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Companies covered: ANP, RGS, SOM, SPL

	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)	69.1%
Cumulative Gain	**502%**
Av. annual gain (13 yrs)	**20.6%**

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Bioshares

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

Strong Quarter for Somnomed Signals Pivotal Year Ahead

Somnomed (SOM: $1.26) has just delivered an exceptional quarter with strong growth. Overall unit growth for the quarter of the company's oral splints used for the treatment of sleep disorders was a very solid 23.6%. Sales growth was even more impressive with a 41.4% increase over the previous corresponding period (pcp), largely due to a weaker Australian dollar.

In the December quarter the company sold more than 11,000 devices. The Asia pacific region increased sales by 13%. Europe continued to perform exceptionally well, recording a 52% growth in unit sales. However, sales in the US increased by only 10%. Nevertheless there are signs the US has turned the corner with stronger growth ahead expected, with 23% growth in unit sales achieved in November and 31% growth achieved in December over the pcp.

Europe – OAT is a First Line Therapy in Sweden and Holland

Somnomed has been achieving strong growth in Europe for some time now and for one key reason. In Sweden and Holland oral appliance therapy (OAT) such as Somnomed's Somnodent devices, is prescribed as a first line therapy. This means that patients who have an AHI (number of apneas per hour) of more than five are recommended OAT even before CPAP therapy.

In Sweden OAT has about 55% of the market, with CPAP around a 45% market share. In Holland, OAT has more than 35% market share, up from 8%-10% three years ago. Somnomed's CFO Neil Verdal-Austin said that 'Once we see that (strong market share) numbers just climb. We have real proof that is happening now.'

In those countries, the access channels for Somnomed's devices are simpler, with less leakage, according to Verdal-Austin. Patients see their GP, then undergo a sleep test, and are then fitted with an oral splint. All the costs are paid for by the one government body (county councils in Sweden) and it is more difficult for the patient to exit this treatment loop than it is for instance in Australia. The benefit to the county councils is they have a healthier population, that is working and that is functioning at work. This preventive healthcare system no doubt reduces future healthcare costs.

All countries in Europe where Somnomed sells its products provide some type of reimbursement for Somnomed's devices. In Germany, the company is making some headway with achieving better reimbursement, however, the progress is slow.

European sales now make up around 30% of total sales. In the last two years, Somnomed has acquired four distributors in Europe (Holland, Sweden, France and Germany), which allows it to coordinate sales and reimbursement better. The company does not have any immediate plans for additional acquisitions is Europe, although it is seeking to enter additional regions in Europe.

Cont'd over

USA

The company's operations in the US have definitely turned the corner according to Verdal-Austin. The new lower-priced Herbst product is being accepted well, the company has signed on some new, large dental businesses to adopt the Somnodent products, and it has converted some of its competing accounts over to Somnodent. There is some impact from the company's investment in marketing its products to the medical sector (rather than dental sector). However this impact is difficult to measure.

The company is due to start a trial next month with managed care group Kaiser Permanente. While this will only be a small study, the aim is to achieve a policy change with this group, to have oral appliance therapy adopted throughout its centres. Achieving a change in the way sleep therapy is practised by such a large managed care organisation will be an important inroad into competing head-to-head with the CPAP suppliers in the US.

In the second quarter, the company generated a net positive cashflow of $620,000. It can be expected that increasing free cashflow will be invested into the building of the company's sales and marketing initiative in the US.

Summary

We expect 2014 will be a pivotal year for Somnomed. Its European market is delivering outstanding growth and there are signs that the US is returning to strong growth. We expect Somnomed to achieve sales of around $28 million this year. With a market value of $56 million, the stock is trading at a prospective 2.0 times sales. The company finished the year with $4.0 million in cash.

Bioshares recommendation: **Buy**

Bioshares

Antisense Posts Encouraging Interim Results from Phase II Acromegaly Study

Antisense Therapeutics (ANP: $0.14) has reported some encouraging results from its Phase II trial with its antisense drug candidate ATL1103 in the treatment of patients with acromegaly.

