Biotech Daily

Friday October 18, 2019

Daily news on ASX-listed biotechnology companies

*** ASX DOWN, BIOTECH EVEN: OPTHEA UP 7.5%; RESONANCE DOWN 10%**

*** DR BOREHAM'S CRUCIBLE: CLINUVEL PHARMACEUTICALS**

*** CSL: PROF JOSEPH CHIAO, PHARMING LAWSUIT ON HA DATA**

*** ONCOSIL RECEIVES $3.8m R&D TAX INCENTIVE**

*** CLINUVEL 1.5m, $48m CEO DR PHILLIPE WOLGEN RIGHTS AGM**

*** PHARMAXIS 927k CEO GARY PHILLIPS RIGHTS AGM**

*** STARPHARMA 671k CEO DR JACKIE FAIRLEY RIGHTS AGM**

*** CELLMID TO VOTE ON 3m CEO MARIA HALASZ OPTIONS**

*** BIONOMICS 2nd STRIKE AGM**

*** RACE 5.5m DIRECTORS OPTIONS AGM**

*** REGENEUS CEO LEO LEE 15m OPTIONS AGM**

*** ALTHEA COMPLETES CANADA PEAK ACQUISITION**

*** NOXOPHARM: 'GLUTAMATE-INHIBITOR FOR BRAIN CANCER'**

*** MERCHANT FUNDS REDUCES TO 5% OF RHYTHM**

*** MERCHANT TAKES 12% OF AUSCANN**

MARKET REPORT

The Australian stock market fell 0.52 percent on Friday October 18, 2019, with the ASX200 down 35.0 points to 6,649.7 points. Sixteen of the Biotech Daily Top 40 stocks were up, 15 fell, seven traded unchanged, and two were untraded. All three Big Caps fell.

Opthea was the best, up 25 cents or 7.5 percent to $3.58, with 441,708 shares traded. Dimerix climbed five percent; Compumedics, LBT and Patrys improved more than four percent; Medical Developments, Neuren and Optiscan rose more than two percent; Genetic Signatures, Oncosil, Pro Medicus, Telix and Volpara were up one percent or more; with Ellex, Next Science and Starpharma up by less than one percent.

Resonance led the falls, down 1.5 cents or 9.7 percent to 14 cents, with 1.3 million shares traded. Cyclopharm, Cynata and Imugene fell four percent or more; Avita, Impedimed, Orthocell, Prescient and Proteomics were down three percent or more; Actinogen, Mesoblast and Paradigm shed more than two percent; Clinuvel was down 1.55 percent; with Cochlear, CSL, Nanosonics, Polynovo and Resmed down by less than one percent.

DR BOREHAM'S CRUCIBLE: CLINUVEL PHARMACEUTICALS

By TIM BOREHAM

ASX code: CUV

Share price: $31.85

Shares on issue: 48,960,633

Market cap: $1.56 billion

Chief executive officer: Dr Philippe Wolgen

Board: Stan McLiesh (chairman)*****, Dr Wolgen, Brenda Shanahan, Willem Blijdorp, Dr Karen Agersborg, Susan Smith

***** Retiring at the AGM, expected in November

Financials (year to June 30, 2019): revenue $31.05 million (up 22%), net profit $18.1 million (up 37%), earnings per share 36.6c (up 37%), cash balance $54.3 million (up 50%), dividend per share 2.5 cents (up 25%).

Major identifiable holders: Dr Wolgen 6.73%, Fidelity Investment Management 5.45%, Ender1 LLC (Sean Parker) 5.4%.

While proclaiming the US Food and Drug Administration's approval of Clinuvel's rare skin disorders drug Scenesse as a "momentous occasion for an Australian biotech company" CEO Dr Philippe Wolgen avoids any hubris.

"I'm very careful about using the word success because the minute you proclaim success, the next day the house falls down," he says.

Dr Wolgen's reticence is understandable, given Clinuvel's quest for the FDA's stamp of approval as a 'serious' drug took more than 14 years.

