Biotech Daily

Friday August 9, 2024

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: AVITA UP 8%; NEUREN DOWN 5.5%**

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

*** NEUREN: 'NNZ-2591 SIGNIFICANTLY IMPROVES ANGELMAN SYNDROME'**

*** AVITA H1 REVENUE UP 18% TO $40m; LOSS UP 74% TO $52m**

*** IDT UP-TO $4m SANOFI mRNA FOLLOW-UP CONTRACT**

*** CHIMERIC, CELL THERAPIES TO MAKE CAR-T CELLS IN AUSTRALIA**

*** CARDIEX TAKES $1.12m MITCHELL ASSET RDTI LOAN; TOTAL $2m**

*** ALLEGRA TAKEOVER BID 'UNCONDITIONAL'**

*** NEUROTECH 1m DIRECTOR OPTIONS, 60m FENIX SHARE, RIGHTS EGM**

*** WASHINGTON H SOUL PATTINSON BELOW 5% OF AMPLIA**

*** BREAKTHROUGH VICTORIA LOSES CEO GRANT DOOLEY; BOARD CHANGES**

MARKET REPORT

The Australian stock market was up 1.25 percent on Friday August 9, 2024, with the ASX200 up 95.7 points to 7,777.7 points. Twenty-nine of the Biotech Daily Top 40 stocks were up, eight fell, two traded unchanged and one was untraded. All three Big Caps rose.

Avita was the best, up 20 cents or eight percent to $2.70, with one million shares traded.

Alcidion and Universal Biosensors climbed more than seven percent; Immutep improved 6.7 percent; Imugene and Percheron were up more than five percent; Atomo, Curvebeam, Dimerix, Nova Eye, Polynovo and Resonance rose more than four percent; Clarity was up 3.7 percent; Clinuvel, Cochlear, Medadvisor, Medical Developments, Mesoblast, Paradigm, Prescient and Pro Medicus rose more than two percent; 4D Medical, Aroa, Compumedics, CSL, Emvision, Impedimed and Telix were up one percent or more; with Cyclopharm, Genetic Signatures, Resmed and Starpharma up by less than one percent.

Neuren led the falls, down 94 cents or 5.5 percent to $16.15, with 1.9 million shares traded. Amplia lost 3.7 percent; Micro-X and SDI shed more than two percent; Nanosonics, Opthea and Orthocell were down more than one percent; with Proteomics down by 0.6 percent.

DR BOREHAM'S CRUCIBLE: AROVELLA THERAPEUTICS

By TIM BOREHAM

ASX code: ALA

Share price: 14 cents; **Shares on issue:** 1,050,775,660; **Market cap:** $147.1 million

Chief executive officer: Dr Michael Baker

Board: Dr Thomas Duthy (chair), Dr Baker, Dr Debora Barton, Dr Elizabeth Stoner, Gary Phillips

Financials (June quarter 2024): receipts nil, net cash outflows $1.82 million, cash balance $12.7 million, quarters of available funding: 7.0

Identifiable major shareholders: Merchant Funds Management 6.02%, Richard Mann (Mann Beef Pty Ltd) 6.16%, MB Investment Capital 2.64%

Fickle fashion trends don't just apply to apparel: a hot area two years ago, the cell therapies sector is struggling to retain investor interest amid hyped-up expectations, clinical setbacks and high development and manufacturing costs.

In the frank words of Arovella chief Michael Baker: "It's in the worst shape it has been since the highs of 2018 to 2020."

Dr Baker points to lay-offs and shutdowns among the expanding US cell manufacturing companies. "A lot of them came out of the woodwork but should not have and will eventually fall away," he says.

Cell therapy refers to extracting human cells from a patient or donor and tricking them up so they can fight disease more effectively.

There's a silver lining to the malaise: pharmaceutical companies are still paying big dollars for the emerging players, even at early (phase I) clinical phase.

Arovella is seeking to overcome the problems of CAR-T (chimeric antigen receptor) therapies by involving invariant natural killer (INKT) T- cells, one of the body's strongest immune cells which Dr Baker dubs the "soldiers of the blood stream".

