Biotech Daily

Friday June 25, 2021

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: TELIX UP 13%; RESONANCE DOWN 9%**

*** DR BOREHAM'S CRUCIBLE: IMUGENE**

*** PROTEOMICS: 'PROMARKERD TEST COULD SAVE $51b PER YEAR'; HALT**

*** J&J, NAVBIT LAUNCH SPRINT NAVIGATION FOR HIP REPLACEMENT**

*** ELLUME, DELTA AIR LINES DEAL FOR SARS-COV-2 TEST KITS**

*** CRONOS: SAIPH MARIJUANA SKIN PRODUCTS FOR JAPAN, HONG KONG**

*** TOTAL BRAIN $1.8m LOAN**

*** ADALTA TAKES $1.7m RADIUM RDTI LOAN**

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*** STATE STREET TAKES 5% OF COCHLEAR**

*** DR ALAN FINKEL, NEBULA, HOWITT REDUCE TO 5% OF COGSTATE**

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MARKET REPORT

The Australian stock market was up 0.45 percent on Friday June 25, 2021, with the ASX200 up 32.7 points to 7,308.0 points. Twenty of the Biotech Daily Top 40 stocks were up, 11 fell, eight traded unchanged and one was untraded.

Telix was the best, up 74 cents or 13.1 percent to $6.37, with 2.1 million shares traded. Avita and Pharmaxis climbed more than six percent; Antisense was up 5.6 percent; Impedimed, Optiscan and Volpara improved four percent or more; Amplia, Clinuvel, Imugene, Nanosonics, Neuren, Polynovo and Universal Biosensors rose more than two percent; Cochlear, Next Science and Oncosil were up more than one percent; with Genetic Signatures, Medical Developments, Orthocell, Pro Medicus and Resmed up by less than one percent.

Resonance led the falls, down 1.5 cents or 8.8 percent to 15.5 cents, with 275,083 shares traded. Prescient lost 7.5 percent; Immutep fell 4.4 percent; Actinogen and Cynata were down more than three percent; Compumedics, Cyclopharm, Opthea and Patrys shed more than one percent; with CSL, Mesoblast and Starpharma down less than one percent.

DR BOREHAM'S CRUCIBLE: IMUGENE

By TIM BOREHAM

ASX code: IMU

Share price: 37 cents; **Shares on issue:** 4,936,304,190; **Market cap:** $1.83 billion

Chief executive officer: Leslie Chong

Board: Paul Hopper (executive chair), Ms Chong, Dr Axel Hoos, Charles Walker, Dr Lesley Russell, Dr Jens Eckstein

Financials: (March quarter 2021): revenue nil, cash outflows $4.64 million, cash on hand $29.4 million (a further circa $30 million of listed and unlisted options are expected to be converted within the next two years)

Identifiable major holders: Richard John Mann & Family 5.93%, Paul Hopper 4.09%, Dr Nicholas Smith 2.7%, Leslie Chong 1.56%, Private Portfolio Management 1.35%.

Trick question: excluding CSL, which ASX drug developer boasts the biggest market capitalization?

The answer is not the $1.3 billion stem cell play Mesoblast, which at one stage was worth north of $2 billion. And it's not the cancer diagnostics and therapeutics house Telix Pharmaceuticals (with a current worth of $1.26 billion).

What about the rare skin disorders group Clinuvel, which has an approved drug and is revenue producing? Sorry - no cigar.

Since the start of April, Imugene has risen fourfold and is now valued at $1.73 billion, having briefly been worth $2.3 billion.

"Our investors have been very happy of late," trills chief executive Leslie Chong, who joined the company in late 2015 from big pharma Genentech.

The Imugene scene over time

Led by the aptly-monikered Dr Warwick Lamb, Imugene started out as an animal health company in the 1990s and then dabbled in enhanced generics including vitamin D and ibuprofen formulations.

In late 2013, the company acquired the private Biolife Science Queensland, an immune-oncology play based on Medical University of Vienna know-how. This introduced Imugene's lead molecule HER-Vaxx, which targets HER-2, as in human epidermal growth factor receptor-2.

The deal also introduced legendary biotech wheeler-and-dealer Paul Hopper to Imugene and he was duly appointed chair.

In August 2018, Imugene acquired the rights to B-cell peptide vaccines (notably the PD1 checkpoint inhibitor) from Ohio State University and Mayo Clinic.

