



Biotech Daily

Wednesday June 7, 2017

Daily news on ASX-listed biotechnology companies

- * **ASX FLAT, BIOTECH DOWN: BIONOMICS UP 8%, STARPHARMA DOWN 8%**
- * **ANAESTHESIA: RCT DATA FABRICATION, NON-RANDOM SAMPLING**
- * **BIOTECH DAILY EDITORIAL: TRIAL TRANSPARENCY**
- * **IMAGION \$12m IPO FOR NANO-MAGNETIC CANCER TEST**
- * **ATCOR SIGNS NEPHROLOGY ASSOCIATES FOR SPHYGMOCOR**
- * **OVENTUS: 'PILOT TRIAL MOUTH GUARD EQUALS CPAP'**
- * **LINKS, LOTSA, LAURENCE FREEDMAN BELOW 5% IN BIONOMICS**
- * **PHARMAXIS APPOINTS DR KATHLEEN METTERS DIRECTOR**

MARKET REPORT

The Australian stock market slipped 0.01 percent on Wednesday June 7, 2017 with the ASX200 down 0.3 points to 5,667.2 points.

Twelve of the Biotech Daily Top 40 stocks were up, 15 fell, 10 traded unchanged and three were untraded.

Bionomics was the best, up three cents or 7.9 percent to 41 cents with 4.1 million shares traded.

Osprey climbed 5.6 percent; Benitec was up 3.45 percent; Medical Developments and Sirtex rose more than two percent; Admedus, Ellex, Neuren, Pharmaxis and Psivida were up more than one percent; with Cochlear, CSL, Mesoblast and Opthea up by less than one percent.

Starpharma led the falls, down 0.3 cents or 8.3 percent to 3.3 cents with 10.2 million shares traded.

Avita and Factor Therapeutics lost more than seven percent; Acrux fell 5.8 percent; Cellmid, Impedimed, Prima, Pro Medicus and Viralytics were down more than three percent; Prana, Reva and Uscom shed more than two percent; Actinogen fell 1.5 percent; with Airxpanders, Nanosonics and Resmed down by less than one percent.

ANAESTHESIA

UK anaesthetist and Anaesthesia editor Dr John Carlisle says that some large randomized controlled trials are not randomized and may have fabricated results.

In an article in the John Wiley & Sons journal Anaesthesia Dr Carlisle wrote: "There was evidence that trials retracted for reasons other than data integrity may have contained corrupt and possibly fabricated data."

"Trials with extreme distributions of means were more likely to contain incorrect or fabricated data than other trials, as has been independently verified," Dr Carlisle said.

The article, entitled 'Data fabrication and other reasons for non-random sampling in 5,087 randomised, controlled trials in anaesthetic and general medical journals', was published on Sunday June 4, 2017, accompanied by an editorial.

The full article is available at: <http://onlinelibrary.wiley.com/doi/10.1111/anae.13938/full>.

Dr Carlisle said that randomized, controlled trials had been retracted after publication because of data fabrication and inadequate ethical approval.

"Fabricated data have included baseline variables, for instance, age, height or weight.

"Statistical tests can determine the probability of the distribution of means, given their standard deviation and the number of participants in each group.

"Randomized, controlled trials have been retracted after the data distributions have been calculated as improbable," Dr Carlisle wrote.

Dr Carlisle said he wanted to explore whether the distribution of baseline data in trials was consistent with the expected distribution and that he wanted to determine whether trials retracted after publication had distributions different to trials that have not been retracted.

Dr Carlisle said he wanted to determine whether data distributions in trials published in specialist anaesthetic journals were different to distributions in non-specialist medical journals.

Dr Carlisle said he analyzed the distribution of means in 5,087 randomized, controlled trials in eight journals between January 2000 and December 2015, chosen because he had electronic access to the full text.

"Trial p values were distorted by an excess of baseline means that were similar and an excess that were dissimilar [with 763 of 5,015 trials or 15.2 percent] that had not been retracted from publication had p values that were within 0.05 of 0 or 1 (expected 10%), that is, a 5.2% excess, $p = 1.2 \times 10^{-7}$," Dr Carlisle wrote.

