Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Cleo Diagnostics

By TIM BOREHAM

ASX code: COV

Share price: 20.5 cents

Shares on issue: 128,500,001

Market cap: $26.3 million

Chief executive officer: Dr Richard Allman

Board: Adrien Wing (chair), Dr Allman, Dr Andrew Stephens, Prof Tom Jobling, Lucinda Nolan

Financials (December half 2023): income $5,386, loss $421,412

Major shareholders: Wing Investment Holdings (Adrien and Michelle) 11.09%, Loumea Investments (Richard Vom) 7.10%, Hudson Institute of Medical Research 5.84%.

For all the advances in cancer diagnostics, some iterations of the cheeky disease continue to evade accurate forms of detection.

That is certainly the case with ovarian cancer, the seventh-most prevalent cancer and with one of the highest mortality rates.

Because a pap smear does not pick up ovarian tumors, there is no early detection test. The diagnosis is made at the time of surgical ovary removal - which obviously is less than ideal.

Enter Cleo Diagnostics, which debuted on the ASX on Tuesday this week, having raised $12 million.

The funds are earmarked to support the commercialization of up to three diagnostic tools, starting with an application to the US Food and Drug Administration for a triaging tool (see below).

“There is no accurate pre-surgical method to diagnose ovarian cancer or to accurately differentiate between cancerous [tissues], versus the much more common benign disease,” says Cleo chief executive Dr Richard Allman.

“This is simply not good enough.”

Cleo hopes to succeed where many an ovarian diagnostics developers have stumbled.

“Ovarian cancer has been a hard area to be in. The number of scientific discoveries has been small in the past 20 to 40 years,” Dr Allman says.

“But we wouldn’t risk doing an IPO in the current climate if our story wasn’t strong.”

About ovarian cancer

It is estimated that 445,700 women globally will be diagnosed with ovarian cancer annually by 2040, a 42 percent increase on 2020. According to Cancer Australia, the current Australian incidence is 11 in 100,000 women.

Ovarian cancer is one of the deadliest cancers because it tends to be undetected until the advanced stages.

Only about 30 percent of women diagnosed at advanced stage will survive beyond five years. But survivability increases to 94 percent if the nasties are detected early.

“By and large you don’t find out you have ovarian cancer until you are at a late stage, because of the location of the tumours deep inside the body,” Dr Allman says.

“It also tends to be asymptomatic or with very general symptoms such as tiredness or abdominal pain.”

By the time they get to late stage, the patients have hundreds of tumors around the abdomen, which means treatments - ‘debulking’ surgery and/or chemo - are not usually successful.

Currently, the standard-of-care diagnoses are trans-vaginal ultrasounds and assays based on the biomarker CA-125, which is overexpressed by ovarian tumors (as well as some other cancers).

Dr Allman says the effectiveness rate of the existing tests is no better than 50 percent: a toss of a coin would be just as useful.

The brains behind Cleo

Cleo was incorporated in November 2021, based on the assets acquired from the Hudson Institute. The Hudson Institute sprung from the 2014 merger of the Prince Henry and Monash medical research institutes.

As with all good medical discoveries, serendipity was involved: Hudson's Dr Andrew Stephens was looking at immune responses in tumors and discovered the bio-marker CXCL-10. The test is backed by more than 10 years of research at the Hudson Institute.

An inflammatory molecule, CXCL-10 is evident only on malignant ovarian tissue and develops very early in pre-cancerous lesions. Cleo continued probing the data and ultimately struck a deal with Hudson for an exclusive worldwide licence to the tech.

An epidemiologist, Dr Allman was the chief scientific officer for Genetic Technologies, where he helped to develop the company's second-generation breast cancer risk tool. Before that, he had an academic career in the UK.

Dr Allman also carried out due diligence for ASX blood test peer, Rhythm Biosciences, which recently won UK Conformity Assessment approval for its bowel cancer test. He then did similar work for Cleo and was convinced enough to join the company full-time.

Accountant and corporate adviser Adrien Wing founded Rhythm and he is now Cleo's chair and biggest shareholder. Fellow Cleo director Prof Tom Joblin is a gynaecological oncology surgeon and founder of the Ovarian Cancer Research Foundation (OCRF).

Another director, Lucinda Nolan, would be familiar to Victorians, having risen to assistant commissioner in the police force. She was then CEO of the Country Fire Authority where she faced political bushfires on all fronts, before heading to the OCRF.

Meanwhile, Dr Stephens is now Cleo's chief scientific officer.

Clinical head start

Cleo is working off the building blocks of two trials carried out by the Hudson Institute, under the auspices of Dr Stephens.

The first trial in 2020 enrolled 275 patients and assessed the ability of the test to distinguish malignant and benign tumors (triaging). The test achieved a sensitivity rate of 90 percent and a specificity of 91.7 percent. Sensitivity is the ability to avoid false negatives while specificity relates to false positives.

