Biotech Daily

Friday March 8, 2019

Daily news on ASX-listed biotechnology companies

*** ASX DOWN, BIOTECH UP: PRANA UP 25%; PATRYS DOWN 8%**

*** DR BOREHAM'S CRUCIBLE: VOLPARA HEALTH TECHNOLOGIES**

*** S&P ASX ALL ORDINARIES: 6 BIOTECHS, AUST ETHICAL IN; 7 OUT**

*** IMMUTEP: 'IMP761 REDUCES PRIMATE T-CELLS', CLINICAL TRIALS**

*** FEDERAL $500k FOR GRIFFITH UNI PLASPROTECT MALARIA VACCINE**

*** FEDERAL HEALTH BOARDS '50% WOMEN'; PROF DOROTHY KEEFE**

*** UNIVERSAL BIOSENSORS LOSES 33% STAFF, CEO RICK LEGLEITER**

*** COCHLEAR: UK NICE EXPANDS HEARING IMPLANT SUITABILITY**

*** IMMUTEP RECEIVES $872k FEDERAL R&D TAX INCENTIVE**

*** WENTWORTH WILLIAMSON TAKES 7% OF TASMANIAN POPPY**

*** ASX SUSPENDS MEDIGARD ON ACCOUNTS**

MARKET REPORT

The Australian stock market fell 0.96 percent on International Women's Day, Friday March 8, 2019, with the ASX200 down 60.1 points to 6,203.8 points.

Fifteen of the Biotech Daily Top 40 stocks were up, 13 fell, 11 traded unchanged and one was untraded.

Prana was the best, up 0.9 cents or 25.0 percent to 4.5 cents, with 1.2 million shares traded. I Genetic Signatures climbed 23.85 percent; Benitec was up 10.3 percent; Immutep improved 6.1 percent; Actinogen, Medical Developments, Paradigm and Proteomics were up more than three percent; Antisense, Cynata and Neuren rose more than two percent; Ellex, Starpharma and Volpara were up one percent or more; with Cochlear, Polynovo and Resmed up by less than one percent.

Patrys led the falls, down 0.2 cents or 8.3 percent to 2.2 cents with 25,000 shares traded. Kazia lost six percent; LBT, Nanosonics and Universal Biosensors fell more than four percent; Uscom was down 3.6 percent; Clinuvel, Mesoblast and Oncosil shed more than two percent, Compumedics, Opthea, Pharmaxis and Pro Medicus were down more than one percent; with CSL down 0.06 percent.

DR BOREHAM'S CRUCIBLE: VOLPARA HEALTH TECHNOLOGIES

ASX code: VHT

Share price: $1.24

Shares on issue: 179,350,158 (51,482,213 subject to voluntary escrow)

Market cap: $222.4 million

Chief executive officer (and co-founder): Dr Ralph Highnam

Board: Paul Reid (chairman)*****, Dr Highnam, Roger Allen, Prof John Michael Brady, John Diddams, John Pavlidis, Dr Monica Saini

Financials (December quarter): receipts $NZ1.9 million, cash burn $NZ2.75 million, cash on hand $NZ17.1 million, estimated current quarter outflows $4.4 million

Major shareholders: Patagorang Pty Ltd (Roger Allen) 11.4%, Dr Ralph Highnam 10.1%, Tina Jennings 5.1%, Harbour Asset Management 5.0%, Prof John Mike Brady 4.4%, Private Portfolio Managers 3.6%, Craigs Private Clients 3.5%, Marcus Sarner 3.3%.

***** To enable the company to have an independent chair, Mr Reid replaced Mr Allen as chairman as of March 1

For the Wellington-based diagnostics play, the mantra of 'breast is best' takes on a different meaning from the nursing mother's self-evident dictum.

Volpara's platform technology is all about improving the detection and diagnosis of breast cancer, which can do with plenty of improvement, despite the ubiquity of the disease.

Unlike so many of its life sciences counterparts, Volpara has stuck to its original purpose.

But it has also expanded its remit from measuring breast density to introducing software for screening clinics to improve their efficiency and patient experience.

Women with dense breasts - and that's 40 to 50 percent of the female populace - are at much greater risk of contracting breast cancer.

What's more, the dense tissue comes up white on a mammogram - as does a tumor. As a result, 20 to 30 percent of cancers are missed in this cohort.

After 10 years of development, Volpara has entered commercialization stage and is now being judged by the market on its ability to generate recurring revenue.

Volpara founder and CEO Dr Ralph Highnam is a global expert on breast density, which refers to the level of glandular tissue versus fat in the appendages.

