Biotech Daily

Friday February 10, 2023

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: GENETIC SIGNATURES UP 10%**
- MESOBLAST DOWN 10%

*** DR BOREHAM'S CRUCIBLE: IMAGION BIOSYSTEMS**

*** VAXXAS STARTS PHASE I NEEDLE-FREE INFLUENZA VACCINE TRIAL**

*** AROVELLA, IMUGENE TAKE CAR-INKT, ONCARLYTICS TO MOUSE TESTS**

*** CYTIVA: ACURABIO TO MANUFACTURE PLASMID DNA**

*** IMUGENE WINS US B-CELL PD1-VAXX PATENT**

*** M&G REDUCES TO 6.8% OF STARPHARMA**

*** PERENNIAL TAKES 8.2% OF LUMOS**

MARKET REPORT

The Australian stock market fell 0.76 percent on Friday February 10, 2023, with the ASX200 down 56.6 points to 7,433.7 points.

Twelve of the Biotech Daily Top 40 stocks were up, 18 fell, eight traded unchanged and two were untraded. All three Big Caps fell.

Genetic Signatures was the best, up 7.5 cents or 9.7 percent to 85 cents, with 39,580 shares traded. Cyclopharm, Imugene and Resonance rose more than seven percent; Compumedics climbed 5.6 percent; Antisense, Atomo and Opthea improved four percent or more; with Medical Developments, Neuren, Starpharma and Telix up by less than one percent.

Mesoblast led the falls, down 11.5 cents or 9.75 percent to $1.065, with 5.5 million shares traded; followed by Next Science down 7.5 cents or 9.0 percent to 75.5 cents with 69,163 shares traded.

Pharmaxis, Polynovo and Proteomics lost more than six percent; Avita, Emvision and Nova Eye were down more than five percent; Clinuvel, Kazia and Prescient fell four percent or more; Dimerix, Patrys and Pro Medicus were down more than three percent; Nanosonics shed 2.6 percent; Cochlear, Cynata, Resmed and Universal Biosensors were down more than one percent; with CSL and Volpara down by less than one percent.

DR BOREHAM'S CRUCIBLE: IMAGION BIOSYSTEMS

By TIM BOREHAM

ASX code: IBX

Share price: 2.7 cents; **Shares on issue:** 1,121,318,534; **Market cap:** $30.3 million

Executive chair: Robert (Bob) Proulx

Board: Robert Proulx, Michael Harsh, David Ludvigson, Jovanka Naumoska, Mark Van Asten, Dianne Angus

Financials (December quarter 2022): receipts $88,000, cash outflows $454,000, cash balance $4.44 million, quarters of available funding 9.8

Identifiable major holders: Manhattan Scientific (4.6%), The Board of Regents of the University of Texas System 0.94%, Hoajie Li 0.98%, Robert Proulx 0.55%.

Imagion chief Bob Proulx reckons the oncology imaging innovator has achieved far more with its initial, early-stage breast cancer study results than investors might appreciate.

Carried out in Australia, the phase I trial showed the first signs that the company's approach of detecting tumors with magnetic nanoparticles was safe - and might work.

"As far as I know, it was the first time ever … that someone has taken an iron oxide particle with a targeting ligand [molecule] and put it in a patient," Mr Proulx says.

The results were deemed significant enough to be the subject of a 'poster' presentation at last December's San Antonio Breast Cancer Symposium, attended by a cluster of 3,000 oncologists.

And there's more.

This week, the company announced that an independent, blinded review by a panel of expert breast cancer radiologists supported the potential of the company's Magsense particles to detect tumor cells in lymph nodes, via magnetic resonance imaging (MRI) machines.

This means the company can shelve expensive plans to develop its own device, in favour of commercializing the particles themselves (see below).

"We don't have to worry about building a proprietary machine or commercializing a new piece of equipment," Mr Proulx says. "We can sell our particles at any hospital that has an existing MRI."

While Imagion initially is focused on human epidermal growth factor receptor-2 (HER2) type breast cancer, other solid tumours including prostate and ovarian cancers are also in its sights.

Los Alamos project goes off with a bang

Imagion combines the use of magnetically detectable nanoparticles with biological agents, to detect certain solid cancers.

Imagion's underlying technology was created by a Los Alamos, New Mexico physicist called Edward R Flynn, who tinkered with magnetic sensors after his wife contracted breast cancer.

