Biotech Daily

Friday September 11, 2020

Daily news on ASX-listed biotechnology companies

*** ASX DOWN, BIOTECH EVEN: IMMUTEP UP 7.5%; IMUGENE DOWN 6%**

*** DR BOREHAM'S CRUCIBLE: KAZIA THERAPEUTICS**

*** DOHERTY INSTITUTE: 'COVID-19 T-CELL IMMUNE RESPONSE LOW'**

*** FEDERAL $3.7m FOR 3D MEDITECH COVID-19 NASAL SWAB DEAL**

*** PRO MEDICUS, NY UNI $25m IMAGING CONTRACT; RESEARCH DEAL**

*** ELLUME ADDS QIAGEN SARS-COV-2 ANTIGEN TO ANTIBODY TEST**

*** FDA SUGGESTS IMPROVEMENTS FOR POLYNOVO NOVOSORB TRIAL**

*** GENETIC TECHNOLOGIES BREAST CANCER RISK TEST ON SALE IN US**

*** OPTHEA 4m DIRECTOR OPTIONS AGM**

*** REGENEUS 15.3m DIRECTOR OPTIONS AGM**

MARKET REPORT

The Australian stock market fell 0.83 percent on Friday September 11, 2020, with the ASX200 down 49.1 points to 5,859.4 points.

Sixteen of the Biotech Daily Top 40 stocks were up, 15 fell, seven traded unchanged and two were untraded.

Immutep was the best, up 1.5 cents or 7.5 percent to 21.5 cents, with 4.7 million shares traded. Medical Developments climbed 3.7 percent; Impedimed, Optiscan, Orthocell and Uscom rose more than two percent; Actinogen, Cochlear, Pro Medicus and Starpharma were up one percent or more, with Clinuvel, CSL, Nanosonics, Neuren, Opthea, Polynovo, Universal Biosensors and Volpara up by less than one percent.

Imugene led the falls, down 0.3 cents or 6.25 percent to 4.5 cents, with 12.9 million shares traded. Antisense, Oncosil, Osprey and Proteomics lost more than three percent; Alterity, Cynata, Genetic Signatures and Kazia shed more than two percent; Compumedics, Paradigm, Prescient and Telix and were down more than one percent; with Avita, Mesoblast and Resmed down by less than one percent.

DR BOREHAM'S CRUCIBLE: KAZIA THERAPEUTICS

By TIM BOREHAM

ASX code: KZA; **Nasdaq code:** KZIA

Share price: 96.5 cents; **Shares on issue:** 94,623,369; **Market cap:** $91.3 million

Chief executive officer: Dr James Garner

Board: Iain Ross (chairman), Bryce Carmine, Steven Coffey, Dr Garner

Financials (year to June 30 2020): revenue nil, other income $995,000*****, loss of $12.47 million, cash on hand $8.8 million

***** Consists mainly of $968,000 R&D tax rebate

Major identifiable holders: Willoughby Capital 13.06%, Platinum International Health Fund 9%, MNA Family Holdings (Hishenk Pty Ltd super account) 2.27%, Hishenk Pty Ltd (Michael Abolakian) 1.63%

In winning rare paediatric disease designation in the US for an aggressive childhood brain cancer last month, Kazia picked up one of the hottest tickets in the biotech world: a priority review voucher from the US Food and Drug Administration.

While they sound like meaningless paperwork, the vouchers are valuable and fungible, having changed hands for as much as $US350 million ($AUD490 million). More recent transactions have coalesced between $US150 million and $US200 million.

The quirk of the incentive scheme for drug developers is that the vouchers are validated on approval of a drug. Thus, the expedited review timeline is only relevant for another late-stage developer, typically a big pharma company, rather than the initial holder. One advantage is that the documents can be submitted over time and signed off as needed - which is a big thing.

"If you can launch a $1 billion drug six months earlier it's worth half a billion dollars," says Kazia chief executive James Garner. "The idea is not so much we use it but sell it to someone else."

A fortnight later, on August 20, the FDA also awarded fast-track designation for Kazia's lead drug paxalisib (formerly GDC-0084), for the brain cancer glioblastoma.

And four days after that, Kazia's paxalisib picked-up an FDA orphan drug designation for malignant glioma, which includes the rare and aggressive kids' disease diffuse intrinsic pontine glioma, for which it won the rare paediatric disease award. Investors have not been impervious to the upbeat tidings, with Kazia shares doubling since then.

