# Biotech Daily

Friday February 4, 2022

*Daily news on ASX-listed biotechnology companies*

*** ASX UP, BIOTECH DOWN: PROTEOMICS UP 10%; ONCOSIL DOWN 7%**

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

*** PROTEOMICS, QIMR VALIDATE OESOPHAGEAL CANCER BIOMARKERS**

*** FEDERAL $15m FOR ADELAIDE CANCER GENOMICS LABORATORY**

*** TELIX TO BE PROMOTED INTO ASX200**

*** RESPIRI, M-TELEHEALTH $33k 2nd WHEEZO ORDER; REIMBURSEMENT**

*** EXOPHARM TELLS ASX: 'AIRM NEWS MATERIAL, CLARIFICATION NOT'**

*** CLARITY RECEIVES $3.3m FEDERAL R&D TAX INCENTIVE**

*** FIL REDUCES TO 7.3% OF STARPHARMA**

## MARKET REPORT

The Australian stock market was up 0.59 percent on Friday February 4, 2022, with the ASX200 up 42.1 points to 7,120.1 points.

Thirteen of the Biotech Daily Top 40 stocks were up, 21 fell, five traded unchanged and one was untraded.

Proteomics was the best, up 10 cents or 10.2 percent to $1.08, with 56,687 shares traded. Micro-X climbed 8.7 percent; Pharmaxis was up five percent; Genetic Signatures rose 4.55 percent; Patrys was up 3.85 percent; Clinuvel rose two percent; Imugene, Kazia, Opthea, Orthocell, Resmed and Starpharma were up more than one percent; with CSL, Next Science and Pro Medicus up by less than one percent.

Oncosil led the falls, down 0.3 cents or 6.8 percent to 4.1 cents, with 1.2 million shares traded. Telix lost 5.3 percent; Avita, Cyclopharm, Emvision, Medical Developments, Neuren and Resonance were down more than three percent; Alcidion, Amplia, Antisense, Atomo, Cynata, Dimerix and Volpara shed two percent or more; Immutep, Nova Eye, Paradigm and Universal Biosensors were down more than one percent; with Cochlear Mesoblast and Polynovo down by less than one percent.

# DR BOREHAM'S CRUCIBLE: EBR SYSTEMS INC

**By TIM BOREHAM**

**ASX Code:** EBR

**Share price:** 71 cents

**Shares on issue (Chess depository instruments):** 267,925,340 CDIs

**Market cap:** $190.2 million

**Chief executive officer:** John McCutcheon

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

**Financials* (half year to June 30 2021):** income $US258,566, expenses $US10.23 million, net loss $US15.9 million, cash balance circa $A115 million (post IPO)

***** One US dollar equals A71c

**Major identifiable shareholders (% of fully diluted):** Brandon Capital (partners and clients) 19%, MH Carnegie and co 11.7%, Split Rock Partners LP 9%, Ascension Ventures 4.3%, Allan Will 2.9%, John McCutcheon 2.7%

Sick to death of faulty leads that break well before the expiry of their expected useful lives?

When it comes to mobile phone leads, we all know the dread of supporting Apple's multi-trillion market cap by constantly buying replacements.

But when it comes to embedded pacemaker leads, patients literally could be sick to death.

The nub of the problem is that electrical leads are the weakest part of so called CRT (cardiac re-synchronization therapy) devices, with a circa four percent failure rate each year.

CRT is the standard-of-care for moderate to severe heart failure due to desynchrony, using lead-based cardiac pacing devices to coordinate the beating of the left and right sides of the heart.

"The longer you have it in the more likely you are to have a failure at some point," chirps EBR Systems CEO John McCutcheon.

"CRT [devices] last 10 years before the battery needs to be replaced, but leads can fail before that."

To be clear, the heart device giants Medtronic, Abbott and Boston Scientific do have wireless pacemaker devices for the right ventricle.

But EBR tackles the specific problem of the left ventricle, which, for physiological reasons, is harder to access than the right-side equivalent (see below).

Based in the US, EBR listed on the ASX on November 24 last year, having raised $110 million at $1.08 apiece in the biggest life sciences initial public offering to date.