"They are rabid killers and we can manufacture them so they are even more potent and then we will give them to patients," he says.

Arovella's lead blood cancer program is about to enter phase I trials, but the company is also eyeing developing the world's first CAR-INKT therapies to tackle gastric, oesophageal and pancreatic cancers.

"This is a very important area for the large pharma companies and we are happy to be in a very niche area of the sector," Dr Baker says.

Straight as an arrow

Arovella started as Eastland Medical in 2001, listing first for syringes and then its unsuccessful Artimist sublingual malaria treatment. Eastland became Suda Pharmaceuticals in 2012 developing a spray-based oral drug delivery platform called Oromist, and took the insomnia treatment, Zolpimist, to market.

Biotech entrepreneur Paul Hopper took over as executive chair in 2019 and oversaw sweeping changes: appointing Bioscience Managers investment guru Dr Baker as CEO, ditching the oral delivery program and closing the company's Perth headquarters.

In June 2021, Arovella signed a deal with Imperial College London to acquire its invariant natural killer T (INKT) cell platform. INKT cells are a rare variant of T-cells. The acquired program, ALA-101 targets a blood cancer marker called CD19 (see below).

In October 2021, the company changed its name to Arovella, which derives from arrow (as in targeted drug delivery) and novel (as in new therapies).

Mr Hopper quit the board in June 2022, with Dr Thomas Duthy eventually becoming chair. Dr Duthy's day job is heading Neurotech, which is developing cannabinoid-based treatments for childhood neurological disorders.

In September 2022, Arovella entered a joint development program with the ASX-listed Imugene - of which Mr Hopper is chair - but in March this year Imugene said it no longer wanted to continue.

Prêt à porter cells

The US Food and Drug Administration has approved six CAR-T treatments, all of them targeting CD19 or the B-cell maturation antigen (BCMA) for blood cancers (leukaemia, lymphomas and multiple myelomas). But because of the incidence of secondary malignancies, albeit low, they all come with an FDA 'black box' warning.

Most of the treatments are based on using the patient's own cells - the autologous approach - which is more bespoke but takes longer, is more expensive and uses potentially compromised cells.

Arovella seeks to avoid the problems with the allogeneic method, by which cells are derived from healthy donors. The doses are stored at minus 170°C and are shipped to clinical sites when needed.

Dr Baker notes that bog-standard T-cells account for 70 percent of the body's immune cells, while 10 to 15 percent are 'natural killer' (NK) cells. The elite INKTs make up 0.1 to 1.0 percent.

"Both [T-cell and NK cells) have limitations: T-cells can't be used off-the-shelf unless they are genetically engineered, which requires an extra step," he says. "NK cells can be given from one person to another, but the desired level of activity has not been seen to date."

Manufacturing - dull but important

Dr Baker says Arovella didn't invent INKT cells - nature did - but the company's smarts are tied up in a multi-step manufacturing process that can be done in numerous ways.

"Manufacturing doesn't sound that interesting but it is an enormous milestone for us," he says. "It turns us from a potentially one-product company to a platform company with a number of shots at goal."

Dr Baker says CAR-Ts are curing patients, but the autologous approach means doses have to be made every single time.

In the US, more than 80,000 lymphoma and more than one million gastric cancer patients are diagnosed every year.

"How do you manufacture that many doses of cells with proper quality control?" he asks. "If you have to quality control every dose there is a bottleneck."

ALA-101 trial, here we come

Arovella's lead program, ALA-101, is showing early promise as a treatment for CD19-expressing blood cancers.

Earlier mouse work involved the rodents being infused with CD19-expressing, aggressive B-cell acute lymphoblastic leukaemia cells. At the 90-day mark, 95 percent of those treated with ALA-101 (CAR19-INKT cells) remained alive, while only 60 percent of those treated with CAR-T therapies survived.

This week, the company said it had received a response from the FDA for its pre-investigational new drug (IND) meeting for its planned phase I study, with the feedback providing "clear and achievable" requirements for a submission.

