Biotech Daily

Friday September 27, 2024

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market edged up 0.1 percent on Friday September 27, 2024, with the ASX200 up 8.5 points to 8,212.2 points.

Fourteen of the Biotech Daily Top 40 companies were up, 17 fell and nine traded unchanged. All three Big Caps fell.

4D Medical was the best (see below), up 18.5 cents or 41.6 percent to 63 cents, with 9.2 million shares traded. Syntara climbed 8.3 percent; Neuren was up 6.4 percent; Alcidion, Cyclopharm and Medadvisor were up five percent or more; Emvision, Mesoblast and Universal Biosensors were up more than three percent; Nova Eye rose 2.9 percent; Compumedics was up 1.7 percent; with Genetic Signatures, Pro Medicus and Proteomics up by less than one percent.

Resonance led the falls, down 0.35 cents or 5.6 percent to 5.9 cents, with 35,116 shares traded. Atomo and Paradigm lost five percent; Actinogen and Imugene fell four percent; Curvebeam was down three percent; CSL and Cynata shed more than two percent; Aroa, Avita, Cochlear, Dimerix, Immutep, Opthea, Orthocell and Telix were down one percent or more; with Clarity, Polynovo, Resmed and SDI down by less than one percent.

DR BOREHAM'S CRUCIBLE: CYNATA THERAPEUTICS

By TIM BOREHAM

ASX code: CYP

Share price: 21 cents; **Shares on issue:** 180,676,271; **Market cap:** $37.9 million

Chief executive officer: Dr Kilian Kelly

Board: Dr Geoff Brooke (chair), Dr Kelly, Dr Paul Wotton, Dr Darryl Maher, Janine Rolfe

Financials (year to June 30, 2024): revenue nil, loss of $9.74 million ($14.27 million deficit previously), cash of $6.2 million (down 61%)

Identifiable major holders: Phillips Asset Management (Bioscience Managers Translation Fund) 13%, Fidelity Investment Management 10%, Fujifilm 4.5%, Kenneth Wilson 1.97%, Aily Lamb 1.3%, Ross Macdonald 1.1%

Stem-cell therapies promise to revolutionize treatments for a range of diseases including graft-versus-host disease (GvHD), osteoarthritis, wounds treatment and fibrotic maladies.

More than 1,200 stem cells trials have taken place over the last decade, covering 300 indications, but approvals have been elusive.

One enduring problem is obtaining enough of the precious cells from donors to service patients in a cost-effective manner. The quality of cells also varies from donor to donor.

Cynata is the only clinical-stage company in the world trialing induced pluripotent stem cells (IPSCs), from which the healing agent - mesenchymal stem cells (MSCs) - are derived.

IPSCs promise to produce a limitless number of high quality and high potency doses from a single donor.

Cynata is based on its "revolutionary" stem-cell manufacturing platform, Cymerus. "It's a real game changer as to how these therapies can be produced at scale," says Cynata chief Dr Kilian Kelly.

"The major obstacle to commercialization has been that standard manufacturing methods require ongoing new donors. That approach is associated with ongoing challenges of potency, consistency and scale."

After its trial enrolments were hampered by the pandemic, Cynata is getting to the pointy end with four trials underway, with three of them reporting between late this year and early 2026.

The studies cover GvHD, Cynata's quasi-lead indication, knee osteoarthritis, diabetic foot ulcers and kidney transplants.

Getting to the bottom of Cynata

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

The Cymerus platform 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.

In June 2023, Cynata's chief operating officer, Dr Kelly, became CEO, with incumbent Dr Ross Macdonald having retired after 10 years in the job. Dr Kelly had senior roles at influenza drug house Biota and stem-cell peer Mesoblast.

In 2019, Cynata forged an alliance with Fujifilm, with Fujifilm funding the development of CYP-001 (the GvHD therapy) in return for the global selling rights. But Fujifilm decided to emphasize its own cell manufacturing and the rights reverted to Cynata in 2021.

What's the problem?

The conventional stem-cell cultivation process involves obtaining donated tissue such as bone marrow and isolating the mesenchymal stem cells (MSCs)and growing the cells in the laboratory (culture expansion).

The process starts with a small number of MSCs, but many more are needed to treat only one patient. MSCs lose potency when they undergo culture expansion, which means new donors are constantly required.

