Biotech Daily

Friday May 8, 2020

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market was up 0.5 percent on Friday May 8, 2020, with the ASX200 up 26.9 points to 5,391.1 points. Twenty-one of the Biotech Daily Top 40 stocks were up, 10 fell, eight traded unchanged and one was untraded. All three Big Caps fell.

Paradigm was the best for the third day in a row on no news, up 30 cents or 12.5 percent to $2.70, with 5.5 million shares traded. Optiscan climbed 10 percent; Patrys was up 8.3 percent; Cynata improved 7.6 percent; Orthocell rose 6.1 percent; Actinogen, Dimerix and Telix were up more than five percent; LBT, Medical Developments and Opthea were up more than four percent; Ellex, Immutep, Proteomics and Resonance were up three percent or more; Pharmaxis, Universal Biosensors and Uscom rose more than two percent; Volpara was up 1.5 percent; with Nanosonics and Next Science up by less than one percent.

Amplia led the falls, down 0.5 cents or five percent to 9.5 cents, with 17,000 shares traded. Antisense and Oncosil lost more than four percent; Clinuvel fell 3.1 percent; CSL, Kazia, Mesoblast and Starpharma shed more than two percent; Cochlear, Neuren, Polynovo and Pro Medicus lost more than one percent; with Resmed down 0.6 percent.

DR BOREHAM'S CRUCIBLE: CYCLOPHARM

By TIM BOREHAM

ASX code: CYC

Share price: $1.25

Market cap: $99.1 million

Shares on issue: 79,283,398

Chief executive officer: James McBrayer

Board: David Heaney (chairman*****), Mr McBrayer, Tom McDonald

Financials (calendar 2019 year): revenue $14.08m (up 5%), loss after tax $2.91m (previously $118,000 surplus), underlying profit $887,000 (down 37%), final dividend per share 0.5c (steady), cash balance $12.6m (up 116%)

Identifiable major shareholders: Anglo Australian Christian and Charitable Fund 16.9%, Barings (UK) 14.61%, Karst Peak Capital 12.19%, Australian Ethical 10.34%, Chemical Overseas Ltd 10%, CVC Ltd 8.9%, Mr McBrayer 5.4%

***** Former chairman Vanda Gould ceased being a director in November last year, after being found guilty of attempting to pervert the course of justice in relation to a major tax fraud.

After 12 years of attempting to access the US market for Cyclopharm's nuclear medicine technology, chief executive and part-time saxophonist James McBrayer hopes to hear some sweet notes from the US drugs and devices gatekeeper before the month is out.

On March 30 Cyclopharm said it had lodged a new drug application (NDA) with the US Food and Drug Administration for its lung ventilation imaging agent Technegas, to detect pulmonary embolisms (blood clots).

The FDA has a 60-day timeline to either approve or reject the application which makes May 27, D-Day for the company.

Despite the company's setbacks over the years, Mr McBrayer is talking "when" rather than "if" in terms of accessing the world's biggest nuclear medicine, by far.

"We are confident of securing approval within the next 12 months," he says.

Cyclopharm's hopes were further enhanced by the FDA's decision to waive the $US2.9 million ($AUD4.6 million) application fee.

‘Safe and efficacious’

Cyclopharm’s patented Technegas currently is used in 59 countries to detect pulmonary embolisms and has been used on four million patients.

“That puts us up with the biggest multinationals in terms of product reach,” Mr McBrayer says. “We have had no attributed adverse events with Technegas. It’s as safe and efficacious as you would ever get.”

The company estimates the US pulmonary embolism detection market at $US90 million a year. “We expect to gain a 50 percent share of this market in the first two to three years, rising to 80 percent over five to seven years,” Mr McBrayer says.

The FDA application has been made under the regulator’s 505(b)2 mechanism, which is based on reviewing existing ‘literature’ (the learned tomes about usage) and metadata analysis, rather than clinical trials.

Going nuclear

Dubbed as a ‘pseudo gas’, Technegas consists of teeny tiny dry carbon nanoparticles irradiated with the isotope Technetium-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 at the bedside in a generator 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 computed tomography camera. The nanoparticles have a six-hour radioactive life, after which they are eventually dispersed through normal lung excretion.

While Technegas historically has been used for pulmonary embolism, it also can be used for other respiratory ailments such as chronic obstructive pulmonary disorder (COPD) and asthma.

Technegas was invented in the mid-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 on January 2007 after raising $11 million at 30 cents apiece.

A pharmacist, Mr McBrayer joined in June 2008, taking over from John Sharman who went on to head up Medical Developments. Mr McBrayer headed the nuclear medicine mob Syncor Australia, as well as Lipa Pharmaceuticals. He also held a business development role at waste manager Cleanaway, so don’t accuse him of not getting down and dirty.

