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## **CEO INTERVIEW WITH AEGIS EQUITIES RESEARCH**

Antisense Therapeutics Limited is pleased to release the attached transcript of an interview given by Chief Executive Officer, Mr Mark Diamond, to John Kessell, Healthcare Analyst, Aegis Equities Research.

### ***About Antisense Therapeutics Limited***

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. Its mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets.

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## Antisense Therapeutics Limited

Sector: Health Care

The following is a transcript of an interview conducted by John Kessell, Healthcare Analyst at Aegis. For more on Antisense Therapeutics (ANP) see our Blue Book series at [www.aer.com.au](http://www.aer.com.au) or go to the ANP website at [www.antisense.com.au](http://www.antisense.com.au)



John Kessell – Healthcare Analyst

The company, Antisense Therapeutics, is based on antisense compounds licensed from US strategic partner, ISIS. What exactly are antisense drugs, and why does the company believe that this class of drugs has promise?

ANP CEO – Mark Diamond

Antisense technology is an innovative way of making highly targeted and thereby, highly effective medicines. Antisense drugs differ from most conventional medicines in their mechanism of action. Conventional drugs work by binding directly with disease-causing proteins to block or inhibit their action. Antisense drugs work a step earlier by blocking the production of the disease-causing protein in the first instance.

As their mechanism of action is very specific for the disease target, antisense drugs generally are perceived to be more targeted in treating a disease than their conventional drug counterparts. That's one of the primary reasons that Antisense Therapeutics is excited by this technology.

There are now 20 antisense drugs in clinical development, at least half of which are in late stage development, and so it is an area where there's a significant amount of innovation. ISIS, who are a world leader in the field of antisense technology, has 17 drugs in development, either in its own pipeline or with partners.

The technology has been under development for a number of years, and, as such, it has been through various iterations or improvements, from first to second generation

antisense technology. These improvements have resulted in compounds that are both safe and highly effective. The improvements that have come with the second generation antisense technology have widened the application of these drugs to a broad group of diseases, including, of course, multiple sclerosis (MS), which we are very interested in.

The drugs have the same basic chemical structure or backbone, as we describe it, and therefore have very similar pharmacokinetic and safety profiles, which means that when we're looking at the progress of the second generation antisense drugs through the clinic, we get a very good impression of how our compound is likely to perform in later stage clinical trials.

So, this is a very mature technology, where not only have we been able to establish the safety and activity of these compounds but we also know how to manufacture these drugs and administer them effectively to patients. Thus, owing to its maturity, the technology has a much lower risk profile than that of other technologies that haven't advanced as far in the clinic.

The second generation antisense drugs are more stable, potent and less toxic. These drugs are being applied in a broad range of diseases. ISIS has, as its most advanced second generation antisense drug, a drug that it's developing for the treatment of high cholesterol. This agent has shown remarkable activity in clinical studies to date. Over three months of treatment, this drug has shown to be performing as good as, if not better than, any other current agent available for treating high cholesterol.



Also, this drug has shown to be well tolerated. Importantly, the doses that ISIS has used in this particular clinical study are similar to what we're using in our Phase II clinical trial, which gives us a great deal of confidence about the safety profile of our drug. ISIS has successfully completed one-year safety studies on this cholesterol-lowering agent and is due to commence registration studies this year, which are directed at getting the compound approved.

Hence, the technology has advanced a long way. There have been very critical improvements made to this technology. So, from our perspective, the technology is living up to its promise of delivering drugs that are very effective in treating human diseases.

John Kessell – Healthcare Analyst

ATL1102 is currently in Phase IIa trials for multiple sclerosis. This drug targets the same receptor as Biogen Idec and Elan's antibody drug, Tysabri. Tysabri was taken off the markets for just over 12 months due to concerns about rare reports of the drug being associated with a fatal neurological condition, PML.

Tysabri was allowed back on the market by the FDA in July 2006, but what does Tysabri's association with PML mean for Antisense's drug, ATL1102, given that they share the same receptor?

ANP CEO – Mark Diamond

When the news broke that Tysabri had been withdrawn from the market because of its association with the fatal neurological condition, PML, Antisense Therapeutics decided to halt its clinical study underway in Europe to assess whether the safety issue associated with Tysabri was in any way relevant to our development plans and if there were any implications for the development of ATL1102.