"The p values of [31 of 72 trials or 43 percent] that had been retracted after publication were within 0.05 of 0 or 1, a rate different to that for unretracted trials, $p = 1.03 \times 10^{-10}$ and the difference between the distributions of these two subgroups was confirmed by comparison of their overall distributions, $p = 5.3 \times 10^{-15}$," Dr Carlisle said.

"Each journal exhibited the same abnormal distribution of baseline means," he said.

"Some p values were so extreme that the baseline data could not be correct.

"Fraud, unintentional error, correlation, stratified allocation and poor methodology might have contributed to the excess of randomized, controlled trials with similar or dissimilar means, a pattern that was common to all the surveyed journals.

"It is likely that this work will lead to the identification, correction and retraction of hitherto unretracted randomized, controlled trials," Dr Carlisle said.

"The distribution of means for baseline variables in randomized, controlled trials was inconsistent with random sampling, due to an excess of very similar means and an excess of very dissimilar means and the distortion in two non-specialist medical journals was indistinguishable from that found in six specialist anaesthetic journals," he said.

"Future work might determine whether this finding is general to all randomised, controlled trials," Dr Carlisle wrote.

BIOTECH DAILY EDITORIAL

Biotech Daily is not aware of any deliberate fraud or accidental statistical variations in any of the peer-reviewed data relating to the companies and organizations we cover.

That is not to say it has not or does not happen, just that we are not aware of any such cases.

Dr Carlisle says he may have made errors in his calculations and data transcription from the more than 5,000 trials he investigated and some trial errors may have been accidental.

Nevertheless, his article is a salient and sobering reminder that there are motives for scientists, academics and researchers to falsify data, for personal gain, for profit for their employing companies or merely "to be published". This should never be the case. And journalists and publications should always immediately correct their errors. But they don't.

What we do know about the Australian biotechnology sector is that a close cousin to fraud and data manipulation is corporate spin and selective data mining.

Biotech Daily prefers to report precise patient numbers in small trials and on some occasions, companies have gone out of their way not to assist. While it is very clear that "75 percent of patients responded" is good news, it is less so when it is really three of four patients in an unblinded pilot trial.

We believe that all scientists, academics and researchers should read Dr Carlisle's article, and should questionable data be published, question it.

David Langsam, Editor

IMAGION BIOSYSTEMS

The Albuquerque, New Mexico-based Imagination is hoping to raise up to \$12 million at 20 cents share to list on the ASX and develop its Magsense cancer diagnostic tests.

The Imagination prospectus said it was founded by Dr Ed Flynn, with Robert Proulx as executive chairman and the company hoped to list on June 20, 2017.

Imagination said there was an unmet medical need for non-invasive detection of specific cancerous tumors and the Magsense "super-para-magnetic relaxometry technology has broad applicability in the diagnosis and staging of cancers and other diseases and provides a platform to commercialize a wide range of products and applications".

The company said it had spent directly and through grants about \$US18 million in developing the Magsense technology and initial end-use applications.

Imagination said the technology used nanoparticles labelled with cell-specific targeting antibodies which could be injected intravenously or by other routes of administration.

The company said that the nanoparticles could then be magnetized by a low-field magnetic pulse and their location detected by superconducting quantum interference device detectors in its Magsense instrument.

Imagination said that Magsense nanoparticles attached to bio-marked cancer cells lost their induced magnetization more slowly than an unattached particle, so only those particles attached to their target tumor were measured, with unattached nanoparticles not detected.

The company said that the Magsense system did not expose the patient to ionizing radiation or radioactive tracers.

Imagination said the technology had not been tested in humans.

The prospectus is available at: <http://bit.ly/2s2X9Nk>.

ATCOR MEDICAL

Atcor says it has signed a two-year healthcare delivery network agreement with the Oak Brook Illinois-based Nephrology Associates of Northern Illinois and Indiana.

Atcor said that it would provide Sphygmocor non-invasive central blood pressure and arterial stiffness systems to Nephrology Associates practices throughout the region.

