



Biotech Daily

Friday November 16, 2018

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market slipped 0.09 percent on Friday November 16, 2018 with the ASX200 down 5.4 points to 5,730.6 points.

Sixteen of the Biotech Daily Top 40 stocks were up, 12 fell, six traded unchanged and six were untraded.

Avita was the best, up 1.6 cents or 19.75 percent to 9.7 cents with 64.4 million shares traded.

Airxpanders climbed 13.9 percent; Neuren improved 7.5 percent; Immutep and Starpharma were up more than five percent; Ellex, Imugene, Nanosonics and Orthocell were up more than four percent; Bionomics, Cynata and Polynovo were up more than three percent; Telix rose 2.7 percent; Optiscan was up 1.6 percent; with Clinuvel, Medical Developments and Resmed up by less than one percent.

Factor Therapeutics led the falls, down 0.1 cents or 33.3 percent to 0.2 cents with 49.1 million shares traded.

Prescient lost 10.6 percent; Impedimed fell 5.8 percent; Uscom was down 3.6 percent; Compumedics, LBT, Mesoblast and Oncosil shed more than two percent; Dimerix, Opthea and Volpara were down more than one percent; with Cochlear, CSL and Pro Medicus down by less than one percent.

DR BOREHAM'S CRUCIBLE: REGENEUS

By TIM BOREHAM

ASX code: RGS

Share price: 20 cents; **Shares on issue:** 208,885,143; **Market cap:** \$41.8 million

Chief executive officer: John Martin

Board: Dr Roger Aston (chairman), John Martin, Prof Graham Vesey (chief scientific officer), Barry Sechos, Dr Glen Richards, Leo Lee

Financials (year to June 30 2018): revenue \$611,000 (previously \$10.1 million* profit), loss of \$5.2 million (previously \$3.3 million profit*), cash of \$1.02 million (previously \$4.1 million)

* The previous numbers reflect payment of an \$8.9 million licencing fee from Tokyo's AGC Asahi Glass. The 2017-'18 revenue includes a \$576,000 licencing fee

September quarter: revenue nil**, cash outflows \$815,000, cash balance \$2.7 million, estimated current quarter outflows \$1.8 million

** The company received \$2.4 million in government grants and tax incentives

Major identifiable shareholders: Prof Vesey and Vesey Investments 7.6%, Thomas Mechtersheimer 2.9%, John Martin 3.5%, Dr Ben Herbert 1.45%, Dr Richards 1.1%.

With its early to mid-stage stem cell and cancer immunotherapy programs in the human and veterinary spheres, Regeneus has its fingers in some very hot pies.

But investors are waiting for something very specific: a pending licencing deal in Japan for Progenza, an off-the-shelf treatment for osteoarthritis pain.

On the company's indications, they might not be waiting for much longer with a deal expected by early next year or even by Christmas.

Regeneus is already in rarefied company in Japan, having struck a 50:50 partnership with the country's biggest drug manufacturer, AGC.

The licencing partner would fund the phase II trials and be responsible for distribution.

CEO John Martin says Regeneus was interested in five potential licencing partners, which was whittled to three, all of which are currently in due diligence.

In up-front monetary terms, he says the offers are similar.

"It's not a case of whose money is better but whether it will deliver a better outcome in terms of phase II and marketing."

Eyes on Japan

Mr Martin says only 16 Australian companies to date have struck technology licencing deals with the Japanese, who usually are content to buy our coal and iron ore.

Regeneus will follow the path of stem cell leader Mesoblast, which already has an approved product in Japan in alliance with partner JCR: the graft-versus-host disease treatment Temcell, which it acquired from Osiris in 2014.

Cynata is partnered with Fujifilm and is seeking Japanese regulatory approval for its graft-versus-host disease treatment Cymerus.

Mr Martin says normally drug developers focus on the US, but Asia (notably Japan) is much more advanced. In the case of stem cells, the development push comes right from the top: Prime Minister and graft-versus-host disease sufferer Shinzo Abe.

"I don't know of any major stem cell deal where the Japanese aren't on the other side of it," Mr Martin says. "Australian companies are well thought of in this space."

The Regeneus evolution

The brainchild of prolific inventor Prof Graham Vesey, Regeneus was founded in 2007 by Prof Vesey and Dr Benjamin Ross, both of whom have Macquarie University links.

"Stem cells from adipose [or fat] tissue are not super novel, but he came up with a formulation of stem cells based on what they secrete and how they drive the therapeutic effect," Mr Martin says.

The company listed in 2013 after raising \$10 million at 25 cents a share, with an focus was on adipose stem cells in the veterinary sector and then an autologous human product called Hiqcell. (Autologous means the cells are derived from the patient's own tissue.)