In 2019, Imugene acquired the global licence for CF33, a chimeric vaccinia (pox) virus developed by City of Hope's ebullient chair of surgery, Prof Yuman Fong. The tech was owned by the private Vaxinia, in which Mr Hopper and Prof Fong were major investors.

In May 2021, the company announced that it had licenced a novel oncolytic virus called CD19 (as in cluster differentiation) from California's City of Hope cancer centre. The terms were undisclosed but involved an immaterial cash payment.

The facts on HER-vaxx

HER-Vaxx is Imugene's oldest and most advanced program.

Aimed at gastric cancer, a phase II gastric cancer trial, with sites in Eastern Europe and India, enrolled its first patient in March 2019. As opposed to the mechanism of action of ready-made antibody treatments such as the top-selling Herceptin, HER-Vaxx activates the patients' own immune system to produce its own HER-2 antibodies.

HER-2 is overexpressed in 10 to 30 percent of breast, gastric, ovarian and pancreatic cancers.

In an interim analysis last November, Imugene reported a "statistically significant" benefit.

There were 27 evaluable patients in the interim analysis which resulted in an overall survival (the primary endpoint) of 14.2 months for patients on HER-Vaxx plus chemotherapy, versus 8.8 months for chemo alone.

In January, 2021 Imugene completed the recruitment of 36 advanced gastric cancer patients and in April, reported a statistically significant number of events had occurred - that is, data on 24 patients - to establish the secondary endpoint of PFS was met.

The company is now awaiting nature to take its course (yep - the patients to die) in order to log the overall survival results.

Of course, the longer the patients live, the better the data.

As for the B-cell peptide program, Imugene is also developing a checkpoint inhibitor called PD-1 (as in programmed cell death-1).

Imugene's PD1-Vaxx targets non-small cell lung cancer (NSCLC), the most common lung cancer. The program centres on phase I high-strength dosing of patients who have failed checkpoint inhibitor drug therapy.

What alpha is better?

Some eyebrows were raised about the company's use of a 'one-sided' P (probability) value in the gastric cancer study, which produced a flattering 'hazard ratio' of 0.418.

The 'one sided' P value refers to the company setting a probability factor of 10 percent (for the nerds: alpha = 0.1). A registrational study (aimed at drug approval) requires a two-sided alpha of five percent (alpha = 0.05).

This means that in the Imugene's case there is less than a 10 percent risk that the effect they saw was purely by chance, as opposed to less than five percent. The use of a one-sided alpha meant the trial designers expected a positive treatment effect, so the probability bar was lowered.

Ms Chong says setting alpha at 0.1 is normal in phase II or signal-seeking proof-of-concept studies, while the measure is also acceptable for phase II immunotherapy studies.

Why? A smaller number of patients or events are required to complete the study at a lower cost, while providing "meaningful and significant statistics that could well lead to further development" of a drug.

Unleashing the CF33 armoury

As with other oncolytic viruses, CF33 causes tumor cells to rupture and then trains the immune system to recognize the diseased cells and exterminate them. Pre-clinical work suggests that CF33 infiltrates all kinds of solid tumors and replicates rapidly, spreading easily to other malignant cells

Imugene's CF33 program centres on Check-Vacc (CF33 plus the PD-L1 transgene), targeting triple negative breast cancer. Imugene hopes to get US Food and Drug Administration clearance by early July, with enrolment targeting 30 patients starting shortly after.

Then there's Vaxinia, the most potent oncolytic virus in the company's armoury.

After the usual toxicology work, the company plans an "ambitious" study of 86 patients with solid tumors that have metastasized despite previous treatment. These include head neck and shoulder cancers, advanced melanoma, and gastric, breast, lung, renal, bladder and colorectal cancers. Throw in pancreatic cancer (potentially) and that's pretty much the A-Z of tumors.

The latest pickup

Coupled with CF33, CD19 is intended to enable CAR-T (as in chimeric antigen receptor T-cell) therapies. Chimeric antigen receptor T-cells are T-cells that have been genetically engineered to produce an artificial T-cell receptor for use in immunotherapy.

The proposed combination therapy has been dubbed onCARlytics – geddit? Basically it involves souping up the virus to include CD19 (CD19 transgene).