The study will be in two parts: a dose escalation stanza with nine to 12 patients and then a phase Ib expansion to more patients, with an IND application to be lodged by April 2025.

Targeting solid tumors

In October 2023, the company licenced a technology around the protein Claudin18.2 (CLDN18.2), from the Chinese-US Sparx Group. Known as ALA-105, the program uses the same manufacturing platform, but with a different lentivirus carrying the genetic material to make a CAR-targeting CLDN18.2.

CLDN18.2 is expressed on gastric, pancreatic and oesophageal cancers and some ovarian and lung cancers (not healthy cells). The company is using its INKT cell platform to target such solid tumors.

“This is because of the INKT cell’s ability to infiltrate tissues and tumors, to block cells that promote tumor survival and to release cytokines to stimulate an immune response,” Dr Baker says.

Dr Baker says CLDN18.2 is positioned to be like the next human epidermal receptor growth factor-2 (HER-2), the common biomarker expressed in one in five breast cancers and some bladder, ovarian, pancreatic and stomach cancers.

He notes that a CLDN18.2 targeting drug, Astellas Pharma’s zolbetuximab was approved in Japan for gastric cancers, while an FDA application has been lodged. While the drug is based on a monoclonal antibody rather than a cell, Dr Baker says the drug validates the CLDN18.2-targeting approach even though trial results were pretty ordinary.

In January, after 18 months of effort, Arovella made its first lentivirus - which delivers the requisite genetic material to the INKT cells.

Tickling up

In January, Arovella further licenced a cytokine ‘armoring’ tech called IL-12-TM, from the University of North Carolina’s Lineberger Comprehensive Cancer Center. (IL stands for interleukin and TM is trans-membrane not just the trade mark.)

As the name suggests, the technology will strengthen the INKT platform’s ability to target solid tumors; and was developed by Prof Gianpietro Dotti, who is on Arovella’s scientific advisory board.

Animal data published in Nature Communications shows IL-12-TM “enhances CAR-INKT persistence, and therefore cell numbers, which provides better anti-tumor activity (including solid tumors such as neuroblastomas)”.

The Viagra of the immune-oncology sector, the program could result in more potent and longer lasting INKT cells.

Finances and performance

At the end of the June quarter, the company had cash of $12.7 million following a $12.5 million placement - enough to start dosing patients and capturing data. The over-subscribed offer was struck at 10 cents a share, with attaching one-for-one options exercisable at 15 cents a share within the next three years.

Shareholder assent was required but investors waved the proposal through at a May meeting.

Over the last 12 months Arovella shares have traded between 4.0 cents (August 2023) and 19 cents (February 2 this year). They hit a record low of two cents in early 2023, but surged 180 percent in the past year.

Dr Baker says the register has transformed since 2020. The biggest holders are the ubiquitous Merchant Group and beef baron Richard John Mann, who has invested in other biotechs including Imugene.

Almost ‘virtual’ in nature, the company prides itself on a low cash burn and you will rarely find Dr Baker at the pointy end of the plane.

Sizing the rivals

The CAR-T space has competition from dozens of drug developers, with a good smattering of NK-focused companies as well. But the INKT space is a different matter: Arovella ranks among only five of them globally. And setbacks have abounded.

(Quasi) rivals are the Nasdaq-listed, $US76 million market cap MINK Therapeutics (phase I stage) and the private, pre-clinical Appia Biotech (which is in partnership with cell therapy leader Kite Pharma). The nearest exemplar to Arovella, Appia uses a different manufacturing method but is not yet in clinical trials.

Deals included Astrazenca acquiring Graycell last December for $US1 billion up-front for a phase Ib technology.

Dr Boreham’s diagnosis:

Dr Baker says now that the company has a genuine platform, it will sniff around for new CAR-T programs that leverage the know-how.

“We are constantly looking for ‘CARs’ like this that we can integrate into our manufacturing platform and develop for a range of cancers.”

The company cites one million new diagnoses of gastric and oesophageal junction cancers a year, with 789,000 deaths. That makes them the fourth most fatal cancer.

