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	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)	62.5%
Cumulative Gain	**479%**
Av. annual gain (13 yrs)	**20.1%**

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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 - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph: 0403 850 425
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.

Viralytics Reports More Positive Data from Phase II Melanoma Study

Viralytics (VLA: $0.36) has reported more data from its Phase II trial with its oncolytic virotherapy, CAVATAK, which uses the coxsackievirus Type 21 vurus to treat metastatic melanoma.

Of the 54 patients due to be enrolled, the company has now enrolled 49 with the remaining five due to be enrolled by the end of the year. Of those enrolled, 35 have hit the six month point (on an immune related progression free survival basis) with 12 achieving irPFS at six months, or 34% of patients.

Other information emerging from the study is survival data. Of the 16 patients evaluable, nine have survived one year (54%), which compares very well with the Amgen oncolytic virus drug candidate T-Vec which achieved 58% survival in a similar Phase II study. Amgen is now awaiting final Phase III survival data to see if the company can file the drug for approval. The mean overall one year survival rates from a review of 42 Phase II melanoma trials, treated with a range of compounds is 25.5% according to the company.

There are possible synergies between the Amgen's and with Viralytics' therapies, where potentially the drugs could be used in series, with a second oncolytic virus used once patients' immune systems start to build antibodies to the first therapy.

Viralytics plans to initiate a randomised Phase II trial of CAVATAK in the second half of 2014. In moving the drug forward, testing of the therapy will need be used in combination with new melanoma drugs reaching the market. It is becoming a more competitive landscape with recent approvals in the filed including Yervoy from Bristol-Myers Squibb (sales of US$700 million in 2012 after launch in 2011), which also acts on the immune system, and Zelboraf from Roche (sales of US$250 million following launch in 2011). The company says there is a major problem with existing treatments relating to resistance and drug toxicity.

In other measures from Viralytics' ongoing Phase II study, of the 38 patients who have been on treatment for at least 12 weeks, one patient experienced a complete response and eight patients achieved a partial response (24% objective response). This is in line with T-Vec which achieved an objective response of 26% in its Phase II trial. Amgen acquired the T-Vec technology from Biovex in a US$1 billion deal that included a US$425 million upfront payment.

An advantage of using immune therapy in cancer treatment is the generally strong safety profile of such therapies. To date, Viralytics' CAVATAK therapy has not shown to cause any serious adverse events. Specific data that needs to still be seen with CAVATAK is the effectiveness of the therapy in treating distant tumours (i.e. those other than the tumours where the virus is injected). The company has indicated that the therapy is active in distant tumours although no overall details have yet been reported.

Cont'd over

Clinuvel Pharm. Approaches All-Important Regulatory Crossroad

It has been a very long journey for Clinuvel Pharmaceuticals (CUV: $1.325) and the drug it is developing for the treatment of sunlight intolerance and skin discoloration (vitiligo).

In February last year, the company submitted its new drug application with the European regulator, the EMA. The EMA's review is one of the longest in the regulator's history, which is not surprising given the technology. Clinuvel is currently completing responses to questions from the EMA which should be submitted by the end of the year. The final review process should then start in January next year, with an expert panel review expected in March 2014. Clinuvel expects it will make an oral presentation to the regulator in 2014 H1, which will precede a decision from the EMA.

Reasons for Lengthy Assessment

Clinuvel's drug is used to prevent severe reactions to the sun in certain people with a condition known as EPP. It is also being trialed for the treatment of vitiligo.

Clinuvel has spent considerable time and effort in proving that its drug, delivered as a depot injection that lasts two months, is safe, and it would appear that regulators are comfortable with its safety profile according to the company. Over 900 people have been administered the drug, receiving 2,746 implants in total and there have been 2,192 aqueous injections of the product as well with no serious adverse events linked to the drug.

The product has been given to patients through a compassionate use program, and the drug is also currently commercially available in Italy and Switzerland. Since 2010, 79 people in these countries have received 528 implants. In FY2013, the company generated $1.5 million from sales in Italy and Switzerland.

While the safety profile of the drug is good, there are two important factors that the EMA will consider. The first is the potential for the drug to be abused, for those seeking a natural tan by injection. Board Chair StanMcLiesh said at the recent Clinuvel AGM there is a concern about whether this drug will become the 'ultimate off-label product'. He believes the company has addressed abuse concerns through risk management plans.