Learning from the Canadian experience

US lung clinicians have long looked wistfully over the border to Canada, where Technegas was approved way back in 2003.

In that market, Mr McBrayer says, Technegas has “almost 100 percent” replaced the long-standing method, called Xenon-133.

“The only market that still uses Xenon-133 for diagnostic lung ventilation imaging is the US, because Technegas isn’t there.”

As a so-called “true” gas, Xenon-133 requires a negatively pressured room and a method to trap gases expelled by the patient. “That’s pretty claustrophobic for someone who thinks they might be dying of a pulmonary embolism,” Mr McBrayer says.

He adds that Xenon-133 is a “lower energy” isotope, which means it produces only two-dimensional images of the lung’s peripheral bits. Then there’s another Technetium-99 based agent called DPTA, which is short for: diethylenetriaminepentaacetate

You can say that again: Di-ethylene-triamine-penta-acetate.

Officially used for renal (kidney) imaging, DPTA has been deployed off-label for pulmonary embolisms.

Cyclopharm claims Technegas is superior to DTPA because of the shortcomings of DTPA’s liquid aerosol (nebulizer based) delivery system.

When dispersed from the pressurized canister the molecules !!! droplets expand, which can create airways turbulence as the droplets swirl and coalesce.

“The result is a splotchy image and you can’t see what’s going on,” Mr McBrayer says.

In the US, computed tomography pulmonary angiography (CTPA) is the main way to diagnose pulmonary embolisms.

A sensible silly question

Can we ask a silly question? If Technegas is so superior, why have the FDA’s best brains not allowed it in the land of the free and wheezing?

(In journalism there are no silly questions, although asking a visiting dignitary what they think of a country five minutes after they have landed comes close).

Mr McBrayer says when he came on board, the company had had “a few missteps” with the FDA. ”My focus was to reset the relationship and work out just what we needed to do to get this across the line.”

There are a few ‘dog ate my homework’ factors.

Firstly, Technegas can be classed as either a drug or a device, but in the US it is categorized as both.

“We have also kicked some own goals,” Mr McBrayer says. “We wanted to get to market as quickly as possible and we thought the FDA would take this real-world evidence as enough. But that doesn’t work; you still have to show the [clinical] data.

“We have had some poor [contract research organization] partners and that took us down a blind alley.”

Originally the FDA demanded a prospective phase III trial, but the company was unable to recruit the 240 patients targeted.

The brief US government political shutdown last year didn’t help, while the Covid-19 plague has pretty much halted all clinical trials. Nonetheless the company is within “striking distance”, with 200 patients enlisted for the now stalled study.

Since then, the FDA has approved DPTA for detecting pulmonary embolisms, having previously been used ‘off label’.

The significance is that Cyclopharm’s data comparing Technegas with DPTA has now been legitimized (also under the 505 (b)2 pathway) and will add weight to the FDA application.

Bear in mind that the FDA always preferred a technetium-99 based trial to be compared with another technetium-99 based product (DPTA).

“They gave us a leg up,” Mr McBrayer says. “On any guidelines our product in comparison is superior especially with patients with small airways.”

Acronym soup

Then there’s the bureaucratic aspects of dealing with the FDA, which boasts 8,800 employees spread across the country (not just at Maryland HQ).

On the drugs side, Cyclopharm’s application is overseen by the Centre for Drug Evaluation and Research (CDER).
CDER is a sub group of the Division of Medical Imaging and Radiation Medicine (DMIRM), which in turn is an arm of the Office of Specialty Medicine (OSM).

Because Technegas is also classed as a device, the application also has to be vetted by the Centre for Devices and Radiological Health (CDRH).

The presence of FDA, CDER, CDRH, OSM and DMIRM reps means that the company’s regulatory meetings swell to 15 participants or more and are PDC*****.

***** pretty damned crowded

Financials and performance

An enduring dividend paying entity, Cyclopharm is a black swan of the mid-tier biotech space.

Officially Cyclopharm is loss making, having reported a $2.91 million post-tax deficit in calendar 2019 compared with a previous $118,000 surplus. But in underlying terms, the company made $887,000, down 37 percent. This number excludes $3.84 million of FDA expenses and $1 million of litigation costs relating to a squabble with former employees.

The company dispensed a steady interim dividend of half a cent, or one cent for the full year (also unchanged).

As of balance date the company had budgeted $US8.8 million for the FDA filings, with $US7.6 million already expended. Of course, the $US2.9 million fee waiver will ease the burden.

