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In this edition...
Solid progress is being made by many companies in the biotech sector. Among these is Starpharma which has secured an important licensing deal with condom manufacturer SSL International. Starpharma stands to receive over $100 million in milestone payments and royalties. And Sunshine Heart finally received the greenlight from the FDA for the US trial of its C-Pulse device, albeit conditional on some minor change being made to the trial protocol. We also update readers on a new found focus at Proteome Systems and a note a key milestone ahead in the December quarter for Clinuvel Pharmceuticals.

Companies covered: CUV, PXL, SHC, 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)	70.0%
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 - current)	-10.0%
Cumulative Gain	**87%**
Av Annual Gain (7 yrs)	**17.8%**

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Bioshares

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Edition 280

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

Starpharma Secures Major Licensing Deal

Starpharma Holdings (30 cents) has secured its most important commercial agreement to date, signing an exclusive licensing deal with the maker of the Durex condom, **SSL International Plc**. The agreement covers the use of Starpharma's microbicide, Vivagel, in SSL's condoms worldwide. The product is expected to be on the market within 18 months and to deliver Starpharma *over* $100 million in milestone payments and royalties.

What is incredibly appealing about the Vivagel product is that there are no effective microbicides available on the market and very few in development. Nonoxinol-9 (N-9), which was previously used, has in fact been found to increase the probability of sexually transmitted diseases. Starpharma's Vivagel works not only as a spermicide, as did N-9, but also very effective at killing viruses such as HIV and HSV-2 (herpes virus).

Spermicides have previously been incorporated into around 30%-40% of condoms on the market and SSL commands around 30% of the global branded condom market. The estimate of future income for Starpharma is spread over the life of the company's patents – roughly the next 15 years – however, this figure assumes SSL will not increase its current market share. There is the potential for the total future income stream to be considerably higher if the product is well accepted by consumers. Condoms with an effective microbicide can also command a 50% pricing premium.

Ex-vivo trials will be conducted and it is expected that a small human safety study will be needed before the product gets to market. Both companies will be involved in final product development and regulatory submissions. Manufacturing of the active ingredient will be conducted by third parties on behalf of SSL.

Future milestones will be payable on regulatory submission of the product, regulatory approval, and the achievement of sales targets. According to Starpharma's CEO, Dr Jackie Fairley, SSL is extremely excited by this product and the concept of a condom with virocide properties has also received very positive feedback from consumers.

Starpharma is also commercialising Vivagel as a standalone product to prevent the transmission of sexually transmitted diseases, such as HIV and herpes, to be sold both in developing countries and in major western markets such as the US. These programs are being funded by the NIH grants of US$26 million. The company has a collaborative deal with another unnamed condom manufacturer for developing countries outside of the regions covered in the SSL deal.

Starpharma is capitalised $54 million with $7.5 million in cash at mid year. This cash balance should increase with the receipt this quarter of an upfront payment from SSL. The company generated $9.9 million in the last financial year from government grants and royalty and licensing revenue.

Bioshares recommendation: **Speculative Buy Class A**

Proteome Systems Applies Focus

Proteome Systems (PXL 10.5 cents; Cap'n $ 26 million) will focus on the two areas where its intellectual property assets and expertise look to be succeeding. The first is in its diagnostic hardware platform, where the first product will be WheatRite, due for commercial release in Canada this year. The second is in biomarker discovery for infectious diseases. Its leading program here is a rapid diagnostic test for active tuberculosis, with **Becton Dickinson** (BD) having an option over the test.

Over the last two months Proteome Systems has cleaning out its cupboard of technology assets, focusing on what works, has clear competitive advantage and on where the company has leading expertise. In August this year it indicated it would exit the therapeutics business which it entered through the small acquisition of **Eukarion** in 2005. A month earlier the company cancelled its prostate cancer diagnostic program due to limited market potential for such a product. And in May this year it out-licensed its GlycomIQ software and its chemistry sugar database to **Agilent Technologies**.

Over the nine years since the business was started, there has been a continued search for the right business model for the company. The clarity of direction for the company is a welcomed step. How the field of proteomics following the genomics boom was going to pan out was uncertain. Proteome Systems' initial punt on a massive expansion in the use of 2D electrophoresis systems, and to develop hardware to service this growth, failed badly. The company has since decided to use its proteomics (discovery of proteins and their functional use) expertise to find unique protein biomarkers that can be incorporated in the new point-of-care diagnostics.

Lead product – WheatRite

WheatRite will be used by farmers to determine the most ideal time to harvest their wheat crop. The product was initially developed in conjunction with **Bayer Cropscience Pty Ltd**, an Australian subsidiary of **Bayer Cropscience AG**. The test uses a unique point-of-care test platform developed by Proteome Systems, with the WheatRite chemistry from Bayer.

