Biotech Daily

Friday October 6, 2023

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market was up 0.41 percent on Friday October 6, 2023, with the ASX200 up 28.7 points to 6,954.2 points. Seventeen of the Biotech Daily Top 40 stocks were up, 18 fell, two traded unchanged and three were untraded.

Patrys was the best, up 0.2 cents or 28.6 percent to 0.9 cents, with 13.3 million shares traded. Dimerix climbed 19.35 percent; Actinogen was up 9.5 percent; Amplia and Cynata were up more than eight percent; Next Science rose 7.9 percent; Alcidion and Micro-X were up four percent or more; Prescient and SDI climbed more than three percent; Nanosonics rose two percent; 4D, Antisense, Clinuvel, Telix and Universal Biosensors were up one percent or more; with CSL and Polynovo up by less than one percent.

Nova Eye led the falls, down three cents or 12.5 percent to 21 cents, with 293,981 shares traded. Cyclopharm lost 8.8 percent; Impedimed and Starpharma were down more than six percent; Immutep and Orthocell shed more than five percent; Atomo and Imugene fell more than four percent; Emvision, Neuren and Proteomics were down more than three percent; Genetic Signatures and Mesoblast shed more than two percent; Medical Developments, Resmed and Resonance were down more than one percent; with Avita, Pro Medicus and Volpara down by less than one percent.

DR BOREHAM'S CRUCIBLE: CYCLOPHARM

By TIM BOREHAM

ASX code: CYC

Share price: $2.50; **Shares on issue:** 93,896,326; **Market cap:** $234.7 million

Chief executive officer: James McBrayer

Board: David Heaney (chair), Mr McBrayer, Kevin Barrow, Dianne Argus, Professor Gregory King

Financials (half year to June 30, 2023): revenue $16.5 million (up 44%), sales revenue $15.7 million (up 37%), net loss of $2.89 million ($2.56 million deficit previously), interim dividend per share 0.5c (steady), cash balance $18 million (down 11%)

Identifiable major shareholders: Anglo Australian Christian and Charitable Fund 14.2%, Barings Acceptance 12.3%, Chemical Overseas Ltd 8.6%, CVC Ltd 7.1%, Mr McBrayer 5.5%

Many Aussie biotechs have endured a long wait for the US Food and Drug Administration (FDA) to approve - or reject - their drugs and devices, but Cyclopharm's three-decade quest for the agency's imprimatur surely must set the record.

At 12.39 am last Saturday, Sydney time, CEO James McBrayer's mobile phone chirped with the news that the agency had approved his company's tool for three-dimensional imaging of pulmonary embolisms and other lung diseases, called Technegas.

This was consistent with the Friday deadline (Washington time) under the FDA's protocol, which allows the gatekeeper 180 days to accept or reject an application.

In response to an earlier entreaty, the FDA issued a 'complete response letter' in June 2021. This required Cyclopharm to satisfy the agency on aspects of manufacturing the product, which the company duly fulfilled.

"I was half awake, half asleep, which has been the case for several weeks," Mr McBrayer says of the magic moment.

"When they [the FDA] asks you a question they don't give you too much time to respond, so I was like a fire engine ready to go at any time of the day or night."

Cyclopharm's attempts at gaining approval in the world's biggest nuclear medicine market dates to 1991. But this time around, a further rejection would have been quite a shock given the FDA was emitting more warm signals than a bucket of plutonium.

"We knew that we went above and beyond what they were looking for, just to be sure that we didn't leave anything to chance," Mr McBrayer says.

Cyclopharm's case is strengthened by the fact that Technegas is approved and used in 64 countries - including Canada where it has been deployed for two decades.

FDA consent would open a market for pulmonary embolism diagnosis worth $US180 a year, while its tool can also be used for other lung ailments (see below).

Cooking with Technegas

Cyclopharm's patented Technegas currently is used to detect pulmonary embolisms - lung clots - and has been used on 4.5 million patients.

The FDA approval is for "visualisation of pulmonary ventilation", which covers common conditions including chronic obstructive pulmonary diseases (COPD), asthma and - if anyone still cares - Covid. The assent also covers kids six years or older, without the requirement to do more trials.

As with elsewhere, Cyclopharm's remit is to encroach into the imaging market dominated by computer tomography (CT), as well as older two-dimensional nuclear techniques.

Manufactured at the bedside, Technegas consists of teeny-tiny, dry-carbon nanoparticles irradiated with the isotope Technetium-99 (produced from decaying molybdenum-99). The particles are 150 nanometres and to put that in context a sheet of paper is about 100,000 nanometres thick.