In fact, he completed an Oxford D Phil (doctorate of philosophy) on the topic, which no doubt provoked many a titter among his fellow scholars.

Volpara was last year's second best performing BDI-40 price wise, surging 198.5 percent despite a sharp retraction in December after a lacklustre quarterly report and slower than expected progress on new contracts.

Volpara's evolution

Initially, Volpara started with Volpara Density, a tool to measure breast density and thus identify at-risk women for more frequent examinations.

Volpara then devised Volpara Enterprise: automated tools used by clinics to improve the efficiency and performance of sites with multiple x-ray machines.

At a recent major radiology shindig in Chicago Volpara launched Volpara Live!, a tool that assists clinicians in real time.

The company claims it's the first such point-of-care tool - and who are we to argue?

Volpara Enterprise enables clinicians to detect a sub-standard image before the patient has left the clinic, avoiding the need for an expensive recall.

(It can detect whether different companies' mammography machines are applying optimal - rather than painful or insufficient pressure and whether the x-ray dose is correct.)

Volpara's revenue mix is shifting from up-front capital amounts to a 'software as a service' model that involves a monthly per-patient subscription payment.

In the 2017-'18 year, the number of sites signing up for Volpara Enterprise climbed from 14 to 57.

In October 2018, NZ screening chain Breastscreen Central became the first public body to purchase the enterprise software.

Trials are continuing with Britain's National Health Service.

Other takers for the enterprise software are the Sloan Kettering Cancer Centre in New York, the MD Anderson in Houston, the Stanford University Hospital in California, the University of Virginia Medical Centre, Women's Breast Imaging Perth, the Auckland Breast Centre and Mercy Radiology.

Holland density trial a Dutch treat

One impediment to clinics taking up Volpara's product suite has been the lack of formal proof of the efficacy of density-based screening via a proper randomized trial.

But now Volpara has the smoking gun evidence after the results of a large Dutch screening trial - carried out over eight years - were aired at the European Congress of Radiology in Vienna.

Based on a screening of 40,000 women – with a subset of 400,000 screened women overall deemed to be extremely dense breasted - the trial showed a dramatic drop in "interval cancers" when patients were screened with an x-ray, Volpara Density and then magnetic resonance imaging (MRI).

Interval cancers tend to be detected by symptoms - which usually reflects an advanced stage - a year or two after a screening has returned a negative result and prior to the next scheduled screening, hence 'interval'.

That's either because the cancer was hidden by dense tissue, or was extremely fast growing.

Extremely dense-breasted women are defined as having breasts with 15.5 percent or more of the fibrous material. In this cohort, standard mammographies have a sensitivity of 61 percent (in other words, only six in every 10 cancers are detected).

The rate of interval cancers in extremely dense-breasted women is normally 4.4 per thousand, but the trial results in a reduction to around one per thousand.

The trial - aptly named Dense - wasn't a test of Volpara Density as such, but was aimed at determining whether MRIs were a cost-effective way of reducing the number of interval cancers.

In an ideal world every woman with a positive diagnosis should have an MRI, but the trouble is they are five to six times more expensive than a standard mammography. MRIs also require use of a contrast agent and can generate false positives.

The trial resulted in a low false positive rate of seven percent - that is, women who have biopsies that turn out not to be cancer - with plans afoot to reduce that further.

US evidence suggests the false positive recall rate for breast x-rays is around 10 percent.

Dr Highnam says the trial has "massive implications" for breast cancer screening globally.

"Screening programs have been waiting for randomized controlled trials to show the benefit of density-based screening," he says.

"Finally, now they have a way forward to optimize their screening protocols."

The trial was funded by several charities as well as Bayer AG (which makes MRI contrast agents) and was overseen by renowned Dutch epidemiologist Prof Carla van Gils, of the University Medical Centre Utrecht.

Given the role of Volpara Density in assessing breast density, Dr Highnam said the results were expected to result in “increasing international interest in automated breast density solutions”. Such as … er … Volpara Density.

Investors agreed, pushing Volpara shares eight percent higher on the day.

USA, or bust

Volpara’s quest to dominate the US market is being helped by an expanding number of states issuing breast density screening guidelines.

In February, Georgia became the 38th state to do so, with the guidelines now covering close to 90 percent of US women.

Dr Highnam notes the US Food and Drug Administration recently issued guidelines to improve the quality of mammography and provide more information to patients, especially about breast density.

These guidelines have remained untouched since 1997. So, while breasts conceptually haven’t changed in that time, the imaging technology certainly has.

In September, a new FDA clearance under the 510k pathway expanded the information algorithms can provide to clinicians.

