Biotech Daily

Friday March 9, 2018

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market was up 0.34 percent on Friday March 9, 2018, with the ASX200 up 20.3 points to 5,963.2 points. Seventeen of the Biotech Daily Top 40 stocks were up, 13 fell, nine traded unchanged and one was untraded. All three Big Caps rose.

Factor Therapeutics was the best on no news, up 0.7 cents or 17.5 percent to 4.7 cents with 1.4 million shares traded.

Uscom climbed eight percent; Prana improved 5.6 percent; Admedus, Bionomics, Dimerix, ITL, Orthocell and Pharmaxis were up three percent or more; Actinogen, Medical Developments and Optiscan rose more than two percent; Avita, Cochlear, Compumedics, Nanosonics, Resmed and Volpara were up one percent or more; with CSL and Polynovo up by less than one percent.

Cyclopharm led the falls, down eight cents or 7.4 percent to $1.00 with 10,000 shares traded.

Mesoblast and Opthea lost more than five percent; Immutep fell four percent; Genetic Signatures and LBT were down more than three percent; Benitec shed 2.6 percent; Starpharma and Telix were down one percent or more; with Ellex, Neuren, Pro Medicus and Sirtex down by less than one percent.

DR BOREHAM'S CRUCIBLE: AVITA MEDICAL

By TIM BOREHAM

ASX code: AVH; **US OTCQX code:** AVMXY

Share price: 5.8 cents

Market cap: $59.1 million

Shares on issue: 1,018,402,660

Chief executive officer: Dr Michael Perry

Board: Lou Panaccio (chairman), Dr Michael Perry, Jeremy Curnock Cook, Louis Drapeau, Damien McDonald, Prof Suzanne Crowe

Financials (December half): sales revenue $788,295 (up 51%), other revenue $3.7 million (up 19%), net loss $7.3 million (previously $4.8 million loss), cash $11.8 million.

Identifiable shareholders: Regal Funds Management 6.89%, One Funds Management (Asia Pacific Health Fund) 7.46%, Paul Cozzi 3.3%, Fats Pty Ltd 1.66%, Ateq Investments 1.5%, Adam Kelliher 1.09%

Immortalised by Perth-based queen of burns Prof Fiona Wood, the regenerative skin house finally is eyeing an entry into the US market - a decade after its Recell treatment started to be approved in 16 other countries.

As with so many biotech plays, Avita has been a slow burn indeed, having had several strategy and management revamps.

Despite all the hope and promises, Avita stock is trading at close to decade lows.

But Avita is not without friends, with a pending US approval decision looming as a pivotal moment in the company's chequered history.

Formerly Clinical Cell Culture, the company changed its name to Avita in June 2008 after a merger with Visiomed and a 10-for-one share consolidation.

At one time Avita did a line in respiratory products such as the Funhaler, an asthma spacer pitched at encouraging young 'uns to take their medication through "auditory and visual" devices, complete with bells and whistles for children who didn't like breathing. At $50 it didn't compete well with the standard $20 spacer for kids who did like breathing.

Now, it's all about Recell.

"I believe the technology is so good and so undervalued that we are in a great position," says CEO Dr Mike Perry.

Management merry-go-round

True to Avita's sharper US focus, a management cleanout last year saw the three most important acronyms – CEO, CFO and COO – replaced.

A former war correspondent, chief executive officer Adam Kelliher survived a bullet during the Balkans war and for two years ran Avita with "energetic service". But last year he handed in his flak jacket because he was unwilling to relocate to the US.

A Novartis exec, Dr Perry moonlighted as an Avita director from 2013 and then retired from his day job in April last year. Given his experience in US commercialization and distribution, Dr Perry was the right bloke in the right spot.

Recell unpeeled

Seeing you asked, Recell is a rapid cell harvesting device that enables surgeons to treat skin defects using patients own cells collected during surgery.

It means that surgeons can prepare a small quantity of cells on site, rather than sending a biopsy to the lab. In effect, the donor area is multiplied 80 times, and cut less skin from one part of a body to heal another part.

The result of this autologous harvesting is a spray-on skin, so let's call Avita the WD-40 of burns care.

From 2008, Recell was approved for use in 16 jurisdictions including Europe, Canada, Brazil, Japan, Australia and New Zealand.

Recell shot to fame after Prof Wood, a former Avita director, used the spray-on technique to treat the Bali bombing burns victims in 2002.

Globally 7,000 patients have been treated to date, with no safety problems.

US here we come

Avita's focus on the US is not surprising, given it's a $US5.7 billion burns market.

In September last year Avita filed a pre-marketing approval application (PMA), with US Food and Drug Administration approval "anticipated" by October this year.