The gas-like substance is freshly brewed by heating a carbon crucible to 2,700 degrees Celsius and inhaled by the patient via tubing. Only three to four breaths are required.

The gas works as an imaging agent, allowing three-dimensional viewing with a gamma or single photon emission CT camera. The nanoparticles have a six-hour radioactive life, after which they are eventually dispersed through breathing.

Sounds like our cup of tea

Technegas was invented in the 1980s by Australian University biomedical engineer Prof Bill Burch. Over a cup of tea, he partnered with industrialist Ian Tetley to form Tetley Medical.

Technegas was commercialized after being approved in Europe in 1988. Cyclopharm was incorporated in 2005 and listed in January 2007, after raising $11 million at 30 cents apiece.

Technegas was approved in Australia in 1986 - when Bob Hawke still presided over the land - and in Europe since the early 1990s.

A pharmacist, Mr McBrayer joined in June 2008, taking over from John Sharman who went on to head up Medical Developments and then Universal Biosensors. Mr McBrayer headed the nuclear medicine mob Syncor Australia, as well as Lipa Pharmaceuticals.

Sizing up the US market

The company hopes to emulate the experience of Technegas in Canada, where it has snared close to 100 percent of the nuclear medical ventilation market.

The company estimates the US pulmonary embolism market at $US180 million per annum, with four million procedures a year.

Currently, about 85 percent of patients are imaged with computed tomography pulmonary angiography, or CTPA, with nuclear imaging confined to patients unsuited for this imaging (they may be pregnant, have poor renal function or are allergic to the imaging agents).

Initially, the company will target this 15 percent of the market, which accounts for 600,000 procedures annually and is valued at $US90 million.

Based on Cyclopharm's experience in the Canadian market and globally, the company reiterates expectations it can achieve a 50 percent share over the next two to three years, rising to more than an 80 percent over a three-to-five-year period.

If the company can then help to double the share of nuclear imaging to 30 percent, the addressable market rises to $US180 million

Anticipating approval, the company has been assembling 200 Technegas generators at its facility at Kingsgrove in inner Sydney. Initially, the company expects to have rolled out 20 generators at high-volume sites by the end of 2023, expanding to 300 by the end of 2024.

These units give rise to ongoing revenue from consumables such as the carbon billets, single-use tubing and the crucibles which disintegrate in the mini nuclear reactor as part of the process.

Crucially, Technegas is subject to an existing reimbursement code for pulmonary embolism imaging procedures, which is 'agnostic' in terms of the diagnosis method used.

Broker Bell Potter assumes revenue of $US140 per exam across 480,000 procedures, equating to initial total revenue $US103 million.

What's wrong with current methods?

If the current diagnosis methods were OK, Technegas would not stand a chance. But they're not.

Currently, the nuclear medicine diagnosis is by way of an isotope called Xenon-133, which requires a negatively-pressured room and a method to trap gases expelled by the patient.

Then there's another Technetium-99 based liquid aerosol agent called DPTA, which is indicated for renal (kidney) imaging but has been deployed off-label for pulmonary embolisms.

To date, computed tomography pulmonary angiography (CTPA) has been more effective than the nuclear imaging options. But Cyclopharm claims Technegas surpasses all of them in terms of avoiding both false positives and false negatives.

Given that, Technegas in theory should snare a market share of way more than 30 percent.

“But I will be beaten-up if I get too greedy,” Mr McBrayer says. “We will never completely displace CT because it is fast and it is available around the clock, whereas nuclear medicine departments typically aren’t open 24-7.”

Drug or device – or both?

A quirky aspect of the approval was that it was approved as a drug and a device combination. which Mr McBrayer dubs as “very novel”.

Called a Technegas “system” in FDA-speak, the generator is regulated as a drug.

Mr McBrayer said the most difficult issue for the FDA is that Technegas is manufactured and delivered at the point-of-care, that is, the bedside.

Without the usual batch quality control exerted over a factory-made product, the FDA wanted to ensure the consistent reproducibility of key components.

After two visits to the Kingsgrove facility, the FDA inspectors were satisfied about the quality of manufacturing.

Financials and performance

Cyclopharm posted sales revenue of $15.7 million for the half-year to June 2023, 37 percent higher, with a net loss of $2.89 million.

The revenue uptick was attributed to strong sales of consumables, especially in Europe. Sales of patient administration set - the equivalent of the KFC family combo bucket with all the requisite consumables - rose seven percent to $5.61 million.

Generator sales fell 15 percent to $1.4 million because of half-to-half revenue lumpiness, but remain well above pre-Covid levels.

