Biotech Daily

Friday December 3, 2021

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: RESONANCE UP 5%; PRESCIENT DOWN 6.5%**

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*** TOTAL BRAIN LOSES CFO EMIL VASILEV; NEW CFO WANTED**

MARKET REPORT

The Australian stock market was up 0.22 percent on Friday December 3, 2021, with the ASX200 up 16.0 points to 7,241.1 points. Sixteen of the Biotech Daily Top 40 stocks were up, 14 fell and 10 traded unchanged.

Resonance was the best, up 0.5 cents or 4.8 percent to 11 cents, with 602,285 shares traded. Actinogen improved four percent; Compumedics, Kazia, Nova, Pro Medicus and Starpharma climbed three percent or more; Neuren, Pharmaxis and Polynovo rose more than two percent; Genetic Signatures, Resmed and Universal Biosensors were up more than one percent; with Avita, Clinuvel, Medical Developments and Nanosonics up by less than one percent.

Prescient led the falls, down 1.5 cents or 6.5 percent to 21.5 cents with 1.5 million shares traded. Alterity fell 4.2 percent; Cyclopharm, Mesoblast and Osprey lost more than three percent; CSL, LBT, Patrys and Volpara shed more than two percent; Cochlear, Cynata, Immutep, Imugene and Paradigm were down one percent or more; with Proteomics and Telix down by less than one percent.

DR BOREHAM'S CRUCIBLE: MESOBLAST

By TIM BOREHAM

ASX code: MSB
Nasdaq code (American depository shares): MESO

ASX shares on issue: 648,696,070
Nasdaq ADSs: 129,739,214

ASX share price: $1.555; **Market cap:** $1.01 billion

Chief executive officer: Prof Silviu Itescu

Board: Joseph Swedish (chair), Prof Itescu, William Burns, Donal O'Dwyer, Dr Eric Rose, Michael Spooner, Philip Facchina, Shawn Cline Tomasello

Financials (September quarter 2021): revenue $US3.59 million (up 175%), loss of $US22.7 million (previously a $US25.3 million deficit), cash balance $US116.0 million (down 15%), borrowings $US96.4 million (up 2.2%)
Year to June 30, 2021: revenue of $US7.46 million (down 77%), loss of $US98.8 million (previously $US77.2 million deficit), cash balance $US136.9 million (up 5.8%), debt $US94.24 million (up 5%) - $US1.00 = $A1.41

Identifiable major shareholders: Prof Silviu Itescu 10.8%, M&G Investment Group 8.2%, Thorney Holdings 5.3%.

When we last covered the stem cell developer in March 2019, the world was a different place in which medical knowledge pertaining to viruses and vaccines was the preserve of virologists and epidemiologists (which, by the way, no one could spell).

But as our former French friends say: *plus ça change, plus c'est la même chose*.

At the time, Mesoblast founder and CEO Prof Silviu Itescu was "95 percent" certain the company would do what no other Aussie biotech in phase III trial stage had achieved. And that was winning US Food and Drug Administration (FDA) approval for a new therapy.

As it happened, that accolade went to the public, not-for-profit Medicines Development for Global Health and Mesoblast is still awaiting its maiden FDA approval, for its proposed treatment for children's graft-versus-host disease (GvHD) called remestemcel-L.

The company got awfully close, with an FDA oncological expert committee overwhelmingly recommending approval, but the FDA itself would not budge and demanded at least one additional trial.

Then Covid hit and Mesoblast entered the race to develop an effective treatment for the respiratory effects of Covid-19 and is pursuing late-stage treatments for chronic heart failure and chronic lower back pain.

The company is extremely keen on GvHD approval because it will show the FDA is comfortable with its mesenchymal stem cell platform, acquired from US pharma group Osiris Therapeutics in 2013. In turn, this will help its Covid-19 program.

The story to date

For close to two decades Mesoblast has taken investors on a whipsaw up-and-down journey that makes New Jersey's Kinga Ka - dubbed the world's scariest roller coaster - look like a merry-go-round ride.

The world's biggest listed player in mesenchymal stem cells and so-called precursor cells, Melbourne's Mesoblast was founded by Prof Itescu. The company listed on the ASX in 2004 and then on the Nasdaq in late 2015. The Osiris assets were acquired in 2013.

