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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Adalta

By TIM BOREHAM

ASX code: 1AD

Share price: 10 cents; **Market cap:** $20.4 million; **Shares on issue:** 203,945,613*****

Chief executive officer: Dr Tim Oldham

Board: Dr Paul MacLeman (chair), Dr Oldham, Dr Robert Peach, Dr David Fuller, Liddy McCall (Yuuwa rep, Dr James Williams alternate)

Financials (June quarter 2020): revenue nil, cash burn $1.1 million, cash on hand $3.4 million, loan facility $2.1 million**, quarters of available funding 3.1
***** Includes 40 million shares issued under the placement component of the $4 million placement, and $4.1 million rights offer announced on August 11, 2020, but not included in the cash position above
****** Consists of funds advanced by Radium Capital as a forward payment for 80 percent of the company's expected research and development tax incentive for the 2019-'20 year.

Identifiable major shareholders***: Yuuwa Capital 26.5%, Platinum Asset Management 12.4%, Meurs Holdings 5.1%, Knight61 Investments 1.9%, Citicastle (Leon Serry) 1.7%
******* post placement, ahead of the rights issue

The truth be told, kicking off recruitment for a phase I trial should be more of a passing remark in a drug developer's routine update, rather than a monumental milestone on the corporate timeline.

But tell that to investors in Adalta, who pushed shares in the fibrotic diseases specialist up by as much as 40 percent, after the company's July 23 revelation (of sorts) that it had treated its first participants in an idiopathic pulmonary fibrosis trial.

As Winston Churchill said, possibly after a few stiff drams: “This is not the end. This is not even the beginning of the end. But it is, perhaps the end of the beginning.”

Adalta chief Dr Tim Oldham prefers a ‘spotty teenager’ analogy: “We are an adolescent biotech company getting its coming of age moment with the first product coming through to the clinic,” he says.

“That was always going to be a catalyst for us then doing more.”

When the fish are biting

Adalta has joined the conga line of life sciences going to the well, raising $4 million in a placement and seeking $4.098 million more in a rights issue.

As of June 30, Adalta had $3.4 million in the vault, enough to fund the volunteer stage of its planned phase I safety study.

But when the fish are biting - sharks, in Adalta’s case - you immerse the rod in said well.

“Being a biotech, we are always going to need to raise money anyway,” Dr Oldham says.

Inspired by sharks

A spin off from Latrobe University and the CSIRO, Adalta listed in August 2016 after raising $10 million at 25 cents apiece.

Adalta’s program revolves around AD-214, its lead I-body (standing for “intermediate” group of immunoglobulin or immunoglobulin-like domains, which is not quite as snappy) candidate. A type of protein, AD-214 mimics the cell characteristics of sharks. The souped-up AD-214 molecules are engineered with two loops that mimic the shape of shark antibodies.

As any marine biologist would tell you, sharks are among the oldest living organisms and their hardy and adaptive antibodies are part of the reason. These antibodies are called “Ignars” - which sounds like the noise a shark would make when chomping on a surfer’s leg. (Seeing as how you asked, it’s actually immunoglobulin new antigen receptors.)

The AD-214 loops are twice the length of human antibodies, and are said to access nooks and crannies to latch on to drug targets that evade normal monoclonal antibodies.

The core mechanism of action is that the compound binds to the protein CXCR4, which is not a Star Wars ‘droid but a receptor over-expressed in the unhealthy fibrotic tissue.

The idea is that AD-214 binds to the lung tissue and blocks the migration of cells implicated in fibrosis, without impacting the healthy cells.

Tackling a difficult disease

The company's key target idiopathic pulmonary fibrosis (IPF) is "irreversible, unpredictable progressive and incurable". As 'idiopathic' implies, no-one knows what causes it.

Worldwide about 300,000 people suffer from idiopathic pulmonary fibrosis, with an average survival of less than four years.

Adalta claims the two available treatments - Boehringer Ingelheim's nintedanib and Roche's pirfenidone - have safety limitations and poor efficacy.

While Adalta cites a $3 billion idiopathic pulmonary fibrosis market, the company really wants to develop AD-214 as a 'platform' for interstitial lung disease (ILD), of which idiopathic pulmonary fibrosis accounts for 25 to 30 percent.

CXCR4 is upregulated in all ILDs. Other fibrotic conditions of interest are age-related macular degeneration and kidney and liver conditions such as the difficult to treat non-alcoholic steato-hepatitis (NASH).

Mr Oldham admits Adalta is not the only developer targeting idiopathic pulmonary fibrosis, but is the only one pursuing the CXCR4 target.

"Our mode of action is to engage the cells responsible for alleviating the inflammatory and fibrotic processes, as opposed to the other drugs that block the signals those cells are sending," he says.

"We are stopping those cells that drive those processes from getting to the fibrotic tissue in the first place."

Changing of the guard

Dr Oldham joined the company in October last year, after the sudden departure of the long-serving and energetic Sam Cobb in August.

"I was attracted to Adalta because there aren't that many Aussie biotechs doing more than just eyeing a product to be sold," Dr Oldham says. "At Adalta I saw something with this platform that was designed to solve difficult drug targeting challenges."

Dr Oldham worked at the original Mayne Pharma and then ran the Asia Pacific region for Mayne's acquirer, Hospira. He also has worked at Tijan Ventures and McKinsey and was CEO of Cell Therapies (Peter MacCallum Cancer Centre's cell manufacturing subsidiary).

