Biotech Daily

Friday May 26, 2023

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: NEXT SCIENCE UP 24.5%; IMMUTEP DOWN 15%**

*** DR BOREHAM'S CRUCIBLE: EBR SYSTEMS INC**

*** FISHER & PAYKEL REVENUE DOWN 6% TO $1.5b, PROFIT $233m**

*** MESOBLAST Q3 REVENUE DOWN 4% TO $3m, LOSS DOWN 13% TO $28.5m**

*** IMMUTEP: 5 OF 37 EFTI HEAD, NECK CANCER COMPLETE RESPONSES**

*** OPTISCAN REQUESTS 'CAPITAL RAISING' TRADING HALT**

*** HYPERION TAKES 5% OF FISHER & PAYKEL HEALTHCARE**

*** MEDADVISOR: KATE HILL, COTIVITI'S BRETT MAGUN DIRECTORS**

*** BIO-MELBOURNE MEDICAL TECHNOLOGY MANUFACTURING FORUM**

MARKET REPORT

The Australian stock market was up 0.23 percent on Friday May 26, 2023, with the ASX200 up 16.6 points to 7,154.8 points. Seventeen of the Biotech Daily Top 40 stocks were up, 14 fell, eight traded unchanged and one was untraded.

Next Science was the best, following its AGM, up 12 cents or 24.5 percent to 61 cents, with 168,407 shares traded.

Cynata climbed 14.8 percent; Volpara was up 10.2 percent; Patrys rose 9.1 percent; Impedimed improved 7.1 percent; Pharmaxis was up six percent; Orthocell and Resonance were up more than five percent; Atomo and Mesoblast climbed more than three percent; Dimerix, Paradigm and Proteomics rose more than one percent; with Cochlear, Emvision, Genetic Signatures, Polynovo and Pro Medicus up by less than one percent.

Immutep led the falls, down 5.5 cents or 14.9 percent to 31.5 cents, with 7.2 million shares traded. Both Alcidion and Antisense lost 4.8 percent; Avita, Medical Developments and Opthea shed more than two percent; Micro-X, Neuren, Prescient, Resmed, Telix and Universal Biosensors were down one percent or more; with Clinuvel, CSL, Cyclopharm, and Nanosonics down by less than one percent.

DR BOREHAM'S CRUCIBLE: EBR SYSTEMS INC

By TIM BOREHAM

ASX Code: EBR

Share price: $1.165; **Shares on issue (CDIs):** 270,838,632; **Market cap:** $315.5 million

CEO: John McCutcheon

Board: Allan Will (executive chair), John McCutcheon, Dr Chris Nave, Trevor Moody, Dr Bronwyn Evans, Dr David Steinhaus, Karen Drexler

Financials* (calendar 2022 year): income nil, net loss $US33 million (previous loss $US39.8 million), cash balance $US63.5 million (down 19%)**

* $US1.00 = 68 Australian cents

** Includes $US48.07 million of marketable securities (government and corporate bonds).

Major identifiable shareholders: HESTA 17%, Hostplus 17%, Brandon Capital (partners and clients) 7.7%, MH Carnegie Funds 14.87%, Split Rock Partners LP 9.87%.

A heartfelt round of applause for EBR Systems, which now has the requisite evidence to seek US approval for its leadless device to enable stimulation of the tricky left ventricle.

On Monday, EBR revealed its 183-patient pivotal study for its Wise device - as in 'wireless stimulation endocardially' - passed the key efficacy and safety hurdles.

In the words of EBR chief John McCutcheon, the trial "crushed" both primary safety and efficacy endpoints (see below).

"It is the most significant accomplishment in our company's history and it puts us on the path to [US Food and Drug Administration] approval and commercialisation," he says.

The top-line results were presented to cardiac specialists gathered at the Heart Rhythm Society's annual meeting in New Orleans - a tough crowd indeed.

Having earlier won European marketing assent, EBR is now girding for FDA approval under the fast-track and breakthrough drug designation pathways.

About EBR

Based in Sunnyvale in California's Silicon Valley, EBR was founded in 2003 by electrophysiologist Dr Debra Echt, ultrasound scientist Dr Axel Brisken and former pacemaker engineer Richard Riley … EB&R.

Dr Echt saw a problem with leads and thought there was a better way to defibrillate. The founders then found a way to stimulate the heart leadlessly.

