Biotech Daily

Friday August 7, 2020

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: KAZIA UP 57%; AMPLIA DOWN 7%**

*** DR BOREHAM'S CRUCIBLE: EXOPHARM**

*** 4D OPENS UP 98% IN OVERSUBSCRIBED $56m IPO FOR IMAGING**

*** KAZIA: FDA RARE KIDS DISEASE STATUS FOR PAXALISIB FOR DIPG**

*** G MEDICAL $5m PLACEMENT**

*** ALLEGRA IMPROVES SPINAL FUSION CAGE IN COVID-19 DELAYS**

*** SOUTH KOREA ALLOWS CYNATA CYMERUS STEM CELL PATENT**

*** M&G REDUCES TO 11% OF MESOBLAST**

*** KARST PEAK, ADAM LEITZES REDUCE TO 11% IN GENETIC SIGNATURES**

*** DIRECTOR MICHAEL STORK DILUTED TO 7% IN PATRYS**

*** PAINCHEK REQUESTS 'CAPITAL RAISING' TRADING HALT**

*** ADALTA REQUESTS 'CAPITAL RAISING' TRADING HALT**

*** REGENEUS REQUESTS 'JAPANESE LICENCING DEAL' TRADING HALT**

*** PRESCIENT APPOINTS PROF PHILLIP DARCY ADVISOR**

*** MGC: 'IN-VITRO STUDY BACKS ARTEMIC FOR COVID-19'**

MARKET REPORT

The Australian stock market fell 0.62 percent on Friday August 7, 2020, with the ASX200 down 37.4 points to 6,004.8 points. Fifteen of the Biotech Daily Top 40 stocks were up, 19 fell and six traded unchanged. All three Big Caps fell.

Kazia was the best, up 32 cents or 57.1 percent to 88 cents with 8.7 million shares traded. Osprey and Telix climbed more than six percent; Oncosil improved 4.55 percent; LBT and Cynata were up more than three percent; Antisense, Medical Developments and Mesoblast rose two percent or more; Avita, Nova and Pro Medicus were up more than one percent; with Neuren, Starpharma and Volpara up by less than one percent.

Amplia led the falls, down one cent or 7.4 percent to 12.5 cents, with 608,861 shares traded. Alterity lost 7.1 percent; Resonance retreated 6.7 percent; Actinogen fell four percent; Cyclopharm, Genetic Signatures and Resmed lost more than three percent; Clinuvel, Compumedics, Impedimed and Uscom shed more than two percent; CSL Imugene, Nanosonics, Opthea, Orthocell, Polynovo and Prescient were down more than one percent; with Cochlear, Next Science, Paradigm and Proteomics down by less than one percent.

DR BOREHAM'S CRUCIBLE: EXOPHARM

By TIM BOREHAM

ASX code: EX1

Share price: 28.5 cents

Market cap: $27.2 million

Shares on issue: 95,472,000

Chief executive officer: Dr Ian Dixon

Board: Jason Watson (chair), Dr Dixon, David Parker

Financials (June quarter 2020): revenue nil, cash outflows $2.15 million, cash on hand $1.74 million, quarters available cash 0.81.

Identifiable major shareholders: Altnia Holdings (Dr Dixon) 29.3%, Michael Francis McMahon/Susan Lesley McMahon 2.4%, Oldview Enterprises (The Priestley Account) 1.5%, Anthony John Locantro 1.4%.

Given the scientifically complex nature of Exopharm's quest to develop exosomes into therapeutics, it's good to see that founder and chief executive Ian Dixon hasn't lost sight of the commercial basics.

He says: "Biotechnology is about spending investors' money to get to some kind of revenue - or a big deal - while building value along the way with many steps."

Indeed.

With Exopharm in early clinical stage, there are many more baby steps required before the company can claim any success with harnessing exosomes, which are touted as an alternative to stem cell therapies.

Dr Dixon reminds investors of the great experience with penicillin, which was discovered and then developed through hard graft (and a dose of serendipity).

"Out of the greatest of crises some of the greatest discoveries are made and two or three great minds can make a huge difference," he says.

Exopharm was founded by Dr Dixon, who also co-founded the ASX stem-cell play Cynata Therapeutics. He was also a director of the previously ASX-listed Cell Therapies, which produced adult stem cells for the pure-play stem cell champion Mesoblast.

