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

CEO: John McCutcheon

Board: Allan Will (chairman), John McCutcheon, Dr Christopher 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.