"When bone marrows are used a source of stem cells, the big limitation is that only a certain amount of product can be made from one donation," Dr Kelly says.

A single dose requires around 200 million MSCs.

"People will debate what the limit is - a few hundred doses might be able to be made from the one donation, or a few thousand," Dr Kelly says. "But that's kind of irrelevant, because for a common condition you will need to make more than a few thousand doses."

One research paper suggests IPSCs can multiply by 10 to the power of 72 – an amount well beyond the capacity of your columnist's calculator.

Seeking a better GvHD therapy

Cynata's completed phase I trial was the first time any patient had been treated with IPSC-derived MSCs - their own cells or otherwise. GvHD occurs when transplanted bone marrow material rejects the body (this is the opposite to usual organ transplants, when the body does the rejecting).

The phase I results compared well with separate (non-Cynata) phase III trial results for the Novartis kinase inhibitor drug ruxolitinib (brand name Jakafi or Jakavi), approved for sale in the US for acute steroid-resistant GvHD.

The bottom line was that at 28 days the overall response rate for Cymerus was not much better than ruxolitinib, but at two months Cynata had a 73 percent overall response rate, compared with 40 percent for ruxolitinib and 22 percent for best-available treatment (BAT).

At 18 months, overall survival for Cynata was 60 percent, compared with 38 percent for ruxolitinib and 36 percent for the BAT.

Phase II trial enrolment of 60 patients with high-risk acute GvHD is expected to complete by the end of 2024, with results in the second half of 2025.

The company has 'orphan' drug designation in the US for GvHD, which confers benefits such as seven years' marketing exclusivity post-approval. Dr Kelly says it's possible that the drug could win approval in the US without a phase III effort because it is a rare disease with a significant unmet need.

Knees …

An ongoing phase III trial for moderate knee osteoarthritis sufferers is being carried out at two sites, overseen by the University of Sydney and aided by a $2 million grant from Australia's National Health and Medical Research Council (NHMRC).

The investigator-led trial was at the volition of Prof David Hunter, rheumatologist and professor of medicine at the University of Sydney and Royal North Shore Hospital.

Dubbed Sculptor, the 320-patient, 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. Three injections are administered directly to the joint, with the second one after three weeks and the third after a year.

The patients are not about to have a knee reconstruction - but they are likely to need one without intervention. The trial is fully recruited, with the last patient visit slated for late 2025 and results due in 2026.

Dr Kelly says the researchers are looking for a disease-modifying effect, based on the anti-inflammatory properties of the MSCs.

"We don't except the MSCs to regrow cartilage, but by addressing the inflammation we can stop the further degeneration of the cartilage," he says. "If we can stop the degeneration and manage pain and inflammation, that's good enough."

… and kidneys

Given the ability of stem cells to prevent solid-organ rejection, the Liden University Medical Centre in the Netherlands is conducting (and funding) a Cymerus kidney transplant trial.

"This one is approved and ready to go with enrolments under way soon," Dr Kelly says.

Results from the first cohort are expected early next year.

Current anti-rejection (immune suppressant) drugs are extremely toxic and - ironically - cause kidney damage and increase the risk of cancer. In other words: not ideal.

… and diabetic foot ulcers

In the case of diabetic foot ulcers, Cynata has a novel product that combines its stem-cell therapy with a wound dressing. The latter was licenced from the private Adelaide company Tekcyte in 2021 but in July, Cynata acquired Tekcyte's Cytopatch intellectual property for a payment of shares worth $230,000.

For the ongoing phase I trial of 30 patients, dubbed CYP-001, the company released data from the first eight patients after 10 weeks' follow up.

"We saw really encouraging results, a median reduction of more than 88 percent in the active group compared with 51 percent for the control group," Dr Kelly says. "We are hoping to see a similar pattern when we see the full results [from all patients] late this year or early next year."

The company will seek to partner the program.

Will donors be needed at all?

In a separate development, Murdoch Children's Research Institute (MCRI) researchers have developed stem cells that closely resemble human blood stem cells.

The MCRI's Prof Elizabeth Ng said the development paved the way for these laboratory-grown cells to be used in blood stem cell and bone marrow transplants. By taking blood stem cells from the same patient, it is hoped that GvHD can be avoided.

