Biotech Daily

Friday September 8, 2017

Daily news on ASX-listed biotechnology companies

*** ASX DOWN, BIOTECH UP: DIMERIX UP 11%, BENITEC DOWN 4%**

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

*** BOEHRINGER 2nd PHARMAXIS PXS-4728A TRIAL TRIGGERS $15m**

*** ALLEGRA RAISES $1.3m, SECOND PLACEMENT FOR $1.4m MORE**

*** MEMPHASYS, TRANSOCEAN SETTLE DISPUTE**

*** JAPAN PATENT FOR PRIMA IMP731 FOR TRANSPLANT REJECTION**

*** DAVID NEATE TAKES 10.5% OF SIENNA**

*** DRH, DAVID HANNON INCREASE, DILUTED TO 8% OF NOXOPHARM**

*** PRO MEDICUS APPOINTS DR LEIGH FARRELL DIRECTOR**

MARKET REPORT

The Australian stock market was down 0.3 percent on Friday September 8, 2017 with the ASX200 down 17.3 points to 5,672.6 points.

Fifteen of the Biotech Daily Top 40 stocks were up, 10 fell, 12 traded unchanged and three were untraded. All three Big Caps were up

Dimerix was the best, up 0.1 cents or 11.1 percent to one cent with 1.1 million shares traded.

ITL and Pharmaxis climbed more than seven percent; Polynovo was up 6.1 percent; Compumedics improved 5.3 percent; Cellmid was up 4.2 percent; Atcor and Living Cell rose more than three percent; Actinogen, Avita, Clinuvel, LBT, Orthocell, Pro Medicus and Resmed were up more than one percent; with Cochlear, CSL and Sirtex up by less than one percent.

Benitec led the falls, down half a cent or four percent to 12 cents with 111,700 shares traded.

Universal Biosensors lost 3.85 percent; Airxpanders, Neuren, Osprey, Reva and Viralytics were down more than one percent; with Impedimed, Medical Developments and Starpharma down by less than one percent.

DR BOREHAM'S CRUCIBLE: CLINUVEL PHARMACEUTICALS

By TIM BOREHAM

ASX Code: CUV

Share price: $6.90; **Shares on issue:** 47,735,227; **Market cap:** $329.4 million

Chief executive officer: Dr Philippe Wolgen

Board: Stanley McLiesh (chairman), Dr Philippe Wolgen, Brenda Shanahan, Elie Ishag, Willem Blijdorp

Financials (2016-'17 year): revenue $17.0 million (up 165%), maiden net profit $7.11 million (previous loss $3.15 million), cash of $23.7 million (2015-'16: $13.8 million)

Identifiable shareholders: Lagoda Investment Management 11 percent, Fidelity Investments 9.6 percent, Dr Wolgen 7.8 percent, Ender 1 LLC (Sean Parker) 4.9 percent.

Clinuvel chief Dr Philippe Wolgen describes the drug developer's journey as "counter-current to arrive at the present point" - and don't we love the former cranio-facial surgeon and enthusiastic soccer player's quaint Franco-Dutch phraseology.

"Rather than traversing along the fastest imaginable and plotted route to success, we have frequently been impelled to take tortuous avenues to achieve our objectives," he told shareholders recently.

Unlike the majority of ASX-listed drug plays, at least Clinuvel has navigated these tortuous routes. It actually has a drug on market - to treat rare skin intolerance to sunlight - which makes the company a rarity in itself. Revenues are flowing and the company posted a substantial $7.1 million maiden profit.

Safe tanning appeal fades

Wolgen's "tortuous" reference could well refer to Clinuvel's origins as Epitan, which as the name suggests was pitching a synthetic peptide, melanotan, as a safe tanning agent.

The earnest Dr Wolgen put paid to all of that malarkey when he joined the company in 2005, although the US Food and Drug Administration had already refused approval two years earlier. Since then the company stuck to a serious clinical program for the technology, now known as Clinuvel's lead drug Scenesse (afamelanotide).

