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Bioshares

31 January 2014
Edition 537

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

Companies covered: BLT, MSB, VLA, Cash Analysis

	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)	66.0%
Cumulative Gain	**491%**
Av. annual gain (13 yrs)	**20.4%**

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Viralytics Cashes Up

Viralytics (VLA: $0.33) has announced a $27 million capital raising which will give it the funds needed to complete a Phase II trial of its oncolytic virotherapy in late stage melanoma patients and a Phase I/II intravenous dosing trial of CAVATAK in patients with solid tumours. The money will also fund a randomised Phase II trial of CAVATAK in melanoma patients, which is scheduled to commence later this year.

The funding will come in three parts. An initial $6 million will be placed under the company's current placement capacity. A second tranche of $16.9 million is subject to shareholder approval. Up to $4.1 million will be raised by a 1 for 6 non-renounceable entitlement offer, and shareholders will also have the right to top up under the entitlement offer if there is a shortfall. The record date for the rights issue is February 7.

The capital raising is noteworthy because 12 institutional investors will enter the Viralytics register, up from a nil figure. This is the basis for the capital raising being described as transformational. The institutional investors include four who will have holdings of greater than 5%. There will also be more than four specialist healthcare investors.

Comments

The transformation of Viralytics since the days when it relied on convertible note financing from La Jolla Cove Investment Partners is nothing short of remarkable. Why has a company with no institutional support to date been able to secure capital almost equal to its capitalisation of $27.1 million at the date of the deal?

The first reason is Amgen's acquisition of oncolytic virotherapy company Biovex in March 2011 for US$407 million in cash up front and contingent payments of US$575 million. The therapy acquired by Amgen, now named talimogene laherparepvec, is nearing completion in a 440 patient Phase III trial, with overall survival results expected by mid year.

A second reason is that Viralytics secured the services of corporate finance teams with a track record of successful capital raisings. Bell Potter was the lead manager for the financing and Roth Capital partners was the sole US placement agent. Bell Potter dominated ASX life science raisings in 2013, being associated with $270 million's worth of financings at Mesoblast, GI Dynamics, Neuren Pharmaceuticals and Bionomics.

A third reason is that in the context of surging levels of investment interest in biotech, especially in the US, Viralytics was a rare and very appealing value proposition.

A fourth but perhaps pre-eminent reason, is that data emerging from the company's open label study is positive, showing a 60% survival rate at one year.

Bioshares recommendation: **Speculative Buy Class B**

Mesoblast Delivers Very Positive Phase II Results From Spinal Disc Repair Trial

Mesoblast (MSB: $5.88) has generated positive data from its spinal disc repair trial that will allow the company to move into Phase III studies. The results showed a clear improvement against baseline and benefit over the control groups across a number of parameters. The strength of the results means that a Phase III trial of only 300-400 patients will be needed. That trial is expected to commence this year and take about 12 months to enroll patients.

Trial Design

Mesoblast tested two doses of its stem cell therapy – a 6 million (6M) cell dose and an 18 million (18M) cell dose. There were two control groups. One was a saline solution and the other hyaluronic acid (HA). There were 20 patients in each of the control arms and 30 patients in each of the treatment arms. The patients participating had experienced moderate-severe lower back pain for more than six months which was caused by early stage disc degeneration. The trial was conducted in the US and in Australia. The patients were followed for 12 months after having been given one injection into the spine of either the stem cells (in a solution of HA) or the control solutions.

Results

What was very encouraging about these Phase II results is the positive outcomes across a range of measures.

Pain Reduction

A clinically important measure in people living with back pain is the ability to reduce pain by more than 50%. In the stem cell treated arms, 69% and 62% of trial participants reduced their pain by more than half in the 6M and 18M dose arms. This compares to 35% of patients who received HA and 31% who received saline having pain levels reduced by more than half. The control effect was also distorted as those in the control arms were taking twice as much opioid medication.

On most of the pain measures recorded, statistical significance was achieved. The exception was in the mean pain reduction in the 18M where the p-value was 0.11. These results highlight a clear benefit from only a small patient population.

