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Bioshares

29 August 2014
Edition 566

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

Companies covered: ACW, SOM, UCM, VHL

	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 - May '14)	26.6%
Year 14 (May '14 -)	15.7%
Cumulative Gain	**421%**
Av. Annual gain (14 yrs)	**17.2%**

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Forrest Capital Launches Alzheimer's Disease Drug Play

Perth-based Forrest Capital has used Actinogen (ACW: $0.047) as the vehicle for its fifth biotech play, acquiring University of Edinburgh spin-out Corticrine, an Alzheimer's disease drug discovery and development company.

Actinogen has up until now been focused on a project in the cancer stem cell space but was initially founded to develop actinomycetes, gram-positive organisms found in soil, as antibiotics.

Forrest Capital's biotech investments to date have included Patrys (now exited), Oncosil Medical, Cynata Therapeutics and Imugene, representing a diversified group of technologies and investment return models.

Dr Jason Loveridge and Martin Rogers will join the board once the Corticrine acquisition has been approved by shareholders.

Actinogen will issue 125 million shares for the acquisition of Corticrine. In conjunction with the acquisition, Actinogen will issue 100 million shares to raise $2 million. On completion, the company should hold $3 million in cash.

The University of Edinburgh will hold approximately 11% of Actinogen on completion of the acquisition. The founders of Corticrine will hold approximately 35% of Actinogen.

The Corticrine Asset

Corticine has developed a molecule, UE2343, which inhibits 11-beta-hydroxysteroid dehydrogenase (11beta-HSD1). 11beta-HSD1 is an enzyme which generates cortisone, which is then converted to the active hormone cortisol which in turn activates glucocorticoid receptors. The treatment hypothesis for Alzheimer's disease is based on the observation that patients with too much cortisol (known as Cushing's Syndrome) exhibit memory loss. The theory is that dampening the production of cortisol will improve cognition.

The general role of cortisol is to regulate immune, metabolic and cardiovascular responses to stressful stimuli. However, if stress levels are sustained, then the levels of cortisol are also sustained above normal levels, leading to disease permanently exacerbated states or conditions, such as Cushing's Syndrome. The modulation of 11beta-HSD1 has mostly previously been explored in the areas of diabetes and metabolic syndromes, hypertension and cardiovascular disease risk management.

Corticrine has also shown in animal studies that small molecule inhibition of 11beta-HSD1 reduces amyloid-beta plaque burden and plasma amyloid-beta, as well as improving cognitive function and providing cognitive protection.

Cont'd over

– Actinogen cont'd

UE2343 is an orally delivered drug candidate with high bioavailability. A synthetic manufacturing process has been developed to allow kilogram-scale manufacture. Patents and applications for the compound run beyond 2028.

Phase I Program

Corticrine has completed a single ascending dose Phase I study of UE2343 in 48 patients, which showed the compound was well tolerated with no adverse toxicities.

A Phase I multiple ascending dose study of UE2343 in 20 healthy volunteers is planned to commence in 2015. While the goal will be to explore PK, PD and toxicology endpoints, secondary endpoints will evaluate changes in hippocampal signalling during memory tasks and study the inhibition of systemic HSD1 as measured by whole body D3-cortisol generation rate.

A Phase II efficacy study is planned to commence in late 2015 or early 2016.

Commentary

The Corticrine acquisition is attractive for several reasons. The first is that this equity funded deal is clean and gives both Corticrine founders and the University of Edinburgh access to plenty of upside should UE2343 progress successfully through the clinic and ultimately a sale transaction to a large pharmaceutical company.

Second, the UE2343 research program has received significant funding to date, from the Wellcome Trust Seeding Drug Discovery program. Furthermore, the pre-clinical, clinical and manufacturing work done to date means that the company is a short distance from investigating the efficacy of the compound in a pivotal trial in 2016.

Third, UE2343 importantly represents a new approach for the treatment of Alzheimer's disease. Much of the focus over the last decade has focused on directly attacking or neutralising the beta-amlyoid plaque which is characteristic of the disease in its later stages. There have been a number of spectacular and expensive failures with this approach yet the approach remains popular as the table on next page shows.

