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In this edition...
A rare event took place this week, the listing of a life science firm on the ASX. While Bluechiip is the second life science listing to take place this year, it is the first proper IPO, since Bioniche's listing in January follows its primary listing on the Toronto Stock Exchange. Positive developments have occurred at Bionomics, which has had its MS drug collaboration with Merck Serono extended, Sunshine Heart has successfully completed an animal trial of a fully implanted C-Pulse heart assist system and Mesoblast has shown that its stem cell product Revescor increases blood supply to damaged heart muscle. And news from the annual ASCO meeting brings both positive and negative news for local melanoma drug developers, Viralytics and Patrys.
The Editors
Companies Covered: BCT, BNO, PAB, PXS, SHC, VLA

	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	-6.7%
Cumulative Gain	**293%**
Av Annual Gain (10 yrs)	**21.2%**

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Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au

David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph:03 9348 9317
Email: pachacz@bioshares.com.au

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Bioshares

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

Bluechiip Lists on the ASX

After months of planning and effort, Bluechiip (BCT: 23 cents) has listed on the ASX, making it only the second biotech to list this year, after **Bioniche** listed in January this year. Bluechiip raised $3 million and listed at 25 cents a share. It finished the week slightly down on its share price, at 23 cents, with the market valuing the business at $17.5 million.

Bluechiip is commercialising a passive tracking technology with its primary initial market being used to label and monitor cryogenically stored medical samples. Existing RFID systems can not operate below -25C and can not sense temperature, although that feature can be added in with additional sensors. The Bluechiip technology uses microbeams in tiny chips that resonate at unique frequencies to identify samples. The chips can be attached to the sample or embedded in the vial during the manufacturing process.

Bluechiip CEO, Brett Schwarz, said that there is an existing market in clear need of such a product. However, the challenge over the next 12 months is to have its manufacturing process up and running to supply material.

The chips will be manufactured by a third party in Italy, which has existing experience in manufacturing silicon chips for the computer industry. However, the final process involves laser ablation to store the unique identification information on each chip. This last step in the process has been held up because the company has, until now, not been able to acquire a specialised instrument at a cost of $1.3 million. The funds raised via the IPO will pay for this equipment and allow commercial manufacturing to proceed. Schwarz is planning to have commercial product available by mid 2012.

Interim Measure

In the meantime, the company will look to release evaluation kits, which include small numbers of chips and chip readers. These kits can be sold to customers, as has been industry practice with RFID systems, whereby customers can conduct their own testing with the technology on a small number of samples. The goal is to have these kits available in the next three to six months.

Another goal this year for Bluechiip is to have its product adopted by vial and tube manufacturers, who would embed the chips in their product ranges. This would allow end users to purchase storage vessels with Bluechiip's identification system already in place.

Cont'd on page 4

Mesoblast Releases More Positive Heart Trial Data; Annouces Plans for New Suite of HF Products

The data from Mesoblast's (MSB: $8.60) Phase II congestive heart failure trial continues to be positive and in new ways. The initial results released in January this year showed a significant reduction in major coronary events from just one injection of the company's adult stem cell therapy, called Revascor. This week the company released more positive information around improvements in blood flow to the heart muscle.

Of the 60 patients in the Phase II study, 22 had reduced blood flow to the heart muscle. In the patients treated with Revascor (17 patients), there was a 51% reduction in this condition called myocardial ischemia, compared to no change in the control group.

The company is now planning to develop a suite of therapies for people with heart failure, including those suffering from poorly addressed chronic angina, heart attack patients and people with congestive heart failure.

A Phase III study is expected to start in early 2012 in congestive heart failure. The company has submitted a Clinical Trial Application with European regulators to start a Phase IIb study in 225 patients who have suffered a heart attack, and it is filing an IND application in support of a Phase II study in around 150 patients patients with chronic refractory angina by years end.