Surgical Intervention

Fewer patients receiving the stem cell therapy required subsequent surgical intervention, with 6.9% of the 6M group and 3.3% in the 18M group needing intervention such as injected steroids of spine fusion. This compared to 10% in the HA group and 25% in the saline group.

Opioid Use

The amount of opioid use in both the 6M group and the 18M was lower than the saline group, by 23% and 42% respectively. The HA group opioid use was 6% lower than the saline group. These results were not statistically significant (p=0.17 in the 18M group).

Improvement in Disc Stability

Measurement of disc stability gives an indication of physical improvement in the disc. Increased translational movement is linked to disc instability and disc degeneration. There was less translational movement in the 18M group (1.3%) and the 6M group (2.0%) compared to the HA group (2.5%) and the saline group (3.5%). Statistical significance was achieved between the groups with a p-value of 0.021.

Safety

The only adverse events, noticed across all groups, was back pain, which was transient, following injections into the spine. Also important was that the stem cells did not trigger any immune response.

Duration of Response

It was found that the treatment effect in the second six months was better than the first six months. While the effect of the control started to wear off after six months, the opposite was found with the treatment arms. Of interest will be the treatment outcome at 24 months. This cell therapy may offer the advantage of a single treatment lasting more than year, whereas pharmaceutical intervention needs to be ongoing.

The clinical investigator of the trial said that this treatment has the potential to change the treatment paradigm for spinal disease. Mesoblast CEO Silviu Itescu said that the most pleasing aspect of the trial was the predictability of the human data from the large animal data that had been generated.

Discussion

An appealing aspect of this potential product for Mesoblast is that there are limited treatment options for people with early stage disc degeneration that results in lower back pain. The most aggressive therapy is injection of steroids into the spine, however this only lasts for around six weeks. Patients with this injury must simply wait for the disc degeneration to continue at which time spinal fusion therapy is deemed to be appropriate.

Another advantage is that specialists dealing with early stage disc degeneration already deliver injections into the spine for steroid treatment, so once a stem cell therapy is approved, it can easily be incorporated as a standard of care.

Phase III Studies

An important consideration for the company in moving into the Phase III study is the optimal dose of stem cells to use. The results were not clear on which dose delivered the better clinical outcome. Mesoblast CEO Silviu Itescu indicated that the company may even consider taking two doses into the pivotal study. The lower dose is more appealing from a cost of goods perspective.

The next stage for the company is to have discussions with regulators around the Phase III trial design. Mesoblast has $250 million to fund its business activities and can afford to conduct the Phase III studies independently. However, the company has indicated it will need to find a sales and marketing partner for the product, with those discussions underway. Mesoblast is seeking to find a partner to also move its spinal fusion trial forward.

Cont'd over

– Mesoblast cont'd

One regulatory aspect for the company is that it must ensure consistency of product from a manufacturing perspective. This is an issue that all stem cell players will have to address.

A Phase III study will likely involve 60% of patients from the US and 40% from Europe. That trial is expected to start in the next few months and take 12 months to enroll. There was no issue for recruitment in this Phase II study, with the investigators contacted by patients from across the US. There was no need to advertise in the Phase II study but advertising will be used for the pivotal trial.

In Japan, the government has lowered the bar for stem cell therapies, where approval will be considered where the therapy is shown to be safe and there is some evidence of efficacy. To gain approval in Japan, a trial of around 100 people may be necessary, although it is unclear whether data from a non-Japanese patient pollution will be acceptable for approval in Japan. The company is assessing its approach for the Japanese market.

Market Size and Pricing

The selling price of this therapy is expected to be between $5,000-$10,000. There are 3.5 million people in the US living with early stage disc degeneration (2.5 million in Europe) and over 600,000 seek treatment each year. That represents a market size of at least $3-$6 billion a year in the US, but could potentially be higher if an effective therapy such as this reaches the market.

Focusing on this earlier stage indication (rather than later stage spinal fusion) increases the market size and is also a more open market with no effective incumbent products on the market.

Phase III Teva/Mesoblast Heart Failure Trial

The details of Teva Pharmaceutical Industries' Phase III trial in chronic heart failure trial has been submitted with www.clinicaltrials.gov. Teva is Mesoblast's partner with this study.