Of Cyclopharm's revenue of $14.08 million, 75 percent was derived from "patient administration sets" - the consumables - with a further 18 percent derived from selling the generators. The consumables are the aforementioned crucibles, which disintegrate in the mini nuclear reactor, as well as single-use tubing.

In 2019 the average cost of a generator was $37,219, while the consumables were worth $58.30 per patient.

The company has the long-term support of private equiteer CVC and Australian Ethical. Hong Kong fundie Karst Peak Capital joined the register after taking $9.77 million of shares in a placement last December at $1.15 a share - a then 12 percent premium.

But the biggest holder is now the Anglo Australian Christian and Charitable Fund, with a 16.9 percent stake. "We are truly blessed," Mr McBrayer quips.

Cyclopharm shares have been volatile during Covid-19 market meltdown, having hit a record $1.50 on April 17 but also trawled a 12-month low of 73 cents on March 20.

The shares hit a 10-year low of 12 cents in March 2013.

Covid-19? Seeing you ARDS-ed

Are you thinking what I'm thinking, B2?

As a respiratory imaging agent, Technegas could be used for acute respiratory distress syndrome (Ards), the pneumonia-like condition that causes most Covid-19 fatalities.

In March, Cyclopharm told the ASX that it had reports of increased use of Technegas to differentiate between Covid-19 and pulmonary embolism where laboratory tests results are not fast enough.

“Yes, we have a potential part to play in tackling Covid-19, but it’s early days in how it’s being used and we are getting various early reports,” Mr McBrayer says.

“We have been speaking to key opinion leaders to see what this unique technology can do.

“We’re not talking about Technegas, but nuclear medicine as a whole.”

So, when it comes to Covid-19 Cyclopharm is not sitting on its Ards.

Nor is it making any spurious claims: “If my background was in marketing rather than pharmacy, I might have been drawn to those, but you have the responsibility to tell the truth,” Mr McBrayer says.

And in late breaking news

The European Journal of Nuclear Medicine and Molecular Imaging gave Cyclopharm’s Technegas the ‘Image of the Month’ award for identifying trachea-bronchitis in a Covid-19 patient that otherwise might have been missed.

Dr Boreham’s diagnosis:

Mr McBrayer concedes the existing imaging methods - including non-nuclear CT scanning - would work just as well as Technegas with healthy patients.

“But these patients are not healthy.”

Cyclopharm’s opportunities beyond pulmonary embolisms are easy to glean, given COPD and asthma are much bigger markets.

In the longer term, China looms as a “tricky but interesting” market.

But in the short term, Cyclopharm’s laser-like focus is on its two-decade old quest to enter the US market.

Without the US access, Cyclopharm has performed solidly but unspectacularly since listing and it can only do so much.

“Being a small company, we need to focus on keeping the doors open and investing what we can, when we can,” Mr McBrayer says.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Unlike Cyclopharm’s single-use vessels, here’s hoping his own Crucible won’t disintegrate under the pressure

FEDERAL GOVERNMENT

The Federal Government says it will invest $16.2 million in eight research projects “to beat ovarian cancer”.
A media release from Federal Health Minister Greg Hunt said ovarian cancer had the lowest survival rate of all female cancers, with only 43 of 100 women diagnosed surviving past five years.
Mr Hunt said the research would help “understand the underlying factors that contribute to the development and progression of ovarian cancer and how best to managed and treat this devastating condition”.
The media release said the projects included the University of Newcastle repurposing a drug for treatment-resistant ovarian cancer; the University of Melbourne’s high throughput discovery of drug combinations for low-grade serous ovarian cancer; and Monash University’s granulosa cell tumor research and measurement of adherence to best practice guidelines for managing ovarian cancer.
The Government said further projects included Griffith University’s phase II trial assessing exercise intervention during chemotherapy; the Queensland Institute of Medical Research’s investigation into variations in care, survival aetiology and risk factors; and the University of Queensland’s use of extracellular vesicles for early detection, monitoring and therapeutic intervention, and its new radio-imaging agent to guide targeted therapy.
The Government said the funding was from the Medical Research Future Fund’s Emerging Priorities and Consumer Driven Research Initiative.
For more information go to: www.heatlh.gov.au/mrff.

