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In this edition...
Experts from the front-line of medicine, be they physicians, surgeons or diagnosticians, can supply investors with detailed insights about products in development. Sunshine Heart hosted a briefing by US surgeon Dr Sanjeev Aggarwal, who has pioneered a minimally invasive technique for implanting SHC's C-Pulse device. His observations on the device and challenges in treating heart failure are well worth noting. pSivida has opened up as an attractive investment opportunity, as its partner Alimera re-submits Iluvien to the FDA. Bionomics has significantly re-cast its share register and boosted cash resources. Hexima has set a date for a vote on a proposal to de-list the company. And we discuss the FDA's approval of Merck's boceprevir on Biotron's own HCV compound BIT225.
The Editors
Companies Covered: BIT, BNO, HXL, PVA, SHC

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - May '10)	49.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 now commenced	-1.2
Cumulative Gain	**316%**
Av Annual Gain (10 yrs)	**21.2%**

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Bioshares

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Edition 407

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

Sunshine Heart's C-Pulse Device – Expert Review

Sunshine Heart (SHC: 6.3 cents) this week conducted a roadshow on the east coast of Australia with a leading US cardiac surgeon who specialises in heart transplants, LVAD (heart pump) implants and now in Sunshine Heart's C-Pulse device. Dr Sanjeev Aggarwal, the Director of Mechanical Circulatory Support at **Saint Luke's Mid American Heart and Vascular Institute** in Kansas City, gave a short presentation before opening Q&A sessions with local investors interested in how Sunshine Heart's device is placed as a potential mechanical cardiac therapy.

Dr Aggarwal's hospital has more than 600 beds and is ranked one of the top 10 cardiac transplant facilities in the US. Dr Aggarwal has conducted over 160 LVAD implants, and performs around 50 heart transplants every year and 40 LVAD implants a year. He can justifiably be classified as an expert in this field. He is helping pioneer the C-Pulse system, being involved in Sunshine Heart's feasibility trial, having conducted five of the 20 implants. In particular, Dr Aggarwal has pioneered the minimally invasive surgery procedure (MIS) used in implanting the C-Pulse system, which assists the heart function through counter-pulsation using a balloon wrapped around the aorta.

Dr Aggarwal believes the number of heart failure cases is expected to double over the next 20 years in the USA. Heart failure affects more people than the top six cancers combined according to Dr Aggarwal.

Appeal of the C-Pulse System

Dr Aggarwal is independent and is not tied to any particular technology or device. What has intrigued Dr Aggarwal about Sunshine's system is that it is designed for use in Patients with Class III heart failure, where most other devices such as LVADs are designed for use in more seriously ill patients, those being diagnosed as having Class IV heart failure.

While there are around 200,000-300,000 patients in the US with Class IV heart failure, the number with Class III heart failure is substantially higher, at around 1.5 million people in the USA said Dr Aggarwal.

Perhaps the most important point made by Dr Aggarwal was the breakthrough that occurred with this device in being able to deliver it with minimally invasive surgery. Dr Aggarwal said that it is a 'massive deal' that the device can be implanted now without

– Sunshine Heart cont'd

splitting the chest (median sternotomy). Dr Aggarwal says having a MIS approach is a 'deal changer'. Some cardiologists will not refer Class III heart failure patients if it requires a median sternotomy.

The C-Pulse device can now be implanted through an incision the same size as that required to implant a pacemaker. And most patients have an existing pacemaker. The procedure takes Dr Aggarwal only 45 minutes to implant the C-Pulse device, with a total operating time of around 75 minutes in total.

Another one of the key distinctions is that this is device is an 'extravascular' system, meaning it does not come in contact with the blood. This means the patient does not require anti-coagulant medication.

Patients with Class III heart failure are not staring death in the face, said Dr Aggarwal, but their quality of life is impeded. With the C-Pulse system the patient can turn the system off at any time, for instance when the grandchildren arrive, and turning off the system does not cause a fatal effect, as with the LVAD systems. This feature is a significant quality of life advantage. However, patients often do not turn the C-Pulse off for long, according to Dr Aggarwal, with patients soon noticing the difference when they are disconnected.

