Biotech Daily

Friday November 5, 2021

Daily news on ASX-listed biotechnology companies

*** ASX UP, BIOTECH EVEN: ACTINOGEN UP 6%; CLINUVEL DOWN 12.5%**

*** DR BOREHAM'S CRUCIBLE: ANTISENSE THERAPEUTICS**

*** PREVATEX RAISES $2.2m**

*** PROTEOMICS: 'PROMARKERD BEATS STANDARD-OF-CARE TESTS'**

*** PHARMAUST RIGHTS OPTIONS RAISE $514k**

*** VISIONEERING: 'NATURALVUE REDUCES MYOPIA PROGRESSION'**

*** VISIONEERING LAUNCHES NATURALVUE ENHANCED MULTIFOCAL LENS**

*** IQ3: 41%-OWNED ONCOTEX LICENCES GOLD COMPOUNDS FOR CANCER**

*** BLACKROCK TAKES 5.8% OF AVITA**

*** VANGUARD TAKES 5.2% OF AVITA**

*** PARADICE TAKES 8.4% OF IMPEDIMED**

*** JM FINANCIAL REDUCES TO 9.8% OF UNIVERSAL BIOSENSORS**

*** REGAL FUNDS BELOW 5% IN ADHERIUM**

*** QUINCY STREET TAKES 6.3% OF ZELIRA**

*** AUSBIOTECH APPOINTS GEOFFREY KEMPLER CHAIR**

*** POLYNOVO LOSES 7-YEAR CEO, M-D PAUL BRENNAN; 'DIFFERENCES'**

*** VISIONEERING APPOINTS DR ASHLEY TUAN CMO**

MARKET REPORT

The Australian stock market was up 0.39 percent on Friday November 5, 2021, with the ASX200 up 28.9 points to 7,456.9 points. Fifteen of Biotech Daily Top 40 stocks were up, 15 fell, nine traded unchanged and one was untraded.

Actinogen was the best, up one cent or 6.1 percent to 17.5 cents, with 5.5 million shares traded. Proteomics climbed 5.6 percent; Pharmaxis and Resonance improved more than four percent; Imugene and Pro Medicus were up more than three percent; Optiscan and Telix rose more than two percent; Cochlear, Immutep, Nanosonics and Prescient were up one percent or more; with CSL, Cyclopharm, Medical Developments, Mesoblast and Paradigm up by less than one percent.

Clinuvel led the falls, down $5.06 or 12.5 percent to $35.50, with 550,148 shares traded. Alterity and Antisense lost more than six percent; Polynovo was down 5.4 percent; LBT, Starpharma, Universal Biosensors and Uscom fell four percent or more; Opthea and Osprey were down more than three percent; Genetic Signatures, Next Science and Volpara shed two percent or more; Orthocell was down 1.9 percent; with Neuren and Resmed down by less than one percent.

DR BOREHAM'S CRUCIBLE: ANTISENSE THERAPEUTICS

By TIM BOREHAM

ASX code: ANP

Share price: 22.5 cents; **Shares on issue*:** 574,476,343; **Market cap*:** $129.3 million
***** Ahead of this week's $20 million share placement and $16.8 million one-for-9.4 rights offer, at 24 cents a share to raise $16.8 million. Combined, the raisings will increase shares on issue by approximately 153.3 million or 22%

Managing-director: Mark Diamond

Board:** Dr Charmaine Gittleson (chairman), Mr Diamond, Robert Moses, Prof Graham Mitchell, Dr Gary Pace, Dr Gil Price, William Goolsbee
****** Prof Mitchell, Mr Goolsbee and Mr Moses retire at this year's AGM

Financials (year to June 30, 2021): revenue nil, loss of $8.06 million (previously $5.9 million deficit), cash of $6.02 million*** (up 48%).

Identifiable major holders*:** Platinum Asset Management (sub 5%), Citicastle Pty Ltd (Leon Serry) 2.5%, Altor Capital 2.20%, Esarad Holdings 1.84%, Dale Anthony Reed 1.79%
******* Ahead of $36.8 million capital raising

Even under the best circumstances when things flow smoothly, drug development entails mind-numbing leg-work before the elation of selling the therapy for the benefit of sick people and for the enrichment of investors.