Being an autologous product, regulatory approval was not required and Regeneus happily marketed the product for some years through a handful of Gold Coast and Sydney clinics.

But management then twigged that drug companies and clinicians were demanding allogeneic stem cell treatment, that is, using material derived from elsewhere and forming a more convenient off-the-shelf treatment.

Specifically, the company's work centres on a sub-set of secretions called exosomes.

Mr Martin describes these agents as the "first responder at an accident site", in that they give the body the signal to repair a cartilage, rather than being the direct regeneration agent.

Regeneus's key products are Progenza and Sygenus, a topical dermatological treatment for acne. The key difference is that Progenza consists of the cells and the secretions, while Sygenus contains the secretions only.

Does this matter? Well, sort of: Progenza is clearly classified it as a regenerative medicine while Sygenus is more of a biologic, which means a longer approval process.

All about Progenza

Technically speaking, Progenza cells excrete cytokines and growth factors to reduce inflammation and heal damaged and diseased tissue.

In its local phase I study called Step, the company enrolled 20 patients with moderate to severe knee pain.

In May 2017, the company reported the usual safety signals. But it also found a significant and “rapid and sustained” reduction in knee pain, as well as significant improvement in cartilage volumes and “positive signs of disease modification”.

In late 2016, Regeneus signed an exclusive deal with Asahi Glass (AGC), by which the maker of beer (and lots of other stuff) manufactures Progenza for the Japanese market.

Regeneus and AGC also formed a joint venture to develop and commercialize Progenza for osteoarthritis and all inflammatory indications in Japan. The Japanese venture has established a cell production facility at AGC’s Yokohama Research Centre and it is developing processes for commercial manufacture.

Progenza has also been granted Advanced Therapy Medical Therapy (ATMT) classification in Europe. This recognizes Progenza as a regenerative therapy within the EU.

... and Sygenus

Sygenus showed a strong analgesic effect in post-operative pain study, with longer lasting effects compared with morphine.

The study was the “first to demonstrate this effect from mesenchymal stem cells and their secretions”.

With acne, Sygenus in topical gel form showed reduced appearance of lesions after six weeks. With age spots, 95 percent were smaller and 63 percent were smaller and lighter after eight weeks of treatment.

... and dogs

Our four-legged friends aren’t being ignored, either. The company has a program called Cryoshot for canine osteoarthritis and Kvax, a canine cancer vaccine.

No, they’re not barking mad: these are huge markets. Thus far, the company has treated more than 5,000 tail-waggers for osteoarthritis, and has not received a single written complaint.

“It’s a good program,” Mr Martin says. “Not many companies have been able to get through a stem cell product for canine orthopaedics.”

“We have an established relationship with one of the biggest vet pharma companies in the world and we may have something to say about this over the next month or so.”

Finances and performance

Regeneus lost \$5.18 million in 2017-'18 compared with a \$10.1 million profit previously. This sounds like an undesirable trend but the 2016-'17 numbers reflected an \$8.9 million milestone payment from AGC

If the licencing deal is struck, another payment is due in the June quarter of 2019. How much? Think in terms of a \$US5 million payment but also a 50 percent share of any upfront licence fees from a putative clinical partner.

At the end of September, Regeneus held \$2.7 million in cash. The company has a \$1.4 million loan facility from Sydney’s Paddington Street Finance, repayable at the next AGC milestone, the receipt of a 2018-'19 R&D payment or by September 30, 2019.

Otherwise, the company hasn’t raised any equity funding in four and a half years.

Over the last 12 months Regeneus shares have meandered between 10.5 cents in March this year and 23.5 cents in July. They peaked at 60 cents in November 2013.

Dr Boreham’s diagnosis:

The proof of Regeneus’s success lies in sealing the vaunted Japanese deal and we always get nervous when boards nominate timelines for these transactions which are notoriously hard to execute.

As usual, we have the flattering comparison in terms of other global deals. In January, Takeda Pharma, Japan’s biggest pharma company, acquired Belgian regenerative medicine company Tigenix for a cool \$US630 million.

The Regeneus board has been unusually stable and includes the five original directors including chairman and biotech legend Dr Roger Aston.

While the Aston-Martin combination drives the show, a notable addition to the board is veterinarian Dr Glen Richards, a judge on the Shark Tank commercial television show and founder of the listed vet clinic chain (and now takeover target) Greencross.

With the team racing for the finish line, it’s all eyes on the Japanese.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Like the dogs he would love to have his belly fat removed and re-injected to make his knees, wrists and hips work properly again.