Another potential advantage is that the increased blood flow to the heart muscle can help the heart muscle recover, because it is counter-pulsating with the heart (and not taking over the heart function like LVADs). And a critical component of the MIS procedure is the short recovery time, which is similar to that of a pacemaker.

People can be effectively controlled with drug therapy however that doesn't prolong life, according to Dr Aggarwal. Another of the advantages of the C-Pulse system is that it doesn't 'burn other options', if a sternotomy is not required, allowing other procedures to be conducted that may require sternotomies in the future (inferring there is a limited number of times surgeons will consider splitting a patient's chest in two).

C-Pulse Not Suitable for all Class III Heart Disease Patients

The C-Pulse system will not be suitable for all people with Class III heart failure. People with calcium or plaque build up in the ascending aorta are immediately excluded said Dr Aggarwal. It is also not known what the long term effect of counter-pulsation using a device such as the C-Pulse.

Infection is an issue with all operations and devices, particularly where there is a drive line protruding through the skin, as is the case with the C-Pulse system and LVADs. However, the level of infection is directly linked to the diameter of the drive line. Infections can also relate to the hospital. Dr Aggarwal stated that none of his five C-Pulse patients experienced an infection.

The most suitable people for a C-Pulse system would be Class III heart failure patients whose arteries are not blocked by plaque, patients who can not tolerate current medications, and those who have had 'acute decompensated heart failure', a sentinel event where one third of patients are no longer alive after 12 months.

Take Up Will all be Data Driven

Moving forward, the interest in the C-Pulse system will be data driven, suggested Dr Aggarwal. Results from the 20 patient feasibility trial will be presented at heart conference between September 18-21.

In terms of how long the C-Pulse system should last for, Dr Aggarwal said one year would be a minimum period. CEO Dave Rosa said the C-Pulse system is certified for five years function. Dr Aggarwal has had one LVAD patient last for four and a half years.

Results

Dr Aggarwal says that some patients from the feasibility trial have reduced the quantity of diuretics taken following a C-Pulse implant. However the best measure for Dr Aggarwal is simply how the patient feels. One patient who has been implanted with a C-Pulse system, is now able to walk up six flights of stairs, something that Dr Aggarwal joked he would have trouble doing.

Future Therapies

Dr Aggarwal said there will be no single bullet for the treatment of heart failure in the future, with drug therapy, mechanical systems and cell therapies all likely playing a role.

Forthcoming Pivotal Study

In the first quarter of next year, SHC expects to begin a 270 patient pivotal study, which will cost up to $35 million. Half of the patients in the study will receive a C-Pulse system. The company will start approaching sites for this study in a few months time.

Summary

Many of the points made by Dr Aggarwal the company has been making for the last 10 years. However to hear these features first hand from a cardiac surgeon at the front-line adds significant weight to the C-Pulse argument.

In terms of the progress the company is now making, CEO Dave Rosa said that 18 months ago, people were not returning his calls. Now people are independently approaching the company.

Sunshine Heart is capitalised at only $64 million, with $9.3 million in cash at the end of March. C-Pulse looks like it is well on the way to progressing its therapy to a commercial reality in the area of mechanical circulatory support systems. A major driver for this stock will be the release of the results from the feasibility study in the third quarter of this year.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Bionomics Completes $14 Million Placement

Bionomics (BNO: $0.63) announced this week the completion of a capital raising through the placement of 25 million shares at 57 cents to international and local institutional investors, raising $14.25 million.

Significant investor Start-up Australia also placed 60 million of its shares at 57 cents to international and local institutional investors. Start-up retained an 8.2% interest in Bionomics, following its divestment and the capital raising placement.

The 57 cent price is the volume weighted average of Bionomics share price from the 30th of March to May 11 and is a 21% discount from the stock's closing price of 72 cents on May 12.

