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In this edition...
The work of investors is made easier when a trailblazer emerges to provide the yardstick to measure both itself and its followers. Oncosil Medical is seeking to bootstrap itself on Sirtex Medical's success in educating the market on the role that selective radiotherapy can play in treating certain cancers. The companies are not competitors. However, together they enable some useful comparative insights to made e.g. in terms of ease of delivery, which will help investors appreciate the Oncosil approach to treating pancreatic cancer. Cogstate and Prana Biotech both presented at seminar in Melbourne this week, with the event reinforcing both the challenges and opportunities for diagnosing and treating Alzheimer's disease.
Companies covered: CGS, IPD, ISN, LBT, NEU, PBT, OSL

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - Current)	36.7%
Cumulative Gain	**387%**
Av. annual gain (12 yrs)	**16.6%**

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Bioshares

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Edition 515

Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies.

The Oncosil Medical Plan – Follow Sirtex!

Oncosil Medical (OSL: $0.088) is developing a cancer ablation therapy (termed Oncosil), similar to the therapy that Sirtex Medical has very successfully commercialised. Oncosil Medical has moved what was a shelved technology back into a commercialisation pathway, putting together a highly experienced management team and board, with additional funding the remaining step to advance this program.

The Oncosil product is a nuclear medicine device, similar to Sirtex's Sir-Spheres. Its regulatory pathway will be similar, with it not considered a pharmaceutical product. Oncosil's management has been quick to highlight that this is not a competing product to Sir-Sphere's. Oncosil will be used to irradiate tumours in the pancreas, where Sir-Spheres are used only for the treatment of primary and secondary liver cancers.

The Oncosil product was originally developed by pSivida. However that company ran out of cash during the GFC and the project was shelved. pSivida completed several Phase I and Phase II studies. Oncosil was acquired by way of a back door listing into Neurodiscovery, and at the end of June this year the company had $3.4 million in cash.

Oncosil's CEO is Neil Frazer, the brother of Ian Frazer who developed the Gardasil vaccine for prevention of HPV. Neil Frazer is highly experienced in pharmaceutical product developed, having brought 10 products to market in his career and is looking to make Oncosil product number 11.

Oncosil's Chief Scientific Officer is Dr Peter Knox, who was formerly CSO of Amersham International, which in 2004 was acquired by GE Healthcare for US$9.5 billion. The chairman is biotech entrepreneur Martin Rogers, who was formerly CEO of Prima Biomed. Roger Aston is also on the board as a non-executive director.

Pancreatic Cancer

At a company briefing this week, Frazer said that 80% of people diagnosed with pancreatic cancer are dead within one year. Only one out of six people respond to the chemotherapy drug gemcitabine, and only one in five are suitable for surgery, which Frazer says is a very radical process, with the tumours very difficult to access. People with pancreatic cancer die from either an obstruction of the bile duct or metastases to the liver.

The annual market for the treatment is expected to reach US$1.2 billion by 2015. Over 280,000 people are diagnosed worldwide with pancreatic cancer each year, and Oncosil's treatment is suitable for 10%-15% of that patient population.

Aside from chemotherapies that deliver a median survival of less than six months, external beam radiation is also used but is unpopular because of its side effects. Frazer believes there are no threats to the Oncosil product from emerging therapies, with immune therapies likely to be useful in future for deep-seated tumours like pancreatic cancer.

Cont'd over

Suitability of Oncosil Therapy – Early Stage Cancers

The Oncosil therapy is ideally suited for patients with localised tumours in the pancreas that are around 1-2 cm in length. It is not suitable for generalised pancreatic tumours. It is most suitable for early stage cancers. Oncosil will seek approval for a single treatment approach. Once approved, Oncosil may consider gaining approval for additional treatments, and may also look at applying this therapy for the treatment of brain and lung cancers.

Oncosil P32 properties compared with Sir-Spheres

The Oncosil therapy uses the pSivida biosilicon technology. It combines porous silicon with phosphorus, which is placed into a neutron reactor to make the P32 radioisotope. P32 has a half-life of 14.3 days, compared to Sirtex's Yttrium-90 half-life of 2.7 days. The maximum dose of the Oncosil therapy is 7% of tumour volume.

Frazer said that Oncosil is easier to deliver that Sir-Spheres, with it being 80% easier to deliver than Sir-Spheres. The Oncosil therapy takes only 30 minutes to deliver and is conducted as an out-patient procedure.

The safety profile of Oncosil is also favourable. In one case where the entire dose was delivered incorrectly into the blood stream, there were no side effects because the radiation was dissipated in the blood stream.