But he's happy to highlight that not only has Clinuvel become one of the few Australian biotechs to obtain fully-fledged FDA approval, it did so while beating the key financial metrics outlined in a 2006 business plan.

At the time, management decreed the drug needed to be developed for under $200 million, compared with the typical $400 million to $600 million for a phase III drug.

It also needed to be done with a maximum 250 percent share dilution, costs not exceeding $12 million a year, a cost of capital of under 10 percent and a return on equity of more than six percent. The company was also to become dividend paying when it achieved profits within 10 years.

As things transpired, the drug cost $129 million with only a 165 percent share dilution and a return on equity of more than 20 percent.

The company posted its first meaningful profit in 2016-’17 and paid a maiden 2.0 cents a share dividend a year later.

Okay, so a slight miss on the 10-year deadline.

Average annual costs over the period also were $12.75 million and not $12 million as targeted.

But investors who pushed Clinuvel shares 60 percent higher after the October 9 news were hardly going to quibble about these slippages.

Out of the shadows

After two years of pontification, the FDA czars approved Scenesse as an adult treatment for the rare condition erythropoietic protoporphyria, or EPP.

EPP is an inherited metabolic disorder that causes a severe reaction to sunlight because of a dearth of the compound protoporphyrin nine (PPIX) in blood and tissues.

PPIX is activated by visible light and ultraviolet radiation, causing tissue damage and howling pain. Scenesse binds to the melanocortin 1 receptor on skill cells and sets in motion a “cascade of cellular events” to activate melanin and create a prophylactic barrier.

In other words, the drug tans the skin - a side effect that has been both a boon and a bane for the company’s development (more on that later).

Scenesse is a formulation of the peptide afamelanotide. About the size of a rice grain, the Scenesse shots are injected subcutaneously in a 16mg dose and ooze their goodness for two months (after which the patients have another one).

EPP affects about one in 140,000 people, equating to about 5,000 to 10,000 sufferers.

Life is hell for these folk, a.k.a. shadow chasers, who are confined indoors all day.

If at first you don’t succeed …

While Clinuvel flies the Australian flag, Scenesse evolved from lab work by four scientists at the University of Arizona in 1987.

In 1995 the owners applied for investigational new drug status with the FDA, based on marketing claims of a “tanning solution by chemical induction”.

The FDA demurred.

Epitan was incorporated in 1999 and back-door listed on the ASX in 2000, before changing its name to Clinuvel in 2006.

In 2003, the molecule was out licenced to an Australian team, which fronted the FDA again. “The FDA labeled it as the next injectable Botox,” Dr Wolgen rues.

In 2004, the company tried yet again and the agency’s rejection was more pointed.

“The FDA said they would not allow it ever to come to market for reasons of efficacy, tolerability and lifestyle use,” Dr Wolgen says.

A former facio-cranial surgeon and almost professional soccer player, Dr Wolgen joined the company in 2005 and set it on a new direction: a Europe-focused and strict medical agenda.

Changing course to Europe

Management was spurred by the breakthrough results of a five-person Swiss trial that showed the patients increased their tolerance to sunlight 11-fold.

“The [Clinuvel] board was quite strict and said the technology was quite promising but there is no guarantee it is going to generate returns,” Dr Wolgen says.

In pursuit of “financial proof-of-concept” the company zeroed-in on Italy, where the government formally supported drugs addressing an unmet need (as long as they had the support of the relevant medical community).

Rome agreed to subsidize 23 percent of the cost of the users, which then was EUR5,375 ($A8,810) per injection (up to six per year are required). Swiss insurers then said they were willing to subsidize the drug.

“So, we went back to Australia and said ‘we think there are people willing to write a cheque for it’,” Dr Wolgen said.

After a “hefty” board debate, the company decided to offer Scenesse for compassionate use (that is, free) to needy patients.

“There are pros and cons to do doing this,” Dr Wolgen says. “If you start incurring costs and distribute free of charge, it also sets a precedent for insurers to delay and not pay.”

“That was a difficult and pivotal decision, but for two years we did it across Europe and in Australia.”