The oncolytic virus (CF33) infiltrates solid tumors and expresses CD19 on the cell surface, so that a CD19 directed target (such as a CAR-T drug) would work in combination. As we noted in our recent piece on Mr Hopper's freshly listed Chimeric, CAR-T is a sexy new area of immunotherapy attracting hot investor interest.

But Ms Chong stresses that CD19 is not a CAR-T play, per se.

What CD19 does - or what it's hoped to do - is tag cancer cells for CAR-T or other CD19 directed therapies in destruction of solid tumors.

To date the US Food and Drug Administration has approved four CD19 CAR-T therapies, but only for blood cancers (B-cell lymphomas and acute lymphoblastic leukaemia).

Ms Chong says "supercharging" CF33 and CD19 is a "revolutionary new paradigm in combination therapy" allowing combination use with CAR-T drugs. Under the City of Hope deal, Imugene has been bestowed the global rights to develop CF33-CD19. This is in return for the upfront fee, annual maintenance fees, milestone payments and royalties.

Lucrative options

It's never a good look when a company's top brass lighten their personal holdings, as Messrs Chong and Hopper recently did.

But the duo was selling ordinary shares to exercise wildly in-the-money options before they expired at the end of June.

Ms Chong sold a tad over 4.48 million shares to convert 50 million options, at a cost of $2.14 million (approximately 4.2 cents apiece). At the time of disposal in late May the shares were worth $1.8 million, give or take a few bob. Mr Hopper sold 1.5 million to convert 25 million options at a cost of $1.07 million.

Post transaction, Ms Chong retains 77 million shares (current market value $29 million) and Mr Hopper has 201.4 million ($76 million).

"Paul has sold 1.01 percent of his holdings and he has never sold in seven years," she says of her chairman.

Ms Chong adds that she didn't exactly have $2 million under her couch cushion; hence the need to sell the shares to buy the options.

The upshot is that Imugene has $3.2 million of funds - the option exercise proceeds - it did not have previously.

But the disclosure could have been better: a laudatory statement mentioned the options purchase, but not the accompanying share sales (which were disclosed in the standard ASX release).

Finances and performance

Thanks to in-the-money options, Imugene won't be short of a dollar as the options are exercised over the next two years.

All in all, there are circa $30 million of options out there and -not surprisingly - holders are converting them sooner rather than later given the bonanza gains on offer.

The company has listed options that will bring in $9.9 million this year and a further $12.3 million in 2022. These are exercisable at 4.5 cents to 5.4 cents.

Then there are $11 million of unlisted options - held by board and management - exercisable from 4.0 cents to 4.5 cents.

As of the end of March the company had just over $29 million in the bank.

Imugene shares hit a record of 47 cents on May 26, having changed hands for as low as one cent in mid-2013.

Northern Queensland beef baron Jack Mann accounts for just over five percent of the register.

Dr Boreham's diagnosis:

Two years ago, Ms Chong declared that the conductor had blown the whistle and the Oncolytic Express was about to leave the station.

Well move over, Fat Controller: Imugene's spectacular valuation uplift since then suggests the Oncolytic Express has been upgraded from Puffing Billy to bullet train.

"That train has certainly got a lot bigger," Ms Chong says. "We have basically five trials that are in the clinic, or will be in the clinic this year or next."

Given the early nature of Imugene's programs it's hard to know on which track the company will end up, and it's unlikely to be an express service to drug development.

The company may well be shunted off the ASX line by being acquired.

Ms Chong notes the blood cancers targeted by the four approved CAR-T drugs account for only 10 percent of all cancers, with the therapies working 60 to 90 percent of the time.

"Imagine if we could get solid tumors to react in that way," she says.

"That would be revolutionary and the most significant drug [discovery] you could imagine."

Disclosure: There's a strong one-sided probability that Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort.

