Biotech Daily

Monday April 3, 2017

Daily news on ASX-listed biotechnology companies

*** MARCH BDI-40 UP 10%, ASX200 UP 3%, BIG CAPS UP 5%**
- MESOBLAST UP 46%, PRANA 40%, VIRALYTICS 32%; IDT DOWN 17%, ELLEX 14%

*** TODAY: ASX UP, BIOTECH EVEN: BENITEC UP 6%, PRANA DOWN 13%**

*** OPTHEA CLAIMS OPT-302 + LUCENTIS WET AMD SUCCESS; $45m RAISING**

*** MOUSE DATA BACKS BENITEC DDRNAI BB-301 FOR OPMD**

*** BIONOMICS: 'BNC101, CHECKPOINT INHIBITOR FOR CANCER IN MICE'**

*** USCOM CONSORTIUM EU $2m FOR BETTER SPACERS**

*** NOMINATIONS CLOSE FOR $750k SCIENCE PRIZES APRIL 12**

*** SUDA FILES ARTIMIST APPLICATION TO TGA**

*** HUNTER HALL REDUCES TO 5.5% OF SIRTEX**

*** M&G GROUP TAKES 13% OF MESOBLAST**

*** THORNEY TAKES 5.8% OF MESOBLAST**

*** ALLAN GRAY REDUCES, AGAIN, TO 15% OF PHARMAXIS**

*** ALVIN BLUMENTHAL, SUBURBAN BELOW 5% OF CRESO**

*** AVITA RELEASES 3.5m ESCROW CEO LOAN SHARES**

*** UNIVERSAL BIOSENSORS TO RELEASE 26k ESCROW SHARES**

*** CRESO TO RELEASE 4m ESCROW SHARES**

*** PHYLOGICA LOSES CO SEC NATASHA FORDE, GRAEME BODEN STAYS**

MARKET REPORT

The Australian stock market was up 0.13 percent on Monday April 3, 2017 with the ASX200 up 7.8 points to 5,872.7 points. Fifteen of the Biotech Daily Top 40 stocks were up, 15 fell, five traded unchanged and five were untraded. All three Big Caps were up.

Benitec was best, up one cent or 5.88 percent to 18 cents with 459,361 shares traded, followed by Viralytics up 5.83 percent to $1.27 with 646,578 shares traded. ITL rose 4.3 percent; Impedimed and Living Cell were up more than three percent; Airxpanders, Cellmid, Clinuvel, Genetic Signatures, Mesoblast and Pro Medicus improved more than two percent; Atcor, Resmed, Sirtex and Universal Biosensors were up more than one percent; with Cochlear, CSL and Nanosonics up by less than one percent.

Prana led the falls, down 0.9 cents or 12.7 percent to 6.2 cents with 431,349 shares traded. Dimerix lost 7.7 percent; Psivida and Resmed fell more than four percent; Pharmaxis was down 3.45 percent; Factor Therapeutics and Orthocell shed more than two percent; Admedus, Avita, Bionomics, Ellex, Medical Developments, Neuren and Oncosil were down more than one percent; with Compumedics down 0.9 percent.

BIOTECH DAILY TOP 40 INDEX (BDI-40)

March was a very good month for the Biotech Daily Top 40 Index (BDI-40), which climbed 10.0 percent, compared to the ASX200 up 2.7 percent.

Sirtex strengthened its hold as the largest biotech by market capitalization at $1,033 million, closely followed by the resurgent Mesoblast at $976 million – having briefly broken the billion dollar barrier last week – and Nanosonics at $923 million.

The Nasdaq Biotechnology Index (NBI) fell 1.25 percent in March, while the collective three Big Caps of Cochlear, CSL and Resmed (which are not included in the BDI-40) climbed 4.7 percent in March and 23.2 percent for the year to March 31, led by the Magic Pudding of CSL, up 6.2 percent in March, with Cochlear up 3.6 percent and Resmed retreating 0.7 percent (see charts below).

