Biotech Daily

Friday May 27, 2022

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: COMPUMEDICS UP 12%**
- MEDICAL DEVELOPMENTS DOWN 7%

*** DR BOREHAM'S CRUCIBLE: OPTHEA**

*** COMPUMEDICS FORECASTS SALES ORDERS UP 19% TO $42m**

*** RACE READY FOR PHASE II ZANTRENE FOR AML TRIAL**

*** IMMUTEP: IMP321 SHOWS 'FAVOURABLE ANTI-TUMOR ACTIVITY'**

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*** NOXOPHARM: 'IDRONOXIL, CISPLATIN INCREASE RESPONSE, IN-VITRO'**

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*** NEXT SCIENCE TO LOSE CEO JUDITH MITCHELL IN 2023**

*** PHARMAUST TO LOSE CSO DR RICHARD MOLLARD**

MARKET REPORT

The Australian stock market was up 1.08 percent on Friday May 27, 2022, with the ASX200 up 76.8 points to 7,182.7 points. Twenty of the Biotech Daily Top 40 stocks were up, 14 fell and six traded unchanged.

Compumedics was the best, up two cents or 11.8 percent to 19 cents, with 66,500 shares traded. Actinogen climbed 7.1 percent; Dimerix was up 6.9 percent; Amplia, Antisense, Neuren and Universal Biosensors were up more than four percent; Alcidion and Polynovo improved more than three percent; Genetic Signatures, Mesoblast, Resmed, Resonance and Telix rose two percent or more; Emvision, Immutep and Opthea were up more than one percent; with Avita, Cochlear, Nanosonics, Pro Medicus and Volpara up by less than one percent.

Medical Developments led the falls, down 19 cents or seven percent to $2.53, with 88,919 shares traded. Prescient lost 5.7 percent; Cyclopharm, Kazia and Nova Eye fell more than four percent; Next Science was down 3.55 percent; Paradigm and Starpharma shed more than two percent; Cynata, Orthocell, Pharmaxis and Uscom fell more than one percent; with Clinuvel, CSL and Proteomics down by less than one percent.

DR BOREHAM'S CRUCIBLE: OPTHEA

By TIM BOREHAM

ASX code: OPT

Nasdaq code: OPT (American depositary shares, each equal to eight Australian shares)

Share price: $1.335; **Shares on issue:** 351,939,280; **Market cap:** $469.8 million

Chief executive officer: Dr Megan Baldwin

Board: Dr Jeremy Levin (chairman), Dr Baldwin, Michael Sistenich, Lawrence Gozlan, Dan Spiegelman, Dr Julia Haller, Dr Susan Orr, Quinton Oswald

Financials (half year to December 31, 2021): revenue $91,218 (down 54%), loss of $37.7m (previous deficit $28.2m), cash $88.2m (down 43%)

Identifiable major shareholders: Regal Funds Management 12.58%, Baker Brothers Life Sciences 8.2%, Jagen Pty Ltd (Liberman family office) 3.3%

The back-of-the-eye disease house is zigging rather than zagging, with its shares lifting more than 30 percent over the last month while the rest of the biotech sector has sagged like a failed sponge.

Do investors have special visionary powers? There's no apparent reason behind the share surge, with first results from the company's phase III registration trial not due to mid-2024.

One likely reason is that Opthea chief Dr Megan Baldwin has been making up for lost Covid lockdown time and has been hitting the (virtual) conference circuit hard.

This month, it was Citi's and HC Wainwright global life science shindig, as well as Retina World Congress in Florida. In March, Dr Baldwin fronted Oppenheimer's virtual conference and coming up is the Bascom Palmer Eye Institute's Angiogenesis, Exudation and Degeneration 2022 "gath" (which is what the young ones call events these days).

Dr Baldwin notes there's an element of catch-up, in that the shares were hit hard 12 months ago.

"We were trading at a ridiculous valuation for the stage we are at," she says. "So, it's all about letting the market in both the US and Australia know we are in the final stages and getting the word out there."

The final stanza consists of two phase III pivotal trials to assess - or confirm - the efficacy of Opthea's treatment for wet age-related macular degeneration (wet ADM), the biggest cause of blindness for over 60s.

"We are one of the few biotech companies in Australia taking on a phase III asset development," Dr Baldwin says.

Opthea's vision statement

Wet AMD is marked by loss of vision caused by degeneration of the central portion of the retina (the macula).

Blood vessels grow abnormally under the retina, resulting in leakage of fluid and protein from the vessel. The condition can set in quickly, with patients losing their vision in as little as 10 weeks.

A so-called 'trap inhibitor', OPT-302 is a fusion protein that blocks the activity of two proteins, vascular endothelial growth factors C and D (VEGF-C and VEGF-D).