In this table of selected Phase I programs drawn from active clinical trials as posted on clinicaltrials.gov, eight programs are based on targeting beta-amyloid and its clearance. Twenty-one Phase I programs were selected from a search which yielded 44 trials categorized as Phase I Alzheimer's studies. Biomarker and certain country specific (i.e. Japan) studies were excluded. The Phase I status was selected because of their likely generally stronger contemporary relationship to UE2343 with respect to vintage.

Fourth, as Bionomics' recent US$508 million plus royalties deal with Merck attests, novel treatment paradigms, even at the preclinical stage, can grab the attention of large pharmaceutical companies, even if the approach may prove to be more beneficial in treating symptoms rather than be disease modifying.

Fifth, despite the losses incurred in Alzheimer’s disease by large pharmaceutical companies and also by many smaller companies, the appetite for drug discovery and development is high because a genuinely disease modifying drug has not been found and the market opportunity - read, economic burden - is huge.

Sixth, a shift to developing drugs to treat prodromal (pre symptomatic) as well as mild-to-moderate Alzheimer’s disease has taken place, where the delay or deferral of the advanced stage is the objective. This is because the underlying biology of Alzheimer's disease begins ten or more years before symptoms appear.

This is a direction which should bias the chances of success for many companies currently developing drugs to treat Alzheimer's disease. And coupled to the introduction of clinical trial management tools, such as Cogstate's Precision Recruitment tool, then decreased costs of drug development could pave the way for increased chances of success for companies such as Actinogen, or more likely, a potential acquirer.

These factors mean that Actinogen is likely to be a significant outperformer in the not too-distant future.

Assuming the issue of all shares specified under the transaction, Actinogen is capitalised at $20 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Selected Early Stage Alzheimer's Disease Clinical Trials (Active or Yet to Recruit)

Company	Intervention	Mechanism/s	Route of Delivery	Indication	Status
Biogen Idec/ Eisai	BAN2401	Monoclonal antibody - binds to soluble Aß protofibrils	IV	MCI, Mild AD	Phase I, 24 pts
Medipost [Korea]	NEUROSTEM	Umbilical cord derived mesenchymal stem cells	Intra-ventricular	AD	Phase I/IIa, 40 pts
Abbvie	ABT-957	Calpain inhibitor	Oral, 2 x day	MtM AD	Phase I, 20 pts
Uni California (SF)	TPI-287	Microtubule inhibitor (taxane class of drugs)	IV	MtM AD	Phase I, 33 pts
Uni California (SF)	Allopregnanalone	Naturally occurring brain steroid (3alpha, 5alpha-tetrahydroprogesterone)	IV	MCI, Mild AD	Phase I, 32 pts
American Society of Thermalism and Climatology	Transcranial Magnetic Stimulation	Excitatory stimulation over the prefrontal and parietal cortex, to stimulate brain derived neurotropic factor	External stimulation	AD	Phase I/II, 100 pts
Axon Neuroscience SE	AADvac1	vaccine directed against tau proteins: axon peptide 108-KLH conjugate	sc (3 injections)	MtM AD	Phase I, 30 pts
Life Extension Foundation	Etanercept	TNF-alpha fusion protein - addressing inflammation and oxidative stress	Perispinal	MtM AD	Phase I, 12 pts
Kyowa Hakko Kirin (licd from Immunas Pharma Inc)	KHK6640	anti-amyloid beta (Aß) peptide antibody	IV (?)	Prodromal AD, MtM AD	Phase I, 62 pts
Johnson & Johnson (Janssen)	JNJ-54861911	targets a-beta processing	Oral, 2 x day	Prodromal AD	Phase I, 40 pts
Regenera Pharma (Israel)	RPh201	a botanical extract, also applied to wound healing	sc	MtM AD, AD	Phase I,II, 56 pts
Neutrotrope Bioscience	Bryostatin 1	Macrolide lactone; Protein Kinase C (PKC) modulator; memory regulation	IV	AD	Phase I, 15 pts
Eli Lilly	LY3002813	anti-amyloid beta (Aß) antibody	IV,sc	MCI, MtM AD	Phase I, 100 pts
AHAMMS (China)	UC-MSC	Ubilical cord derived Mesenchymal Stem Cells	IV	AD	Phase I, Phase II, 30 pts
Russell Swerdol	S-Equol (AUS-131)	Stimulation of estrogen receptor beta, promoting mitochondrial function	Oral, 2 x day	Very mild, to mild AD	Phase I
Biogen Idec	BIIB037	anti-amyloid beta (Aß) antibody	IV	Prodromal, MtM AD	Phase I, 160
AstraZeneca	MEDI1814	anti-amyloid beta (Aß) antibody	IV,sc	MtM AD	Phase I, 242 pts
Veterans Affairs (USA)	tDCS	transcranial direct current stimulation	External stimulation	MCI, AD	Phase I, 200 pts
Icure Pharmaceuticals	Donepezil Patch	acetylcholinesteraze inhibitor	Transdermal	AD	Phase I, 24 pts
ReXceptor	Bexarotene (Targretin)	retinoid x receptor (RXR) agonist, targeting clearance of Aß, by stimulating production of ApoE	Oral, 3 x day	AD	Phase I, 12 pts
GlaxoSmithKline	GSK2981710	medium chain tryglycerides (6-10 carbon fatty esters of glycerol) [the ketogenic diet hypothesis=neuroprotection]	Oral, liquid	Age-related cognitive decline	Phase I, 88 pts

