Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Regeneus

By TIM BOREHAM

ASX code: RGS

Share price: 14 cents; **Market cap:** $38.9 million; **Shares on issue:** 277,824,988

Chief executive officer: Leo Lee

Board*: Barry Sechos (chairman), Prof Graham Vesey (chief scientific officer), Dr John Chiplin, Dr Alan Dunton, Leo Lee

***** Dr Glen Richards stepped down in June

Financials (June quarter 2020): receipts nil ($1.64 million, year to June 30), cash burn $376,000, debt $1.1 million, cash on hand $982,000, 10.3 quarters of funding

Identifiable major shareholders: AGC Inc 8%*****, Vesey Investments 5.72%, Leo Yao Lee 4.86%, Thomas Mechtersheimer 2.21%

***** AGC has not yet converted its contractual rights into ordinary shares but is expected to do so.

The roller-coaster of the emerging stem cell therapies sector was tumbling on Wednesday and soaring on Friday.

Sector leader Mesoblast suffered the Hump Day blues after the US Food and Drug Administration dissed the company's data supporting its approval application for its proposed graft-versus-host disease (and Covid-19) therapy Remestemcel-L.

The shares lost a third of their value. But the week ended on a much happier note after the FDA's advisory committee voted nine to one in favor of approval.

On a more pleasant note, Regeneus shares soared as much as 82 percent on Tuesday, after Japanese partner Kyocera finally signed a licencing agreement for its stem-cell based knee osteoarthritis treatment, Progenza.

For Regeneus, the news follows the signing of a memorandum of understanding in March this year - but also more than a year of background discussions.

In demanding an exclusive negotiating period and heavy due diligence, Kyocera had committed to a decision by the end of September so - unusually - this one wasn't struck at the eleventh hour.

"This agreement … provides a clear commercialization pathway for Progenza and [opens up] a significant market given osteoarthritis potentially affects more than 25 million people in Japan alone," says Regeneus chief Leo Lee.

Mr Lee says the company targeted Japan because in effect it has a "regulatory superhighway" for cell therapies.

"You only need one study and then you can get to market. That's why other companies are also targeting Japan."

These other parties include Mesoblast, which is marketing the graft-versus-host disease (GvHD) treatment Temcell (acquired from Osiris in 2013).

Also, Cynata and Japan's Fujifilm has struck a global worldwide deal to commercialize Cynata Therapeutics' GvHD treatment, Cymerus.

About Regeneus

Regeneus is all about fat-derived mesenchymal stem cells: or rather the secretions from these cells that have the ability to be clinically developed to treat multiple candidates.

Progenza is an off-the-shelf (allogeneic) treatment for osteoarthritis pain. Progenza cells secrete cytokines - a protein that regulates the cells and sends signals to them - and other growth factors.

Osteoarthritis pain is usually treated with non-steroidal anti-inflammatory drugs, which may induce side effects including stomach ulcers and gastrointestinal bleeding.

Regeneus focuses on a subset of secretions called exosomes - and your columnist need not explain what they are because we did so last week with our coverage of Exopharm.

In 2016, Regeneus entered a Japanese joint-venture alliance with stem-cell manufacturer AGC, an arm of Mitsubishi AGC Asahi Glass.

The idea was that AGC would manufacture the Regeneus cells, licence its technology and introduce a commercial partner.

As it happened, there was a carve-out provision that annulled the tie-up if a commercial partner wanted to manufacture the drug as well. Then - lo and behold - Kyocera came along.

As part of the December 2019 divorce pact, AGC received $US2.5 million for services rendered, convertible to Regeneus shares.

While Kyocera has not yet done the paper-work, it it's expected to avail itself of this option to pick up eight percent of the Regeneus register.

Board cleanout spells strategic shift

Regeneus was the brainchild of inventor Graham Vesey and was founded by Prof Vesey and Dr Benjamin Ross. Both have strong Macquarie University links.

The company was pursuing numerous human and animal health indications until early 2019, when the board decided to focus on the Progenza programs.

In January 2019 then chief executive John Martin resigned to pursue other opportunities, to be replaced by Mr Lee (an existing director).

Chairman (and biotech legend) Dr Roger Aston resigned shortly thereafter, to be replaced by fellow biotech legend Dr John Chiplin and the Florida-based Dr Alan Dunton.

Mr Lee had held numerous big pharma roles, including as regional head for Merck Sharp and Dohme.

He has lived in Japan for 10 years but spends about half his time in Sydney. Mr Lee went to Taiwan for a holiday in February and has been marooned there ever since, because both Japan and Australia closed their borders.