Sirtex Medical's Sir-Spheres deliver a much higher dose of radiation than that emitted by P32 Oncosil (about five times as much). P32 is currently used for several other medical therapies said Frazer, including blood-based treatments.

Frazer said that Oncosil's CSO, Dr Peter Knox, has considerable experience in this space, having previously been involved with the sale of beta seeds used in prostate cancer brachytherapy at Amersham. Sales of these seeds (which Bioshares understands are used in over a third of patients with prostate cancer) generates sales of $1 billion a year according to Frazer.

Clinical Trial Results to Date

Pilot Study 1

A pilot study was previously conducted with Oncosil, with patients receiving gemcitabine two weeks prior to Oncosil therapy. In this study in 17 patients with pancreatic cancer, four achieved a partial response over the 24 weeks of the trial, 10 achieved stable disease, and three patients had progressive disease. The median progression-free survival was 121 days (four months) and median overall survival was 10 months, compared to typically 5.7 months achieved with gemcitabine treatment alone. Patients also achieved an average 35% reduction in pain during the trial.

Pilot Study 2

A second pilot study was conducted but stopped after only six patients were enrolled due to a change of product focus by the company conducting the trial (pSivida). This was a dose escalating study, using doses up to four times as high as the first pilot study. The therapy was well tolerated and stable disease was reported in all six patients.

Registration Study

Oncosil is now preparing to conduct its registration study, which will permit it to market the drug in Europe, the US and other regions. The study will involve between 100-300 patients across 20 centres and is expected to cost up to $12 million to complete. The study is expected to take one year to recruit and a further year to obtain results.

The study's endpoints will be progression-free survival, overall survival, quality of life (including reduction of pain), and safety. The therapy has shown to numb pain at and around the tumour site in previous studies.

Oncosil is due to have a pre-IDE meeting with the FDA before the end of the year. It also needs to finalise its regulatory approach for Europe. Its options for Europe at the moment are to gain CE Mark approval without a registration study, which will allow it to sell the therapy in Europe but not market it, or, to assess the first 20 patients in the registration study and file that data with the European regulator. The registration study is expected to start in the first quarter of 2014.

Royalty Obligation

Oncosil has a royalty obligation to pSivida for any sales of the product. This will be low initially and will increase as a percentage based on the achievement of sales milestones. The terms are typical of a mid-stage licensing deal. In our view, this would indicate that royalty obligations would be in the low-to-mid double digits once sales targets are reached.

Summary

Financial conditions have improved considerably since the GFC. That has meant that dormant assets such as Oncosil's can be returned to the development pathway. Oncosil has put in place an experienced and knowledgeable team that has the capabilities, both financial and medical product development, to successfully commercialise this product.

Oncosil is capitalised at $21 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Alzheimer's Disease Seminar – 'There is a Tsunami Coming!'

The BioMelbourne Network hosted a breakfast seminar this week on the topic of Alzheimer's disease. This is a sector that investors need to watch very closely and it is one that is changing rapidly because of an ageing population, advances in technology and changes to the regulatory regime overseeing product development in the area.

In response to the question: what has been the big change in the field of Alzheimer's disease?, Professor Geoffrey Donnan, Director of The Florey Institute of Neuroscience and Mental Health, said 'we can now look at the brain like we never could before. Amyloid beta plaques and the tau protein involved with this disease can now be imaged in people with Alzheimer's disease (when they are still alive).'

The ABIL Study

Professor Christopher Rowe spoke about the ABIL study (the Australian Imaging Biomarkers and Lifestyle study of ageing), which is the largest brain amyloid imaging study in the world. The study was set up in 2006. If involves multinational healthcare companies such as Merck, Pfizer and GE Healthcare, and local biotech Cogstate.

The ABIL study is following 1,000 people, with 60% recruited in Melbourne and 40% in Perth. People involved in this study include both health volunteers and people with signs of cognitive decline.

The forward looking figures for Alzheimer's disease in world populations are somewhat alarming. Rowe said that currently there are around 300,000 people living with Alzheimer's disease in Australia and this is expected to increase to one million by 2050. Alzheimer's disease is responsible for 70% of dementia. At the age of 60, one in 100 people will have Alzheimer's disease, and this increases to 25% of the population by the age of 85.

Currently only mild stimulants are approved for the treatment of Alzheimer's disease but nothing tackles the underlying disease.

The ABIL study is being recognised globally. It is the first human imaging study also using the Fluorine-18 labelled PET tracer to pick up the amyloid protein, and is also the first human imaging study for a specific PET tracer for the tau protein. There are more than 1500 citations now annually for this study, and the study was awarded the best imaging paper by the Alzheimer's Association in both 2012 and 2013.