We would like to say the share price hasn't missed a beat, but the stock is trading some 30 percent under par in a market that's become wary of big-ticket life science listings.

**WISE-ing up on leadless devices**

Based in Sunnyvale in California's Silicon Valley, EBR was founded in 2003 by electro-physiologist Dr Debra Echt, ultrasound scientist Dr Axel Brisken and former pacemaker engineer Richard Riley.

While the former two have left the building, Mr Riley remains an adviser to the company

At the, er, heart of EBR is its device called Wise (as in wireless stimulation endocardially).

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

Around 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).

As with all decent inventions, Wise came about in a roundabout way: Dr Echt saw a problem with leads and thought there was a better way to carry-out defibrillation.

The founders then found a way to stimulate the heart leadlessly.

The Northern California-based John McCutcheon joined EBR in 2019 and managed to sneak in several trips to Australia before the curse of Covid struck.

More than 35 years ago, Mr McCutcheon started out at American Hospital Supply in sales and marketing and then went entrepreneurial, working in a number of start-ups.

"I sometimes find myself in small companies taken over by large companies and quickly realize it's not where I thrive and try to find the next start-up opportunity," he says.

EBR listed on the Australian bourse because it was too young for the Nasdaq.

More to the point, it was backed by a slew of big-name Australian private investors pre-listing, including MH Carnegie and Brandon Capital. These investors bought - rather than sold - into the initial public offer.

The company also had close links with superannuation funds, who were keen for the company to pursue an ASX listing. Industry super fund investors include Australian Super, HESTA and Hostplus.

**Left behind**

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. So [clinicians] have less concern about clot formation on the right side, but [are] very concerned about the left side,” Mr McCutcheon says.

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).

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 heart.

Within 30 to 45 days the device is covered by heart tissue, which ameliorates the risk of clots and means it won’t interfere with the heart mechanics such as valves and capillary muscles.

The Wise is described as the size of a grain of cooked rice - and certainly smaller than the arborio variety. Because it doesn’t have an inbuilt battery, the device is only five to six percent the size of other wireless pacemakers.

**In the clinic**

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

Granted, 31 percent experienced “serious adverse events”. But given the subjects had a 30 percent of dying within a year, it no doubt was a chance worth taking.

EBR is in the final stages of enrolling for pivotal US trial, called Solve-CRT, as the basis for a pre-market approval (PMA) submission to the US Food and Drug Administration.

The most stringent device marketing application, the PMA process evaluates the safety and effectiveness of class III medical devices.

The trial aims to enrol a minimum of 183 patients across about 60 sites.

“We aim to finish enrolment in the first half of 2022,” Mr McCutcheon says. “We already have CE mark [European approval], but it’s costly to commercialize initially. So, we want to be strategic and get FDA approval and then commercialize more broadly”.

Australian approval is expected shortly thereafter.

**So why hasn’t anyone thought of it before?**

Mr McCutcheon says heart giants Medtronic, Abbott and Boston Scientific all made bets on leadless pacemakers for the right heart - and assumed they would be small enough for the left side.

“We are the only tech in the foreseeable future that can fill that gap,” he says. “Why? Because it’s hard.

“A lot of people would like to do what we do clinically, but we are not aware of anybody with published patents or early work. We don’t see anyone in this space for quite some time, if ever.”

**Finances and performance**

To get EBR this far, shareholders have tipped in more than $US200 million and eventually they will be tapped for more.

Currently, the company is in pre-revenue stage and that won’t change in a hurry.

The company estimates the market is worth $US2.1 billion, but with additional applications this number goes as high as $US7.5 billion to $US8.5 billion.

The cost of the devices will be shaped by reimbursement, which translates to around $US35,000 in the US and an average $US20,000 in the addressable non-US markets such as Germany, France, the UK and Australia.

“As we mature, and our [cost of goods sold] goes down, we will look to other countries [such as parts of Asia] where distributors would be required,” Mr McCutcheon says.

Distribution-wise, the company plans to take the direct approach initially.

“It’s a concentrated market,” Mr McCutcheon says. “We know many of the electro-physiologists on a first-name basis. We have their cell ’phone numbers and emails, they’re not hard to contact.”