For the 12 months to March 31, 2017, the BDI-40 was up 7.1 percent, the ASX200 was up 15.4 percent and the NBI was up 12.5 percent.

And March was definitely medical marijuana month, with Zelda up 200 percent to $30 million, followed by Creso up 175 percent to $33 million on a Brazilian distributor, MMJ up 161.8 percent to $144 million, Botanix up 54.5 percent to $17 million and Medlab Clinical up 11.1 percent to $90 million, with several claiming import and trial approvals.

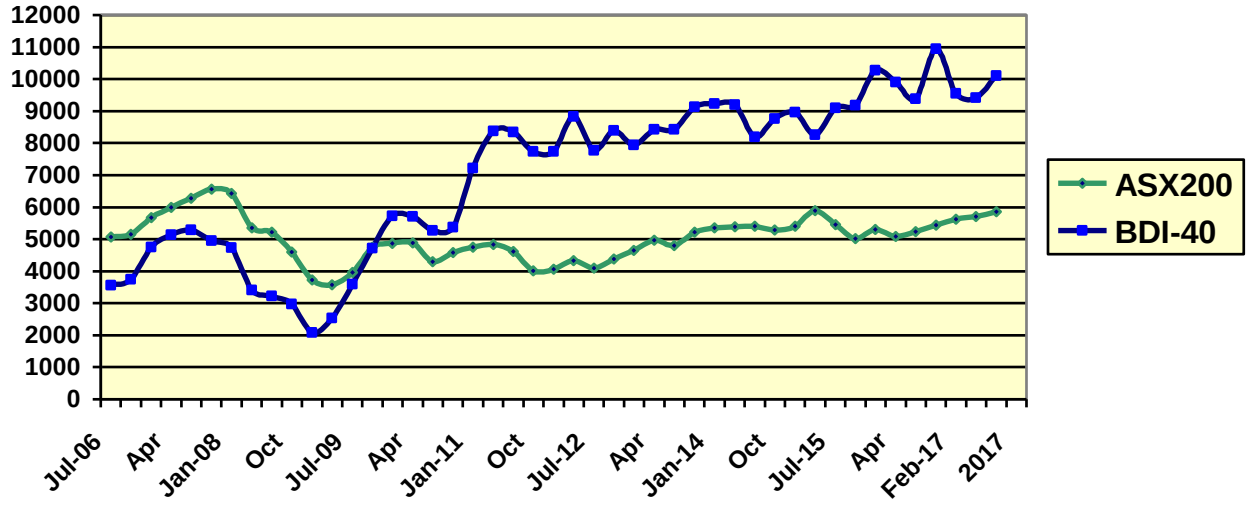
The BDI-40 saw 23 companies climbing, 11 by more than 10 percent and 16 falling, with just four by more than 10 percent, while ITL held steady at $45 million.

Mesoblast improved on clinical announcements, but surprised by climbing higher on a discounted capital raise, up $309 million or 46.3 percent to close the month at $976 million, followed by Prana reporting good clinical news for the first time in five months, up 40.1 percent to $38 million, Viralytics (31.5%), Living Cell (29.8%), Pro Medicus (26.9%), Compumedics (23.1%), Cellmid, (17.6%) and Genetic Signatures (15.8%).

IDT led the few notable March falls, down 16.6 percent to $35 million, followed by Ellex (13.6%), Atcor (13.3%) and Avita (11.4%).

Outside the BDI-40, GI Dynamics, Immuron, Imugene, LBT, Medibio, Optiscan and Paradigm were all recovering or showing new promise.

BDI-40 v ASX200 Jun 30, 2006 to Mar 31, 2017- Adjusted



OPTHEA

Opthea expects to raise $45 million on its claim of safety and biological activity in its first-in-human phase I/IIa trial of OPT-302 for wet age-related macular degeneration.

In announcements to the ASX and a teleconference, Opthea chief executive officer Dr Megan Baldwin and study investigator Prof Pravin Dugel said the trial met its safety and efficacy endpoints, including biological activity at the low dose of 0.3mg of OPT-302.