The treatment already has compassionate-use status in the US, with 80 patients treated to date.

The PMA application is supported by two randomized and controlled US-based clinical trials.

The first compared Recell alone versus standard of care for spilt thickness skin grafts for second degree burns patients. The 102-patient effort saw a 97.5 percent reduction in donor skin required.

The second was for third degree burns patients and compared Recell with mesh and skin graft, or split thickness graft alone. In these cases, an average of 32 percent less donor skin was required.

It BARDA be good

Avita has a powerful and deep pocketed partner in the US: the Biomedical Advanced Research and Development Authority (BARDA). BARDA stockpiles medicines for mass disasters and supports biotechs with potentially useful drugs and devices.

In September 2015, BARDA chipped in $US16.9 million for pre-approval clinical program and then in June 2016 stumped up a further $US8 million for an economic model. The agency then came good for $US24.3 million of paediatric research in September last year.

Last year, BARDA ordered $US7.5 million of Recell kits and potentially could order $US30 million more, depending on the agency's view of how much stock is needed to cover any impending disaster.

Or more to the point, how much it can afford.

Avita is also working on a reimbursement strategy with US funders.

"Our pricing studies are ongoing," Dr Perry says. "We still haven't locked in a US price but are confident we will get reimbursement (either under existing codes or a new code)."

Dr Perry says it's one of the few times in his storied career when he has overseen a new product that both greatly improves the standard of care, but also reduces treatment costs.

Avita's numbers

Avita has been an enthusiastic capital raiser over the last decade, with the latest whip 'round (in November last year) pulling in $16.9 million via a $4.5 million private placement and $12.4 million rights issue.

The deal enabled long-time holder Hunter Hall (now Pengana) to exit, thus obviating a share overhang. But at a rock-bottom 4.5 cents a share, the placement didn't exactly please remaining investors.

With $11 million in the bank, Avita may need to find more of the folding stuff, but Dr Perry says any raising is likely to be modest.

Avita shares are popular with retail investors, who account for 60 to 70 percent of the register. Management loves 'em to bits but the trouble is they take profits every time the stock looks like having a sustained run.

Frustrated, management is mulling re-domiciling to the Nasdaq, citing superior valuations. For example, US stem-cell burns house Renovacare is valued at $US300 million, without yet undertaking clinical trials.

But plenty of Australian companies have been re-rated by the better-informed US investors and it's nearly always downwards.

What's the US market worth?

Seeing you asked again, here's a handy guide: there are about 500,000 US burns patients a year, with perhaps 15,000 suitable for Recell treatment.

Dr Perry says the average patient requires three to three and a half kits, so let's say 50,000 kits a year. Multiply that by an average cost of $US5,000 to $US8,000 per kit and that equates to a $US250 million to $US400 million market.

Avita is also exploring areas such as venous leg ulcers, diabetic foot ulcers and repigmentation, as well as regenerative cell and gene therapies.

Dr Boreham's diagnosis:

After years of frustrating investors, Avita now looks more focused as it pursues the US market. BARDA's backing helps, although ongoing support is never assured (as holders in the 'flu drug house Biota, formerly Aviragen and now Vaxart, would attest).

Investors should be aware that Avita has stiff competition, whether it's crusty surgeons opting for the good ol' skin grafts or the lattice style-products developed by the likes of ASX counterpart Polynovo (which BARDA also funds).

Given Recell is already widely used globally, Avita should be performing much better share price wise.

If it doesn't, the company will either try its luck on Nasdaq, get taken over or become a pot stock.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Fortunately, his only personal experience with burns has been sideburns in the 1970s and an occasional scolding from Mother.

THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH

The Walter and Eliza Hall Institute says the discovery of a cancer signature in mice could lead to blood test for patients not responding to adenocarcinoma lung cancer.

The Institute said that some patients with the aggressive lung cancer did not respond to immunotherapies currently used to treat other cancers.

WEHI said that the research showed "a unique molecular signature in the blood" that could be used to detect the lung cancers with a blood test.

The Institute said that the study focused on the role of two cell signalling pathways KEAP1/NRF2 and PI3K, which were known to be involved in human lung cancer adenocarcinomas.

The research article, led by Dr Sarah Best and Dr Kate Sutherland and titled: 'Synergy between the KEAP1/NRF2 and PI3K Pathways Drives Non-Small-Cell Lung Cancer with an Altered Immune Microenvironment' was published in Cell Metabolism with an abstract available at: https://www.sciencedirect.com/science/article/pii/S1550413118301177.

"More than one in five lung adenocarcinomas have alterations in the KEAP1/NRF2 pathway, suggesting it is a major cancer driver," Dr Sutherland said.