Broker Morgans forecasts the company to break even in 2026 on an underlying earnings basis, with projected revenue of $US95 million. This, of course, assumes FDA approval, with the company targeting US sales by as early as the December half of 2023.

EBR shares have traded as low as 62 cents (in late January) … and the market gods have not been kind generally.

**Dr Boreham's diagnosis:**

As reported by the Australian Financial Review, MH Carnegie principal Mark Carnegie believes EBR will be the "next Cochlear and change lives around the world". Having invested $40 million in EBR to date, the prominent venture capitalist is certainly putting his money where his mouth is.

Mr McCutcheon isn't getting carried away with comparisons to the $13 billion market cap hearing implant maker, stressing management's focus on ensuring the company is self-sustaining. He also knows that tapering back on research and development would be as fatal for the company as a full-blown coronary.

"My experience with medtech is you never want to stop innovating, you always keep advancing. That way, if competitors get interested you are one or two steps ahead with fresh patents."

Deficient as it may be, the current technology has certainly advanced since the 1950s Furman pacemaker, which relied on a cord being tethered to mains power.

As is always the case, winning regulatory approvals is a worthy aim but does not guarantee widespread take-up of a device. And Wise is EBR's sole focus, so there's single-product risk.

Mr McCutcheon says cardiologists are amenable to technology, but are data driven and don't grasp at something just because its new.

"It will come down to the sweet spot of which patients benefit the most," he says. "We have doctors that love it, with patients that couldn't be treated in any other way."

EBR will only succeed if it complements, rather than competes with, the big three heart device companies.

"We fulfil an unmet need and that's why clinicians are happy to see us," Mr McCutcheon says. "Our potential competitors are happy to see us because we solve a problem."

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He has often told an editor he has been working on an "interesting lead" when in fact he has been at the pub, but this time it's for real.***

## PROTEOMICS INTERNATIONAL LABORATORIES

Proteomics says it has completed a 300-patient biomarker validation study with the Queensland Institute of Medical Research Berghofer for oesophageal adeno-carcinoma.
Proteomics said oesophageal adeno-carcinoma was the most common form of oesophageal cancer in Australia and it was working with the Institute to develop “a simple blood test … using a panel of biomarkers … initially identified by QIMR Berghofer researchers” (BD: Oct 9, 2020).
The company said that the analysis “sought to demonstrate the robustness of the biomarkers across laboratories through a series of analytical and clinical validation experiments”.
Proteomics managing-director Dr Richard Lipscombe said the research studied multiple proteins in the blood associated with early-stage oesophageal adeno-carcinoma.
“From these we’ve been able to identify a select panel of biomarkers with the potential to be used as a diagnostic test,” Dr Lipscombe said.
“Importantly we have also completed validation of the panel using blood samples from more than 300 patients,” Dr Lipscombe said.
The company said that the results of the study, titled ‘Translation Proteomics: Establishing a Mass Spectrometry Assay for Biomarkers of Oesophageal Cancer’ were presented today at the Lorne Proteomics Symposium in Victoria.
Proteomics said the results “showed several protein biomarkers … were statistically significant in identifying oesophageal adeno-carcinoma”.
The company said that the study focused on Barrett’s oesophagus, a pre-malignant condition that is a major risk factor for oesophageal adeno-carcinoma.
Proteomics said that Barrett’s oesophagus affected about two percent of the population and occurred when the oesophagus was damaged by acid reflux.
The company said patients were currently screened using invasive and costly endoscopy procedures and with the Institute would finalize arrangements for the future development of the biomarkers into a diagnostic test for oesophageal cancer.
Proteomics was up 10 cents or 10.2 percent to $1.08.