PROTEOMICS INTERNATIONAL LABORATORIES

Proteomics claims its Promarkerd prognostic blood test for diabetic kidney disease can save US payers $US384 billion ($A505.7 billion) over 10 years.
Proteomics said Promarkerd was the “only” test capable of predicting the onset of diabetic kidney disease and Boston Healthcare Associates modelled the impact by comparing its Promarkerd with the current standard-of-care test for diabetic kidney disease in patients with type 2 diabetes but who otherwise had no sign of kidney disease.
Proteomics said the US had 31 million adults with diabetes and if each spent $US150 a year for the test, it would total $US8.9 billion a year but “could produce savings of $US473 billion over 10 years”.
The company said the savings would be “primarily from slowing the progression of diabetic kidney disease, followed by benefits from delaying or preventing dialysis and kidney transplants, and a reduction in dialysis crashes.
Proteomics managing-director Dr Richard Lipscombe said that “testing patients with type 2 diabetes every six to 12 months with Promarkerd would enable early intervention for those at high-risk of developing diabetic kidney disease”.
“This would decrease the need for expensive late-stage interventions, such as dialysis and kidney transplants … and assist in stratifying which patients would receive new [diabetic kidney disease] preventative therapeutic treatments,” Dr Lipscombe said.
The company said it would present the findings at the American Diabetes Association’s 81st Scientific Sessions on June 26, 2021 at 1.30pm (AEST).
Proteomics requested a trading halt “pending the release of the presentation”.
Trading will resume on June 29, 2021 or on an earlier announcement.
Proteomics last traded at 92.5 cents.

JOHNSON & JOHNSON MEDICAL, NAVBIT

Johnson & Johnson says it will launch the Navbit Sprint navigation, using global positioning systems (GPS), to align acetabular cups in hip replacements.
In a media release, Johnson & Johnson said it had partnered with private Sydney company Navbit to bring Sprint to operating theatres in Australia.
The company said the cost of revision hip replacements in Australia in 2018-’19 was about $137.6 million, with dislocation 20.3 percent of revision procedures, or about $27.9 million a year, with the incidence of revision due to dislocation reduced by 31 percent where navigation was used, implying a saving of about $8.7 million a year.
The company said Sprint was “a compact, single use medical device designed to assist surgeons in placing and aligning the acetabular cup”, which used GPS technology to provide feedback to the surgeon on the position of the cup throughout the procedure.
The company said that despite advances in technique, accuracy of cup placement was variable due to factors such as the anatomy of the pelvis, stiffness of the spino-pelvic area, functional positions of the pelvis, its position at set-up and movement during surgery, reference frames used and the way angles were measured.
Navbit co-founder and orthopaedic surgeon Prof Bill Walter said that existing hip navigation technologies were seldom used, as they were” cumbersome and complicated”.
“Achieving the right alignment without technology is actually quite difficult, even for the most highly trained surgical eye,” Prof Walter said.
Johnson & Johnson said that the Navbit Sprint had been included on the Australian Register of Therapeutic Goods following assessment by the Therapeutic Goods Administration and had been cleared by the US Food and Drug Administration and granted Conformité Européenne (CE) mark.

ELLUME

Ellume says it has a partnership with Delta Air Lines to provide its US Food and Drug Administration emergency use authorized Sars-Cov-2 test kits to its customers.
Ellume said the in-home rapid antigen severe acute respiratory syndrome coronavirus (Sars-Cov-2) tests were available for $US50 ($A66) and could be shipped to a home address or picked up locally after purchase from Delta's website.
Ellume is a public unlisted company.

CRONOS AUSTRALIA

Cronos says it has launched cannabidiol-based hand and body care products, Ablution cleanser and Tranquility moisturizer, in Japan and Hong Kong.
Cronos said the Saiph products were formulated for sensitive skin and allergy tested to Japan cosmetic standards.
The company said its Ablution gel-based hand and body cleanser contained 350mg of Japan-compliant cannabidiol and the Tranquility moisturizer had 700mg of Japan-compliant cannabidiol.
Cronos was untraded at 10.5 cents.

TOTAL BRAIN

Total Brain says it has an unsecured loan agreement for $1.8 million from shareholders and a third-party lender.
Total Brain said the loan from 19.9 percent substantial shareholder Zoltan Varga, managing-director Louis Gagnon, directors David Torrible, David Daglio, chief operating officer Matt Mund, and an unrelated undisclosed third-party non-professional lender would be for five months over five months at 12 percent interest per annum.
The company said the loan and accrued interest were repayable in cash during the term with no pre-payment penalty or was due at the end of the term.
Total Brain said the loan would be used for general working capital requirements, to finalize a licencing transaction, and other outstanding contracts.
Total Brain was up one cent or 3.1 percent to 33 cents.

