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Daily news on ASX-listed biotechnology companies

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.