"It's been a really busy time for us and it's great to see some of these efforts bearing fruit," Dr Garner says.

High profile victims of rare disease

The most common form of brain cancer, glioblastoma, killed both former Republican presidential candidate John McCain as well as Beau Biden, son of current Democrat challenger Joe Biden. In an election year Kazia ain't taking sides!

Local victims include broadcaster Stan Zemanek, Sydney surgeon and reality TV star Chris O'Brien and journalists Andrew Olle and Matt Price.

The disease is relatively rare but not extremely so, with about 133,000 new cases a year - 12,500 of them in the US.

The paediatric treatment pertains to the truly rare and aggressive diffuse intrinsic pontine glioma (DIPG), which affects 300 to 500 kids in the US each year and maybe one-tenth as many here.

"It's a very aggressive tumor with no existing drug treatment," Dr Garner says. "The average survival from diagnosis is around nine to 10 months, so this is the absolute definition of unmet medical need."

Kazia's ancient roots

Kazia was formerly known as Novogen, Australia's second oldest listed biotech behind Circadian (now Opthea). Novogen bought GDC-0084 from Glioblast Pty Ltd, which had earlier licenced the compound from Roche's Genentech.

Interestingly, Glioblast was owned by biotech Hall of Famer Paul Hopper and Leslie Chong, who oversaw development of GDC-0084 while at Genentech (she now heads up the ASX-listed Imugene).

Founded by Dr Graham Kelly, Novogen listed on the ASX in 1994 and then on the US Nasdaq in 1998. In its tortured history, Novogen has had many guises, including a developer of veterinary products and women's natural health supplements and red clover leaf derivatives for cancer.

Dr Kelly left the company in 2005 after a strategic difference of opinion with the board, only to return as CEO in 2012. He departed (again) in 2015 to found the now ASX-listed Noxopharm.

Novogen's board recruited Dr Garner in 2016 to take the company along a more commercially-focused path, rather than dabbling in early stage stuff that never went anywhere.

Novogen then engaged in a legal spat with Noxopharm over intellectual property, which was settled in 2017.

In that year Novogen changed its name to Kazia, which is Hebrew (or possibly Polish) for "this is a meaningless yet pleasant enough name which no one else had trademarked" – and not to be mistaken for 1970s cheap children's keyboards.

In the clinic

The core problem with glioblastoma is that there's been little progress treating the condition over the last two decades. While breast and lung cancer drugs have been repurposed, they don't quite hit the spot. The usual treatment is a drug called temozolomide.

Paxalisib inhibits a signalling pathway called PI3K, which is expressed in 85 percent to 90 percent of glioblastoma tumors.

Interim results from a 30-patient, phase II study showed a five months' median extension in overall survival to 17.7 months, compared with 12.7 months for the control group on temozolomide.

Progression free survival time (that is, the tumor not spreading) extended from 5.3 months to 8.4 months.

The company is about to enter a phase III pivotal study, in view of fronting the US FDA for marketing authorization.

In an unusual yet efficacious approach, Kazia plans to join a worldwide study called GBM Agile. (GBM being shorthand for glioblastoma).

Created independently of any individual drug company, GBM Agile aims for a standardized approach that generates data in a format the FDA likes to see. The long-term study involves drug developers slotting in their drug for a certain period, with the collaborative approach creating economies of scale.

The first entrant to the study is a Bayer-owned drug called Stivarga (regorafenib).

"That part is currently recruiting as we speak. Paxalisib should be the second drug to join, and that is slated to start recruiting by the end of the year," Dr Garner says.

"GBM Agile will recruit up to 200 patients on paxalisib, and roughly the same number in the control arm, so that would imply something like a 400 to 450 patient study."

However, there's an element of uncertainty because the study is adaptive (tweaked along the way). "If we get an answer after, say, 150 patients on paxalisib that the drug clearly works, then the study stops there," Dr Garner says.

A sound metho-dology

Kazia's work is predicated on the notion that temozolomide isn't effective for two-thirds of glioblastoma patients, which sounds like a big fat fail to us.

But it all depends on whether patients have a 'methylated' or 'unmethylated' form of the disease. We won't go into the technical differences, but they relate to genetic factors.

Dr Garner says the ‘methylated’ group will respond to temozolomide, with an average life extension of six to seven months.