The Northern California-based Mr McCutcheon joined EBR in 2019. After earlier sales and marketing roles at American Hospital Supply, he worked at a number of start-ups where he discovered his entrepreneurial flair.

EBR listed on the ASX on November 24, 2021, having raised $110 million at $1.08 apiece.

Have a heart

While heart patients have long been used to the wonders of pacemakers, there's a big problem with the embedded leads of the ticker-kickers (formally known as cardiac re-synchronization therapy, or CRT devices).

CRT is the standard-of-care for moderate to severe heart failure due to desynchrony.

"This is where the right ventricle contracts before the left ventricle, resulting in reduced efficiency and the heart not pumping enough blood to meet the body's needs," Mr McCutcheon says.

About four percent of pacemaker leads fail every year - a better performance rate than mobile phone leads but with more dastardly consequences. The longer the pacemaker is in there, the higher the chance of failure.

One reason the left ventricle is trickier is because it circulates arterial blood straight to the brain. The right side (venous blood) circulates through the lungs and is less prone to clotting. Given the left-side leads are more likely to create a clot, they are currently placed in the surrounding coronary sinus and the stimulation occurs outside the chamber (epicardial pacing).

Wise up

Wise is an implantable cardiac system to provide left ventricle pacing stimulation, in conjunction with a co-implanted system that provides right ventricular stimulation.

The size of a grain of cooked rice, the Wise device is embedded in the heart and is powered by a sub-cutaneous battery close to the ticker.

A transmitter picks up the groove of the right ventricle and sends a signal to the Wise electrode, which converts ultrasound energy to electrical energy to stimulate the left ventricle. The transmitter sits between the ribs and is flush to the skin, so is unobtrusive and not noticeable to the patient.

More than 350 patients have been embedded with the device to date, with the first Australian patient implanted in February 2018.

In essence, Wise enables CRT for patients otherwise unable to receive lead-based devices, or who are at high risk from an upgrade procedure (from implanted pacemaker or defibrillator to lead-based CRT).

Wise is the only wireless device small enough to stimulate the left side of the heart and deliver CRT.

Also, Wise will be the only therapy for patients with existing leadless pacemakers who develop pacing-induced heart failure - and about 30 percent of users do so within four years.

The company is also developing a rechargeable battery that is around one-third of the size of the current iteration and smaller than those used in standard pacemakers.

Trial nails it

Carried out in Australia, the US and the UK, the 'Solve-CRT' study was a single-arm, pivotal trial for patients with acute and chronic lead failures and high-risk upgrades.

The patients already had failed lead-based CRT and had no other options.

The primary efficacy endpoint was a 9.3 per cent reduction in left ventricular end systolic volume (LVESV), a key heart function measure.

"Patients with heart failure have dilated hearts and Solve-CRT aimed to reverse this," Mr McCutcheon says.

The safety endpoint was that at least 70 percent of patients needed to be free of complications such as vascular events, strokes, thrombosis, cardiac perforation or battery problems.

As it happened, the trial showed a 16.4 percent reduction in LVESV, with a probability score ('p' score) of 0.003.

The rate of non-complication was 80.9 percent, with an even lower p score of 0.001. In other words, these results were in no way a fluke.

Given the success, the trial has finished earlier than planned although the company will continue to invest in studies to treat bradycardia (slow heart beats).

To support its successful European approval application, EBR earlier carried out a 35-patient study which resulted in biventricular pacing (a good thing) in 97 percent of participants one month after the implant.

Who are the 'Goldilocks' patients?

In theory, Wise is relevant for all of the New York Heart Association four classes of heart failure (class I being the least sick and class IV being very ill).

Class I patients could be treated in cases where they were former class II and class III patients who received a benefit from CRT, but then subsequently had a lead failure.

“The implanter would choose to treat them now, rather than wait for them to deteriorate,” Mr McCutcheon says. “Class II and III are the ‘just right’ group where they are very sick, but not too sick.”

“We can treat Class IV, but these patients are very, very ill.”

Mr McCutcheon adds that Wise could reverse the damage created by pacemakers (pacing-induced heart failure) and prevent it, if deployed early enough.

Finances and performance

Mr McCutcheon says the success of the trial results removes the “binary risk that all medical technologies face in meeting clinical regulatory hurdles”.

In other words: the trials don’t meet the primary endpoints and any amount of ‘data mining’ can’t save them.

EBR lost $US33 million ($A48 million) in 2023, an improvement on the $US40 million deficit previously but a chunky deficit nonetheless.