Opthea is developing OPT-302 as a wet AMD combination therapy with the existing drugs Lucentis (ranibizumab) and Eylea (aflibercept), which only block VEGF-A.

About half the market is treated off-label with Avastin, an old cancer drug.

"The existing therapies are no good for 45 percent of patients, because the disease process is more complex than just blocking VEGF-A," Dr Baldwin says. "We are basically targeting a mechanism of resistance to the current standard-of-care treatments, which are blockbuster agents in themselves."

The company is also interested in diabetic macular oedema (DME), but this program has been "paused" after disappointing clinical results (see below).

Getting in the rhythm

Opthea is the renamed iteration of Circadian Technologies - the first ASX-listed biotechnology company.

Founded by biotech doyen Leon Serry, Circadian was "an incubator" for companies including the Victoria state-founded Amrad, (later renamed Zenyth and sold to CSL). Other companies in its portfolio were Metabolic (which became Calzada before morphing into Polynovo), Antisense and Optiscan.

Circadian dabbled in a number of applications including melatonin for jet-lag (hence the name), drugs for Alzheimer's disease and cancer diagnostics before focusing on eye ailments.

Circadian acquired the VEGF portfolio in 2008 and the company changed its name to Opthea in December 2015. Dr Baldwin was anointed CEO in February 2014, having been at Circadian since 2008 in roles including overseeing the OPT-302 program.

In October 2020, the company launched a US offering of American depositary shares, now listed on the Nasdaq Select Global Market.

The company aimed for $US160 million but ended up raising $US128 million - which is still nothing to sneeze at ...

Clinical trial triumphs and tribulations

In August 2019, Opthea shares jumped as much as 160 percent after the company released the results of its keenly-awaited phase IIb trial for wet AMD.

The trial enrolled 366 previously untreated patients across 110 sites, testing a combination of Opthea's OPT-302 with the standard of care therapy, ranibizumab (Lucentis). The results showed this combined treatment produced "statistically significant and clinically meaningful" results, with a mean "visual acuity gain" after 24 months.

But the biotech gods are fickle: in June 2020 Opthea shares were birched after the company revealed underwhelming phase IIa data from its 144-patient diabetic macular oedema (DME) trial. Affecting a younger, working age demographic, DME is a blindness-inducing condition that also involves retinal leakage.

Dr Baldwin says the results were unflattering because the patients had been treated with the standard-of-care and were not treatment naïve. This made the visual acuity hurdle harder to surmount.

"It was a noisy data set," she says. "But when we teased out the patients that had a very consistent anti-VGEF-A treatment with Eylea, we saw the clinical benefit."

What's next?

Naturally, the market's attention is now focused on the phase III wet AMD trial, which is open in 25 countries across 200 sites. The company has been recruiting for a year, with patient uptake gaining pace post pandemic.

The two studies, Shore and Coast, are in combination with ranibizumab and aflibercept, respectively. This is to obtain broader approval for use with any type of VEGF inhibitor. Each trial aims to enrol 990 patients and are sham controlled, triple masked, randomized and all the other things one would expect from a properly constructed clinical program.

While the target patient population is similar, Opthea is boosting its odds of success by not recruiting a non-responsive subset of patients with a lesion called RAP. RAPpers accounted for about 10 percent of phase IIb patients.

The analysis will also be "enriched" by first assessing the 80 percent patients that fared best in the previous trial. Eventually, though, the whole patient population will be analyzed.

"We are very comfortable with how we have designed it and how we plan to analyze it," Dr Baldwin says.

Pretty Chronic for Vision

While Opthea is not into RAP, it's quite happy to enrol patients with a wet AMD variant called polypoidal choroidal vasculopathy (PCV), by which fluid leaks and bleeds from abnormal blood vessels.

“It means vessels that are … in the back of the eye grow as polyps,” Dr Baldwin says. It is especially prevalent in Asian populations and is said to be the most common form of Wet AMD, globally.

In the phase IIb trial,18 percent of the 366 treatment-naïve patients had PCV.

After six months, the standard-of-care cohort had a seven-letter improvement on the eye chart, but those treated with OPT-302 had twice the improvement (a further 6.7 letters).

Dr Baldwin says the phase III effort should include a similar proportion of PCV patients, or perhaps more, given that more Asian centres are participating. She says the company possibly could launch a supplemental PCV-specific study, probably in collaboration with Asian experts.

Finances and performance

In the current climate for biotechs, cash is king, so it’s heartening that at the end of March Opthea had $88 million crisp ones in the bank.

The not-so-good news is that the company chewed through $37.7 million in the December 2021 half, with $31.8 million devoted to research and development.

“Retinal studies are not cheap,” Dr Baldwin says. “We have no need to raise capital but we will keep monitoring as we move along.”

In February, the company entered an at-the-market equity program, by which the company can sell up to $US75 million of its ordinary shares in the form of its American depositary shares.