By the numbers

The Kyocera deal sees Regeneus receives $US19m ($A27 million) of upfront, development and regulatory milestones. This includes $US9 million upfront, of which Regeneus received $2 million at the signing of the memorandum of understanding.

The company also stands to pocket single to high double-digit royalties on sales.

Kyocera stumps up for all manufacturing, development and commercialization costs - which is likely to be at least equal to the $27 million paid to Regeneus.

“From that perspective it was a significant vote of confidence in Regeneus from a multinational such as Kyocera,” Mr Lee says.

In a phase I study in 2018, Progenza met all safety and efficacy endpoints. Under Tokyo's fast-track approval system, Kyocera should only need to carry out a phase II study.

Crucially, the deal pertains only to osteoarthritis in Japan: Regeneus can do deals with other parties outside Japan for Progenza.

Regeneus can also license Progenza for other indications in Japan, but Kyocera has first right of refusal.

The company says the upfront payments will provide "sufficient cash runway" until Progenza's commercial launch in Japan.

The company raised $5.54 million a year ago in a placement and rights issue at eight cents apiece.

On the debt side, Regeneus owes $1.1 million to Mr Lee and also has a $4 million loan facility from Mr Lee and Paddington Street Finance, an entity linked with chairman Barry Sechos.

The debt will be repaid - and the facility retired - when the Kyocera funds roll in.

Regeneus stock peaked at 60 cents in November 2013, shortly after listing at 25 cents a share.

The shares hit a record low of five cents in March, during that infamous Covid-19 meltdown when investors should have been buying as if there were no tomorrow.

It certainly felt like it.

What's next?

The company is keen to carry out a phase II trial for knee osteoarthritis in the US, funded by the Kyocera cash.

Firstly, it needs to build a factory to make the stem cells, which should take 12 months or so.

Mr Lee says the company is also keen on running an Australian proof-of-concept study for neuropathic pain, such as back pain and a face condition called trigeminal neuralgia.

"The company has interesting data round neuropathic pain," he says. "We just have to pick the right disease area and we will be doing that in the near future."

Mr Lee says the company has had "good discussions" with the deep pocketed US National Institutes of Health about lower back pain and other ailments currently treated with opioids.

"We believe there will be a lot of interest in accelerated therapies and we see funding coming through the NIH," he says.

Covid-19, acne and other stuff

Meanwhile, Regeneus is engaged in “ongoing discussions” with potential European partners.

In the US the company wants to carry out a phase II study before partnering.

The company, by the way is interested in Covid-19, but does not have an active program.

A recap: most Covid-19 victims who die do so because of acute respiratory distress syndrome (Ards), which is the body’s inflammatory immune over-reaction to the virus.

Mr Lee says the company’s stem cells are just as applicable to stem cells as any other’s (read Mesoblast’s or Cynata’s platforms).

“But there are already hundreds of clinical studies out there,” he says. “It’s always harder catching up with a trend than to develop something that will have high unmet needs in future.”

Regeneus also has a second-string drug candidate called Sygenus, which is slated as a topical acne treatment. Mr Lee says Sygenus has “tremendous potential” but work is at an early stage and progress has been, well, spotty.

Meanwhile, the company’s cancer vaccine and animal health businesses are for sale to the highest bidder.

Mr Lee should take this as a compliment: he wouldn’t make for a good used car salesman as he admits that cancer vaccine science has been superseded by immune stimulation therapies.

“But with animal health we are still talking and there’s a ‘for sale’ sign on it.”

Dr Boreham’s diagnosis:

The beauty of the Kyocera deal is that it delivers Regeneus the up-front folding stuff without significant ongoing costs.

Thus, the deal will fund the manufacturing of the drug and the extension programs.

We shouldn’t gloss over the fact that Progenza is not yet approved in Japan.

But with the local Kyocera doing the paperwork, the chances of communication or cultural misunderstandings are greatly reduced.

On industry numbers cited by Regeneus, the Japanese osteoarthritis market is worth $US350 million ($A490 million) a year.

Mr Lee estimates a specific Progenza addressable market of five million patients in Japan, 4.5 million in the US and five million in Europe.

Hang on! How can Japan (population 126 million) be a bigger market than the US (330 million) and on par with Europe (500 million)?

The answer is that US patients are younger and more likely to undergo knee surgery or resort to short term pain relief, rather a stem cell treatment.

Last September Dr Chiplin promised your columnist that in five years' time the company would be in a range of well-advanced pain and inflammation products - presuming the company had not been acquired in the interim.

We won't forget!

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. The truth be told, he probably will forget.