Mesoblast's setbacks include the heart trial failing to meet primary endpoints, a botched Nasdaq listing and a decision by Teva to walk away from the heart program tie-up.

Where it all stems from

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, and arthritis to (previously) diabetes.

The company receives royalties or milestones on two non-US approved products: for GvHD in Japan (Temcell, marketed by JCR Pharmaceuticals) and for perianal fistulas in Europe (Alofisel, marketed by Tigenix). Perianal fistulas are a common complication of Crohn's disease.

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 out 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. The inflammation mechanism-of-action means the platform is relevant for conditions including heart failure, back pain, GvHD and rheumatoid arthritis.

The heart of the matter

In 2018, a phase III, 159-patient investigator-led trial of Revascor (rexlemestrocel-L) for chronic heart failure failed to reach its primary endpoint of temporarily weaning patients from left-ventricle assist devices. The patients had New York Heart Association (NYHA) class III or IV heart disease and had failed standard-of-care drugs.

Mesoblast shares tumbled 28 percent on the news, but the narrative quickly moved on from what Prof Itescu dubbed “academic” endpoints set by the regulators.

The company turned to data showing Revascor reduced gastro-intestinal bleeding by 76 percent and hospitalization by 65 percent. In June 2019, the company won FDA orphan drug status for the gastro-intestinal bit, but not much seems to have happened since.

In 2020, Mesoblast’s own 537-patient, phase III, cardiac trial also missed its primary endpoints, but the company said it reduced cardiac events.

In a ‘late breaking’ presentation to the American Heart Association’s pow-wow in November 2021, the co-principal investigator, and Texas Heart Institute boss, Dr Emerson Perin outlined a “significant relationship” between the presence of systemic inflammation (as quantified by a protein biomarker) and rexlemestrocel-L treatment.

‘Late breaking’ is not about a Jimmy Olsen scoop for the Daily Planet, but is original work completed after submission deadline. The contents must be deemed to be of urgent and significant scientific important.

The gist of the findings is that when combined with standard-of-care, rexlemestrocel-L reduced the incidence of cardiovascular death, heart attacks and strokes by 33 percent. This was in relation to NYHA class II and class III patients. Of the 301 patients with high inflammation, the efficacy increased to 45 percent.

The company and the FDA are discussing the way forward, with the agency likely to require a confirmatory study for the highly inflamed cohort.

Graft-versus-host disease

Graft-versus-host disease (GvHD) affects about half of all allogeneic (off-the-shelf) bone marrow transplant recipients. The company carried out three paediatric trials which in effect showed remestemcel-L improved the “dismal survival” of kids with chronic forms of the disorder.

“This is surely one of the cruelest diseases, striking - and often taking innocent, young children who have already undergone the ordeal of a bone marrow transplant,” chair Joseph Swedish told the company’s AGM this week.

Mesoblast thought FDA approval was a dead cert after an FDA advisory committee voted overwhelmingly in favor of the data, but then the agency itself requested that Mesoblast do more work.

It was thought the agency would demand an additional adult trial, but the talks now centre around quality control aspects such as potency assays to ensure consistent batches.

“We do not believe we will have to do any further clinical study for remestemcel-L and GvHD,” Prof Itescu says.

Acute respiratory distress syndrome (ARDS)

Last December, Mesoblast's data safety monitoring board (DSMB) advised to call it a day with the 223 patients recruited for its Covid trial, rather than the targeted 300. The trial pertained to ventilator-dependent patients with moderate to severe acute respiratory distress syndrome or ARDS - the cause of most Covid fatalities, and the DSMB opined the trial was unlikely to achieve the stated primary endpoint of a 43 percent reduction in ventilated patients at 30 days.

Mesoblast argued that better patient management meant that fatalities had declined overall and the issue was all about trial design.

Not one for turning, Mesoblast has ploughed on with analyzing the patient data. In July, the company said remestemcel-L reduced mortality through 60 to 90 days in the pre-specified population under 65 years old, by 48 percent. The company plans to move forward with an additional phase III trial in Covid-19 ARDS and is discussing trial protocols with the FDA.

In November 2020, Mesoblast and Novartis entered a deal to commercialize a Covid treatment. The compact, which is yet to be finalized, involves a potential $US50 million cash injection, $US25 million in equity and up to $US1.25 billion in additional milestones.