Alzheimer's disease starts 30 years before dementia occurs. Using the now available PET imaging techniques, after 12 years when beta amyloid starts to be deposited in the brain, imaging can detect the build up of beta amyloid, which can tell the patients and doctors whether that person will go on to develop Alzheimer's disease.

Rowe said that we are about to be hit with a flood of new clinical trials in this space. Never has there been more interest in the field of Alzheimer's disease. Rowe said that the ABIL study is Australia's best and most productive Alzheimer's disease research program but it receives no direct government support.

US Commitment to Brain Diseases

In the US, in April this year US President Obama launched the Brain Initiative to prevent, treat and cure brain disorders. The US Government will contribute US$100 million to the initiative, which is not substantial in relation to the US NIH budget, which the Obama administration is decreasing. However, it has researchers excited because of the expectation that there will be more funding behind the initial commitment.

Microsoft founder Paul Allen has formed the Allen Institute for Brain Science, which has a target to effectively treat and prevent Alzheimer's disease by 2025.

Rowe said that things are moving fast in this space. 'At present we are leaders in some areas. There is a tsunami coming!'

Prana Biotech. – The Role of Executive Function

CEO of Prana Biotechnology, Geoffrey Kempler, said that there are 36 million people in the world living with dementia. Kempler said that the company's lead company, PBT2, which is currently in Phase II trials in Alzheimer's disease and in Huntington's disease, works on four levels. It is an anti-amyloid, is neuroprotective, neurorestorative, and improves executive function.

Kempler said that Alzheimer's disease is due to an abnormal interaction between proteins and metals, which results in the formation of amyloid plaques said Kempler. PBT2 works by reducing beta amyloid aggregation in the brain, and also helps clear and degrade the plaques. PBT is neuroprotective by reducing tau hyperphosphorylation and it promotes neuronal regrowth.

A healthy brain requires metals, such as copper, zinc and iron, to form new memories. But in Alzheimer's disease these metals are bound up in amyloid deposits. Kempler said that PBT2 liberates these metals and restores them to neurons.

But executive function is also important in Alzheimer's disease, not just memory. Kempler quoted Craig Ritchie from the Imperial College London in saying that we have turned Alzheimer's disease into a memory problem. Executive function deterioration comes in three years before memory symptoms start to appear. This manifests in symptoms such as depression, apathy and personality changes. In a previous clinical trial, PBT2 was shown to significantly ($p=0.042$) improve executive function over a 12 week period. PBT2 targets both memory and executive function said Kempler.

The search for effective therapeutics for Alzheimer's disease is littered with failures. Seven Phase III trials conducted by some major pharmaceutical groups, including, Pfizer, Johnson & Johnson, Eli Lilly, Bristol-Myers Squibb and Baxter, have failed in this disease.

A learning from some of these trials is to ensure that patients actually have Alzheimer's disease. In the Eli Lily trial, it was found that 30% of participants did not even have the disease.

Phase IIb Alzheimer's Disease Trial Progress

Prana is conducting a Phase IIb trial in Alzheimer's disease, which the company is mid-way through. In this trial, 40 patients have been recruited with earlier stage Alzheimer's disease. The patients are being treated for 12 months with PBT2 and are compared to a placebo arm. The company is measuring cognition (using the NTB test), distribution of amyloid plaques in the brain using the PIB imaging agent, as well as changes in brain volume and brain energy utilisation.

The first endpoint for the company will be to see a difference in beta amyloid deposits in the brain of the treated group compared to the control group. The second endpoint will be to achieve an improved outcome in cognition in the treatment arm.

The last patient was enrolled in November last year and the trial is expected to finish in December this year. Results are expected in March next year.

Kempler said that the company came very close to concluding a licensing deal with a major pharmaceutical company previously but were thwarted by the GFC.

Phase IIa Huntington's Disease Trial

Prana has completed a 109 patient Phase IIa trial in Huntington's disease. The results are due by October this year at the latest, with analysis now underway.

THREAD Study – Now enrolling….

Associate Professor David Darby from the Florey Institute presented a very interesting longitudinal study he is involved with, called the THREAD study. This study will seek to enrol 10,000 people over he age of 50 years before they show any signs of cognitive decline.

This internet-based study, will have participants assessed remotely each month using tests including the Cogstate test (Darby was one of the founders of Cogstate). When a person in the study starts to experience a deterioration in cognition, and if there is no explained reason for that change, then they will have their brain imaged. If there are visible signs of Alzheimer's disease, then those people will be offered rapid enrolment into clinical studies with emerging drug treatments.