CHILDREN'S MEDICAL RESEARCH INSTITUTE

Sydney's Children's Medical Research Institute says it will work with Boston's Logicbio Therapeutics on gene therapies for children with genetic liver and other organ diseases. The Institute said that the two organizations would develop new adeno-associated virus (AAV) vectors to transport a healthy copy of a gene into a patient's cells to either replace or edit the faulty gene.

CMRI said that the program was led by Prof Ian Alexander and Dr Leszek Lisowski and the partnership would involve developing synthetic adeno-associated virus capsids "capable of overcoming many of the current limitations of existing viral vectors".

The Institute said that under the partnership Logicbio it would hold exclusive worldwide commercial rights to developed vectors with the goal of commercializing the new capsids as widely as possible.

Dr Lisowski said the partnership was "confident that we can further improve on the performance of current AAV vectors, expanding their utility in a range of tissues, while also improving manufacturability and reducing cost".

"We're trying to get to a point where instead of a liver transplant in a very young infant, we can genetically repair the liver without major surgery," Prof Alexander said.

"It's a very exciting time to be doing gene therapy," Prof Alexander said.

"At the moment, we can routinely produce vectors in the lab, but to move to much larger clinical scales it is very costly and involves long, overseas waiting times for clinical trials," Dr Lisowski said. "For one person it could be between \$300,000 to \$1 million for a single treatment."

"That means the therapies are not going to be available to most of the public any time soon," Dr Lisowski said.

"We aim to change that, to reduce costs and local waiting times for trials so these cures are more widely and more quickly available," Dr Lisowski said.

"While the initial focus is on liver, the technology has the potential to expand to other disease targets, involving the brain, the heart, kidneys, bone marrow and pancreas," Dr Lisowski said.

Logicbio chief executive officer Fred Chereau said his company was "optimistic that we can significantly improve the performance of AAV vectors through this collaboration".

"These next-generation vectors will strengthen our platform and expand our pipeline [and] we also expect them to bolster other important approaches to genetic medicine, including gene therapies," Mr Chereau said.

The Children's Medical Research Institute said that the New South Wales State Government would provide funding for facilities to manufacture gene transfer vectors in Western Sydney, to be run by Prof Alexander and Dr Lisowski.

AVITA MEDICAL

Avita says it has completed hiring of the 20-member sales team to support the US launch of Recell spray-on skin for acute thermal burns.

Avita said that sales team was "in the process of completing a rigorous training program, including on-site training within burn centres, in preparation for the market launch of the Recell system".

The company said that 32 US burns centres were reviewing Recell or had begun ordering and were taking deliveries of the product.

Avita said the sales team included clinical training specialists to train surgeons and nurses and assist burn centres in their use of the Recell system.

Avita was up 1.6 cents or 19.75 percent to 9.7 cents with 64.4 million shares traded.

STARPHARMA

Starpharma says DEP-docetaxel and DEP-cabazitaxel show “significant” benefits over gemcitabine or albumin-bound paclitaxel for pancreatic cancer in mice.

Starpharma said that its dendrimer enhanced product (DEP) versions of docetaxel and cabazitaxel products, showed “significant efficacy and safety benefits over gemcitabine alone, albumin-bound paclitaxel, marketed as Abraxane, alone and in combination, in the human pancreatic cancer mouse model.

The company said the results “were despite the fact that these standard pancreatic cancer treatments, gemcitabine and/or Abraxane showed limited activity in this model”.

Starpharma said that DEP-cabazitaxel alone and in combination with gemcitabine, and DEP-docetaxel in combination with gemcitabine, resulted in complete tumor regression and 100 percent survival, significantly outperforming each standard treatment, gemcitabine and Abraxane alone and in combination.

The company said that DEP-docetaxel alone significantly outperformed both gemcitabine and Abraxane, in terms of both tumor regression and survival.

Starpharma said that pancreatic cancer was “a leading cause of death among oncologic diseases, with a one-year relative survival rate of 20 percent and a five-year survival rate of seven percent.

The company said that gemcitabine was commonly used both alone and in combination with Abraxane in pancreatic cancer as a first line treatment.

Starpharma said that Abraxane had sales of about \$US1.2 billion and gemcitabine had peak sales prior to patent expiry of \$US1.7 billion.

The company said that DEP-docetaxel was in phase II trials, both alone and in combination with nintedanib and DEP-cabazitaxel was in phase I/II trials.

Starpharma chief executive officer Dr Jackie Fairley said the results for both DEP-docetaxel and DEP-cabazitaxel, showing complete tumor regression and 100 percent survival in this pancreatic cancer model were “very impressive compared with the standard treatments of gemcitabine and/or Abraxane”.

“Given pancreatic cancer has one of the lowest survival rates, it remains an area of significant unmet medical need,” Dr Fairley said.