However, the company is sitting on cash of $US63 million, which should tide the company over to revenue stage after expected FDA approval - and sales - next year.

In addition, meeting the primary endpoints also enables the company to draw on $US20 million of debt, the second tranche of a facility provided by Chicago’s Runway Growth Finance Corporation for a five-year term.

The company drew an initial $US20 million at the time of signing the deal in July last year.

A further $US10 million can be drawn on FDA approval, but given that facility expires in June 2024 the company will not be likely to be able to avail of it.

As is usually the case, Wise’s commercial prospects will be shaped by US reimbursement, currently around $US35,000 in the US and an average of $US20,000 elsewhere.

Given the cardiac community is fairly small, EBR will sell directly in the US initially, but is amenable to using distributors elsewhere.

Valuing the stock at $1.55 a share post FDA approval, broker Morgans forecasts a $36 million loss this year and $32 million deficit in calendar 2024. Rival broker Wilsons reckons the stock is worth $1.50 a share and calculates peak sales at $US650 million per annum.

EBR shares traded at a low of 62 cents in late January this year. After Monday’s trial results they spurted like a ruptured artery by as much as 19 cents, or 21 percent to a record $1.07 a share.

Total addressable market

The company estimates the current total addressable market at $US2.5 billion, consisting of chronic heart failure ($US1 billion), high-risk upgrades ($US800 million), leadless upgrades ($US400 million) and acute lead failure ($US300 million).

There were 228,000 CRT sales globally in 2020, with the US accounting for 97,000. In 2024, this number is expected to grow to 272,000, 112,000 of them in the US.

Mr McCutcheon says that once Wise is accepted by clinicians, the device will access the $US2.5 billion-plus market.

The market grows to $US7.1 billion when first-line CRT treatment, de novo implants for bradycardia, international expansion and leadless upgrades are taken into account.

“We may also see implanters deciding to implant a combination of a leadless pacemaker and Wise, as a frontline treatment in patients they feel will benefit from totally leadless CRT,” Mr McCutcheon says.

In these cases, the patient would not have an existing pacemaker or implantable cardioverter-defibrillator (ICD).

Mr McCutcheon says with further technological advancements, Wise could displace standard CRT and become a standalone device without need for a co-implant.

Dr Boreham’s diagnosis:

The Wise devices further evolution of the pacemaker since the advent of the Furman, a box-sized device attached to mains power.

We used to laugh at the 1990s ‘brick mobile phones’, too.

While innovation will continue to occur elsewhere, Mr McCutcheon reckons the company has a decent head start on any competitors, with no rival device in the offing.

By overcoming the left ventricle problem, EBR is also a step ahead of the pacemaker/medical device giants Medtronic, Abbott Laboratories and Boston Scientific.

Mr McCutcheon says the trial results vindicate the faith of the company’s shareholders that include Mark Carnegie, Brandon Capital and industry super funds HESTA, Hostplus and Australian Super.

“Our trajectory has not always been linear - we have faced setbacks along the way,” he says. “Now EBR has huge addressable market with no direct competition, as a live CRT therapy that is complimentary to other leadless technologies.”

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. His career trajectory to date has been anything but linear.

FISHER & PAYKEL HEALTHCARE CORPORATION

Fisher & Paykel Healthcare says revenue for the year to March 31, 2023 was down 6.0 percent to $NZ1,581,100,000 ($A1,473,534,000), with profit down 33.6 percent to $250,300,000 ($A233,310,000).
Fisher & Paykel said revenue came from sales of hardware products to hospitals, including sales of its Evora mask for obstructive sleep apnoea and its homecare products.
Fisher & Paykel said it would pay a dividend on July 7 of 27.1 NZ cents a share to shareholders on the record date of June 27, 2023, up 2.3 percent from the previous year.
The company said earnings per share fell 33.7 percent to 43.3 NZ cents, net tangible assets per share rose 4.2 percent to $2.72, with cash and equivalents of $NZ121.0 million.
Fisher & Paykel fell $1.51 or 6.3 percent to $22.48 with 2.6 million shares traded.

MESOBLAST

Mesoblast says revenue for the three months to March 31, 2023 was down 3.6 percent to $US1,939,000 ($A2,965,000), with net loss down 12.7 percent to $US18,646,000 ($A28,512,000).
Mesoblast said that for the nine months to March 31, revenue fell 32.9 percent to $US5,362,000 with net loss after tax down 14.2 percent to $US59,970,000.
The company said revenue from Japanese sales of Temcell for the three months to March 31, 2023 was $1.8 million.
The company said diluted loss per share for the three months was down 22.9 percent to 2.53 US cents, with cash and cash equivalents of $US48,799,000 at March 31, 2023 compared to $US76,760,000 at March 31, 2022.
Mesoblast was up four cents or 3.85 percent to $1.08 with 2.2 million shares traded.