In July this year, that development agreement was superceded by a new agreement with the Bayer Cropscience parent company in Germany. Bayer Cropscience will begin selling the test into the Canadian market in the next two months. Bayer Cropscience has conducted market research on the product in the US and Europe which has indicated there should be considerable demand for the test.

In Canada there are 5.5 million truckloads of wheat produced each year, where wheat is controlled through a single grain commission. The product may be used by farmers, who are asking for this type of test, and also by the Canadian Grain Commission for testing the quality of each truckload of wheat and therefore pricing. The technology will allow separation of rain damaged wheat loads in quality control systems as well as guiding farmers for the best time to harvest their crop. Wheat has become a highly valued commodity and the benefit in harvesting the product at the most ideal time has increased.

The WheatRite Test

If it starts to rain just before harvest time, the wheat grains may begin to germinate which produces an enzyme called alpha amylase. This enzyme starts to break down the starch which reduces the quality of the flour.

The current test for this level of sprout damage is called the Falling Number Test, which measures the amount of time taken for a plunger to fall to the bottom of a precision bore glass filled with a heated paste of the wheat meal and water. In high quality wheat it takes over 300 seconds for the plunger to fall and less than 300 seconds for lower quality wheat. It does not measure directly the level of amylase. The WheatRite test has the potential to complement this test and potentially even replace it.

The Proteome System test is a simple point-of-care disposal test that uses antibodies to directly measure the level of alpha amylase. It can deliver a simple visual result in the disposable test, or a semi-quantitative readout using an electronic reader being developed by Proteome Systems, called the ReadRite scanner.

There is currently no simple test kit available for this test and the current Falling Number Test is causing frustration with users. The test is open to variability, is time consuming (the Canadian Wheat Commission can only conduct 24 tests a day), and not all receival sites have the capability to conduct the test. The ability of the Proteome Systems hardware in the vertical flow through DiagnostIQ platform, which was designed specifically for this test, to accept coarse grain samples in a simple disposable format is what makes this test unique. The test takes less than 10 minutes to complete and is very accurate, although needs to be calibrated for the type of wheat.

It is expected the test will be sold to the receival sites first, then marketed to the farmers. Canada produces 5% of the world's wheat supply, which is grown on 55,000 wheat farms. The test may also have particular appeal is some Eastern European and South American countries where the Falling Number Test for wheat quality has not been adopted.

Proteome Systems will receive an annual license fee from Bayer Cropscience and ongoing royalties (single digit). Initially, Proteome Systems will manufacture the WheatRite test with larger quantities to be manufactured by a third party. It is expected that in the second year on the market a meaningful royalty stream should be achieved. Bayer Crop Science has started marketing the test into Europe as well and expects to begin marketing into the US.

The agreement with Bayer Cropscience also covers the development of a second agricultural diagnostic product which is expected to reach the market in 2010. Once again it will use the Bayer Cropscience reagents with the Proteome System point-of-care diagnostic platform.

Cont'd on page 4

IND Receipt a Key Milestone for Clinuvel Pharmaceuticals

Clinuvel Pharmaceuticals (CUV: 26 cents) is developing a peptide drug CUV-1647 that is designed to treat skin disorders that are occur as a result of excessive sun exposure. Generally speaking, CUV-1647 does not treat disease as such but provides UV and photo-protective benefits.

CUV-1647, which has now been designated afamelanotide by the World Health Organisation, is currently being evaluated in several conditions, including erythropoietic protoporphyria (EPP) or severe light sensitivity, polymorphous light eruption (PLE) and in transplant patients who are at risk of contracting skin cancer (such as actinic keratoses). Another condition being investigated is solar urticaria, which is the equivalent of an 'allergic' reaction to ultraviolet light (but where no other treatments are available).

Afamelanotide is an analogue of the hormone alpha-MSH (melonin stimulating hormone). The compound stimulates the release of melanin, which induces pigmentation of the skin. The duration of drug action is short lived but the pigmentation effects lasts for up to two months.

Afamelanotide is currently being evaluated in two Phase III trials and two Phase II trials.

Recent developments

Absolute Capital Management exit

Since 2006 European investor Absolute Capital Management Holdings has been a significant investor in Clinuvel. This investor recently disposed its 20% stake in Clinuvel, with the stock being placed to a dozen primarily Australian institutional investors, including eight new investors. The release of this stock overhang and dispersal into the hands of a greater number of institutional shareholders is a positive for the company.

Orphan drug designations

Throughout 2008, Clinivel has received orphan drug designations from the European Medicines Agency, (the EMEA), the Swiss agency, Swissmedic, and the US FDA. In general orphan drug designations are granted when the number of patients suffering from a disease or condition that is too small to warrant the investment in drug development within normal commercial parameters. Various regulatory concessions, market benefits and exclusivities become available to the sponsoring firm.