Opthea said 20 patients were in the phase I dose ranging trial, which tested 0.5mg Lucentis in combination with 0.3mg, 1.0mg and 2.0mg of OPT-302 as well as 2mg OPT-302 as a monotherapy, with 31 patients in the randomized, phase IIa, dose expansion trial comparing 2.0mg OPT-302 as a monotherapy to the same dose in combination with 0.5mg Lucentis, across previously treated and naïve patients.

Following the teleconference, Dr Baldwin told Biotech Daily that given the small numbers in the 51-patient, multi-armed trial there was no clear dose response, but the low dose of 0.3mg had shown a biological response, as did the 1.0mg and 2.0mg doses, injected monthly for three months.

Dr Baldwin said that OPT-302 was tested as a monotherapy and demonstrated an increase in visual acuity of 5.6 letters on the early treatment diabetic retinopathy study (ETDRS) eye-chart at 12 weeks, whereas the previous phase III Lucentis (ranibizumab) 'Marina' trial showed that controls had a continuous decrease in acuity, while those receiving Lucentis had a response plateau at three months.

Dr Baldwin said the vascular endothelial growth factor (VEGF) C and D combination in OPT-302 was complementary to the VEGF-A in Lucentis and improved visual acuity as well as sub-retinal fluid levels and mean central subfield thickness.

Prof Dugel, who is also Retinal Consultants of Arizona managing-partner and a clinical professor at the University of Southern California Eye Institute, said that age-related macular degeneration patients had a mean of 17 injections of Lucentis with no improvement and it was significant that there had been improvement with three injections of OPT-302.

Prof Dugel said the two aims of the trial were whether OPT-302 was safe and the result was "outstanding" and whether there was biological activity, which he said there was.

Opthea said that 49 patients were evaluated, the two deaths were unrelated to study drugs, and OPT-302 alone and in combination was safe and well-tolerated at all doses.

The company said that 44 patients (89.8%) maintained or gained vision at 12 weeks, with 18 naïve patients having the best response of an increase in 10.8 letters at 12 weeks.

Opthea said that the drug combination improved vision in 19 prior-treated patients by an average 4.9 letters and reduced both central subfield thickness and sub-retinal fluid in both naïve and prior treated patients, with 72 percent of naïve patients having a complete resolution of sub-retinal fluid and central subfield thickness reduced to near normal levels.

Opthea said it expected to raise $35 million in a placement at 93 cents a share, a 14.8 percent premium to the closing price before last week's trading halt, and would offer a one-for-14 rights issue to shareholders at the record date of April 5, with the offer opening on April 10 and closing on April 24, 2017, to raise a further $10 million.

Dr Baldwin said that with the company's existing funds and the expectation of the 43.5 percent Federal Government Research and Development Tax Incentive, Opthea would be able to fund a three-arm, 350-patient, randomized, controlled, phase IIb trial of OPT-302 in combination with Lucentis for wet age-related macular degeneration, with top-line results in 2020, as well as a 90-patient, phase IIa trial of the combination for diabetic macular oedema with results by the end of 2018, and a phase IIa trial for wet age-related macular degeneration patients with a sub-optimal response to anti-VEGF-A treatment.

Opthea remained in a trading halt at 81 cents.

BENITEC BIOPHARMA

Benitec says that pre-clinical mouse data shows that DNA-directed RNA-interference can correct oculo-pharyngeal-muscular dystrophy.

Benitec said that oculo-pharyngeal-muscular dystrophy (OPMD) was a rare progressive muscle-wasting disease caused by mutation in the poly(A)-binding protein nuclear 1 (PABPN1) gene and was characterized by eyelid drooping, swallowing difficulties and proximal limb weakness.

The company said that the studies showed that a DNA-directed RNA-interference (ddRNAi) approach to silence and replace the mutant PABPN1 protein resulted in "the correction of the muscular dystrophy and of key clinical features of OPMD including a progressive atrophy and muscle weakness associated with nuclear aggregates of insoluble PABPN1".