Cyclopharm also does a nice line in third party sales of other products, which contributed almost half the revenue ($7.3 million, up 120 percent).

Relatively speaking, the potential Technegas sales of $US180 million highlight the significant of the US approval.

Cyclopharm is an oddity among biotechs in that it pays a modest dividend of one cent a year, but retains cash of $18 million.

Given the company no longer has the costs of seeking US approval, presumably the cash will swell and a capital raising will not be needed.

The company spent $440,000 on legal costs during the half, but the expenditure was worthwhile because the company won $440,000 in a settlement pertaining to a long-running patent spat.

Cyclopharm shares edged up a modest 1.4 percent after the FDA assent, to a 12-month high of $2.87. Given the approval was widely expected, the market already had accounted for the upside.

Cyclopharm shares traded at a 12-month low of $1.17 in late December 2022. They traded at a record $3 in late 2021 and trawled an all-time low of 14 cents in February 2013.

Dr Boreham's diagnosis:

As with the FDA's approval of Neuren Pharmaceutical's drug for Rett syndrome, the Cyclopharm story is one of endurance amid a wall of obstacles.

Over time, Cyclopharm made mistakes including assuming the FDA would accept 'real world' evidence, rather than requiring a formal clinical trial.

The drug-versus-device aspect also muddied things, while the company chose some less-than-desirable contract research partners.

A keen saxophonist, Mr McBrayer in 2021 promised we would hear some "sweet notes" from the FDA - rivalling the sax solos in Gerry Rafferty's Baker Street or George Michael's Careless Whisper.

Beyond pulmonary embolisms, broader markets beckon and the company has an active clinical program to capture the opportunities.

For instance, the chronic obstructive pulmonary disease (COPD) diagnosis market is estimated to be to be 30 times bigger than the pulmonary embolism market.

Valuing Cyclopharm at $4.25 - 50 percent above current levels - Bell Potter projects a $500,000 underlying loss on revenue of $59 million in calendar 2024.

The company should really hit the right note in calendar 2025, with the broker predicting $14.5 million profit on turnover of $59 million.

With the discordant delays now a thing of the past, patient investors can now relax to the harmonious flutter of US revenues and a gently ascending share price.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He's also like a fire engine, ready to go – but only before midnight.

ANATARA

Anatara says stage one of its 61-patient, phase I/II trial of gastrointestinal reprogramming, or Garp, reduced irritable bowel syndrome (IBS) by 56 percent and met safety objectives.

In August. Anatara said it had dosed all 70 patients in the first stage of its phase I/II trial of Garp, and that the treatment was a “multi-component, coated complementary medicine” that included its pineapple stem-based bromelain (BD: Aug 31, 2023).

Today, the company said after eight weeks of treatment, the study showed the 20 placebo patients had a 36 percent reduction compared to their baseline irritable bowel syndrome severity score compared to 56 percent for low dose patients and 50 percent for the 21 high dose patients.

Anatara said the low dose had been selected for stage two of the trial.

The company said that a 50 percent reduction in irritable bowel syndrome (IBS) scores translated to “a significant positive change in day-to-day life, a benefit that cannot be understated”.

Anatara said it was “not surprised or concerned about the high placebo response as the medical literature shows that IBS clinical trials typically have a high placebo response on average of about 40 percent, very much in line with today’s results”.

The company said the primary endpoints for the trial included change in irritable bowel severity, treatment-related adverse events, with the secondary endpoints relief compared to baseline, improved anxiety and depression compared to baseline, change in irritable bowel syndrome quality of life and safety markers.

Anatara said exploratory endpoints included plasma levels of inflammatory markers, use of “rescue” medication in the study group and alterations in gut microbiota with respect to diversity and balance.

Anatara said it would expand to stage two of the trial, with a possible 50 patients, and a preliminary indication of meaningful efficacy.

The company said the data analysis suggested that stage two may require as few as 50 participants on the optimum low dose of product versus the placebo group to achieve the desired primary endpoint of at least a 20 percent improvement, or reduction, in irritable bowel syndrome severity scores, and noted that this 20 percent reduction had already been achieved in stage one.

Anatara said “as is the case with statistical analysis, increasing the population … is expected to provide statistically significant p-values”.

Anatara executive chair Dr David Brookes said the results were “a very pleasing and not unexpected outcome from the stage one interim analysis given the trial design”.

“To confirm safety and the optimum dose with a meaningful indication of efficacy was the intention of stage one of the trial,” Dr Brookes said. “The company is buoyed by this milestone and looks forward to advancing the Garp project.”