FDA Introduces New Guidelines

An important development in the field of Alzheimer's disease (AD) drug development came in February/March this year when the FDA released guidance on early stage drug trials in AD, acknowledging that the hurdle of treating late stage patients has been too high.

According to the FDA, this includes potentially enriching the patient population with those patients most likely to progress to 'more overt dementia', and that in mild cognitive impairment, preventing or slowing cognitive decline might be enough to show evidence of efficacy (using a time-to-dementia metric). In a second change proposed by the FDA (accelerated approval mechanism under CFR 314.510), a drug could be approved on a single primary efficacy measure, but then would need follow-on studies.

To date there are 1,370 people enrolled in the study. People interested in participating in this study should contact David Darby (ddarby@unimelb.edu.au).

Cogstate

Cogstate's Chief Scientific Officer, Paul Maruff, presented on the role of its cognition test in Alzheimer's disease. The company's goal is to 'industrialise' the scientific information that has been obtained to date for the medical field. This is being achieved firstly in the Canadian market, in conjunction with the company's partner Merck.

In Canada, the product (named Cognigram) has been structured as a typical pathology test, where the doctor writes a script, and the patient then goes to a pathology group to have the test conducted. To date around 1,000 people in Canada have been evaluated with the Cognigram test since it was launched in March this year.

The test is now part of a continuing education program for general practitioners in that market, and Cogstate/Merck are moving towards reimbursement from the Canadian government.

Bioshares

Bioshares Model Portfolio (9 August 2013)

Company	Price (current)	Price added to portfolio	Date added
Invion	$0.070	$0.060	August 13
IDT Australia	$0.320	$0.260	August 13
Viralytics	$0.295	$0.300	August 13
Circadian Technologies	$0.240	$0.270	March 2013
Tissue Therapies	$0.275	$0.255	March 2013
Benitec Biopharma	$0.300	$0.040	November 2012
Nanosonics	$0.780	$0.495	June 2012
Somnomed	$1.16	$0.94	January 2011
Cogstate	$0.360	$0.13	November 2007
Universal Biosensors	$0.71	$1.23	June 2007

Portfolio Changes – 9 August 2013

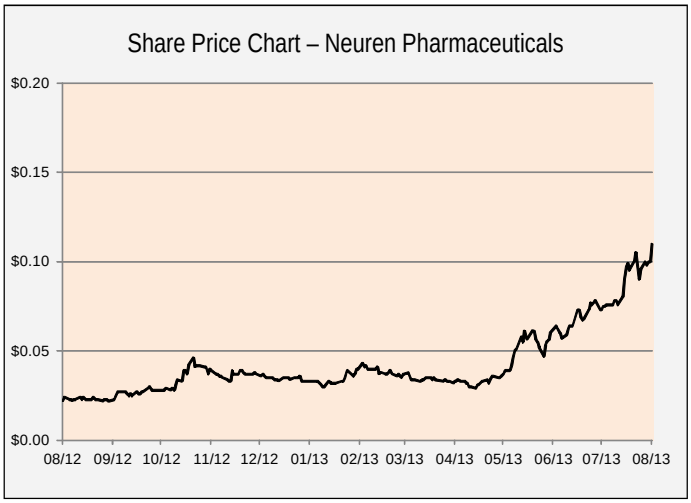
IN:

No changes.

OUT:

No changes.

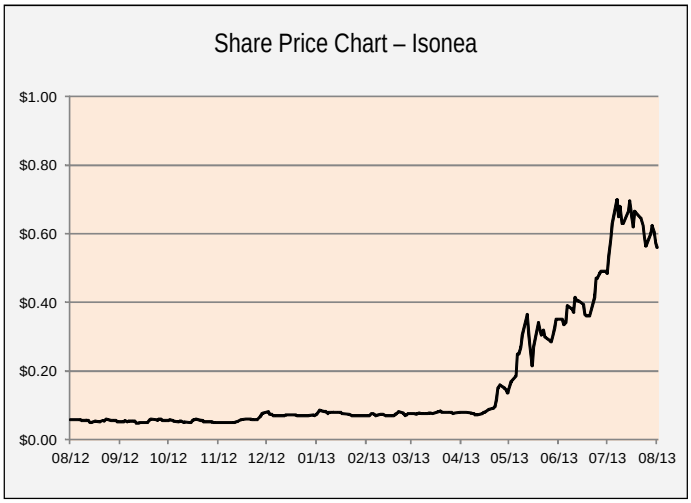
Stock Watch



Neuren Pharm. (NEU: $0.11; Cap'n: $135 million)

Neuren Pharmaceutical's shares have had a spectacular run over the last 12 months, increasing by 378%. Recently, the company was forced to address social media commentary about the effects of its drug NNZ-2556 on subjects in its Rett Syndrome trial, to state that 'the clinical benefit, if any, of NNZ-2566 compared to placebo will not be known until treatment assignment is unblinded and the trial data are analysed.' This is an appropriate comment. However, the company's capitalisation of $135 million is unwarranted given the company's orphan drug focus on the one hand, but also its program in the very difficult area of traumatic brain injury.

