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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Antisense Therapeutics

By TIM BOREHAM

ASX code: ANP

Share price: 2.5 cents

Shares on issue: 371,586,638

Market cap: $9.3 million

Chief executive officer: Mark Diamond

Board: Robert Moses (chairman), Prof Graham Mitchell, Dr William Goolsbee, Dr Gary Pace, Mark Diamond

Financials (March quarter): revenue nil, cash burn $392,000, cash $562,000*****, estimated current quarter cash outflows $550,000

***** A rights issue and placement in April raised $5 million.

Identifiable holders: Australian Ethical 19.3%, Platinum Asset Management 5.7%, Opthea Ltd 2.77%, Bin Liu 2.72%, Glen Bull 2.3%, CVC Ltd 2.27%, Citicastle Pty Ltd 2.22%

Having spun-out from Circadian Technologies in 2001, Antisense rates as one of the oldest listed biotechs that have stuck to its original purpose (in this case, novel gene-silencing therapies).

Unusually, Mark Diamond has been CEO for all that time and he vies with Bionomics' Deborah Rathjen and Compumedics' Dr David Burton as the sector's longest serving biotech helmsperson.

Another oddity of Antisense is that as far as we're aware it's the only biotech headquartered in the leafy Melbourne suburb of Toorak. (Opthea, formerly Circadian, moved all the way to South Yarra a few years ago.)

But longevity and a toffy address aren't the reasons why institutional investors have taken a shine to Antisense. Rather, it's the company's focus on Duchenne muscular dystrophy (DMD), a genetic degenerative muscular condition that affects only boys.

DMD has similar disease features to multiple sclerosis (MS), which was the company's initial focus and still hopes to pursue. Antisense is also seeking a treatment for acromegaly, a growth disorder that causes the enlargement of hands, face and feet usually caused by a non-cancerous tumor.

Cashed up

After a $5 million capital raising, Antisense is all cashed up with somewhere to go with its RNA-targeted therapeutics. RNA refers to ribonucleic acid, which is present in all cells and carries instructions from DNA to control the development of proteins. (DNA stands for deoxyribonucleic acid, but I'm sure we all knew that.)

The Antisense program is based on two molecules, ATL1102 and ATL1103 - licenced from global antisense technology leader Ionis Pharmaceuticals (formerly ISIS before a certain terrorist group pilfered the name).

ATL1102 targets MS and DMD, while ATL1103 has acromegaly in its sights.

The raising was backed by Australian Ethical, which took a $580,000 placement and $1.1 million in the subsequent rights issue. Other participants in the raising were Platinum Asset Management, ASX-listed private-equiteer CVC and Leon Serry (the biotech sector doyen who founded Circadian Technologies).

Mr Diamond says the institutions are squarely focused on the company's upcoming phase II trial for DMD, with the raising made possible after the company won approval for the study. "That is where we are spending most of the funding," he says.

Making sense of Antisense

As well as being the name of the company, antisense is a platform first identified in the late 1970s.

Typically, most drugs work by directly binding to the target protein to treat a disease. However these targets are limited to 500 proteins, whereas the human genome (30,000 genes) control thousands of different ones.

Antisense drugs focus on the RNA 'messengers', thus tackling a much wider array of targets. While the effect is the same - the protein production is inhibited - there are key advantages.

In the company's words: "Antisense drugs don't require the complex and time-consuming analysis of the structure of the target protein that is required for conventional (small molecule) drugs."

Once the company has identified a therapeutic application and corresponding gene target, an antisense inhibitor compound can be designed within hours suitable for use in research and clinical trials.

Antisense drugs are rapidly and effectively absorbed in the blood, but they do have side effects. These are "generally predictable, occur at high doses and are well understood."

In the clinic

Antisense has completed phase II studies for acromegaly and MS and has ethics approval for a local phase II trial pertaining to DMD.

With ATL1102, Antisense targeted patients with relapsing remitting MS (ATL1102 is an antisense inhibitor of the VLA-4 protein a recognised MS target).

The MS trial produced evidence that the drug "significantly reduced the number of brain lesions in patients with relapsing-remitting MS".

The trial met the primary endpoint with a 54.4 percent reduction in the cumulative number of new active brain lesions (compared with placebo).

With DMD, the company received assent in late February for a phase II trial at the Melbourne Royal Children's Hospital neuromuscular centre.

This will enrol 10 wheelchair-bound boys between 10 years and 18 years, weighing 25kg to 60kg. The trial will assess the safety and tolerability of ATL1102, but also efficacy in terms of the blood and imaging markers of inflammation and muscle damage.

The DMD trial is due to start by June this year, with first results by June next year.

Mr Diamond says the drug tackles inflammation that exacerbates muscle fibre damage. Currently, inflammation is managed by cortico-steroids which, while improving muscle strength, have multiple side effects.

Tragically, most boys do not live beyond their 20s.

"If we show good activity in DMD that could be highly supportive of an MS study," Mr Diamond says.

Acromegaly progress

Acromegaly, meanwhile, is caused by a benign tumor of the pituitary gland that causes an excess growth hormone and insulin-like growth factor 1 (IGF-1).

ATL1103 reduces the expression of the growth hormone receptor in the liver, thus reducing serum (or blood) IGF-1 (sIGF-1).

Antisense's phase II trial met its efficacy endpoint with a significant reduction in sIGF-1.

ATL-1103 is intended to be as a second-line therapy, when other treatments have failed, but the company hopes that it could be eventually be a first-line therapy.

With acromegaly affecting 85,000 adults in the US and Europe, ATL1103 has been granted orphan drug status in US and Europe.

Antisense wants to establish an early access program status with European regulators, with the company preparing enough of the raw material to treat 15 patients for one year.

Dr Boreham's diagnosis:

The road to progress for Antisense has been full of potholes and investors have needed the patience of Job.

"We have had a couple of setbacks along the way but we built up a lot of knowledge and awareness," Mr Diamond says.

In a major setback, Teva pulled out of an exclusive worldwide development and commercialization deal for MS. Announced in February 2008, the tie up involved a $US2 million upfront payment and up to $US100 million of milestone payments.

But in March 2010 Teva determined the drug no longer suited its "product profile".

Teva was also thought to have been concerned with toxicology issues in an earlier pre-clinical trial.

Multiple sclerosis is a lucrative market worth $US20 billion and the company is hopeful of grant funding from the US National Institutes of Health and/or the US MS Society.

Dr Bill Goolsbee was chairman of the Nasdaq-listed immunotherapy house Sarepta Therapeutics and is a key part of the Antisense story. In 2016, Sarepta went from a $US50 million market cap when it gained FDA approval for its Exondys 51 DMD drug (which has a different mechanism of action from ATL-1102) and is now worth $US6 billion.

Antisense might be happy with a similar uplift.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort and does not live in Toorak, but has passed through there once in a battered Volkswagen.