“For instance, Volpara can now refine breast density scoring when there is an area of the breast that is especially dense and provide an overall sensitivity score for the exam,” Dr Highnam says.

Finances and performance

Volpara’s third (December) quarter was a curate’s egg of good and not so good, with over-expectant investors latching on to the latter. The company booked record receipts of $NZ1.9 million ($1.82 million), up 192 percent on the September quarter. It also lost $NZ2.8 million.

Typical of “cloud” subscription models, revenue is recognized over the life of the contract which means short-term revenues are more constrained. But as subscriptions grow, more annuity income is generated and annual recurring revenues ensue.

Given that, Volpara chalked up annual recurring revenue (ARR) of $NZ755,000, taking the financial year-to-date run rate to $NZ5.6m, up 56 percent.

Management also guided to an 85 percent increase in ARR in the financial year to March 2019.

While 85 percent growth sounds bouncy enough, management had set an “aggressive but plausible” target of 150 percent growth.

The company attributes the lag mainly to slower than anticipated uptake by new sites in the US, partly the result of Volpara’s need to blood a new sales force.

Volpara subsequently had a record January and Dr Highnam says February has shaped up “okay” as well. At last count. the company had signed 113 customers across 300 sites, and was expecting to sign a further 25 to 30 by the end of March.

The company looks to be sound, cash wise, having raised $20 million from institutions in April last year.

On current expectations, Volpara is expected to remain unprofitable in 2018-’19, (which we’ll know soon enough because the Kiwi company reports its full year to March 31), before posting modest earnings in 2019-’20 and immodest ones thereafter.

Meanwhile Volpara shares have traded in a range from 61 cents to $1.55 over the last 12 months.

Dr Boreham’s diagnosis:

Given the duration of the trial and the number of patients involved, the Dense trial results promise to be a pivotal point in Volpara’s short history.

But for the time being, it’s a matter of wearing out the shoe leather to get those US imaging sites on board. After all, the US market accounts for 95 percent of expected revenue.

Volpara has some interesting backers in Australian entrepreneur Roger Allen, founder of Computer Power group and the venture capital firm Allen & Buckeridge. Founding director Mike Brady isn’t of Up There Cazaly fame, but a professor of oncological imaging at Oxford University.

Dr Saini is a former medical director of GE Health and a breast screening guru.

Mr Reid and Mr Diddams are serial company directors in Australia and NZ, so there’s a nice balance of commercial, medical and entrepreneurial on the board.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. So as to not make a boob of himself, especially on International Women’s Day, he does try to stay abreast of things.

STANDARD & POORS DOW JONES INDICES

Six biotechnology companies and Australian Ethical Investment will join the Standard & Poors ASX All Ordinaries Index, from March 18, 2019, with seven to be removed.
The S&P Dow Jones Indices announced the changes today, including Auscann, Avita Medical, Clover Corp, Opthea, Paradigm and Volpara joining the largest 500, by market capitalization, of the 2,282 ASX-listed companies.
The S&P Indices removed Airxpanders, Bionomics, Impedimed, Medlab Clinical, Reva, Somnomed and TPI Enterprises from the index.
Australian Ethical is a substantial investor in a number of ASX-listed biotechnology companies.
A list of companies in which Australian Ethical was invested at September 30, 2018 is available at: https://www.australianethical.com.au/companies-we-invest-in/.

IMMUTEP

Immutep says a non-human primate animal model shows that IMP761 decreases inflammatory T-cell infiltration induced by intra-dermal injection of an antigen.
Immutep said that the pre-clinical study of IMP761, an LAG3 agonist antibody being developed for the treatment of autoimmune diseases, was presented at the Congress of European Crohn's and Colitis Organisation conference in Denmark on March 7, 2019.
The company said that the in-vivo results were "consistent with earlier in-vitro studies … on the immunosuppressive activity of IMP761".
Immutep said that compared to control animals, CD3+ or CD8+ T-cell infiltration was inhibited by IMP761 for both tested sub-cutaneous doses (0.03mg/kg and 0.3mg/kg) as observed via immunofluorescence staining of T cells in the skin tissue test site biopsy".
The company said that multivariate analysis of the test site parameters (erythema, CD3, CD4 and CD8 T cell infiltration) "showed a significant decrease of this antigen-specific T-cell induced intradermal reaction, compared to the control group".
Immutep said that at the site of chronic inflammation, auto-immune memory T-cells were stimulated by the same self-peptides repeatedly, acquiring an "exhausted" phenotype.
The company said it used LAG-3, a marker for exhausted memory T-cells, to target the self-reactive T-cells in the animals.
Immutep said that as LAG-3 was a T-cell co-inhibitory receptor, "we developed an agonist antibody, IMP761, to increase LAG-3 down-modulation of T-cell receptor signaling in these autoimmune T-cells".
Immutep chief medical and scientific officer Dr Frédéric Triebel said that better targeted immune-suppressive antibodies "should address the root cause of autoimmune diseases by specifically silencing the auto-immune memory T-cells accumulating at the disease site".
"By increasing the physiological negative feedback loop of LAG-3 on T-cell receptor signaling in response to self-peptides, IMP761 is preventing the activation of all downstream inflammatory pathways," Dr Triebel said.
Immutep said it would advance IMP761 into clinical development and had begun cell line development for manufacturing.
Immutep chief executive officer Marc Voigt said the IMP761 pre-clinical study was "very encouraging".
"We believe that IMP761 represents a new, more targeted therapeutic approach working upstream from currently available immunosuppressive therapies," Mr Voigt said.
Immutep was up 0.2 cents or 6.1 percent to 3.5 cents with 2.8 million shares traded.