Antisense Therapeutics is testing its drug candidate in 24 patient Phase II trial, with interim, three month results available from the first eight patients. In those eight patients, half received a lower weekly dose of 200mg per week, and half received a higher dose of 400mg a week.

In the lowest dose, there was 'no consistent reduction' in the serum IGF-1 levels. Reducing circulating IGF-1 levels in the blood is know to effectively treat acromegaly, which is an excessive growth of organs and limbs in the body.

In those four patients receiving a higher dose, a 30% reduction in IGF-1 levels was achieved after 14 weeks. A 30% reduction in IGF-1 levels is expected to deliver an appropriate clinical benefit. However the patients in this trial had very high IGF-1 levels, between 2.4-5.0 times normal, and their IGF-1 levels were not reduced to within the normal range. The company indicated that normal starting iGF-1 levels for patients with acromegaly is 1.8 times normal.

Completion of enrolment into the trial is expected early this year. Antisense is considering a small add-on study with higher doses of the drug, however that comes with the risk of adverse events such as liver toxicity, which is a risk with high doses of antisense drugs. There were no serious adverse events reported in this trial.

Antisense is capitalised at $20 million. The company held $4.0 million in cash at the end of September (which includes an expected R&D tax rebate).

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Starpharma Announces Phase I for DEP-Docetaxel

Starpharma (SPL: $0.705) announced that it has received approvals to commence a Phase I trial of its dendrimer-enhanced docetaxel (DEP-Docetaxel) cancer treatment candidate at the Alfred Hospital in Melbourne. Other sites may be added to the trial.

The trial will enrol approximately 30 patients with advanced or metastatic cancer. The trial is a dose escalation study with the primary objective to establish a maximum tolerated dose.

A secondary objective is to establish a dose for Phase II studies. The drug will be delivered intravenously once every three weeks.

Potential Advantages of DEP-Docetaxel to Docetaxel (Taxotere)

Starpharma has established in pre-clinical studies that DEP-Docetaxel has a half life more than 60 times greater than Taxotere, the orginator drug marketed by Sanofi. Starpharma has also established that the accumulation of DEP-Docetaxel in tumours is 40 times greater than that for Taxotere. One implication is that lower overall doses could be administered.

Another advantage that DEP-Docetaxel appears to offer over docetaxel is that DEP-Docetaxel does not cause neutropenia, which occurs in 75% of patients receiving docetaxel. If this is confirmed in clinical studies, it may become the basis for building a strong commercial foundation for the drug.

A further advantage is that a chemical used to make docetaxel more soluble, polysorbate 80, is not required in Starpharma's formulation. This means that injection reactions (which can sometimes be fatal) should not occur.

Patents covering DEP-Docetaxel extend to 2032.

The Abraxane Model

A model for Starpharma's development of DEP-Docetaxel is Celgene's Abraxane, which was first approved in 2005. Celgene obtained Abraxane through its acquisition of Abraxis Bioscience for US$3.2 billion in October 2010.

Abraxane is a solvent-free formulation of paclitaxel, an agent similar to docetaxel, in which the active drug is bound with albumin. Patents covering Abraxane expire in the US in 2026 and in Europe in 2022.

Abraxane is approved for the treatment of metastatic breast cancer after failure of other therapies, in the US, Europe and Japan. It is also approved for the treatment of non-small cell lung cancer, as a first line treatment in combination with carboplatin. Most recently it has been approved in the US and Europe for the treatment of metastatic adenocarcinoma of the pancreas in combination with gemcitabine.

Sales of Abraxane

	2010	2011	2012	2013 (9 mo)	2013 (9 mo) (annualised)
Sales (US$)	$71.4	$385.9	$426.7	$447.1	$596.1
% change		440%	11%	na	140%

Sales of Abraxane have grown strongly since 2010, with CY2013 figures approaching US$600 million on an annualised basis.

It is still to be determined if DEP-Docetaxel will be developed as a competitor to Abraxane in indications such as metastatic breast cancer, or developed to treat other cancers.