The article, co-written by Benitec chief scientific officer Dr David Suhy, entitled 'PABPN1 gene therapy for oculo-pharyngeal-muscular dystrophy', was published in Nature Communicationsand is at: http://www.nature.com/articles/ncomms14848.epdf.

Benitec said that the data was generated in the A17 mouse model that expressed the mutant PABPN1 gene and mimicked most of the features of human oculo-pharyngeal-muscular dystrophy patients.

The company said the findings were central to European orphan drug designation for the oculo-pharyngeal-muscular dystrophy program earlier this year (BD: Jan 22, 2017).

"These published results have been critical for establishing the proof of concept that a ddRNAi approach may be able to treat this orphan disease," Dr Suhy said.

"Furthermore, this program highlights one of the unique aspects of the Benitec technology that is not readily attainable by other gene therapy approaches," Dr Suhy said.

"Specifically, through our unique approach to gene silencing and gene therapy, we are able to knock out the mutated form of the gene and have the ability to express a normal copy to restore function," Dr Suhy said.

"We are extremely excited about the progress we have made with our OPMD program and, with our European orphan drug designation, we look forward to streamlining the process towards regulatory approval," Dr Suhy said.

Benitec said it had been working with research groups headed by Prof George Dickson at London's Royal Holloway University and Dr Capucine Trollet at the Paris, France-based Myology Research Center.

The company said the collaboration was begun at the Royal Holloway and had shown that the combination of two recombinant adeno associated virus vectors, one allowing the inhibition of mutated PABPN1 by ddRNAi, and the other expressing a functional PABPN1, "significantly reduces the amount of PABPN1 nuclear aggregates, decreases muscle fibrosis, reverts muscle strength to the level of healthy muscles and normalizes the expression of RNA".

Benitec said that the efficacy of the combined treatment was also confirmed in cells derived from oculo-pharyngeal-muscular dystrophy patients.

The company said that with its collaborators, it was pursuing the advance of BB-301, a next generation, follow-on ddRNAi therapeutic for the treatment of oculo-pharyngeal-muscular dystrophy, that combined both the silence and replace strategy of mutant PABPN1 into a single vector.

Benitec said that BB-301 was in preclinical development and it planned to begin US Food and Drug Administration investigational new drug application-enabling studies later this year, with a phase I/II study in oculo-pharyngeal-muscular dystrophy patients expected in 2018, subject to toxicity results and future regulatory review.

Benitec was up one cent or 5.9 percent to 18 cents.

BIONOMICS

Bionomics says that pre-clinical mouse data supports its BNC101 anti-LGR5 cancer stem cell drug candidate for solid cancers.
Bionomics said the data would be presented at the American Association for Cancer Research meeting in Washington, DC in a poster entitled 'Targeting the LGR5 complex with BNC101 to improve checkpoint inhibitor therapy in colorectal cancer' and demonstrated "complementary anti-tumour activity between BNC101 and checkpoint inhibitors".
The company said that LGR5 positive cancer stem cells were highly prevalent within metastatic colorectal cancer and led to a higher tumor recurrence in patients.
Bionomics said that emerging data showed that cancer stem cells could generate an environment in the tumor that suppressed the immune system from functioning as it normally would to attack tumor cells.
The company said that checkpoint inhibitors were a form of immunotherapy that increased the ability of the immune system to recognize and destroy tumor cells that would otherwise escape immune surveillance, but in the presence of cancer stem cell derived immune suppressive factors, checkpoint inhibitors might not be able to function to their highest potential.
Bionomics said that in the the mouse model of colon cancer treatment with BNC101 and a checkpoint inhibitor was associated with a greater reduction in T-regulatory cells, an immune suppressive cell and a modest increase in tumor attacking cytotoxic T-cells compared to treatment with a checkpoint inhibitor alone.
The company said that further preclinical data showed the ability of BNC101 to induce the recruitment of natural killer cells to the LGR5 positive cells through an effect known as antibody-dependent cell-mediated cytotoxicity.
Bionomics said that targeting the LGR5 positive cancer stem cell component of colorectal cancer with BNC101 might release potential suppression of checkpoint inhibitor activity to leverage greater therapeutic benefit to colorectal cancer patients.
Bionomics fell half a cent or 1.3 percent to 37 cents.

