Biotech Daily

Friday September 21, 2018

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: LBT UP 14%; ELLEX DOWN 13%**

*** DR BOREHAM'S CRUCIBLE: PARADIGM BIOPHARMA**

*** US FDA APPROVES AVITA RECELL FOR SEVERE BURNS**

*** ELLEX TRIAL MISSES ENDPOINT; AMD PROGRESS SLOWED TREND**

*** IMUGENE HIRES AMBIOPHARM FOR KEY-VAXX; PATENT APPLICATION**

*** ACRUX DIRECTOR 'RIGHTS', POTENTIAL SPILL AGM**

*** IDT AGM TO VOTE ON DIRECTORS, POTENTIAL 2nd STRIKE SPILL**

*** OBJ 60% DIRECTORS FEES HIKE, POTENTIAL SPILL AGM**

*** COGSTATE AGM TO VOTE ON 1m CEO BRAD O'CONNOR OPTIONS**

*** FIL TAKES 10.5% OF RESAPP**

*** MGC REQUESTS 'CANADA MARIJUANA DEAL' TRADING HALT**

*** MEDIBIO DIRECTOR JACK COSENTINO OUT, JENNIFER SOLITARIO IN**

MARKET REPORT

The Australian stock market was up 0.41 percent on Friday September 21, 2018 with the ASX200 up 25.1 points to 6,194.6 points. Twenty-two of the Biotech Daily Top 40 stocks were up, nine fell, five traded unchanged and four were untraded. All three Big Caps rose.

LBT was the best, up 1.5 cents or 14.3 percent to 12 cents with 4,670 shares traded. Cyclopharm climbed 10 percent; Avita improved 8.9 percent; Neuren was up 7.2 percent; both ITL and Pro Medicus were up 6.7 percent; Mesoblast and Orthocell climbed more than five percent; Dimerix, Imugene, Osprey and Polynovo improved more than four percent; Clinuvel, Nanosonics, Oncosil and Opthea rose more than two percent; Actinogen, Factor, Medical Developments, Paradigm and Pharmaxis were up more than one percent; with Cochlear, CSL, Resmed and Volpara up by less than one percent.

Ellex led the falls, down 11 cents or 13.3 percent to 71.5 cents with 1.4 million shares traded. Airxpanders lost 9.1 percent; Reva was down 7.4 percent; Prescient fell 5.4 percent; Benitec and Impedimed lost more than three percent; with Genetic Signatures, Starpharma and Telix down by less than one percent.

DR BOREHAM'S CRUCIBLE: PARADIGM BIOPHARMA

By TIM BOREHAM

ASX code: PAR

Share price: 94 cents

Shares on issue: 126,273,316

Market cap: $118.7 million

Chief executive officer: Paul Rennie

Board: Graeme Kaufman (chairman), Paul Rennie, John Gaffney, Christopher Fullerton

Financials (year to June 30, 2018): revenue $53,899 (up 110.4%), loss of $6.2 million (up 44.8%) cash of $2.4 million (down 5.6%).

Identifiable holders: Paul Rennie 18.1%, MJGD Nominees (technology vendor) 4.9%, other board and management 2.8%, Irwin Biotech (technology vendor) 4.3%.

***** Bank interest

****** The company received $955,317 from the exercise of in-the-money options during the quarter and then a further $464,285 in July. It is expected to bank a further $571,428 by the end of August.

It's a case of everything old is new again at Paradigm, which is seeking to repurpose a very old drug for orthopaedic and viral arthritic indications.

When it comes to spruiking the virtues of Paradigm's anti-inflammatory lead compound pentosan polysulfate sodium (PPS), Adelaide stockbroker David Baker speaks from personal experience.

A partner of Paradigm's house broker Baker Young, Baker has used PPS injections to clear up his arthritis.

Baker is not PPS's only advocate: the drug is widely used by 40 to 50 past and present AFL footballers to clear up knee and joint complaints and osteitis pubis, or groin inflammation.

Former Carlton and Adelaide star and Brownlow medalist Greg 'Diesel' Williams says PPS turned him from a virtual cripple to a re-energized guy able to go a full round of golf.

It had similar restorative effects on former Carlton high flyer (literally) Andrew Walker.

“He could hardly walk between practice sessions and had every available therapy thrown at him - but didn’t respond to any of it,” says Paradigm chief Paul Rennie. “He is now running between 20 and 30 kilometres a week and has no knee pain and is playing [country] football again.”