Following the capital raising we estimate Bionomics cash holding to be $23 million.

The placements and capital raising achieve several objectives for Bionomics. Firstly, the company has now substantially repositioned its share register so that it has a stronger and improved spread of institutional investors who have also flagged a longer term commitment according to Bionomics CEO Deborah Rathjen. Secondly, with cash reserves lifted from around $6 million at the March quarter to an estimated $23 million including proceeds from the sale of its Thebarton facility, it has put itself in a comfortable position as it seeks to license BNC210, its novel anti-anxiety compound.

The value of retaining of strong cash reserves should not be under-estimated because potential Big Pharma licencees can exploit weakness found in a small biotech's cash position to excessively bias deal terms in their favour.

The improved cash position may even allow Bionomics to consider other development options for BNC210 if potential licencees struggle with the deal terms set by Bionomics.

CEO Deborah Rathjen said institutional investors were not only attracted to platform characteristics of Bionomics, but also to the results from the BNC210 trial and the opportunity it represents. The company's drug discovery and drug pipeline were also highlighted as attractive features as was the company's Multicore drug development technology, which entered the company courtesy of its merger with Illiad Chemicals in May 2005. A further attraction was forthcoming news flow for the cancer compound BNC105.

Drug development is a high risk endeavour which can be mitigated by companies developing more than one compound, in different indications and exploiting different mechanisms of action. This strategy is apparent in the Bionomics business model. De-risking can also occur in other ways. What is less apparent is that both BNC210 and BNC105 are drug candidates based on other compounds, modified to overcome limitations (BNC105) and applied to a quite different clinical setting (BNC210).

Bionomics is aiming to partner BNC210 before the end of the calender year. Interim data from from the BNC105 mesothelioma trial is expected this quarter.

Bionomics is capitalised at $217 million.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

pSivida – Alimera Sciences ReSubmits Iluvien for FDA Approval

This week pSivida's (PVA: $3.85) partner **Alimera Sciences** resubmitted their new drug application with the FDA for their drug candidate, Iluvien. Iluvien is a corticosteroid depot injection for the treatment of diabetic macular edema (DME).

Alimera was asked to resolve to issues around its third party manufacturing sites. The FDA also wanted to see additional information around its control groups and the specifications on the packaging, manufacturing and sterilisation procedures. The third party issues have been resolved and the company has supplied the additional information.

Alimera also supplied 36 month safety and efficacy data that has become available, even though the original requirement was for 24 month data only. It has also provided information on a subgroup of patients, those patients who had been diagnosed with DME for three or more years. There was not statistical difference in efficacy between this subgroup and the whole patient population.

Efficacy Peaked at 30 Months

Overall, the efficacy was shown to peak at 30 months, with 33.6% of patients in trial A and 42.4% of patients in trial B gaining 15 letters (three lines on the eye chart) or more improvement. At 36%, this fell marginally to 31.8% in trial A and 36.4% in trial B.

At 36 months, in both trial A and B, statistical significance was achieved at 30 weeks, 33 weeks but not at 36 weeks in the full patient population. In the sub group, statistical significance was achieved at 36 weeks. Presumably Alimera and pSivida will not want their potential patient population reduced to only those who have had DME for more than three years.

The safety aspect of the therapy looks acceptable, with 35% of patients experiencing intra-ocular pressure, however in most cases that can be resolved with eye drops. In 3.7% of patients, an incisional surgical procedure was required.

Competition from Lucentis

The competition to this therapy is **Roche**'s Lucentis, which is currently into the third year of two Phase III trials. Lucentis has shown better two year data than Iluvien, with 45.7% of patients gaining a 15 letter or more improvement in eyesight. However the drug needs to be injected every month.