In 2012 the company sought European marketing approval, with management fronting a presentation at London’s Canary Wharf where regulators from all 28 European Union member states were represented (we’re talking pre-Brexit times, of course).

“We thought if the Europeans had the audacity to approve the drug that certainty would count in the US as they would not need to take regulatory leadership,” Dr Wolgen says.

The European Medicines Agency approved Scenesse for EPP in late 2014 and the company launched the drug in Europe in 2016.

The secrets of Clinuvel’s success

Clinuvel has done a couple of things differently to attain the holy grail of FDA approval. Firstly, it stayed headquartered in Melbourne Australia. “In 2005 there was a tendency to go to the US and Europe because that is where notionally there is the talent to develop it,” Dr Wolgen says.

“But we went the other way. We said we have a base here and tax incentives and there is a good infrastructure.”

Secondly, Clinuvel retained control of distribution in house. “We said if you built this knowledge in-house you would be mad to give it out of your hands and let others determine the destiny of your best molecule.”

The in-house approach - which relates to functions over and above distribution- was a key factor in helping the company to contain costs.

Finances and performance

Clinuvel generated its first meaningful revenue in 2015-’16 - $6.4 million - and then turned its first profit of $7.11 million in 2016-’17.

For the year to June 30, 2019, the company reported an $18.1 million net profit, up 37 percent on revenue of $31 million (up 22 percent).

Clinuvel is coy about likely US revenue, given big pharma has been roughed up by both sides of US politics, with price-gouging accusations. To ameliorate these concerns, the company has adopted a policy of uniform global pricing.

In Europe, the treatment costs EUR55,000 to EUR85,000 ($A90,000 to $A140,000) a year, depending on the number of injections required. At the midpoint, treating a mere 1,000 patients implies annual revenue of $A115 million.

Of course, much depends on the availability of reimbursement, but Dr Wolgen notes that US insurers are already stumping up for US patients to be treated in Europe.

(In the UK, the company is struggling to win reimbursement from the National Institute for Health and Care Excellence - NICE – which isn’t being so nice about the matter).

Dr Wolgen says the company has taken a selective approach to pursuing supportive shareholders with deep pockets and a longer-term view. The register includes Fidelity and billionaire Napster founder Sean Parker.

“We wanted to build a registry of investors that fitted the way we go about our business,” Dr Wolgen says. “We have consciously kept the share register clean and tidy.”

As of June 30, Clinuvel had $54 million of cash and given its revenue generating status it won’t be bothering holders for more of the folding stuff in the foreseeable future. Clinuvel shares have traded as low as $1.13 (December 2013) and as high as $45.88 (after the October 9 news).

Dr Boreham’s diagnosis:

Clinuvel’s home-spun success makes the failed $2.17 a share, $95 million takeover offer from Retrophin in 2014 look like pure larceny. In hindsight, of course.

Clinuvel certainly has done a sterling job of generating revenue from such a low patient base, but Dr Wolgen agrees that investors are expecting wider applications.

“Will the company grow only on this technology or does it need more,” he asks, rhetorically. “The answer is there has to be more. We have an organic strategy [labs in Singapore developing next molecules] and we are going to grow inorganically by [acquisitions] and licencing other technologies.”

Clinuvel is targeting a pigmentation disorder called vitiligo, which affects about 45 million people. Known as the Michael Jackson disease in some circles, vitiligo causes the skin to go pale, generally in blotches.

Since 2010, Clinuvel has carried out two vitiligo trials in Singapore and the US, with “significant” results. But there have been unexpected obstacles unrelated to efficacy.

“We went to Singapore and discovered … it was culturally unacceptable to become so dark. But African-Americans were delighted to [get] back their pigmentation.”

Clinuvel’s criterion for the next indication is simple: “there has to be a high unmet need and no alternative in sight.”

This, we assume, precludes safe tanning but we did hear something about an over-the-counter sunscreen in development.