= programs targeting Aß

MtM= Mild to Moderate
MCI= Mild Cognitive Impairment

Uscom Aims for Profitability

Uscom is setting its target for moving into profitability some time in this financial year. It's been a pivotal 12 months for Uscom (UCM: $0.27), which has seen sales of its core product, the USCOM 1A, increase by 83% to $1.05 million, and has seen the company integrate its second product into the business, called BP+, from the acquisition of Pulsecor in June last year.

The USCOM 1A is a unique product that provides non-invasive measurement of cardiac output. The BP+ product provides non-invasive measurement of central blood pressure and is not unique.

Drivers of Sales Growth in FY2014

Most of the sales in the last financial year were from the USCOM 1A product. The company achieved strong sales growth because it had increased its total number of distributors from 15 to 27, improved the distribution margins, and awareness of the benefits of the product continued to grow with now between 450-500 publications covering the technology.

Drivers For FY2015

For this financial year, there will be two main drivers for growth, and potentially a third. The first is from continued growth in USCOM 1A sales. The second will be from launch of the company's second cardiac measurement product, the BP+, with manufacturing having commenced in June. And in 2015, the company is expecting to receive CFDA approval in China for BP+. Uscom has a distribution agreement with Pioneer Pharma, which involves a five year, $7 million contract to sell into China, once regulatory approval is received in China.

Integration of the Pulsecor Business

The last 12 months has been a very busy period for the company integrating the Pulsecor business into Uscom. This has included tightening up the existing regulatory process for BP+, transferring those approvals to Uscom and integrating the Pulsecor IP into Uscom.

During the year the company received CE Mark approval for BP+ to allow the company to start selling BP+ into Europe. And this week, the company received TGA approval to start selling the device in Australia. FDA approval has already been received. However further regulatory work may be required with respect to additions or changes with BP+, including software enhancements.

The company is currently conducting a manufacturing run of 180 BP+ devices in Sydney. Its USCOM 1A product is also manufactured at the same facility.

Summary

Uscom CEO Rob Phillips said the goal for the company this financial year is to transition to profitability, which is not reliant on sales from the Chinese distribution deal coming online. “The USCOM 1A product is changing clinical practice and saving lives. The commercial risks are really diminishing,” said Phillips. Having established an expertise in the cardiac diagnostic space and with distribution channels having been set up, Phillips said there is the opportunity also for further product acquisitions in this space.

