Biotech Daily

Friday March 15, 2019

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market slipped 0.07 percent on Friday March 15, 2019, with the ASX200 down 4.4 points to 6,175.2 points. Nineteen of the Biotech Daily Top 40 stocks were up, 10 fell, eight traded unchanged and three were untraded.

Genetic Signatures was the best, up 14.5 cents or 13.7 percent to $1.205, with 175,856 shares traded. Antisense climbed 8.6 percent; Cynata was up 6.55 percent; Avita, Imugene and Mesoblast were up more than five percent; Proteomics improved 4.9 percent; Starpharma and Uscom were up more than three percent; Impedimed, Prana, Pro Medicus and Telix rose more than two percent; Actinogen, Kazia, Medical Developments, Nanosonics and Opthea were up more than one percent; with Clinuvel and Cochlear up by less than one percent.

Osprey led the falls, down one cent or 8.7 percent to 10.5 cents with 2.5 million shares traded. Optiscan fell four percent; Benitec, Compumedics, Ellex, LBT, Orthocell, Prescient and Resmed shed three percent or more; Volpara was down 1.6 percent; with CSL and Paradigm down by less than one percent.

DR BOREHAM'S CRUCIBLE: MESOBLAST

By TIM BOREHAM

ASX code: MSB; **Nasdaq code (American depository receipts):** MESO

ASX Share price: $1.27

ASX Market cap: $633.3 million

ASX shares on issue: 498,626,208

Nasdaq ADRs on issue: 99.8m.

Chief executive officer: Prof Silviu Itescu

Board: Brian Jamieson (chairman)*****, Prof Itescu, William Burns, Donal O'Dwyer, Dr Eric Rose, Michael Spooner, Joseph Swedish, Shawn Tomasello

***** Mr Jamieson retires at the end of March. His successor as chairman is yet to be announced.

Financials (December half): revenue of $US13.5 million ($A18.8 million), loss of $US44.1 million ($A61.5 million), cash balance $US77 million ($A108 million)

Identifiable major shareholders: M&G Investment Group 13.7%, Prof Silviu Itescu 14.4%, Capital Group 7.95%, Thorney Holdings 5.1%.

Mesoblast founder and CEO Prof Silviu Itescu says he's "95 percent" certain the stem cell drug developer is on the cusp of doing what no other Aussie biotech in phase III trial stage has done in its own right: winning US Food and Drug Administration approval for a new therapy.

In which case it's 95 percent certain that Mesoblast should be worth a lot more than its current depressed valuation - perhaps many times more.

The drug in question is Remestemcel-L, a treatment for graft versus host disease (GvHD) that afflicts half of all allogeneic bone marrow transplant recipients. Via its Japanese partner JCR Pharma, Mesoblast won Japanese approval and Temcell is generating royalties for Mesoblast.

Mesoblast is currently investing in a US sales force to sell the GvHD drug. Because half of bone marrow procedures in the US are carried out by 15 centres, it doesn't involve too many feet on the ground.

Prof Itescu says US approval would open up more than a market for which there is no other treatment.

“GvHD for us will be a bellwether for the whole platform,” he says. “It will send a signal that US regulators are comfortable with mesenchymal stem cells, our manufacturing capability and safety.”

The program is based on mesenchymal stem cell assets acquired from US pharma group Osiris Therapeutics in October 2013, for which Mesoblast paid $US50 million in cash and scrip plus $US50 million in milestones.

Prof Itescu’s own developed cells are called mesenchymal precursor cells and they are in development for everything from congestive heart failure, lower back pain, arthritis and (previously) diabetes.

A tortured path

The world biggest listed player in mesenchymal stem cells and so-called precursor cells, since listing in 2004, Mesoblast has had more false starts than the Sydney to Melbourne fast rail.

From a peak valuation of $2.5 billion, Mesoblast’s market cap has withered to around $600 million. Culprits include a heart trial that failed to meet primary endpoints, a badly executed Nasdaq listing and Teva’s decision to walk away from the heart program.

Or maybe the whole darn thing is just taking too long.

Still, Mesoblast is in the unprecedented position of having two approved therapies on market, while it’s also in the throes of two phase III trials.

The company has also scheduled a pow-wow with the FDA to discuss potential fast track approval for its heart drug Revascor, as a preventative for gastrointestinal bleeding in artificial heart patients.