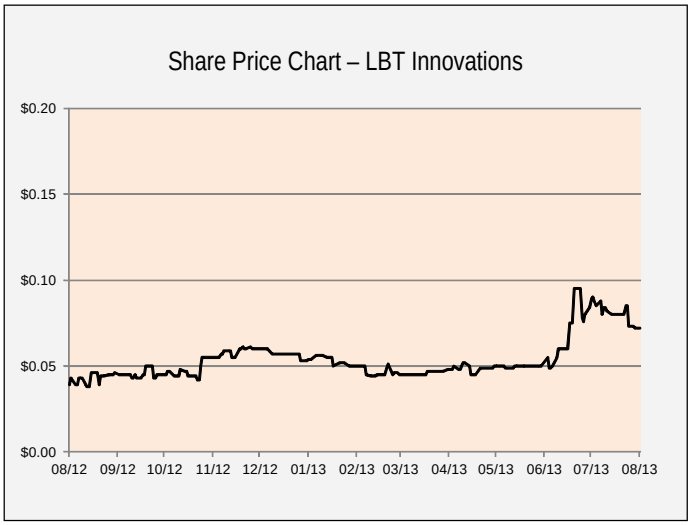
Bioshares recommendation: **Sell**



Isonea (ISN: $0.56; Cap'n: $144 million)

Isonea is one of the few emedicine plays listed on the ASX. Isonea's share price peaked recently at 70 cents, yet its current share price is still up 884% from a year ago. However, it would appear that profit taking has already commenced with Isonea shares. The company recently raised $13.5 million through a share placement, so it now has the funds to market its AirSonea asthma monitoring device in the US and in Australia. However, investors should not underestimate the difficulty of launching a new ehealth product, in either the US or Australia. Sales are more likely to build slowly after launch, which is planned for January 2014 in the USA.

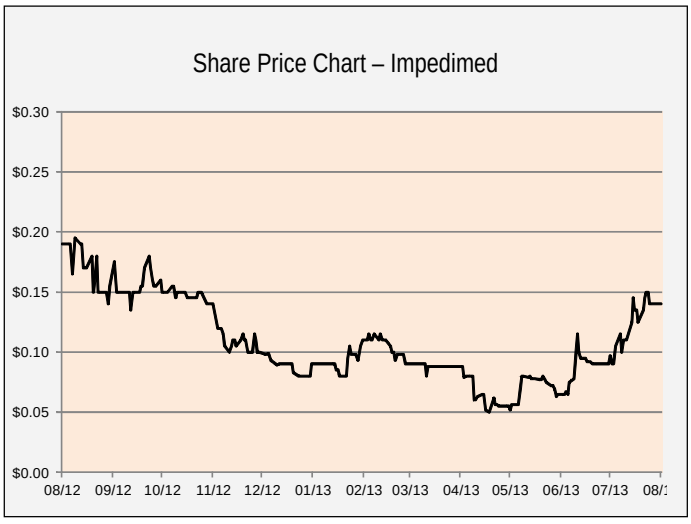
Bioshares recommendation: **Sell**



LBT Innovations (LBT: $0.072; Cap'n: $7 million)

The LBT Innovations share price almost doubled recently following its announcement of its joint venture agreement with Hettich AG for the development of its Automated Plate Assessment System. The company's base cash position is now secured for the medium term. LBT Innovations is a small but solid company that has stayed focused on developing innovative solutions for the microbiology lab. This stock is more suited to the long term investor with a penchant for accumulating the stock at opportune times.

Bioshares recommendation: **Speculative Buy Class B**



Impedimed (IPD: $0.14; Cap'n: $25 million)

Is Impedimed a turnaround story in the making? The company's share price has increased from recent low of 5 cents to 14 cents (+180%). The company reported sales growth of 51% for FY2013 and its net operating cash flow for the June quarter was down 48% from the same quarter a year ago. With a board renewal program in place and an intense focus on cost control, Impedimed 'Mark II' is a stock to monitor . However, key drivers will be the awarding of an AMA Cat. I code for reimbursement, coupled to changes to product labelling for its L-Dex device so that the device can be used to diagnose and detect lymphodema.

Bioshares recommendation: **Speculative Buy Class B**

How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion, Circadian Technologies

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