"It was the classic scenario of a scientist wanting to do something about it," Mr Proulx says.

The technology resided in diagnostics house Senior Scientific, which was acquired by the New York based nano-medicines group Manhattan Scientifics. The relevant activities ended up within the newly-formed Imagion, which listed on the ASX on June 22, 2017 after raising $12 million at 20 cents a share.

The listing means Imagion is headquartered in Melbourne, but most of its activities take place in San Diego (where Mr Proulx resides).

Avoiding biopsies with better diagnosis

But what is the problem Imagion is purporting to solve? After all, there are at least five ways of imaging the body, currently.

Mr Proulx says x-rays are great for detecting broken bones, while ultrasounds are cheap and ideal for showing up foetuses and abnormalities

Computed tomography (CT) and positron emission tomography (PET) scans are also useful, but have their limitations (the latter uses radioactive tracing agents).

MRI scans are superior resolution-wise and will detect an "anatomical problem", such as a fibrotic mass.

"But none of these methods can tell you whether a suspicious spot or lesion is cancerous or not."

The idea of Magsense is to avoid unnecessary biopsies.

"When a breast cancer is detected, the first thing the patient wants to know is whether it has spread to the lymph nodes," Mr Proulx says.

"An ultrasound might tell whether a lymph node is larger or misplaced and [whether to do] a biopsy, but what if we can give the answer non-invasively?"

The 'non-invasive' angle is especially pertinent for prostate cancer detection, given the biopsy sample is obtained via a 12-pronged tool inserted up the rectum.

We're glad we got to the bottom of that one.

Making sense of Magsense

Imagion's Magsense platform involves injecting iron oxide nanoparticles combined with cancer-specific targeting antibodies or small molecules, contained within a solution.

"A detectable magnetic particle is coupled to cancer-specific targeting molecules, so when the nanoparticle is injected into the patient it will circulate and will seek out the cancer cells," Mr Proulx says.

The nanoparticles attached to the cancer cells lose their magnetism more slowly than the unattached ones, acting as a magnetic beacon. In the case of breast cancer, HER2 refers to an antigen that expresses the human epidermal receptor.

"Some antibodies are specific to that receptor. So, if you put the antibody on our particle it will bind to those cancer cells," Mr Proulx says.

If there no cancer, the particles will circulate harmlessly and the iron oxide eventually will be excreted via the liver.

"Everything about this is biologically safe; we are using antibodies or peptides that the body already recognises, with a detectable iron oxide particle," Mr Proulx says.

Thanks, patients

Carried out in Australia across four sites, the breast cancer trial opened in December 2020, but because of Covid lockdowns it didn't enrol its first patient until May 2021.

As announced in early December last year, the results from the first six-patient cohort hit the primary endpoint of safety and tolerability.

The research also showed the imaging agent to be detectable by both MRI and the company's proprietary relaxometry technology. In other words, Magsense could "help discriminate potentially cancerous nodes from normal ones".

Patients were given a 30-milligram dose, compared with more than 1,000mg over three days for a popular iron-based anaemia drug.

"We can say with high confidence a dose of our Magsense particle is very unlikely to cause metabolic upheaval in the liver," Mr Proulx says.

Unlike most safety trials that use healthy volunteers, the trial custodians were interested in HER2 patients to explore the 'efficacy' angle.

Mr Proulx says the trial was burdensome for the participants, who were subject to an MRI, the nanoparticle dosing and then another MRI and a biopsy.

Given it was strictly a research study, there was nothing in it for them.
"It took a very special person to be willing to volunteer for our study," Mr Proulx says.

MRI decision will save a fair (s)quid

Following the supportive opinion of the three-person expert panel led by principal investigator Dr Jane Fox, Imagion has made the commercial decision not to develop its own device.

To explain: the nanoparticles are subject to a low magnetic pulse, with their location detected by an ultra-sensitive ‘super-conducting quantum interference device’ (yep - a Squid).

The company expected revenue would be by way of the fabled printer and cartridge model, by which the hardware (the measuring stations on which the patients lie) virtually given away.

Mr Proulx says the devices were to have been developed by the Melbourne-based design house Planet Innovation. But advancing them would have taken at least 18 months and would have cost “many millions” of dollars. Given Imagion had parked device development for the last two years, the decision is more a case of freeing-up future funding, rather than generating current cost savings.