Antisense certainly knows about the drudgery as it seeks US and European regulatory approval to progress human trials for its ATL1102 treatment for the rare genetic disorder Duchenne muscular dystrophy (DMD).

Things were progressing at a glacial pace, but this week the company announced the equivalent of the melting ice caps - debated (and we use the term loosely) at this week's Glasgow talkfest.

In news we would file under 'boring but important', the European Medicines Agency in effect approved the company's Paediatric Investigation Plan, a blueprint for how the company would develop its Duchenne muscular dystrophy drug on the Continent.

The approval - or final positive opinion, strictly speaking - opens the way for Antisense to carry out a phase IIb/III trial across 30 European sites in nine countries.

"This study could turn out to be a pivotal trial," says Antisense chief executive Mark Diamond. "In other words, if we get the requisite data showing significant clinical improvement in upper limb function, we could submit for European approval."

Not wanting to waste the moment, Antisense also rounded up $20 million in an institutional placement, with a follow-on rights issue slated to raise a further $16.8 million.

A chunky $36.8 million? There's nothing boring or unimportant about that.

Biotech goes upmarket

But let's step back a bit. The only biotech based in the ritzy Melbourne suburb of Toorak, Antisense sprung from Circadian Technologies (reputed to be the first ASX-listed biotech).

Mr Diamond has the status of the longest-serving CEO of any Australian biotech, having joined Antisense just after the Twin Towers toppled in 2001.

Antisense's key asset is ATL1102, licenced from the Nasdaq-listed Ionis Pharmaceuticals (formerly ISIS, but Middle East events encouraged a name change).

Initially, Antisense focused on 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 expression of proteins.

In 2010, big pharma Teva pulled out from an exclusive global deal with Antisense to develop ATL1102 for multiple sclerosis.

A phase IIa trial showed that ATL1102 was good for cleaning up brain lesions, but the dosage was very high (400 milligrams compared to 25 milligrams for the DMD trials).

Antisense's second compound, ATL1103, targeted acromegaly. But in August 2019 an early access program was shelved after the company learned 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.

DMD in the spotlight

Now, Antisense's sights are firmly on ATL1102 as a treatment for Duchenne muscular dystrophy, a rare genetic degenerative muscular condition that affects only boys and is regressive, fatal and poorly treated.

DMD is caused by a mutation in the muscle dystrophy gene, leading to severe progressive muscle loss and premature death. The current standard of care, corticosteroids, have limited efficacy and significant side effects when used continuously, as required.

The disorder affects about one in 3,500 males from birth to 18 years, or about 48,000 boys in the US and Europe. It's the biggest fatal genetic disorder.
In-licenced from drug developer Ionis, ATL1102 is an antisense inhibitor of the VLA-4 protein, also known as CD49d, a target for the treatment of multiple sclerosis.

ATL1102 inhibits the inflammation caused by the lack of the protein dystrophin, which erodes muscle function.

Antisense's key evidence to date is the outcome of a phase II study, carried out at the Melbourne's Royal Children's Hospital's neuromuscular centre. The trial enrolled nine non ambulant (wheelchair bound) patients, who were treated with ATL1102 over six months (with all but one remaining on the standard-of-care, cortico-steroids).

The boys' muscle function was then compared with the recorded results from 20 boys treated with corticosteroids only. This data was held by leading DMD expert Prof Eugenio Mercuri, of Rome's Catholic University.

Measuring up

In results dubbed as statistically significant, the ATL1102-treated boys performed better on the muscle function assessment score after 24 weeks.

How is the improvement measured? Good question.

The relevant gauge is the Performance of Upper Limb Function (PUL2) test. The RCH patients scored a mean improvement of 0.89 when dosed with ATL1102, which doesn't sound like much until compared with the Rome boys, who saw an average decline of 2.0.

Also, 78 percent showed no change or an improvement, compared with 33 percent for the control group.

The Continental way

Initially, management targeted the US Food and Drug Administration to win the requisite trial approvals, but then re-focused on the European Medicines Agency.

