Biotech Daily

Friday July 21, 2023

Daily news on ASX-listed biotechnology companies

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*** PETERS TAKES 19.45% OPTISCAN**

*** MEURS DILUTED TO 12% OF ADALTA**

*** AUSBIOTECH LAUNCHES CELL & GENE INDUSTRY STRATEGY**

MARKET REPORT

The Australian stock market fell 0.15 percent on Friday July 21, 2023, with the ASX200 down 11.1 points to 7,313.9 points. Seven of the Biotech Daily Top 40 stocks were up, 22 fell, eight traded unchanged and three were untraded. All three Big Caps were up.

Starpharma was the best, up 5.5 cents or 14.9 percent to 42.5 cents, with 860,827 shares traded. Alcidion climbed 4.8 percent; Kazia was up 3.85 percent; Emvision and Universal Biosensors rose more than two percent; Pro Medicus and Resmed were up more than one percent; with Cochlear, CSL and Cyclopharm up by less than one percent.

Avita led the falls, down 54 cents or 9.3 percent to $5.29, with 559,038 shares traded, followed by Patrys down 9.1 percent to one cent, with 1.6 million shares traded. Micro-X and Pharmaxis lost more than eight percent; Atomo and Medical Developments were down more than six percent; Orthocell fell five percent; 4D Medical and Impedimed fell more than four percent; Amplia and Paradigm were down more than three percent; Next Science, Polynovo and Volpara shed more than two percent; Clinuvel, Dimerix, Immutep, Mesoblast, Nanosonics and Neuren were down more than one percent; with Telix down by 0.2 percent.

DR BOREHAM'S CRUCIBLE: CYNATA THERAPEUTICS

By TIM BOREHAM

ASX code: CYP

Share price: 13.5 cents; **Shares on issue:** 179,631,786; **Market cap:** $24.25 million

Chief executive officer: Dr Kilian Kelly

Board: Dr Geoff Brooke (chair), Dr Kelly, Dr Paul Wotton, Dr Darryl Maher, Dr David Atkins, Janine Rolfe (CEO and director Ross Macdonald retired on June 30 2023, with director Dr Stewart Washer)

Financials (March quarter 2023): revenue nil, cash outflows $2.97 million, cash balance post-raising about $17.5 million, end of quarter cash $13.5 million

Identifiable major holders: Phillips Asset Management (Bioscience Managers Translation Fund) 13.1%, Fidelity Investment Management 10%, Fujifilm 4.5%

The changing of the guard is not just evident at Buckingham Palace: barely a week goes by without an ASX-listed biotech announcing a new person at the helm.

In the case of the junior stem-cell therapy developer, incumbent Dr Ross Macdonald announced his retirement after 10 years in the job, to be replaced with chief operating officer Dr Kilian Kelly.

Dr Kelly joined the company at the same time as Dr Macdonald, who was brought in by Cynata's Perth-based backer Forest Capital (as was director Dr Stewart Washer, who has also left the building). Before then, Dr Kelly had senior roles at influenza drug house Biota and stem-cell peer Mesoblast.

Unlike with some other regime changes in the sector, Dr Kelly says there are likely only to be peripheral changes in terms of how he runs the joint.

"Everyone CEO has slightly different views, but we will continue to focus on the existing programs," he says.

Cynata's clear priority is to advance its phase II clinical trial for graft-versus-host disease, or GvHD - an immunological condition that afflicts bone-marrow recipients and is usually fatal for patients resisting steroid treatment.

Cynata is a case of Covid interruptus in that this program – as well as an investigator-led one for knee osteoarthritis – was seriously delayed by the pandemic.

The perceived lack of headway has resulted in Cynata shares losing more than 60 per cent of their value over the last year - a fact not lost on Dr Kelly.

"We have been absolutely hammered and effectively are at all-time lows," he says.

The birds and the bees of iPSCs and MSCs

Cynata is all about harvesting induced pluripotent stem cells (iPSCs), from which mesenchymal stem cells (MSCs) are derived.

MSCs are adult stem cells which can be isolated from human and animal sources and can produce more than one kind of specialist cell.

Cynata says iPSCs are economically advantageous in that they are generated from a donation from a single donor, resulting in product consistency, scalability and potency.

'Pluripotent' means the iPSCs could develop into any type of adult cell. They can be derived from anywhere in the body - typically skin and blood - and grown in limitless quantities in the lab.

Known as Cymerus, Cynata's platform for making MSCs stems from the University of Wisconsin-Madison, the centre of US stem cell research. The University's Prof Igor Slukvin co-founded Cynata, with the aim of licencing the technology from the Wisconsin Alumni Research Foundation.