Mesoblast is capitalised at $2.4 billion.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Bionomics – Kv1.3 Program With Merck Serono Extended

Bionomics (BNO: $0.65) announced a one year extension of its research collaboration with **Merck Serono** that covers the development of compounds for the treatment of Multiple Sclerosis which target the potassium ion channel Kv1.3.

Under the terms of the deal, Bionomics may receive milestone payments of up to US$47 million for each compound that is successfully developed.

The subset of MS that the Kv1.3 program is directed at is Relapsing Remitting MS, which represents about 80% of MS patients. This market is served by the injected interferon-beta 1a drugs Avonex, Rebif, Betaseron, the myelin-like injectable decoy Copaxone, Tysabri (an injected antibody) and Gilyena (an orally administered immuno-suppressive). Rebif is marketed by Merck Serono.

Kv1.3 blockers target rogue T-cells (effector memory T-cells) that over-express by as much as 50 times the Kv1.3 potassium channel, compared to another potassium ion channel (iKCa-1). Ion channels are pore-like cell membrane proteins that control electrical gradients in cells.

Cont'd on page 4

Sunshine Heart Completes Study on Fully Implantable C-Pulse

For Sunshine Heart (SHC: 5.7 cents) to have its heart assist system widely adopted as a realistic therapy for patients with Class III heart disease (as opposed to Class IV stage patients), we have for been of the view that two hurdles needed to be overcome (see *Bioshares* 362).

The first was that the device needed to be able to be implanted through a minimally invasive surgery (MIS) procedure, rather than a median sternotomy, known in the trade as 'cracking the chest' in half. This has now been achieved and it's likely most future procedures with use MIS.

The second hurdle that should vastly expand the realistic market for this device is for it to be fully implantable. This week Sunshine Heart announced that it had successfully completed its first animal study with a fully implantable system.

The company said it had achieved this milestone one year ahead of schedule. Of significance, the company said that its ultimate goal is to develop a fully implantable device that will connect to a patient's existing pacemaker from which it will receive it electrical control signals.

CEO Dave Rosa said it was easier than he had expected to develop a working version of a fully implantable system. One of the reasons the outcome was achieved so rapidly is that the company's original intellectual property was around a fully implantable system and the company founder, Will Peters, continues to be involved with product development. The company has also accessed a third party's TET (transcutaneous energy transfer) system.

The company trialed three different systems, and a working system was achieved very quickly. The system absolutely supported the animal, said Rosa, for about two hours before it was stopped. The implanted system may have lower power requirements, with the driver implanted only 1-2cm from the aorta.

The next stage is to complete device development. However, at this point, the focus is on finalising product optimisation for the device to be used in the forthcoming pivotal study. Rosa said for some US investors following the company, just to show that a fully implantable system is achievable has been a very important event.

Next up for the company is the release of results from the 20 patient feasibility study, which are due out in the next quarter. And from there the company will look to start a major pivotal study. The results from the feasibility study, if positive, should generate strong interest both from investors and potential acquirors of the technology.

Sunshine Heart is capitalised at $58 million and had $9.3 million in cash at the end of March.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

ASCO Annual Meeting 2011– New Melanoma Treatments Discussed

The annual meeting of the American Society of Clinical Oncology concluded in Chicago last week. A session was devoted to a presentation by Dr Jedd Wolchok from **Memorial Sloan Kettering** on the results of a Phase III trial of ipilimumab, an antibody developed to treat melanoma.

Ipilumimab, known by its trademark name of Yervoy (**Bristol-Myers Squibb**), was approved earlier this year by the FDA for the treatment of unresectable or metastatic melanoma. The drug is delivered intravenously in four doses over three weeks.

Yervoy is a monoclonal antibody that blocks cytotoxic T-lymphocyte antigen 4 (CTLA-4). CLTA-4 is a negative controller of T-cell activity, which means that blocking it can allow for a freed-up T-cell response to deal with cancer cells.

Melanoma remains one of the most difficult treat classes of cancer, with until the recent approval of Yervoy, treatment relying on several older drugs including dacarbizine as the approved standard of care, albeit very poor, and with other drugs such as aldesleukin, temozolomide and carboplatin also used.