The company has finalized the design of its proposed European study, and is likely to enrol 114 patients across two dose arms of different strengths, as well as a placebo arm. All boys will continue to be treated with corticosteroids. Under the open-label design, the boys will continue to use ATL1102 after the 12-month trial period.

In Europe there are about 20,000 boys with DMD, about half which are non-ambulant and thus eligible for the trial.

Mired down in monkey business

Meanwhile, the FDA process has been bogged down by the agency's insistence on a longer toxicology study than the six-month monkey-based trial proposed by the company in a "cogent and well supported" entreaty (Mr Diamond's words).

The FDA wanted 12 months but in a classic compromise it agreed to nine months, to be submitted before the trial reaches six-month dosing of children.

The toxicology study has been delayed because of a shortage of specially-bred monkeys, many of which are obtained from China.

The FDA is yet to approve the study, which of course would need to be carried out on US soil. Having said that, it's possible that data from the European trial could be taken into account.

The good news is that the agency is happy with the Royal Children's Hospital trial outcomes as the basis for a larger US study.

About a year ago, the FDA awarded Antisense 'rare paediatric disease designation' (RPDD) for ATL1102. RPDD designation includes a rare paediatric disease review voucher, which is an express-lane ticket for FDA approval. These bits of paper can be on-sold for many millions of bucks - and usually are.

Antisense also has 'orphan drug' designation from the FDA and the EMA.

"Orphan drug status brings additional benefits, like 10 and seven years of market exclusivity in Europe and the US respectively and waiving of certain registration fees which can be quite substantial," Mr Diamond says.

The Sarepta experience

Antisense is buoyed by the experience of the Nasdaq-listed Sarepta Therapeutics, which has won approval for not one, but three, DMD drugs.

So doesn't Sarepta thus have the market covered already?

Not so, says Mr Diamond.

The three drugs each pertain to a form of genetic mutation and, collectively, cover only 25 percent of DMD patients. They also have a different mechanism of action.

Mr Diamond says ATL1102 potentially could be used in conjunction with Sarepta's therapies, to treat both ambulant and non-ambulant boys.

He adds that Sarepta won FDA approval without showing improvement in disease progression in controlled, randomized studies.
Instead, the FDA was convinced by an improvement in dystrophin levels in the boys' muscles. Sarepta was knocked back by the European regulator, which won't accept such surrogate endpoints.

In any event, Antisense will keep an eye on the competition with former Sarepta directors William Goolsbee and Gil Price on the Antisense board.

Mr Diamond notes that Sarepta was smaller than Antisense before its first drug was approved. Now the company commands a $US7.6 billion market capitalization and chalked up September quarter sales of $US167 million.

Finances and performance

As of June 30, 2021 Antisense had $6 million of cash in the bank, having expended $2.28 million in the June quarter and $6.6 million in the 2020-'21 year.

Mr Diamond was clear that the company would need more cash for a European trial and hence this week's raising, struck at 24 cents a share (an 18.6 percent discount to the last closing price of 29.5 cents on October 27.

While the shares are currently trading below the rights offer price, shareholders are being induced with one option for every two shares, exercisable at 48 cents each.

Broking analysts covering the stock estimate a European trial to cost about $35 million and Mr Diamond isn't exactly arguing with that.

A US trial could cost a similar amount, although some savings may be possible if offshore data is allowed. While an equity raising seems the most likely route, a partnering arrangement is possible.

Late last year, Antisense raised $8.5 million in an oversubscribed placement and share purchase plan, which followed a $1.6 million in a placement in March 2019 and a $5 million placement in 2019.

Antisense shares over the last 12 months have wandered between nine cents (mid December 2020) and 25 cents (January and April this year). When we last looked at Antisense in September 2019 the stock traded at 5.3 cents for a market cap of $22 million, so investors have been rewarded for their patience.

Dr Boreham's diagnosis:

Antisense has some other tricks up its sleeve to reduce fibrosis in other human diseases, including a recently-inked collaboration with the Murdoch Children's Research Institute (at the RCH) on other rare inflammatory disorders.