Cynata back-door listed in October 2013 via the shell of green nappy maker Eco Quest.

Turning Japanese

There are strong Japanese links with Cynata, in that Kyoto University's Dr Shinya Yamanaka won a Nobel Prize in 2012 for his pioneering work in iPSCs.

In late 2019, Cynata forged an alliance with Fujifilm, which had long forsaken happy snaps for medical applications.

The deal involved Fujifilm funding the development of CYP-001 (the GvHD therapy) in return for the global selling rights, with Cynata in line for milestone and royalty payments.

A planned global trial was derailed by Covid and then Fujifilm's decision to emphasize cell manufacturing rather than developing its own stem-cell products.

In 2021, Fuji and Cynata agreed that the development rights would revert to Cynata, but the parties signed a new agreement with the parties agreeing to establish a Cymerus manufacturing plant in Japan.

Interestingly, stem cell leader Mesoblast's only approved therapy to date is for steroid-resistant GvHD in Japan (marketed by JCR Pharma).

Japan also features strongly because former Prime Minister Shinzo Abe was a huge supporter of cell therapies and regenerative medicine.

Mr Abe was assassinated in July last year, after he had left office, but his legacy is regulation allowing accelerated approval of any kind of regenerative medicine therapy.

Good vibes Here Dudes

The original idea was that Fujifilm was to carry out a trial for GvHD using Cymerus, scheduled by the end of (Covid-ridden) 2020.

“We have put Japan on ice and are now moving forward with a global phase II trial, with sites in the US, Australia and Europe,” Dr Kelly says.

The 60-patient, randomized, blinded, controlled trial will be run at multiple centres in the US, Europe and here, with the first sites (in Europe) expected to open in August.

The trial will compare patients receiving the standard-of-care steroids with a placebo, versus those receiving steroids and the stem cell potion.

Dr Kelly says it’s possible - just possible - that the GvHD trial could support marketing approval in the US without a follow-on phase III effort.

“No regulation says you have to do a phase III trial; you need data from an ‘adequate and well-controlled’ trial to support efficacy and safety,” he says. “It is a rare disease with a significant unmet need, so we tick those boxes.”

The phase I effort met all endpoints, with the results aired at the International Society of Cell and Gene Therapies’ shindig in Paris in early June. The delegates heard that nine of the 15 patients treated with CYP-001 survived at the two-year mark. This compared “highly favorably with previously published outcomes, including for current steroid-resistant GvHD drugs”.

The trial marked the first time any patient had been treated with iPSC-derived MSCs - their own cells or otherwise.

A treatment we kneed

While GvHD is Cynata’s lead indication, a phase III trial for moderate knee osteoarthritis sufferers is about to get underway under the auspices of the University of Sydney.

Aimed at enrolling 440 patients, the double-blinded, placebo-controlled trial will assess the effect of injected Cymerus over two years, the co-primary endpoints being patient-assessed pain reduction and reduced cartilage loss. Recruitment is expected to be completed by the end of 2023.

The trial is sponsored by the University of Sydney and fully funded by a $2 million grant from the National Health and Medical Research Council (NHMRC). Dr Kelly estimates that if Cynata had to fund the trial, it would cost $20 million to $30 million. Cynata will provide the product and is entitled to access all the data.

Dr Kelly says the patients are not about to have a knee reconstruction - but they are certainly headed in that direction: “Hopefully we can intervene and at a minimum resolve the pain and inflammation and stop it from getting worse.”

Given the NHMRC is providing the cheque, the trial sites are Australia-only, but the results could be acceptable to overseas agencies.

“It’s a very exciting trial and a huge opportunity for us to get a huge trial done without paying for it at commercial rates,” Dr Kelly says.

Stay focused …

Astonishingly, more than 1,200 MSC trials have taken place over the last decade, covering 300 indications. The main diseases of interest are GvHD, heart disease and osteo-arthritis and fibrotic indications such as idiopathic pulmonary fibrosis.

Cynata is involved in early-stage trials for diabetic foot ulcers and renal transplants. An Adelaide-based diabetic foot ulcer trial aims to enrol 30 patients, randomized against the standard-of-care dressing.

“This one’s a bit different, because we are applying the cells topically, using a dressing,” Dr Kelly says. “The number of cells we need is less than a million cells compared with an intravenous infusion of up to 200 million cells. So, it could be a more cost-effective approach.”

Preliminary data from patients in the trial has been “promising”.

