Biotech Daily

Friday July 7, 2023

Daily news on ASX-listed biotechnology companies

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*** ADHERIUM LOSES CO CO SEC MARK LICCIARDO**

MARKET REPORT

The Australian stock market lost 1.69 percent on Friday July 7, 2023, with the ASX200 down 121.1 points to 7,042.3 points. Six of the Biotech Daily Top 40 stocks were up, 22 fell, 11 traded unchanged and one was untraded. All three Big Caps fell.

Atomo was the best of the six, up 0.3 cents or 5.6 percent to 5.7 cents, with 4.3 million shares traded. Starpharma climbed 4.9 percent; Prescient rose 2.4 percent; with Alcidion, Antisense and Volpara up by more than one percent.

Micro-X led the falls, down 1.5 cents or 12 percent to 11 cents, with 155,571 shares traded. Actinogen and Cynata lost more than seven percent; Kazia was down 5.9 percent; Resonance fell 4.3 percent; Avita, Compumedics, Dimerix, Immutep and Nova Eye were down more than three percent; Clinuvel, CSL, Impedimed, Polynovo and Telix shed more than two percent; 4D Medical, Cochlear, Nanosonics, Neuren, Orthocell, Paradigm and Pro Medicus were down more than one percent; with Genetic Signatures, Opthea and Resmed down by less than one percent.

DR BOREHAM'S CRUCIBLE: MICROBA LIFE SCIENCES

By Tim Boreham

ASX Code: MAP

Share price: 31 cents

Shares on issue: 344,136,473 (48,031,314 in ASX escrow)

Market cap: $106.7 million

Chief executive officer: Dr Luke Reid

Board*: Pasquale Rombola (chair), Prof Ian Frazer (deputy chair), Prof Gene Tyson, Dr Hyungtae Kim, Richard Bund, Jacqueline Fernley

***** Dr Caroline Popper resigned in mid-June 2023 for personal reasons

Financials (March quarter 2023): revenue $1.01 million (up 61%), receipts $1.24 million, loss of $5.9 million, cash of $35.4 million, quarters of available funding: six

Major shareholders: Sonic Healthcare 19.99%, Perennial Value Management 11.7%, SA Microba Holdings (Mr Bund) 9.2%, Tiga Trading 7.17%, Macrogen Inc 5.2%, Boysenholtz Pty Ltd 5%, Gingko Bioworks Inc 4%

Inside the human gut, trillions of bacteria are doing their job and contrary to common belief it's not all about forcing their chunderous host to reach for the bucket.

On the contrary, the complex ecosystem is vital for maintaining human health in terms of digestion and boosting immunity. In the words of Luke Reid, the head of the only ASX-listed microbiome-testing outfit, Microba, they are crucial to maintaining health and treating or preventing a range of chronic conditions.

The science of how the bugs do this has not been well understood, although knowledge is increasing rapidly in areas such as treating irritable bowel disease (IBD).

The smart bugs are also known to produce neuro-transmitters that can affect the brain, as well as metabolites that work systemically through the body and impact various organs and systems.

Microbiome companies are attracting hot commercial interest and since listing just over a year ago, testing outfit Microba has seen a proliferation of deals and partnerships in the sector.

In the past six months the US Food and Drug Administration (FDA) has also approved two microbiome-based drugs, both to treat Clostridium difficile (a germ that causes colon inflammation).

The latest in a number of big-ticket partnerships, Microba and Sonic Healthcare last November sealed a deal by which the ASX-listed pathology giant sells Microba's kits across its extensive global network.

This week, the parties agreed to sell Microba's infectious diseases platform (called Metapanel) in Australia.

Adding to the intrigue, Merck & Co has just snapped up the irritable bowel disease and Crohn's disease specialist Prometheus Biosciences for $US10.8 billion ($16.2 billion).

From a germ of an idea

Microba was formed in 2017 based on intellectual property acquired from the University of Queensland. Also involved were the University of California Berkeley, Massachusetts Institute of Technology and the Joint Genome Institute.

Microba listed on April 5, 2022 at a subscription price of 45 cents, with the initial public offer raising $30 million.

Microba's tech was developed by co-founders Prof Philip Hugenholtz and Prof Gene Tyson.

The latter is an executive director and the former chairs its scientific advisory board.

CEO Dr Reid was an associate director of Uniquest Pty Ltd and, before that, held roles at plant geneticist Dupont Pioneer.

Dr Reid met the two professors at Uniquest while working on unrelated tech and the rest - as they say - is history.