In 2014, the European regulator approved Scenesse to treat erythropoietic protoporphyria, or EPP, an extreme sun intolerance afflicting about 5,000 people - colloquially known as shadow chasers - globally.

Strictly speaking, the drug treats the phototoxic side effects of severe burns and anaphylactoid reactions.

While it may seem odd that Clinuvel targeted such a small market, one way of looking at it is that the company is proving Scenesse with a most extreme skin condition.

Clinuvel also cites a market of 45 million people for broader target disorders such as vitiligo, the loss of pigmentation in dark-skinned people that affects about one percent of the population. (Michael Jackson was the most famous sufferer, before he killed himself with an anaesthetic drug in a cautionary tale of off-label usage).

Scenesse is approved for EPP in Europe, with the $17 million of revenue including the first 12 months of commercial sales in the Netherlands, Italy, Austria and Germany.

The full-year revenue includes $4.83 million of revenue granted under special access schemes that recognise the rarity and untreated nature of the condition.

The UK National Institute of Health Care and Excellence (NICE) is evaluating Scenesse in terms of special availability to adult patients and reimbursement by the National Health Service. And in April this year German insurers agreed on a reimbursement regime "aligned to the company's uniform global pricing policy".

Clinuvel's clinical focus is now on a phase II, Singapore-based trial for vitiligo, "evaluating the use of Scenesse in diverse patient groups with various skin complexities".

Coming back for more

In a July update, Clinuvel reported two quarters of growth for Scenesse, with 98 percent of the European EPP patients treated for the first annual cycle coming back for a second round of photo-protection. The treatment costs about $US28,000 a year.

After the European Medicines Agency approved Scenesse in 2014, Dr Wolgen said one reason for the consent was the company's reassurance the drug would not be used for "off label" purposes (such as safe tanning).

That was a spit-on-the-hand, Scout's honour pledge, but it seems the regulators are a suspicious lot. "Despite our proclamations, European regulators still seek evidence and confirmation of our exclusive supply to EPP patients," Dr Wolgen says.

"At times I have been surprised by the lack of realisation of leading regulatory authorities as to the significance of public statements made by listed companies, including Clinuvel," he says.

We can think of a reason: a few of them elsewhere are known to stretch the truth.

Out of the shadows

The US market also beckons: in July last year the FDA granted Scenesse fast track approval status for EPP and subsequently accepted Clinuvel's data as adequate for a new drug application.

The FDA is happy to receive a rolling series of dossiers on how the drug is faring.

The process is helped by the real life European experience of Scenesse, with no emerging safety concerns.

In the meantime, Dr Wolgen says, US EPP patients are requesting information on the availability of the drug, which has made a profound difference to many of the patients treated.

“Knowing that there is a treatment available while not being able to obtain it must be an unspeakable frustration of many patients in the US,” Dr Wolgen says.

“The regulatory hurdles to make a novel drug available are increasingly high and the administrative processes after drug approval have become complex and time consuming,” Dr Wolgen says.

Dr Boreham’s diagnosis:

The commercialization of Scenesse comes after 11 years of development and 17 years as a listed entity. In drug development land, it’s a rare example of plugging away and actually getting somewhere.

Dr Wolgen, who helped bolster the share register with the addition of the likes of billionaire Napster founder Sean Parker, can take a bow.

In glorious hindsight, the board was right to snub New York’s Retrophin that lobbed a hostile $2.17 a share offer in July 2014, valuing the company at about $95 million.

The shares have traded between $1.13 and $8 over the last decade, with the company evolving from Epitan in 2000.

Clinuvel established a level 1 American depository receipt program and these days close to 12 percent of all shares on issue are held as these instruments.

The fundamental constraint of EPP is that it’s such a small market, although Scenesse reportedly has changed the lives of sufferers who need not hide in the broom cupboard on a sunny day.

While it’s too late for Michael Jackson, a vitiligo treatment would help to justify Clinuvel’s current $300 million-plus market capitalisation.

Punters should expect to hear more about from the company at its November annual general meeting when it unveils its ‘2020 Strategy’, hopefully not the same one proposed by former Sirtex chief executive officer Gilman Wong.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. One could say his knowledge of the topic runs only skin deep.