## FEDERAL GOVERNMENT

The Federal Government says it has allocated $15 million to help establish an innovative cancer genomics laboratory in South Australia.
A media release from Federal Health Minister Greg Hunt said that the laboratory would be established within Adelaide’s SA Pathology, formerly known as the Royal Adelaide Hospital’s Institute of Medical and Veterinary Science.
The media release said that the laboratory would “strengthen South Australia’s capacity in genomic diagnostic testing, which [was] key to finding new pathways for prevention, diagnosis, and treatment of cancer”.
“While survival rates in Australia are high by world standards, we still lost almost 50,000 people to cancer last year,” Mr Hunt said. “This is why medical research is so important.”
“Genomics uses a person’s own genetic makeup to analyze and understand their disease and unlock personalized treatments,” Mr Hunt said.
“By analyzing DNA to work out how to target and destroy cancer cells, we can get a better understanding of what medicine or treatment will work best for a patient,” Mr Hunt said.
The Federal Government said it had allocated more than $150 million across 40 research projects as part of the Medical Research Future Fund’s $500 million Genomics Health Futures Mission, as well as $50 million for Omico, a nationwide network of cancer research and treatment centres to develop genomic testing.

## STANDARD & POORS DOW JONES INDICES, TELIX PHARMACEUTICALS

Standard & Poors says Telix will replace Sydney Airport in the S&P-ASX200, prior to the open on February 10, 2022, pending a scheme of arrangement court approval.
Standard & Poors said that it was awaiting final court approval of the scheme of arrangement for Sydney Airport to be acquired by Sydney Aviation Alliance Pty Ltd.
Telix fell 38 cents or 5.3 percent to $6.81 with 1.6 million shares traded.

## RESPIRI

Respiri says that M-telehealth has placed a second order for its Wheezo asthma management device worth about $US24,000 ($A33,600).
In December, Respiri said it had a five-year, 1,000 Wheezo unit-per quarter deal, worth $208,000 with the Delray Beach, Florida-based M-telehealth (BD: Jan 16, 2022).
The company said that the devices would be provided by M-telehealth to “key decision makers … to allow for the critical review, testing and evaluation required to expedite the piloting of Wheezo which are the first and most difficult steps in seeking to secure reimbursement” and inclusion in management protocols.
Respiri said that more than 600 customers had been targeted and many had requested Wheezo devices.
Respiri was up 0.2 cents or four percent to 5.2 cents with 2.2 million shares traded.

## EXOPHARM

Exopharm has told the ASX that working with the Astellas Institute for Regenerative Medicine was material, but the subsequent clarification was not.
The ASX said that on Friday January 28, 2022, before the Monday January 31 announcement of the collaboration, Exopharm’s share price increased 10.3 percent from 39 cents to 43 cents, and further increased 12.5 percent after the announcement on January 31 from 43 cents to an intra-day high of 48.5 cents.
According to Commsec data, following the clarification on February 1, the company’s share price closed down 5.2 percent at 45.5 cents.
The ASX asked Exopharm whether the information in the original announcement and the clarified announcement were material, and when the company became aware of that information.
Exopharm said that the clarified information comprised minor word changes and clarifications, as well as an amendment to the referencing of a quote.
Exopharm clarified its statement that “initial services will…” to “initial services are designed to seek to validate” its technology platforms to manufacture exosomes for Astellas, firstly at Exopharm’s facilities in Melbourne followed by the Astellas facilities in Massachusetts.
The company said it first became aware of the information on the execution of the agreement over the weekend of January 29 and 30, and early in the morning of January 31, 2022 with the information released prior to the commencement of trading on January 31, 2022
Exopharm said its projects with the Institute would potentially start in March 2022, where it had previously said it would start in March 2022.
The company said that clarification changed the agreement to “anticipates”, rather than “enables” laboratory work to demonstrate the effectiveness of its technologies using AIRM’s cell-based therapeutic technologies.
Exopharm was unchanged at 44 cents.

## CLARITY PHARMACEUTICALS

Clarity says it has received $3,262,861 from the Australian Tax Office under the Federal Government Research and Development Tax Incentive program.
Clarity said the rebate related to research and development expenditure for the year to June 30, 2021.
Clarity was up 1.5 cents or 2.1 percent to 72 cents.

## STARPHARMA

FIL (Fidelity) Limited says it has reduced its substantial share-holding in Starpharma from 33,514,716 shares (8.32%) to 29,778,237 shares (7.31%).
The Sydney-based, FIL said that it bought, sold and transitioned shares between October 14, 2020 and October 15, 2021 at prices ranging from $1.1906 to $2.1986 a share.
Starpharma was up 1.5 cents or 1.5 percent to $1.03.