– Cont'd over

Hexima De-listing To Go To The Vote

Plant technologies company Hexima (HXL: $0.30) has announced a date for a General Meeting [10AM, June 9, 2011] for shareholders to vote on the de-listing of the company. The company listed in August 2007, at $1.25 a share, after raising $40 million. The company's CEO at the time of listing was Dan O'Brien, who made way for Josh Hofheimer in July 2008. In turn, Hofheimer did not renew his contract in July 2010, with Ross Dobinson stepping in as Executive Chairman in that month.

In an Explanatory Memorandum, the company put forward three arguments for the de-listing. The first was that the company's share price had traded between 17.5 cents and 53 cents in the last twelve months, with (it implied) no recognition being made for commercial and technical progress made by the company over the period.

We observe that since its listing, Hexima has successfully completed three years of field trials of its technology in cotton, initiated one major licensing agreement with **Dupont/Pioneer Hi-bred** covering anti-fungal applications of its technology in corn and soy crops, built a corn transformation facility at La Trobe University and advanced its fungal resistance program considerably. **Dupont/Pioneer Hi-bred** and **Monsanto** have also taken out research licenses covering Hexima MGEV, multiple gene vector technology.

Secondly, with low trading volumes, the company was being " 'priced' on what are marginal trades" and thirdly, "the implied market capitalisation of the Company impairs the Company's ability to derive value from its technologies in negotiations with commercial partners."

The board, which comprises Ross Dobinson (Executive Chairman) , Prof. Marilyn Anderson, Hugh Morgan, Prof. Jonathan West and Stephen Skala, has unanimously recommended the de-listing, with all the major shareholders also endorsing the move, according to Dobinson.

While the de-listing removes the ability of shareholders to readily sell shares, Dobinson said that a 'grey' facility could be set-up for shareholders looking to sell or buy shares. As an unlisted public company the company is still bound by the same laws that bind public companies.

A de-listing would free the company from adherence to continuous disclosure rules. Together with a de-coupling from a 'marginal trades' derived market capitalisation, these factors could strengthen Hexima's position in commercial negotiations as and when they arise in the future. Those commercial negotiations, we would add, could also extend to M&A discussions.

Dobinson also stated that "when you have a long term growth story, with next-to-no news flow and no need to raise capital", then the need to be listed disappears. He said there is "no compelling reason to stay listed", adding that "you do what is logical, and staying listed is not logical."

We support the recommendation of board to de-list Hexima if it results in strengthening the company's negotiatiating position with existing or potential commercial partners.

Hexima currently holds cash of $16.5 million and is capitalised at $24 million.

Bioshares recommendation: **Vote for the de-listing**

Bioshares

– sPivida cont'd

Our expectation is that Alimera should gain approved for Iluvien. The FDA will give a decision within six months. An FDA approval will trigger a US$25 million milestone payment from Alimera to Psivida. Psivida will also receive a 20% profit share from sales. US analysts have predicted annual sales of Iluvien of between US$250 million – US$800 million.

Alimera is capitalised at US$261 million (with US$44 million in cash after debt) and pSivida has a market value of US$82 million excluding warrants. pSivida had US$23.1 million in cash at the end of March. The company has 10.2 million warrants outstanding (excluding those with an exercise price over US$10). If these were all exercised, the company would raise an additional US$59 million, giving the company US$82 million in funds. Its market capitalisation on a fully diluted basis would be US$119 million.

Subtracting the cash, including that from exercised warrant, would give pSivida a technology value of only US$37 million. Excluding consideration of the warrants, the company's current technology value is only US$59 million. And if Iluvien is approved, pSivida receives a US$25 million milestone payment, giving the company a technology value of only US$31 million on an undiluted basis.