Cynata carried out pre-clinical work on renal transplants, with the Liden University Medical Centre in The Netherlands. Early results suggest MSCs can improve tolerance and avoid solid-organ rejection. Dr Kelly says current anti-rejection (immune suppressant) drugs are extremely toxic and – ironically - cause kidney damage and increase the risk of cancer.

“Anyone who uses them would love to not have to use them.”

Warning: AO content

Cynata’s GvHD trial is ‘adults only’, but the company would look to include children in any expansion study.

Meanwhile, Cynata’s stem cell ‘frenemy’ Mesoblast is awaiting a US August 2 D-Day to see if the FDA will accept its marketing application for its paediatric GvHD treatment.

Dr Kelly notes that about 90 percent of GvHD patients are adults, although there’s the prospect of the off-label use of Mesoblast’s kids’ treatment in grown-ups.

Despite the prospect of a rival product in the world’s most important market, Dr Kelly says he would be pleased if Mesoblast won approval.

“It would be a tick for all MSC-based therapies,” he says. “We would rather compete [with Mesoblast] than compete with nothing.”

Finances and performance

Cynata is riding out the funding nuclear winter that has enveloped the biotech sector.

In early April, the company completed a placement to raise $5 million at 21.5 cents, a then 2.5 percent discount to the prevailing price.

An oversubscribed share purchase raise $2,050,000, at 15.5 cents apiece, with one-for-two options exercisable at 30 cents. The funds will be used to support the GvHD trial, costing about $10 million.

Cynata shares peaked at a 12-month high of 44 cents in August last year and a record high of $1.80 in 2019. They sunk to a record low of 10.5 cents on July 4 this year.

Post raising, Cynata has about $17.5 million in the bank, not much less than its $23 million market capitalization.

Dr Boreham's diagnosis:

Research house Oliver Wyman estimates there are 4,000 cases of GvHD a year in the US. The firm says the newly-diagnosed market is worth $US85 million ($A125 million) and the steroid-resistant market is $US125 million (because of higher pricing for this smaller, but more difficult sector).

"If you don't get acute GvHD under control quickly, the prognosis is terrible – 80 to 90 percent mortality in two years," Dr Kelly says. "But we must be realistic. Steroids are very cheap and work in around 30 to 50 percent of patients. So, there will be a tendency to use steroids in milder cases to see if they do work."

While expensive, the stem cell therapies are attractive to payors (insurers) because patients don't have to take the drug forever.

In some cases, the GvHD is "completely resolved" in days, although given their underlying malignancies patients should not expect a telegram from the King.

"But they stand a chance, which is why there is a willingness to pay for fairly expensive treatments," Dr Kelly says.

Cynata's lowly valuation leads investors to ponder the 'sliding doors' moment of Sumitomo's 2019 provisional $2 a share cash bid for the company, which didn't get over the line. But Dr Kelly is unfazed.

"Objectively it's hard to explain why we would be worth less now than 10 years ago, when we didn't even have a manufacturing process," he says. "My view is it is clinical data that will change the course of the share price."

Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He has a strong suspicion he is worth less than he was 10 years ago in inflation-adjusted terms

ANTEOTECH (FORMERLY ANTEO DIAGNOSTICS)

Anteotech says an online article states it has been accused of “misusing confidential information of London’s Ferroglobe Innovation SL with whom [it] previously collaborated”.
In 2019, the then Anteo said it had an agreement with Madrid’s Silicio Ferrosolar for the integration of silicon into anodes for lithium-ion batteries (BD: Jun 25, 2019).
Yesterday, in an announcement titled ‘Clarifying Statement’ the company said it “rejects this allegation and will vigorously defend any such allegation should it be made”.
Anteotech said Ferroglobe had made an application to an unspecified Court “to seek preliminary discovery of the company’s confidential material for it to be able to assess whether or not it wishes to allege that there has been misuse of Ferroglobe’s confidential information, which the company rejects”.
Biotech Daily made several attempts to contact Anteotech to clarify which Court was hearing the matter but had no response at the time of publication.
Anteotech said that it was defending that application.
The company said that on July 19, 2023, the unspecified Court “rejected orders sought by Ferroglobe and made orders put forward by the company requiring Ferroglobe to provide financial security for the company’s costs after which the company will provide certain patent applications by the company to Ferroglobe for review under a strict confidentiality regime”.
Ferroglobe’s website said it produced metallurgical products for consumers and industrial applications and was “the largest merchant producer of silicon metal in the Western World, and a … producer of silicon-based alloys and manganese-based alloys”.
Anteotech was up 0.1 cents or 2.6 percent to 3.9 cents with 1.4 million shares traded.