Exopharm listed on the ASX on December 2018, having raised $7 million at 20 cents apiece.

What are exosomes?

For those too afraid to ask, exosomes are small particles produced by cells that deliver therapeutic properties to other cells to reduce inflammation or promote regeneration.

Trillions of exosomes are produced by stem cells, but like hair follicles they decline with age. Exosomes are also known as extracellular vesicles, or EVs, but have nothing to do with Teslas or other electric vehicles.

Exopharm is developing two products. The first is naïve EVs, which are made from stem cells and platelets and designed to be a new class of regenerative medicine.

A new discipline, engineered extracellular vesicles are the result of drugs or proteins being added to the vehicles to create new treatments for specific viruses, cancers, cardiac diseases, infectious and neurological conditions and even erectile dysfunction.

But much of the exosome challenge lies in extracting and purifying the agents as drug products, with clinical progress slowed by manufacturing limitations. So, it's just as well Exopharm holds a technology called ligand-based exosome affinity purification (Leap), which allows for efficient manufacturing.

Exopharm chief commercial officer Dr Chris Baldwin says Exopharm's strategy is to solve the manufacturing problems using naïve exosomes and then play with engineered EVs.

"EVs are how stem cells work," he says. "They contain RNA (ribonucleic acid) instructions inside and get sent out into the body to tell the cells how to grow and adapt."

The clever extracellular vesicles also have a dressing on the outside to ensure the messages are embedded in the cells in the desired way.

Dr Baldwin notes that many developers of mesenchymal stem cell therapies are refocusing on the active ingredients - exosomes - because they can be turned into an off-the-shelf product in a more economic and safer way.

"With our Leap technology we are creating the capacity to extract the active ingredient and turn it into something that can be commercialized."

Clinical delays

Exopharm holds the claim to fame of being the first company to launch a human clinical trial with an autologous exosome drug candidate, via its Plexoval I study. (Autologous material is obtained from the same individual).

The 20-patient study aimed to evaluate the safety, tolerability and biological activity of its initial EV product called Plexaris, for wound healing. The first human guinea pigs were dosed in January, with one 15-strong cohort assessed on wound healing and the remaining five appraised for "biological activity".

But then along came the cursed Covid-19 and on April 1 the company said the trial was suspended, with recruitment numbers likely to be reduced. It was no joke.

Management now hopes for a restart and is also eyeing a safety trial of a variant allogeneic (off the shelf) prospect, Plexaris OS (as in off-the-shelf, not actually overseas), aimed at conditions including dry aged -related macular degeneration.

The company has also engineered Plexaris as Plexodox, which has undergone in vitro testing as an anti-cancer agent.

Plexodox was loaded with the off-patent cancer drug doxorubicin, with the Petri dish results showing the combo killed “considerably more” lung cancer cells than doxorubicin itself.

While off-patent, doxorubicin is a commonly used treatment generating $1 billion of revenue a year. It is hoped that Plexodox will increase its efficacy at lower doses and reduce side effects.

Did someone mention Covid-19?

Yep, you gotta have a Covid-19 angle these days.

Exopharm is designing extracellular vesicles to produce an effect that Dr Baldwin dubs “flattening the curve within the body”.

You see, viruses are so dangerous because they interfere with the process of the extracellular vesicles delivering the messages. In effect they turn the cell into a virus factory, with the multiplied germs released into the bloodstream.

With the coronavirus, the outside ‘spike’ proteins enable the virus to enter cells with an angiotensin-converting enzyme 2 (ACE2) receptor on the outside. Once inside the cell, the RNA allows for virus replication.

Exopharm is working on an engineered EV product, Fortrexo Cov that would defeat the virus’s cunning replication strategy by sending out RNA instructions of its own.

Dr Baldwin adds the platform may be applicable to other diseases such as Huntington’s disease and glioblastoma (brain cancer): anything that needs an “internal agent of action”.

New digs, same gig

Via the safety of a webinar, the company recently showcased its new facility at the Baker Institute, in Melbourne’s appropriately-named Commercial Road.

The premises merges the company’s hitherto separate manufacturing and research digs and was done at the height of the Covid-19 plague allowing key experiments to re-start two days later.

“We used literally anything our scientists could borrow from our partner institutions,” says chief operating officer Gregor Lichtfuss.