Uscom is capitalised at $22 million. The company made a loss of $1.5 million last year and has just under $1.6 million in cash.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Virax To Start Two Phase II Cancer Studies In 1H 2015 With Pathway Oncology Acquisition Assets

In May this year, Virax Holdings (VHL: $0.006) acquired Pathway Oncology to gain access to that company's oncology assets, which includes a small molecule called GGTI-2148. Virax will pay up to 240 million VHL shares ($1.4 million), pending the achievement of certain clinical milestones. Pathway has licensed the rights to the technology from Yale University and the Moffitt Cancer Center in the US.

The program had previously completed encouraging preclinical studies and a Phase I trial in 13 patients with solid tumours. These patients had exhausted available drug treatments. Even in the advanced cancer patients GGTI-2418 was able to stabilise disease in four of the 13 patients. The stabilisation was seen as the dosages of the drug candidate increased. Importantly there was no overt toxicity seen with the drug candidate. The acquisition also came with ample GMP manufactured material to start the clinical trials said Virax CEO Rob Crombie.

Phase Ib/II Studies To Start 1H 2015

Virax is planning to start two Phase Ib/II studies in the first half of next year. One is in patients with multiple myeloma, and the other is in breast cancer. The multiple myeloma trial will be conducted at the Moffitt Cancer Center in Florida and the Principal Investigator has been appointed. The Phase Ib trial will involve around 10-20 patients as a bridging dose escalation study with about 30-50 patients treated in total. It will be recruiting patients who have become refractory (non-responsive) to the front-line drug Velcade.

The Phase Ib/II breast cancer trial will recruit up to 80 patients in total. This will involve a lead-in section of the trial, looking at treatment alone with the Virax drug candidate, GGTI-2148. This is because the Phase II trial will be a combination treatment with the cancer drug paclitaxel. The Principal Investigator, Joseph Sparano, from the Albert Einstein College of Medicine in New York, has been appointed.

Mechanism Of Action Of GGTI-2148

GGTI-2148 is believed to have a dual mechanism of action. It arrests uncontrolled cell cycle growth by inhibiting the cancer growth enzyme GGTI (geranyl-geranyl transferase I). “GGTI catalyzes lipid modification of many Ras-related proteins that are found aberrantly activated in around 30% of all human cancers,” said Crombie. GGTI-2148 also directly causes apoptosis of the cancer cells.

GGTI-2148 To Be Trialed As A Combination Therapy

GGTI-2148 is initially being developed for treatment in combination with existing cancer therapeutics. Importantly, GGTI-2148 is believed to sensitise patients to existing cancer therapies once patients have become refractory to treatment.

This approach has an important advantage, both for clinical studies and well as a commercial product. The benefit is that patients are not required to change treatment regimes, but will be treated with GGTI-2148 and then resume previous drug treatment. Combination drug treatments can add complexity to the regulatory pathway. However an important difference for Virax is that is also developing a diagnostic tool that will allow the clinicians to understand when GGTI-2148 therapy is being effective.

Cancer Diagnostic For Use With GGTI-2148

In May this year, Virax acquired an exclusive option to in-license a novel cancer biomarker, called p27, from the Moffitt Cancer Center. The level of the p27 protein is found to drop considerably in patients with cancers such as breast cancer, which leads to uncontrolled cell growth. The Moffitt Cancer Center has done considerable work with this protein and found that Virax's drug candidate GGTI-2148 has an impact on restoring levels of p27 and thereby arresting the uncontrolled cell growth associated with cancer.

If GGTI-2148 is being developed as a combination therapy to resensitise patients who have become refractory to drug therapy, then having a diagnostic marker to tell clinicians when patients are ready for resuming original drug therapy after treatment with GGTI-2148 will add considerable clarity to the drug therapy regime. It will also provide information to clinicians as to which patients are likely to respond to drug treatment.

Crombie believes there will not be difficulty in recruiting patients into the multiple myeloma trial because clinicians are desperate to find a way to treat patients who have become refractory to the standard of care, Velcade, to which there is a high level of resistance. And the big point to stress said Crombie is that patients are not being removed from the standard of care.

Final Steps before Commencement of Phase II Trials

Virax is currently working on completing the trial designs. An IND has been previously filed and received from the FDA. This IND package has been transferred to Virax and will need to be re-opened. Virax will be meeting with the FDA towards the end of this year to “ensure the drug program is aligned with the FDA's expectations,” said Crombie.