Mechanism of action

Using a proprietary process, Mesoblast selects precursor and stem cells from the bone marrow of healthy adults, creating a master cell bank. This cell kitty is then expanded into thousands of doses for off-the-shelf use, without the need for tissue matching.

Mesoblast is targeting a common market across all its disease indications: inflammation.

In the case of heart disease, tissue macrophages churn our inflammatory factors that damage heart muscle, cause fibrosis and vascular dysfunction.

The stem cells respond to severe inflammation by switching the culprit macrophages ‘off’ and converting them to nice cells that actually protect the heart muscle.

“This is the central mechanism in each of our disease states: heart failure, back pain, GvHD and rheumatoid arthritis,” Prof Itescu says. “We have the potential to make a big difference in some very big disease states where inflammation is central.”

What's what at Mesoblast

Mesoblast's approved therapies are for the aforementioned Temcell in Japan, as well as for perianal fistulas in Europe (renamed Alofisel for that market).

The fistulas are the number one surgical complication for Crohn's disease sufferers, occurring in about one in every 10 patients.

Ahead of a commercial launch in Europe, Mesoblast's global partner Takeda is negotiating pricing and reimbursement and also undergoing phase III fistula trials in the US.

"It's not one of our core products but it demonstrates that our intellectual property [IP] is the dominant IP in the mesenchymal stem cell space," Dr Itescu says.

Mesoblast is funding two phase III trials off its own bat in view of FDA filings: a whopper 566-patient one for chronic heart failure and a 404-patient effort for chronic lower back pain caused by disc degeneration.

Via its Chinese partner Tasly, Mesoblast is seeking Chinese approval for a phase III chronic heart failure trial.

Have a heart

The key motivation for the heart trial is that current medications such as beta blockers and statins have been around for 20 years or more. Meanwhile, heart disease is growing at a faster rate than ever with eight million new patients expected by 2030 in the US alone.

"We are targeting patients with class three or four disease, the sickest 15 to 20 percent of patients who have failed standard-of-care drugs," Prof Itescu says.

"Once you are in class three heart failure the likelihood of death over the next two years is as high as 20 percent. Once you are class four or end-stage heart failure, your chance of mortality in 12 months is 50 percent."

He says any Tasly heart trial should generate data to support an FDA filing, or the US data could be used to support a Chinese application. "The closer they are in terms of patient population and endpoints the easier it is to use both filings," Dr Itescu says.

The point about endpoints

"Primary endpoint" is a sensitive term at Mesoblast's Collins Street HQ after a 159-patient trial of Revascor for end-stage patients using left ventricle assist devices (LVADs or heart pumps) came a cropper last year.

Well, in the eyes of the market it did, because the shares tumbled 28 percent.

In short, the trial - carried out by independent investigators at New York's Mt Sinai School of Medicine and funded by the US Government National Institutes of Health - did not meet its primary endpoint of temporarily weaning patients from the LVADs.

But Prof Itescu stresses the "academic" endpoint was set by the investigators - not Mesoblast - and was never viewed by the FDA as clinically relevant.

"That [weaning] was not something of any interest to us," he says. "What we were interested in, based on FDA guidance in writing, was reducing the major clinically meaningful problem of recurrent hospitalizations from major gastrointestinal bleeding."

"And we did. We reduced bleeding rates by 76 percent and hospitalization by 65 percent and these numbers were identical to an earlier pilot trial."

Mesoblast is now using an "innovative" endpoint that measures hospitalizations - a measure not targeted in early stage heart patient trials because thousands of patients are required to show a statistically valid result.

Under what's known as 'joint frailty' model commonly used in cancer patients, the total burden of the disease is taken into account.

The secondary endpoint - the time to and incidence of mortalities - is simple enough. The ideal data package will result in reduced deaths and hospitalizations, but not reduced hospitalizations because more of the patients are dying.

Finances and performance

Mesoblast lost a cool $US44.1 million during the half, on revenue of $US13.5 million (including $US11 million of milestone payments from Tasly).

But with a cash balance of $US92 million, Mesoblast is well placed to absorb inevitable further losses as the phase III trials advance. The December balance of $US77 million was bolstered by a payment of $US15 million in January from Hercules Capital, triggered after the company met its bleeding and hospitalization secondary heart endpoints.

Given Mesoblast's sickly share price, management has steered clear of equity funding in favor of innovative non-dilutive debt funding.