CYNATA THERAPEUTICS

Cynata says it has ethics approval for a 24-patient, open label, randomized, controlled trial of its Cymerus mesenchymal stem cells for adults in intensive care with Covid-19.
Cynata said the patients with respiratory distress would be administered either Cymerus mesenchymal stem cell infusions and standard-of-care or standard-of-care alone.
The company said the primary endpoints of the trial would be safety and tolerability up to day-28 and improvement in hypoxaemia levels, or low levels of oxygen in the blood caused by compromised lung function, by day-7.
Cynata said the trials would be conducted in collaboration with the Cerebral Palsy Alliance Research Institute and Covid-19 Stem Cell Treatment Group investigators, and it expected to begin recruitment, subject to finalization of agreements with study centres in New South Wales.
The company said start-up activities for trials of its CYP-001 for graft versus host disease would continue despite the Covid-19 pandemic.
Cynata was up five cents or 7.6 percent to 70.5 cents with 2.6 million shares traded.

LBT INNOVATIONS

LBT says the South Australian Government has extended the date to make its third $1.5 million drawdown to December 31, 2020.
In 2018, LBT said it would receive $4 million, with an instalment of $1 million, which it received in May 2019, and two instalments of $1.5 million by December 31, 2019, one of which it received in June 2019 (BD: Aug 28, 2018, May 9, Jun 27, 2019).
Today, the company said the final instalment was subject to achievement of operational milestones.
LBT was up half a cent or 4.55 percent to 11.5 cents.

PAINCHEK
Painchek says it has a notice of allowance from the Australian Patent Office for its smartphone pain assessment and monitoring application.
Painchek said the patent, titled 'A Pain Assessment Method and System' would protect its intellectual property until August 18, 2035.
Painchek fell half a cent or three percent to 16 cents with 7.6 million shares traded.

HERAMED
Heramed says it has appointed Medtech Edge subsidiary Advanced Pregnancy Solutions (APS) to distribute its Heracare "hybrid maternity care platform".
Heramed said it would pay APS a marketing and setup fee of $11,500 and monthly business development, consulting and management fees of $3,850 for six months to access Medtech's contracts, amplify Heracare's exposure and secure pilot projects.
The company said that within six months, it would jointly develop a business model based on monthly subscriptions to share revenue between Heramed and APS.
Heramed fell one cent or 8.3 percent to 11 cents.

ELIXINOL GLOBAL
Elixinol says it has sold land owned by wholly owned subsidiary Nunyara Pharma to a private individual for $2,560,000, with settlement scheduled for May 22, 2020.
Last year, Elixinol said the Australian Office of Drug Control had granted Nunyeara a medicinal cannabis manufacturing license (BD: Jul 17, 2019).
Today, the company said it would use the funds from the sale to support its marijuana food additives strategy.
Elixinol was up one cent or 3.2 percent to 32.5 cents.

PHARMAUST
Pharmaust has requested a trading halt "pending an announcement regarding disclosure of clinical trial results".
Trading will resume on May 12, 2020 or on an earlier announcement.
Pharmaust last traded at 10 cents.

THC GLOBAL GROUP
THC has requested a trading halt "pending an announcement with respect to a material acquisition".
Trading will resume on May 12, 2020 or on an earlier announcement.
THC last traded at 30 cents.

MICRO-X
Managing-director Peter Rowland says his 12,425,000 share-holding has been diluted below five percent in a placement and through the conversion of convertible notes.
Last month, Micro-X said it had raised $8.75 million through a placement and hoped to raise a further $6.25 million in a one-for-5.6 underwritten entitlement offer at 14 cents a share (BD: Apr 17, 2020).
Micro-X was unchanged at 13.5 cents with 1.2 million shares traded.

OSPREY MEDICAL

In three separate ceasing substantial notices, Brisbane's CM Capital and Melbourne's Australian Super say they have ceased their substantial holdings in Osprey.
Last month, Osprey said it raised $10,244,920 through a three-for-one renounceable entitlement offer at 1.2 cents per Chess depositary interest (BD: Apr 29, 2020).
Today, CM Capital said it held 34,040,899 shares and Australian Super said it held 34,302,093 shares, and they were both diluted below five percent in Osprey.
Osprey was unchanged at 0.9 cents with 4.4 million shares traded.

NOXOPHARM

Noxopharm says it has appointed Fred Bart as a non-executive director.
Noxopharm said that Mr Bart had been "chairman and managing director of numerous private and public companies since 1980, specializing in manufacturing, technology, property and marketable securities".
The company said that Mr Bart was currently the chairman of Electro Optic Systems and Audio Pixels and a director of Weebit Nano and Immunovative Therapies, an Israeli company involved in in the manufacture of cancer vaccines.
Mr Bart was appointed a director of Genetic Technologies in 1996, chairman in November 2008 and was due to be re-elected in 2009 but on the day of the meeting he resigned and the resolution was withdrawn (BD: Sep 18, Nov 19, 2008; Nov 26, 2009).
Noxopharm was untraded at 19.5 cents.