FEDERAL GOVERNMENT

The Federal Government says it will match Rotary clubs and provide $500,000 to raise funds for the Griffith University Plasprotect Malaria Vaccine Project.
A media release from Federal Health Minister Greg Hunt said the funding would come from the Medical Research Future Fund and would be used by Brisbane's Griffith University for clinical trials to test the effectiveness of the Plasprotect malaria vaccine.
The Government said Plasprotect had "proven highly effective in animal trials and has been shown to be safe in humans, with the next step to undertake human clinical trials".
The media release said malaria affected more than two hundred million people and killed more than 450,000 people each year, including thousands of Australians.
The Government said that since 2016, the National Health and Medical Research Council had provided more than $52 million to support malaria research.

FEDERAL GOVERNMENT

The Federal Government says health portfolio boards have reached more than 50 percent for the first time.
A media release from Federal Health Minister Greg Hunt said the "health portfolio's gender balance is currently 51.6 percent for ministerial appointments to boards and committees".
"As we mark International Women's Day, I am delighted to announce that health portfolio's gender balance is currently 51.6 percent for ministerial appointments to boards and committees … up from 43.4 percent two years ago," Mr Hunt said.
The Government said that Cancer Australia had appointed University of Adelaide professor of cancer medicine Prof Dorothy Keefe as its chief executive officer.

UNIVERSAL BIOSENSORS

Universal Biosensors says it has reduced staff by one third, including its new chief executive officer Rick Legleiter.
Universal Biosensors said it had "ceased employment of approximately one third of its workforce in Rowville, Melbourne".
"This cost reduction initiative is expected to deliver an annualized saving of approximately $3.0 million," the company said.
In 2017, Universal Biosensors said Mr Legleiter was appointed chief executive officer and it would make a decision on his replacement following Siemens negotiations, to end on June 8, 2019 (BD: Aug 7, 2017; Feb 11, 2019).
Universal Biosensors fell one cent or 4.35 percent to 22 cents.

COCHLEAR

Cochlear says the UK National Institute for Health and Care Excellence (NICE) has expanded the suitability criteria for its cochlear implants in the National Health Service.
Cochlear said the threshold for eligibility was reduced to 80 decibels hearing loss (dB HL) at two or more frequencies without the use of a hearing aid, down from 90 dB HL.
The company said advocacy and community associations, healthcare professionals and key groups including the British Academy of Audiology, the British Society of Audiology and the British Cochlear Implant group campaigned for the expansion of patients suitable for its implants.
Cochlear was up 28 cents or 0.2 percent to $177.42 with 214,178 shares traded.

IMMUTEP

Immutep says it has received $872,351 from the Australian Tax Officer under the Federal Government Research and Development Tax Incentive program.
Immutep said the rebate related to research and development expenditure for the year to June 30, 2018.

TPI (TASMANIAN POPPY INDUSTRIES) ENTERPRISES

Sydney's Wentworth Williamson Management says it has increased its substantial holding in TPI from 4,872,614 shares (6.01%) to 5,795,086 shares (7.15%).
In a substantial shareholder notice signed by Wentworth Williamson director and portfolio manager James Williamson, the company said it acquired the shares between December 31, 2018 and March 5, 2019 but failed to state the price paid as required under the Corporations Act 2001.
TPI fell seven cents or 6.7 percent to 98 cents.

MEDIGARD

The ASX says it has suspended Medigard immediately as "operations and financial conditions are not adequate to warrant the continued quotation of its securities".
Medigard said that the suspension would continue until the company was able to demonstrate compliance with Listing Rules 12.1 and 12.2.
Medigard last traded at two cents.