“To be able to drive our developments efficiently we need to be able to do it ourselves … and control the entire development and manufacturing process. Only then will we be able to be truly masters of our own destiny.”

Dr Lichtfuss describes the company as “tightly integrated in the Melbourne biosciences ecosystem”. In particular, it has research facilities with two leading hospitals and three research bodies: “relationships that give us access to world-leading technologies and experts”.

Finances and performance

As of June 30, 2020, Exopharm had a cash balance of a tad over $1.7 million, which is a little too slender for comfort. Fortunately, management isn’t exactly splashin’ it about on travel to international conferences, so lockdowns do have their silver linings.

“Exopharm’s finances are in good shape and we are being very careful with the cash we have, using the money to make advances and produce results,” Dr Dixon says.

“We have cut back on some costs to preserve the runway and keep our people confident about their employment.” (The company has 25 full-time equivalent staff).

Dr Dixon says the company should be able to start its second Plexoval study (the allogeneic one) with existing funding. Beyond that, funding options include non-dilutive sources such as partnering, but these routes are time consuming with uncertain results.

“Funding will continue to come from our investors who understand the story and see the potential of exosomes as the new mode of medicine,” he says. “We will adjust our activities to match the funding we have access to.” As you do.

Exopharm shares plunged from 35 cents on February 12 this year to a record low of 14.5 cents on March 23, in what might turn out to be the shortest and sharpest market ‘flash crash’ in history. The shares peaked at 61 cents on February 1, 2019.

Hurry, hurry!

Despite the progress and promise, Dr Dixon admits the company is “not building value as fast as we would like to, or need to.” He adds: “we need to move fast or we will be overrun by others”.

For example, exosome developers Evox Therapeutics in the in the UK and Codiak in the US have done four big pharma deals between them in the last two years, with $US50 million plus up-front payments and potential billion-dollar milestones.

As of January, at least three rivals aimed to start trials this year, with several more, close behind.

“Some of these companies are pivoting into exosome product development after previously focusing on stem cell research,” Dr Dixon says.

While EVs are mooted as a replacement for stem cell therapy, Dr Baldwin believes the two approaches are complimentary.

“It will never be a low-cost treatment,” he says. “A vast majority of patients that are treated with stem cells can be treated with EVs with better consequences.”

Dr Boreham’s diagnosis:

Dr Baldwin notes that it’s one thing to have active ingredients that work and another thing to have a commercial product.

But he deploys a 2400-year old analogy to prove there are precedents for commercializing a therapy such as naïve EVs.

“If you were a Greek with a headache, you would go to Hippocrates and he would hand you a packet of bark to make some tea,” he says.

The remedy worked, but the active ingredient didn’t turn into a proper medicine until 1888 when Bayer introduced acetylsalicylic acid (or Aspirin as we better know it) – and became one of the biggest pharma companies on the back of that magic bark.

Dr Dixon draws similarities with the $2.3 billion ASX stem cell leader Mesoblast, in that both companies have platform technologies that can be used for multiple purposes.

Apart from the cell/non-cell distinction, the duo’s business models are similar: “manufacture the products and show they are safe and effective and take products into partnerships and sales”.

Still, we stress again that Exopharm is at an early stage and its development will be governed by what is - or isn’t - in the kitty.

And speaking of which, it’s an ideal time to raise capital, with investors amenable to anything with a coronavirus angle.

Dr Baldwin, by the way, reckons we shouldn’t get too excited about the company curing coronavirus anytime soon.

“I really hope it doesn’t because we are really not close to something,” Dr Baldwin says.

“We hope a vaccine comes along well before us. But it demonstrates our technology and if it successful this is what we’ll use for Covid-23 or Covid-25.”
Perish the thought!

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He is thus not bound by the Hippocratic Oath but did let out a few when he hit his thumb with a hammer the other day.