“These results are particularly interesting given we also observed stable disease for more than 20 weeks in a pancreatic cancer patient with DEP-docetaxel in our phase I trial,” Dr Fairley said.

Starpharma was up 7.5 cents or 5.1 percent to \$1.535 with 1.3 million shares traded.

OPTISCAN IMAGING

Optiscan says that founding director Peter Delaney will resign as chief technology officer on November 22, 2018 and will continue as a consultant.

Optiscan said that Mr Delaney was a founding director in March 1994 and was appointed managing-director in June 1994, through the company’s ASX listing in 1997, before becoming director of technology in 2002, a role he held until May 2016 when he resigned from the board after 22 years and assumed the role of chief technology officer.

The company said that Mr Delaney had “a pivotal role in the technical development and commercialization of Optiscan's patented confocal microscope technology and its application in many areas of pre-clinical and clinical research and clinical practice”.

“We all wish him the very best and thank him for all he has done for Optiscan,” the company said.

Optiscan was up 0.1 cents or 1.6 percent to 6.5 cents.

MEDIBIO (FORMERLY BIOPROSPECT)

After the market closed, Medibio said that board spill resolutions to its annual general meeting associated with Bioprospect's Elias Leo 'The Gun' Khouri failed.

In October, Medibio said shareholders would vote to remove chairman Chris Indermaur and director Andrew Maxwell and appoint Benjamin Richardson, Peta Slocombe and Elias Khouri as directors (BD: Oct 16, 2018)

The company said it had received a Section 249D of the Corporations Act 2001 notice from Mr Khouri and associates to remove Mr Indermaur and Mr Maxwell and appoint Mr Richardson, Ms Slocombe and Elias Khouri as directors (BD: Oct 1, 2018).

Today, the company said the spill resolutions were opposed with more than 101 million votes with more than 21.2 million votes in favor.

Medibio said that the remuneration report earned a first strike with 36,937,102 votes (29.9%) against and 86,431,893 votes (70.1%) in favor.

The company said that the meeting approved the ratification of the prior issue of shares, the 10 percent placement capacity and the election of directors Peter Carlisle, Patrick Kennedy and Dr Franklyn Prendergast.

Medibio was unchanged at 3.8 cents.

THE HYDROPONICS COMPANY

Up to 30.2 percent of votes at the Hydroponics extraordinary general meeting opposed the issue of in-the-money staff options and director shares.

Hydroponics said the strongest opposing vote was to the issue of 2,000,000 options exercisable at 40 cents each to the company's head of hydroponics Jason Colquhoun, with 13,910,356 votes (30.2%) against and 32,103,795 votes (69.8%) in favor.

The company said that all resolutions faced dissent with all but two of the 13 resolutions opposed by 19 percent of voters or more.

In October, Hydroponics said it proposed to issue chief executive officer Ken Charteris 4,000,000 options, pending performance conditions and exercisable at 75 cents and \$1.20; Jason Colquhoun 2,000,000 options exercisable at 40 cents by December 31, 2020; chairman Steven Xu 190,000 shares; and directors Lou Cattelan and Gary Radcliff 95,000 shares each; along with votes on the employee option plan, the prior issue of shares and options, approve the 10 percent placement capacity and change the company name to THC Global Group (BD: Oct 12, 2018)

Hydroponics closed at 53 cents on October 12, 2018.

The company's most recent Appendix 3B new share issue announcement said it had 89,373,122 shares quoted on the ASX, 37,514,450 shares in escrow or 126,887,572 shares in total, meaning the opposition to Mr Colquhoun's options was 10.96 percent of the shares in the company, sufficient to requisition extraordinary general meetings.

Separately, Hydroponics said its wholly-owned subsidiary Vertical Canna Inc had "a binding agreement to conduct due diligence" to buy an unnamed Canadian company which was becoming a licenced producer of cannabis.

The company said that on acquisition, it would build "a full-scale cannabis growing facility ... able to offer direct retail sales in addition to supporting other commercial sales".

Hydroponics said its objective was for Vertical Canna "to pursue a build out of a vertically integrated cannabis business across North America through strategic acquisitions and partnerships with a focus on short paths to profitability with strong potential for value development ... [and] Vertical Canna is currently developing a new retail cannabis and equipment brand which will soon be available across stores in Canada".

Hydroponics fell half a cent or 0.9 percent to 54 cents.

PAINCHEK

Painchek says it has received \$751,385 from the Australian Tax Office under the Federal Government Research and Development Tax Incentive program.

Painchek said the rebate related to research and development activities for the year to June 30, 2018.

Painchek was up 0.3 cents or 6.7 percent to 4.8 cents.