Chronic lower back pain

With 50 percent of US opioid prescriptions pertinent to chronic lower back pain, Mesoblast is targeting reduced use of these addictive substances.

In February this year, a phase III trial of rexlemestrocel-L for chronic lower back pain caused by disc degeneration also failed to meet its primary endpoints but showed the therapy provided a "safe, durable and effective" alternative, with best results when dispensed early in treatment.

A trial of 404 patients showed at least two years of pain reduction, relative to a saline placebo. Of the 168 patients prescribed opioids, there was a 40 percent reduction in opioid use over this period.

German pharma house Grunenthal has the European and Latin American rights to the back pain indication. Mesoblast is entitled to $US112.5 million ahead of a European launch, of which $US17 million has already been received. Cumulative milestone payments could reach $US1 billion.

Chronic back pain affects about 30 million Americans and 40 million Europeans.

Finances and performance

Mesoblast has a history of steep losses, but it also has been adept at raising big licks of capital when needed. The company reported a $US100 million pre-tax loss in the year to June 2021, taking losses over the last five years to $US442 million.

The company derived modest revenue from Temcell: $US7.2 million in the 2021-'21 year (up 10 percent) and $US2.4 million in the September quarter (up 90 percent year-on-year).

Following a $US110 million private placement, Mesoblast has a cash balance of $US136.9 million as of June 30 2021.

Then there's the debt. In 2018, Mesoblast entered a $US75 million facility with Hercules Capital Inc, $US50 million of which had been drawn.

In late November 2021 the company repaid the facility after negotiating a $US90 million arrangement with Oaktree Capital Management (with $US60 million drawn down). The first three years of the five-year loan are interest free.

Mesoblast also has a $US40 million eight-year facility with Novaquest, which has been $US30 million drawn at a 15 percent interest rate.

The aforementioned Novartis deal, if executed, is another source of funding.

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.

Dr Boreham's diagnosis:

It's been another frustrating 12 months for Mesoblast.

As chair Swedish told this week's pow-wow: "2021 has been a rollercoaster year for the world and a challenging year of both meaningful progress as well as some setbacks for Mesoblast."

He adds that the company's core therapies have "continued to deliver results that demonstrate their lifesaving potential in addressing four complex medical disorders".

One way of looking at Mesoblast is it's in an exciting position with three phase III trials. If the FDA approves just one of them, more meaningful revenues will flow. Broker Bell Potter estimates peak sales of $US137 million a year for the GvHD therapy.

As exemplified by investors taking a short position in the stock, the alternative view is that Mesoblast is a serial disappointer that's running out of excuses.

What's certain is that investors need to keep a tight grip on the guard rail as the roller coaster ride continues.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He has submitted many articles after deadline but is yet to cry: "hold the front page!"

REDHILL BIOPHARMA

Redhill says a 269-patient trial shows that Talicia is about 50 percent more effective in eradicating Helicobacter pylori in obese patients than active comparators.

Redhill said that Talicia, a further developed version of the Sydney-based Giaconda's Heliconda, eradicated Helicobacter pylori in patients with a body mass index of 30kg/m^2 to 40kg/m^2 at 88.1 percent compared to the active comparator at 62.9 percent ($p < 0.008$).

The company said that Talicia eradicated Helicobacter pylori in patients with a body mass index of more than 40kg/m^2 at 90.9 percent, compared to 31.8 percent for the active comparator.

In 2010, Israel's Redhill bought Myoconda (RHB-104), Heliconda (RHB-105) and Picoconda (RHB-106) from Sydney's Giaconda (BD: Aug 17, 2010).

Today, the company said that the research article, titled 'Eradication by Low-Dose Rifabutin Triple Therapy (Talicia) is Unaffected by High Body Mass Index' was published in the journal Gastrohep "showing the high efficacy of Talicia in eradicating Helicobacter pylori irrespective of patient BMI and level of obesity in clinical trials".

The article is available at: https://onlinelibrary.wiley.com/doi/full/10.1002/ygh2.494.

The research article said that Talicia was compared with placebo and the active comparator, a combination of amoxicillin and omeprazole, treated for 14 days and followed up at 28 to 59 days post-therapy.