He is currently on the board of the ASX listed generics maker Acrux, which is headed by old Hospira/Mayne chum Mike Kotsanis.

"We swapped roles," he says. "I was leading Europe when Hospira acquired Mayne and Mike was leading Asia-Pacific."

So glad about MAD and SAD*

The phase I trial had been running a little behind schedule, partly because of an issue with processing samples from the mouse proof-of-concept study. Fortunately, a reanalysis confirmed the expected positive results.

The first stage of the study has started recruiting 44 healthy volunteers, at seven dose levels. The company then plans to enrol a minimum 15 IPF patients for a single ascending dose (SAD), with a further 12 subject to multiple ascending dose (MAD) treatment.

“We are not expecting efficacy data, but we expect to demonstrate where AD-214 is engaging CXCR4, which will give us great information about the mechanism of action.”

Imagin’ that

With the help of a $1 million grant from the Medical Research Future Fund, Adalta is developing a “radio-labelled” version of AD-214, for positron emission tomography (PET) screening.

This allows the company to measure receptor occupancy in the target fibrotic tissue and understand the interplay between white blood cells and the lung tissues of fibrotic patients.

“This was a really important breakthrough, because now we had a way to visualize AD-214 in the lungs of patients,” Dr Oldham says.

Without it, the phase I study would have enrolled only healthy volunteers and been of less use.

“In effect, Adalta now has a more powerful phase I study,” Dr Oldham says. “It means we will have a study that is fit for partnering, rather than just for safety data. It is a much more robust, important study than would have been possible otherwise.”

Still on imaging, in September last year the company entered a research collaboration with GE Healthcare to evaluate I-bodies that might be used as imaging agents in GE’s PET scans. The initial target is granzyme B, which is not a vitamin but a biomarker of anti-cancer activity by a person’s immune system.

Dr Oldham says the GE tie-up validates the commercial appeal of Adalta’s program.

The mandatory Covid-19 angle

Fibrosis and acute respiratory distress syndrome (Ards) - are you thinking what I’m thinking, B2?

It doesn’t take a pyjama-clad Lady Cavendish to realize that Ards, the usual cause of coronavirus mortalities, is a fibrotic/inflammatory disorder.

“We have been pretty careful about jumping on the Ards and Covid band-wagon,” Dr Oldham says, adding that in-vitro data suggests AD-241 can modulate the inflammatory cells responsible for Ards (or cytokine release syndrome).

Dr Oldham says it appears that two-thirds of people hospitalized with Covid-19 will end up with lung fibrosis.

“We are devoting our efforts to how we might think about that application,” he says. “We know from severe acute respiratory syndrome (Sars) that six months after recovery, patients still have inhibited respiratory function.”

But rather than fruitlessly chasing teddy bears around the lounge room, Adalta’s top bananas won’t get distracted from the company’s core programs.

Finances and performance

The one-for-four rights offer closes on September 2, after which Adalta should have $11 million with which to play. The offer is not underwritten.

Under the GE Healthcare deal Adalta has pocketed GBP100,000 ($A182,752) upfront, with GE funding the discovery program over eight to 11 months.

“Effectively we are developing a drug for free, with additional milestones and royalties if GE takes a drug to clinic,” Dr Oldham says.

Ahead of the capital raising, he estimated the company would need at least $10 million to implement its plans over the next three years.

“We are quite encouraged by the capital markets and the feedback we are getting from our shareholders, especially the top 10 or 20 for our growth strategy.”

Speaking of the register, Adalta is 26.5 percent owned by the Perth-based venture capital fund Yuuwa Capital.

Yuuwa was established in 2009 with investment from the Australian Federal Government’s Innovation Investment Fund.

Private holders include former Fortescue Metals CEO Peter Meurs, who also owns a wad of Adalta shares in his own right.

While Yuuwa has been supportive, the fund has a sunset date of late 2022, having been extended from late 2019 in March last year.

Because the fund does not have a mandate to invest more, it abstained from the placement and rights issue and this reduced its holding from 32.9 percent. If all the rights are taken up its holding could reduce to as low as 22 percent.

The good news about Adalta shares is that they have recovred from their Covid-19 meltdown, when the shares cratered to a record low of 4.1 cents (on March 23).

The stock hit a record high of 37 cents in March 2018.

Dr Boreham's diagnosis:

A key question is what happens after the phase I results, presuming they are successful.

The obvious answer is a phase II trial, but Dr Oldham notes that big pharma is partnering on idiopathic pulmonary fibrosis programs early in the piece.

In November last year, Roche acquired Premedior for $US390 million ($A540 million) up front, with potential $US1 billion milestones. Premedior's lead program is a phase II idiopathic pulmonary fibrosis trial.

"My objective is to have a list of two or three companies willing to produce a term sheet by the time we get to the partnering window by the end of next year."

Alternatively, there's a pathway to a "relatively low cost" phase Ib or phase II trial, possibly in combination with another drug.

In the meantime, investors should look out for the top-line safety data next January, as well as an update on the GE collaboration later this year.

Dr Oldham says the company will be "thoughtful about where we go next".

On the fourth anniversary of Adalta's listing, unrequited shareholders will be relieved that post-raising this tiddler is at least swimming somewhere and not destined for shark bait.

* With apologies to Dr Seuss

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He's also not a marine biologist either, but knows that if you want a shark to let go of your leg you punch it in the face.