BOTANIX PHARMACEUTICALS

Botanix says it has “firm commitments” to raise $12.5 million through a non-underwritten placement to institutional investors at 12.0 cents a share.
Botanix said the price was a 13.4 percent to the five-day volume weighted average price.
The company said the proceeds would extinguish future milestone and royalty payments due to the Boulder, Colorado-based Fresh Tracks Therapeutics Inc from whom it had bought its sofpironium bromide topical gel.
In 2022, Botanix said that it would pay the Miami, Florida-based Brickell Biotech up to $US17 million ($A25 million), plus royalties for sofpironium bromide gel for excessive underarm sweating (BD: May 4, 2022).
According to the Fresh Tracks website Brickell Biotech rebranded to Fresh Tracks on September 7, 2022.
In September, Botanix said it filed a new drug application to the US Food and Drug Administration for sofpironium bromide for excessive sweating (BD: Sep 26, 2022).
Today, Botanix said it was obliged to pay Fresh Tracks $US4 million on FDA approval of the gel, $US4 million if approval was extended to another indication (such as for palmar or plantar hyperhidrosis) and $US4 million for approval in the UK or Europe.
The company said it was obliged to pay sales milestones of up to $US160 million on reaching milestones, including the first $US75 million of net sales and up to $1.8 billion of sales, as well as royalties ranging from 12 percent to 20 percent on net sales.
Botanix said that in exchange for $US8.25 million “all of these future financial obligations due would be extinguished”.
Botanix executive chair Vince Ippolito said that a single upfront payment “potentially saved up to $US160 million in milestone and royalty payments”.
Botanix fell one cent or 6.9 percent to 13.5 cents with 7.9 million shares traded.

VOLPARA HEALTH TECHNOLOGIES

Volpara says customer receipts for the three months to June 30, 2023 rose 27.4 percent to $NZ11,048,000 ($A10,197,094) compared to the prior corresponding period.
Volpara said that annual recurring revenue from its breast mammography software of was up 28.8 percent to $NZ34.9 million ($A31.8 million).
The company said it had a net cash inflow of $NZ9,000 for the three months to June 30 with cash and equivalents of $NZ12,107,000, compared to $NZ15,152,000 in 2022.
Volpara managing-director Teri Thomas said the three months was “a great quarter” with recognition by Microsoft and continued growth of the customer base.
“What matters most is the positive impact on families and our growth and financial strength allow us to explore ways to expand that impact,” Ms Thomas said.
“We could not be more pleased,” Ms Thomas said
Volpara fell 2.5 cents or 2.7 percent to 91 cents.

MACH7 TECHNOLOGIES

Mach7 says it has a five-year, $3.7 million deal with the Tusla, Oklahoma-based Diagnostic Imaging Associates, to provide its E-Unity diagnostic viewer.
Mach7 said the agreement was based on a subscription model and would expand the use of E-Unity beyond the original 75,000 annual study agreement for mammography reading to 1.2 million studies a year.
Mach7 chief executive officer Mike Lampron said the Tusla, Oklahoma-based Diagnostic Imaging Associates was “a large, growing practice that is benefiting from the shift in diagnostic imaging from acute care to ambulatory settings and we are delighted to now provide its 70-strong radiologist practice with the full functionality of our zero-footprint E-Unity diagnostic viewer”.
Mach7 was up four cents or 4.4 percent to 95 cents.

STARPHARMA HOLDINGS

Starpharma says its targeted cancer diagnostic DEP HER2-zirconium has shown “improved sensitivity” in a HER2-positive breast cancer model in mice.
Starpharma said that the dendrimer enhanced product (DEP) diagnostic was a designed to diagnose, stage and monitor human epidermal growth factor receptor 2 (HER2) positive cancers with greater sensitivity.
The company said that, in mice, the diagnostic had a “favorable bio-distribution profile …excellent imaging contrast between tumor and normal tissues” and showed rapid uptake and a 25 percent higher level of tumor accumulation, as well as achieving 40 times more drug in tumor than blood.
Starpharma said it planned to conduct clinical testing of DEP-HER2-zirconium and other DEP radio diagnostics and therapeutics.
Starpharma chief executive officer Dr Jackie Fairley said that radio diagnostics and therapeutics and HER2 therapeutics were “both rapidly growing categories with a number of highly successful product launches in recent years”.
“The application of Starpharma’s DEP technology in the radio [diagnostics and therapeutics] area presents a substantial opportunity to expand the commercial opportunity for DEP,” Dr Fairley said.
“The DEP platform offers greater flexibility which allows a wide range of radioisotopes to be utilized, Dr Fairley said.
Starpharma was up 5.5 cents or 14.9 percent to 42.5 cents.