The company's deputy chair, Prof Ian Frazer needs no introduction as the co-inventor of the Gardasil and Cervarix cervical cancer vaccines.

The guts of the company

Microba has three arms: microbiome services (testing), drug development and a proprietary database of 1.2 million microbial genomes covering 5,000 species.

The company launched its first product, Microba Insight, in Australia in July 2018. Consumers buy the test online for $349 and send back a stool sample, for which they receive a summary of their gut microbiome.

Patients outside a healthy range are provided with advice including dietary recommendations.

In 2019, the company followed up with a gut microbiome measuring product, Metabiome, for healthcare professionals in Australia and New Zealand through a distribution partnership.

Consumers aside, users of the test include healthcare practitioners and research entities (such as biotechnology and food companies).

In late February this year the company launched three test variants under the new brand Co-Biome: Metaxplore, Metaxplore GI and - you guessed it – Metaxplore GI Plus.

Pitched at clinicians, these tests are designed to be interpreted shortly before the patient appointment.

The Metaxplore tests include tweaks such as the ability to identify nine specific pathogens and to provide a microbiome profile of more than 28,000 species.

“We can also analyse published data, put it through algorithms and identify novel parts of the microbiome,” says Microba therapeutics head, Prof Trent Munro.

Central to Microba’s story is the geographically diverse microbiome databank, which the company has accumulated over the last four years.

This bug library will help the company to pin down “novel and therapeutic leads not identified by others”.

Take your partners

Microba is chuffed about the partners with which it has drawn a dance card.

Sonic Healthcare aside, Microba has partnerships with sector leader Genova Diagnostics, North America’s biggest gastrointestinal pathology providers.

Others are Synlab, Europe’s biggest pathology lab chain, the Nasdaq-listed Illumina and the New York-listed, Bill Gates-backed Ginkgo Bioworks.

Microba has also just signed a Middle Eastern compact with artificial intelligence outfit G42.

Dr Reid describes the distribution model as “very high margin and very scalable”.

Under the “Intel inside” model, the company delivers the raw data underpinning the clinical reports. The partners do the sales, marketing, distribution and processing.

“Early on we decided we didn’t have to own every customer in every market and that it was better to work with the best leaders with deep channels into markets,” he says.

Via these partners, Microba has access to 35 countries. Of these, 13 have been “operationalised” compared with the eight promised by June 2023.

News you can use

Dr Reid says the company's tests emphasise "actionable information".

The reports are designed to be simple, so that a clinician can glean the key information five minutes before the patient visit.

From the report, patients can be advised of corrective actions such as a change of diet or a prescription of good ol' antibiotics to treat a known pathogen.

"We have always been rigorous and conservative with what we bring to individuals," he says.

As well as providing patient-specific results, Microba curates and grades all the relevant available clinical literature and this also determines the actions available to the patient.

In the clinic

The company has just launched a phase I trial for lead drug candidate MAP 315 for the inflammatory bowel disease of ulcerative colitis.

In June, the company enrolled the first of 32 healthy patients, 24 of them on active treatment over 14 days and eight on placebo.

The results are expected to be announced in December this year and - if successful - will lead to a phase II efficacy study.

Microba chose ulcerative colitis because there's a significant unmet need, with patients suffering frequent flare-ups.

Other potential targets are colon cancer, diabetes, non-alcoholic steato-hepatitis (Nash or fatty liver disease), Alzheimer's disease, rheumatoid arthritis, anxiety and depression.

On the immune-oncology front, the company is interested in using microbiomes to enhance the efficacy of approved checkpoint inhibitors.

Pre-clinical microbiome mouse melanoma models - and do excuse the alliteration - showed a "significant reduction in tumor size" when Microba's "therapeutic leads" were used in combination with a checkpoint inhibitor.

"As pharma companies look at ways to differentiate their immunotherapy products, we believe Microba presents a compelling opportunity as a combination therapy," Dr Reid says.

Meanwhile, Microba and Ginkgo are targeting the development of novel therapies for three autoimmune disorders.

A poo-nami of approvals pending?

In November 2022, the FDA approved Ferring Pharmaceuticals and Rebiotix's Rebyota, a "microbiota restorative therapy" for irritable bowel disease sufferers.

In late April, the agency gave the nod to two Clostridium difficile therapies: Seres Therapeutics and Nestle's SER-109, now called Vowst.

Has everyone finished eating? Great!

A key downside of the two approved products is that they are based on faecal donations: the poo of healthy subjects.

The procedure has been made more elegant by freeze-drying the faeces and encapsulating the material but - let's face it - the procedure is always going to have some image problems, given they are rectally administered.

