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In this edition...
With the AGM season in full swing, more than a handful of biotech companies have taken the opportunity to time their annual reporting meetings with announcements regarding new investments or new product development opportunities. Biota announced at its AGM the acquisition of two companies with early stage programs in the field of antibiotics. Starpharma put foward a plan to develop Vivagel as a treatment for bacterial vaginosis. Starpharma also conducted its AGM while in a trading halt, in effect while it completes a capital raising. Capital inflows have certainly opened up for well structured, advanced stage biotechs, with QRxPharma announcing a $23 million placement.

The Editors
Companies Covered: ACR, BTA, HXL, SPL,UBI

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - Current)	80.6%
Cumulative Gain	**251%**
Av Annual Gain (9 yrs)	**22.0%**

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Bioshares

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

Starpharma Seeks New Product Opportunity for Vivagel

Starpharma (SPL: $0.60) is one of the few platform technology companies in the biotech space listed on the ASX. Platform technology companies are those from which multiple products or applications can be derived from a core technology base, which in the case of Starpharma is dendrimer chemistry. Although dendrimers can be constructed using different chemical base units, they can be constructed in a very precise and uniform fashion, often but not always conforming to a star shape, but certainly using branch-like structures.

The dendrimer construct itself is not always the active molecule, with additional chemical groups added to the surface or bound within the larger dendrimer macromolecule as a payload. Starpharma's Priostar dendrimers (partnered with **EMD Merck**) are used to deliver siRNA and DNA into cells. Another product, Stratus CS (partnered with **Siemens Healthcare**) has been developed as cardiac diagnostic. The dendrimer molecules in this application have antibodies attached to their surface.

An attractive feature of dendrimer chemistry is that it offer chemists the ability to build large molecules in a very precise fashion.

Capital Flows Again

Capital is well and truly flowing into biotech sector once again. This week **QRxPharma** announced a fully underwritten $23 million placement. The funds will be used largely to complete the Phase III trials of the company's lead drug candidate, MoxDuoIR, an immediate release opioid combination, and to file this drug candidate for approval in the US.

The raising will include a private placement and a renounceable rights issue. It will be fully underwritten by RNS Morgans Corporate.

Starpharma has also announced a capital raising that appears to be targeted at the development of Vivagel as a treatment for bacterial vaginosis.

AGM Notes

Although platform technology stocks have not been a favourite with investors for many years, Starpharma's share price has appreciated by 140 % over the last twelve months. As highlighted at the company's AGM, Starpharma has recorded a year of solid progress (a "seminal year" in the words of the chairman Peter Bartels) and in particular, the market has become better informed of the potential revenue prospects for one of the company's partnered programs.

Starpharma has a partnership with **SSL International** for the coating of Vivagel , a dendrimer product which incorporates anti-viral compounds which inhibit HIV and HSV-2, on certain condom products to be marketed by SSL. Although Starpharma has stated that it expects to receive more than $100 million in receipts from the arrangements, which in-

Cont'd over

– from page 1

cludes double digit royalties of net sales, the potential exists for greater revenues where a higher proportion of Vivagel is used as in condom coatings. For example, if a 'high' proportion is used Starpharma could receive $30 million per annum, assuming SSL maintains a 40%-42% market share. Sales of Vivagel coated condoms are expected to commence in 2011. Starpharma estimates that its investment to date in application of Vivagel as a condom coating is $3 million.

Opportunity in Bacterial Vaginosis

As announced at its AGM this week, Starpharma is currently in a trading halt while completes a capital raising. Based on remarks made by CEO Jackie Fairley at the AGM, our inference is that the funds would primarily be devoted to a new application of Vivagel to treat the condition of bacterial vaginosis (BV). According to Starpharma, as many as 21 million women experience BV infection in the US alone. While antibiotics are currently used to treat the infection, they are not fully effective (less than 50%) and the driver for developing new medicines is to bring down the recurrence rate, and therefore reduce the reliance on antibiotics.

Vivagel was found to be effective in resolving BV when the company was conducting safety studies. So somewhat serendipitously, the company has found a promising new drug development opportunity for Vivagel.