"The ability to take any cell from a patient, reprogram it into a stem cell and then turn these into specifically matched blood cells for transplantation will have a massive impact on these vulnerable patients' lives," she said.

The work is at mouse study stage, with a human trial expected in five years. Cynata's work is far more advanced.

Dr Kelly says the news validates the use of IPSCs (which the researchers deployed).

"In the short term it doesn't have any direct effect on Cynata, but it does validate that … IPSCs really are the way to make cell-based therapies."

Finances and performance

At the end of June, Cynata had $6.2 million in the bank, enough to sustain the company until the second half of 2025. Cynata does not cover the cost of the kidney and knee trials.

The company last went to the funding well in mid-2023, raising $7 million in a placement and share purchase plan at 21.4 cents apiece.

Dr Kelly says there are “various sources of funding for the company” including potential corporate partnerships.

Over the last 12 months Cynata shares have prevaricated between 11 cents (December 4 last year) and 34 cents (June 13 this year).

They peaked at a five-year high of $1.71 in September 2019.

Dr Boreham’s diagnosis:

So far, only one stem-cell therapy has been approved in Europe (for a complication of Crohn’s disease) and in Japan, Korea and India for GvHD. Mesoblast’s Temcell is approved in Japan for GvHD.

In what would be a US first, leading stem cell exponent Mesoblast expects approval of a therapy for paediatric GvHD, which accounts for 10 percent to 20 percent of cases.

Cynata, not surprisingly, is angling for the rest.

While Cynata’s GvHD program has grabbed most of the attention in recent years, it’s the smallest indication in terms of potential value.

Citing various research sources, the company appraises the GvHD market at $US600 million ($A880 million), compared with $US9.6 billion for diabetic foot ulcers, $US5.9 billion for kidney transplants and a monstrous $US11.6 billion for knee osteoarthritis.

Misty-eyed, long-term, Cynata investors might recall that Sumitomo in 2019 made a provisional $2 a share cash bid for the company, which was not progressed.

Five years later and considerable clinical advancement later, the company is worth only a fraction of that.

Bugger!

The glass-half-full stance on Cynata is that only one of the four trials has to hit the jackpot for the company to be worth closer to the value of Mesoblast - circa $1 billion - rather than its current humble worth.

“This is an incredible exciting time for the company,” Dr Kelly says.

“Each of these trials is important in their own right because they can show the potential for MSCs to fulfil a huge unmet need.”

Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort, which is a bit of a bugger.

FLOREY INSTITUTE, MONASH UNIVERSITY

The US Food and Drug Administration says it has approved Bristol-Myers Squibb Cobenfy (xanomeline and trospium chloride) oral capsules for schizophrenia in adults.

The FDA said that Cobenfy, formerly known as Karxt, was is “the first anti-psychotic drug approved to treat schizophrenia that targets cholinergic receptors as opposed to dopamine receptors, which has long been the standard-of-care”.

The US regulator said that schizophrenia was “a leading cause of disability worldwide”.

FDA executive Dr Tiffany Farchione said the drug “takes the first new approach to schizophrenia treatment in decades … [and the] approval offers a new alternative to the anti-psychotic medications people with schizophrenia have previously been prescribed”.

The FDA said that about one percent of Americans had the illness and it was one of the world’s 15 leading causes of disability.

The Florey Institute said that research fellow Prof Brian Dean made the original discovery that led to the development of Karxt.

Prof Dean said his research “in the 1980s and 1990s, with colleagues including Elizabeth Scarr, showed that muscarinic receptors in the brain were involved in the pathology of schizophrenia”.

“In 2000, we proposed that a drug that activated the muscarinic M1 and M4 receptors would alleviate the symptoms of schizophrenia,” Prof Dean said.

“The licencing of the drug Cobenfy, a drug with that exact mechanism of action, has now validated our proposal,” Prof Dean said. “[This] heralds a new era in treating the symptoms of schizophrenia as it is the first drug that does not act on dopamine neurotransmission in the brain.”

Prof Dean said the licencing of the drug emphasized the need for basic discovery research as a vital component of discovering new ways to treat disorders of the brain.

The Florey Institute’s Prof Jess Nithianantharajah said “this landmark event underscores the incredible neuroscientific advancements that have been made in recent years to transform therapeutic discovery”.