The technique also involves significant manufacturing challenges and it is not exactly scalable.

"There's no doubt oral therapy will be better efficacy-wise," Prof Munro says.

Finances and performance

At the time of the Sonic Healthcare deal, management said the resulting revenues from the partnering deals should become apparent in the second (June) half of the current financial year.

Lo and behold, the March quarter showed revenue of a tad over $1 million, 60 percent up year-on-year. The company also lost close to $6 million, but still has $35 million in the bank.

Success in the US market is always a key factor for a diagnostics outfit. In that respect, Dr Reid says the company has a "thoughtful" US reimbursement strategy and investors should expect some news "in the not-too-distant future".

In the meantime, he says, there's a "significant sizable" local market for both testing products.

As part of last year's deal, Sonic Healthcare invested $17.8 million to acquire a 19.99 percent holding in Microba - the maximum allowable stake without launching a takeover offer.

The Microba register is chock-full of institutions including Thorney Investments (Tiga Trading) and Perennial Value Management.

Since listing Microba shares have traded between 14 cents (mid-October last year) and 42 cents (mid-February this year).

Safe but useless?

There's plenty of hype in the supplements industry about probiotics: micro-organisms that are claimed to benefit the gut when ingested.

Typically derived from dairy sources, most of these pills and potions are 'generally recognized as safe' category: they will not kill you, but may not necessarily benefit you.

The poor disclosure opens an opportunity for Microba to enter the sector with products that are properly scientifically validated.

Probiotics aren't sourced from the natural gut microbiome because they can't tolerate oxygen, so are harder to make.

A key aspect of Microba's smarts is being able to handle and replicate the bacteria in the lab.

"We have a role to play in supplements but from a very scientifically-validated perspective," Dr Reid says.

Dr Boreham's diagnosis:

Most biotechs talk about their hopes and intentions for big-ticket partnering deals, which we take with the proverbial grain of sodium chloride seasoning.

With its Sonic and Genova tie-ups, Microba is looking the real deal.

Bear in mind the company has no intention of going all the way on its own, either down the testing or drug development paths.

Ultimately, Dr Reid expects microbiome testing to become as routine as blood testing and will treat a range of inflammatory and mental health disorders.

"Our vision is [that] in the not-too-distant future this should become like a routine blood test," he says.

Not surprisingly, investors often probe management on the virtues of the testing side of the business vis-a-vis the nascent therapeutics side.

"If we nail therapeutics, it would be significantly larger than testing," Dr Reid says. "But the testing business in its own right could be really significant."

Given that, Microba is like one of those trillions of bacteria: a small bug in a very large pond but that leaves all the more room to grow.

Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He works by gut feeling alone.

COGSTATE

Cogstate says it could benefit from the US Food and Drug Administration full approval of Eisai Co and Biogen's lecanemab, marketed as Leqembi, for Alzheimer's disease.
Cogstate quoted the FDA saying: "Leqembi is the first amyloid beta-directed antibody to be converted from an accelerated approval to a traditional approval for the treatment of Alzheimer's disease".
"The drug works by reducing amyloid plaques that form in the brain, a defining pathophysiological feature of the disease," Cogstate quoted the FDA.
The company said that the confirmatory phase III Clarity Alzheimer's disease study of lecanemab met its primary endpoints showing a statistically significant reduction of a clinical decline in a global clinical study of 1,795 participants with early Alzheimer's disease.
Cogstate was not party to the collaborative arrangement between Eisai and Biogen in respect of the confirmatory clinical study, nor did it have access to or awareness of information relating to the treatment other than as publicly released.
The company said that "the upside revenue for [its] healthcare business is expected to be dependent upon the release, reimbursement and availability of proven Alzheimer's treatments".
Cogstate said that in 2020 it granted Eisai exclusively rights to develop and distribute its digital cognitive assessment technologies in healthcare and other markets worldwide, but specifically excluded the clinical trials market, in which Cogstate marketed its products independently (BD: Oct 26, 2020; Sep 28, 2022).
Cogstate fell half a cent or 0.3 percent to $1.565 with 1.9 million shares traded.

IMRICOR MEDICAL SYSTEMS

Imricor has provided further details about its $30 million three-year drawdown equity facility with Luxembourg's Gem Global Yield LLC (BD: Jul 6, 2023)
Imricor said that Gem Global would pay the higher of 90 percent of the 15-day average closing bid price, or a fixed floor price nominated by Imricor in its draw-down notice.
Imricor was up half a cent or 1.1 percent to 45 cents.