The trial is listed as starting last month. It will enroll 1730 patients with the expected completion date August 2018. The trial is not yet recruiting. Six clinical sites have been listed in the US.

Summary

Mesoblast arguably has a leading position in the commercial stem cell field. Its strong position allows it raise funds to conduct pivotal studies, as well as acquire competing technologies, such as the Osiris assets bought last year.

The positive Phase II early disc disease result supports movement into a Phase III program. A challenge for all stem cell players will be to get regulators to sign off on manufacturing consistency, where batch to batch consistency can be validated.

Mesoblast is capitalised at $1.9 billion.

Bioshares recommendation: **Speculative Class A - Look to Buy Opportunistically Below $5**

Bioshares

Benitec Cleared for Gene Therapy RNAi Trial

Benitec (BLT: $0.82) has received clearance from the FDA to proceed with its Phase I/II study of its RNAi therapy for the treatment of patients with chronic Hepatitis C (HCV) infection. This is a major milestone for the company.

The first of the two sites in the US has commenced enrolment of patients. A total of 14 patients will be enrolled into the study, with five different doses being explored. Patients will receive a single dose via an intravenous infusion. Six weeks after the first patient has been treated, a second patient will be treated with the same dose if there are no adverse events. From there the dose will be escalated if safety is cleared. It is expected that the third highest dose will reach a therapeutic level.

Open Label Study

The trial is an open label study, so material progress will be released to the market. It is expected that some safety data will emerge by mid year, and some efficacy data by the end of the year. The trial is expected to be completed by the end of 2015.

The primary endpoint in the study is safety. The secondary endpoint is efficacy, which will be mainly measured by changes in viral load. However the company will also be looking at shRNA levels in the liver, which is the target organ, which will initially be measured by taking liver biopsies. The company will also look to measure this same effect (shRNA production) by taking blood samples through a proprietary assay, which will be validated from the early biopsy samples.

Patients in the trial will have failed other treatments (not including the recently approved drug Sovaldi from Gilead Sciences). The patients will have chronic infection but patients with liver fibrosis will be excluded. The Benitec technology uses a virus (AAV) to deliver DNA into liver cells which initiate an RNAi response to inhibit HCV in the cells by silencing three HCV genes.

Chief Business Officer Carl Stubbings was delighted by the prompt response from the FDA in clearing the trial with no questions regarding the company's IND application and two days earlier than the standard 30 day clearance process.

Benitec had $5.1 million in cash at the end of last year. The company is capitalised at $70 million.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