In the meantime, Clinuvel has a five to seven-year window to make hay from the EPP indication before rivals wake up to the enormous potential that even an obscure disease can present.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He admittedly was sceptical about the company’s chances but has now seen the light.

CSL

CSL says it filed a lawsuit against former senior scientist Prof Joseph Chiao regarding information “he intended to provide to Pharming Healthcare Inc”.

The Leiden, Netherlands-based Pharming Group NV posted on its website that it “categorically denies having had any involvement in the alleged abstraction of proprietary information by Dr Joseph Chiao from his former employer CSL”.

Biotech Daily attempted to contact Prof Chiao, but had not received a reply at the time of publication.

In August 2018, Prof Chiao was a co-author of an article, titled ‘Training patients for self-administration of a new subcutaneous C1-inhibitor concentrate for hereditary angioedema’ published in Wiley’s Nursing Open journal.

CSL has developed and is marketing Haegarda for hereditary angioedema.

Pharming has commercialized Ruconest for hereditary angioedema.

CSL told Biotech Daily that it filed the suit in the US District Court for the Eastern District of Pennsylvania on October 1, 2019.

CSL did not provide details of Prof Chiao’s employment, but according to his Linkedin page, he was CSL Behring’s senior medical director and therapeutic area head in July 2016 and was previously a professor in the University of Florida’s Department of Pathology where he worked from July 1994 to May 2000.

CSL said in a media release that Prof Chiao “deliberately downloaded highly sensitive, proprietary commercial information and trade secrets that we believe he intended to provide to Pharming Healthcare Inc, and where [Prof] Chiao recently began working”.

CSL said that, “based on our investigation to date, no identifiable patient data was obtained by Chiao”.

“Any data involved was de-identified, aggregated information regarding the way that patients use CSL Behring’s and other products,” CSL said. “We have no reason to believe these files contain any patient-specific or identifiable information.”

“We are confident that our swift actions, including retrieval of the data and the initiation of court proceedings, has protected our data and intellectual property from use or disclosure by Chiao or Pharming,” the company said.

“We take the protection of our propriety business information extremely seriously and will vigorously pursue our pending legal action,” CSL said.

“As a company that upholds our core values, including integrity, we are deeply disappointed by Chiao’s actions,” the company said.

Pharming said it was included in the injunction obtained by CSL Behring “to prevent possible transmission of proprietary documents and data to Pharming, which CSL claimed had been removed from its systems by Dr Chiao”.

Pharming said it recently hired Dr Chiao as its medical director.

The company said that the injunction was “aimed at giving CSL time and opportunity to investigate how and what was taken, and whether or not Pharming was involved and/or has received any of the abstracted data or documents”.

Pharming said it “did not induce or encourage Dr Chiao to breach any rules or contract terms or in any way to remove any data from his former employer”.

Pharming said it had not received or seen any proprietary CSL information from Dr Chiao or any other source.

Pharming said it was cooperating with CSL in the cyber-interrogation of all of Pharming’s systems and with US judiciary authorities to demonstrate its innocence of any wrongdoing.

“In accordance with the injunction, Dr Chiao has been suspended pending the outcome of the court hearing,” Pharming said.

CSL fell $1.62 or 0.6 percent to $250.97 with 528,319 shares traded.

ONCOSIL MEDICAL

Oncosil says it has received $3,782,089 from the Australian Tax Office under the Federal Government Research and Development Tax Incentive program.
Oncosil said the rebate comprised of $3,780,856 and $12,333 in interest and related to research and development expenditure for the year to June 30, 2019.
Oncosil was up 0.1 cents or 1.1 percent to 9.5 cents with 3.3 million shares traded.