One is a facility with Novaquest, by which the capital is not paid until the company reaps revenue from Remestemcel in the US.

"This sort of financing does not exist in Australia but is commonplace in the US," Prof Itescu says. "When we have a strong share price we would probably do equity. The good news is that in the US structured financing is very attractive."

Over the last decade Mesoblast's ASX shares have traded as high as $9 (October 2011) and as low as $1.03 (December last year). Around eight percent of Mesoblast stock is 'shorted' which means it's in the hands of arbitrageurs who have sold the stock in the hope of buying it at a lower price.

NASDAQ ‘victory’

When Mesoblast dual-listed on the Nasdaq in November 2015 - accompanied by a $US63m capital raising - it was assumed the American depositary receipts would benefit from those sophisticated Yankee investors re-rating the stock.

It didn’t pan out that way - the shares dropped by one-third - but the company claims victory anyway.

Why? The primary aim of the exercise was to enhance liquidity and this is what occurred. The twist is that the boosted volumes have related to the ASX ‘home’ stock, not the Nasdaq ADRs. But the Nasdaq listing has removed the impediment of most US funds being confined to stocks subject to US governance.

Dr Boreham’s diagnosis:

Mesoblast has its fans and detractors - possibly not much in between - and finally the company is at a juncture where one camp will be proved right and the other wrong.

The US institutions covering the stock are firmly in the bullish camp: Cantor Fitzgerald ascribes a ‘price target’ for the ADRs, currently trading at $US4.39 a share, of $US23. Maxim Group and Oppenheimer guesstimate they’re worth $US16 and $US14, respectively.

Despite its zeal, Cantor Fitzgerald cites the heart failure program as the biggest market opportunity, but ascribes only a 40 percent chance of success. It also notes that Mesoblast’s core patents expire in 2029.

The short-term proof lies in whether the FDA does indeed approve Remestemcel-L for GvHD and then whether it bestows fast-track status on the gastrointestinal bleeding program.

Meanwhile, the back-pain program offers a potential solution to the US scourge of opioid abuse.

Prof Itescu says the brutal truth is that 50 percent of drugs will fail after phase III stage. Even so, Mesoblast is confident of joining the pantheon of ‘Aussie global biotech champions’ alongside the likes of CSL and Cochlear.

“Australian investors need to understand [that drug development] is not for the faint-hearted,” he says. “It’s expensive, but this is how you build an industry. You can’t skimp on it and it’s not for short term returns.”

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He’s 95 percent sure he doesn’t really understand the science of stem cells but neither does the market.

GI DYNAMICS

GI Dynamics says a 61-patient study of its Endobarrier for obesity and type 2 diabetes study, found that 10 of 35 patients on insulin were able to discontinue their treatment.
GI Dynamics said that England's Sandwell and West Birmingham Hospitals principal investigator Dr Robert Ryder presented the results of the study, titled 'UK First NHS Endobarrier Service for Advanced Type 2 Diabetes and Obesity: One-Year Outcomes in All Patients Treated', at the Diabetes UK Professional Conference 2019 in Liverpool last week.
The company said that the data showed that the Endobarrier duodenal insert resulted in a statistically significant reduction in blood glucose levels measured by HbA1c, as well as body weight, liver fat and cardiovascular disease risks.
GI Dynamics said the data was collected from the first implant in October 2014 to the last explant in November 2018.
The company said that of the 61 patients, 35 were on insulin prior to treatment and at explant, 10 discontinued their use of insulin.
GI Dynamics said the most significant outcome measure was the average 2.2 percentage points reduction of HbA1c at 12 months from 9.5 percent to 7.3 percent ($p < 0.001$) with an average weight loss of 15.9kg, from 122.6kg to 106.7kg ($p < 0.001$).
The company said there were statistically significant reductions of $p < 0.001$ on all measures including body mass index (BMI), blood pressure, cholesterol and alanine amino-transferase (ALT), except for the reduction of high density lipo-protein.
GI Dynamics said that Dr Ryder analyzed the potential impact of Endobarrier on 10-year cardio-vascular disease risk for patients with type 2 diabetes and obesity and found that about "eight of 100 patients would avoid coronary heart disease or a stroke event over the next 10 years".
"The final outcome from this study … suggests Endobarrier can provide significant improvements for patients with long-standing poorly controlled diabetes and obesity, who have been unable to manage their diabetes with standard treatment options," Dr Ryder said.
"Further evidence and research suggest Endobarrier contributes to the reduction of other comorbidities associated with type 2 diabetes and obesity," Dr Ryder said.
GI Dynamics chief executive officer Scott Schorer said the data "continues to develop the breadth of support for clinical efficacy of Endobarrier in a real-world clinical setting".
"The significant reduction of HbA1c, weight and improvement in numerous markers, including reduction in cardiovascular risk and elimination of insulin use for 28 percent of patients, is substantial," Mr Schorer said.
GI Dynamics was up 0.3 cents or 20 percent to 1.8 cents.

