisense drug designed to act at an earlier stage of the disease process by preventing excessive amounts of VLA-4 being produced.

With its highly specific mechanism of action and well tolerated drug chemistry, ATL1102 may potentially provide important advantages over Antegren™ in the cost of therapy and method of delivery, as well as improved effectiveness.

The recent Antegren™ news provides Antisense Therapeutics with greater confidence in the likely success of ATL1102. Also, the submission of the Antegren™ application to the FDA will establish a path to regulatory approval for ATL1102 and commercially and scientifically validate the Company's MS drug development strategy.

4. Financial Information

Antisense Therapeutics recently announced its financial results for the six-month period to 31 December 2003.

For the half-year, Antisense recorded a loss of $1,626,940 (2002: $3,882,283), which included an income tax benefit of $371,820 (2002: $nil) and the expensing of all research and development costs incurred.

There were a number of major reasons why the loss was less than what was recorded in the same period in 2002. Among them was the receipt of an R&D Start Grant for the ATL1101 psoriasis project ($638,700) and a cash rebate received in relation to the Research and Development Tax Concession ($371,820).

The Company also had less research and development costs this half-year, with the majority of the costs of the manufacturing, development and formulation of ATL1102 having been incurred in 2002.

Also during this six-month period to 31 December 2003, the company raised $10.4 million through the issue of new shares. Of this amount, $5 million was raised through a private placement to Australian institutions and professional investors and a further $5.4 million was raised pursuant to the company's Share Purchase Plan.

Cash Reserves now stand at $15 million.

ANTISENSE THERAPEUTICS

For release: 24 February 2004

Successful Animal Study Results Demonstrate Potential New Treatment for Growth and Sight Disorders

Highlights

- Demonstration of efficacy in pre-clinical animal studies of new antisense compound
- Results to be presented at International Scientific Symposium
- Outcomes comparable to leading therapeutics
- Major disease applications including acromegaly and diabetic retinopathy
- Patent applications lodged
- Development to commence on new compound (ATL1103)

Results of Animal Studies

Antisense Therapeutics Limited is pleased to announce that an antisense inhibitor designed to block the Growth Hormone receptor (GHr) gene has produced definitive results in an experimental system in mice. This confirms its potential as a treatment for diseases associated with excessive growth hormone action. These diseases include acromegaly (an abnormal growth disorder of organs, face, hands and feet), diabetic retinopathy and wet age-related macular degeneration (AMD). The latter disorders are common diseases of the eye and major causes of blindness.

The targeting of GHr with our proprietary antisense compound inhibits growth hormone activity, thereby reducing levels of the hormone insulin-like growth factor-1 (IGF-I) in the blood. Acromegalic patients are known to 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. 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 in patients.

Antisense Therapeutics' animal studies for the GHr antisense compound were conducted at the University of Queensland by Professor Michael Waters, internationally recognised for his research on GHr and disorders related thereto. These studies demonstrated that the compound significantly reduces blood levels of IGF-1 in mice, an effect which, if reproduced in humans, should provide therapeutic benefit to acromegaly patients and potentially to diabetic retinopathy sufferers.

The animal study results are to be presented by Dr George Tachas, Antisense Therapeutics' Director of Drug Discovery, at the International GH-IGF Symposium, Cairns, Queensland on April 19, 2004.

Growth and Sight Disorders – Markets, Current Treatments
The most widely used pharmaceutical treatment for acromegaly is the drug octreotide (Sandostatin™), however a significant percentage of patients do not respond to this therapy while other patients experience adverse reactions with this therapy. The latest drug to be approved in Europe and the US for the treatment of acromegaly is pegvisomant (Trovert™, Somavert™). Pegvisomant is effective in a larger percentage of patients than octreotide although it requires more frequent (daily) dosing by injection than the long acting form of octreotide which is surgically implanted (intragluteal). Sales of pegvisomant are projected to reach US$500M per annum.

The study results for our GHr antisense compound are comparable to those achieved by pegvisomant in an equivalent animal model. Our GHr antisense compound may have important clinical advantages over pegvisomant and octreotide, including more convenient route of administration and less frequent dosing.

There are presently no pharmaceutical therapeutics approved for the treatment of diabetic retinopathy. There are also no standard and effective therapies for most AMD patients. Given the high unmet medical need for such diseases the market potential for effective medicines is estimated to be several billion dollars.

Patent applications have been lodged covering all disease indications for GHr antisense.

Outlook
Following the success of the animal efficacy studies and in light of the significant commercial potential of the compound, the company has decided to move this project, named ATL1103, into development. Orders for bulk quantities of the active pharmaceutical ingredient, to be formulated into injectable product for use in the preclinical safety studies, are expected to be placed with our collaboration partner Isis Pharmaceuticals, Inc, within the first half of 2004.

This result from our drug research pipeline confirms Antisense Therapeutics' ability to use the most advanced second generation antisense technology to quickly and inexpensively generate and test new antisense compounds for clinically validated targets in important human diseases.

About Acromegaly
Acromegaly is a serious chronic life shortening disease triggered by excess secretion of growth hormone (GH) by benign pituitary tumours. Oversupply of GH overstimulates liver, fat and kidney cells, through their GH receptors, to produce excess levels of Insulin-Like Growth Factor-I (IGF-I) in the blood manifesting in abnormal growth of the face, hands and feet, and enlargement of body organs including liver, kidney and heart. The primary treatments for acromegaly are to surgically remove the pituitary gland and/or drug therapy to normalize GH and serum IGF- I levels. In North America, Europe and Japan there are approximately 40,000 diagnosed acromegaly patients with about half requiring drug therapy. Drug treatment costs vary depending on dosage and frequency of administration ranging from A$14,000-$33,000 per patient per year

About Diabetic Retinopathy and Age Related Macular Degeneration (AMD)
Diabetic retinopathy and wet age-related macular degeneration (AMD) are two of the leading causes of vision loss. Over 5 million Americans aged 18 and older are affected by diabetic retinopathy. Around 12,000-24,000 patients with diabetic retinopathy lose their eyesight

each year in the US alone. These conditions are caused by new blood vessel formation in the retina or macula (the central part of the retina). In diabetes, high blood glucose can cause oxygen deprivation, which can stimulate factors that induce additional blood vessels in the retina. In AMD similar factors are thought to stimulate blood vessel production in the macula. These new blood vessels may break and bleed into the eye leading to scarring within the eye. Whilst there are drugs to control diabetes, patients with Type I diabetes who have had their disease for more than 10 years have a 90% chance of developing retinopathy, and about 20% of patients with Type II diabetes will get the disease. Surgical ablative treatments such as photocoagulation (laser therapy) are available but are not completely effective, may cause partial vision loss, and can only be used a limited number of times.

About Antisense Therapeutics Limited

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

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