Other than dodgy knees (osteoarthirits and bone marrow oedema lesions), current targets are viral arthritis, Ross River virus and Chikungunya (not a Sri Lankan village but like Ross River a viral infection spread by mosquitoes).

Phase I work relates to allergic rhinitis (yep, hay fever), chronic obstructive pulmonary disease and allergic asthma - proving that the plural of anecdote is not evidence.

Last year the company’s phase IIa hay fever trial didn’t meet its primary endpoints, having touted that it could earn $1 billion a year. The company blamed the formulation, so back to the drawing board on that one.

A new sense of purpose for old drug

Used in humans for more than 60 years, PPS is a semi-synthetic drug made from beech-wood hemicellulose.

Johnson & Johnson sells an oral formulation under the name Elmiron, to treat a painful bladder disease called interstitial cystitis. PPS is also used to treat deep vein thrombosis.

Paradigm secured a 20-year agreement Germany’s Bene Pharmachem, which makes the only US Food and Drug Administration-approved form of PPS.

Paradigm then listed on August 18, 2015, having raised $8 million at 35 cents apiece in an oversubscribed raising.

Paradigm’s driving forces are 18 percent shareholder Mr Rennie and chairman Graeme Kaufman.

Mr Rennie was Mesoblast’s head of product development. Mr Kaufman needs no introduction as former chairman of Bionomics and IDT, a former Cellmid director and continuing IDT director. He also was chief financial officer at CSL and an executive vice-president at Mesoblast.

Repurposing a drug means much lower development costs.

There’s also a 25 percent chance of successful development compared with 10 percent for a de-novo drug, with the development timeline abbreviated from 10 to 17 years to three to five years.

Paradigm intends to pursue the FDA’s 505(b) (2) pathway, by which the company can use historical data, in this case from Bene Pharmachem, to support the application.

About 30 percent of approved new drugs are either reformulated drugs or combination drugs, so Paradigm's approach is not especially unusual.

Paradigm also has the rights to a line of exosomes, which are bodies secreted by human cells and linked to the regeneration characteristics of stem cells.

Clinical progress

In all about 400 patients (mainly osteoarthritis sufferers) have been treated with PPS under the Therapeutic Goods Administration's special access scheme.

The latest clump of results for 25 osteoarthritis patients reported a 60 percent reduction in pain (as self-assessed by the patient) after six weeks of treatment.

Across 100 patients, the average pain reduction to date has been a little over 50 percent.

Of course, this "real world" stories of broker's dodgy joints and footy stars' knackered knees does not amount to clinical evidence. Hence, the company has launched two key formal clinical trials for osteoarthritis and Ross River virus.

Paradigm has just finished recruiting 126 patients for the osteoarthritis trial, a randomized, double-blinded, placebo-controlled effort across six Australian sites.

The patients have concurrent bone marrow lesions, which result from fluid build-up in the bone marrow, which is generally the result of a ruptured anterior cruciate ligament or degenerative osteoarthritis.

First results from this trial are expected in the December quarter. Paradigm has also recruited 20 patients for its phase IIa Ross River trial.

But last year its shares halved in value after the 80-patient phase IIa trial for allergic rhinitis failed to meet its primary endpoint.

Fast-track approval

Mr Rennie notes that for a 505 (b) application, the "real world" data can supplement the clinical data and enhances the chances of approval.

"Given the fact we are targeting chronic pain, the likelihood of fast-track approval is very high," he says.

He hopes for a small pivot trial of as few as 100 patients, rather than the usual thousands. The slimmed-down requirement raises the prospect of Paradigm funding the drug to approval stage, rather than finding a partner (which is always an option).

Initial results are expected this quarter for the Ross River trial and by the end of the calendar year for the orthopaedic trials.

Financial and performance

With a cash balance of around $4 million, Paradigm says it is adequately funded for the current trials, with potential capacity fund any phase III stuff.

Paragon received $955,317 from the exercise of in-the-money options during the quarter and then a further $464,285 in July. It expects to bank a further $571,428 by the end of August and the company also expects a $2 million Federal Research and Development Tax Incentive in September.

Paradigm shares have more than trebled over the last year and have traded as high as 96 cents in mid-July this year, and as low as 25 cents in August last year.

Dr Boreham's diagnosis

Surely there's no market for an effective remedy for dodgy knees and joints?

Just kidding!

The size of the global osteoarthritis market is estimated at $US5 billion a year, with 33 million creaky Americans alone suffering these ailments and a further three million here.