Mr Proulx says it would have been “problematic” to expect a hospital to shell out around $US500,000 for a device, especially if it was only relevant for breast cancer detection.

He adds the idea of a proprietary device platform is not altogether dead.

“There are some new, really small sensors and we are looking at developing a detector more like an ultrasound device than a big Squid,” he says.

These devices could be deployed cost-effectively at general practitioner !!!!!GP clinics, perhaps as a triage tool whereby only positive results are sent for an MRI.

“This bodes well for our proprietary technology because we can skip over the expensive machines … and move to something more ubiquitous in terms of implementation.”

Finances and performance

Imagion recorded December quarter cash outflows of $454,000, albeit after receiving a $2.5 million Federal Research and Development Tax Incentive payment.

The company also gleaned $88,000 of revenue, taking the calendar 2022 tally to $350,000. This income derived from selling the particles to third parties for research in other fields such as animal vaccines and hypothermia.

In November 2020, Imagion raised $6 million in a placement at 8.5 cents per share.

In 2021, the company garnered $4.8 million from the exercise of in-the-money options at five cents per share. The company currently has $6 million of options on issue, with a three-cent exercise price.

Imagion's base of 8,500 investors have seen the share price fall from a peak of 20 cents in February 2021 to as low as two cents (in January this year).

The shares traded as low as one cent at the onset of the pandemic, in March 2020. This week they perked up to 3.3 cents after the MRI decision, briefly rendering the aforementioned options in-the-money.

Finger in the wind

Mr Proulx says the breast cancer trial was never meant to be statistically significant; rather, it was a "finger in the wind" as to whether Magsense looked like working.

Imagion's next task is to expand the trial globally, with an eventual registration study requiring perhaps 500 patients. The company may also introduce a 'de-escalation' component to the study, to test with doses lower than 30 milligrams.

Last September, the company presented research on Magsense for prostate cancer to the World Molecular Imaging Congress in Miami, Florida.

Preclinical work provided "strong evidence the company's [technology] has the potential to target prostate cancer tumours expressing the prostate specific membrane antigen [PSMA] with high specificity".

Dr Boreham's diagnosis:

Mr Proulx says initially the company identified 150 applications for non-invasive cancer imaging, but honed that down to only 20 that would fly in a commercial sense.

For example, pancreatic cancer is a large unmet market, but a tricky one as the tumors don't express a particular biomarker.

"We focus on where the unmet medical need is and whether we have an imaging solution to tackle that," Mr Proulx says.

"We are focused on cancer applications where the biology is reasonably well known and we can target them by putting the biology on our particles."

That said, breast, prostate and ovarian cancers alone are a $US4.5 billion market opportunity.

Despite this week's price fillip, Imagion's "impatient and frustrated" holders (the company's words) remain to be convinced about the company's prospects.

"We are undervalued for a clinical stage company, but it is what it is," Mr Proulx says.

Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He considers himself to be undervalued, but it is what it is.

VAXXAS PTY LTD

Vaxxas says it has begun its 150-patient, phase I trial of inactivated seasonal influenza vaccine quadrivalent (IIV4) using its needle-free vaccine technology.

Vaxxas said the trial would assess the safety, tolerability and immunogenicity of an IIV4 candidate in about 150 healthy participants, aged 18 to 50 years, who had not received an influenza vaccine within the last six months and had received no vaccines of any kind for at least 30 days prior to participating in the study.

The company said the trial was being conducted at three University of the Sunshine Coast sites in Brisbane, Morayfield and Sippy Downs.

Vaxxas said that its high-density micro-array patch (HD-MAP) needle-free vaccine technology would use the commercially available IIV4 from an unnamed bio-pharmaceutical company, which targeted four strains of the influenza virus and offered "broad immune coverage against the 'flu viruses expected to circulate across the globe for a given 'flu season".

Last year, Vaxxas said it had raised $US23 million ($A34 million) in a placement led by Sydney's Oneventures and the University of Queensland University's commercialization arm Uniquest Pty Ltd for its clinical programs, including its needle-free Covid-19 vaccine and installation of manufacturing lines (BD: Dec 6, 2022).