Carried out in 2022, the second trial assesses 271 patients with an elevated risk of ovarian cancer as part of a broader biomarker panel. The test detected malignancies at an early stage with more than 90 percent accuracy, with the "potential" to do so at a pre-cancerous stage. More work is required. Cleo expects a learned medical journal to publish an article on its findings based on 'alpha prototype' work (academic data).

Targeting triage

Yet unnamed, the Cleo assay is a non-invasive in-vitro blood test to determine the presence and recurrence of ovarian cancers.

The targeted CXCL-10 is over-expressed on ovarian cancers - but not the more common benign tissue. The test consists of an immune-assay, control proteins and algorithms.

Cleo is working on three uses, but the primary commercial focus is on a pre-surgical triage test for symptomatic women.

“They may have had abdominal pain or an abnormal ultrasound, but the doctor still doesn’t know whether it is an ovarian cyst or a tumour,” Dr Allman says.

The only way of finding out is to excise the suspicious matter with surgery - but 90 percent of the time the lump will be benign.

Under the FDA’s 510(k) route, the company merely would have to prove the product is not inferior to the existing diagnostics. Cleo notes there already are two FDA approved products targeting the CA-125 biomarker. But any commercial Cleo test most likely would be multi-panel, in that CA-125 would also be targeted for maximum efficacy.

Other applications

Cleo is also eyeing a mass screening test for non-symptomatic women and a post-surgery recurrence test to gauge whether cancer has returned.

With recurrence, the CA-125 based assays have been found wanting.

“There’s more clinical complexity and uncertainty around timelines with this one, because the patients might have a recurrence after several weeks or months,” Dr Allman says.

With screening, all women aged over 50 would - or should - be eligible.

“We are de-risking this one by carrying out our first study in high-risk women with a BRCA [gene] mutation or a strong family history of ovarian cancer,” Dr Allman says.

Given that, a shorter trial with fewer patients is possible.

Finances and performance

Post IPO, Cleo has 128,500,001 shares on issue, compared with 45,000,001 previously (to be exact).

The public offer consisted of 60 million shares at 20 cents apiece, plus 16 million convertible notes - part of a seed capital round - converted at 50 cents apiece.

Dr Allman says the company has enough funding to bring the triage test to market, “with a little bit of fat to initiative the recurrence and screening studies.” These secondary studies are expected to start next year.

Getting a screening test to market would require more funding, but the company will not go back to market until it has runs on the board with the FDA triage application.

In the US, about one million patients will have an abnormal ultrasound result each year, requiring referral to a specialist.

Similar triage type tests are reimbursed at about $US890 ($A1,390) which implies a $US1 billion-plus addressable market.

In the hands of the Hudson Institute, the technology was backed to the tune of $5 million by the National Health and Medical Research Council and the Ovarian Cancer Research Foundation (mainly the latter).

If the test is approved in the US, the UK, Europe or Japan, Cleo needs to pay $1.5 million to the Hudson Institute.

Given the joyousness of such a landmark occasion, we’re sure investors wouldn’t mind this modest impost.

Cleo shares ranged between 19.5 cents and 23 cents immediately after Tuesday’s debut and the last time we looked they were trading at par with the 20-cent issue price.

Check out the competition

The Cleo prospectus lists six global developers of blood-based ovarian cancer assays, three of which have products on market.

To be honest, the competitive landscape is blurred.

The Texas-based Aspira Women’s Health has a multi-biomarker test called Ovasuite, including a triage function. Pennsylvania’s Fujirebio Diagnostics also has a combination tool called Roma.

The roll-call includes the ASX listed Inoviq, which has been focused on breast cancer but is developing an ovarian cancer diagnostic for patients already diagnosed or in remission. This assay targets the CA125 biomarker. Inoviq is also tapping its separate exosome platform, Exo-Net as a broader screening tool.

We would be remiss not to mention the ASX listed Healthlinx, which tried to develop a multi-marker blood test called Ovplex. Healthlinx morphed into a social media company - never a good sign - before disappearing from the ASX boards altogether

Cleo is also keen to avoid the experience of Rhythm Biosciences, which made an "incorrect regulatory move" resulting in a surprise rejection by Australia's Therapeutic Goods Administration.

"There are learnings to be had from other peoples' hiccoughs, but there are bigger learnings to be had from successful companies," Dr Allman says.

In the non-cancer space, he cites Cellestis, which developed a niche antibody diagnostic for tuberculosis and was acquired by China's Qiagen for a tidy $355 million in 2011.

Dr Boreham's diagnosis:

Management has set a clear target of FDA approval within 24 months for the triage test, with commercial sales in the US six months thereafter.

"Two and a half years is very ambitious. I'm not aware of another Australian biotech that has delivered on a timeline like that," Dr Allman says.

Given that the Hudson has worked on the test for 10 years, Dr Allman says his goal is achievable, because management has focused on risk reduction every step of the way. In other words, the company is not chancing the FDA process by presenting half-baked data.

"It would be easy to build a black box research company around a diagnostic, with no clear line of sight to a commercial product," he says.

"We have worked hard at de-risking the company, not just from a science perspective but an investor perspective."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. His idea of optimal risk management is not to get out of bed in the morning, but that is not always practical.