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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: 5.3 cents

Shares on issue: 420,103,487

Market cap: $22.3 million

Chief executive officer: Mark Diamond

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

Financials (year to June 2019*): revenue $76,266 (up 198.5%), loss of $2.94m (previously $2.33m loss), cash of $2.9m (up 52.9%).

***** During the year the company also received a $284,000 R&D Tax Incentive relating to the 2017-'18 year

Identifiable holders: Australian Ethical 19.96%, Citicastle Pty Ltd (Leon Serry) 6.15%, Platinum Asset Management 7.56%, Opthea 2.77%, Bin Liu 2.72%, Glen Bull 2.3%, CVC 2.27%.

After 18 years at the helm of Antisense, Mark Diamond has outlasted all of his peers after the sector's elder stateswoman, Bionomics' Dr Deborah Rathjen, bowed out in January.

"I do feel like the old man of biotech," Mr Diamond says. "But you are always learning about new facets of the business."

One lesson is that a biotech's purpose and strategy and evolve over time.

In the case of Antisense, the Circadian Technologies spin-off was focused on ATL1102, a treatment for multiple sclerosis (MS), based on 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.

Now, Antisense's sights are firmly on a close cousin to MS, Duchenne muscular dystrophy, a rare genetic degenerative muscular condition that affects only boys.

About DMD (and acromegaly)

Duchenne muscular dystrophy is caused by a mutation in the muscle dystrophy gene, leading to severe progressive muscle loss and premature death (patients usually die in their 20s).

"We never anticipated we would develop a drug for Duchenne muscular dystrophy," Mr Diamond says.

Antisense's second compound, ATL1103, has acromegaly in its sights, but in August the company said the program had been put on the backburner after learning, unexpectedly, that more clinical work would be needed to access the European market.

Acromegaly is an enlargement of hands, face and feet usually caused by a non-cancerous tumor.

Both molecules are licenced from global antisense technology leader Ionis Pharmaceuticals (formerly ISIS before a certain terrorist group gave the moniker some poor connotations).

A multiple sclerosis drug is not entirely off the agenda, but do read on ...

Shooting the 'messenger'

Typically, most drugs work by binding to the target protein directly to treat a disease.

However, these targets are limited to about 500 proteins, whereas the human genome (30,000 genes) controls thousands of different ones.

First developed in the last 1970s, antisense drugs focus on the ribonucleic acid 'messengers', thus tackling a much wider array of targets.

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.

As a result, an antisense inhibitor compound that's suitable for use in research and clinical trials can be designed within hours.

Sweating on trial results

The challenge of managing Duchenne muscular dystrophy is to reduce the inflammation that exacerbates muscle fibre damage - and that's what ATL1102 aims to do.

The recent uptick of investor interest in Antisense stems from pending results for the company's phase II trial, due by the end of the year.

Carried out at the Melbourne Royal Children's Hospital's neuro-muscular centre, the trial involves nine wheelchair-bound patients, aged between 10 and 18. These kids are being administered a weekly 25 milligram dose of ATL1102 over 24 weeks.

But safety first!

The results from the first four patients showed no dosing issues or any harm done.

While primary endpoints of the study relate to safety and tolerability, the efficacy of the drug will also be assessed in terms of "disease processes and progression".

In simpler terms, this means whether the boys' upper limb strength and functions have improved.

"We are conscious that people are aware that we are getting to the sharp end of the study," Mr Diamond says.

"We will have all patients complete dosing in November and the results reported shortly thereafter, even though the study continues beyond that."

Given the study is open label - meaning both the researchers and the patients know what's being administered - the company may be able to report some interim results before the last patient is dosed.

"To be comfortable ... we need a significant number of patients completing 12 weeks of dosing," Mr Diamond says.

A D&M with the EMA over DMD

Management is now preparing to meet the European regulator, the European Medicines Agency to win assent for a follow-on phase IIb Duchenne muscular dystrophy trial.

Mr Diamond envisages the study would involve about 100 patients, with 12 months dosing at a higher dose. The trial would compare results to a control arm of patients on standard-of-care cortico-steroids.

“We have been given advice by our own independent regulatory consultant that based on the data generated we should get support for a longer study,” he says.