The other main question regulators must ask is whether the drug provides 'clinical meaningfulness'. By way of example, in the company's Phase III trial in the US, patients on drug had a median direct sunlight exposure of 64 hours over six months (36 minutes a day) compared to 47 hours (26 minutes per day) on placebo. This result was not statistically significant (p=0.107). There was a large range between patients, with the longest exposure in the active arm being 650 hours over six months compared to 224 hours in the placebo arm. There is also the consideration of how quickly (or rather slowly) patients will change practices on the drug after avoiding direct sunlight all of their lives.

On other measures, patients on the active arm had three times more pain free periods lasting more than two hours than those on placebo. And there was a statistically significant improvement in quality of life in those taking the drug. The EMA has also requested to see the latest data from the US Phase III trial.

US Regulatory Approval

The next stage for Clinuvel in the US is to have a pre-NDA meeting with the FDA. The FDA will be interested in the clinical relevance of this treatment believes Wolgen. Wolgen also believes the FDA is very proactive in learning directly from the experiences of patients with this disease.

Summary

The stock has a high risk in 2014 as it moves through the uncertain regulatory process in Europe. It has a good chance of receiving a positive decision from the EMA given its very solid development work. If that occurs, at its low market value, Clinuvel's share price has room considerable growth in 2014.

The company is capitalised at $51 million with $11 million in cash at the end of September. Clinuvel will receive around $0.5 million through the R&D tax rebate in Australia.

Bioshares recommendation: **Lighten [Revaluate At Key Points During the Regulatory Review Process]**

Bioshares

– Viralytics cont'd

Viralytics is capitalised at $31 million. It had $3.3 million at the end of September and in October announced it had received $1.9 million in an R&D tax rebate. The company will need to raise additional funds before it initiates its randomised Phase II study in the second half of 2014.

Viralytics plans to license or sell the asset once it has reached a key value creation milestone. This point may be the release of final Phase II data from the current trial.

Viralytics expects to have full six month irPFS data in Q3 2014, with one year survival data in Q1 2015. The company expects to report further data at a major oncology conference in Q2 2014.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Corrections to last week's analysis of Antisense Therapeutics

Please note the following corrections:

In the current Phase II trial underway with ATL1103 in patients with acromegaly, there is no placebo arm, and the patients will start with a 600mg dose, not 650mg. Patients in this trial will have IGF-1 levels from 30% above normal to levels more than double normal levels (not 30%-100% above normal). Also note that while acromegaly is an orphan drug disease and Antisense does not specifically have orphan drug designation.

With respect to Antisense's MS program, Antisense believes the previous adverse events seen in a preclinical animal model were seen at all doses, not just at high doses as indicated. CEO Mark Diamond has further indicated the company is conducting toxicology testing now only at the doses it expects the drug will be used in the next Phase IIb study.

Five Stock Wrap

Company	Uscom	**Code**	UCM	**CMP**	$0.15	**Cap'n ($M)**	$11.4	**Cash ($M) 30/6**	$1.2	**SI**	**1.1**

- Uscom markets a non-invasive cardia monitor, the USCOM 1a, which measures blood flow across the heart valves using Doppler waves
- UCM acquired NZ company Pulsecor in June, to obtain its Cardioscope BP+ central blood pressure measurement device
- Cardioscope BP+ competes with products from Atcor Medical, Healthstats International, I.E.M Gmbh, Tensiomed and BP Labs
- UCM recorded sales of $0.638 M for FY13 ($0.864 M , FY12); losses of -$1.4 M for FY13 (-$1.8 M , FY12)
- SEPT: Raised $1 M to support sales efforts
- SEPT: Hired new global sales manager, UK based Steve Hakem
- OCT: Signed a 5 yr $6.6 M minimum purchases agreement (for Uscom products) with China Pioneer Pharma Holdings in October
- *(Note that the arrangement does not commence until approval is received by Chinese FDA)*
- NOV: This week appointed Medsource-SW as distributor in Southern USA
- Company's strength is possesion of products with approvals in place in most sales territories
- Company's weakness is that it sells a low turnover, long sales cycle, high value capital good (but BP device now complements that)

Comment: With fresh resources and new agreements, UCM is now better placed to grow sales

Bioshares recommendation: **Speculative Buy Class B** | Timing -

Company	Reva Medical	**Code**	RVA	**CMP**	$0.585	**Cap'n ($M)**	$193.8	**Cash ($M) 30/9**	$27.9	**SI**	**1.2**