The company went through an exhaustive assessment process with a group of leading MS experts. We brought together a medical advisory board of key opinion leaders in the field of MS and it was this board's opinion that

Antisense Therapeutics should continue with the development of ATL1102, as it felt the drug had very exciting prospects for the treatment of MS.

These experts also understood that while ATL1102 shared the same biological target as Tysabri in VLA4, the drugs had different mechanisms, with ATL1102 being an antisense drug and Tysabri being a monoclonal antibody. The medical advisory board believes this difference may be germane to the safety issue that had been observed with Tysabri.

The medical advisory board was also aware that PML observed in the clinical trials of Tysabri occurred when the drug was used in combination with Interferon or in an immuno-compromised setting. As we did not intend to use ATL1102 in either of these settings, the board perceived the risk of observing PML safety issues in our clinical trial to be very low.

Hence, we've continued with the development of ATL1102. We've been advised by our Medical Advisory Board to incorporate into our study a process for monitoring the PML safety issue. PML is caused by a virus, the JC virus. In our study, we're able to monitor the activation of this particular virus. Importantly, to date in our study, we've seen nothing that would suggest that our drug is having any impact on the JC virus state of these patients.

We believe, however, that it's very important to focus on the positive attributes of Tysabri, which is that targeting VLA4, as Tysabri does, has led to the development of the most efficacious drug for treating patients with relapsing-remitting MS to date.

Tysabri is significantly more effective than anything that's either on the market or in development for treating MS. So, it's a very exciting target, and we are in a unique position by being able to work on this particular target. We have the ability to avoid or circumvent patents that prevent others from targeting VLA4 in MS.



We know that VLA4, or targeting VLA4, is likely to have a role in other disease indications such as rheumatoid arthritis, asthma and inflammatory bowel disease. We have a unique position in that we know that we do not infringe on relevant intellectual property and we're very excited by the prospect of having a drug that's not only as efficacious as Tysabri but also potentially safer. Thus, we believe we have the prospect of a blockbuster drug.

John Kessell – Healthcare Analyst

Tysabri's global sales have grown rapidly since its reintroduction in July 2006 to reach US\$48M in the first quarter of calendar year 2007. What sort of annual sales do you see as being achievable for Tysabri and how does this relate to ATL1102's market potential?

ANP CEO – Mark Diamond

Market analysts have been predicting the blockbuster potential of Tysabri for some time now and I can say that Biogen Idec has also recognised that this drug has the potential to out sell the company's other drug that it markets for the treatment of MS, Avonex, which has sales in excess of a billion dollars.

The current market for MS drugs is US\$5B. There are four drugs on market, each selling for more than a billion dollars. Biogen has estimated that the market will grow to US\$11B by 2016. A significant portion of this growth will come through the growth of Tysabri sales in the market. Biogen Idec have identified that there are potentially around 300,000 patients in whom the current therapy is not meeting their clinical needs.

At an annualised cost of treatment of US\$20,000- US\$30,000 a year, a drug would only need to take 10% of that particular potential market to have sales in excess of a billion dollars. So the market opportunities are very significant for Tysabri, and this would apply to our drug as well, which has the same biological target as that of Tysabri. So we would see ourselves having the same-sized market opportunity for our drug but with important advantages over Tysabri, including being cheaper, easier dose and, possibly, safer.

John Kessell – Healthcare Analyst

Turning to the Phase IIa trial for ATL1102, what are the objectives of this trial?

ANP CEO – Mark Diamond

The Phase IIa trial is being conducted to confirm both the activity and the safety of ATL1102 in the treatment of patients with relapsing-remitting MS. The primary objective of this study is to show a reduction in MS lesions in the brain of these patients. This is assessed via magnetic resonance imaging, which is a recognised clinical end-point for the treatment of MS.

Our study is an 80-patient placebo-controlled, double blind, randomised trial. This is a high standard of running an MS trial and was confirmed by the experts on our medical advisory board, who had reviewed the trial design for our study. So, our objective is to complete a high-quality study with outcomes that will attract a quality partner to continue the development of ATL1102.