Mr Rennie points to a number of recent transactions that should spur investors. For example, in July last year Servier paid $US346 million for the European rights to Galapogas, an oral therapy for osteoarthritis.

If anything, Paradigm's closest cousin is the Nasdaq-listed Flexion, which has had a drug approved for slow-release corticosteroids.

"It's a good proxy for us in terms of market cap and clinical trial design," Mr Rennie says.

While the ongoing results of the special access program are encouraging, investors will be holding their breath for the first phase IIb results by the end of this year.

"This will be a major inflexion point for us," Mr Rennie says. "It will be one of the first clinical trials worldwide for a non-opioid, non-steroid based treatment."

Of course, with all inflexion points the trial results have to inflex the right way.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He goes weak-kneed at the suggestion of a cure for dodgy joints.

AVITA MEDICAL

Avita says the US Food and Drug Administration has approved its Recell wound treatment for severe thermal burns in patients 18 years and older.

Avita said that its Recell point-of-care, spray-on skin had been approved to treat second and third-degree burns with sales expected to begin before the end of 2018.

In 2008, the then Clinical Cell Cultures said that following its merger with Visiomed to become Avita, it would begin the regulatory approval process for the Prof Fiona Wood-invented Recell, having shelved Cellspray and Cellspray XP (BD: Jun 4, 2008).

An Avita executive told Biotech Daily that Recell first received Conformité Européenne (CE) mark in 2005 and Australian Therapeutic Goods Administration approval in 2006.

In a teleconference today, chief executive officer Dr Mike Perry said he expected a US paediatric registration-directed trial to begin in the next one or two weeks.

Dr Perry said that in the US, 500,000 patients a year were admitted to hospital with severe burns, with 3,400 deaths from burn injuries each year.

Avita said the addressable market for Recell was about $US200 million ($A274.3 million).

Dr Perry said that the Recell skin harvesting system would sell for about $US5,000 to $10,000 per kit with each kit able to cover up to 10 percent of body area wounds.

In a media release, Avita said that two randomized, controlled clinical trials supporting the FDA approval showed that treatment of acute burn wounds with the Recell system required substantially less donor skin than required with conventional split-thickness autografts to achieve closure of burn wounds.

Avita said that the reduction in donor skin requirements provided clinical benefits to patients and significant reductions in the cost of treatment.

“Today’s approval of the Recell system marks an important milestone for us and provides a new way to treat burns for the thousands of patients with significant unmet medical needs,” Dr Perry said.

Dr Perry said the company appreciated its collaboration with the US Biomedical Advanced Research and Development Authority (BARDA) which had funded recent trials and supported Recell development.

Avita said the Recell system could be used alone in the treatment of partial-thickness burns, or in combination with autografting for the treatment of full-thickness burns.

The company said that a small skin sample was collected and immersed in its proprietary enzyme solution to separate the skin cells to produce the spray and the resultant suspension included keratinocytes, fibroblasts and melanocytes, which played “a critical role in wound healing”.

“The suspension is then sprayed directly onto the prepared burn wound, providing a broad and even distribution of live cells across the entire wound bed,” Avita said.

The company said Recell could treat a wound up to 80 times the donor sample, so a sample about the size of a credit card could cover a patient’s entire back.

Avita said its first US Recell trial compared treatment against conventional split-thickness autografts in patients with deep partial-thickness, or second-degree, burn injuries and showed that Recell required 97.5 percent less donor skin than standard-of-care, resulting in a statistically significant reduction in pain, increased patient satisfaction, improved donor scar outcomes and wound closure comparable to standard-of-care.

The company said the second trial showed that Recell with split-thickness autografts for third degree burns used 32 percent less skin than standard-of-care ($p < 0.001$).

Avita said that in addition to the two trials, Recell had been used for more than 90 burn patients under an FDA compassionate use program and more than 65 patients under an FDA continued access program.

Avita was up 0.8 cents or 8.9 percent to 9.8 cents with 31.2 million shares traded.

ELLEX MEDICAL LASERS

Ellex says its 292-patient, laser therapy trail for intermediate age-related macular degeneration missed its primary endpoint, but showed a trend to slow progress.

Ellex said that the three-year, randomized, multi-centre 'Lead' trial showed a reduction in the rate of progression to late stage age-related macular degeneration (AMD) in 76 percent of patients who received the retinal rejuvenation (2RT) treatment.

