ISSN 1443-850X

Companies covered: **ANP, IXC**

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-35.8%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - May '14)	26.6%
Year 14 (May '14 - May '15)	23.0%
Year 15 (May '15 - May '16)	33.0%
Year 16 (May '16 - May '17)	16.8%
Year 17 (May '17 - May '18)	-7.1%
Year 18 (May '18 - May '19)	-2.3%
Year 19 (May '19 - May '20)	39.5%
Year 20 (May '20 - Current)	3.9%
Cumulative Gain	1032%
Av. Annual gain (19 yrs)	17.3%

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence No. 258032
Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info[at}bioshares.com.au

David Blake - Editor/Analyst
Ph: (03) 9326 5382
Email: david[at]bioshares.com.au

Mark Pachacz - Editor/Analyst
Ph: 0403 850 425
Email: mark[at]bioshares.com.au

Individual Subscriptions (48 issues/year)
$500 (Inc.GST)
Edition Number 844 (25 May 2020)

Bioshares

25 May 2020
Edition 844

Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies

Extract from Bioshares –

Antisense Therapeutics Reports Consistent Positive Results for Phase IIa DMD Study

Antisense Therapeutics (ANP: $0.069) has reported the full results from its Phase IIa study of its drug candidate ATL1102 in boys with Duchenne Muscular Dystrophy (DMD).

Previous data had shown that the antisense compound achieved an improvement or stabilisation of the degenerative muscle wasting disease compared to historical data at six months. The full data set provides consistent outcomes supporting the mechanism of action of the drug with improved patient outcomes.

Safety Profile

The primary outcome from the study was the safety profile of ATL1102. ATL1102 had previously been evaluated at much higher dose of 400mg per week in a Phase II trial in patients with relapsing-remitting multiple sclerosis. That study delivered a successful outcome on efficacy, however on safety, there were concerns, with thrombocytopenia (low platelet levels) in 22% of patients emerging as an issue, which is reversible when treatment stops.

In this recent Phase II study in boys, using just 25mg weekly (1/16th of the dose) for six months (compared to two months treatment in the MS study), there was no evidence of an adverse effect on platelet levels.

The main side effects were injection site reactions, because the compound was delivered by subcutaneous injection. This is a common side effect with antisense drugs. Similar to a previous study with another antisense drug in treating acromegaly, Antisense used a microneedle injection system to ameliorate this reaction. Antisense CEO Mark Diamond said that over time, injection site reactions reduced in the boys, with all nine boys in the study completing the full treatment. A skin discoloration was also seen at the site of injection.

Efficacy Results – A Mean Gain in PUL2.0 Score of 0.9

Previously it had been reported by the company that seven of the nine boys in the study, who were all wheelchair bound, showed either an improvement or no worsening of the strength as assessed by the PUL2.0 test. The mean gain in this score was 0.9 points. This compares to a study conducted by Pane et al which followed boys at a similar age (16.4 years compared to a mean age of 14.9 years in the Antisense study) where the mean result at six months was -1.09.

ATL1102 works by inhibiting CD49d expression on T-cells. T-cells are responsible for resolving infection or other issues in the body such as inflammation. In DMD, the inflammation follows the muscle wasting and this process is exacerbated by the T-cells that

Cont'd over

migrate from the blood stream to the sites of inflammation.

Antisense learnt of this correlation from work by other researchers (Pinto-Mariz *et al*) who found that patients with DMD with higher levels of CD49 expressing T-cells had more severe and rapid progression of their disease and that inhibiting CD49 expression could be a way to slow the disease.

Previously the company reported from this study that the level of T-cells deceased over the 24 weeks of treatment, and particularly those expressing CD49, confirming the mechanism of action. It was also found that these levels of T-cells in the blood bounced back four weeks after treatment had finished.

In new information, it was found that this T-cell data correlated with effects on strength in the nine boys. In most (six) of the boys who improved or stabilised their strength, once treatment stopped, the CD49 T-cell levels rebounded, but did not increase with the two boys whose strength deteriorated over the six months.