CLINUVEL PHARMACEUTICALS

Clinuvel says it proposes to issue 1,513,750 performance rights to chief executive officer Dr Phillippe Wolgen in recognition of his work on Scenesse for erythropoietic protoporphyria.
At the market close today the performance rights were worth about $48.2 million and the company said the rights would vest pending conditions.
Last week, Clinuvel said that Scenessde had been approved by the US Food and Drug Administration.
Dr Wolgen was appointed chief executive officer to win approval for Scenesse on November 28, 2005 (see Dr Boreham's Crucible, above).
The company said it would vote on a special resolution to increase its non-executive directors' fee pool by 27.3 percent from $550,000 to $700,000.
The company said it would vote to adopt its remuneration report and to re-elect directors Brenda Shanahan and Susan Smith.
The meeting will be held at the Events Centre at Collins Square, Tower 2, Level 5, 727 Collins Street, Melbourne, on November 20, 2019 at 10am (AEDT).
Clinuvel fell 50 cents or 1.55 percent to $31.85 with 243,606 shares traded.

PHARMAXIS

Pharmaxis says its annual general meeting will vote to grant chief executive officer Gary Phillips 927,000 performance rights.
Pharmaxis said the performance rights would vest based on overall company performance and in two tranches on June 30, 2021 and June 30, 2022.
The company said it would vote to adopt its financial and remuneration reports and to re-elect non-executive director William Delaat.
Pharmaxis said it would vote on a special resolution to amend its constitution.
The meeting will be held at the offices of Computershare, Level 3, 60 Carrington Street, Sydney, on November 21, 2019 at 2:30pm (AEDT).
Pharmaxis was unchanged at 20.5 cents.

STARPHARMA HOLDINGS

Starpharma says its annual general meeting will vote to issue 670,996 performance rights, worth $849,750 to chief executive officer Dr Jackie Fairley.
Starpharma said 134,199 rights would vest on June 30, 2021 with 536,797 rights vesting on September 30, 2022, pending performance hurdles.
The company said the value for each right represented a volume weighted average price of $1.2664 on June 30, 2019.
The meeting will be held at the RACV City Club, Level 2, 501 Bourke Street, Melbourne, on November 21, 2019 at 4.00pm (AEDT).
Starpharma was up half a cent or 0.45 percent to $1.125.

CELLMID

Cellmid says its annual general meeting will vote to issue 3,000,000 options to chief executive officer Maria Halasz, and 2,500,000 shares to Dennis Eck in lieu of cash.
Cellmid said it proposed to issue Ms Halasz 1,000,000 short term incentive options and 2,000,000 long term incentive options, all exercisable within five years, at a 10 percent premium to the 30-day volume weighted average price to the date of issue, and vesting on June 30, 2020 and June 30, 2022, respectively, provided that Ms Halasz remained employed by the company at those dates.
The company said it proposed to issue director Mr Eck 2,500,000 shares at 20 cents a share, in lieu of a cash payment for his $50,000 average annual director's fees.
The company said the meeting would vote on the adoption of the remuneration report, the re-election of director Bruce Gordon, and the ratification of the issue of placement shares.
The meeting will be held at Automic Group, Level 5, 126 Phillip Street, Sydney, on November 19, 2019 at 2pm (AEDT).
Cellmid was unchanged at 19.5 cents.

BIONOMICS

Bionomics says its annual general meeting will vote on its remuneration report and a potential second-strike board spill.
Last year, Bionomics said its remuneration report was opposed by 46,479,971 votes or 37.2 percent, providing the first trigger for a potential board spill at this year's annual general meeting (BD: Nov 14, 2018).
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 meetings is required to vote on a board spill and if passed by more than 50 percent of votes, the directors must stand for re-election at a subsequent meeting within 90 days.
If the spill vote fails, the trigger is reset to no opposition.
Bionomics said it would vote to adopt the remuneration report, to elect directors chairman Dr Errol De Souza, Alan Fisher and Mitchell Kaye.
The meeting will be held at the Adelaide Convention Centre, Room L1, West Building, North Terrace, Adelaide on November 20, 2019 at 11am (ACDT).
Bionomics fell half a cent or 4.55 percent to 10.5 cents.