EYEPOINT PHARMACEUTICALS (FORMERLY PSIVIDA CORP)

Eyepoint says revenue for the six months to December 31, 2018 was up 122.2 percent to $US2,928,000 ($A4,135,020) with net loss after tax up 280.1 percent to $US44,720,000 ($A63,155,120).
Last month, Eyepoint said it launched Yutiq, formerly known as Durasert, for posterior segment uveitis in the US (BD: Feb 5, 2019).
Eyepoint said diluted loss per share was up 89.3 percent from 28 US cents to 53 US cents at December 31, 2018 and it had cash and cash equivalents of $US42,261,000 at December 31, 2018 compared to $US38,776,000 at June 30, 2017.
Eyepoint fell 13 US cents or 5.02 percent to $US2.46 ($A2.46) with 399,578 shares traded.

NEXT SCIENCE

Next Science says it hopes to raise $35 million at $1.00 a share to commercialise its Xbio anti-bacterial technology and list on the ASX under the code NXS in April.

The Sydney-based Next Science said that the 35,000,000 shares would be 19.54 percent of the issued share capital implying a market capitalization of $179.1 million on completion of the initial public offer.

The company said it was founded by chief technology officer Dr Matt Myntti in 2012 and its non-toxic technology platform had “proven efficacy in eradicating biofilm-protected bacteria” which accounted for 90 percent of all bacteria, including the antibiotic-resistant methicillin-resistant Staphylococcus (golden staph), Escherichia coli (E coli) and Staphylococcus.

Next Science said the Xbio platform destroyed biofilms, the surface films formed by bacteria to act as shields, and treated infections by making the bacteria more vulnerable to attack by antimicrobials, antibiotics and the body’s natural immune defences.

The company said that Xbio acted as a protective barrier against bacterial infections and provided optimal healing conditions by keeping wounds moist.

Next Science said that it had four US Food and Drug Administration-approved Xbio-based products on sale in the US: Bactisure, a sterile lavage to remove biofilm and bacteria from open surgery; Blastx, an antimicrobial wound gel for chronic wounds; Torrentx, an antimicrobial wound wash for use in accident and emergency departments and approved by the FDA as an over-the-counter drug; and Surgx, a sterile wound gel to help reduce surgical site infections.

The company said it had distribution agreements with Zimmer Biomet for Bactisure, and 3M Company for Blastx.

Next Science chairman George Savvides said the Xbio technology “could change the way chronic wound infections are treated and prevented in the future”.

A spokesperson for the company said that chief executive officer Judith Mitchell formerly worked for Johnson & Johnson and Cochlear.

The spokesperson said the board included Lang Walker investment director and former Neuren director Bruce Hancox, with companies of which Lang Walker is the beneficiary holding 43 percent of the company following the initial public offer.

“The funds raised from the IPO will be used for development activities across medical devices, over-the-counter drugs and prescription pharmaceutical,” Ms Mitchell said.

“Our aim is to launch four more Xbio-based products by the end of … 2019, taking the total to eight, with additional products in the development pipeline for rollout over a number of years,” Ms Mitchell said.

Next Science said the offer was expected to close on April 4, and the company hoped to list on the ASX on April 29, 2019 under the code NXS.

The company said that Patersons Securities was the lead manager for the offer and the prospectus was available at: www.nextscience.com.

Next Science is a public unlisted company.

SUDA PHARMACEUTICALS

Suda says its anagrelide has a potential role in cancer treatment.

Suda said it could be used as a chemo-preventative product by reducing platelet numbers, thereby reducing “the proliferative and protective effect that platelets exhibit on metastatic cells”.

Suda was unchanged at half a cent with 1.1 million shares traded.