4D MEDICAL (FORMERLY 4DX)

4D opened on the ASX at $1.47, a 98.0 premium to its 73 cents price in its $55.79 million initial public offer to commercialize its non-invasive respiratory imaging platform.
In July, 4D said the XV technology was a four-dimensional lung imaging technology that used mathematic models and algorithms to convert X-ray scans into quantitative data to help physicians manage patients with respiratory diseases (BD: Jul 8, 2020).
The company said at that time, the XV technology was designed to be compatible with existing hospital equipment and was delivered through an internet-based 'software-as-a-service' model for hospitals and clinics on a pay per use basis.
4D said its XV Technology had US Food and Drug Administration 510(k) approval, was currently sold in the US and it had 43 patents and applications, included 15 granted patents in the US, Australia, the European Union and Asia.
Today, 4D said it had 264,762,406 shares and 20,666,069 options on issue and the fully underwritten $55.79 million capital raising valued the company at $193.28 million.
At the closing price of $1.59 the 4D market capitalization is $420.97 million.
4D said the offer proceeds would be used for marketing, clinical trials and trade shows, operating expenditure, research and development, US sales and distribution, intellectual property and trademarks, and to pay selling shareholders and selling holders.
The company said its board comprised chair Bruce Rathie, managing director Dr Andreas Fouras, non-executive directors Li Bianchi, Dr Robert Figlin, Lusia Guthrie, John Livingston and Julian Sutton and executive director Heath Lee.
The company said its management team included chief executive officer and founder Dr Fouras, chief financial officer Mr Lee, company secretary Charlene Stahr, head of engineering Aidan Jamison and head of sales and marketing Paul Cooke.
4D said Bell Potter Securities and E&P Corporate Advisory were joint lead managers.
4D climbed closed up 86 cents or 117.8 percent at $1.59 with 37.2 million shares traded.

KAZIA THERAPEUTICS

Kazia says it has US Food and Drug Administration rare paediatric disease designation for its Paxalisib, or GDC-0084, for diffuse intrinsic pontine glioma.
Kazia said diffuse intrinsic pontine glioma was a rare and highly-aggressive childhood brain cancer.
In 2018, the company said the FDA had granted orphan drug designation to GDC-0084 for the brain cancer glioblastoma multiforme (BD: Feb 23, 2018).
Today, Kazia said rare paediatric disease designation (RPDD) could be granted to drugs in development for serious or life-threatening diseases which primarily affect children and had fewer than 200,000 new cases a year in the US.
The company said that designation gave potential access a priority review voucher at the time of a marketing authorization for diffuse intrinsic pontine glioma (DIPG).
Kazia chief executive officer Dr James Garner said that "although glioblastoma remains our primary focus for Paxalisib, we have been devoting increasing energy to developing the drug in childhood brain cancer as well".
"For patients diagnosed with DIPG, there are currently no FDA-approved drug treatments, and the average survival from diagnosis is around 9.5 months," Dr Garner said.
"The granting of RPDD by the FDA recognizes our efforts and achievements so far and leaves us well placed to move Paxalisib forward as a potential therapy for DIPG," Dr Garner said.
Kazia was up 32 cents or 57.1 percent to 88 cents with 8.7 million shares traded.

G (GEVA) MEDICAL INNOVATIONS

G Medical says it has “firm commitments from institutional and professional investors” to raise $5 million in a placement at five cents a share.
G Medical said the funds would be used to scale up its diagnostic testing facility operations, expand its US sales team and increase manufacturing volumes of the Prizma device and G Medical Patch to fulfill anticipated orders.
G Medical said Sydney’s MST Financial was the lead manager of the placement.
G Medical fell 0.7 cents or 11.1 percent to 5.6 cents with 7.7 million shares traded.

ALLEGRA ORTHOPAEDICS

Allegra says that Covid-19 restrictions have delayed the study of its spinal fusion cage device in sheep, but it has used the time to improve device.
Last year, Allegra said it had begun a trial in Lyon, France of its biodegradable strontium-hardystonite-Gahnite (Sr-HT-Gahnite) spinal fusion cage for bone neck fusion in sheep (BD: Nov 15, 2019).
Today, the company said it had to delay the implantation of the last group of sheep but had used the time “to implement recent advancements in 3D printing technology” which improved the device.
Allerga said that it had observed fractures of the implants during the six-month study, as the neck mobility and the domed shape of the sheep cervical inter-vertebral disc were significantly different to human cervical spine, on which the design was based.
The company said the revised design would improve the strength of the implant significantly and allow for the physiological differences in the animal model.
Allegra said it expected to resume with the study in January 2021, subject to restrictions, and the confirmatory clinical trial in Australia would be delayed.
Allegra was up 1.5 cents or 6.4 percent to 25 cents.