Commentary

The move by Starpharma to develop improved versions of existing drugs, such as DEP-Docetaxel and DEP-Oxaliplatin has merit especially where its dendrimer technology can decrease toxicities of existing compounds and also improve clinical outcomes. The ability to access the faster 505(b)(2) approval pathway is also attractive.

Taxotere is now off patent, with generic versions being marketed by Sandoz, Hospira, Accord Healthcare and Actavis. Therefore interest in a superior patent protected version from large pharmaceutical companies could be expected to grow. Together with the benefits listed above for DEP-Docetaxel, it has the potential to make an attractive licensing proposition.

The main threat to the commercial prospects for DEP-Docetaxel will stem from the introduction of new therapeutic interventions for cancer.

Summary

Although recent advances in the technology-enabled cancer generics program are a positive for Starpharma, a **Sell** recommendation is placed on the stock because its current market capitalisation of $200 million does not align with the consistent underperformance of other programs in the business, including the condom coating program, the Vivagel for bacterial vaginosis program and various agrochemical programs. Starparma states that it has signed on most of the top ten agrochemical companies, the first being signed in 2009. However, the status of these relationships appears to be of a research and collaboration nature rather than having advanced to the product development stage, all the while remaining mostly invisible to shareholders because of confidentiality agreements.

Bioshares recommendation: **Sell**

Bioshares

Regeneus' HiQCell: More From The OSCARS Trial

Since listing in September at 25 cents, Regeneus' (RGS: $0.48) share price has increased by 92%, although the stock peaked at 66 cents in late November. The company is now capitalised at $88 million

The surge in the stock price, which followed a very lack lustre post-IPO period could be attributed to a lift in corporate profiling activities outside of the company's home state of New South Wales, the US Department of Agriculture's approval of its canine cancer autologous vaccine product, and from new laws passed in Japan designed to fast track regenerative medicine products to that market.

Bioshares placed a **Sell** recommendation on Regeneus soon after listing. Is that recommendation still warranted? In our IPO Profile of Regeneus in *Bioshares* 517, the lack of a statistically insignificant result in the Regeneus's OSCARS study of HiQCell, its osteoarthritis product was noted. Further noted was a patent challenge made by Norwood Immunology. A concern raised in *Bioshares* 521 focused on the scalability of the company's business, in particular the capital required to grow the business.

Since then the company has released an interim report on the OSCARS trial, obtained a US DA approval for its canine cancer vaccine and signed Lonza to manufacture its allogeneic (off the shelf) treatment for musculoskeletal conditions in dogs.

HiQCell and the OSCARS Trial

HiQCell is an autologous cell therapy product for the treatment of musculoskeletal conditions and which is available in Australia.

The therapy requires the harvesting of cells from adipose tissue (fat). This source material is rich in mesenchymal stem cells, immune cells, muscle cells, endothelial cells and pericytes which are collectively termed the stromal vascular fraction.

In the 40 patient OSCARS trial, subjects diagnosed with osteoarthritis in the knee received a single injection of HiQCell in a test knee. Cartilage degradation was measured at base line and at six months.

However, the endpoint for the Phase II trial was reduction in pain symptoms. The problem with the trial was that both the treatment group and control arm recorded very similar decreases in reported pain symptoms at each reporting point out to 12 months. A likely explanation for the similarity in results for both arms is that use of pain medication that has clouded the results.

The results from MRI scans of the treated knees in the OSCARS trial have now been made available and offer a better understanding of the therapy. MRI mapping revealed that loss of cartilage was slowed at the six month point for both groups, and that for both groups more patients stabilised than progressed.

Despite that, MRI mapping showed that there was a much higher number of subjects in the treatment group in the trial with the most severe grading of osteoarthritis, compared to the placebo group. The inference is that HiQCell delivered an efficacious result because the results were skewed by the greater numbers of patients with a grading of the most severe OA.

Measures of a non-invasive marker of cartilage damage, CTX-II, showed a 31% increase for the placebo group, between baseline and six months, whereas the levels of this marker decreased in the treatment group. This supports the view that HiQCell slows cartilage damage.