VICTORIA GOVERNMENT, PRAXIS PRECISION MEDICINES

The Victoria Government says the Cambridge, Massachusetts-based Praxis Precision Medicines will establish its Asia-Pacific headquarters in Parkville, inner Melbourne.
A media release from Victoria Minister for Economic Development and Industrial Relations Tim Pallas said Praxis was a biotech company founded on research with the Parkville-based Florey Institute of Neuroscience and Mental Health to deliver new medicines for patients with disorders including epilepsy, autism and mental illness.
Praxis founder and chief executive officer Dr Kiran Reddy said that "with the help of the Victorian Government, we've been able to build relationships with Victoria's renowned research institutes and skilled partners that has helped us to establish our footprint here and access local talent".
The Government said the new research centre would create at least 100 jobs, with hundreds of local jobs expected in the expansion of Praxis' projects and clinical programs.
Mr Pallas said "more and more global players are choosing Victoria as their home base in Australia and Praxis moving to Parkville will not only create jobs and boost the economy, it will potentially improve the lives of millions of people".

LATROBE UNIVERSITY, WINTERMUTE BIOMEDICAL

Melbourne's Latrobe University says antibiotics company Wintermute Biomedical has moved its US operations to Latrobe's Research and Innovation Precinct.
Latrobe University said Wintermute had developed and patented a broad-spectrum antibiotic with potential in treating a wide range of infectious diseases, including skin diseases and would take the drug to Australian human clinical trials.
Latrobe said Wintermute chief executive officer Dr Geoff Rogers, who won the Prime Minister's Prize for New Innovators in 2018 and chief operating officer Dr Priscilla Rogers were from Melbourne.

CLINUVEL PHARMACEUTICALS

Clinuvel says it has discussed an appeal and a managed access deal for Scenesse for erythropoietic protoporphyria with the UK National Institute of Health and Care Excellence.
Clinuvel said it met with the National Institute of Health and Care Excellence (NICE) Highly Specialised Technology Committee to evaluate Scenesse for erythropoietic protoporphyria (EPP) in Manchester on March 14, 2019, the third meeting with the committee since 2017.
The company said it discussed the grounds of appeal upheld by NICE in 2018 and the possibility of a managed access agreement for Scenesse for the prevention of phototoxicity in adult erythropoietic protoporphyria patients (BD: Oct 10, 2018).
The company said the committee would issue new final evaluation documents, but timelines had not yet been disclosed.
Clinuvel was up 17 cents or 0.6 percent to $28.81 with 708,515 shares traded.

BIONOMICS

Bionomics says interim executive chairman Dr Errol De Souza will continue as executive chairman until June 30, 2019.
Bionomics said Dr De Souza's salary would be $18,000 a month for 10 days a month, equivalent to $216,000 a year for 10 days a month for 12 months.
Bionomics was up half a cent or 2.8 percent to 18.5 cents.

DORSAVI

Dorsavi says it will reduce costs by up to 40 percent, including a 28.5 percent cut to chief executive officer Dr Andrew Ronchi's base salary.
Dorsavi said that Dr Ronchi agreed to a pay cut from $US310,000 ($A437,627) to $US221,500 ($A312,691.55).
The company said it would reduce corporate and marketing overheads and would focus spending on its existing core products for large multi-national company applications.
The company said non-executive directors would accept options instead of directors' fees from March 1, 2019.
Dorsavi was unchanged at 3.5 cents.

SHAREROOT

Shareroot says it has appointed Michelle Gallaher as its chief executive officer.
Shareroot said Ms Gallaher co-founded The Social Science, a company she sold to Shareroot last year, continuing on as managing director.
The company said Ms Gallaher was involved with the Media Consent project, "a platform that integrates data from social media wearables and clinical trials" (BD: Jan 9, 2019).
Shareroot said Ms Gallaher was formerly the chief executive officer of Bio-Melbourne Network and co-founded the not-for-profit advocacy group Women in STEMM Australia and skincare start-up company Skinlife.
The company said Ms Gallaher was a fellow of the Australian Institute for Management, won the Telstra Victorian Business Woman of the Year award and Victorian Entrepreneur of the Year award in 2017, and in 2018 was inducted into the Victorian Honor Roll for Women.
Shareroot was up 0.05 cents or 50 percent to 0.15 cents with 3.3 million shares traded.