CYNATA THERAPEUTICS

Cynata says that South Korea’s Intellectual Property Office has allowed a patent application covering its Cymerus mesenchymal stem cell technology.
Cynata said the patent, titled ‘Methods and materials for haemato-endothelial differentiation of human pluripotent stem cells under defined conditions’, would cover the ability to manufacture mesenchymal stem cells from a single donation to create therapeutic stem cell products and provided commercial rights until March 12, 2034.
The company said that the patent was owned by the University of Wisconsin–Madison’s Wisconsin Alumni Research Foundation and exclusively licenced to Cynata.
Cynata was up 2.5 cents or 3.9 percent to 67 cents.

MESOBLAST

M&G Investment Funds says it has reduced its substantial holding in Mesoblast from 72,470,118 shares (12.48%) on May 18 to 65,668,769 (11.24%) on August 5, 2020.
The London-based M&G said the previous notice was given on May 18, 2020.
On May 27, M&G said it reduced its holding in Mesoblast from 70,636,115 shares (13.15%) to 70,068,935 shares (12.05%) (BD: May 27, 2020).
Today, M&G said it sold shares between May 22 and August 5, 2020, with the single largest sale 3,030,445 shares for $13,152,295 or $4.34 a share.
Mesoblast was up 10 cents or 2.3 percent to $4.40 with 8.4 million shares traded.

GENETIC SIGNATURES

Karst Peak Capital and Adam Leitzes say they have reduced their holding in Genetic Signatures from 18,934,528 shares (13.30%) to 15,934,528 shares (11.17%).
The Hong Kong and Cayman Islands-based Karst Peak and Mr Leitzes said that on August 5, 2020 they sold 3,000,000 shares for $7,350,000 or $2.45 a share.
Genetic Signatures fell nine cents or 3.6 percent to $2.40.

PATRYS

Patrys director Michael Stork and Stork Holdings say their 98,773,814 shares in Patrys have been diluted from 9.20 percent to 6.91 percent.
The Ontario, Canada-based Mr Stork said the shares were diluted on August 5, 2020 following a share issue by the company.
Earlier this week, Patrys said it had applications for $1,789,620 in its fully-underwritten entitlement offer at 1.2 cents a share to raise $4,290,371 (BD: Aug 4,2020).
Patrys was unchanged at 1.3 cents with 7.2 million shares traded.

PAINCHEK

Painchek has requested a trading halt pending the “announcement of a capital raising”.
Trading will resume on August 11, 2020 or on an earlier announcement.
Painchek last traded at 13 cents.

ADALTA

Adalta has requested a trading halt “for the purpose of considering and executing a capital raising”.
Trading will resume on August 11, 2020 or on an earlier announcement.
Adalta last traded at 10.5 cents.

REGENEUS

Regeneus has requested a trading halt “pending an announcement … in relation to a licencing agreement in Japan”.
Trading will resume on August 11, 2020 or on an earlier announcement.
Regeneus last traded at 11 cents.

PRESCIENT THERAPEUTICS

Prescient says it has appointed Prof Phillip Darcy to its scientific advisory board.
Prescient said Prof Darcy was the head of cancer immunotherapy at Melbourne’s Peter MacCallum Cancer Centre, a chimeric antigen receptor-T (CAR-T) expert, and a National Health and Medical Research Centre senior research fellow.
Prescient fell 0.1 cents or 1.7 percent to 5.7 cents with 1.8 million shares traded.

MGC PHARMACEUTICALS

MGC says pre-clinical in-vitro laboratory tests has shown that its Artemic could be used "as an immune-modulatory agent for the treatment of Covid-19".

MGC said in-vitro studies at Israel's Myplant Bio research laboratory "were designed to test the effect of Artemic and its ingredients, consisting of artemisinin, vitamin-C, curcumin [and] Boswellia serrata, on responses of human peripheral blood mononuclear cells to inflammatory stimuli".

Last week, the company said its mouse study of Artemic for severe acute respiratory syndrome coronavirus-2 (Sars-Cov-2) showed no adverse results in standard toxicity measures (BD: Jul 27, 2020).

MGC was up 0.3 cents or 13.6 percent to 2.5 cents with 107.3 million shares traded.