RACE ONCOLOGY

Race says it will vote to issue 5,500,000 options to directors' Dr Daniel Tillett, Dr William Garner, Dr John Cullity and Chris Ntoumenopoulos.
Race said it would vote to issue 2,500,000 options to director Dr Tillett, exercisable at 19 cents each within three years, and 1,000,000 options each to directors' Dr Garner, Dr Cullity and Mr Ntoumenopoulos, exercisable at 25 cents each within two years.
Race said it would vote to adopt its remuneration report, elect directors Mr Ntoumenopoulos and Dr Tillett, and approve a 10 percent placement capacity.
The meeting will be held at the Vintage Room, RACA, 89 Macquarie Street, Sydney on November 22, 2019 at 11am (AEDT).
Race fell half a cent or 3.85 percent to 12.5 cents.

REGENEUS

Regeneus says it will vote to issue chief executive officer Leo Lee 15,000,000 options for his appointment and a restructure of his remuneration.

Regeneus said it would vote to issue Mr Lee 5,000,000 options at the time of his appointment as chief executive officer, granted in four tranches and vesting upon satisfaction of performance conditions to January 31, 2021.

The company said the options would expire five years from the date of the grant of options, with 2,500,000 exercisable at 20 cents a share and 2,500,000 exercisable at 25 cents a share.

Regeneus said it would vote to issue Mr Lee 10,000,000 options as part of the restructure of his remuneration, granted in three tranches and vesting upon satisfaction of performance conditions to December 31, 2023.

The company said the options would expire five years from the date of the grant of options, with 3,500,000 exercisable at 10 cents a share, 3,500,000 exercisable at 15 cents a share and 750,000 each exercisable at 20, 25, 30 and 35 cents a share.

Regeneus said it would vote to ratify the prior issue of 29,250,000 shares, approve an additional 10 percent placement capacity and re-approve its share option plan.

The company said it would vote to adopt its remuneration report and o re-elect directors Dr John Chiplin and Alan Dunton.

The meeting will be held at the offices of Dentons Australia, Level 16, 77 Castlereagh Street, Sydney on November 21, 2019 at 3pm (AEDT).

Regeneus was unchanged at 8.1 cents.

ALTHEA GROUP HOLDINGS

Althea says it has completed the acquisition of Canada marijuana extraction and contract manufacturing business Peak Processing Solutions.

In July, Althea said it had raised $30 million in a placement and would give former Peak director Greg Battersby and employee shareholders $C4.1 million ($A4.5 million) in cash and 25,851,846 shares to fund the acquisition (BD: Jul 25, 2019).

Althea was up 2.5 cents or 3.9 percent to 66 cents.

NOXOPHARM

Noxopharm says it will apply its glutamate-inhibition technology to the treatment of the brain cancer glioblastoma multiforme.

Noxopharm said the glutamate brain chemical played “a key role in driving the aggressive nature of [glioblastoma multiforme] growth”.

The company said that with the University of New South Wales, it had selective glutamate-inhibitor drugs in its chemical library, which would expedite its path to the clinic.

Noxopharm was up three cents or 8.6 percent to 38 cents with 1.3 million shares traded.

RHYTHM BIOSCIENCES

Merchant Funds Management says it has reduced its substantial shareholding in Rhythm from 6,600,000 shares (6.55%) to 5,347,636 shares (5.31%).

The Perth, Western Australia-based Merchant said that between September 20 and October 17, 2019 it sold 1,252,364 shares for $218,180.65 or an average of 17.4 cents a share.

Rhythm was untraded at 17 cents.

AUSCANN GROUP HOLDINGS

Merchant Funds Management says it has increased its substantial shareholding in Auscann from 36,237,639 shares (11.43%) to 39,400,000 shares (12.43%).

The Perth, Western Australian-based Merchant said that between October 14 and 18, 2019 it bought and sold shares, with a single largest purchase of 2,687,639 shares for $808,952 or 30.1 cents a share.

Last Friday, after the market closed Merchant Funds said it became a substantial holder in Auscann with 36,237,639 shares (11.43%), acquired from Canopy Growth Corp, buying the shares off-market for $5,435,645 or 15 cents a share (BD: Oct 14, 2019).

Auscann was unchanged at 27 cents with 2.7 million shares traded.