"These cancers are very aggressive, are resistant to standard therapies and have a poor prognosis, so new therapies are urgently needed," Dr Sutherland said.

WEHI said that adenocarcinoma accounted for about 40 percent of lung cancers and was often associated with a history of smoking but was also the most commonly diagnosed lung cancer in non-smokers.

The Institute said that adenocarcinoma occurred more frequently in females and in young people than other types of lung cancer.

Dr Best said the study showed that the tumors had characteristics indicating they were likely to respond well to immunotherapy.

"This is extremely important because these tumors are chemotherapy and radiotherapy resistant, meaning there are effectively no current treatments for these patients," Dr Best said. "Using preclinical models, we showed for the first time that these tumors have the markers that respond to anti-PD-1 [programmed cell death-1] and anti-CTLA-4 immunotherapies, which are some of the most exciting new cancer therapies being investigated in the clinic".

"But more importantly, we showed that these immunotherapies were effective in fighting the tumors and leading to tumor regression in our preclinical models," Dr Best said.

Dr Best said the research showed that non-stop signalling caused by mutations in the KEAP1/NRF2 and PI3K pathways caused lung adenocarcinomas to develop.

"This is the first time anyone has shown that these alterations directly cause lung adenocarcinomas," Dr Best said.

"With this knowledge, we can further investigate how targeting those pathways could lead to therapies for these aggressive and hard-to-treat cancers," Dr Best said.

Dr Sutherland said the unique molecular signatures found in the blood could be a tool to identify patients who would respond to immunotherapies, or even as an early detection test for these cancers.

"Working with our colleagues Dr David De Souza and Prof Malcolm McConville at Bio21 Institute, we were able to identify a unique … trail that the cancers leave behind in the blood," Dr Sutherland said.

"Our hope would be that the test could identify patients likely to respond to immunotherapies, but also that it could be a simple, non-invasive blood test for the early detection of these lung cancers," Dr Sutherland said. "The next steps would be to analyse human samples to prove the same is true in lung adenocarcinoma patients, but we need more funding for that work to continue".

FEDERAL GOVERNMENT

Federal Health Minister Greg Hunt says research applications are open for $10 million “to help find new treatments for low survival cancers and diseases”.
A media release from Mr Hunt said that low survival rate cancers were caused nearly 40 percent of cancer deaths in 2017 and the funding would create opportunities for new trials.
The Government said that people living with low survival diseases and their health professionals faced challenges, including delays in diagnosis, difficulties accessing treatments and finding the right care.
“We are committed to continuing to invest in research to find the answers to these challenges,” Mr Hunt said.
The media release said that trials targeting low survival cancers and diseases with higher relative mortality rates, such as mesothelioma, pancreatic and lung cancer and/or spinal muscular atrophy and other low survival conditions, could be funded under the program.
The Government said that the funding was available under the Medical Research Future Fund Low Survival Cancers and Diseases Grant Opportunity.
Application close on April 18, 2018 and details for applicants are available at: https://www.nhmrc.gov.au/grants-funding/apply-funding.

OBJ

OBJ says a 24-patient study shows that its Active Kneeguard magnetic transdermal system reduces osteoarthritis pain and improves movement.
OBJ said that Curtin University’s Prof Tony Wright reported that the randomized, double-blind study compared 48-hour administration of a magneto-phoresis enhanced transdermal ibuprofen (5%) patch to placebo trialled on six male and 18 female volunteers with medically diagnosed painful knee osteoarthritis.
The company said the primary outcomes were the visual analogue scale (VAS) rating of movement pain and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores, with secondary outcomes pain at rest and stiffness.
OBJ said the study sought to show its magnetic array-back hydrogel technology could be used with third party therapeutic drugs such as ibuprofen.
The company said there were significant differences between the active patch and the placebo patch for all primary outcomes with VAS for movement pain ($p < 0.001$), WOMAC pain score ($p = 0.004$) and WOMAC function score ($p = 0.003$), indicating that patients had less pain and improved function during the 48-hour active patch session.
OBJ said there were significant improvements across most of the secondary outcome measures and 18 of the 24 patients (75%) reported no skin reactions to either placebo or active patches, with slight skin redness reported by five active patch participants and six placebo patients, all associated with the adhesive tape rather than the gel.
Prof Wright said that it was “clear that the Active Kneeguard device containing ibuprofen (5%) with magneto-phoresis produced a significantly greater reduction in pain and improvement in function than the placebo device”.
“This was particularly the case for movement related pain,” Prof Wright said. “There was also a clear improvement in function based on the WOMAC function score.”
“The anti-inflammatory effect of ibuprofen may also be linked to the improvement in stiffness … reported by many participants, and the reduction in pressure sensitivity indicated by the significant improvement in pressure pain thresholds,” Prof Wright said.
OBJ said that 22 of the 24 patients (92%) “considered themselves either better or much better following the active patch treatment”.
OBJ was up 0.1 cents or 2.9 percent to 3.5 cents with 4.3 million shares traded.