PHARMAXIS

Pharmaxis says a Boehringer Ingelheim phase IIa trial of oral BI 1467335 for non-proliferative diabetic retinopathy will trigger a EUR10 million ($14.9 million) payment.

In August, Pharmaxis said the Germany-based Boehringer's trial of BI 1467335, formerly known as PXS-4728A acquired in 2015, for non-alcoholic steato-hepatitis triggered a EUR18 million ($A26.9 million) payment (BD: Mar 12, 2015; Aug 25, 2017).

Today, the company said that non-proliferative diabetic retinopathy without centre-involved diabetic macular oedema was the second indication for the drug is developed.

Pharmaxis said the trial, entitled 'Randomized study of orally-administered BI 1467335 in patients with non-proliferative diabetic retinopathy without centre-involved diabetic macular oedema' (Robin), would enrol 100 patients with moderately severe to severe non-proliferative diabetic retinopathy without centre-involved diabetic macular oedema.

The company said the primary objectives were to establish proof-of-clinical-principle and to evaluate the safety and tolerability of BI 1467335.

Pharmaxis said that patients would be randomized to either BI 1467335 or placebo for a 12-week treatment period and a 12-week follow-up, with a subsequent phase IIb study to confirm and extend the findings.

The company said that BI 1467335 was an oral inhibitor of amine oxidase, copper containing 3 (AOC3), also known as vascular adhesion protein-1 (VAP-1), or a semi-carbazide-sensitive amine oxidase (SSAO).

Pharmaxis said that diabetic retinopathy was the leading cause of vision-loss in adults aged 20 to 74 years and progresses from mild non-proliferative diabetic retinopathy to moderate and severe non-proliferative diabetic retinopathy, characterized by retinal haemorrhages and vascular changes in the retina, to proliferative diabetic retinopathy characterized by the growth of new blood vessels on the retina.

The company said that diabetic macular oedema, characterized by retinal thickening from leaky blood vessels, could develop at all stages of retinopathy.

Pharmaxis said that of an estimated 285 million people with diabetes mellitus worldwide, about one third had signs of diabetic retinopathy and of these, a further one third of diabetic retinopathy was vision-threatening with severe non-proliferative diabetic retinopathy, proliferative diabetic retinopathy and diabetic macular oedema.

Boehringer Ingelheim chief medical officer Dr Christopher Corsico said the second indication phase IIa trial was "important news for the millions of patients threatened by losing their vision".

"Boehringer Ingelheim is committed to developing novel treatments designed to address unmet medical need and improve public health and looks forward to studying this novel compound in [non-proliferative diabetic retinopathy] patients," Dr Corsico said.

Pharmaxis chief executive officer Gary Phillips said he was "delighted that our partner Boehringer Ingelheim has decided to pursue a second indication for the drug acquired from Pharmaxis in 2015".

"It will be very rewarding for the Pharmaxis team to see another group of patients benefit from our initial work," Mr Phillips said.

"The deal structure negotiated with [Boehringer Ingelheim] recognized the potential that the drug had in multiple indications so expanding the development plan to include diabetic retinopathy as well as [non-alcoholic steato-hepatitis] means that we will receive a EUR10m milestone payment when the first patient is dosed in the [diabetic retinopathy] phase IIa study and that all the potential development milestones in the deal [EUR418.5 million or $A625 million), would be payable to Pharmaxis should both indications be approved," Mr Phillips said.

Pharmaxis was up two cents or 7.4 percent to 29 cents.

ALLEGRA ORTHOPAEDICS

Allegra says it has commitments to raise $1.3 million in two-tranche placement at 15 cents a share.
Allegra said that the first tranche of 5.3 million shares would be issued under the company's 15 percent placement capacity, with the second tranche subject to shareholder approval and the annual general meeting on or about October 27, 2017.
The company said that shareholder approval would be sought for the issue of 3.333 million shares to Robinwood Investments Pty Ltd, an entity related to director Anthony Hartnell.
Allegra said the funds would be used to commercialize the Sr-HT-Gahnite bone project, the establishment of a pilot manufacturing facility, regulatory process submissions and the manufacture of a three-dimensional spinal cage.
The company said it would seek shareholder approval to raise a further $1.4 million in private placement at 15 cents a share.
Allegra was up three cents or 23.1 percent to 16 cents.