The company believes that it could over a 24 month period, conduct one Phase II study and two Phase III studies, which could give rise to a licensing opportunity in the 25%-30% royalty range. The Phase II study would enrol in the order of 100 subjects for the purpose of dose determination, with testing for clinical cure after seven days and prevention of recurrence. The Phase III studies would have similar goals, with the exception of dose determination. Each Phase III study would enrol approximately 200 patients.

The product development proposal for Vivagel as a treatment for BV is attractive for several reasons. In the first instance, it builds on a significant body of clinical development already conducted, with safety studies completed for Vivagel. The two year timeline is a reasonably short period of time in which to see substantial pharmaceutical product value creation and related to this is the proposed investment outlay; Starpharma holds the view that the clinical development of Vivagel for BV will cost between $9-$10 million.

Axiron Inspiration?

The proposed program bears comparison to Acrux's Axiron product development (see next page), which this year successfully completed Phase III evaluation for treating testosterone deficiency in males, convincingly addressing the US FDA requirements. Axiron was developed on the back of a $22.5 million fund raising in July 2007. Acrux has sufficiently de-risked that program so that the chances of Axiron being licensed on very attractive terms, or being acquired is very high.

Summary

While more recent investors have certainly seen their investment in Starpharma perform well, it is beginning to look like long term holders of the stock will see a positive return on their investment in the near-to-mid term. Starpharma has flagged that other partnerships are being pursued, which when added to the current portfolio of partnerships, can only strengthen the company's revenue prospects.

Starpharma is capitalised at $124 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Acrux – The Zulu Principle at Work

Investment book *The Zulu Principle*, a text recommended by a *Bioshares* reader, is based on the concept of focus, to specialise in a narrow area and to become a relative expert in that field. It also stresses the importance of selecting an investment area where you have a competitive edge, finding a market that is under-exploited by professional investors. There is very little that is unknown about leading stocks, according to author Jim Slater and private investors are more likely to find a bargain in under-exploited or under-researched areas of the stock market, specifically small growth stocks. These investment ideologies underpin, we would argue, the investment ideology taken at **Bioshares**.

With biotech, as with most business ventures, a little bit of luck is often involved.

The opening paragraph of *The Zulu Principle* discusses the involvement of luck in investment with two quotes. Famous golfer Gary Player once said the harder you work, the luckier you get. And Elmer Letterman put it a different way: Luck is when preparation meets opportunity. The point of these quotes is they are both very applicable to Acrux in its current position.

Two years ago, Acrux decided to raise $22.5 million to fund the final clinical development of Axiron, a topically delivered male testosterone product. Over that two years, the testosterone product market has been blown open, with the market size accelerating and with multi-million and billion dollar deals having been done in recent weeks alone. An article in this week's *Business Week* (9 November), titled “Testosterone Is Sure Looking Virile”, highlights the massive interest in this market now with "youth-crazed boomers making it a billion-dollar industry".

The article states that in the 12 months to June 2009, sales have increased by 25% to just under US$840 million. At the end of September this year, **Abbott Laboratories** acquired **Solvay Pharmaceuticals** for US$6.6 billion, to acquire products including the leading testosterone product on the market, called Androgel. Androgel accounts for about 20% of Solvay’s sales.

According to Acrux, Androgel generated sales of US$554 million in the 12 months to March this year. In August this year, Endo Pharmaceuticals struck a $210 million deal with the Prostraken Group, including a US$10 million up front payment, for access to its testosterone gel product for the USA alone. The product has been submitted for approval with the FDA.

The article in *Business Week* also discusses the black box warnings that have been placed on existing testosterone gel products, specifically because of transmission of the gel to others including from the hand that is used to apply the gel. The effects from this transmission include temporary symptoms of puberty in children and increased aggression in children.

Axiron’s Points of Difference

What makes the Acrux product distinction increasingly valuable is that not only does in not need to be applied to a large surface area on the torso like competing gels – Axiron is applied in the armpit – it also uses a product applicator where the hand does not come in contact with the gel. While the FDA has concerns over existing products, Acrux's Axiron could arguably receive a favourable review from the FDA with the product's ability to substantially reduce unwanted transmission of the testosterone hormone.

