Biotech Daily

Thursday June 30, 2022

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market fell 1.97 percent on Thursday June 30, 2022, with the ASX200 down 132.1 points to 6,568.1 points. Eleven of the Biotech Daily Top 40 stocks were up, 20 fell and nine traded unchanged.

Micro-X was the best on no news, up 2.5 cents or 21.7 percent to 14 cents, with one million shares traded. Proteomics climbed 17.0 percent; Paradigm and Starpharma were up more than 10 percent; Emvision and Universal Biosensors were up more than seven percent; Actinogen was up 6.4 percent; Medical Developments improved 3.9 percent; Neuren rose 2.4 percent; Amplia and Orthocell were up more than one percent; with Cochlear up 0.35 percent.

Genetic Signatures led the falls, down 14 cents or 10.8 percent to $1.16, with 52,353 shares traded. Compumedics lost 8.8 percent; Antisense and Avita retreated more than six percent; Cyclopharm, Mesoblast and Resonance were down more than five percent; Prescient and Volpara fell more than four percent; Pharmaxis and Polynovo were down three percent or more; Imugene and Next Science shed more than two percent; Atomo, Clinuvel, Immutep, Nanosonics, Opthea and Telix were down more than one percent; with CSL, Pro Medicus and Resmed down by less than one percent.

DR BOREHAM'S CRUCIBLE: PARADIGM BIOPHARMACEUTICALS

By TIM BOREHAM

ASX code: PAR

Share price: 96.5 cents; **Shares on issue:** 232,680,798 (5,085,003 in ASX escrow)

Market cap: $224.5 million

Chief executive officer: Marco Polizzi

Board: Paul Rennie (chair), Dr Donna Skerrett, John Gaffney, Amos Meltzer, Helen Fisher

Financials (March quarter 2022): receipts $14,000, cash outflows $15.2 million, cash balance $39.8 million, quarters of available funding 2.63 (the company received an $8.2 million Federal Research and Development Tax Incentive in early June)

Identifiable major holders: Paul Rennie (Kzee Pty Ltd) 8.7%, Nancy Edith Wilson-Ghosh 1.68%.

Paradigm Biopharmaceuticals' investment relations guy Simon White is a bit different to your average biotech corporate gun for hire, given he's actually tried the remedy he is promoting.

A footballer with the AFL's Carlton Football Club, Mr White had no fewer than eight knee surgeries over his eight-year, 87-game playing career, including multiple reconstructions.

When the defender retired in 2017, his joints were not in a good way.

"I was having really bad night ache. I would go for a run and I would be awake for five or six hours because I couldn't get comfortable."

After trying everything from stem cells to liposuction, he went to Carlton club doctor Philip Bloom and joined the 400 or so sportspeople the medico had treated with the reinvented old drug pentosan polysulfate sodium (PPS).

PPS is not approved, but is used under the Therapeutic Goods Administration's special access scheme.

Three years on, Mr White is sleeping much more soundly and still pulling on the boots for amateur team East Doncaster (Eastern Football League).

Mr White's Carlton team mate, the high-flying Andrew Walker has also benefited from PPS, his aerial gymnastics having extracted a heavy toll on his knees.

"I played him in a pre-season scratch match last year and he is still moving as well as he ever has," Mr White says.

Paradigm's long list of athlete patients - including Carlton legend Mark 'Diesel' Williams - exemplifies the persuasive power of real world evidence (RWE).

But while the US Food and Drug Administration is more receptive to RWE, anecdotes don't quite have the gravitas of a large scale, properly-constructed, clinical trial.

On that note, the agency finally has allowed Paradigm to forge ahead with two phase III trials that will prove (or otherwise) that its repurposed drug is the bee's knees.

Zilosul by the doseful

Okay - let's take a step back.

Renamed Zilosul by Paradigm, PPS is an anti-inflammatory compound made from beech-wood hemicellulose (don't laugh: aspirin used to be made from willow bark). Over time, PPS has been used to treat a bladder condition and deep vein thrombosis.

As far as osteoarthritis goes, there are commonly prescribed non-steroidal anti-inflammatory drugs, which the company claims are often ineffectual at the dealing with the root cause, or opioid-based painkillers.

So far Zilosul has been used on about 600 patients, mainly through special access schemes but also in a 112-patient phase IIb trial.

As well as AFL kickers of the Sherrin football, 10 American (National Football League) footballers have also been treated for their creaking joints, under a US special access program.

A phase II trial has also been carried out (see below).

As well as dodgy knees, Paradigm is eyeing other conditions including viral osteoarthritis (Ross River fever) and the rare disease muco-poly-saccharidosis (MPS). Given the inflammation angle, Covid-19 is also in the mix.