Funding

In May Virax raised $3.0 million. At the end of June the company had $3.8 million in funding, which is sufficient to support the business through to mid 2015 according to the company.

Summary

Virax has acquired some interesting cancer assets. The assets have been developed at prestigious medical research centres in the US and the company has commitment from similarly respected hospitals to conduct its clinical studies in patients with breast cancer and multiple myeloma.

Funding will be an item the company to address in the next six months. Given the company's very low market capitalization, of $6 million, it's a stock with potential if it can finalise its IND, transition into its Phase II programs and ensure prompt recruitment.

Bioshares recommendation: **Pending Patent Review**

Bioshares Model Portfolio (29 August 2014)

Company	Price (current)	Price added to portfolio	Date added
LBT Innovations	$0.130	$0.130	July 14
pSivida	$5.040	$3.800	May 14
Invion	$0.085	$0.089	February 14
Impedimed	$0.360	$0.245	December 13
Analytica	$0.035	$0.025	December 13
Imugene	$0.017	$0.022	November 13
Oncosil Medical	$0.105	$0.155	September 13
IDT Australia	$0.270	$0.260	August 13
Viralytics	$0.275	$0.300	August 13
Tissue Therapies	$0.370	$0.255	March 2013
Somnomed	$1.94	$0.94	January 2011
Cogstate	$0.270	$0.13	November 2007

Portfolio Changes – 29 August 2014

IN:
No changes

OUT:
No changes

Somnomed Full Year Results Briefing

Somnomed (SOM: $1.94) has been conducting briefings following the release of its full year accounts.

Somnomed recorded revenues of $25.8 million for FY2014 , a 40% increase from the previous year. EBITDA increased 26.5% to $1.05 million.

EBITDA, when adjusted for investments in the US managed care team , acquisition and legal costs in Europe, and new market set up costs, was $3.3 million, or 12.9% of sales. Executive Chairman Peter Neustadt said that the goal was to bring the EBITDA margin to 20% in four years time and in the longer term to 25%.

Somnomed expects that going forward in the US sales will cover the costs of the US investments in its medical team. This includes a Chief Medical Officer, a Medical Advisory Board, a billing department, a medical education department, a medical sales department and a managed care department.

The company's gross margin is expected to be maintain in the high 60% range, with benefits flowing from the phasing in of digital production technologies to decrease freight costs.

Net average sales per unit was $639, which represented an increase of 13%. Factors behind the increase included exchange rate effects and the acquisition of a distributor which means that Somnomed received the benefits of a full selling price.

Somnomed is now active in 27 countries and in almost all operates of its own accord i.e. sells direct. Sales by volume were 11% in the Asia Pacific region, 36% in Europe and 53% in the USA.

The company's marketing strategy is now built on a medical channel, directed at physicians with dentists providing the fulfilment channel. "The dentist is our pharmacist," said Neustadt, with 5,000 dentists registered to fit the Somnodent range of sleep therapy appliances.

There are now 17 clinical studies published on continuous open airway therapy (COAT) therapy. COAT refers to dental splints such as the Somnodent devices. Several clinical studies are expected to be published in the near future, focusing on the relationship between Somnomed's product and co-morbidities.

Studies comparing COAT to CPAP show that by and large the two approaches are comparable, except that CPAP is generally better in the management of interruptions. However, according to Neustadt, breathing interruptions aren't considered as important as other measures. “Insurers are not happy,” he said, because “they see the flood of patients coming but don’t see CPAP as the way to go.”

Somnomed quoted a Frost and Sullivan survey, which forecast the oral appliance market in the USA to grow from 180,000 - 200,000 patients fitted with device in 2013 to grow to over 1 million in 2020. In value terms this is an increase from US$63 million in 2013 to US$343 million in 2020. This is across all price segments. According to Neustadt, Somnomed has 45% share of the upper price segment in the USA.

Somnomed is capitalised at $96 million.

Bioshares recommendation: **Buy**

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

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