The Wolchok study reported a survival benefit of 2.1 months [11.2 months versus 9.1 months] for Yervoy over dacarbizine.

The Study enrolled 502 patients with stage III and stage IV melanoma who had received no prior therapy.

Yervoy was approved on the basis of results received from one Phase III trial in 673 patients. What was interesting about this study was that patients were selected on the basis testing positive for HLA-A2*0201 genotype, which means that patients would respond to a co-administered gp100 peptide vaccine. The endpoint of the three arm trial was to compare Yervoy plus the gp100 peptide, to the gp100 peptide arm.

The study reported a statistically significant overall survival benefit of 10 months for Yervoy, 10 months for Yervoy with gp100, and 6 months for the gp100 arm, showing that adding the vaccine to Yervoy made no appreciable difference to therapy.

Adverse event profile of Yervoy – fatalities reported.

However, Yervoy is not without some series issues on the safety front. Yervoy comes with a boxed warning label, which warns of severe immune-mediated adverse reactions including enterocolitis, hepatitis, dermatitis, neuropathy and endocrinopathy, which were mostly observed when the drug was administered.

In the Yervoy Phase III study that formed the basis of its approval, 15% of patients in the Yervoy only arm and 12% of patients in the Yervow plus gp100 arm experienced immune related adverse reactions. The most common adverse event was enterocolitis, which saw a 7% rate occur in both arms. Fatalities associated with enterocolitis, hepatotoxicity, dermatitis, and neuropathy were reported.

Vemurafenib – An Oral Drug

Another drug in Phase III development for the treatment of melanoma is vemurafenib (**Roche/Plexxikon**), which is targeted to patients with the BRAF V600E mutation. Vemurafinib is administered orally, twice a day. While the Phase III trial in 675 patients is not complete, interim results show a survival benefit at six months for the 84% vemurafenib arm and 64% in the dacarbazine arm. The full study results will not be available until May 2014. However, it was reported in *Nature Reviews Drug Discovery* that Roche and Plexxikon expected to submit vemurafenib for approval this year.

Viralytics – Cavatak ASCO Poster

Viralytics (VLA: $0.083) is developing Cavatak, an oncolytic virotherapy, to treat melanoma, in addition to other advanced solid cancers.

The company presented a poster on Cavatak at ASCO, covering the Phase I study of the therapy as administered intra-tumourally to nine Stage IV melanoma patients. Although, no objective responses were recorded, Viralytics reported five out of nine patients experienced transient reductions in tumour volume.

The introduction of Yervoy as a new standard of care will raise the bar for Cavatak by most likely forcing the evaluation of Cavatak against Yervoy in at least one of two Phase III studies. This assumes it successfully completes it planned Phase II program, which is currently the subject of an IND application re-assessment with the FDA.

While Cavatak may possibly be limitated in the therapeutic setting if anti-(cocksackie-)virus antibodies are produced, its benefit arises from a potentially far more favourable safety profile, in addition to its tumour lysing ability. In the Phase I study Cavatak was reported as being well tolerated, with no patients experiencing any serious adverse events that were connected to the administration of Cavatak

Bioshares recommendation: **Speculative Buy Class B**

Also of Relevance: Patrys – PAT-SM6

Although not discussed at ASCO due to its current clinical status, Patrys (PAB: $0.11) is developing an antibody, PAT-SM6, for the treatment of melanoma, as well as for solid tumours. It expects to report on a nine patient Phase I study for PAT-SM6 in the second half of 2011. The company plans to run an extension study in 18 patients, increasing the dose up to 9 mg/kg.

PAT-SM6 binds to the GRP78 receptor, which is found on 98% of cancer tissues examined by the company. This receptor is the first to be targeted by any drug developer. GRP78 could well be an attractive target because of it role in suppressing processes that result in cell death (apoptosis).