- Reva Medical is developing the ReZolve2 bioresorbable coronary stent
- Has now enrolled its 87th patient in CE Mark trial (total number is 125)
- 65 pts have passed the 30 day follow up period; no major coronary adverse events reported (no heart attacks, no thrombosis)
- RVA anticipates submitting for a CE Mark in 2014, followed by authorisation in 2015 Q1
- Is competing with Abbotts XIENCE stent (in early sales in EU) and Elixir Medical's DESolve system, (yet to begin sales in EU)
- The investment rationale is that the global stenting market will shift from metal to bioresorble stents
- Stated in conference call that it expects to commence clinical trials of a stronger, thinner next generation product in 2014
- This is a sound decision because the market is responsive to technically superior products that deliver clinically superior benefits

Comment: RVA is making steady progress towards completion of the pivotal CE Mark trial

Bioshares recommendation: **Speculative Buy Class B** | Timing -

Company	Unilife	**Code**	UNS	**CMP**	$0.510	**Cap'n ($M)**	$307.1	**Cash ($M) 30/9**	$10.2	**SI**	**0.2**

- Unilife manufactures and supplies injectable drug delivery systems, focusing on biologics and vaccines
- OCT: signed a supply agreement of the Finesse system with Sanofi in September, 2013, exclusively for Sanofi's anti-thrombotic drugs
- Has received a US$5 M milestone payment, with a potential $10 M to follow
- NOV: signed a supply agreement with AstraZeneca's biologics group Medimmune for wearable injection systems
- Unilife expects revenues from Medimmune to commence 2014 Q1; other terms not disc.
- Company posted losses of US$63 M in FY13 and $52 M in FY12; At 30/6 was carrying debt and obligations of US$38 million
- Product sales have been minimal for last two years. Unilife expended US$21.7 M on R&D in FY2013 (US$23.1 M, FY13)
- Has access to US$22.5 M loan facility

Comment: UNS share price has run ahead of expectations; weak cash position a potential drag on working capital requirements

Bioshares recommendation: **Sell** | Timing -

Company	Resonance Health	**Code**	RHT	**CMP**	$0.013	**Cap'n ($M)**	$4.7	**Cash ($M) 30/9**	$0.9	**SI**	**5.2**

- RHT markets the non-invasive MRI test Ferriscan for iron overload; has recorded solid growth in volume sales over last four years
- However, sales of $1.5 M for FY2013 showed no change from the previous year's figure; 50% of sales stem from clinical trials
- Is developing HepaFat-Scan for fatty liver disease and a liver fibrosis test
- Announced contract with European imaging business Alliance Medical to offer FerriScan in the UK and potentially elsewhere in Europe
- RHT reports that some US insurers are paying for the test; company has submitted an application for a CPT code
- Ferriscan received FDA approval as a companion diagnostic for the drug deferasirox (wording covers identification and monitoring)
- Anticipates FDA decision for HepaFat in 2014 Q1
- Market opportunity in fatty liver disease is very large; an improved diagnostic tool could improve liver surgery outcomes
- RHT has been slowly building the foundations for growth into areas beyond iron overload market (but which has validated the product)

Comment: RHT has a low market profile; however, an FDA approval in 2014 could trigger a re-rating

Bioshares recommendation: **Speculative Buy Class B** | Timing -

Company	PharmAust	**Code**	PAA	**CMP**	$0.013	**Cap'n ($M)**	$18.7	**Cash ($M) 30/9**	$3.51	**SI**	**6.3**

- Pharmaust recently acquired Pitney Pharmaceuticals, and is now largely focussed on the life sciences
- 100% owned drug services (synthetic & med chem) business Epichem recorded sales of $1.3M in FY13 (85% to offshore customers)
- Biotech entrepreneur Dr Roger Aston joined the board as Executive Chairman in August 2013.
- PAA is developing an existing veterinary antiparasitic compound (PPL-1) . Expects Phase I/II to commence in FY2014
- The albendazole (ALB) program addresses treatment of ascites - the collection of fluid within the peritoneal cavity) with a known cmpd
- Albendazole has poor solubility in water; opportunity exists to optimise formulation and route of administration (and file use patents)
- In the next 12 months PAA will seek to file an IND for ALB, commence optimisation trial and initiate Phase II/III trial
- Well positioned to take advantage of the R&D Tax Incentive scheme as a service provider *and* as a drug developer
- With 1,440 million shares outstanding a capital consolidation could occur, following similar consolidations at e.g ANP and BLT