The company said the primary endpoint was progression to late AMD in the treated eye of 2RT patients, with 13.6 percent of the 2RT group and 17.2 percent of the control group developing late AMD (p = 0.122).

"Although not statistically significant, there was a trend favoring the Ellex 2RT treatment group," Ellex said.

The company said that "post hoc analyses showed that intervention with Ellex 2RT in patients who did not have co-existent reticular pseudo-drusen at the start of the trial (76% of patients) resulted in a significant treatment effect (p = 0.002) and a clinically meaningful 77 percent reduction in the rate of progression from intermediate to late AMD versus placebo".

Ellex said that the purpose of the Lead trial was to investigate the safety and efficacy of nano-second laser treatment as a prophylactic intervention for the early stages of AMD to slow progression.

Ellex said that the principal trial investigator was Melbourne's Centre for Eye Research Australia head of macular research and deputy director Prof Robyn Guymer.

The study results article, titled 'Sub-Threshold Nanosecond Laser Intervention in Age-Related Macular Degeneration: The LEAD Randomized Controlled Clinical Trial' was published in the journal Ophthalmology, with an abstract available at: https://www.aaojournal.org/article/S0161-6420(18)32135-3/fulltext.

The journal article reported that progression was slowed for the 222 (76·0%) participants without co-existent reticular pseudo-drusen (RPD) at baseline (p = 0.002) while an increased progression rate was observed for the 70 (24·0%) participants with RPD with sub-threshold nanosecond laser intervention treatment (p = 0·002) and differences between the groups in serious adverse events were not significant.

The article concluded that sub-threshold nanosecond laser intervention "may have a role in slowing progression for those without coexistent RPD and may be inappropriate in those with RPD, warranting caution when considering treatment in clinical phenotypes with RPD".

"Our findings provide compelling evidence for further trials of the 2RT laser, but they should not be extrapolated to other short pulse lasers," the article concluded.

Ellex chief executive officer Tom Spurling said that the significant reduction in the risk of progression to late AMD in the large subset of patients without coexistent RPD "confers a significant first-mover advantage for our proprietary Ellex 2RT technology in these patients".

"As indicated by the trial authors, the Lead clinical results are unique to Ellex 2RT and cannot be extrapolated to other thermal or non-thermal laser treatments," Mr Spurling said. "We estimate the number of intermediate AMD patients without RPD to represent at least approximately 15 million patients annually in Ellex's existing 2RT markets."

"With no currently approved treatment options available for AMD in its early stages in these markets, or indeed anywhere in the world, we believe the Lead data will be of significant clinical interest to retinal specialists and ophthalmologists seeking an intervention for patients with the early stages of AMD," Mr Spurling said.

Ellex fell 11 cents or 13.3 percent to 71.5 cents with 1.4 million shares traded.

IMUGENE

Imugene says it has appointed the North Augusta, South Carolina-based Ambiopharm to manufacture its Key-Vaxx cancer vaccine for a proposed phase I clinical trial.
Imugene said the "clinical good manufacturing practice" batch was part of the pre-clinical development for the proposed programMed cell death-1 (PD-1) trial in 2019.
The company said it had filed a new provisional patent titled 'A Vaccine Composition and Uses Thereof' with the Australian Patent Office to protect PD-1 vaccine candidates designed to generate an antibody immune response against PD-1.
Imugene said the application "greatly expands the number of candidates protected in the highly-valued checkpoint inhibitor landscape" and added to the PD-1 method of treatment patent filed in February 2018.
Imugene was up 0.1 cents or 4.55 percent to 2.3 cents with 21.3 million shares traded.

ACRUX

Acrux says its annual general meeting will vote to grant directors 800,000 free "rights" and a potential 'Second Strike' board spill vote.
Last year, the Acrux annual general meeting gave the remuneration report a 'first strike' with 55.1 percent against and 44.9 percent in favor (BD: Oct 26, 2017).
Under the Corporations Amendment (Improving Accountability on Director and Executive Remuneration) Act 2011 any company sustaining a vote of 25 percent or more against the remuneration report in two successive annual meetings is required to vote on a board spill and if passed by more than 50 percent of votes the directors must stand for reelection at a subsequent meeting within 90 days.
Today, Acrux said it proposed to issue chairman Ross Dobinson 320,000 rights, with 160,000 rights each for directors Dr Timothy Oldham, Dr Simon Green and Dr Geoff Brooke.
The company said the rights would vest over four years from January 1, 2018, "subject to service and do not include a performance vesting condition".
Acrux said that non-executive directors' remuneration had not been adjusted since 2014 and issuing the rights in lieu of increasing cash remuneration was "prudent".
The company said that the meeting would vote on the re-election of Dr Oldham.
The meeting will be held at Pitcher Partners, Level 13, 664 Collins Street, Melbourne on November 1, 2018 at 10am (AEDT).
Acrux was up half a cent or 1.85 percent to 27.5 cents.