But what is PPS's origin?

Janssen Pharmaceuticals (Johnson & Johnson) sells an oral formulation of PPS under the name Elmiron, to treat a painful bladder disease called interstitial cystitis.

Paradigm has an exclusive supply deal with the only approved PPS maker, Germany's Bene Chempharma.

Otherwise, Paradigm has patents on the relevant indications in injected oral or topical form. The patents run until 2035 or 2040.

The company describes the supply deal with Bene Chempharma - under which Bene receives a two percent royalty - as being as good as patent protection.

Paradigm management shifts

Paradigm was founded by Paul Rennie and Graeme Kaufman and listed on the ASX on August 18, 2015, having raised $8 million at 35 cents apiece.

Mr Rennie was Mesoblast's head of product development. Mr Kaufman was CSL's chief financial officer through the plasma behemoth's privatization, was a Mesoblast executive vice president and Bionomics chair.

Mr Kaufman stepped down as Paradigm's chair and as a director in June 2020 for health reasons. Last November, Mr Rennie ceded his chief executive role and is the new chair.

Director and chief medical officer Dr Donna Skerrett stepped up as acting head banana, but she can now return to chief medical officer duties after the appointment of US healthcare executive Marco Polizzi.

Clocking on from July 1, Mr Polizzi has 30 years' pharma industry experience in varied commercial roles. At Sandoz, he created a hospital and speciality markets unit and he also established new divisions at Mallinckrodt Pharmaceuticals and JHP Pharma.

Mr Polizzi will remain US based, which is okay in our books given that's where the pivotal trial is taking place.

Clinical update (and recap)

As reported in December 2018, the local phase IIb trial showed that 46 percent of patients had a 50 percent or more reduction in pain after 53 days, compared with 22.5 percent for the placebo group. The trial injected PPS into the knee and compared it to injected saline.

Interestingly, at the time broker Morgans broke from the cheer squad and dubbed the phase IIb (and follow up) osteoarthritis results as "unconvincing and lacking substantive clinical evidence". Party poopers!

The FDA concurred and in April 2020 the FDA knocked back Paradigm's request for approval, which was predicated on one planned phase III trial and "published literature" (no, not Emily Bronte).

"We'll have two adequate and well-controlled phase III trials, thanks," the regulator told the company.

Having been on FDA 'clinical hold' for the best part of nine months, the requested two phase III confirmatory and pivotal trials are now underway.

Enrolling about 900 and 735 knee osteoarthritis patients respectively, the pivotal and confirmatory trials will be carried out across 56 sites, about half of them in the US. The remainder are in Europe, Britain and Australia.

The treatment involves weekly self-administered injections over six weeks.

In the US the key endpoint is pain, using the 24-question Western Ontario and McMaster Universities (Womac) pain scale. Knee function is a secondary endpoint.

In Europe pain and function (versus placebo) are the secondary endpoints.

Later this year, the company hopes to release interim data from a phase II exploratory study of the disease modifying potential on knee osteoarthritis patients, looking at disease progression biomarkers and radiographic imaging of any bone marrow lesions.

Paradigm is also carrying out two smaller phase II studies for muco-poly-saccharidosis, in view of a co-development deal to progress it beyond that.

Finances and performance

While Paradigm had just under $40 million in the bank as of the end of March - and in June cashed a $8.9 million Federal Research and Development Tax Incentive - the harsh reality is that it will need more lucre to complete the trials. Bell Potter assumes a circa $70 million raising in 2023.

Paradigm has not disclosed the cost of the trials, although the $80 million has been bandied around. Or at least we've bandied that number around …

In the happier days of yore, Paradigm raised $35 million in 2020 and a monstrous $78 million (via a placement and rights offer) in 2019.

Over the last 12 months, Paradigm shares have lurched between $2.53 (early November 2021) and 90 cents currently. They peaked at $4.20 in late January 2020. The shares have lost 53 percent of their value over the last 12 months and were kicked out of the ASX300 in March. But don't take it personally: that fate befell a number of other biotechs.

Compelling economics …

Based on the work of a global market research company using de-identified patient data from payers (insurers) and doctors, Paradigm is confident that it can charge $US2,500 per course of treatment.

Management hopes that by the time a new drug application is filed in 2025, re-treatment data will be available. The significance of this is that the drug would be able to treat osteoarthritis as an ongoing chronic condition and this would be on the label.

"We are looking at a second line therapy for pain and function at the moment," Mr White says. "This doesn't bring in the fact that we will investigate disease modifying properties that would have taken the price through the roof."