MEMPHASYS

Memphasys says it has settled a statement of claim from its former corporate advisor Transocean Securities Pty Ltd, through mediation.
Last year, Memphasys said it received a statement of claim from Transocean following a statement that it had "terminated the mandate on August 26, 2016 for cause" and appointed Platinum Road as its corporate advisor (BD: Sep 20, Nov 21, 2016).
In 2016, the company said Transocean was claiming it did not have the right to terminate its mandate and appoint Platinum Road as it had an exclusivity arrangement with Transocean.
Memphasys said that on July 28, 2016 it demanded a refund of net fees charged for underwriting fees wrongly charged by Transocean and Transocean was seeking to recover damages, including the value of the monthly retainer between April 2016 and December 2017, 50,000,000 underwriter options and fees that would have been earned by Transocean on subsequent funding.
Today, Memphasys said that the terms of the settlement were confidential
Memphasys fell 0.1 cents or 25 percent to 0.3 cents with one million shares traded.

PRIMA BIOMED

Prima says the Japan Patent Office has granted a patent covering IMP731 for treating or preventing organ transplant rejection or treating an autoimmune disease.
Prima said that the patent, entitled 'Cytotoxic anti-LAG-3 monoclonal antibody and its use in the treatment or prevention of organ transplant rejection and autoimmune disease' would provide intellectual property rights through to April 30, 2028.
The company said the patent was filed as a divisional application directed to its IMP731 antibody originally developed by Immutep SA, now a wholly owned subsidiary of Prima.
Prima said that the granted claims provided broad protection for the antibody and use of the antibody in the manufacture of a medicine for treating or preventing organ transplant rejection or treating an autoimmune disease.
The company said that the rights for the development of the IMP731 antibody were granted to Glaxosmithkline in December 2010, which began first-in-human clinical trials of a proprietary antibody (GSK2831781) derived from IMP731.
Prima was unchanged at 2.1 cents with 4.4 million shares traded.

SIENNA CANCER DIAGNOSTICS

David Neate says he has increased his substantial shareholding in Sienna from 17,002,970 shares (9.43%) to 18,852,970 shares (10.46%).
The Portsea, Victoria-based Mr Neate said he bought 1,850,000 shares on market on August 3 and September 5, 2017 for $296,678 or 16 cents a share.
Sienna was up one cent or 7.7 percent to 14 cents.

NOXOPHARM

DRH Superannuation and David Hannon say they have increased and been diluted in Noxopharm from 7,526,273 shares (10.01%) to 7,905,627 shares (7.76%).
The Sydney-based DRH Superannuation substantial shareholder notice said that the registered shareholders included its DRH Superfund No2, RAH (STC) Pty Ltd and Mr Hannon.
DRH said that it received 1,424,808 'performance shares' for free on November 23, 2016, with Mr Hannon and RAH selling shares between September 21, 2016 and August 29, 2017.
Noxopharm was up three cents or 9.4 percent to 35 cents.

PRO MEDICUS

Pro Medicus says it has appointed Dr Leigh Farrell as a non-executive director, effective from September 8, 2017.
Pro Medicus said Dr Farrell held a Bachelor of Science and a Doctorate of Philosophy from Monash University and was currently the Princeton, New Jersey's Certara's head of corporate strategy and business development (BD: Sep 8, 2016; Aug 2, 2017).
The company said that previously he was chairman and chief operating officer of D3 Medicine, acquired by Certara in 2016.
Pro Medicus said that Dr Farrell had extensive experience in corporate strategy, joint ventures, intellectual property strategy, business development and licencing as well as having worked for a range of biotechnology, pharmaceutical companies, universities and corporate advisory consultancy practices.
Pro Medicus was up five cents or one percent to $4.95.