In 2019, Redhill said that the US Food and Drug Administration had approved Talicia, an oral capsule, delayed-release combination of the antibiotics, amoxicillin and rifabutin, and a proton pump inhibitor, omeprazole (BD: Nov 5, 2019).

The company said in 2019 that Talicia was the only rifabutin-based therapy approved for Helicobacter pylori infection and was designed to address the high resistance of Helicobacter pylori bacteria to current clarithromycin-based standard-of-care therapies.

Today, Redhill said that "high BMI and obesity are known risk factors for Helicobacter Pylori eradication treatment failure".

The company said that previous studies showed that the failure rate of clarithromycin triple therapy could increase by nearly 300 percent in patients with a high BMI, from nearly 15 percent in patients with a BMI of less than 25kg/m^2 to 45 percent in subjects with a BMI greater that 25kg/m^2.

Lead author, the University of Michigan's Prof John Yung-Chong Kao said that "with more than 70 percent of American adults being overweight or obese, it is important to understand the influence of patient BMI on Helicobacter pylori eradication treatment success".

"These data support that low-dose rifabutin-containing therapy such as Talicia can be considered as a first line therapy to treat Helicobacter pylori infection particularly in patients with high BMI," Prof Kao said.

Redhill said "no cases of rifabutin resistance were identified" in the study, compared to a pooled clarithromycin resistance rate of more than 17 percent across all BMI groups.

The company said that generally, no differences were identified in the safety of Talicia across BMI groups, consistent with its overall safety profile.

Redhill chief medical officer Dr June Almenoff said that the "obese population experiences more infections and thus has more antibiotic exposure than the general population, potentially leading to higher rates of antibiotic-resistant organisms"

"Given the medical risks associated with obesity, it is especially important to use highly effective treatments such as Talicia, to provide patients with a high probability of cure with first-line treatment," Dr Almenoff said.

On the Nasdaq, Redhill was up two US cents or 0.74 percent to $US2.74 ($A3.87) with 890,093 shares traded.

CSL

CSL says that it “notes the recent speculation about [its] involvement in potential offshore [mergers and acquisitions] activity.

In an announcement to the ASX titled ‘Response to speculation’, CSL said it “regularly assesses strategic opportunities that can improve its business, improve the health of people around the world and provide value to shareholders”.

The company said that there was no certainty that any transaction would result from CSL's consideration of such opportunities and if any transaction did result, when such a transaction would occur.

The Australian Financial Review has been reporting that CSL has been allegedly raising money to acquire the St Gallon, Switzerland Vifor Pharma.

According to Six Swiss Stock Exchange Vifor Pharma had a current market capitalization of CHF8,160,750,000 ($A12,549,508,400).

Vifor Pharma’s website said Abbas Hussain was the company’s chief executive officer since August 2021 and was previously a director of CSL.

In 2017, CSL said that Mr Hussain had been appointed a director effective from February 14, 2018 and earlier this year “regretfully” accepted his resignation following his appointment to Vifor (BD: Dec 13, 2017; Jun 25, 2021).

In 2018, Cochlear said it had appointed Mr Hussain as a director and in July this year, said he had resigned (BD: Nov 20, 2018; Jul 20, 2021).

CSL fell $7.63 or 2.5 percent to $297.67 with 847,979 shares traded.

KAZIA THERAPEUTICS

Kazia says its 30-patient, phase II, clinical study of oral paxalisib as a first-line therapy for glioblastoma shows a three month overall and progression-free survival benefit.

In March 2018, Kazia said it begun its phase II trial of GDC-0084 for patients newly diagnosed with glioblastoma multiforme or brain cancer, with a focus on dose optimization (BD: Mar 29, 2018).

Today, the company said that a dose of 60mg once daily was identified as the maximum tolerated dose and selected for future studies.

Kazia said that the median overall survival in the intent-to-treat population was 15.7 months, which compared “very favorably” to 12.7 months historically reported with the use of temozolomide in this patient group.

The company said the median progression-free survival in the intent-to-treat population was 8.4 months, a “substantial increment” over the 5.3 months associated with temozolomide.

Kazia said the safety profile of paxalisib was “highly consistent” with previous studies, including hyperglycaemia, oral mucositis and skin rash among the most common drug-related toxicities.

