# Biotech Daily

Friday May 24, 2019

*Daily news on ASX-listed biotechnology companies*

*** ASX, BIOTECH DOWN: ANTISENSE UP 6%; LBT DOWN 12.5%**

*** DR BOREHAM'S CRUCIBLE: ONCOSIL MEDICAL**

*** IMMURON TO RAISE $2.9m**

*** ANTISENSE ATL1102 DMD TRIAL ENROLLED**

*** STARPHARMA: DEP-IRINOTECAN, CETUXIMAB KILL CANCER IN MICE**

*** MGC CLAIMS 'MARIJUANA TOXIC TO GLIOBLASTOMA', IN-VITRO**

*** NAOS TAKES 18.5% OF BTC HEALTH**

*** GOODBYE PHOSPHAGENICS, WELCOME AVECHO**

## MARKET REPORT

The Australian stock market fell 0.55 percent on Friday May 24, 2019, with the ASX200 down 35.8 points to 6,456.0 points.

Ten of the Biotech Daily Top 40 stocks were up, 18 fell, nine traded unchanged and three were untraded.

Antisense was the best, up 0.3 cents or six percent to 5.3 cents with 23.9 million shares traded.

Pharmaxis climbed 5.7 percent; Cyclopharm, Immutep and Uscom were up more than three percent; Clinuvel, Oncosil and Telix rose more than one percent; with CSL, Neuren, Resmed and Starpharma up by less than one percent.

LBT was this week's yoyo, on Monday's FDA approval for its APAS Independence; today retreating two cents or 12.5 percent to 14 cents, with 7.2 million shares traded.

Proteomics lost 6.1 percent; Imugene was down 5.6 percent; Osprey and Volpara fell more than four percent; Kazia was down 3.3 percent; Genetic Signatures, Impedimed, Medical Developments, Nanosonics and Opthea shed more than two percent; Avita, Cochlear, Dimerix, Mesoblast, Paradigm and Pro Medicus were down one percent or more; with Compumedics and Polynovo down by less than one percent.

# DR BOREHAM'S CRUCIBLE: ONCOSIL MEDICAL

**By TIM BOREHAM**

**ASX code:** OSL

**Share price:** 6.7 cents; **Market cap:** $42.3 million; **Shares on issue:** 630,708,788

**Chief executive officer:** Daniel Kenny

**Board:** Dr Chris Roberts (chair), Daniel Kenny, Dr Roger Aston, Dr Martin Cross, Mike Bassett

**Financials (March quarter 2019):** revenue nil, cash burn $2.8 million, cash of $10.2 million, estimated current quarter cash burn $2.65 million.

**Identifiable major shareholders:** Regal Funds 10.6%, Webinvest (Otto Buttula) 3.84%, Daniel Kenny 3.2%, Bannaby Investments (Keith Kerridge) 3%, Tisia Nominees 2.9%, Australian Ethical 2.6%, Dr Roger Aston 2%

We all know the Brits don't need an excuse for a tea break, but for Oncosil a promised cuppa with the country's drug regulator appeals well beyond a fortifying Earl Grey.

The targeted radiation house and its investors are in a state of flux after the British Standards Institute (BSI) refused to grant approval for the company's treatment for inoperable pancreatic cancer, which kills 95 percent of sufferers within five years.

Approval was meant to be a dead cert - or so the company thought - but instead the po-faced authorities decreed the evidence showed "insufficient clinical benefit at this time".

In the pre-Brexit milieu, approval by the BSI is a proxy for obtaining pan European (CE mark) approval.

While Oncosil shares swooned 69 percent after the BSI's snub, it's not as if the company is in the same 'failed trial' cohort of Factor Therapeutics (wound healing), Innate Therapeutics (multiple sclerosis) and, more recently, Actinogen (Alzheimer's disease).

In CEO Daniel Kenny's view, the setback related more to the way the dossier was presented, rather than the integrity of the data.

"[The regulator] needed to join the dots and that's not being condescending or critical to anyone," he says, meaning all the data was there, but like Labor's franking credits policy could have been explained a wee bit better.

Another complicating factor was that Oncosil's application marked the first time an advisory body called the Clinical Oversight Committee was involved in the approval process for an active implantable medical device.

"[The process] was new to everybody," Mr Kenny says.

As it stands, the BSI's stance does not amount to a CE Mark rejection, but if the 'non decision' is not overturned it certainly will be.

"I'm not blaming BSI for the situation but I'm not saying we submitted a poor application," Mr Kenny says.

Undeterred by the setback, Oncosil director Martin Cross on April 1 peeled off $19,253 to buy $358,333 shares at 5.3 cents apiece - and then on May 7 ponied up $20,496 for 230,000 more (at 8.9 cents apiece). On April 2, fellow director Michael Bassett lashed out $44,247 for 800,000 shares, paying 5.5 cents apiece.

Who said the battered Labor Party was the preserve of the True Believers?