IDT AUSTRALIA

IDT says its annual general meeting will vote to re-elect directors and could face a Second Strike board spill resolution
Last year, IDT had a remuneration report first strike with the meeting voting 48.8 percent against the report and 51.2 percent in favor (BD: Oct 24, 2017).
In 2017, IDT said its proposed increased placement capacity failed, with 57.5 percent of votes against and 42.5 percent in favor.
Today, IDT said the meeting would vote to elect chairman Alan Fisher and director Hugh Burrill.
The meeting will be held at Deloitte Touche Tohmatsu, Level 10, 550 Bourke St, Melbourne, on October 23, 2018 at 10am (AEDT).
IDT fell one cent or 6.45 percent to 14.5 cents.

OBJ

OBJ says that its annual general meeting will vote on an increase to the directors' fee pool by 60 percent to $400,000 and a potential 'Second Strike' vote.
Last year, OBJ earned a remuneration report first strike with the meeting defeating the resolution 57.95 percent to 42.05 percent (BD: Nov 9, 2017).
In 2016, the placement capacity faced 34.4 percent dissent with the remuneration report passed easily (BD: Oct 28, 2016).
The company said that the meeting would vote on the remuneration report, the approval of an additional 10 percent placement capacity and the election of director Antonio Varano.
The meeting will be held in the Formal Dining Room, University Club of Western Australia, Hackett Entrance 1, Hackett Drive, Crawley, Western Australia on October 25, 2018 at 10am (AWST).
OBJ was up 0.2 cents or 9.1 percent to 2.4 cents.

COGSTATE

Cogstate says its annual general meeting will vote to issue chief executive officer Brad O'Connor 1,000,000 options and to re-elect directors.
Cogstate said that the options would be exercisable within five year and at four cents above the closing price on the date of the meeting, "subject to the company meeting or exceeding its 2018-'19 budget" with one third vesting two years from the issue date and the balance 12 months after.
The company said the meeting would vote to approve the 10 percent placement facility and on the re-election of directors Martyn Myer and David Dolby.
The meeting will be held at the Business Centre, Level 6, Tower Two, 727 Collins Street, Melbourne, on October 24, 2018 at 11am (AEDT).
Cogstate fell one cents or 1.6 percent to 61 cents.

RESAPP

FIL Limited says it has increased its substantial holding in Resapp from 60,848,856 shares (9.23%) to 69,313,051 shares (10.52%).
The Hong Kong, London and Sydney-based FIL said it bought, sold and "transitioned out" of shares between June 20, 2017 and September 19, 2018, at prices ranging from seven cents to 32 cents, as well as buying 3,565.962 shares in its recent $7.5 million placement at 22 cents a share (BD: Sep 19, 2018).
Resapp was up one cent or 4.3 percent to 24.5 cents with 11.6 million shares traded.

MGC (MEDICAL GRADE CANNABIS) PHARMACEUTICALS

MGC has requested a trading halt pending an announcement "regarding a material commercial transaction with a Canadian cannabis company".
Trading will resume on September 25, 2018 or on an earlier announcement.
MGC last traded at 4.8 cents.

MEDIBIO

Medibio says that former chief executive officer Jack Cosentino has resigned as a director and Jennifer Solitario has been appointed head of corporate health.

In August, Medibio said that managing-director and chief executive officer Jack Cosentino would “cease … effective from August 28, 2018” but provided no explanation for his departure (BD: Aug 29, 2018).

Today the company said the Perth-based Ms Solitario was “a proficient leader with more than 20 years of experience in the health insurance industry” and was formerly HBF Health executive general-manager overseeing benefits management, pharmacy, community and corporate “wellness” business units, managing benefits payments of more than $1 billion.

Medibio said it had hired Finnesse Partners to find a new chief executive officer,

The company said that “Ms Slocombe … [was] no longer employed by the company” but did not elaborate on her role.

Medibio fell 0.1 cents or 1.4 percent to 7.2 cents with 1.1 million shares traded.