The effect of the treatment was even more pronounced on the most severe OA group (Grade 4). The nine placebo subjects in this group saw their CTX-II levels increase by 43% over 6 months, whereas the treatment group stayed roughly in line with the measurement made at baseline.

Levels of macrophage inhibitory factor (MIF) were also significantly reduced in the treatment group at the six month point.

Commentary

The additional analysis from the OSCARS trial is welcome since there appears to be evidence emerging at the molecular level of the ability of the therapy to slow cartilage degeneration.

What would now make sense for the company to do (even though the product is available commercially) is conduct a second larger trial, staged to run over a longer period (e.g. two years) and in which repeat injections are given to a cohort of patients. Although the company has established a patient registry for HiQCell, the question of repeat dosing is one which is largely going unanswered in the world cell therapy. More importantly, instead of using pain scores as an endpoint, Regeneus could now justify using a combination of bi-lateral radiographic and MRI scans, and biomarkers to develop a reliable measure of efficacy.

Summary

The most attractive investment feature of Regeneus is that it has a human therapy product on the market. Another product in development, its 'secretions' product, which uses factors secreted from adipose tissues, could have market potential well beyond acne.

The company could benefit from hiring staff with strong operational credentials in running high-value-product clinic based business (such as IVF clinic) and, with those staff in place, evaluate the merits of setting up its own chain of clinics in Australia, rather than act as a wholesaler to specialists working from their own clinics. This is an important business model question for Regeneus.

The challenge for the company is on the funding front. The company's estimated cash position post -listing was $9.3 million. These funds are likely to be expended quickly and a capital raising this year is by our estimate, a very likely event. Entry into the stock may be warranted following such an event.

Bioshares recommendation: **Sell**

Bioshares

Bioshares Model Portfolio (24 January 2014)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$0.880	$0.620	December 13
Impedimed	$0.235	$0.245	December 13
Analytica	$0.028	$0.025	December 13
Imugene	$0.020	$0.022	November 13
Oncosil Medical	$0.140	$0.155	September 13
Invion	$0.085	$0.060	August 13
IDT Australia	$0.390	$0.260	August 13
Viralytics	$0.320	$0.300	August 13
Tissue Therapies	$0.325	$0.255	March 2013
Benitec Biopharma	$0.825	$0.40	November 2012
Somnomed	$1.26	$0.94	January 2011
Cogstate	$0.380	$0.13	November 2007
Universal Biosensors	$0.53	$1.23	June 2007

Portfolio Changes – 24 January 2014

IN:
No changes

OUT:
No changes

VALE Alan Woods

It is with great sadness that we report that Alan Woods, a long-term supporter and some would say a founding father of angel capital investment in the Australian biotechnology industry, passed away on the 2nd of January. Alan was a successful entrepreneur and together with family members built David Bull Laboratories which was later sold to Faulding. Alan had an unusual mix of technical understanding, commercial savvy and vision which led him to become a founding investor in Biota Limited, one of Australia's earliest biotech start-ups. This continued a legacy of his grandfather's interest in influenza treatment which never wavered.

Alan not only invested in the sector but supported other entrepreneurs and, for example, was crucial in the establishment of Medica Holdings Limited, a listed Pooled Development Fund. Medica went on to establish several other biotechnology companies.

Bioshares extends its sympathy to all of the Woods family.

"Alan was a conservative investor and for him to back Australian biotechnology the way he did provided a major endorsement to entrepreneurs and Australian research. Alan always remained close as a shareholder, supporter and friend"…… Kevin Healey

"He was the first angel investor I ever encountered, and by far the most angelic. He understood the neuraminidase story at a time when big pharma were all rejecting it out of hand, invested his own money in Biota and convinced others to do the same, negotiated a win-win with Glaxo at its most arrogant, dealt effectively with both Machiavellian managers and unworldly academics, found consensus among the many and varied views of a thoroughly opinionated Board (I was one of them), and throughout it all remained calm, unflappable and charming to all concerned. He was a great man."……Peter Andrews AO

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