Comment: PAA mixes early and mid stage assets with a cash business, with early out-licencing a positive de-risking strategy

Bioshares recommendation: **Speculative Buy Class B** | Timing -

Notes: PE - Price/Equity ratio SI - Survival Index (refer to Bioshares 527 for explanation)

Bioshares Model Portfolio (15 November 2013)

Company	Price (current)	Price added to portfolio	Date added
Imugene	$0.022	$0.022	November 13
Oncosil Medical	$0.115	$0.155	September 13
Calzada	$0.076	$0.073	September 13
Invion	$0.105	$0.060	August 13
IDT Australia	$0.435	$0.260	August 13
Viralytics	$0.360	$0.300	August 13
Circadian Technologies	$0.250	$0.270	March 2013
Tissue Therapies	$0.225	$0.255	March 2013
Benitec Biopharma	$0.555	$0.40	November 2012
Somnomed	$1.24	$0.94	January 2011
Cogstate	$0.450	$0.13	November 2007
Universal Biosensors	$0.54	$1.23	June 2007

Portfolio Changes – 15 November 2013

IN:
No changes..

OUT:
No changes.

Invion Update – Smoking Cessation IND Split; Zarfirkulast In-license

Invion (IVX: $0.105) announced that the FDA will split the company's IND for IVX-102 (nadalol) (oral delivery). This means the smoking cessation in patients with existing COPD indication will be overseen by the Division of Anesthetics, Analgesia and Addiction Products (DAAAP) , which is headed by Dr Bob Rappaport.

The oversight of the 'stricter' pulmonary indications of asthma (and others) will remain with the Division of Pulmonary, Allergy and Rheumatology Products (DPARP).

The rationale for the splitting the IND is that the DAAAP traditionally has overseen smoking cessation medicines and would be the division responsible for regulatory review for INV-102.

A new IND number will be created with a 30 day review period to follow. The company does not expect the primary endpoint nor the number of patients expected to be enrolled in its Phase II trial to change. The trial, which is underway, intends to enrol a total of 130 subjects, with 65 in each arm. Interim results are expected in 2014 H1 (previously 2014 Q1).

The DPARP division will retain oversight of the safety data pertaining to INV102.

In *Bioshares* view, there is some risk attached to this change of FDA divisional oversight in so far as DAAAP may be need more time to build its understanding of nadalol and mechanism of its action in the pulmonary setting.

Zarfirlukast In-licence

Invion recently in-licensed Zarfirlukast from AstraZeneca, with a $500,000 payment due within 12 months from January 2014. Zarfirlukast is an oral leukotriene receptor antagonist approved for the treatment of chronic asthma in adults and children over five

This drug was first developed by Invion's CMO Dr Mitchell Glass, when he was at AstraZeneca. The goal is to resurrect the inhaled version of the drug, which had been shelved for portfolio reasons by AstraZeneca, despite the completion of seven trials.

Invion's inhaled version of zarfirlukast would be re-formulated. The earlier version used chloro-fluorocarbons as the propellent.

One possibility for the inhaled zarfirlukast program is to see if it can be used as an additive therapy with *severe* asthma patients who also might benefit from INV-102 (nadalol) treatment. Patients with allergic asthma are observed to have elevated leukotrine levels. There is also a strong leukotrine signal in some COPD patients, a group which has never been therapeutically addressed by AstraZeneca or Merck.

In short, zarfirlukast extends Invion's reach into the pediatric population while INV-102 (nadalol) extends the company reach into the moderate-to-severe asthma population, thereby broadening its foundations in respiratory medicines.

Next Steps

The company will initiate studies to determine the feasibility of using a metered dose inhaler, which would be followed by stability studies and limited toxicology studies. Within 12-18 months, Invion would then file an IND for the drug.

The inhaled zarfirlukast program is a very good fit with Invion's nadalol program. Investors can gain confidence from the fact that the drug's original developer is once again driving the program.

Invion is capitalised at $49 million and retained cash of $1.75 million at September 2013.

We anticipate that company will look to raise additional funds in the near future, given its latest Survival Index figure was 0.4 .

Bioshares recommendation: **Speculative Hold 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: Starpharma Holdings, Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phylogica, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Atcor Medical, Invion, Circadian Technologies

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