But if you’re ‘unmethylated’, expect to live another 12 days or so.

“We can tell in advance whether they will benefit from the drug with absolute accuracy,” Dr Garner says.

Did you know?

Kazia’s annual report informs us that randomized clinical trials were supposedly first devised by 18th Century Scottish doctor James Lind, who worked on the high seas with the British Navy.

Observing high mortalities from scurvy, the good doctor assigned one group of scorbutic sailors oranges and lemons, while the other received the standard of care: seawater.

No surprises for guessing which cohort emerged the healthier.

It is not recorded whether Doc Lind’s methods received ethics committee approval before the voyage.

Partner wanted for second-string therapy

Kazia also has a legacy ovarian cancer drug candidate called Cantrixil (regorafenib), which has passed phase I scrutiny with results pending.

“We don’t see us taking it forward single handedly,” Dr Garner says.

“The drug has shown promise. But ovarian cancer is a complex space and there are lots of new therapies coming along.”

Ideally, the company would like to find a partner with deeper pockets and more technical expertise in ovarian cancer.

Finances and performance

Presciently, Kazia beat the biotech sector’s rush to raise capital by going to the well in April and gathering $9 million in a placement and share purchase plan.

The company also raised $4 million the previous October.

“We have money well into next year at this stage,” Dr Garner says. “We are in the nice position in that we are not under pressure to do anything.

“It’s still a very uncertain market. Coronavirus isn’t going away, we have the US presidential election and some of the implications of the pandemic are yet to register.”

Kazia shares touched a 12-month low of 37 cents on May 11 this year, but then soared to a record high of $1.12 on August 20. The shares touched a record low of 32 cents on June 21 last year.

Dr Garner says the Nasdaq listing (American depository receipts) used to account for two to three times the turnover of the local shares. But more recently the interest from local investors has been more pronounced.

In June 2016, Kazia was valued at less than $4 million, compared with circa $95 million now.

Dr Boreham's diagnosis:

The harsh reality of cancer drug development is that the treatments usually offer more time, rather than a curative. As we noted, paxalisib at this stage looks like adding five months.

Depending on the cost of the drug, maybe there's a cost-benefit trade-off. But any brain cancer doctor would be happy to offer the drug in the context that less than five percent of glioblastoma patients will live beyond five years after diagnosis.

Dr Garner says the company has reached an "endgame" where management starts to focus on commercialization options.

Not surprisingly, Kazia is keen on adding value to the compound with more clinical work. Beyond that, management's "base case" is licencing the drug to a larger company or companies.

Kazia should also be considered a takeover target, although we have to say that foreign biotech acquirers are much more frequently talked about than spotted on our shores.

"We want do whatever is the best opportunity for patients to access the drug and the best value for shareholders," Dr Garner says.

Meanwhile the rare paediatric priority review voucher scheme is due to expire in September, although it might be extended by whoever wins the keys to the White House.

But it's likely that at least there will be a freeze on new issuances, which makes the current paper out there more valuable. In theory, at least.

Dr Garner says the company exemplifies the old gag about overnight success being 10 years in the making.

"There's definitely a sense the Australian market is waking up to the stock - and not before time," he says.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Being in locked-down Melbourne he would gratefully accept any 'get-out-of-jail free' voucher.

THE PETER DOHERTY INSTITUTE FOR INFECTION AND IMMUNITY

The Peter Doherty Institute says that “killer T-cells … are present at much lower levels in people with Covid-19, compared to influenza or glandular fever”.

The Institute said that killer T-cells, or CD8 (cytotoxic) T cells were key immune cells in fighting viral infections and were integral to mounting an effective and rapid recovery from viruses such as influenza.

The Institute said its research team looked at 22 Covid-19 samples from patients who had asymptomatic, mild or moderate illness and T-cells in people who express a T-cell recognition protein called human antigen leucocyte (HLA) serotype HLA-A2 and found that the “key immune cells weren’t stimulated optimally for rapid proliferation and expansion to fight [severe acute respiratory syndrome coronavirus 2 (Sars-Cov-2)]”.

The research article, titled ‘Suboptimal SARS-CoV-2−specific CD8+ T cell response associated with the prominent HLA-A*02:01 phenotype’ was published in the US Proceedings of the National Academy of Sciences and is available at: https://www.pnas.org/content/early/2020/09/09/2015486117.