“More broadly our expectation is that this complementary medicine’s rejuvenating gastrointestinal tract effects will provide relief for sufferers of non-specific [gastrointestinal tract] symptoms and be an adjunctive therapy in other medical indications, such as inflammatory bowel disease,” Dr Brookes said.

Dr Brookes said he felt the company was “well placed to efficiently conduct stage two”.

“We are also looking forward to sharing the data and discussing the results with other corporates and already interested potential partners following the analysis of stage one of the IBS trial,” Dr Brookes said.

“The trial was more challenging than anticipated and highlighted the difficulties that sufferers of IBS deal with from day to day,” Dr Brookes said. “The company has learnt from these tribulations and I feel is now well placed to efficiently conduct stage two.”

Anatara was untraded at 3.3 cents.

NEUROTECH INTERNATIONAL

Neurotech says the-patient, phase I/II trial of its marijuana-based NTI164 showed “highly significant clinical improvements” in children with neuro-psychiatric disorders.

Neurotech said the trial of children with paediatric auto-immune neuro-psychiatric disorders associated with streptococcal infections (Pandas) and paediatric acute-onset neuro-psychiatric syndrome (Pans) met the primary endpoint of anxiety and depression, with a 30 percent improvement in overall symptoms from high severity at baseline to low severity from week 4 onward (p = 0.016).

The company said the primary endpoint was measured by a change in the revised patient’s anxiety and depression scale, with a mean score of 58.2 from a baseline of 83.7.

Neurotech said once treated with 20 milligrams per kilogram per day of NTI164 all sub-domains of revised child anxiety and depression scale “improved significantly” at 12 weeks.

The company said the improved subdomains included a 32 percent improvement for social phobia, 28 percent for panic disorder, 15 percent for major depression, 36 percent for separation anxiety, 42 percent for general anxiety and 47 percent for obsessive-compulsive behaviors.

Neurotech said the second primary endpoint was patient illness severity and the study showed 12 weeks of treatment led to an 18 percent mean clinical global impression-severity of illness improvement, from 5.0 at the start of the trial to 4.1 (p = 0.0005).

The company said that clinical global impression-severity of illness improvement was “strong” with five patients (33%) “much improved” and 10 children (67%) “minimally improved after four weeks; with eight children (53.3%) “much improved”, six (40%) “minimally improved” and one patient with no change after 12 weeks.

Neurotech said the trial’s secondary endpoints included improvements to a range of scale scores but the trial was “not statistically powered for any secondary endpoints”.

The company said although there were no serious adverse events in the trial, nine adverse events occurred in three patients, six of which “were possibly related to the medication” including four events of vomiting and two events of nausea, with the other three reactions from unrelated viral infections.

Neurotech said that none of the “adverse events were serious and were not considered to interfere with the patient’s functioning” with no additional treatment required, except for the viral infection requiring pain relief and saline mouth wash.

The company said all 15 patients would continue with treatment for 54 weeks under the extension phase of the trial.

University of Sydney and Children’s Hospital at Westmead co-principal investigator of the trial Prof Russell Dale said researchers were still waiting on “further evidence of genomic molecular changes from baseline measures and after 12 weeks of treatment to correlate this meaningful clinical response we have seen with biological evidence of effect”.

Neurotech executive director Dr Thomas Duthy said the company “commenced this clinical trial based on a small number of scientific publications that highlighted recurring, neuroinflammatory processes in these difficult to treat patients”.

“With our established evidence in autism and supportive pre-clinical data we took the decision to run this world-first trial of NTI164 with Prof Dale and Prof Fahey, which has shown very strong benefits for these children over 12 weeks of daily treatment,” Dr Duthy said.

“Given the lack of safe and effective treatments for Pandas/Pans with associated distressing symptoms and significant caregiver burden we remain very hopeful of an accelerated development plan for NTI164 to bring this therapy to market,” Dr Duthy said.

Neurotech fell half a cent or 7.5 percent to 6.2 cents with 10.9 million shares traded.

CSL, ASSOCIATION OF AUSTRALIAN MEDICAL RESEARCH INSTITUTES (AAMRI)

The Association of Australian Medical Research Institutes says it has selected six finalists for its inaugural $35,000 Rising Star Award.

In June, AAMRI said the award was for mid-career researchers, with eight-to-15 years of post-doctoral experience (BD: Jun 30, 2023).

Today, the Association said the finalists included Monash University's Prof Yen Ying Lim, the Peter Doherty Institute's Prof Laura Mackay, the University of Adelaide's Prof Jose Polo, the Sydney St Vincent Hospital's Prof Joseph Powell, Melbourne's Royal Children's Hospital's Prof Andrew Steer and Melbourne's Burnet Institute's Prof Joshua Vogel.