US and European regulatory feedback also suggests the company could do a smaller trial for hip osteoarthritis and also win a label for that.

Hips and knees account for 70 percent of the total addressable market for osteoarthritis.

…. but the natives are restless

Presumably reflecting investor frustration at the long development path, shareholders voted a remuneration report second strike at the January 25 annual general meeting, as well as a proposal to grant incentive shares to Mr Rennie.

In fact, a whopping 68 per cent of voting holders opposed the latter. The remuneration proposal didn't meet the 75 percent approval threshold, with 38 percent of shareholders voting against.

Given the same thing happened last year, the 'no' vote was deemed a second strike, which triggered a motion to spill the board. But as is the case with the vast majority of second strikes, investors weren't quite so bolshie and soundly rejected the spill vote.

The AGM, by the way, was delayed to enable an in-person meeting, as allowed under covid rules. As it happened, the jamboree was held virtually, anyway.

Dr Boreham's diagnosis:

The Paradigm story caused quite a tizz among the company's retail-heavy register - at least before it dawned on investors that the FDA wouldn't be convinced by sportsmen's yarns about a miraculous cure alone. The global biotech sector's dramatic retreat - a function of general risk aversion and the end of the era of cheap money - doesn't help.

Of course, the problem goes beyond athletes: there are more than 30 million osteoarthritis sufferers in the US and about three million here.

To a degree, the phase III trial results are binary, in that the endpoints will or won't be met. "The reality is that if your lead program fails, you are on Struggle Street," Mr Rennie told your columnist in April 2020.

But in this age of data mining patient subsets, something is likely to be salvageable from a poor result. And pain - though very real - is a subjective measure.

Given America's entrenched opioid problem, the FDA could well give the benefit of the doubt if the trial results are half decent. In Bell Potter's words: "Zilosul has the potential to become one of the largest selling drugs of all time if the claims of disease modification and pain reduction are met."

Mr White notes that with trial sites in multiple geographies, the trial could open up approval in Europe and Australia and possibly Canada: "the market might have missed that a bit."

With multiple approvals, Paradigm would truly be kicking goals. But for the time being it's a quarter-by-quarter proposition - against a stiff breeze - as the crucial trials unfold.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. But he does have a decent set of patellofemorals and tibiofemorals and that's all he kneeds.

PROTEOMICS INTERNATIONAL LABORATORIES

Proteomics says it has identified a “panel of statistically significant biomarkers for endometriosis” through a clinical validation study with samples from 857 patients.
Proteomics said the study, with Melbourne’s Royal Women’s Hospital and the University of Melbourne, compared 857 samples across three groups: 468 women who had been diagnosed with endometriosis through a laparoscopy, and two control groups, 147 healthy individuals, and 242 patients with symptoms but no clinical diagnosis.
The company said the study was successful in identifying a panel of several plasma proteins that were statistically significant ($p < 0.05$) at differentiating samples from the laparoscopy-confirmed endometriosis positive group against those with symptoms but no clinical diagnosis.
Proteomics said the next phase of validation would use the biomarkers to build a diagnostic model to test sensitivity and specificity and would take about one month.
The company said it intended to present the results of both the clinical validation study and the diagnostic model at a conference and then seek to confirm the clinical performance of the test in an independent patient cohort.
Proteomics said it had signed a material transfer agreement with Perth’s St John of God Subiaco Hospital Gynaecological Cancer Research Group to access about 250 samples from patients with either clinically confirmed endometriosis or other benign conditions.
The company said the current detection standard was a laparoscopy, involving the insertion of a camera into the pelvis through an incision in the abdominal wall.
Proteomic said that endometriosis was a highly complex condition with a broad spectrum of clinical indications, and further work might be required to detect variations.
Proteomics managing-director Dr Richard Lipscombe said the company was “excited to have passed this significant milestone on our way to developing what we hope will be the world’s first non-invasive test for endometriosis”.
“The clinical validation results are the foundation for turning the biomarkers into a new diagnostic test for endometriosis,” Dr Lipscombe said.
“The statistical modelling and subsequent independent study will prove if we have a viable, novel, non-invasive test for endometriosis, and we believe this program will garner significant interest, both commercially and in the clinic,” Dr Lipscombe said.
Proteomics said that endometriosis affected one-in-nine women and cost Australia $9.7 billion each year, with “no simple way to test for the condition, which often causes pain and infertility”.
Proteomics was up 13.5 cents or 17.0 percent to 93 cents.