Commercially speaking, why focus on rare disorders?

Mr Diamond says while multiple sclerosis is a much bigger market, it's also crowded. So, if a rare disease isn't too rare, it can be more lucrative with lower development costs.

As we said at the outset, regulatory argy-bargy is not exactly fascinating for investors, but behind the scenes there's real progress at Antisense

What's clear is that after two decades in the chair, Mr Diamond isn't about to throw in the towel. And if the European trial founders, it won't be for lack of cash.

Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He tried to enter Toorak once, but was turned back by blue rinse border control.

PREVATEX PTY LTD

Prevatex executive chair Dr Greg Collier says the company has completed a series A capital raise of $2,231,005 at $2.29 a share.

Dr Collier told Biotech Daily that the valuation of the company to about $12.2 million .

In a letter to shareholders, Dr Collier said that Brisbane's Probiotics Australia had invested $625,000 for 272,926 shares or 5.0 percent of the company which would convert at the completion of stage 3 of the manufacturing agreement.

Dr Collier said that funds would be used for "upscaling the manufacturing of Prevotella copri which it was developing to treat food allergies.

Last year, Prevatex said that a multi-institutional study found the maternal microbiome was impacted by family size and the presence of Prevotella copri was associated with a reduced food allergy risk in infants (BD: Mar 25, 2020).

Probiotics Australia operations manager Joe Liu said that the first batch of freeze-dried viable Prevotella copri had been produced.

"There are significant economic and technical challenges that exist around the manufacture of next-generation probiotic species, specifically those that are strictly anaerobic," Mr Liu said.

Mr Liu said Probiotics Australia had overcome the challenges to develop economically-viable media formulations, customized bio-processing equipment pipelines and had produced a viable freezed-dried active pharmaceutical ingredient, with the next-stage of development, commercial-scale production of the active pharmaceutical ingredient.

Prevatex is a private company, in which Biotech Daily editor David Langsam owns shares.

PROTEOMICS INTERNATIONAL LABORATORIES

Proteomics says an 857-sample study shows that its Promarkerd "outperforms current standard-of-care tests" in predicting kidney function decline in type 2 diabetes.

Proteomics said the retrospective study of Fremantle Diabetes Study samples showed Promarkerd correctly identified 84 percent of patients with normal kidney function who later experienced kidney function decline "that would be missed by standard of care tests".

The company said Promarkerd measured the level of three biomarkers and combined them with clinical data in an algorithm to provide low, moderate or high-risk scores.

Proteomics said Promarkerd identified 89 percent of patients with abnormal kidney function who declined further over the course of the study.

The company said high risk patients were 21 times more likely to develop diabetic kidney disease within four years than those classified as low risk; and patients classified as moderate were eight times more likely than low-risk patients to develop the disease.

In 2019, Proteomics said its Promarkerd immunoassay, in-vitro diagnostic for diabetic kidney disease had been validated in a 100-patient study (BD: Sep17, 2019).

Today, Proteomics said the research was presented at the American Society of Nephrology meeting being held from November 4 to November 7, 2021.

The company said the results were being presented as a poster, titled 'A Comparison of Promarkerd to Standard of Care Tests for Predicting Renal Decline in Type 2 Diabetes' and compared the test to current standard of care tests, the estimated glomerular filtration rate (eGFR) and the urinary albumin to creatinine ratio (ACR).

Proteomics managing-director Dr Richard Lipscombe said that Promarkerd "gives doctors the data they need to support early introduction of preventive medications to slow the progression of [diabetic kidney disease] in high-risk patients, closer monitoring of risk factors in moderate-risk patients, and rationalized treatment options in low-risk patients".

Proteomics was up 5.5 cents or 5.6 percent to $1.04.

PHARMAUST

Pharmaust says it has raised $514,144 of a hoped for $792, 281 in its one for four entitlement options offer (BD: Oct 1, 2021) (AVW: Oct 1, 2021).
Pharmaust said the options were exercisable at 20 cents by October 31, 2023.
The company said JP Equity Partners was the lead manager to the offer and would allocate and issue the shortfall.
Pharmaust was up one cent or 10 percent to 11 cents.