A Land Grab

The *Business Week* article says that testosterone is the fastest growing prescribed therapy in the US$80 billion anti-aging industry. The booming market is "now spurring a land grab by companies that make it". There is also the use of testosterone with women to increase low libido, with the FDA admitting that 25,000 prescriptions each year are being written off label for this use. Acrux also has a testosterone program for this application in women's which is moving towards Phase III trials.

What is also exciting companies on the hunt for acquisitions is that the market for testosterone products has only reached 10% of those men with low testosterone. Furthermore, the markets of India and China remain largely untouched.

Acrux's South African born CEO, Richard Treagus, may be unaware of the Zulu Principle investment philosophy. However, the company is certainly in the right place at exactly the right time with arguably the best testosterone product on offer. It probably did not know the testosterone market would be such a hot area when it first started is testosterone program several years ago but its decision to focus its development efforts on completing clinical development of Axiron alone look set to pay handsome dividends.

As mentioned last week, Acrux has hired **Credit Suisse** as an investment advisor to help negotiate to a commercial partnering transaction, although we would argue an outright acquisition of the company is also a possibility.

Acrux is capitalised at $352 million.

Bioshares recommendation: **Speculative Buy Class A**

Biota Holdings Fills One Part of Its Pipeline

In August this year, Biota Holdings (BTA: $2.68) sent clear signals that it intended to fill gaps in its development pipeline. With the company's royalty stream from Relenza due to end around 2014, the company is determined to ensure there is a steady stream of projects and products moving through to market.

This week the company announced that it had filled one of those gaps, with programs at the lead-preclinical stage of development. Biota will expand from antiviral drug development to the development of antibacterial drugs to combat the 'super bugs' that are becoming increasingly problematic with their resistance to existing antibiotics. The other gap remains in programs moving from Phase I into Phase II.

Biota will acquire the drug development assets of US-based **MaxThera** and UK-based **Prolysis**. Both are privately held companies and both companies have early stage antibacterial drug programs.

Biota will invest at least $40 million into four programs from these two companies over the next three to five years. We estimate that both are at least 18-24 months away from entering clinical development. Prolysis is the more significant of the two acquisitions, with Biota paying $10.8 million in Biota shares. The 20 staff will be maintained in Oxford. The research is based on work conducted by Professor Jeff Errington, who is the Director of the **Institute for Cell and Molecular Biosciences** at **Newcastle University**. He has a strong reputation and is to be invited to join the Biota Board.

For the MaxThera assets, Biota will pay US$1.5 million (US$1.2 million in cash and US$300,000 in shares). The two founders of the company will join Biota and will stay based in Boston. There are expected to be some synergies between the three R&D groups (Melbourne/Oxford/Boston) with the Melbourne team able to conduct medicinal chemistry work for the other teams. It also importantly gives Biota a global presence in major international biotech hubs.

AGM Notes

Both acquisitions were announced at this week's AGM. The company is expected to see a more defined path forward under new chairman Jim Fox. Fox was founder and CEO of **Vision Systems** which was sold in 2007 for $797 million to **Danaher Corporation**. Fox has become a shareholder in Biota during the year. His expectation is that a licensing deal for the company's long acting flu drug program will be completed by the end of this financial year. CEO Peter Cook said there are very promising discussions underway. This laninamivir drug candidate is a prodrug with the active very similar but not exactly the same as zanamivir (Relenza), according to Cook.

The appeal of the company's acquisition programs is that major drug companies have these programs on their target list. If Biota can successfully bring these programs into the clinic, then there should be considerable interest from potential licencees once significant value has been added – within three to four years – which fits the Biota business model. Each program, while being in the same field of antibiotic drug development, has the potential to yield novel products that work via different mechanisms.

Biota's partner for Relenza, **GlaxoSmithKline** has now become a one-stop shop for influenza treatment products, having firmly embraced this market. By the end of 2009, GSK should have the capacity to produce 90 million courses of Relenza in the current delivery device, and 100 million courses in a different rotacap device. This alternative inhaler format has been given temporary approval for use during a pandemic by Swedish regulators.