IMMUTEP

Immutep says five of 37 patients (13.5%) in part C of its Tacti-002 phase II trial of eftilagimod alpha for head and neck cancer have had a “complete response”.
Immutep said the trial is evaluating efti, formerly IMP321, with pembrolizumab (Keytruda) for metastatic second-line head and neck squamous cell cancer.
Last week, the company said its 114-patient, phase II trial of eftilagimod alpha with pembrolizumab for non-small cell lung cancer had a 25.0-month median overall survival (BD: May 17, 2023).
Today, Immutep said 11 of 37 patients (29.7%) had a “strong” response rate, with an overall survival rate for 17 patients (46.0%).
The company said that of the 15 patients with a PD-L1 combined positive score of more than 20, nine (or 60 percent) had a “very promising response”, while the 12-month overall survival rate was 66.7 percent, or 10 patients.
Immutep said the treatment was safe and well tolerated with no new safety signals.
The abstract is available at: https://meetings.asco.org/abstracts-presentations/218549.
Immutep fell 5.5 cents or 14.9 percent to 31.5 cents with 7.2 million shares traded.

OPTISCAN IMAGING

Optiscan says it has requested a trading halt pending an announcement “regarding a material capital raising”.
Trading will resume on May 30, 2023 or on an earlier announcement.
Optiscan last traded at 10 cents.

FISHER & PAYKEL HEALTHCARE CORPORATION

Hyperion Asset Management says it has become a substantial shareholder in Fisher & Paykel Healthcare with 29,384,189 shares or 5.07 percent of the company.
The Brisbane-based Hyperion said that between January 31 and May 23, 2023 it bought and sold shares, with the single largest purchase on May 23 of 496,876 shares for $12,913,769 or $25.99 a share.

MEDADVISOR

Medadvisor says it has appointed Kate Hill as non-executive director, with Cotiviti's US-based director Brett Magun replacing Raeann Grossman, effective May 24, 2023.
In August 2021, the South Jordan, Utah-based Cotiviti said it acquired 43,999,999 shares or 11.66 percent of Medadvsior (BD: Aug 24, 2021).
Today, the company said Mr Magun was Cotiviti's general counsel and corporate secretary and oversaw the company's legal complains functions.
Medadvisor said Mr Magun had more than 25 years as an in-house corporate attorney for companies including Virgin Money US, KPMG in the Netherlands and Bear Stearns in New York City.
The company said Mr Magun held a Bachelor of Science from Boston University and a Doctor of Jurisprudence from Brooklyn Law School.
Medadvisor said Ms Hill was previously an audit partner at Deloitte for more than 20 years, was formerly Kazia company secretary and was currently a director of Artrya and Atmo Pty Ltd.
The company said that Ms Hill held a Bachelor of Science from Bristol University.
Medadvisor was up two cents or 9.1 percent to 24 cents.

BIO-MELBOURNE NETWORK

The Bio-Melbourne Network says it will hold a forum along with its "masterclass" on medical technology manufacturing next week.
The Network said the extra event, titled 'Bio-Forum on regulatory essentials for medtech manufacturing' would include speakers from Israel's Memed, Invetech and Melbourne's CMS Scidoc (Compliance Management Solutions & Scientific Documentation).
The Bio-Melbourne Network said the forum would provide "an overview of regulatory essentials for manufacturers and [medical technology] enterprises, including compliance, traceability and evidence gathering".
The Network said the forum would cover onshore device manufacturing regulations, requirements for operating ISO13485 facilities, working with the US Food and Drug Administration and meeting compliance for US market access.
The Bio-Melbourne Network said that the Bio-Forum was a stand-alone event as well as part A of its masterclass program 'Concept to Creation: The Roadmap to Medtech Manufacturing' (BD: May 4, 2023).
The Network said that the event would be held at the Australian Centre for the Moving Image in Flinders Street, Melbourne, and online on May 30, 2023 from 7:30am to 10am, including networking. For details and registration, go to:
https://biomelbourne.org/event/bioforum-regulatory-essentials-for-medtech-manufacturing/