MEDIBIO (FORMERLY BIOPROSPECT)

Medibio says the US Food and Drug Administration (FDA) has notified it that MEB-001 “in its current form does not meet the criteria for designation as a breakthrough device”.
In February, Medibio said it had lodged a breakthrough device status application with the US Food and Drug Administration for its sleep analysis of depressive burden study algorithm (BD: Feb 27, 2023).
In 2014, the then Bioprospect said it would acquire Invatec for its heart rate variability technology for mental health diagnoses and later said it had changed its name to ‘Medibio’ (BD: Sep 8, Oct 27, 2014).
Today, Medibio said it would review the FDA’s feedback and that results from its trials would inform its “continued engagement” with the FDA.
The company said it expected to schedule a pre-submission meeting with the FDA by the end of 2023.
Medibio was up 0.05 cents or 50 percent to 0.15 cents with 5.4 million shares traded.

INCANNEX HEALTHCARE

Incannex says it has filed an investigational new drug application to the US Food and Drug Administration for its synthetic marijuana IHL-42X for obstructive sleep apnoea.
Incannex said that IHL-42X was a composite of dronabinol, a synthetic marijuana tetrahydrocannabinol (THC) with the carbonic anhydrase inhibitor acetazolamide.
In June, the company said it had appointed Dr John Hudson and Dr Russell Rosenberg as principal investigators for the 45-site, phase II/III trial of IHL-42X for obstructive sleep apnoea (BD: Jun 16, 2023).
Today, Incannex said the application detailed its planned phase II/III trial, with participants to receive either IHL-42X, dronabinol, acetazolamide or placebo and complete daily surveys on their sleep quality, as well as assess sleep, cognitive function and other measures of safety and efficacy.
Incannex fell half a cent or 4.35 percent to 11 cents with 2.3 million shares traded.

OPTISCAN IMAGING

Peters Investments says it has increased its shareholding in Optiscan from 106,500,000 shares (17.188%) to 143,166,667 shares (19.449%).
The Perth-based Peters Investments said it bought 875,000 shares on “various” dates for $86,015 or 9.8 cents a share and acquired 35,791,667 shares on June 22, 2023 through “entitlements” for $2,863,333 or eight cents a share.
Last week, Optiscan said that its one-for-three, pro-rata, entitlement offer had raised $8,784,701 and it had placed the $7,914,115 shortfall to its underwriters, for a total of $16,698,816 (BD: Jul 13, 2023).
Optiscan was up 0.1 cents or 1.2 percent to 8.6 cents.

ADALTA

Melbourne’s Meurs Group says its 53,594,168 share-holding in Adalta has been diluted from 14.62 percent to 12.14 percent.
The Meurs Group said it was diluted by the placement of the shortfall on July 13, 2023.
Last week, Adalta said it had place $1.87 million of its rights offer shortfall, taking the total raised to $3.15 million (BD: July 13, 2023).
Adalta was unchanged at 2.4 cents.

AUSBIOTECH

Ausbiotech says it has launched the ‘National Cell and Gene Manufacturing Blueprint’ an industry strategy to expand Australian cell and gene manufacturing.

Ausbiotech said the blueprint provided recommendations to overcome four major challenges, including the “skills gaps in cell and gene manufacturing, building critical mass in Australia’s [industry], optimizing Australia’s contributions to the … product pipeline [and] tracking and guiding industry growth”.

The industry organization said cell and gene products were a “new frontier” in medicine and had demonstrated life-saving and life-changing results for patients with rare diseases and cancer.

Ausbiotech said that while initial scientific challenges had been overcome, manufacturing and delivery requirements remained complex and diverse, with the increasing number of therapies pushing global manufacturing capabilities and capacity to the limit.

Ausbiotech chief executive officer Lorraine Chiroiu said the report behind the blueprint was an “opportunity to harness Australia’s role in the global cell and gene ecosystem, and to ensure that we are best-placed as a nation to be involved in and benefit from these life-changing therapeutic approaches now and into the future”.

“In order to secure Australia's position as a critical hub for cell and gene manufacturing, timely Government support and funding is essential to fully realising opportunity lying in front of us,” Ms Chiroiu said.

The industry organization said it had partnered with Biointelect, and was supported by the Victorian Government’s Australian Medtech Manufacturing Centre.

The Ausbiotech National Cell and Gene Blueprint is available at: https://www.ausbiotech.org/documents/item/768.