



# Biotech Daily

Friday August 7, 2020

*Daily news on ASX-listed biotechnology companies*

## Dr Boreham's Crucible: Exopharm

By **TIM BOREHAM**

**ASX code:** EX1

**Share price:** 28.5 cents

**Market cap:** \$27.2 million

**Shares on issue:** 95,472,000

**Chief executive officer:** Dr Ian Dixon

**Board:** Jason Watson (chair), Dr Dixon, David Parker

**Financials (June quarter 2020):** revenue nil, cash outflows \$2.15 million, cash on hand \$1.74 million, quarters available cash 0.81.

**Identifiable major shareholders:** Altnia Holdings (Dr Dixon) 29.3%, Michael Francis McMahon/Susan Lesley McMahon 2.4%, Oldview Enterprises (The Priestley Account) 1.5%, Anthony John Locantro 1.4%.

Given the scientifically complex nature of Exopharm's quest to develop exosomes into therapeutics, it's good to see that founder and chief executive Ian Dixon hasn't lost sight of the commercial basics.

He says: "Biotechnology is about spending investors' money to get to some kind of revenue - or a big deal - while building value along the way with many steps."

Indeed.

With Exopharm in early clinical stage, there are many more baby steps required before the company can claim any success with harnessing exosomes, which are touted as an alternative to stem cell therapies.

Dr Dixon reminds investors of the great experience with penicillin, which was discovered and then developed through hard graft (and a dose of serendipity).

“Out of the greatest of crises some of the greatest discoveries are made and two or three great minds can make a huge difference,” he says.

Exopharm was founded by Dr Dixon, who also co-founded the ASX stem-cell play Cynata Therapeutics.

He was also a director of the previously ASX-listed Cell Therapies, which produced adult stem cells for the pure-play stem cell champion Mesoblast.

Exopharm listed on the ASX on December 2018, having raised \$7 million at 20 cents apiece.

### **What are exosomes?**

For those too afraid to ask, exosomes are small particles produced by cells that deliver therapeutic properties to other cells to reduce inflammation or promote regeneration.

Trillions of exosomes are produced by stem cells, but like hair follicles they decline with age. Exosomes are also known as extracellular vesicles, or EVs, but have nothing to do with Teslas or other electric vehicles.

Exopharm is developing two products. The first is naïve EVs, which are made from stem cells and platelets and designed to be a new class of regenerative medicine.

A new discipline, engineered extracellular vesicles are the result of drugs or proteins being added to the vehicles to create new treatments for specific viruses, cancers, cardiac diseases, infectious and neurological conditions and even erectile dysfunction.

But much of the exosome challenge lies in extracting and purifying the agents as drug products, with clinical progress slowed by manufacturing limitations.

So, it's just as well Exopharm holds a technology called ligand-based exosome affinity purification (Leap), which allows for efficient manufacturing.

Exopharm chief commercial officer Dr Chris Baldwin says Exopharm's strategy is to solve the manufacturing problems using naïve exosomes and then play with engineered EVs.

“EVs are how stem cells work,” he says. “They contain RNA (ribonucleic acid) instructions inside and get sent out into the body to tell the cells how to grow and adapt.”

The clever extracellular vesicles also have a dressing on the outside to ensure the messages are embedded in the cells in the desired way.

Dr Baldwin notes that many developers of mesenchymal stem cell therapies are refocusing on the active ingredients - exosomes - because they can be turned into an off-the-shelf product in a more economic and safer way.

“With our Leap technology we are creating the capacity to extract the active ingredient and turn it into something that can be commercialized.”

### **Clinical delays**

Exopharm holds the claim to fame of being the first company to launch a human clinical trial with an autologous exosome drug candidate, via its Plexoval I study.

(Autologous material is obtained from the same individual).

The 20-patient study aimed to evaluate the safety, tolerability and biological activity of its initial EV product called Plexaris, for wound healing.

The first human guinea pigs were dosed in January, with one 15-strong cohort assessed on wound healing and the remaining five appraised for “biological activity”.

But then along came the cursed Covid-19 and on April 1 the company said the trial was suspended, with recruitment numbers likely to be reduced.

It was no joke.

Management now hopes for a restart and is also eyeing a safety trial of a variant allogeneic (off the shelf) prospect, Plexaris OS (as in off-the-shelf, not actually overseas), aimed at conditions including dry aged -related macular degeneration.

The company has also engineered Plexaris as Plexodox, which has undergone in vitro testing as an anti-cancer agent.

Plexodox was loaded with the off-patent cancer drug doxorubicin, with the Petri dish results showing the combo killed “considerably more” lung cancer cells than doxorubicin itself.

While off-patent, doxorubicin is a commonly used treatment generating \$1 billion of revenue a year. It is hoped that Plexodox will increase its efficacy at lower doses and reduce side effects.

### **Did someone mention Covid-19?**

Yep, you gotta have a Covid-19 angle these days.

Exopharm is designing extracellular vesicles to produce an effect that Dr Baldwin dubs “flattening the curve within the body”.