ISLAND PHARMACEUTICALS

Island Pharmaceuticals says the US Department of Defense has granted it $US1.3 million ($A1.95 million) for its phase IIa trial of ISLA-101 for dengue fever.
Island said the Department of Defense's Congressionally Directed Medical Research Program grant was awarded to the Syracuse, New York-based State University of New York, who had partnered with Island to develop ISLA-101.
The company said the grant would support laboratory testing and data analysis and allow it to "significantly expand" on data generated, with the trial to evaluate the effectiveness of ISLA-101 to treat dengue fever.
Island said the Department of Defense grants advanced medical and scientific research and filled research gaps by "funding high impact, high risk and high gain projects that other agencies may not venture to fund".
Island adviser Prof Stephen Thomas said the funding would help "advance ISLA-101, gain a deeper understanding of dengue and facilitate bringing a medical countermeasure to military service members and all those who live at daily risk of being infected".
Island was untraded at 12 cents.

KAZIA THERAPEUTICS

Kazia says paxalisib with radiation has US Food and Drug Administration fast track status for solid tumor brain metastases harboring PI3K pathway mutations.
Kazia said the FDA fast track designation “was based on promising clinical data from an interim analysis of an ongoing phase I clinical trial in which patients with brain metastases from a primary tumor are receiving paxalisib in combination with radiotherapy”.
The company said that all nine evaluable patients responded to the combination.
Kazia said that fast track designation expedited development of pharmaceutical products which showed the potential to address unmet medical needs in serious or life-threatening conditions and provided the company with enhanced access to the FDA.
The company said that drugs granted fast track status might be eligible for accelerated approval and priority review, which might result in faster product approval.
Kazia fell one cent or 5.9 percent to 16 cents.

ADALTA

Adalta says data from a study of AD-214 on the T-cells of three human donors, along with previous studies suggest that AD-214 could be efficacious in bi-weekly infusions.
Adalta said that study looked at the link between AD-214 concentration, C-X-C chemokine receptor type 4 (CXCR4) occupancy and the ability of the CXCR4 expressing cells to migrate under normal signalling cues.
The company said that the study showed that CXCR4 receptor occupancy measured at different AD-214 concentrations was consistent with the receptor occupancy observed in phase I safety studies at the same circulating blood concentrations.
Adalta said that the migration of human T-cells could be inhibited with AD-214.
“Taken together, these results help identify target levels of CXCR4 receptor occupancy and hence circulating concentrations of AD-214, that may be needed for efficacy in fibrotic indications,” the company said.
“Maximal T-cell migration inhibition, and hence potential efficacy against fibrosis, might be achieved by maintaining CXCR4 receptor occupancy above 60-85 percent and meaningful inhibition might be achieved as low as 11-37 percent,” Adalta said.
“Due to the very tight binding of AD-214 to CXCR4, these levels of receptor occupancy can be achieved at very low circulating concentrations of AD-214,” the company said.
Adalta said the phase I study showed that concentrations for maximal inhibition of T-cell migration were maintained for several days after intravenous administration, and for meaningful inhibition for much longer.
“This in turn supports the hypothesis that intravenous administration of AD-214 at clinically convenient two-weekly dosing intervals could be efficacious,” the company said.
Adalta chief executive officer Dr Tim Oldham said “we have known AD-214 is efficacious in animal models of fibrotic diseases and also that it can at least partially block its target receptor for several days and even weeks after a single intravenous infusion”.
“What we have not known is whether we could replicate the therapeutic effect seen in animals at these levels of receptor occupancy and hence at dosing frequencies acceptable in humans,” Dr Oldham said.
“For the first time we have been able to show that we can maximally inhibit a key fibrotic process with as little as 60 percent receptor occupancy and that meaningful inhibition can be achieved at much lower levels,” Dr Oldham said.
Dr Oldham said the data was “extremely valuable” for determining appropriate dosing for AD-214 phase II studies.
Adalta was up 0.3 cents or 10 percent to 3.3 cents with six million shares traded.

IMUGENE

Imugene says the intra-tumoral, phase I trial of its Checkvacc oncolytic virotherapy for triple negative breast cancer will proceed to the fourth dose cohort.
Last year, Imugene said it had dosed the first patient in the third cohort of its dose escalation phase I trial of Checkvacc, or CF33-humanised sodium iodide symporter-anti-programmed death ligand-1 (CF33-hNIS-anti-PDL1) (BD: Aug 10, 2022).
Today, the company said the protocol management team found Checkvacc to be safe with no dose-limiting toxicities and no serious adverse reactions.
Imugene said the trial involved a dose escalation, followed by an expansion to 12 patients at the final dose, which would be the recommended phase II dose.
Imugene was unchanged at 9.2 cents with 18.1 million shares traded.