Decrease in Fat Levels

One of the most important findings from this study is new data that was released around changes to fat levels in the arms. Using MRI, fat levels historically have been shown to increase by 3.9% over six months (Ricotti et al) due to the muscle wasting. However, in this study, the average fat levels decreased by 0.5%. Professor Thomas Voit from the NIHR GOSH Medical Research Centre in the UK and who specialises in DMD said that "Normal transformation of muscle to fat is the hallmark of the progressive muscular dystrophy in these boys. You expect more fat (levels) with every MRI from the age of five and it doesn't stop."

Antisense's new consultant medical director, Dr Gil Price, who was previously a non-executive board member of Sarepta Therapeutics, said on an investor call last week that an MRI is completely objective at that there is "certainly an observed effect".

On the subjective measure of quality-of-life, and measures of changes in respiratory function, there were mixed results, which reflects the low patient numbers in the study.

Discussion

The full results now provide Antisense with corroborating data across a range of measures that is consistent with the effect of the drug in DMD, albeit in small numbers and without a placebo comparison. In this trial, ATL1102 was shown to improve or stabilise muscle strength, when it should be deteriorating, fat levels were stabilised when they should be increasing, CD49 T-cell levels were decreasing as expected with inhibition of CD49 expression from direct action of antisense compound ATL1102, and the boys who appeared to be responding to treatment experienced an immediate increase in the relevant T-cells as treatment stopped.

Dr Price said "What this demonstrates, albeit in a small study, is that we have a drug that is biologically, physiologically and pharmacologically active."

Professor Thomas Voit said "DMD is a relentlessly progressive disease (characterised by) a slow and steady decline in their functions. He said that improvement is never seen. That there was stabilisation or improvement in all domains suggests "this is an unambiguous sign that something is happening." Even substantial stabilisation of disease in non-ambulant boys has not been seen in literature said Professor Voit.

DMD Drug Development News

Earlier this month Pfizer reported results from a Phase Ib DMD study in nine ambulatory boys with its on-off gene therapy. Pfizer aims to move the program into a Phase III study in the second half of this year. However, some US analysts have viewed the results as being inferior to Sarepta's DMD drug which is approved.

Of the nine boys, three experienced serious adverse events although all were resolved by the end of the study. The low dose cohort achieved 24% of normal dystrophin levels, while the high dose achieved 52% of normal levels. These effects were generally sustained at 12 months.

With respect to function, Pfizer reported a median improvement of 3.5 points on the NSAA scale, compared to a 4 point drop than can be expected from historical controls.

A gene therapy approach to DMD would be complementary to additional efforts with a compound such as ATL1102 that seeks to diminish damaging T-cell responses by the body.

Next Steps

Antisense is now progressing its DMD program to a Phase IIb European study, with discussions underway with European regulators. Feedback is pending around mid year, with the potential path for achieving conditional approval reliant on the next study delivering sufficiently positive efficacy and safety data.

Antisense is considering two higher doses for its Phase IIb study. That may involve around 75 boys, with 25 in each arm, including a placebo arm. All boys in the study are likely to be offered to continue in an extension study at the highest safe dose. However, the trial design will need to be approved by the European regulators.

Antisense will source supply of ALT1102 for its pivotal study from a contract manufacturer of oligonucleotides in Boston.

IP Protection and Royalty Obligations

Antisense has accessed its antisense programs from biotech group Ionis Pharmaceuticals. As such, it is required to pay Ionis one third of any revenue it receives from ATL1102, or a single digit royalty is payable to Ionis if Antisense takes the compound through to market on its own.

Antisense has filed therapeutic use and methods patents over ATL1102 for the treatment of DMD which may provide protection to at least 2039 if granted.

Continued over

Summary

For Antisense Therapeutics, its overwhelming focus now is on its DMD program with ATL1102. Discussions with regulators and production of material for trials will be key milestones this year. Other milestones relate to discussions with potential partners, or raising funds for Antisense to manage the Phase IIb study with its own resources.

Antisense is capitalised at $34 million with $5.4 million in cash at the end March.

Bioshares recommendation: **Speculative Buy Class B**

How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Some Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Cogstate, Bionomics, LBT Innovations, Opthea, ResApp Health, Pharmaxis, Dimerix, Adalta, Actinogen Medical, Patrys, Cyclopharm, Emvision, Antisense Therapeutics, Heramed, Imugene, Exopharm, Immutep, Neuroscientific Biopharmaceuticals, Invex Therapeutics