The gastric cancer market was worth $US2.1 billion in 2021 and is forecast to be worth $US10.76 billion in 2031.

The deadliest is pancreatic cancer: in 2020, 496,000 patients were diagnosed and 466,000 died. Stage four pancreatic cancer has a miserable five-year survival rate of one percent.

While earlier-stage biotechs aspire to be taken over, Dr Baker says “at a philosophical level” the company wants to progress its tech to commercialization.

Given the six FDA approved CAR-T products were approved at phase II with fewer than 100 patients, Arovella has a fighting chance.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort - even at a philosophical level

NEUREN PHARMACEUTICALS

Neuren says its 16-patient, phase II trial of NNZ-2591 shows an improvement in 11 of 13 evaluable Angelman syndrome patients, compared to baseline ($p = 0.0010$).

Neuren said that the trial of oral NNZ-2591 for Angelman syndrome "showed a level of improvement from baseline after 13 weeks that was statistically significant … and considered clinically meaningful".

In 2022, Neuren said it began the NNZ-2591 phase II trial in Angelman syndrome patients aged three to 17 years old to examine the safety, tolerability, pharmaco-kinetics and efficacy of an oral liquid dose twice daily for 13 weeks (BD: Jul 12, 2022).

Last year, the company said it had completed enrolment of the trial, with top-line results expected by October 2024 (BD: Dec 20, 2023).

Today, Neuren said the trial dosed 16 participants with NNZ-2591, with escalation in two stages up to the target dose of 12mg/kg during the first six weeks of treatment, subject to independent review of safety and tolerability data.

The company said that two children discontinued due to testing positive for Covid-19 and a third child was unable to comply with required safety monitoring procedures.

Neuren said that 11 of 13 children showed an improvement measured by the Angelman syndrome Clinical Global Impression of Improvement (CGI-I), which was a score by the clinician of the child's overall status compared to baseline.

The company said that of the 13, two were "much improved", nine were "minimally improved" and two showed "no change".

Neuren said the mean CGI-I score was 3.0 ($p = 0.0010$), with two children receiving a score improvement of two, or 'much improved', and all eight children in the three-to-12 years old group showing improvement, with a mean score of 2.9 ($p = 0.0078$).

The company said the trial measured Angelman syndrome caregiver overall impression of change (CIC), an assessment by the caregiver of the child's overall status, scored out of seven, compared to baseline, in 12 of 13 evaluable patients.

Neuren said the mean CIC score was 3.2 ($p = 0.0273$) and that three children received a score of two, or 'much improved', and the eight patients in the three-to-12 years old group showing improvement, with a mean score of 2.8 (0.0078).

The company said that a CIC score for one subject was "inadvertently not completed by caregiver at site visit".

Neuren said that other efficacy results included four children with an improvement in Angelman syndrome clinical global impression of severity score, compared to baseline, as well as more than 50 percent of patients showing an improvement in raw scores on the exploratory endpoint of the Bayley Scales of Infant and Toddler Development.

The company said that in the 16 intent-to-treat patients, NNZ-2591 was "well tolerated and demonstrated a good safety profile … [and that] most treatment emergent adverse events were mild or moderate and most were considered not related to study drug".

The company said treatment emergent adverse events included viral infection in five patients, nasopharyngitis and, or seizure in four patients, upper respiratory tract infection, somnolence and, or constipation in three patients as well as diarrhea, drooling, epistaxis, insomnia, pyrexia, skin abrasion, urinary tract infection and, or vomiting in two patients.

Neuren chief executive officer Jon Pilcher said the results provided "additional confirmation that NNZ-2591 as an oral liquid dose may address the core symptoms of diverse neurodevelopmental disorders, independent of the origin of the underlying genetics".

"We are very grateful to the people in the Angelman syndrome community and at the trial sites in Australia who enabled the successful completion of the trial," Mr Pilcher said.

Neuren fell 94 cents or 5.5 percent to $16.15 with 1.9 million shares traded.