Kazia said it expected to receive a final study report by April 2022.

Kazia chief executive officer Dr James Garner said the company was “delighted to report positive final data from the completed phase II study of paxalisib”.

“The data continue to demonstrate a clear efficacy signal and favourable safety profile, suggesting a meaningful advantage over temozolomide, the existing standard of care, and validating our decision last year to join the GBM Agile pivotal study,” Dr Garner said.

“We have gleaned invaluable insights from this trial, … [and] are increasingly also exploring additional patient populations for which a brain penetrant PI3K/mTOR inhibitor may provide significant advantages over the standard of care,” Dr Garner said.

Kazia was up 4.5 cents or 3.25 percent to $1.43.

ALCIDION GROUP

Alcidion says through a consortium, it has received a $23 million, six-year contract to supply Miya Precision to the Australian Government.
Alcidion said the consortium was led by the Reston, Virginia-based engineering and information technology consulting from Leidos through its subsidiary Leidos Australia.
The company said it would provide longitudinal health records through its Miya Precision product, which would aggregate data from the consortium partners and other systems to establish a consolidated view of every participant's health status and history.
Alcidion said Miya Precision facilitated healthcare communication and task management and delivered clinical decision support for patients.
In April, the company said it was part of a consortium in a contract for stage one of two stages of the Australian Defence Department Healthcare Knowledge Management project, providing its Miya platform to collect data (BD: Apr 15, 2021).
Today, Alcidion said project was expected to begin this month with further options to take up Miya observations and assessments and options to renew for up to 15 years with a possible total contract value for the contract with Leidos of about $50 million.
Alcidion was up 2.5 cents or 7.9 percent to 34 cents with 3.5 million shares traded.

RESONANCE HEALTH

Resonance says it has submitted a 510(k) application to the US Food and Drug Administration for its artificial intelligence enabled Liversmart test.
Resonance said Liversmart combined its two regulatory-cleared products, Ferrismart and Hepafat-artificial intelligence into a single multi-parametric magnetic resonance imaging (MRI) session, avoiding the need for multiple MRI appointments, for "a more complete and comprehensive assessment of a person's liver".
The company said that the FDA application process could take between several weeks and several months "depending on feedback received from the FDA including whether the FDA has substantive questions on the Liversmart dossier and whether additional information is required".
Resonance said Liversmart may be eligible for two new US category III current procedural technology (CPT) codes recently published by the American Medical Association which would become active on January 1, 2022.
Resonance was up half a cent or 4.8 percent to 11 cents.

STARPHARMA

Starpharma says it has distribution agreement with Healthco Australia Pty Ltd to supply one million units of its Viraleze anti-viral nasal spray to Vietnam in the first year.
On Wednesday, Starpharma said Viraleze had been registered for sale in Vietnam and would be launched this week with an initial 100,000-unit contract (BD: Dec 1, 2021).
Today, Starpharma said the distribution agreement was between Perth's Healthco Australia with Ho Chi Minh City's Truong Bao Land and Hanoi's Nam Thanh Trade and Medical Services Company Limited.
Starpharma said the agreement included a commitment to purchase a minimum of one million units of Viraleze units in the first year, "with ongoing performance obligations".
The company said the agreement was for an initial term of five years with provisions for annual extensions, with Viraleze available in Vietnam to retail consumers, clinics, hospitals and pharmacies through local medical distribution networks.
Starpharma was up 3.5 cents or three percent to $1.205 with 1.1 million shares traded.

IDT AUSTRALIA

Sydney's Credit Suisse Holdings says it has become a substantial shareholder in IDT Australia with 12,936,807 shares or 5.39 percent.
Credit Suisse said it bought and sold shares between August 2 and November 30, 2021, with the single largest acquisition 1,469,879 shares for $1,015,833 or 69.1 cents a share.
IDT fell 1.5 cents or 2.8 percent to 52 cents.

TOTAL BRAIN

Total Brain says chief financial officer Emil Vasilev has left the company to "pursue other opportunities".
Total Brain said its finance function would be managed by Sydney's Shaw Downie Chartered Accountants.
The company said it would conduct a search for a new chief financial officer "over the coming months".
Total Brain fell half a cent or 4.55 percent to 10.5 cents.