4.7B Reporting Companies – Cash Balances December 31, 2013

Sorted by Survival Index

	Code	Company	Cash Receipts ($M)	Nett Op. Cash Fl. ($M)	Cash End 31/12/13 ($M)		Survival Index	Comments/Events post reporting date
1	ACL	Alchemia	$5.90	$3.69	$16.10	A	**Not App**	
2	BXN	Bioxyne	$0.80	$0.20	$0.43	A	**Not App**	
3	LBT	LBT Innovations	$0.00	$1.20	$2.08	A	**Not App**	
4	LCT	Living Cell Technologies	$6.89	$0.76	$5.39	A	**Not App**	
5	ADO	Anteo Diagnostics	$2.12	-$0.18	$7.48	A	20.8	
6	AVX	Avexa	$0.00	-$0.47	$10.43	A	11.2	
7	MSB	Mesoblast	$12.37	-$2.29	$21.65	A	4.7	
8	NAN	Nanosonics	$12.37	-$2.29	$21.65	A	4.7	
9	ACW	Actinogen	$0.00	-$0.15	$1.35	A	4.5	
10	CYP	Cynata	$0.00	-$0.69	$6.20	A	4.5	
11	SOM	Somnomed	$12.26	-$0.45	$3.96	A	4.4	
12	BNO	Bionomics	$1.42	-$2.38	$20.47	A	4.3	
13	OBJ	OBJ	$0.04	-$0.74	$5.09	A	3.4	
14	OSL	Oncosil Medical	$0.00	-$1.71	$11.45	A	3.4	
15	NEU	Neuren Pharmaceuticals	$3.85	-$7.72	$24.37	CY	3.2	
16	CDY	Cellmid	$0.89	-$0.70	$4.20	A	3.0	
17	OSP	Osprey Medical	$0.00	-$8.04	$23.29	CY	2.9	
18	PAB	Patrys	$0.58	-$1.93	$10.32	A	2.7	
19	MLA	Medical Australia	$0.00	-$48.35	$250.26	A	2.6	
20	SPL	Starpharma	$0.33	-$6.00	$27.83	A	2.3	
21	ANP	Antisense Therap.	$0.00	-$0.81	$3.71	A	2.3	
22	PYC	Phylogica	$0.00	-$1.11	$4.65	A	2.1	
23	SUD	SUDA	$6.06	-$1.35	$5.53	A	2.0	
24	PXS	Pharmaxis	$2.58	-$12.60	$50.69	A	2.0	
25	IMU	Imugene	$0.00	-$0.62	$2.47	A	2.0	
26	GID	GI Dynamics	$2.54	-$37.38	$66.06	CY	1.8	
27	CUV	Clinuvel Pharmaceuticals	$0.78	-$2.84	$9.75	A	1.7	EMA's review of Scenesse extended to mid-2014
28	PRR	Prima Biomed	$0.00	-$8.35	$28.58	A	1.7	
29	BRC	Brain Resource Corp	$0.49	-$1.08	$3.27	A	1.5	
30	QRX	QRxPharma	$0.00	-$5.96	$17.16	A	1.4	
31	UBI	Universal Biosensors	$15.64	-$16.63	$23.72	CY	1.4	[Dec] Secured up to US$25 M loan facility
32	TIS	Tissue Therapies	$0.00	-$3.98	$10.32	A	1.3	
33	PBT	Prana Biotechnology	$0.00	-$7.49	$19.30	A	1.3	
34	AHZ	Admedus	$4.02	-$3.68	$9.31	A	1.3	
35	PAA	Pharmaust	$0.69	-$1.11	$2.70	A	1.2	
36	HCT	Holista Colltech	$2.88	-$0.70	$1.60	A	1.1	
37	RGS	Regeneus	$0.81	-$2.96	$6.52	A	1.1	
38	ISN	Isonea	$0.11	-$4.80	$10.10	A	1.1	
39	RHT	Resonance Health	$1.07	-$0.36	$0.75	A	1.0	
40	VLA	Viralytics	$0.00	-$1.79	$3.29	A	**0.9**	Is raising $23 M in two tranches
41	AVH	Avita Medical	$1.62	-$3.82	$6.76	A	**0.9**	
42	RVA	Reva Medical	$0.00	-$24.52	$21.67	CY	**0.9**	
43	IPD	Impedimed	$1.59	-$2.81	$4.54	A	**0.8**	
44	SIE	Scigen	$23.54	-$2.46	$1.92	CY	**0.8**	
45	GTG	Genetic Technologies	$2.34	-$5.31	$8.22	A	**0.8**	
46	IVX	Invion	$0.01	-$1.35	$1.86	A	**0.7**	
47	ALT	Analytica	$0.00	-$1.12	$1.43	A	**0.6**	
48	BCT	Bluechiip	$0.00	-$1.03	$1.17	A	**0.6**	CEO resigned 28/1/2014
49	UCM	USCOM	$0.33	-$0.80	$0.76	A	**0.5**	Signed a 5-year $7 M sales agreement for China [in Dec Q]
50	RNO	Rhinomed	$0.01	-$0.81	$0.74	A	**0.5**	
51	BLT	Benitec	$0.16	-$6.10	$5.17	A	**0.4**	
52	BIT	Biotron	$0.00	-$2.64	$2.15	A	**0.4**	
53	UNS	Unilife	$13.21	-$12.40	$7.64	A	**0.3**	Signed supply agg. with Sanofi, Hikma, MedImmune and Novartis in 2013
54	MGZ	Medigard	$0.00	-$0.11	$0.05	A	**0.2**	
55	AGX	Agenix	$0.02	-$0.52	$0.20	A	**0.2**	
56	BNE	Bone Medical	$0.00	-$0.31	$0.04	A	**0.1**	Under restructuring
57	GBI	Genera Biosystems	$0.09	-$0.71	$0.07	A	**0.1**	

Legend:

Not App. : The SI calculation for these companies is not calculated due to the companies reporting positive operational cash flows, or in some cases marginally negative operational cash flows.