Co-author and University of Melbourne researcher Jennifer Habel said the magnitude of the killer T-cells “was only five times higher than those of the naïve immune cells”.

“To give that perspective it is … [an order of magnitude] lower than what we see during an influenza or glandular fever response,” Ms Habel said.

The Doherty Institute says the team looked at the activation profile of these immune cells and found that not only was activation of immune cells “was poor, but in some cases these cells remained … as if they hadn’t been exposed to the virus at all”.

The study’s lead researcher, the University of Melbourne’s Prof Katherine Kedzierska said the findings supported the ‘prime and boost’ vaccine model.

“Knowing the specific T-cells and proteins to target will inform the design of an effective vaccine,” Prof Kedzierska said.

The Institute said that if a vaccine was able to prime the immune system of killer T-cells and then boost them a short time later, the immune response is likely to be much more robust to fight Sars-Cov-2.

Co-author Prof Peter Doherty said that “if the Sars-Cov-2 virus is indeed compromising the killer T-cell response that can be important for recovery”.

“The best bet may be to get the right vaccine before the virus gets to us,” Prof Doherty said.

The Doherty Institute said the research was done in collaboration with Melbourne’s Monash University and Alfred Hospital, the Townsville, Queensland-based James Cook University, Hobart’s University of Tasmania.

FEDERAL GOVERNMENT

The Federal Government says it will pay Port Melbourne’s 3D Meditech $3.7 million for the supply of sterile nasopharyngeal swab kits to test for Covid-19.

In a media release, the Minister for Health Greg Hunt said 3D Meditech would supply the three dimensional (3D) printed nasopharyngeal swab kits, which were listed on the Australia Register of Therapeutic Goods, for distribution among general practitioners, private pathology providers and state and territory governments.

Mr Hunt said the kits would include a nasopharyngeal swab, salt solution, and a bio-hazard bag.

The media release said the first kits would be delivered “this week, with further deliveries continuing weekly until early March 2021”.

PRO MEDICUS

Pro Medicus says it has a seven-year, $25 million contract with New York University's Medical Centre for its Visage imaging technology.

Pro Medicus said the deal was through its subsidiary Visage Imaging and would implement the Visage 7 technology in the New York University Medical Centre's radiology and sub-specialty imaging departments, including six hospitals and numerous additional locations, replacing all existing picture archiving and communication systems (PACS).

The company said the Visage 7 rollout was planned to begin by April 2021.

Separately, Pro Medicus said it had a multi-year research collaboration with New York University Medical Centre to develop enterprising imaging for workflow optimization, integration with multi-vendor reporting platforms and the integration of artificial intelligence (AI) technology, with the Centre joining the Visage AI Accelerator program.

The company said it would establish a research and development hub in New York City for its research and commercialization opportunities in the US.

Pro Medicus chief executive officer Dr Sam Hupert said the collaboration with New York University was "a major milestone for our company".

"Having our own [research and development] presence in North America will enable us to leverage the development and commercialization potential of our Visage AI Accelerator and other programs across our rapidly increasing base of North America's top academic, research-oriented clients," Dr Hupert said.

The New York Medical Centre was renamed New York University Langone following a donation from Kenneth and Elaine Langone.

Pro Medicus was up 28 cents or 1.1 percent to $26.26 with 663,071 shares traded.

ELLUME

Ellume says it is developing a severe acute respiratory syndrome coronavirus-2 (Sars-Cov-2) antigen test for the presence of the virus with partner Qiagen NV.

In August, Ellume said it had applied to the US Food and Drug Administration for approval of its Access Anti-Sars-Cov-2 Total Covid-19 blood antibody test and its Hilden Germany-based partner Qiagen NV had submitted an emergency use authorization application and had 900,000 tests pre-ordered (BD: Aug 27, 2020).

Today, the company said the new test was "a rapid, high-performance Sars-Cov-2 antigen test, for active … infection, on the Qiagen Access platform" and the two products would address the global demand for rapid, accurate diagnostic tests for Sars-Cov-2 infection.

Ellume said the Access anti-Sars-Cov-2 antigen test would be "a rapid, portable test that can detect Sars-Cov-2 antigens in people with active infections using nasal samples [and] like the … antibody test, the antigen test is run on the Access Ehub".

The company said the Ehub was a portable, digital device that provided "reliable results in less than 15 minutes and in as little as three minutes in the case of a strong positive".