The opportunistic arrangement means Opthea can sell shares in dribs and drabs at prices offered by participating buyers - but it doesn’t have to. The amounts raised are likely to be much less than $US75 million.

Over the last 12 months, Opthea shares have traded as low as 81 cents (March 3 this year) and as high as $1.67 (June 17 last year). Historically, they peaked at $3.45 in September 2019 and troughed to 20 cents in June 2015.

Biosimilar but different

Some investors have been concerned about the emergence of biosimilars, which are cheaper copies of existing therapies.

“There’s confusion in the market but we do not compete with biosimilars, they help our price point,” Dr Baldwin says.

“Biosimilars reduce the overall pricing pressure for insurers, which helps us. A cheaper version of [existing] therapies means we have a better opportunity of pricing our therapy at a higher value as we can, which is important for a novel and differentiated product.”

Opthea is even open to the possibility of acquiring a biosimilar company and co-formulating OPT-302 in the same vial.

That way, the standard of care and OPT-302 can be delivered in the one injection.

A Kodiak moment worth forgetting

In February the Nasdaq-listed Kodiak Lifesciences announced that its phase IIb/III trial of its own AMD combination drug candidate, KSI-301, had failed to prove the key intended benefit of requiring less frequent injections into the eye.

As broker Wilsons comments, Kodiak was aiming for a long duration dosing schedule, by which patients would need to be injected only every three to five months.

Inaptly titled Dazzle, the trial was “unable to show non-inferiority to 8-weekly aflibercept (Eylea)” on the eye chart.

In effect, patients needed more doses than expected and Kodiak shares plunged 80 percent on the news.

The results suggest that a new wet AMD treatment needs to show efficacy rather than durability alone.

Dr Boreham’s diagnosis:

Love ‘em to bits and all that, but local investors are known for being a tad impatient.

While the 2024 clinical results timeline seems many a sleeps away, it’s not that long in drug development terms.

Broker Wilsons cites a $US1.5 billion “peak sales opportunity” for the use of OPT-302 as a combination wet AMD treatment.

The company notes that Lucentis and Eylea have revenues in excess of $US12 billion a year and that’s growing over time with the ageing populace.

“Opthea is the only company with a clinical program that has shown efficacy over and above the existing blockbuster agents,” Dr Baldwin says.

“We are on the verge of blockbuster potential, but it takes time to get there. Our strategy is to keep our eye on the prize of an approvable blockbuster therapy that will improve people’s lives.”

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. But he likes to think of himself as a man of vision – if he can find his damn glasses that is.

COMPUMEDICS

Compumedics says revenue for the year to June 30, 2022 is forecast to remain about $35 million, with sales orders up “at least” 19 percent to $42 million.
Compumedics said the difference between revenue and sales was due to “global supply issues, chip shortages/delays and other pandemic related factors” that not all new sales orders received over the year to June 30, 2022 could be shipped and booked as revenue.
The company said it was working to resolve supply issues to return to “more normal shipping timelines” over the next year.
Compumedics was up two cents or 11.8 percent to 19 cents.

RACE ONCOLOGY

Race says it will begin the 17-patient, phase II part of its phase Ib/II trial of Zantrene in combination with fludarabine and clofarabine for acute myeloid leukaemia.
Race said it completed the six-patient, phase Ib dose-escalation part, in “heavily pre-treated” acute myeloid leukaemia patients, and the phase II efficacy stage would use a 4-day schedule of the same Zantrene combination therapy.
The company said the first stage met its endpoint of establishing a recommended dose by identifying the treatment dose level that achieved two or fewer dose-limiting toxicities among the six consecutively treated patients.
Race said efficacy results were “very encouraging”, with one patient showing a complete response based on morphology, two patients having a partial response, two showing no response, and one patient not assessable due to death from infection.
The company said the three patients who showed a response were bridged to an allogeneic stem cell transplant, which it said was “an important positive outcome in [acute myeloid leukaemia] treatment as it offers the patient the potential of long-term remission”.
Race chief medical officer Dr David Fuller said the positive results “in such a heavily pre-treated relapsed or refractory acute myeloid leukaemia population is encouraging, especially with three of the patients being subsequently bridged to transplant”.
Race was up half a cent or 0.3 percent to $1.74.