MICROBA LIFE SCIENCES

Microba says the Asheville, North Carolina-based Genova Diagnostics will make microbiome tests using its platform available to US healthcare practitioners, from today.
Microba said that with Genova it had established a Clinical Laboratory Improvement Amendments and College of American Pathologists (Clia/Cap) certified metagenomic laboratory in North Carolina, enabling rapid turnaround on gut microbiome tests using on Microba’s analysis platform.
Microba chief executive officer Dr Luke Reid said that “scientifically and medically aligned partners such as Genova are important to make our technology rapidly available to practitioners and their patients globally to improve health care”.
“We are pleased to see our testing technology coming to practitioners in North America with a true pioneer and leader in the field of gastro-intestinal testing,” Dr Reid said.
Microba fell 2.5 cents or 11.1 percent to 20 cents.

MEDLAB CLINICAL

Medlab says it will hold an extraordinary general meeting for a 150-to-one share consolidation and list on the Nasdaq offering 4,000,000 post-consolidation shares.
Medlab said the consolidation would reduce its share pool from 342,000,000 shares to 2,280,000 shares, and its option pool from 14,583,333 options to 97,224 options.
The company said it would seek approval for a placement of up-to 4,000,000 post-consolidation shares and attaching warrants, or options, for its Nasdaq initial public offer.
Medlab said that the attaching 4,000,000 warrants would be exercisable at 100 percent to 120 percent of the initial public offer price, within five years.
Biotech Daily calculates that at its current price of 5.0 cents a share, Medlab would trade at about $7.50 a share after the consolidation and the offer could raise up to $30 million.
Medlab said that a Nasdaq listing "offers deeper access to sophisticated investors, specialized biotechnology and healthcare funds, and further positions Medlab Clinical as an advanced biotech company in the world's largest market".
The company said it was "heavily US focused with development, manufacturing, and regulatory activities presently in place … [and with] a significant footprint in the US".
The meeting will be at Building A, Units A5-A6, 11-13 Lord St, Botany, Sydney, and virtually at: www.advancedshare.com.au/virtual-meeting on July 28, 2022 at 10am (AEST)
Medlab was unchanged at 4.8 cents with 2.0 million shares traded.

STARPHARMA

Starpharma says its Viraleze nasal spray has been re-launched online by the UK-based Lloyds Pharmacy, with distribution to pharmacies to begin "shortly".
Last year, Starpharma said it appointed Lloyds Pharmacy as the UK distributor of its anti-viral Viraleze nasal spray, which contained SPL7013 (BD: Mar 25, 2021).
In June last year, Starpharma said it had withdrawn Viraleze from sale in the UK following questions from the regulator on claims about severe acute respiratory syndrome coronavirus-2 (Sars-Cov-2) and Covid-19 (BD: Jun 21, 2021).
Today, Starpharma said Lloyds Pharmacies was "one of the largest pharmacy chains in the UK" with about 1,400 shops and that through its affiliated wholesale arm, AAH, it also supplied more than 14,000 independent UK pharmacies.
Starpharma chief executive officer Dr Jackie Fairley said the company was "delighted to re-launch Starpharma's innovative nasal spray, Viraleze, in the UK through Lloyds Pharmacy's extensive online and retail network".
"Viraleze will be particularly useful in the winter cold and 'flu season given its broad-spectrum of activity against multiple cold and respiratory viruses," Dr Fairley said.
Starpharma was up seven cents or 10.45 percent to 74 cents.

GENETIC TECHNOLOGIES

Genetic Technologies says it has sold its Genetype risk assessment test at 16 medical practices in on the "East Coast of Australia".
Genetic Technologies said the clinics would be able to use the tests for either a single disease or multiple diseases, including breast cancer, colorectal cancer, ovarian cancer, coronary artery disease, prostate cancer and type 2 diabetes.
A spokesperson for Genetic Technologies said the clinics were located "primarily in Melbourne".
The company did not disclose the price or accuracy of the tests.
Genetic Technologies was unchanged at 0.3 cents with 5.2 million shares traded.

NEUROSCIENTIFIC BIOPHARMACEUTICALS

Neuroscientific says that recruiting the first of 30 healthy volunteers for its early-phase trial of Emtinb is a “significant milestone”.
Neuroscientific said the study would assess biomarkers in blood samples for proof of mechanism of activity of Emtinb and the findings would be used to guide efficacy outcomes for trials in patients.
The company said it was exploring Emtinb as a candidate for treatment of neuro-degenerative conditions, such as multiple sclerosis and Alzheimer’s disease.
Neuroscientific managing-director Matt Liddelow said that the recruitment of the first subject “marks another historic achievement for the company and a major milestone in developing Emtinb as a much-needed therapeutic treatment with disease modifying potential for patients with multiple sclerosis and Alzheimer’s disease”.
Neuroscientific was up half a cent or 2.9 percent to 18 cents.