The three agencies granted ODDs to Clinuvel's afamelanotide for erythropoietic protoporphyria and congenital erythropoietic protoporphyria.

Major milestone: IND filing and receipt

A major milestone for Clinuvel in the short term will be the filing of an Investigational New Application with FDA for afamelanotide. This event is expected to take place in the December quarter of this year. If no feedback is received from the FDA after thirty days from the filing, it is regarded that the filing has been accepted.

An IND filing describes the clinical trial protocols a company will follow in generating data to support a regulatory submission to the FDA as well as the results from pre-clinical evaluation programs. And just as importantly the filing will describe manufacturing controls regarding the drug candidate. An IND filing will articulate features of a drug such as its chemical stability and purity.

In 2004 Clinuvel was working towards an IND filing but decided that its regulatory strategy at the time was not acceptable so it aborted the task. The company had set a goal of achieving an IND filing by end-2007, with an end-2008 date now more likely.

A implication of developing an IND submission is that information pertaining to *large scale* quantities of drug compound is required. What has held Clinuvel back is that the company has been working on a polylactide coating technology for its dissolvable drug implant to enable the release of the drug over five days. (Alternative implant technologies would appear to be not be able to meet the shorter release profile demanded by Clinuvel.) Clinuvel is currently developing the scale-up manufacturing requirements of this improved formulation, with a view to moving from manufacturing 100 dose batches to 15,000 dose batches. A key point about the IND process is that specifications for a final product are set at the filing stage so vital information relating to manufacturing costs needs to be ascertained prior to the IND filing.

Clinuvel expects that it may need to conduct some additional pharmacokinetic/pharmacodynamic studies of the new technology in the lead up to the IND filing.

Web-site and photo-protection awareness strategy

One very interesting component of Clinuvel's business development program is that it has developed a web based information program, Xptise, about photoprotection for people who are in need of information on skin, ultraviolet light and melanin production and its connection to photo-protection. Such web-based patient or physician focused information pages are not new in the world of medicine but is it less common to see companies with a single main product still in development to establish such resources.

Clinuvel was compelled by a necessity to develop web based resources so that it could increase its access to potential trial subjects by creating and contributing to awareness of different sun-exposure induced skin conditions.

Clinuvel has, at an early phase in the commercialisation of CUV-1647, begun to build a photo-protection brand, which at this stage is built primarily at the corporate level with the greatest (potential) contribution made by the drug candidate yet to come. The company's allocation of resources to building web-based resources is a reflection of a management that is progressive in its understanding of pharmaceutical brand management.

Cont'd over

Proteome cont'd

Second area - Diagnostics for respiratory infectious diseases

The second area of focus for Proteome Systems is in developing biomarkers used to detect respiratory-based infectious diseases. The lead program here is the test for active TB, over which BD licensed an option in July last year.

In the first phase of the agreement, Proteome Systems is conducting a feasibility study including using its own TB biomarkers and diagnostic point-of-care platform. This is expected to be completed by the end of 2008 and includes upfront and milestone fees. BD then has an option to proceed with full development of the test and commercialization of the product. This program is currently being co-funded by the two companies.

Proteome Systems has completed three out of the four milestones in the feasibility study. The third milestone which has been achieved, related to sample preparation, specifically a standardized preparation of the sputa sample. It has built expertise in handling these samples, which will be applied to developing other tests for respiratory-based infectious diseases using its diagnostic platform. The diagnostic platform, called DiagnostIQ, a vertical flow through test, is designed to work well with crude samples such as blood, sputa, saliva or crushed plants.

The biomarkers have been selected for the first test. If BD elects to exercise its option (in early 2009), it would fund the commercialisation of that program from that point. Proteome Systems would receive a single digit royalty from sales. Proteome Systems believes it is well on the well way to achieving the final milestone, which involves meeting set accuracy levels with the test.

Financials

Proteome Systems has garnered solid support for its business over the last year as its development programs have gained traction. Since last year, the company has raised $14.75 million, including the entry of new US investors including Oppenheimer Funds. It generated $2.3 million in revenue from operations in the last financial year, including $1.5 million from collaborations. It has an estimated $9 million in cash, after making a loss of $8.7 million last year. Its burn rate is expected to decrease to $6 million a year from February next year, after its US operations are closed down.