The company said that Nephrology Associates was the second largest kidney specialist practice in the US and the largest private nephrology practice group in the Midwest, with more than 90 physicians in more than 40 offices.

Atcor said that more than 30 Sphygmocor systems were expected to be sold during the first 12 to 15 months of the 24 month agreement and sales had begun.

The company said that nephrologists were “a key target group for sales of Sphygmocor, due to the high correlation between high blood pressure and kidney disease” and nearly all of their patients could benefit from the Sphygmocor test.

The company said that the Renal Physicians Association sponsored its American Medical Association current procedural terminology-1 (CPT-1) reimbursement code for the Sphygmocor test which took effect in 2016.

Atcor chief executive officer Duncan Ross said the company was “very pleased to have one of the premier nephrology groups in the US adopt Sphygmocor into their medical practice”.

“The benefits of central blood pressure waveform analysis are readily apparent to medical specialists with patients experiencing kidney disease and complex hypertension,” Mr Ross said.

Atcor said it previously announced the signing of a similar network agreement with Emory University and Emory Healthcare in Atlanta, Georgia, with more network agreements expected to be signed “in the near future” (BD: Feb 23, 2017).

Atcor was unchanged at 3.7 cents.

OVENTUS MEDICAL

Oventus says a four-patient trial of its mouth guard and airway pipe for sleep apnoea shows it is equal to similar continuous positive airway pressure mask and pumps.

Oventus said that results from the initial pilot study were presented at the American Academy of Dental Sleep Medicine in Boston on June 2, 2017.

The company said that continuous positive airway pressure (CPAP) was the first line of treatment for sleep apnoea patients and used a pressure pump attached to a mask blowing air into the patient’s airway.

Oventus said that the mask and CPAP system was “not well tolerated [but] it is a multibillion dollar industry with massive unmet needs due to issues associated with current treatment options”.

The company said the early data supported the use of its O2Vent T as a CPAP alternative either as a standalone appliance, or in combination with CPAP, using it as a strapless device and not requiring high pressures or a mask.

Oventus clinical director Dr Chris Hart said that “a high percentage of complications and non-compliance with traditional CPAP are due to mask and pressure related issues” and both were minimized with his product.

“The process to optimise the CPAP interface will be completed in the expanded trial [which was] expected to be finished by the end of the year,” Dr Hart said. “Another trial is now under way in Perth, focussing on specific pressure and flow measurements in the patient’s airway and how the Oventus airway technology influences this.”

Oventus was untraded at 35 cents.

BIONOMICS

Laurence Freedman and associated companies have reduced their shareholding in Bionomics again, from 31,037,837 shares (6.45%) to below substantial.

In April 2016 and February 2017, the group reduced their holding from 40,187,873 shares (9.75%) to 31,037,837 shares (6.45%) (BD: Apr 11, 2016; Feb 24, 2017).

Today, the substantial shareholder notice, signed by the Sydney-based Mr Freedman, said the shares were held through Link Superannuation Fund, Link 405 Pty Ltd, Link Enterprises (International) Pty Ltd and Lotsa Nominees Pty Ltd.

The notice said that the group sold 22,500,000 shares for \$8,859,849 or 39.4 cents a share.

Biotech Daily calculates that the group retains 8,537,837 shares or 1.8 percent of the company.

Bionomics climbed three cents or 7.9 percent to 41 cents with 4.1 million shares traded.

PHARMAXIS

Pharmaxis says it has appointed Dr Kathleen Metters as a non-executive director.

Pharmaxis said that Dr Metters had more than 25 years' experience in the discovery and development of new therapies for serious diseases, including nine years with Merck & Co, known as Merck Sharp & Dohme outside North America, of which four years was as the head of basic research.

The company said that from 2011, Dr Metters was Lycera Corp chief executive officer developing oral treatments for autoimmune diseases and cancer.

Pharmaxis said that Dr Metters held a Bachelor of Science from the University of Manchester Institute for Science and Technology and a Doctorate of Philosophy from London's Imperial College.

Pharmaxis was up half a cent or 1.85 percent to 27.5 cents.