In November, Vaxxas said that it had begun a 44-adult, phase I, safety and tolerability trial of the needle-free delivery of a severe acute respiratory syndrome coronavirus-2 (Sars-Cov-2) vaccine (BD: Nov 9, 2022).

Today, the company said that its HD-MAP could be kept at temperatures up to 40°C for at least 12 months without losing effectiveness, while other needle vaccines had to be stored at two to eight degrees Celsius to remain effective.

Vaxxas chief executive officer David Hoey said administration of a quadrivalent influenza vaccine via a needle-free platform like Vaxxas' HD-MAP has the potential to increase vaccination coverage and uptake.

"Vaccine delivered via HD-MAP patch technology removes the need for needle and syringe, is easy to use, and can potentially be self-administered," Mr Hoey said.

"It also has the potential to simplify distribution by removing or reducing the need for refrigeration," Mr Hoey said.

Vaxxas is a private company.

AROVELLA THERAPEUTICS, IMUGENE

Arovella says with Imugene it will advance to in-vivo testing of Arovella's CAR-iNKT cell therapy (ALA-101) and Imugene's oncarlytics therapy (CF33-CD19), in mice.

Arovella said that in-vitro trials of its chimeric antigen receptor invariant natural killer T-cell (CAR-INKT) and Imugene's Oncarlytics CF33-CD19 oncolytic virus therapy found that when combined, they killed solid tumor cells, and that it would progress to the next stage of testing the combination in mice.

The company said that it expected results from the first stage of testing in "the near term" while results of the second stage were expected in "mid-2023".

Arovella managing-director Dr Michael Baker said the company was "pleased by the first set of data and delighted to continue the partnership with Imugene and its Oncarlytics platform".

"Combining the two platforms made sense scientifically and seeing this play out in practice is exciting, given the impact this combination of therapeutics could have in solid tumors," Dr Baker said.

Arovella was up half a cent or 15.6 percent to 3.7 cents with 9.6 million shares traded.

CYTIVA PTY LTD, ACURABIO PTY LTD

Cytiva says the Brisbane's Acurabio will manufacture plasmid DNA using Cytiva's "bacterial plasmid two-step purification protocol".

Cytiva said Acurabio would provide bio-pharmaceutical contract development and manufacturing services for its bacterial plasmid two-step purification protocol, which it said featured "single-use purification technology which delivers efficiency, high purity level outcome and sustainable process".

Last year, the Federal Government said it would provide $12.6 million to support Cytiva's Springfield Bio-Park Australia project in Ipswich, Queensland (BD: Nov 14, 2022).

The Government said the project would be operated by the Marlborough, Massachusetts-based Cytiva, formerly known as General Electric Life Sciences, and would help "buy new equipment to expand its bio-manufacturing capabilities for high-value medicines".

Today, Acurabio chief executive officer Guillaume Herry said "we are very excited to implement Cytiva's latest technology especially because the access and production of plasmid DNA has been a bottleneck in the advanced therapy market".

"We intend to bring biotechs and biopharma companies a more high-quality plasmid DNA quicker than before to help the development of new therapies such as viral vectors and mRNA," Mr Herry said.

Acurabio is a private company.

IMUGENE

Imugene says the US Patent and Trademark Office has granted a patent protecting its B-cell activating immunotherapy programmed death-1 (PD1-Vaxx), or IMU-201.

Imugene said the patent, titled 'Human PD1 Peptide Vaccines and Uses Thereof,' would protect its intellectual property until 2038.

Imugene was up one cent or 7.4 percent to 14.5 cents with 29.8 million shares traded.

STARPHARMA HOLDINGS

M&G Plc says it has reduced its holding in Starpharma from 31,889,780 shares (7.85%) to 27,859,212 shares (6.81%).

The London-based M&G said that between January 14, 2021 and February 8, 2023 it bought and sold shares, with the single largest sale on January 14, 2021 of 2,020,000 shares for $3,038,650 or $1.50 a share.

Starpharma was up half a cent or 0.9 percent to 56 cents.

LUMOS DIAGNOSTICS

Perennial Value Management says it has increased its holdings in Lumos from 15,730,245 shares (7.09%) to 18,181,615 shares (8.19%).

The Sydney-based Perennial said that it bought the shares between February 3 and 9, 2023, with the single largest purchase on February 3 of 872,795 shares for $26,241 or three cents a share.

Lumos was unchanged at three cents with 1.05 million shares traded.