RACE ONCOLOGY

Race says interim data from its cardio-protection program shows that Zantrene protects against chemotherapy-induced heart damage, in mice.
Race said Zantrene, or bisantrene, protected the hearts of mice from the damaging effects of the chemotherapeutic anthracycline, specifically doxorubicin, even protecting against general toxicity or bone marrow suppression “at higher levels of chemotherapy treatment”.
The company said the results were supportive of clinical trials using Zantrene with anthracyclines to “improve cancer patient treatment and quality-of-life”.
Race chief scientific officer Dr Daniel Tillett said that extending the initial cardio-protection study from cells to hearts was “a major step forward”.
“Zantrene is not only able to protect human heart muscle cells from anthracycline induced death, but that this also applies to hearts in animals,” Dr Tillett said.
“When combined with the historical clinical data around Zantrene heart safety, we believe Zantrene may offer millions of patients a unique combination of cardio-protection with enhanced anti-cancer efficacy,” Dr Tillet said.
“Such opportunities are rare in oncology,” Dr Tillett said.
Race was up nine cents or 4.8 percent to $1.95.

PARADIGM BIOPHARMACEUTICALS

Paradigm says IP (intellectual property) Australia has accepted its patent application, for its pentosan polysulfate sodium, or Zilosul.
Paradigm said the patent, titled ‘Treatment of bone marrow pathologies with polysulfated polysaccharides’, would protect its intellectual property until August 6, 2038.
In March, the company said a final rejection for the same patent from the US Patents and Trademarks Office was ‘not final’ as stated in a research note from stockbrokers Morgans (BD: Mar 9, 2022).
Today, Paradigm said “the prosecution of this patent continues with Paradigm expected to file its response to the US Patent and Trademark Office by the end of July 2022.”
The company said that the first claim of the Australian accepted patent referred to “a method of improving knee function where the subject has a bone marrow lesion and osteoarthritis in a knee by administering pentosan polysulfate sodium”.
Paradigm was up nine cents or 10.3 percent to 96.5 cents with 1.5 million shares traded.

CANN GROUP

Cann Group says the Australian Therapeutic Goods Administration has granted its Mildura Marijuana factory a good manufacturing practice (GMP) licence.
Cann said the licence would allow it to produce active pharmaceutical ingredients, manufacture Satipharm capsules and perform in-house chemical, physical and microbiological tests to show that products met regulatory requirements, and distribute its products through the TGA's approved access pathways.
Cann chief executive officer Peter Crock said that "GMP licencing is the regulatory capstone of the Mildura facility, allowing us to cultivate, extract, manufacture, test, and supply finished products entirely in-house".
"With the licence in place, we can now add additional GMP capabilities in response to market demands," Mr Crock said.
Cann Group rose 4.5 cents or 19.6 percent to 27.5 cents with 2.95 million shares traded.

CRESO PHARMA

Creso says it has a non-binding, non-exclusive deal with Taiwan's China Chemical & Pharmaceutical Co to launch animal healthcare products in Taiwan.
Creso said it would work with China Chemical would work towards a binding agreement by August 31, 2022, under which China Chemical to introduce products made by its target acquisition company Sierra Sage Herbs LLC to the Taiwanese market.
Creso fell 0.1 cents or 2.8 percent to 3.5 cents with 9.9 million shares traded.

MEDIBIO

FIL says it has increased and been diluted in Medibio, from 215,314,445 shares (9.56%) to 215,993,951 shares (7.84%).
Last week, Medibio said it had commitments to raise $1.4 million in a placement at 0.15 cents a share (BD: Jun 22, 2022).
Today, the Hong Kong-based FIL, also known as Fidelity Investment Limited, said that on March 9 and 14, 2022, it bought 679,506 shares in Medibio, for 0.5 cents a share.
Medibio was unchanged at 0.15 cents with 27.3 million shares traded.

VISIONEERING TECHNOLOGIES

Visioneering says it has appointed Dr Allan Rubenstein as an independent non-executive director to replace Zita Peach, from June 29, 2022.
Visioneering said Dr Rubenstein was had been a director of The Cooper Companies for 29 years "one of the largest contact lens companies in the world" and was a director of Plex Pharmaceuticals and Coloursmith Labs, and founded Nexgenix Pharmaceuticals.
The company said Dr Rubenstein held a Bachelor of Arts from New York's Cornell University and a Doctor of Medicine from Boston's the Tufts University School of Medicine.
Visioneering was unchanged at 26.5 cents.