“This is a completely new class of drug, so targets a different brain pathway to all the other existing medications for schizophrenia,” Prof Nithianantharajah said.

“This will be beneficial to the many people for whom the current medications don’t work”, Prof Nithianantharajah said.

“This progress highlights that we are just at the start of an exciting new era in the development of new and better medicines for complex mental health conditions,” Prof Nithianantharajah said.

Separately, Monash University said its scientists had played an “integral role in helping pave the way for Cobenfy.

Monash University’s Prof Arthur Christopoulos said that “until now, all available medicines for the treatment of schizophrenia have predominantly been based on science that essentially dates back to the 1950s”.

“An early discovery of a drug called xanomeline for the treatment of Alzheimer’s disease eventually evolved into a combination therapy of two drugs, xanomeline plus trospium (that is Karxt, now called Cobenfy) which work to simultaneously improve symptoms of schizophrenia while also mitigating specific debilitating side effects,” Prof Christopoulos said.

“The development of Cobenfy represents approximately a 30-year journey involving many dedicated scientists in the pharmaceutical industry and in academia,” Prof Christopoulos said. “Cobenfy represents a whole new class of more targeted medicines; a major advancement for the treatment of schizophrenia and other difficult-to-treat neuropsychiatric and neurological diseases.”

4D MEDICAL

4D Medical says it has a five-year, US distribution deal with Amsterdam's Koninklijke Philips NV for its lung imaging technology.

Last year, 4D Medical said it had an agreement with Philips to include XV technology in its US catalogue, with the partnership allowing Phillips to offer 4D Medical's lung imaging as a screening option for veterans exposed to burn pits (BD: Nov 29, 2023).

In January, 4D Medical said it would work with Philips to expand commercialization of its XV lung imaging technology in the US Department of Veterans Affairs (BD: Jan 22, 2024).

Today, 4D Medical said Philips would be the exclusive seller of its products to US government customers and had non-exclusive rights to sell to all other US customers.

The company said initial transfer pricing had been established, in which Philips would "earn margins between 20 percent and 35 percent" varying by product on sales of XV lung ventilation analysis software (LVAS), computed tomography (CT) LVAS, and Imbio products.

4D Medical said that Philips had "long-established and significant existing commercial partnerships" with 50 percent of Department of Veterans Affairs clinics using Philips imaging products.

4D Medical chief executive officer Prof Andreas Fouras said the two companies would "deliver lung function analyses for all lung disorders" including unexplained dyspnoea, asthma, chronic obstructive pulmonary disease, and interstitial lung disease.

"Philips is a market leading brand with a commanding commercial presence across government and non-government sectors," Prof Fouras said.

"Central to the collaboration … is a drive to address the significant health challenges faced by Veterans due to military toxic exposures," Prof Fouras said. "This … collaboration is a pivotal strategy to provide advanced care and support for those who have bravely served."

4D Medical was up 18.5 cents or 41.6 percent to 63 cents with 9.2 million shares traded.

OSTEOPORE

Osteopore says it expects to raise $20 million from the Cayman Island's Advance Opportunities Fund for a redeemable convertible note at four percent interest.

Osteopore said that pending shareholder approval, the convertible notes would issue in four equal tranches, with each tranche comprising 20 equal sub-tranches of $250,000 each, maturing 36 months from the completion of the drawdown for the first sub-tranche.

The company said it had an initial commitment fee of $50,000 that could be issued in new shares or cash; the note had a conversion price at 80 percent of the average closing price on "any five consecutive business days" as selected by the noteholder during the 45 business days immediately preceding the conversion date.

The company said it would pay "an administration fee of 6.0 percent of the aggregate principal amounts subscribed of each sub-tranche to be paid upon drawdown of each respective sub-tranche".

Osteopore executive chair Mark Leong said that the company had "six consecutive quarters of revenue growth, with our bioresorbable implants now used in more than 120,000 surgeries".

"Our exclusive distribution agreement with Zimmer Biomet not only validates our regenerative technology but also strengthens our market position," Mr Leong said.

"Unlike traditional funding methods, the [redeemable convertible note] can provide us with the flexibility and financial agility to drive our plans forward, aligning with our current growth stage and future ambitions," Mr Leong said.

Osteopore was up 0.2 cents or five percent to 4.2 cents with 2.5 million shares traded.