USCOM

Uscom says it has been awarded EUR1,317,502 ($A1,848,170) to develop a smart spacer and software to promote pulmonary recovery training and drug uptake.
Uscom said it was the second European grant to its Budapest, Hungary subsidiary as a member of a consortium awarded the funds over two years under the Eurostars program.
The company said that it would receive EUR349,480k over the two years.
Uscom said that chronic respiratory diseases were common and increasing and the appropriate choice and delivery of medication could "significantly improve outcomes".
The company said that oral inhaled drugs were improved through the use of spacers and its Spirosonic devices delivered "research quality pulmonary assessment to the clinic and home care".
Uscom said that the project was entitled 'Incentive based smart spacer to promote pulmonary recovery training and drug uptake' and focused on the development of a medical device that increased the efficiency of drug delivery from inhalation dispensers, supported by software to re-inforce the appropriate use of medication.
Uscom executive chairman Prof Rob Phillips said that hundreds of millions of people suffered from preventable chronic respiratory diseases and the research funding focused on solving a clinical problem that results in hundreds of thousands of deaths a year.
Uscom was untraded at 20 cents.

OFFICE OF THE CHIEF SCIENTIST

Australia's chief scientist Dr Alan Finkel says the deadline for nominations for the $750,000 in Prime Minister's Prizes for Science is Wednesday April 12, 2017.

Ina media release Dr Finkel said "the prestigious prizes recognized achievement in Australian science … [for] outstanding teachers, scientists and innovators". for

Dr Finkel said the prizes began in 2000 and "while the Sydney Olympics showed our sporting achievements to the world, the Prime Minister's Prizes for Science recognized the world class capabilities of Australian scientists".

"It was the start of a grand tradition in Australian science and has grown to also include the tremendous contributions of our science teachers and innovators," Dr Finkel said.

"Today, people who were schoolchildren when these prizes commenced are teachers, scientists, and innovators in their own right," Dr Finkel said. "It's their turn to be recognized and for their work to further inspire future generations."

The media release from Dr Finkel's office said that he would chair the selection committee for five of the seven prizes.

The Prime Minister prizes for science and prize for innovation each carry awards of $250,000, with $50,000 each for the Malcolm McIntosh prize for physical scientist, the Frank Fenner Prize for life scientist, the prize for new innovators and the excellence in science teaching in primary and secondary schools prizes.

Nominations close at 5pm on April 12, 2017 and for further details about the prizes or to nominate, go to: www.business.gov.au/scienceprizes.

SUDA

Suda says the Australian Therapeutic Goods Administration has accepted its Artimist for paediatric malaria marketing application for review

Suda said that last year it made a pre-submission to the TGA for Artimist (artemether sublingual spray).

The company said the TGA had 255 days to complete its review and provide an opinion, including potential approval of the Artimist marketing authorization.

Suda said that the application included data from its ART004 phase III pivotal trial in 150 paediatric patients with severe complicated malaria or uncomplicated malaria with gastro-intestinal complications.

The company said that the randomized study showed the superiority of Artimist in reducing parasite count compared to standard-of-care intravenous quinine.

Suda said it was in discussions with parties in relation to a trade sale or partnering agreement as part of the product commercialisation strategy and in parallel had begun pre-planning for a product launch, including negotiations around manufacture and supply chain logistics, pricing models and distribution channels.

Suda chief executive officer Stephen Carter said that "based on the positive results from our clinical studies in paediatric patients and our discussions with the World Health Organisation and other groups, we believe that pursuing a marketing authorisation in Australia will accelerate access to Artimist for patients in malaria-endemic countries".