IMMUTEP

Immutep says data from its Tacti-002 phase II trial of IMP321 with pembrolizumab shows “favorable anti-tumor activity in first line non-small cell lung cancer”.
Last year, Immutep said it had dosed the last of 185 patients in the part A expansion of its phase II Tacti-002 combination study of IMP321, or eftilagimod alpha, with pembrolizumab (Keytruda) for cancers (BD: Nov 19, 2021).
Today, the company said an abstract, titled ‘A Phase II study (TACTI-002) in 1st line metastatic non-small cell lung carcinoma investigating eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab: updated results from a PD-L1 unselected population’ would appear at the American Society of Clinical Oncology’s meeting in Chicago on June 3, 2022, was available at: https://bit.ly/3a19SHl and it would present updated data from all 114 patients in an oral presentation on the same day.
The company said data from Tacti-002, for which the cut-off was January 2022, showed an improved overall response rate in 28 of 75 patients (37.3%), compared to 36.1 percent in its corresponding abstract at the Society’s 2021 meeting, with an improved disease control rate in 55 of 75 patients (73.3%) compared to 66.7 percent last year.
Immutep said the IMP321 and pembrolizumab combination was safe and well tolerated.
Immutep was up half a cent or 1.3 percent to 39.5 cents.

INOVIQ

Inoviq says with the University of Sydney it has presented data supporting its Exo-Net technology as a potential cancer cell type classification method.
Inoviq said the study was titled: 'Differential detection of cancer-derived extracellular vesicles using combined antibody functionalized magnetic beads and infrared spectroscopy', was presented at the International Society for Extracellular Vesicles in Lyon, France, May 25 to 29, 2022.
The company said the presentation concluded that its Exo-Net was "a simple and rapid method for preparing enriched subpopulations of [exosomes] … for spectroscopic analysis.
The poster concluded that extracted exosome samples could be used to determine the relative changes in exosome biomolecular contents from different cancer cell types.
The poster concluded that "distinct clustering of spectra by sample type occurred, indicating that the different sub-populations of cell-derived exosomes could be differentiated using this vibrational spectroscopic method".
Inoviq said the study supported its hypothesis that vibrational spectroscopy could differentiate not only cancer cell type, but phenotype, both of which it said were key determinants to accuracy of disease classification and triage for treatment.
Inoviq fell half a cent or 0.9 percent to 53 cents.

NOXOPHARM

Noxopharm says that idronoxil, the active ingredient in its Veyonda, with cisplatin, encouraged immune-modulation of tumors when compared to control, in-vitro.
Noxopharm said the combination of idronoxil and cisplatin for cell lines of nasopharyngeal tumors was carried out at the University of Hong Kong, and had been accepted for the American Society of Clinical Oncology's meeting in Chicago, June 3 to June 7, 2022.
The company said the combination therapy changed the tumor environment, allowing the infiltration of 67 percent more immune cells into the tumor than observed in the control.
Noxopharm said the combination treatment was found to be more effective against nasopharyngeal carcinoma cells than cisplatin alone.
Noxopharm was up one cent or 4.35 percent to 24 cents.

MICROBA LIFE SCIENCES

Microba says it has appointed Brisbane's Beyond Drug Development as the contract research organization for its phase I trial of MAP315, for ulcerative colitis.
Microba said ulcerative colitis was the most prevalent form of inflammatory bowel disease.
The company said that Melbourne's Nucleus Network was the preferred clinical trial site, with the Basel, Switzerland-based Bacthera to provide clinical doses of MAP315 for the randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability and pharmacokinetics of MAP315 in healthy adults, expected to begin in late 2022.
Microba was up 1.5 cents or 6.1 percent to 26 cents.

LIVING CELL TECHNOLOGIES

Living Cell has requested a trading halt pending an announcement "in connection with an equity raising to be undertaken by way of an institutional placement".
Trading will resume on May 31, 2022, or on an earlier announcement.
Living Cell last traded at 0.5 cents.

COCHLEAR

Cochlear says it has appointed Karen Penrose as a non-executive director, effective from July 1, 2022.
Cochlear said Ms Penrose was currently a director of Ramsay Health Care, Estia Health, Bank of Queensland and Vicinity Centres.
The company Ms Penrose holds a Bachelor of Commerce from the University of New South Wales.
Cochlear was up seven cents or 0.03 percent to $218.50, with 79,435 shares traded.

NEXT SCIENCE

Next Science says managing-director and chief executive officer Judith Mitchell will retire by June 30, 2023, with her replacement to be US-based.
Next Science said that Ms Mitchell had advised the company that for personal reasons, she would not be able to make the long-term commitment to reside in the US and that the company would benefit from a chief executive officer based at its Jacksonville, Florida office.
The company said Ms Mitchell was committed to supporting an orderly transition to a new chief executive officer and would continue as US-based chief executive officer, until a successful transition has been achieved.
Next Science fell three cents or 3.55 percent to 81.5 cents.

PHARMAUST

Pharmaust says chief scientific officer Dr Richard Mollard will resign, following the completion of six months' notice required by his contract.
Pharmaust said Dr Mollard was the chief executive officer of its subsidiary Pitney Pharmaceuticals and had been with the company for five years.
Pharmaust executive chair Dr Roger Aston said the company thanked Dr Mollard "for his efforts for us and wish him well in his future endeavors".
Pharmaust was unchanged at nine cents.