VISIONEERING TECHNOLOGIES INC

Visioneering says a 196-subject six-year study shows its Naturalvue multifocal contact lenses reduce the progression of myopia, or near-sightedness, in children.
Visioneering said the retrospective study was presented at the American Academy of Optometry meeting in Boston and showed that 95 percent of subjects wearing Naturalvue multifocal contact lenses had a decrease in myopia progression compared to baseline and 78 percent showed a decrease in myopia progression of 70 percent or greater.
The company said average myopia progression slowed by about 0.85 dioptre or 85 percent compared to baseline, and was statistically significant at all time-points ($p < 0.05$).
Visioneering said the average myopia progression while wearing the Naturalvue lenses never exceeded more than about 0.25 dioptre from baseline.
Visioneering said an age and ethnicity-matched virtual control group developed from 63 randomized clinical trials was used to compare the effectiveness of Naturalvue lenses to changes observed in children not wearing the lenses
The company said children would have been expected to progress by -1.09 dioptre if not wearing Naturalvue compared with -0.06 dioptre observed with Naturalvue over three years.
Visioneering said every one dioptre less of myopia meant “much better vision and a 40 percent decrease in risk of a major cause of vision loss across a lifetime”.
The company said that 67 percent of the children had complete halting of myopic progression during the period of the study”
Visioneering said it would begin a double-blinded, randomized, controlled study of Naturalvue lenses in myopic children in the US, Canada and Hong Kong, with one-year data, expected mid-2023.
Visioneering was up six cents or 6.45 percent to 99 cents.

VISIONEERING TECHNOLOGIES INC

Visioneering says it has launched its Enhanced multifocal one-day contact lens with a 53-patient study confirming “vision, comfort and handling advantages”.
Visioneering said chief executive officer Dr Stephen Snowdy presented supporting clinical data at the American Academy of Optometry meeting in Boston.
The company said that the Enhanced lenses had the Tripletear lubrication system which included hyaluronic acid “to provide hydration and lubrication, lock in moisture and maintain a clean surface to stabilize tears”.
Visioneering said “the ultra-tapered edge is designed for optimal fit and comfort and to help the natural circulation of tears around the lens” and the lenses had a class 2 ultraviolet blocker for an added layer of protection.
The company said the study confirmed that visual acuity was equal to spectacles, within two letters of best-corrected spectacle vision, 92 percent of daily activities could be completed without glasses and no refit was required for current wearers.

IQ3 CORP

IQ3 says 40.5 percent New York investee company Oncotex Inc has licenced a gold compound platform technology to induce immune responses to destroy cancer cells.
IQ3 said the technology was developed by the University of Texas at Austin, Statesboro's Georgia Southern University and Dayton, Ohio's Wright State University.
The company said the technology would "create innovative therapies capable of overcoming multiple limitations seen within current cancer therapeutics".
The company said the gold-based compounds had "the ability to enter cancer cells and fight them from the inside while disrupting the tumors, making them visible to the human immune system [and starting] a cascade to create killer T-cells that then attack and destroy the remaining cancer".
IQ3 said the collaboration with the University of Texas would evaluate the compounds to determine their potential utility against cancer "over the coming months".
IQ3 and Oncotex chair Dr George Syrmalis said the compound "introduces a novel mode of action, demonstrating tumor-specific immune responses and reinstating immunosurveillance".
"It is expected that through this gold-induced immunogenic cell death, we will be able to provide significant complements to immune checkpoint inhibitors," Dr Syrmalis said.
IQ3 was up 5.5 cents or 55 percent to 15.5 cents.

AVITA MEDICAL

Avita says Blackrock Institutional Trust Company has become substantial shareholder with 1,445,119 US shares or 5.8 percent of the company.
The holding is equivalent to 7,225,595 Chess depository instruments (CDIs).
Avita was unchanged at $5.13 with 468,453 shares traded.

AVITA MEDICAL

Avita says the Vanguard Group has become a substantial shareholder with 1,297,499 US shares or 5.2 percent of the company.
The holding is equivalent to 6,487,495 CDIs.