**The story to date**

A novel form of brachytherapy for pancreatic and liver cancers, Oncosil's treatment involves irradiating tumors from the inside by injecting micro particles with a radioactive isotope. The procedure involves the radiation in liquid form being injected via an endoscope into the tumor. While the procedure takes merely half an hour, the localized radiation is emitted for three months.

The Oncosil technology was invented by current board member Dr Roger Aston and was owned by Psivida (now Eyepoint), which he co-founded.

Formerly Neurodiscovery, Oncosil assumed its current guise by acquiring the British outfit Enigma Therapeutics in 2013. A series of board rejigs from 2014 saw the departure of chairman Martin Rogers, with existing board member Dr Aston becoming chairman. He in turn was replaced by Dr Chris Roberts, best known for running that tiddler called Cochlear for decades.

But Dr Roberts also used to chair Sirtex up to 2002, so has a keen interest in radiotherapy as well as hearing implants. Biotech man about town Dr Aston co-founded Psivida, which owned the Oncosil technology that he invented.

**COC-up or temporary setback?**

Oncosil's key evidence to the Clinical Oversight Committee (COC) was a 42-patient study showing 24 percent of patients had become eligible for curative surgery: in other words, tumor volumes had shrunk to the extent that they could be removed with a scalpel.

As per an agreed protocol, these patients received the standard-of-care chemo, as well as Oncosil's eponymous treatment. Called Panco, this study was carried out across sites in Australia, Britain and Belgium.

The average tumor reduction was 29.7 percent, with a maximum shrinkage of 90 percent. Of the 10 patients undergoing a surgical resection (tumor removal), there was no evidence of cancerous cells in the tissue sample surrounding the excised tumor.

As we see it, the key issue is that Oncosil could not present any survival data (that is, how many patients actually continue to live and breathe over a nominated time frame). But as the trial did not have a control group to compare the treatment data against, this was not possible.

**What now?**

As for that cup of tea, the company expects an embossed invite in the mail shortly, in view of a late May or early June appointment. The company is preparing a detailed response to the COC's initial assessment and a revised clinical evaluation report.

Oncosil chose the CE mark process because, unlike the US Food and Drug Administration (FDA) the authorities don't require randomized trials. As a result, the process is quicker, but post-marketing surveillance is more rigorous.

In 2016, Oncosil was granted US investigational device exemption (IDE), with an initial nine-patient trial, Oncopac-1 confirming the safety of the technology. Separately the company is working on US approval, but there's a mountain of work to be done.

An FDA application would likely require a 300-patient randomized trial comparing Oncosil to the standard-of-care chemotherapy.

But that's open to negotiation. Mr Kenny says that as the company has the benefit of data from 74 implants to date, it can explore other options.

**Brexit explained (not)**

Ever wondered what the Brexit brouhaha means for European drug approvals? So did we.

To date, the BSI has been bestowed with the right to grant CE mark approval for the 28 European Union member countries (this number includes Britain). Post Brexit - if it actually happens - the Brussels health bureaucrats won't be overly enamored with being bossed around by the Brits.

But under a transitional arrangement, BSI approvals technically are granted from the Netherlands, so they will remain synonymous with CE mark approval.
"From Oncosil's view Brexit has been a non-event but it has impacted us in terms of being a distraction for the BSI," Mr Kenny says.

**Finances and performance**

As of the end of March, Oncosil had cash of $10.2 million, enough to keep the candles burning at North Sydney HQ.

But if the full trial goes ahead, the company will need to pony up for more through a capital raising. The last whip 'round raised $16.7 million and brought Australian Ethical and Regal Funds Management to the register.

Oncosil's $42 million market capitalization implies that - as with Dr Cross - investors haven't lost hope. It's not unprecedented in the biotech world to have an initial setback, followed by the joy of approval.

While management remains supremely confident, reimbursement is just as important. Given the poor prognosis, though, it's the sort of treatment desperate patients and their relatives might be willing to pay out of their pockets.

Oncosil shares peaked at 24 cents in January 2016 and plumbed to a low of 4.9 cents after the March 25 British bombshell (down 69 percent on the day). The stock then spiked from 5.2 cents to 8.6 cents in the first week of May, no doubt because of the zealous director purchases.

**Dr Boreham's diagnosis:**

Under previous management, Oncosil has over-promised and under-delivered. In fact, the company promised CE mark approval in 2013.

The delay is unfortunate because there are no drugs in advanced development for pancreatic cancer, which produces 85,000 new cases in Europe and 46,000 new cases in the US annually.

The market is valued at $US2 billion globally (excluding China).

"Pancreatic cancer has been a graveyard for so many drugs in the last 20 years," Mr Kenny says. "We have not dented the five-year survival rate of five to seven percent and we don't see any other disruptive therapies down the line."

Mr Kenny says Oncosil is also watching the China market, where regulators are becoming more amenable to evidence based on overseas trials. "We wouldn't go in without a partner, though."

Japan, the world's second biggest healthcare market, looks too hard a task because of tough regulatory hurdles.

Oncosil has been idly described as a 'mini me' version of liver cancer microspheres house Sirtex Medical, taken over by China's CDH Investments late last year for $1.9 billion after a spirited takeover tussle with Varian Medical Systems of the US.