NOXOPHARM

Noxopharm says it will issue $2.6 million in convertible notes to investors, including $500,000 to a company controlled by non-executive chair Fred Bart.
Noxopharm said that the notes would convert for 9.92 cents, a 20 percent discount to the five-day volume weighted average price to September 6, 2024, and would expire on January 2, 2026.
The company said, as an incentive for participating, investors would receive a total of 420,000 unlisted options, exercisable at 14.88 cents each for three years and expiring September 10, 2027.
Noxopharm said the notes were secured over its Federal Research and Development Tax Incentive and had an interest rate of 12 percent, capitalized until the notes were repaid or converted into shares.
The company said Mr Bart was subscribing through 4F Investments Pty Ltd and would receive up-to 100,000 unlisted options on the same terms as other investors.
Noxopharm was unchanged at 10 cents.

TRAJAN GROUP HOLDINGS

Trajan says its annual general meeting will vote to grant 238,599 options to chair John Eales and directors Dr Rohit Khanna, Tiffiny Lewin and Sara Watts.
Trajan said investors would vote to grant 79,533 options to Mr Eales and 53,022 options each to Dr Khanna, Ms Lewin and Ms Watts, with “a nil exercise price’ within five years from grant.
The company said shareholders would also vote to adopt its remuneration report, re-elect director Robert Lyon, renew its long-term incentive plan and renew its proportional takeover bid provision in its constitution.
The meeting will be held online on October 29, 2024 at 10am (AEDT).
Trajan fell half a cent or 0.4 percent to $1.245.

HERAMED

Heramed says the Australian Therapeutic Goods Administration has cancelled all home-use foetal dopplers devices, including its Herabeat foetal heart rate monitor.
Heramed said a review by the TGA found that a lack of specialized training to use foetal doppler devices could result in “false reassurance of the health of a baby”.
The company said it was now required to reclassify Herabeat to a higher class of regulatory classification with its existing class IIa approval also cancelled.
Heramed said it supported the decision to reclassify and it was actively working on it in consultation with the TGA, and would meet with it in October to finalize its pathway to re-approval.
The company said a product recall had not been instigated, and that the cancellation simply meant that home-use devices could no longer be imported or locally manufactured.
Heramed said that given the amount of Herabeat units already in Australia, which could continue to be used and resold, it expected to “meet market needs until reapproval [was] achieved”.
Heramed was unchanged at 1.8 cents.

PARADIGM BIOPHARMACEUTICALS

The Munich, Germany-based Allianz SE says it has ceased its substantial shareholding in Paradigm, selling 3,935,875 shares.

Allianz said that between May 20 and September 24, 2024 it sold 3,935,875 shares for prices ranging from 19.45 cents to 27.09 cents a share, with the single largest sale of 1,049,734 for $204,071 or 19.45 cents a share.

In May, Allianz said it held 21,308,735 Paradigm shares (6.08%) (BD: May 22, 2024).

According to its latest filing Paradigm had 350,239,346 shares on issue, with Biotech Daily calculating that Allianz held 17,372,860 Paradigm shares or 4.96 percent of the company.

Paradigm fell one cent or five percent to 19 cents with 1.5 million shares traded.

NYRADA

Nyrada says it has “successfully completed” a 14-day NYR-BI03 dog toxicology study, the sixth of nine studies required to begin its first in-human phase I trial.

Nyrada said the trial for its brain injury drug candidate was at a dose “much higher” than the intended human dose, and assessed NYR-BI03’s safety and tolerability profile, focusing on general health, body weight, clinical pathology and pharmacokinetics measuring drug exposure.

The company said it would conduct a rat toxicology study, and in-vitro and in-vivo micronucleus studies, before beginning its phase I human trial, this year.

Nyrada was up 1.1 cents or 19.0 percent to 6.9 cents with three million shares traded.

HEXIMA

Hexima says it has extended the date for satisfaction of conditions for its purchase of Real Thing Entertainment from September 30 to December 16, 2024.

In July, Hexima said it would acquire Real Thing Entertainment Pty Ltd for 789,743,000 shares and 87,215,040 options, raise up-to $7.5 million and hold a 10-to-one consolidation (BD: Jul 24, 2024).

Hexima was unchanged at 1.7 cents.