Ellume said that the Ehub could handle up to eight patient samples, process more than 30 samples per hour and both antigen and antibody tests could be run simultaneously.

The company said that multiple Ehubs could be located at high demand sites with minimal cost, enabling laboratories to run tests to detect both previous and active infections on one device at the same time, with each testing slot operating independently of the others.

The company said that the Access antigen test had a sensitivity of at least 90 percent in symptomatic patients and a specificity of 100 percent.

Ellume said that Qiagen would apply for US Food and Drug Administration emergency use authorization and seek Conformité Européenne registration in Europe.

Ellume is a public unlisted company.

POLYNOVO

Polynovo says the US Food and Drug Administration has made suggestions to improve the protocol for its pivotal trial of Novosorb for full thickness burns

In March, Polynovo said it had filed the results of its 15-patient trial of Novosorb to the FDA with its investigational device exemption application and had expected “approval for the larger pivotal trial IDE in June 2020” (BD: Mar 16, 2020).

In July, the company said the FDA had requested additional information for the trial, including a request for the formalization of the review points (BD: Jul 10, 2020).

Today, Polynovo said that along with its trial partner, the US Biomedical Advanced Research and Development Authority (BARDA), it would incorporate the FDA recommendations “to improve the rigour of the trial with some design and administrative changes … over the coming weeks”.

Polynovo managing-director Paul Brennan said that the “the discussion on aspects of the trial management processes does not have any impact on our US sales or momentum with Novosorb [biodegradable temporizing matrix].”

Polynovo was up one cent or 0.5 percent to $2.15 with 2.8 million shares traded.

GENETIC TECHNOLOGIES

Genetic Technologies says its Genetype for breast cancer risk assessment test kit is available in the US through online sales platform, Intelelabs, for $US249 ($A342).

Genetic Technologies said the test informed individuals their five-year and lifetime risk of developing breast cancer using a combination of clinical risk factors and a polygenic risk score after anaylizing a buccal, or cheek, swab.

The company said test price included the buccal swap kit and the provision of results and potential referrals through telemedicine consultations.

Genetic Technologies chief executive officer Dr George Muchnicki said that Covid-19 had “deterred many women from seeking out standard check-ups, with mammography screening down since March”.

“[For] women who are still not comfortable scheduling their appointment … risk assessment can be a valuable tool to identify women who are at increased risk of breast cancer,” Dr Muchnicki.

Genetic Technologies said that it planned to add Genetype for colorectal cancer and other tests to its US sales platform, as well as launch an online platform in Australia.

Genetic Technologies was up 0.1 cents or 12.5 percent to 0.9 cents with 28.0 million shares traded.

OPTHEA

Opthea says its annual general meeting will vote to issue 4,000,000 options to chairman Lawrence Gozlan and director Dan Speigelman.

Opthea said Mr Gozlan and Mr Speigelman would each receive 2,000,000 options exercisable at 50 percent above the five-day volume weighted average price at the grant date and within four years.

The company said shareholders would vote to adopt the remuneration report, re-elect chairman Geoffrey Kempler and elect Mr Gozlan and Mr Spiegelman as directors, ratify placement shares, and approve the issue of shares for the proposed US Nasdaq initial public offer.

The meeting will be held online on October 12, 2020 at 9am (AEDT).

Opthea was up one cent or 0.4 percent to $2.76.

REGENEUS

Regeneus says shareholders will vote to issue15,279,500 options to chief executive officer Leo Lee and directors Dr Alan Dunton, Dr John Chiplin and Prof Graham Vesey.

Regeneus said its annual general meeting would vote to issue Mr Lee 1,250,000 options exercisable at 20 cents each, 3,500,000 options exercisable at 10 cents and 7,500,000 options exercisable at 14 cents within five years for the finalization of a licencing agreement with Tokyo's Kyocero Corp (BD: Aug 11, 28, 2020).

The company said it would issue Dr Dunton and Dr Chiplin with 1,000,000 options each, exercisable at 10.75 cents by August 31, 2025 and Prof Vesey 1,029,500 options exercisable at 14 cents by August 31, 2025.

The company said shareholders would vote to adopt the remuneration report, to re-elect chairman Barry Sechos and director Prof Vesey, approve a 10 percent placement capacity, and approve the ratification of shares.

The meeting will be held online on October 14, 2020 at 2:30 pm (AEDT).

Regeneus was up half a cent or 2.9 percent to 18 cents.