Summary

Proteome Systems will join the list of an increasing number of biotech companies with products on the market later this year. The take up of the WheatRite product will be followed with interest, with meaningful sales and royalties expected in FY2010. The major upcoming milestone for the company will be the completion of the feasibility study with BD and importantly, if successful, a decision by BD to exercise its option to commercialise this test, which will bring significant validation to the biomarker discovery expertise of Proteome Systems.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Clinuvel cont'd

Risks

Clinuvel is currently managing the development of one compound in several different indications. In this regard, there is no pipeline diversity to mitigate single product risk within the firm. The flipside of this risk attribute is that Clinuvel is able to apply a very strong focus on development objectives for CUV-1647. An appropriate strategy by investors is to diversify an investment in Clinuvel by investing in a portfolio of drug development companies.

Inability to achieve an IND acceptance in a reasonable time period is another major risk for the company going forward.

Summary

The ultimate receipt of an IND application from the FDA will represent a major turning point for Clinuvel, as the company's strategy to unlock the potential pharmaceutical benefits of CUV-1647 will have been agreed to by the regulator of the world's largest pharmaceutical market. In our view, the receipt of an IND is a major de-risking event for a biotech and should increase the intrinsic value of the stock.

The management and board of Clinuvel continues to impress, with the determination of the management to drive the development program as hard as possible an investment plus.

Clinuvel Pharmaceuticals is capitalised at $79 million and held $51 million cash as of June 30, 2008 and is very attractive at current prices.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Sunshine Heart – Receives Conditional Approval from FDA

Sunshine Heart (SHC: 11 cents) shares rose sharply (up 57%) today following the company's receipt of conditional approval by the US FDA for its C-Pulse heart assist device. The conditional approval allows the company to commence clinical trial related activities such as finalising business agreements with hospitals where a number of clinical trials are planned in the US.

The FDA has specified a number of additional minor changes to the company's clinical trial protocol patient record keeping and device labelling, which when finalised, will see the grant of clinical trial approval. Sunshine Heart has stated that it agrees to the FDA proposed changes.

Sunshine Heart expects its clinical trial to commence in the fourth quarter of this year, with up to 20 patients suffering from moderate heart failure to be implanted with the C-Pulse device, a balloon cuff that wraps around the aorta and aids blood flow as air is pumped in and out of the balloon cuff. The trials will be conducted as six sites in the US.

The Sunshine Heart clinical trial submission took longer than expected at the FDA because it was a device that fell between two well understand categories of devices that treat heart conditions, being respectively pacemakers and heart pumps (LVADs, such as Ventracor's VentrAssist). One of a number of areas where the FDA sought additional data was regarding the collection of neurological information, which is required for LVADs. However, because Sunshine Heart's C-Pulse device does not come in contact with blood, it was originally not anticipated that neurological performance information would need be collected. However, the FDA has stipulated that it should be collected.

Following the completion of the 20 patient US trial, Sunshine Heart will apply for marketing approval in Europe.

Sunshine Heart expects to receive reimbursement for the devices used in the trial, potentially using the same heart assist system codes that apply to LVADs. However, detailed reimbursement issues are still being worked out.

Sunshine Heart is capitalised at $32 million and maintained cash of $9.7 million at June 30, 3008.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Bioshares Model Portfolio (12 September 2008)

Company	Price (current)	Price added to portfolio	Date added
Impedimed	$0.80	$0.70	Aug-08
Antisense Therapeutics	$0.06	$0.07	Aug-08
Mesoblast	$1.28	$1.25	Aug-08
Avexa	$0.24	$0.32	Jun-08
Cellestis	$2.15	$2.27	April 2008
IDT	$2.10	$1.90	March 2008
Circadian Technologies	$0.88	$1.03	February 2008
Patrys	$0.26	$0.50	December 2007
NeuroDiscovery	$0.09	$0.16	December 2007
Bionomics	$0.33	$0.42	December 2007
Cogstate	$0.14	$0.13	November 2007
Sirtex Medical	$2.39	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.26	$0.66	September 2007
Starpharma Holdings	$0.30	$0.37	August 2007
Pharmaxis	$2.32	$3.15	August 2007
Universal Biosensors	$0.79	$1.23	June 2007
Biota Holdings	$0.76	$1.55	March 2007
Probiotec	$1.48	$1.12	February 2007
Peplin Inc	$0.40	$0.83	January 2007
Arana Therapeutics	$1.03	$1.31	October 2006
Chemgenex Pharma.	$0.81	$0.38	June 2006
Cytopia	$0.20	$0.46	June 2005
Optiscan Imaging	$0.23	$0.35	March 2005
Acrux	$0.95	$0.83	November 2004
Alchemia	$0.27	$0.67	May 2004

Portfolio Changes – 12 Sept 2008

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: Phylogica, Pharmaxis, NeuroDiscovery, Biotech Capital, Cytopia,Arana Therapeutics, Starpharma Holdings, Cogstate, Xceed Biotechnology, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Proteome Systems

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