RACE ONCOLOGY

Race says it will move to the new RC220 formulation of bisantrene, amending a phase Ib/IIa trial protocol and terminating part of a breast cancer cardio-protection trial.
Race said that the previous RC110 formulation required central venous access, due to its tendency to precipitate in and damage the smaller peripheral veins.
The company said it would “focus its future development activities on the peripheral [intra-venous] administered bisantrene formulation RC220 … [which had a] clear therapeutic advantage related to the combined ease and safety of peripheral IV administration” along with new intellectual property protection.
Race said that the investigator-led, phase II open label, acute myeloid leukaemia trial at Chaim Sheba in Israel had enrolled 20 heavily pre-treated patients with relapsed and refractory acute myeloid leukaemia, with two further patients required to meet the first stage of the two-stage decision point.
The company said that observations had been compelling, with several patients being effectively bridged to allogenic stem cell transplant with curative intent and the trial would enrol the final two patients and report on outcomes over the coming months.
Race said the Bisect phase Ib/IIa trial of bisantrene in acute myeloid leukaemia and myelodysplastic syndromes patients with extramedullary disease had significant recruitment challenges based on the rarity of extramedullary disease and the protocol would be amended to include a broader subset of acute myeloid leukaemia patients who would first receive RC110 plus oral decitabine.
The company said subsequent cohorts were planned to receive RC220 plus oral decitabine as production became available, and the broadened criteria were expected “to significantly enhance recruitment and potentially expand the commercial opportunity”.
Race said the non-interventional part of the phase Ib/II cardio-protection trial in breast cancer patients to be treated with doxorubicin and cyclophosphamide and who had two or more cardiovascular risk factors would be terminated.
The company said the non-interventional section was designed to establishing an effective baseline for comparison purposes, but readily available datasets could be used instead.
Race said that in agreement with the principal investigator, and consultation with international breast cancer specialists and cardio-oncologists, it would terminate the non-interventional AC therapy protocol and allocate the related $3 million to RC220 led programs.
“Importantly, we emphasize that the timeframe for the RC220 interventional breast cancer study is not impacted by this decision and the non-interventional trial would have provided no bisantrene-specific insights,” Race said.
Race was unchanged at $1.30.

MICROBA LIFE SCIENCES

Boysenholtz Pty Ltd says it has been diluted below the 5.0 percent substantial shareholder level through the exercise of employee options.
The Brisbane-based Boysenholtz said the shares were held by Philip Hugenholtz and Penelope Boys.
Last year Boysenholtz said their 17,178,431 Microba shares had been diluted to 5.01 percent, following the issue of shares.
Biotech Daily calculates that Boysenholtz holds 4.99 percent of Microba.
Microba was up one cent or 3.3 percent to 31 cents.

LUMOS DIAGNOSTICS

Melbourne's Planet Innovation says its 68,021,060 share-holding in Lumos has been diluted from 21.98 percent to 19.95 percent.
Planet Innovation said it was diluted by the issue of shares from convertible notes to SBC Global Investment on July 4 and to Lind Global on July 5, 2023.
Last year, Lumos said it had an $8 million, convertible note facility from New York's Lind Partners and Melbourne's SBC Global Investment Fund (BD: Nov 21, 2022).
Lumos was untraded at 8.6 cents.

LUMOS DIAGNOSTICS

New York's Lind Partners Global Fund II LP says it has become substantial in Lumos with 22,500,000 shares or 6.78 percent.
Lind said that the shares were acquired following the Lumos application for quotation of the shares on July 5, 2023, which said the shares were a result of the conversion of convertible notes at one cent per security (see above).

HEXIMA

Sydney's Dr John Tarrant says he has increased his substantial shareholding in Hexima from 23,287,366 shares (13.94%) to 25,791,526 shares (15.44%).
Dr Tarrant said that through Balmain Resources Pty Ltd, Cadex Petroleum Pty Ltd and Plough Lane Superannuation, on June 27 and July 5, 2023, he bought 2,504,160 shares for $51,582, or an average of 2.06 cents a share.
Hexima was unchanged at 2.4 cents.

ADHERIUM

Adherium says Mark Licciardo has resigned as joint company secretary, leaving Brett Tucker the sole company secretary.
In May, Adherium said Mr Tucker replaced Rob Turnbull (BD: May 4, 2023).
Adherium was unchanged at 0.3 cents.