The seasonal market for flu drugs has now increased to US$800 million a year. This is mostly due to a large increase in Japan, where the market has surged from just under US$100 million to around US$250 million a year. By March 2010 **Daiichi Sankyo** is expected to submit laninamivir for approval. Biota will receive a single digit royalty from Japanese sales of this drug, if approved. Outside of Japan, the companies share rights to the compound.

Biota and Daiichi Sankyo's next influenza program, Flunet, is a compound that has shown to have a 4000 times greater potency than Relenza. In terms of resistance issues to Relenza and Tamiflu, Cook said Relenza is less prone to emergence of resistance than Tamiflu, with Cook aware of one case of resistance to Relenza and and with resistance for Relenza more likely to be seen in the future.

In financial year 2009, the company used up $26 million of tax losses. The payment of franked dividends will become an option in 2010. The company is waiting for a ruling from the ATO to see whether its current dividend will be treated as a capital return, an unfranked dividend or a combination of the two. On the question of past litigation costs, Biota spent a total of $50 million.

Jim Fox said that FY2009 had been a transformational year for Biota with Relenza royalties now substantial. Peter Cook said that Relenza is now a blockbuster. Biota can now transform from being a one product success into a sustainable business. According to Fox, the company will return cash to shareholders that is surplus to what the company thinks is a balanced plan.

Biota is capitalised at $ 480 million.

Bioshares recommendation: **Hold**

Bioshares

Biota's newly acquired antibiotic programs

Prolysis

Program	Stage	Target
Gyrase & topoisomerase enzymes	Lead to PC	DNA supercoiling (unw inds bacteria DNA), gram positive bacteria
Cell division inhibitor (in staphylococci)	Hit to lead	Blocks assembly of septum w all

MaxThera

Program	Stage	Target
PPAT enzyme	Lead to PC	Blocks Co-enzyme A energy producing pathw ay
EPT enzyme	Hit to lead	Cell w all biosynthesis

PC - Preclinical

Wheat Begins to Open Up for Hexima

Hexima (HXL: $0.53) is a Melbourne-based agricultural biotechnology company that is developing disease and insect resistance technologies and a multi-gene expression vehicle.

A development that has taken place in 2009 that augers well for Hexima is the creation of a unified voice by wheat farmers in the USA, Canada and Australia, who contrary to previous positions, are now supporting the genetic engineering of wheat varieties to improve productivity and address disease. These groups have observed the substantial benefits, monetary and otherwise, that have flowed to corn growers who have planted GM corn varieties. Since the 1930s, wheat yields have doubled to 40 bushels an acre in the US, whereas corn yields have increased eight fold to 153 bushels an acre. GM corn varieties introduced since the 1990s have contributed to a 36% increase in corn yields in the US.

The US, Canadian and Australian groups intend to work together to synchronize the commercialisation of genetically engineered traits in wheat crops. Wheat is the largest crop grown in the world, with 223 million hectares under cultivation each year.

Where this is especially relevant to Hexima is in the area of fungal disease resistance technologies, for which it has developed anti-fungal proteins. Wheat is subject to fungal diseases, some of which are closely related to those that affect corn. Hexima has licensed its anti-fungal proteins to Du Pont for use in corn and soybean, but retains rights for wheat, barley and other crops.

With wheat farmers from three export-focused production territories now pushing for GM wheat, the recent announcement of an alliance between Hexima and the **Australian Centre for Plant Functional Genomics** is timely and strategic. The partnership will explore opportunities to develop traits that address fungal resistance and environmental stress, such as drought, salinity and mineral deficiencies.

It is worth noting that in July this year Monsanto acquired a **Westbred LLC**, a wheat germplasm company, and adding wheat to its portfolio, it is also signalling that it too has observed a sea change in attitudes by wheat growers.

Monsanto's Dispute with Du Pont

A patent infringement dispute has emerged between two global seed companies, **Monsanto** and **DuPont**, a company which has licensed technology from Hexima. In May 2009, Monsanto sued DuPont to prevent DuPont from using Monsanto's proprietary Roundup Ready herbicide tolerant technologies in soybeans and corn.

DuPont had been developing a product similar to Roundup Ready called Optimum GAT. While developed as a stand alone product DuPont now seeks to stack Optimum GAT with Roundup Ready. However, Monsanto has refused to grant Dupont license rights. Monsanto is suing Dupont for patent infringement and DuPont has counter-claimed, alleging anti-competitive behaviour. This dispute underlines the strategic importance of owning 'must have' traits.