You see, viruses are so dangerous because they interfere with the process of the extracellular vesicles delivering the messages.

In effect they turn the cell into a virus factory, with the multiplied germs released into the bloodstream.

With the coronavirus, the outside 'spike' proteins enable the virus to enter cells with an angiotensin-converting enzyme 2 (ACE2) receptor on the outside.

Once inside the cell, the RNA allows for virus replication.

Exopharm is working on an engineered EV product, Fortrexo Cov that would defeat the virus's cunning replication strategy by sending out RNA instructions of its own.

Dr Baldwin adds the platform may be applicable to other diseases such as Huntington's disease and glioblastoma (brain cancer): anything that needs an "internal agent of action".

### **New digs, same gig**

Via the safety of a webinar, the company recently showcased its new facility at the Baker Institute, in Melbourne's appropriately-named Commercial Road.

The premises merges the company's hitherto separate manufacturing and research digs.

The move was done at the height of the Covid-19 plague and allowed key experiments to re-start two days later.

"We used literally anything our scientists could borrow from our partner institutions," says chief operating officer Gregor Lichtfuss.

"To be able to drive our developments efficiently we need to be able to do it ourselves ... and control the entire development and manufacturing process.

"Only then will we be able to be truly masters of our own destiny."

Dr Lichtfuss describes the company as "tightly integrated in the Melbourne biosciences ecosystem".

In particular, it has research facilities with two leading hospitals and three research bodies: "relationships that give us access to world-leading technologies and experts".

### **Finances and performance**

As of June 30, 2020, Exopharm had a cash balance of a tad over \$1.7 million, which is a little too slender for comfort.

Fortunately, management isn't exactly splashin' it about on travel to international conferences, so lockdowns do have their silver linings.

“Exopharm’s finances are in good shape and we are being very careful with the cash we have, using the money to make advances and produce results,” Dr Dixon says.

“We have cut back on some costs to preserve the runway and keep our people confident about their employment.”

(The company has 25 full-time equivalent staff).

Dr Dixon says the company should be able to start its second Plexoval study (the allogeneic one) with existing funding.

Beyond that, funding options include non-dilutive sources such as partnering, but these routes are time consuming with uncertain results.

“Funding will continue to come from our investors who understand the story and see the potential of exosomes as the new mode of medicine,” he says.

“We will adjust our activities to match the funding we have access to.”

As you do.

Exopharm shares plunged from 35 cents on February 12 this year to a record low of 14.5 cents on March 23, in what might turn out to be the shortest and sharpest market ‘flash crash’ in history.

The shares peaked at 61 cents on February 1, 2019.

### **Hurry, hurry!**

Despite the progress and promise, Dr Dixon admits the company is “not building value as fast as we would like to, or need to.”

He adds: “we need to move fast or we will be overrun by others”.

For example, exosome developers Evox Therapeutics in the UK and Codiak in the US have done four big pharma deals between them in the last two years, with \$US50 million plus up-front payments and potential billion-dollar milestones.

As of January, at least three rivals aimed to start trials this year, with several more, close behind.

“Some of these companies are pivoting into exosome product development after previously focusing on stem cell research,” Dr Dixon says.

While EVs are mooted as a replacement for stem cell therapy, Dr Baldwin believes the two approaches are complimentary.

“It will never be a low-cost treatment,” he says. “A vast majority of patients that are treated with stem cells can be treated with EVs with better consequences.”

## **Dr Boreham's diagnosis:**

Dr Baldwin notes that it's one thing to have active ingredients that work and another thing to have a commercial product.

But he deploys a 2400-year old analogy to prove there are precedents for commercializing a therapy such as naïve EVs.

"If you were a Greek with a headache, you would go to Hippocrates and he would hand you a packet of bark to make some tea," he says.

The remedy worked, but the active ingredient didn't turn into a proper medicine until 1888 when Bayer introduced acetylsalicylic acid (or Aspirin as we better know it) – and became one of the biggest pharma companies on the back of that magic bark.

Dr Dixon draws similarities with the \$2.3 billion ASX stem cell leader Mesoblast, in that both companies have platform technologies that can be used for multiple purposes.

Apart from the cell/non-cell distinction, the duo's business models are similar: "manufacture the products and show they are safe and effective and take products into partnerships and sales".

Still, we stress again that Exopharm is at an early stage and its development will be governed by what is - or isn't - in the kitty.

And speaking of which, it's an ideal time to raise capital, with investors amenable to anything with a coronavirus angle.

Dr Baldwin, by the way, reckons we shouldn't get too excited about the company curing coronavirus anytime soon.

"I really hope it doesn't because we are really not close to something," Dr Baldwin says.

"We hope a vaccine comes along well before us. But it demonstrates our technology and if it successful this is what we'll use for Covid-23 or Covid-25."

Perish the thought!

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He is thus not bound by the Hippocratic Oath but did let out a few when he hit his thumb with a hammer the other day.***