John Kessell – Healthcare Analyst

Dosing of patients in the current Phase IIa trial for ATL1102 was initiated in June 2006. But as of this month, only 20 patients have been dosed. The company has recently added a number of new trial sites across Central and Eastern Europe to accelerate enrolments.

Why has the trial taken longer than expected to enrol patients and what is the basis for your confidence that the trial results will be reported by the end of calendar year 2007?

ANP CEO – Mark Diamond

We encountered challenges in Germany in enrolling patients into the study. Unfortunately, we were not able to meet our expectations in terms of enrolment from the German sites. However, we responded promptly by expanding our trial into Eastern Europe. In January of this year, we received approval to begin dosing patients from three Central and Eastern European countries. The delay was in the time that it took us to get approval from the



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regulatory authorities in these countries to start the study there.

So the 20 patients that have been dosed, as per our last announcement, have essentially been in the period since we received approval to start dosing patients in Central and Eastern Europe. We're expecting to have seven countries involved in this particular trial, with approvals in Russia and Poland expected shortly. It's with the addition of these countries that we are now confident of being able to report our results by the end of the year.

John Kessell – Healthcare Analyst

Assuming future trials all go well, could you map out for us the expected timeline for ATL1102 until commercialisation? When is the best-case scenario for ATL1102 to be launched on the market and how many years of patent protection would this leave it with?

ANP CEO – Mark Diamond

We are looking to find a partner for our drug at the end of the Phase II clinical studies. So, the commercialisation timeline really starts from the end of the year where we'd be expecting to receive significant licensing income from the out-licensing of ATL1102.

Our patent protection on this compound is broad and we are also fortunate to have patents in place in both the US and Europe until 2023. So we've a long patent life on this compound and certainly sufficient patent protection to interest a partner to continue the development of this drug.

John Kessell – Healthcare Analyst

Is Antisense's licence for ATL1102 from ISIS dependent on the company meeting specific milestones within certain time periods or does Antisense have complete security over this licence through the commercialisation of the drug?

ANP CEO – Mark Diamond

Yes, we do have performance milestone obligations in our agreement with ISIS. To date, we have met all of the relevant milestones associated with the development of ATL1102 and that has been confirmed by ISIS. So, we will continue to keep our licences as long as we meet those ongoing performance requirements.

John Kessell – Healthcare Analyst

Antisense also has an early stage drug, ATL1103, which is being developed for use in the growth disorder, acromegaly, as well as for diabetic retinopathy, a common cause of blindness. You are now moving this drug into pre-clinical development. When do you expect ATL1103 to start its first human clinical trial?

ANP CEO – Mark Diamond

We are looking to manufacture the drug to start toxicology studies in the second half of this year. Therefore, we would anticipate commencing a clinical trial of ATL1103 in late 2008. ATL1103 has shown significant results in animal studies to date. We're not only impressed by the quality of the animal data that we've generated on ATL1103 but we also believe that the compound is very exciting because we have a clinical end-point in the reduction of serum IGF1, which we can easily measure in early clinical studies which significantly reduces the risk going into these studies.

We're looking at moving forward initially in the niche indication acromegaly and we anticipate that we will be able to take the orphan drug approval route, where we'd be looking at not only an accelerated approval but expect to have studies that would require a smaller number of patients, thereby reducing development costs.

So, we think it is a very affordable program for Antisense Therapeutics and we are excited by the prospects of being able to move rapidly through development and into the market with this drug.



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John Kessell – Healthcare Analyst

The company had around \$8.5M in cash at the end of March 2007. This is expected to last around 12 months, by which time the results of the Phase IIa trial for ATL1102 are expected to be published.

When would the optimal time to raise the next lot of cash be, how much is the next capital raising likely to be for and how long would you want these funds to last for?

ANP CEO – Mark Diamond

The company currently has sufficient cash to fund the completion of its Phase II clinical trial. Also, as I said earlier, we are looking at the potential partnering for ATL1102 at the completion of the Phase II trials. Thus, we'll continue to assess our cash requirements on an ongoing basis in the light of the possible partnering opportunities for ATL1102.

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*END OF INTERVIEW*

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