Without predicting an outcome for such litigation, the dispute, in which one large company is seeking to exert dominance over another large rival, has the potential to increase the attractiveness of smaller technology development companies such as Hexima, which are developing proprietary crop biotechnologies that large seed companies can adopt in order to sustain revenues and profits and maintain their competitive positions.

In our view, a contest between Monsanto and DuPont is likely to place upwards pressure on emerging technology asset prices, such as those owned by Hexima.

Although the introduction of wheat with genetically engineered traits would be more than a decade away at least, the race to develop new traits and develop varieties with multiple traits is now on. It is more than likely that technologies that improve wheat yields will be acquired by the major seed companies at an early stage if evidence from early field trials is strong enough.
Hexima is capitalised at $42 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Universal Biosensors to Receive US$16 Million Milestone Payment

Universal Biosensors (UBI: $1.88) received a welcome surprise this week when its partner **Lifescan** advised that the glucose blood monitoring product being jointly developed by Universal Biosensors and Lifescan had received a clearance from a regulatory authority (presumed to be the FDA). Glucose blood monitors are an essential device used by diabetics to measure blood sugar levels. The product will use proprietary test strips that are manufactured at UBI's Rowville facility.

The clearance has triggered the payment of a US$16 million milestone payment.

The payment now sees UBI comfortably placed with cash resources of more than $30 million. This is perhaps the most significant immediate news for investors as the milestone payment constitutes substantial non-dilutive funding.

Going forward, the clearance is a removal of key risk for UBI, with a next step being the commencement of manufacturing test strips for stocking purposes. UBI stands to receive approximately 1 cent per strip in royalties. UBI's immediate production capacity in 750 million strips per annum, which can be doubled to 1.5 billion as soon as a second suite is brought on stream. Lifescan sells 4 billion strips per annum in a global market that consumes 16 billion per annum.

UBI stated that it expects to receive income of $25 million following the receipt of regulatory approval, over the next twelve months. This includes the ~$17 million milestone payment, in addition to other fees and quarterly service payments which cover the manufacture of strips.

In February, UBI announced that Lifescan had opted to not proceed towards registration with an initial blood glucose monitor, which was targeted for a launch in 2009 Q2. The development of the re-configured product from initiation to regulatory approval was 10 months, which is an impressive performance.

The UBI whole blood test strip technology offers improvements to the amount of sample required for testing, in the time taken to perform the test, and correction for interference emanating from, for example, the presence of high-dose vitamins or paracetamol in the blood stream.

Universal Biosensors continues to be a very attractive investment opportunity at current prices.

Universal Biosensors is capitalised at $295 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bioshares Model Portfolio (13 November 2009)

Company	Price (current)	Price added to portfolio	Date added
Biodiem	$0.20	$0.15	October 2009
QRxPharma	$1.20	$0.25	December 2008
Hexima	$0.53	$0.60	October 2008
Atcor Medical	$0.20	$0.10	October 2008
CathRx	$0.67	$0.70	October 2008
Impedimed	$0.73	$0.70	August 2008
Mesoblast	$1.24	$1.25	August 2008
Circadian Technologies	$0.70	$1.03	February 2008
Patrys	$0.15	$0.50	December 2007
Bionomics	$0.41	$0.42	December 2007
Cogstate	$0.30	$0.13	November 2007
Sirtex Medical	$6.41	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.28	$0.66	September 2007
Starpharma Holdings	$0.60	$0.37	August 2007
Pharmaxis	$2.45	$3.15	August 2007
Universal Biosensors	$1.88	$1.23	June 2007
Probiotec	$2.60	$1.12	February 2007
Chemgenex Pharma.	$0.93	$0.38	June 2006
Acrux	$2.20	$0.83	November 2004
Alchemia	$0.69	$0.67	May 2004

Portfolio Changes – 13 November 2009

IN:
No changes.

OUT:
No changes.

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.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Pharmaxis, Cytopia, Starpharma Holdings, Cogstate, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Peplin, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical, CathRx, BioMd

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