However, as for Viralytics, the advent of new therapies to treat melanoma, such as Yervoy and vemurafenib, set new thresholds for efficacy but also a clear-cut opportunity to compete on the basis of a superior safety record. Hence, the company's Phase I study (and extension study) which is designed to gather safety data is of considerable importance.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares Model Portfolio (10 June 2011)

Company	Price (current)	Price added to portfolio	Date added
Psivida	$4.00	$3.95	May 2011
Bioniche	$1.01	$1.35	March 2011
Somnomed	$1.30	$0.94	January 2011
Phylogica	$0.072	$0.053	September 2010
Sunshine Heart	$0.055	$0.036	June 2010
Biota Holdings	$1.12	$1.09	May 2010
Tissue Therapies	$0.51	$0.21	January 2010
Hexima	$0.31	$0.60	October 2008
Atcor Medical	$0.13	$0.10	October 2008
Impedimed	$0.61	$0.70	August 2008
Patrys	$0.11	$0.50	December 2007
Bionomics	$0.64	$0.42	December 2007
Cogstate	$0.22	$0.13	November 2007
Sirtex Medical	$4.92	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.85	$6.60	September 2007
Starpharma Holdings	$1.42	$0.37	August 2007
Pharmaxis	$1.15	$3.15	August 2007
Universal Biosensors	$0.96	$1.23	June 2007
Alchemia	$0.67	$0.67	May 2004

Portfolio Changes – 10 June 2011

IN:
No changes.

OUT:
No changes.

Another Setback for CF Drug Development

This week has confirmed how difficult it is to bring a new therapy to market for the treatment of cystic fibrosis and why there hasn't been a new drug approved that treats the underlying disease for the last 16 years. **Vertex Pharmaceuticals** saw its market value fall by US$1 billion in the week (to US$9.9 billion) following the release of some results from its cystic fibrosis drug candidates in late stage development, although the market reaction is perhaps a little overdone.

The company has two drug candidates that seek to address the core protein deficiency that is responsible for the disease. The lead compound is VX-770. The company expects to file this drug candidate for approval in the second half of 2011 in the US and Europe. That compound has shown to be very effective, delivering a sustained 10.5% improvement in lung function at 48 weeks. However, the problem is this compound only works for a small subset of patients (3%-4%) who have a particular mutation (G551d).

The company delivered some Phase II results from a trial combining VX-770 with another drug candidate, VX-809. The trial was short, only one week, however the combination of drugs has the potential to be effective in around 50% of people with CF. However the results do not appear to be a 'game changer' according to one US analyst (Geoff Meacham from JP Morgan).

The implication for Pharmaxis is that new CF therapies are extremely difficult to invent and develop. With Pharmaxis' Bronchitol delivering a sustained improvement in lung function of around 8%, and given that it is safe, it is difficult to see how this therapy could not eventually be approved, given the very high unmet clinical need and its potential to address a broader population of CF sufferers.

Bioshares recommendation (Pharmaxis): **Speculative Buy Class B**

Bioshares

Bluechip cont'd

Schwarz said there are also a number of parties interested in doing pilot studies with the chips in collaboration with the company.

Although there are around a dozen mineral exploration stocks listing every month on the ASX, it still appears to be very challenging task for life science companies to raise capital through an IPO. Investor interest in speculative stocks still appears to heavily weighted towards the resources sector and towards the existing pool of listed biotech stocks but still not a great demand for new listings.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

– *Bionomics cont'd*

The drug discovery goal for the collaboration is to create an orally available compound that has a novel mode of action and which is highly selective for the Kv13 channel but not for the closely related iKCa-1 channel.

As can be seen with the current range of mostly injected treatments, the addition of an oral medicine to manage MS would be a welcome advance.

Kv1.3 blockers may also be beneficial in treating rheumatoid arthritis and psoriasis.

Bionomics is capitalised at $224 million and held cash assets of approximately $24 million at March 31, 2011.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

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, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Mayne Pharma Group, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Mesoblast, Atcor Medical, BioMD, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida

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