Biotech Daily

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*Daily news on ASX-listed biotechnology companies*

# 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 enroll 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.***