The meetings are expected to take place in October or November.

With acromegaly, the company also was striving to establish an early access program in Europe, where ATL1103 has been granted orphan drug status (as it has in the US).

But following a review from an ‘external quality person’, Antisense’s European partner Mytomorrows advised that a new clinical trial would be needed, because the material was being supplied by a different manufacturer.

Bugger!

Antisense says it doesn’t have the resources to undertake such work, but will strive to supply ATL1103 drug product to expert acromegaly clinicians.

Previously, the company said an acromegaly drug could generate $1 million of revenue for the company annually in what’s a $US1 billion ($A1.5 billion) global market.

A lower-dose MS trial?

The Duchenne muscular dystrophy program sprang from an earlier phase II clinical trial, testing how well ATL1102 cleaned up brain lesions of multiple sclerosis sufferers with the relapsing-remitting form of the disease.

ATL1102 is an antisense inhibitor of the VLA-4 protein, a recognized MS target.

Reported in 2014, the 77-patient study showed a 54 percent reduction in the number of new brain lesions (versus placebo) and a 90 percent reduction in existing lesions.

The trouble is, the patients were treated with a very high dose of 400 milligrams.

Management wants to see how the Duchenne muscular dystrophy trial fares with the lower dose (25mg), following a restriction ordered by the US Food and Drug Administration, before a further phase IIb trial for MS.

“We were going to dose patients at a higher dose for two months, but have FDA and Royal Children’s Hospital agreement for six months at the lower dose, which will give the drug a good chance of showing activity,” Mr Diamond says.

In 2010, big pharma Teva pulled out of an exclusive global deal with Antisense to develop ATL1102 for multiple sclerosis, so we would counsel the MS Society not to ditch the Readathon just yet.

Finances and performance

Given biotech's long lead times, it always helps to have some serious names on the register with a long-term perspective.

In March, Antisense raised $1.6 million at 3.3 cents apiece in a placement, supported by existing holders Australian Ethical, Platinum Asset Management and biotech doyen Leon Serry.

The founder of Circadian, Mr Serry drove the Antisense listing.

In May 2018, the same names supported a meaty $5 million raising.

As of June 30, this year Antisense held cash of $2.9 million, with a research and development tax refund to come.

A swag of Antisense options expires at the end of 2019 and could raise $6 million - but the catch is the strike price of 8.0 cents is still well north of the current share price.

Antisense shares have moved in interesting and mysterious ways over the last 12 months, having soared from a low of 1.7 cents on October 15 last year to a high of 6.7 cents five trading days later.

The only reason management could attribute to the 294 percent surge was animal spirits unleashed by an upbeat item on a stockbroker's website.

Dr Boreham's diagnosis:

Despite the MS potential, Mr Diamond has little doubt that the big-name investors are exposed to the stock because of the Duchenne muscular dystrophy program.

There are only 80,000 Duchenne muscular dystrophy sufferers in the US and Europe - one in every 3,500 boys.

"There's nothing for those boys," Mr Diamond says.

"The only real therapy is cortico-steroids which have limited efficacy and really nasty side effects."

Commercially speaking, why focus on such a rare disorder? As fellow ASX-listed drug developer Clinuvel shows, a small market can be highly lucrative if one has the market to oneself.

Mr Diamond notes that while multiple sclerosis may be a much bigger market, it's more crowded.

A further MS trial would require 3,000 or more patients, while the Duchenne muscular dystrophy program is 'doable' within the company's own resources.

Antisense aspires to be the next Sarepta Therapeutics, which has a commercially available Duchenne muscular dystrophy drug that's only effective for 13 percent of patients.

The last time we looked, the Nasdaq-listed Sarepta was valued at $US6.4 billion.

Antisense director Bill Goolsbee was Sarepta's chairman and no doubt he has some decent tips on drug commercialization.

Mr Diamond says while keenly anticipated, the Duchenne muscular dystrophy trial results should not be seen as a binary outcome, in that ongoing positive safety results should be enough to proceed to the next trial.

"But if we can show any confirmation of activity at this lower dose, we will all get very excited."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He recalls reading 76 books for the MS Readathon as a 10-year old, but may have skipped a few pages.