"The acceptance of this filing brings us one step closer to addressing the unmet medical need of severe malaria," Mr Carter said.

"It is a debilitating condition that can cause long-term neurological problems and death," Mr Carter said.

"Children under five years of age are one of most vulnerable groups affected by severe malaria because they lack immunity to the parasite," Mr Carter said.

Suda was up 0.2 cents or 9.5 percent to 2.3 cents with 4.7 million shares traded.

SIRTEX MEDICAL

Hunter Hall Investment Management says it has reduced its substantial holding in Sirtex from 3,857,489 shares (6.69%) to 3,152,884 shares (5.46%).

Hunter Hall said it primarily sold shares between December 28, 2016 and March 30, 2017, with the single largest sale 213,350 shares for $3,032,850 or $14.22 a share

Last year, Hunter Hall said it bought and sold shares between October 30, 2015 and December 9, 2016, acquiring 1,469,666 shares on December 9, following the Sirtex profit warning with for $22,985,301 or $15.64 a share (BD: Dec 9, 2016).

Sirtex was up 30 cents or 1.7 percent to $18.20 with 799,325 shares traded.

MESOBLAST

M&G Investment Funds say it has increased its substantial holding in Mesoblast from equivalent to 46,643,788 shares (12.29%) to 54,026,630 shares (13.44%).

The London-based M&G said it held Australian shares and American depository shares, buying and selling between November 24, 2015 and March 30, 2017, but failed to disclose correctly the price of the shares as required under the Corporations Act 2001.

Mesoblast was up five cents or 2.2 percent to $2.33 with 432,738 shares traded.

MESOBLAST

Thorney Technologies says it has returned to a substantial shareholding in Mesoblast with 24,696,000 shares or 5.77 percent.

Thorney said that it acquired 1,125,000 shares at $2.00 each in the recent placement which raised $52.5 million (BD: Mar 27, 2017)

The company said that the shares were held by Thorney Technologies, Thorney Opportunities, Thorney Investment Group, Waislitz Family Foundation, Jasforce Pty Ltd and Urban Land Nominees.

Previous substantial shareholder notices said that Tiga Pty Ltd and Jamahjo Pty Ltd were related investors.

In 2013 and 2015, Thorney increased its holding in Mesoblast, but was subsequently diluted in placements below substantial (BD: Mar 18, 2013; Apr 17, 2015).

PHARMAXIS

Allan Gray says it has again reduced its shareholding in Pharmaxis, this time from 53,999,216 shares (17.02%) shares to 46,953,709 shares (14.71%).

Allan Gray said it bought and sold shares between September 28, 2016 and Mar 29, 2017 with the single largest sale 3,386,198 shares for $960,373 or 28.4 cents a share.

Allan Gray previously said it bought and sold shares in 2015 and 2016, with the single largest sale 2,990,791 shares for an average of 25.5 cents a share (BD: Sep 30, 2016).

Allan Gray held as much as 19 percent of Pharmaxis in 2011, buying shares at about $1.00, having taken profit in 2010 at $2.96 a share (BD: Apr 23, 20101; Jun 16, 22, 2011).

Pharmaxis fell one cent or 3.45 percent to 28 cents.

CRESO PHARMA

Suburban Holdings Pty Ltd says it has ceased its substantial shareholding in Creso Pharma, but appears to retain 4,046,079 shares.
The substantial holder notice, from Martin Place in Sydney with an indecipherable signature, said that Suburban Holdings was diluted by a placement on March 31, 2017 and transferred and sold shares between March 27 and 31, 2017 for prices ranging from 75 cents to 81.4 cents a share.
Last week, Creso said it had raised $8 million in a placement at 69 cents a share and would offer a share plan to raise a further $1 million (BD: Mar 27, 2017).
Last year, Suburban Holdings Pty Ltd said on the Creso ASX site that it had become substantial in itself with 6,500,000 shares (11.26%), but apparently meant it had become substantial in the marijuana food additive company (BD: Oct 26, 2016).
The notice, signed by Alvin Blumenthal of Rose Bay, Sydney was published on Creso ASX website about the same time as five directors interest notices, including one from Adam Blumenthal who said he held one fully paid share subject to 24 months escrow.
Creso fell one cent or 1.3 percent to 75.5 cents with 1.2 million shares traded.