ADALTA

Adalta says it has taken a $1.68 million a research and development tax incentive loan from Radium Capital at 14 percent interest a year.
Adalta said the loan against its accrued research and development tax incentive rebate for the nine months to March 31, 2021 would "help accelerate discovery activities to expand [its] pipeline".
The company said that repayment was timed to coincide with receipt of the Research and Development Tax Incentive, expected by October 31, 2021.
Adalta was unchanged at 13 cents.

HYDRIX

Hydrix has requested a trading halt pending a material announcement "in connection with the [its] distribution of the Angelmed guardian device".
Trading will resume on June 29, 2021 or on an earlier announcement.
Hydrix last traded at 15.5 cents.

CRESO PHARMA
Creso has requested a trading halt “pending an announcement regarding a material sales and revenue update”.
Trading will resume on June 29, 2021 or on an earlier announcement.
Creso last traded at 14 cents.

COCHLEAR
State Street Corp says it has become a substantial shareholder in Cochlear with 3,289,926 shares or 5.00 percent of the company.
The Boston-based State Street and subsidiaries said between February 23 and June 22, 2021 it made in bought and transferred shares at prices ranging from $200.29 to $246.85 a share.
Cochlear was up $3.83 or 1.6 percent to $248.78 with 150,421 shares traded.

COGSTATE
Former chief scientist Dr Alan Finkel and associates have reduced their substantial shareholding in Cogstate from 9,000,000 shares (6.34%) to 8,975,634 shares (5.25%).
The former Cogstate director, Dr Finkel said that through Nebula Neuro and Howitt Nominees he acquired 900,000 shares in a rights issue for $243,000 or 27 cents a share and between February 2 and June 24, 2021 sold bought 924,366 shares for $1,292,631 or an average price of $1.40 a share.
Cogstate was up 18.5 cents or 15.4 percent to $1.385 with 827,583 shares traded.

ESENSE-LAB
Esense says it proposes to be removed from the official list of the ASX “in the best interest of security holders”.
Esense said it had been suspended from trading on the ASX since July 27, 2020 following an ASX query.
The company said it required funding for its ongoing operational and working capital requirements which since the suspension had been increasingly difficult and it had not benefited from being a listed entity.
Esense said it was in the process of considering alternative listing on the TSX Venture Exchange or the Canadian Securities Exchange following the de-listing.
The company had been attempting to commercialize marijuana “terpenes”.
Esense last traded at 1.8 cents.

CSL
CSL says that it has “regretfully” accepted the resignation of Abbas Hussain as an independent non-executive director, effective immediately.
CSL said that Mr Hussain resigned after being appointed as the chief executive officer of the St Gallen, Switzerland-based Vifor Pharma Group.
The company said that Mr Hussain had been a director since 2017 and thanked him for his contribution.
CSL fell $1.48 or 0.5 percent to $285.13 with 809,863 shares traded.

BIOCURATE

Biocurate says it has appointed Dr Marie Lindner as an independent director and Dr Lindner and Josephine Wu as members of its investment committee.
The University of Melbourne and Monash University joint venture, supported by Victoria Government said Dr Lindner had worked as an executive in pharmaceutical, biotechnology, venture capital and start-up for more than 30 years.
Biocurate said that Dr Lindner specialized in internal medicine and nutrition at the Hospital of the University of Pennsylvania and the Children's Hospital of Philadelphia.
The company said that Ms Wu had more than 19 years' experience in of hedge fund, family office and asset management and was the founder and current chief investment officer of Aionious Capital.

CHIMERIC THERAPEUTICS

Chimeric says it has appointed Dr Li Ren as its head of technical operations.
Chimeric said Dr Ren had "nearly 20 years of experience developing and advancing cell therapy drug candidates from the pre-clinical stage through to commercial licensure."
The company said Dr Ren would be responsible for leading the process and analytical development of chlorotoxin chimeric antigen receptor T-cells (CLTX-Car-T), ensuring the technology transfer to a clinical manufacturing organisation of CLTX-Car-T for future trials.
Chimeric said Dr Ren was previously with Bristol-Myers Squibb and oversaw technology transfer and previously worked for Celgene.
Chimeric fell half a cent or 1.75 percent to 28 cents.

MEDIBIO

Medibio says it has appointed Los Angeles-based Rogers and Cowan PMK for marketing and communications for its mental health application launch in the US.
Medibio fell 0.05 cents or 6.7 percent to 0.7 cents with 2.5 million shares traded.