AVITA MEDICAL

Avita says revenue for the six months to June 30, 2024 was up 17.9 percent to $US26,299,000 ($A39,844,000), with net loss up 73.7 percent to $US34,051,000 ($A51,605,000).

Avita said revenue was from sales of its spray-on-skin Recell technology for wound treatment, with no US Biomedical Advanced Research and Development Authority (BARDA) revenue compared to $US1,157,000 in the prior corresponding period "due to the ending of reimbursable clinical trials".

Avita said sales and marketing costs were up 74.95 percent to $US28,942,000, general and administrative costs rose 14.0 percent to $US16,481,000 and research and development costs increased 4.3 percent to $US10,081,000.

The company said the increased sales and marketing costs were "employee-related costs, including salaries and benefits, commissions, professional fees, and travel expenses" due to its expanded commercial organization to support increased commercial operations.

Avita said sales revenue for the three months to June 30, 2024 was up 29.2 percent to a record $US15,183,000, compared to the previous corresponding period.

The company said diluted loss per US share, equivalent to five Australian shares, was up 69.2 percent to $US1.32, net tangible asset backing per share fell 71.3 percent to 76.41 US cents, and it had cash and cash equivalents of $US17,452,000 at June 30, 2024 compared to $US37,485,000 at June 30, 2023.

Avita was up 20 cents or eight percent to $2.70 with one million shares traded.

IDT AUSTRALIA

IDT says it has a $2.5 million to $4 million "follow-on contract" to develop and manufacture Sanofi Australia's messenger RNA (mRNA) technology for clinical use.

Earlier this year, IDT said it had an initial master service agreement worth between $3 million to $3.5 million, excluding costs relating to storage, shipping and equipment purchase, with the Paris-based Sanofi to formulate and manufacture mRNA-based vaccines for Sanofi's clinical trials in a range of indications (BD: Apr 16, 2024).

At that time, the company said it had "one of the few aseptic sterile fill facilities to complete mRNA downstream processing in Asia Pacific".

Today, IDT said the master service agreement provided "flexibility for Sanofi to choose services from IDT and allows for follow-on work packages".

IDT was up one cent or 8.7 percent to 12.5 cents.

CHIMERIC THERAPEUTICS

Chimeric says it has a collaboration with Melbourne's Cell Therapies Pty Ltd to manufacture its chimeric antigen receptor (CAR) T cells in Australia.

Chimeric said Cell Therapies was a commercial contract development and manufacturing company that specialized in cell therapy, gene therapy, regenerative medicine and cellular immunotherapy products.

The company said Cell Therapies' facilities at the Peter MacCallum Cancer Centre in Parkville, Melbourne, and were Australia's "only biomedical manufacturing facility where CAR-T cells and other 'living' cancer therapies can be made at a commercial scale".

Chimeric chief operating officer Dr Rebecca McQualter said the collaboration was "great progress for Chimeric and aims to provide Australian patients with access to our first in class CAR-T clinical trials".

Chimeric was up 0.2 cents or 12.5 percent to 1.8 cents with 1.6 million shares traded.

CARDIEX

Cardiex says it has an up-to $1,120,000 loan at 18 percent a year with Mitchell Asset Management against its expected Federal Research and Development Tax Incentive.
Last year, Cardiex said it extended a $595,000 loan with Mitchell Asset Management to March 31, 2024 and an up-to $880,000 loan to October 31, 2024, providing “ample time to finalize its … tax incentive registration and lodgement” for 2023-’24 (BD: Nov 20, 2023).
Today, the company said the additional loan meant it had a total principal amount outstanding to Mitchell of $2,000,000, exclusive of any interest owed or other charges.
Cardiex said it expected to receive its Federal Research and Development Tax Incentive by the repayment date of October 31, 2024, and make a “substantial repayment of the amounts owed” that would reduce the amount owed to no less than $520,000.
The company said the $1,120,000 loan was secured against its expected Federal Research and Development Tax Incentive for the year to June 30, 2025, and that the loan had a maturity date of October 31, 2025.
Cardiex was unchanged at six cents.