Oncosil, indeed might become the next Sirtex - but not if the British gatekeepers end up preferring Darjeeling to Earl Grey.

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He has been responsible for plenty of COC-ups over his journalistic career but fortunately no-one died.***

## IMMURON

Immuron says it expects to raise $US2 million ($A2,902,450) through the offer of 500,000 American depositary shares (ADSs) at $US4.00 a share ($A5.80).
Immuron said each ADS was equivalent to 40 Australian shares, implying the capital raise was equivalent to 14.5 cents a share.
The company said it would grant the underwriter a 45-day option for 75,000 ADSs raising a further $US300,000 to cover over-allotments in the offering.
Immuron said the funds would be used for expenses related to the clinical development of its clinical candidates, IMM-124E for fatty liver disease and IMM-529 for Clostridium difficile recurrence, and for working capital.
The company said Fordham Financial Management's Thinkequity represented the underwriters for the raise and it expected the offer to close on May 29, 2019.
Immuron was in a trading halt at 19 cents.

## ANTISENSE

Antisense says it has completed enrolment for its nine-patient, phase II trial of ATL1102 for Duchenne muscular dystrophy.
Last year, Antisense said the trial in non-ambulant boys aged between 10 and 18 years of age with Duchenne muscular dystrophy at Melbourne's Royal Children's Hospital would assess the safety and tolerability of ATL1102 (BD: Jul 16, 2018).
Today, the company said that three patients had completed 24 weeks of dosing, with four in treatment and two screened and scheduled to begin treatment this month, with results expected shortly after completing dosing, which was expected in November 2019.
Antisense was up 0.3 cents or six percent to 5.3 cents with 23.9 million shares traded.

## STARPHARMA

Starpharma says its dendrimer enhanced product (DEP) irinotecan with cetuximab outperforms irinotecan with cetuximab in a mouse model of human colon cancer.
Starpharma said DEP-irinotecan was a nanoparticle formulation of the active constituent of irinotecan, marketed as Camptosar, delivered with cetuximab, marketed as Erbitux.
The company said that the high dose DEP-irinotecan and Erbitux showed 100 percent survival and "complete suppression of tumor growth".
Starpharma said the low dose DEP-irinotecan and Erbitux showed a significantly enhanced survival benefit and enhanced suppression of tumor growth, and in comparison, irinotecan and Erbitux had minimal effect on tumour suppression and survival benefit.
The Starpharma chart showed little difference between the combination of the existing anti-cancer drugs irinotecan and Erbitux and the control vehicle until after day-20 of the trial, but a clear difference at that point with DEP-irinotecan.
Starpharma chief executive officer Dr Jackie Fairley said the results "once again demonstrate the significant advantage conveyed by the DEP platform".
"Combinations using DEP drugs are consistently showing better performance than the same combinations using the originator products, for example Camptosar," Dr Fairley said.
"These results are particularly interesting given we have also previously shown the beneficial effect of using DEP-docetaxel, DEP-cabazitaxel and AZD0466 as part of a combination therapy approach," Dr Fairley said.
Starpharma was up half a cent or 0.4 percent to $1.29 with 1.55 million shares traded.

## MGC PHARMACEUTICALS

MGC says in-vitro research in Slovenia shows that its marijuana derivatives can target cannabinoid receptor proteins in glioblastoma brain tumors.
MGC said it worked with Slovenia's National Institute of Biology and University Medical Centre in Ljubljana to develop protocols to treat high-grade brain tumors such as glioblastoma with cannabinoids.
The company said it also identified the most effective cytotoxic cannabinoids to treat glioblastoma in combination with the chemotherapeutic agent temozolomide.
MGC said the study showed potential for cannabinoids to reduce the viability of glioblastoma cells and target chemotherapy resistant glioblastoma stem cells.
The company said the study supported previous pre-clinical studies that showed that cannabinoids could induce processes that led to anti-tumor responses in some cancers.
MGC managing director Roby Zomer said the "highly encouraging, ground-breaking research is part of our efforts to increase the use of cannabinoids in the treatment of multiple diseases that are currently unresponsive to conventional medicines".
MGC fell 0.1 cents or 1.7 percent to 5.8 cents with 1.15 million shares traded.

## BTC HEALTH (FORMERLY BIOTECH CAPITAL)

Naos Asset Management says it has increased its substantial shareholding in BTC Health from 22,038,246 shares (16.91%) to 30,064724 shares (18.54%).
The Sydney-based Naos said it bought 8,026,478 for $708,376 or 8.8 cents a share on market and in the recent placement which raised $8 million at eight cents a share (BD: May 15, 2019).
Biotech Capital was untraded at 11 cents.

## AVECHO BIOTECHNOLOGY (FORMERLY PHOSPHAGENICS)

Phosphagenics says its name has been formally changed to Avecho Biotechnology and its ASX code will change to AVE on Monday, May 27, 2019.
Phosphagenics was unchanged at 0.3 cents.