ADMEDUS

Admedus says it has a three-year purchasing agreement for cardiovascular surgery and vascular repair with an unnamed US group purchasing organization.

Admedus said the agreement would be effective from April 1, 2018 allowing it to promote its Cardiocel and Vascucel Adapt-treated cow patch products to more than 1,500 hospitals who were part of the organization's $US35 billion network.

The company said it was one of two parties "awarded a purchasing agreement to share the estimated $US5.2 million per annum spend".

Admedus chief executive officer Wayne Paterson said the agreement was "a significant opportunity for Admedus and delivers on a commitment that was made at our [annual general meeting] in November 2017 to expand our market share in the US through a partnership with a major compliant [group purchasing organization]".

"In our most recent financial report we signalled aggressive US growth targets for 2018 and this agreement strengthens our ability to achieve that," Mr Paterson said.

Admedus said that it "looks forward to moving up the supply chain and claiming a greater share of the cardiovascular surgery and tissue repair market in the US".

Admedus was up one cent or 3.85 percent to 27 cents with 2.3 million shares traded.

RESAPP HEALTH

Resapp says its revised US paediatric respiratory diagnosis study has recruited 640 of the intended 1,667 patients at the three hospital sites.

Resapp said the Smartcough-C-2 study would evaluate the Resappdx smartphone application in the diagnosis of childhood acute respiratory disease using cough sounds.

The company said that independent quality assurance of the audio recordings had been performed on-site and a sample of the recordings had been reviewed by Resapp and both reviews would continue throughout the study to ensure that audio quality was maintained.

Last year, the 1,245-patient Smartcough-C trial failed to meet its endpoints, with the company saying that "contrary to instructions and training, a high number of patients were treated before clinical research staff recorded their cough sounds [and] a high number … were also found to contain [other] cough sounds or an unacceptable amount of background noise and interference" (BD: Aug 9, 2017).

In September, the company said it had upgraded the trial protocols and algorithms and this year re-started the trial as Smartcough-C-2 (BD: Sep 4, 2017; Jan 21, 2018).

Resapp chief executive officer Dr Tony Keating said that recruitment exceeded the rate time last year, in part due to this year's worse-than-normal flu season in the US.

"We also note that the improvements we made in training and processes are yielding high quality audio data," Dr Keating said.

Dr Keating said he expected the results of the study by "the middle of this calendar year".

Resapp was up 1.4 cents or 12.0 percent to 14 cents with 15.4 million shares traded.

DIMERIX

Dimerix says it has established an unmarketable parcel facility for holders of 3,703 shares or fewer, worth $500 or less, on the record date of March 8, 2018.

The company said that the number of shares was calculated on the closing price of 13.5 cents, with the price investors would receive to be determined by when and how the shares were sold, but did not disclose how many unmarketable parcels were held, nor the total number of shares involved.

Dimerix was up 0.5 cents or 3.7 percent to 14 cents.

MESOBLAST

The Capital Group says it has increased its substantial holding in Mesoblast from 25,488,187 shares (7.856%) to equivalent to 42,591,080 shares (9.0%).
The Los Angeles, California-based Capital Group said that between March 24, 2015 and March 7, 2018 it bought 14,838,893 shares for an average price of $1.839 and on November 13, 2015 bought 452,800 American depository receipts, equivalent to 2,264,000 shares for $US8.00 ($A11.24) a share, equivalent to $2.48 per Australian share.
Mesoblast fell nine cents or 5.1 percent to $1.68 with 4.2 million shares traded.

VIRALYTICS

Tokyo's Mitsubishi UFJ Financial Group with Morgan Stanley and subsidiaries say they have reduced below the five percent substantial mark in Viralytics.
Last week, the New York, London and Sydney based-Morgan Stanley said that it became substantial with 21,085,696 shares or 7.58 percent buying shares between October 30, 2017 and February 28, 2018 and receiving "collateral" including 9,600,000 shares on February 28 for $15,847,143 or $1.65 a share, with an identical notice filed later by Mitsubishi as a related party (BD: Mar 5, 2018).
Today, Morgan Stanley said it sold shares between March 1 and 6, 2018 with the single largest sale 7,500,000 shares for $12,562,500 or $1.675 a share.
In February, Merck Inc (Merck Sharp and Dohme) said it would pay $502 million to acquire the company, or $1.75 a share (BD: Feb 22, 2018).
Viralytics was unchanged at $1.675.