CSL chief scientific officer Dr Andrew Nash said the researchers were "driving advances in healthcare, from better understanding the basis of diseases to developing new therapies, which may ultimately lead to improved outcomes for patients."

AAMRI said the winner would receive $35,000 and be presented the award by Minister of Health and Aged Care Mark Butler at its annual dinner on October 18, 2023.

NANOSONICS

Nanosonics says its annual general meeting will vote to issue 44,054 service rights and 385,140 performance rights to chief executive officer Michael Kavanagh.

Nanosonics said in addition to Mr Kavanagh's $910,000 annual salary the service rights formed part his short-term incentive, with 50 percent already paid and the remaining 44,054 rights, worth $187,359, vesting if he remained with the company until August 31, 2024, and exercisable from August 31, 2025 until August 31, 2028.

The company said the 385,140 performance rights were part of Mr Kavanagh's long-term incentive pay, vesting on company performance hurdles.

Nanosonics said shareholders would vote to elect directors Dr Lisa McIntyre, Steven Sargent, Dr Tracey Batten and Dr Larry Marshall, and adopt its equity plan and remuneration report.

The meeting will be held on online and at Level 1, Building A, 7-11 Talavera Road, Macquarie Park, Sydney on November 3, 2023 at 11am (AEDT).

Nanosonics was up eight cents or two percent to $4.04 with 594,094 shares traded.

KAZIA THERAPEUTICS (FORMERLY NOVOGEN)

Kazia has requested a trading halt pending an announcement "regarding the proposed trading solely on Nasdaq and proposed delisting of the company's securities from ASX".

In 2017, the then Novogen, changed its name to Kazia Therapeutics and said that following a 10-for-one consolidation it would trade on the ASX under the code KZA, and on the Nasdaq under the code of KZIA (BD: Nov 20, 2023).

Earlier this year, Kazia said it had regained Nasdaq compliance by ensuring that its share price was above $US1.00 for 10 business days (BD: Apr 14, 2023).

Trading will resume on October 10, 2023, or on an earlier announcement.

Kazia last traded at 16 cents.

PARADIGM BIOPHARMACEUTICALS

Paradigm has requested a trading halt pending an announcement on "new clinical data from [its] … phase II clinical trial investigating IPPS in knee [osteoarthritis]".

Trading will resume on October 10, 2023, or on an earlier announcement.

Paradigm last traded at 59 cents.

PHARMAUST

Pharmaust has requested a trading halt pending an announcement related to “results from the phase II canine trial”.
Trading will resume on October 10, 2023, or on an earlier announcement.
Pharmaust last traded at 8.1 cents.

VITURA HEALTH

Vitura says Elizabeth Sarah Jansen, as trustee for the Stanford Investment Trust, has retracted a proposed resolution to appoint Mariota Eddison Smutz as a director.
On Friday September 29, 2023, after the market closed, Vitura lodged an announcement that it had received a notice from Ms Jansen under section 249N of the Corporations Act 2001, to appoint Shane Francis Tanner, Mariota Eddison Smutz, Nathan James Hight and Benjamin David Ngahuia Jansen as directors of the company at its next annual general meeting.
At that time, Vitura said Stanford Investment Trust held more than five percent of the company.
Vitura was up 1.5 cents or 4.55 percent to 34.5 cents.

ANATARA LIFESCIENCES

Anatara says chief operating officer John Michailidis has been appointed an executive director replacing non-executive director Dr Jane Ryan, effective from October 2, 2023.
Anatara said Mr Michailidis would continue as chief operating officer.
The company said Mr Michailidis was currently managing-director of JEM Pharmaceuticals Pty Ltd and had been a director of Factor Therapeutics and Australian Diabetes Educators Association as well as managing-director of Teva Pharma Australia.
Anatara said Mr Michailidis held a Bachelor of Science from La Trobe University and a Master of Business Administration from Harvard University.
Anatara chair Dr David Brookes said the company wished Dr Ryan “the very best with her many endeavors and thank her for years of service”.

MEDIBIO

Medibio says Dr Thomas Young will retire as part-time chief executive officer and become a non-executive director, effective October 6, 2023.
Last year, Medibio said it had appointed Dr Young as part-time chief executive officer and would be paid $US110,000 ($A172,651) a year (BD: Sep 19, 2022).
Today, the company said Dr Young would be paid $4,000 a month, in shares in lieu of cash, subject to shareholder approval.
Medibio said its chief executive officer duties would be shared by the “existing management team” and that it had begun searching for a full-time replacement.
Medibio was untraded at 0.1 cents.