IMPEDIMED

Paradice Investment Management says it has increased its shareholding in Impedimed from 102,899,139 shares (6.898%) to 144,301,807 shares (8.358%).
The Sydney-based Paradice said it bought and sold shares between October 12 and November 2, 2021 with the single largest purchase 32,786,886 shares for $5,000,000 or 15.25 cents a share.
Impedimed was unchanged at 18 cents with 4.8 million shares traded.

UNIVERSAL BIOSENSORS INC

Melbourne's JM Financial Group says it has reduced its holding in Universal Biosensors from 21,968,307 shares (12.38%) to 17,382,413 shares (9.78%).
JM Financial says it bought and sold shares between February 25 and September 30, 2021 with the single largest sale 655,000 shares for $524,000 or 80 cents a share.
Universal Biosensors fell 3.5 cents or 4.5 percent to 75 cents.

ADHERIUM

Sydney's Regal Funds Management says it has ceased its substantial shareholding in Adherium with the sale of 24,502,148 shares.
Regal Funds said it sold the shares on October 19 and November 2, 2021 for $306,930 or an average of 1.25 cents a share.
Adherium fell 0.05 cents or four percent to 1.2 cents with 22 million shares traded.

ZELIRA THERAPEUTICS

Quincy Street Capital LLC says it has become a substantial shareholder in Zelira Therapeutics with 79,908,676 shares or 6.29 percent.
The Park City, Utah-based Quincy Street said it bought the shares on November 3, 2021 for $4,794,521 or six cents a share.
Last month, Zelira said it raised $US5 million ($A6.7 million) in a placement to Quincy Street at six cents a 54 percent premium to its 3.9 cents closing price (BD: Oct 20, 2021).
Zelira was unchanged at four cents with 1.6 million shares traded.

AUSBIOTECH

Ausbiotech says it has appointed Geoffrey Kempler chair and a non-executive director.
Ausbiotech said Mr Kempler would replace Michelle Burke after her nine-year tenure as a director, the maximum possible under the Ausbiotech Constitution.
The industry organization said Mr Kempler was a qualified psychologist and a member of the Monash Institute of Cognitive and Clinical Neurosciences advisory board.
Mr Kempler is a former chair and current director of Alterity, formerly Prana, and a former director of Opthea, previously Circadian.
Ausbiotech said Mr Kempler held a Bachelor in Science from Monash University and a Graduate Diploma from Swinburne University.

POLYNOVO

Polynovo says that seven-year managing-director Paul Brennan has resigned but will "remain in the position for three months to assist with an orderly transfer".
Polynovo chairman David Williams thanked Mr Brennan "for his leadership over the last seven years" but noted "increasing differences with the board in relation to Paul's interaction with the company's senior management team and his management style".
"Accordingly, the board has accepted Paul's resignation," Mr Williams said.
"The board sees this as an excellent opportunity and a catalyst to take the company to another level with a new leader," Mr Williams said.
He said the company was looking for an "outstanding candidate and leader with appropriate sales and marketing experience to spearhead growth in the US and the EU".
Polynovo said that Max Johnston had been appointed interim chief executive officer on a fixed remuneration of $300,000 a year including superannuation.
The company said that Mr Johnston was a director from 2014 to 2020 "and knows the business well".
Polynovo said that previously Mr Johnston was Johnson & Johnson Pacific chief executive officer and an executive director of Johnson & Johnson.
The company said that Mr Williams and US director David McQuillan would work closely with Mr Johnston.
Polynovo fell 10 cents or 5.4 percent to $1.755 with 6.1 million shares traded.

VISIONEERING TECHNOLOGIES

Visioneering says it has appointed Dr Ashley Tuan as its chief medical officer.

Visioneering said Dr Tuan had 27 years' experience in clinical and vision research in myopia, higher order aberrations, presbyopia, refractive surgeries and age-related macular degeneration.

The company said Dr Tuan was most recently the vice president of Mojo Vision and previously worked for Cooper Vision.

Visioneering said Dr Tuan held a Masters in Physiological Optics, a Doctor of Optometry from Ohio State University and a Doctor of Philosophy from the University of California at Berkeley.