AVITA MEDICAL

Avita says that 3,500,000 shares will be released from escrow on April 14, 2017.
Avita's most recent Appendix 3B new issue announcement said that on July 22, 2016, 3,500,000 shares had been released from escrow and there were 36,500,000 escrow shares under the chief executive officer plan, and a previous Appendix 3B announcement in February 2016 said that chief executive officer Adam Kelliher would be entitled to nine tranches of loan shares, with the first four tranches of 3,500,000 shares each dependent on remaining with the company for four years; and the next five tranches of 5,200,000 shares dependent on the 20-day volume-weighted average price reaching 20 cents, 30 cents, 40 cents, 50 cents and 60 cents, within the vesting period.
Avita fell 0.1 cents or one percent to 9.7 cents.

UNIVERSAL BIOSENSORS

Universal Biosensors says that 25,767 shares have been released from escrow and it has 175,827,472 shares available for trading.
The company's most recent Appendix 3B statement said there were a further 549,813 shares held in ASX escrow.
Universal Biosensors was up half a cent or 1.2 percent to 41.5 cents.

CRESO PHARMA

Creso says that 4,342,500 shares will be released from escrow on April 13, 2017.
The company's most recent Appendix 3B statement said there were a further 26,442,501 shares held in ASX escrow.

PHYLOGICA

Phylogica says that Natasha Forde has resigned as a joint company secretary as she is leaving Boden Corporate Services and is resigning from several companies.
Phylogica said that Graeme Boden continued as company secretary.
Phylogica was up 0.2 cents or 6.45 percent to 3.3 cents with 1.5 million shares traded.

BIOTECH DAILY TOP 40 WITH MARKET CAPITALIZATION AT MAR 31, 2017

Company $Am	**Apr-16**	**Mar-17**	**Apr-17**
Cochlear	5,852	7,497	7,767
CSL	46,962	53,676	56,989
Resmed	10,402	13,255	13,156
BDI-20			
Admedus	97	88	83
Airxpanders	236	213	245
Bionomics	154	195	181
Clinuvel	198	321	328
Compumedics	61	78	96
Ellex	84	154	133
Impedimed	326	285	270
Medical Developments	304	273	297
Mesoblast	981	667	976
Nanosonics	567	854	923
Neuren	189	122	125
Opthea	64	134	123
Pharmaxis	86	91	93
Polynovo	155	163	152
Prima	85	68	64
Pro Medicus	346	469	595
Psivida	121	80	86
Reva	468	436	406
Sirtex	1,656	920	1,033
Viralytics	154	219	288
Second 20			
Acrux	101	47	48
Actinogen	44	36	38
Atcor	35	15	13
Avita	56	70	62
Benitec	17	33	35
Cellmid	16	34	40
Cyclopharm	32	50	48
Dimerix	10	13	12
Factor Therapeutics	14	49	51
Genetic Signatures	39	38	44
IDT	69	42	35
ITL Ltd	18	45	45
Living Cell	26	57	74
Oncosil	72	40	45
Orthocell	23	32	29
Osprey	45	106	111
Prana	34	27	38
Starpharma	250	260	247
Universal Biosensors	64	68	72
Uscom	20	25	22

* Biotech Daily editor, David Langsam, owns shares in Acrux, Admedus, Benitec, Mesoblast, Nanosonics, Neuren, Volpara and non-biotechnology stocks. Through Australian Ethical Superannuation he has an indirect interest in a range of other biotechnology companies: **http://www.australianethical.com.au/who-we-invest-in**. These holdings are liable to change.

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