ALLEGRA MEDICAL TECHNOLOGIES

Allegra Innovations Pty Ltd says it has met “all of the outstanding conditions… of the bidder’s statement” and its acquisition of Allegra is “now unconditional”.
In May, Allegra said Allegra Innovations, a related party of director Dr Nicholas Hartnell, would pay 0.4 cents a share in a cash bid, valuing it at $478,444 (BD: May 27, 2024).
Today, the company said its takeover offer and all contracts were “free from all conditions contained in … the bidder's statement that are not satisfied as at the date hereof”.
Allegra Innovations Pty Ltd said it held 80.60 percent of Allegra Medical Technologies and urged “all … shareholders to accept [its] offer without delay”.
Allegra was in a suspension and last traded at 2.9 cents.

NEUROTECH INTERNATIONAL

Neurotech says shareholders will vote to issue 1,000,000 options to director Robert Maxwell Johnston and 10,000,000 shares and 50,000,000 rights to Fenix.
Neurotech said investors would vote to issue Mr Johnston 1,000,000 options exercisable at 16 cents each by April 24, 2026 as part of an incentive component of his remuneration package, in addition to his $50,000 yearly director fees.
The company said that shareholders would vote to issue 10,000,000 shares and 50,000,000 performance rights to contract research organization Fenix Innovation Group Pty Ltd, subject to performance-based vesting conditions.
Earlier this year, Neurotech said it had appointed the Melbourne-based Fenix Innovation Group as its contract research organization for trials of its marijuana-based NTI164 for neurological disorders (BD: Apr 10, 2024).
At that time, the company said it would issue 10 million shares to Fenix, which would be voluntarily escrowed for a year, and would also issue it 50 million performance rights, vesting on completion of certain regulatory and commercialization milestones.
Today, Neurotech said the meeting would vote to ratify the prior issue of placement shares and options as well as vary the terms of incentive options approved to be issued to executive director Dr Thomas Duthy at its 2022 general meeting.
The meeting will be held at BDO Australia, Level 18, Tower 4, 727 Collins Street, Melbourne on September 10, 2024 at 11am (AEST).
Neurotech fell 0.1 cents or 1.5 percent to 6.5 cents with one million shares traded.

AMPLIA THERAPEUTICS

Sydney's Washington H Soul Pattinson says it has ceased its substantial shareholding in Amplia through its more than 20 percent holding in Pengana Capital Group.

Yesterday, Pengana Capital Group said it had ceased its substantial holding in Amplia following the sale of 1,700,000 shares on August 6, 2024 for $222,677, or 13.1 cents a share, with Biotech Daily calculating Pengana retained about 4.92 percent of the company (BD: Aug 8, 2024).

Amplia fell half a cent or 3.7 percent to 13 cents with 10.4 million shares traded.

BREAKTHROUGH VICTORIA

Breakthrough Victoria says that chief executive officer Grant Dooley has resigned after three years building and leading the innovation and commercialization fund.

The Victoria Government-funded Breakthrough Victoria said that Mr Dooley was appointed as its inaugural chief executive officer in November 2021 and would remain with the organization to support its search for a new chief executive officer.

The fund said that Mr Dooley had been "instrumental in building the organization into one of Australia's most active venture capital investors … [investing] in 27 companies, one fund, and six university platforms, with committed capital of more than $350 million".

Breakthrough Victoria chair and former Victoria Premier and Treasurer John Brumby said that the board "extends its gratitude to Grant for his dedication, leadership and commitment to the mission of Breakthrough Victoria".

Victoria Treasurer and Minister for Economic Growth Tim Pallas said that Mr Dooley "played a key role in driving Victoria's innovation and economic growth by leading Breakthrough Victoria as it made important investments in priority sectors like advanced manufacturing and clean energy".

Breakthrough Victoria confirmed that four previous directors, Victoria lead scientist Dr Amanda Caples, Jane den Hollander, Sam Andersen and Kee Wong had resigned.

The organization said that Deirdre Blythe, Monique Conheady and Dr Ian Meredith had been appointed as directors, joining Mark Johnson and Joshua Funder.