Bioshares recommendation: **Speculative Buy Class B**

(pSivida has been added to the Bioshares Model Portfolio)

Bioshares

Bioshares Model Portfolio (13 May 2011)

Company	Price (current)	Price added to portfolio	Date added
Psivida	$3.95	$3.95	May 2011
Bioniche	$1.07	$1.35	March 2011
Somnomed	$1.33	$0.94	January 2011
Phylogica	$0.064	$0.053	September 2010
Sunshine Heart	$0.063	$0.036	June 2010
Biota Holdings	$1.20	$1.09	May 2010
Tissue Therapies	$0.49	$0.21	January 2010
Hexima	$0.30	$0.60	October 2008
Atcor Medical	$0.15	$0.10	October 2008
Impedimed	$0.64	$0.70	August 2008
Patrys	$0.14	$0.50	December 2007
Bionomics	$0.63	$0.42	December 2007
Cogstate	$0.20	$0.13	November 2007
Sirtex Medical	$5.22	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.85	$6.60	September 2007
Starpharma Holdings	$1.29	$0.37	August 2007
Pharmaxis	$3.00	$3.15	August 2007
Universal Biosensors	$1.25	$1.23	June 2007
Alchemia	$0.59	$0.67	May 2004

Portfolio Changes – 13 May 2011

IN:
Psivida has been added in at $3.95. See analysis on page 3.

OUT:
No changes.

Biotron – Update

Biotron (BIT: $0.10) is developing BIT225 as a treatment for Hepatitis C virus (HCV) infection. The compound is being evaluated in a 24 patient Phase II trial, which is nearing completion in Thailand.

This week, the FDA approved **Merck**'s boceprevir (brand name 'Victrelis') as a treatment for HCV. Boceprevir falls within the class of antiviral drugs known as protease inhibitors, and it is the first protease inhibitor approved for HCV treatment. Not far behind and in the same class is **Johnson & Johnson's** teleprevir.

Boceprevir has been approved for use with pegylated interferon and ribavarin, the current standard of care for HCV patients. It is also only approved for patients who are positive for HCV Genotype 1. The drug is administered three times a day in four 200mg capsules with a light snack also recommended as being taken.

Boceprevir is expected to sell at a wholesale price of between US$26,000 and US$48,400 per patient, depending on the length of treatment, according to a report in the *Wall Street Journal*.

Phase III trials of boceprevir showed the drug caused a reduction to non- detectable levels of the virus of about 70% of non-black patients and 40%-50% of black patients.

Comment

While the approval of a new medicine for HCV may on the surface appear to be a setback for Biotron, in fact the opposite is the case. Biotron BIT225 has a unique mode of action and is first in its class. BITT225 targets the p7 ion channel of the virus. Novel modes of action are highly desirable in anti-viral therapy because they can address the problem of drug resistance that emerges over time.

The protease inhibitor class drug boceprevir has been approved for use with standard of care (interferon and ribavarin), and BIT225 is being trialled with the same standard of care drugs. It would be a far greater competitive challenge if boceprevir had been approved as a new monotherapy or first line therapy, which would then change the development hurdles for BIT225 considerably.

The price of the new drug is both a positive and a negative for Biotron. It is positive in that it shows the pricing power a new HCV drug can command. However, increasing demands on insurance companies are likely to see the prices of future HCV therapies be pushed downwards.

Issues with Boceprevir

One of the issues with boceprevir is that it must be taken three times a day in four capsules, for a total of 800mg each time. An administration regime of this nature may result in compliance problems emerging. In contrast, BIT225 is currently being evaluated as a twice daily medicine, in a 200mg and 400mg doses, with a final choice on the optimum dose yet to be made. What has also caused clinicians some concern about boceprevir is that it caused anaemia in about 50% of patients in clinical trials, with fatigue, headache and nausea recording similar or worse adverse event rates.

Why Biotron warrants investor attention is that its Phase II results should be available mid-2011, with its trial designed to show clear evidence of effectiveness of the compound in HCV. However, even if the HCV trial issues a negative result, the same compound will be studied in HIV, offering a second shot on goal, now that the company has secured additional funds for that Phase Ib/IIa trial.

Biotron is capitalised at $15 million and retained cash resources of $1.3 million as of March 31, 2011, adding $1.7 million from an SPP following the end of the quarter.

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

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