A: The SI calculation for these companies is based on the average of the last two quarters of NOCF, annualised.

CY: The SI calculation for these companies is calculated on the average of the last four quarters of NOCF.

Bioshares Model Portfolio (31 January 2013)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$0.820	$0.620	December 13
Impedimed	$0.230	$0.245	December 13
Analytica	$0.025	$0.025	December 13
Imugene	$0.017	$0.022	November 13
Oncosil Medical	$0.145	$0.155	September 13
IDT Australia	$0.400	$0.260	August 13
Viralytics	$0.330	$0.300	August 13
Tissue Therapies	$0.290	$0.255	March 2013
Somnomed	$1.36	$0.94	January 2011
Cogstate	$0.365	$0.13	November 2007
Universal Biosensors	$0.50	$1.23	June 2007

Portfolio Changes – 31 January 2014

IN:
No changes

OUT:
Invion and Benitec have been removed given that both companies will most likely be addressing capital requirements in the near future

4.7B Reporting Companies – Cash Balances December 31, 2013 (Cont'd)

Commentary

Despite a steady decrease in the number ASX listed life science companies which report their cash positions on a quarterly basis, the proportion (70%) of companies holding cash necessary to support activities for a year or more is at a high level.

Atcor Medical no longer reports under the 4B rule because it has run five consecutive quarters of positive net operational cash flows. Biodiem has been removed from the list following its delisting in the December quarter.

Many companies topped up their cash reserves in 2013, with a smaller number of companies likely to follow Viralytics' suit and access fresh funding in the near future. Amongst these we include Benitec which should have less difficulty raising funds now that its Phase I/II trial of RNAi has been approved by the FDA (see previous page). Other companies which we think are likely to raise funds in the near future include Analytica, Invion, and Bluechiip. It would be no surprise to see Reva Medical raise significant funds in the lead up to its CE Mark application towards the end of 2014 for its Rezolve 2 bioresorbable coronary stent.

Pharmaxis, capitalised at $40 million, holds cash of $51 million. Prima Biomed, capitalised at $59 million, holds cash of $29 million. These two companies sit as examples of exposed stocks, whose share prices have fallen by 96% and 88% respectively from their three year highs. Such sizeable cash reserves may appeal to aggressive investors seeking to exploit cash box opportunities.

Each quarter, the majority of ASX listed biotech companies are required to report their cash positions. In turn, a key analytical measure we present each quarter is the 'Survival Index' (SI). The index measures how many years those cash reserves will last, based on a company's recent spending patterns. It is limited because it does not account for companies that may increase spending in the next period of activity.

The index is derived for this quarter by dividing the net operational cash flows (NOCF) for the last six months ending September 30, 2013, annualised into each company's cash assets as recorded at December 31, 2013. For companies that report on December 31 full year basis, the index is based on the full year's net operational cash flows (NOCF). The NOCF is the net of receipts and outgoings incurred in support of operational activities.

As a rule of thumb, companies that present with an SI of less than one are likely to be raising funds to support their activities, or are in the process of doing so. A healthy SI is either two or more. Companies with SIs of less then 0.5 may be in positions of funding stress and investors should investigate such stocks with a greater degree of concern.

Small cap life science companies that are not required to comply with the 4.7B Rule include: Acrux, Advanced Medical Design and Manufact., Immuron, Cogstate, Circadian Technologies, Clovercorp, Compumedics, Cryosite, Cyclopharm, Ellex Medical Lasers, IDT, ITL Corp, Calzada, Medical Developments Int., Novogen, Optiscan Imaging, Progen Pharm., Phosphagenics and Atcor Medical.
pSivida, a re-domiciled company, does not comply with the 4B Rule.

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: Starpharma Holdings, Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Tissue Therapies, Viralytics, Phylogica, pSivida, Antisense Therapeutics, Benitec BioPharma, Admedus, Calzada, Invion, Circadian Technologies, Imugene, Analytica

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