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**In this edition...**
Starpharma's Phase III trials of Vivagel as a treatment for bacterial vaginosis did not meet their primary endpoints, halting plans for that indication in the US market. The result was contrary to positive Phase II results and it will take at least four months to find out if trial subjects upset the apple cart by breaching protocols. What the company does learn may be put to good use in Phase III prevention of recurrence trials. Non-invasive cardiac monitor company Uscom intends to publish astonishing results from a study of its device when used to manage patients with septic shock. The technology is life saving and the data compelling. Bluechiip is shifting gears, with the focus on driving sales. Board and management changes at Genetic Technologies have introduced uncertainty with that stock.
**Companies Covered: BCT, GTG, SPL, UCM**

| | 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 - current) | -13.3% |
| **Cumulative Gain** | **199%** |
| **Av. annual gain (11 yrs)** | **17.8%** |

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# Bioshares

**30 November 2012**
**Edition 483**

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

## *Starpharma's Phase III BV Treatment Trial Fails to Meet Primary Endpoint*

Starpharma Holdings (SPL: $1.16) released the results of its Phase III trials of Vivagel for the treatment of bacterial vaginosis (BV). The primary endpoint of Clinical Cure at Test of Cure (Days 21-30) was not met.

The company had completed one Phase III trial (SPL7013-015) across 18 sites in the US, in which 247 subjects were randomised to receive Vivagel (126 subjects) or a placebo gel (121 subjects).

A second identical Phase III (SPL7013-016) trial was run across 11 sites in the US and 9 sites in Europe in which 249 subjects were randomised to receive Vivagel (126 subjects) or a placebo gel (123 subjects).

The results ran counter to that obtained in a Phase II trial of Vivagel, which generated a statistically significant Clinical Cure at Test of Cure result for Vivagel.

In both Phase III studies, an unexpected *improvement* in Clinical Cure in the *placebo group* was observed, from the End of Treatment time point (2-5 days post treatment) to the Test of Cure time point (2-3 weeks post treatment).

Starpharma CEO Jackie Fairley described the results as 'excruciatingly frustrating', pointing to the possibility that factors entered the clinical trial process to confound the results, so as to not give a true picture of the treatment capabilities of Vivagel, consistent with the positive Phase II results.

The company will now embark on a review process to determine, in detail, what might have caused the confounding results, with breaches of trial protocol a leading area of interest.

One hypothesis advanced by Fairley was that subjects who received Vivagel may have recommenced sexual activities, in response to treatment success which may have then reactivated the symptoms of bacterial vaginosis.

A second hypothesis was that some subjects receiving the placebo may have resorted to self-administration of antibiotics as a response to failure to clear symptoms. Starpharma identified two trial sites, from which if the data was excluded, a statistically significant Test of Cure (i.e. primary endpoint) result was achieved for the whole study.

The company expects a review of the Phase III trial to take four months to complete. However, that is an early estimate made by the company, and it could quite likely take longer.

*Cont'd over*

**Bioshares Model Portfolio (30 November 2012)**

| Company | Price (current) | Price added to portfolio | Date added |
|---|---|---|---|
| Psivida | $1.32 | $1.550 | November 2012 |
| Benitec | $0.013 | $0.016 | November 2012 |
| Nanosonics | $0.495 | $0.495 | June 2012 |
| Osprey Medical | $0.38 | $0.40 | April 2012 |
| QRxPharma | $0.78 | $1.66 | October 2011 |
| Somnomed | $0.85 | $0.94 | January 2011 |
| Cogstate | $0.345 | $0.13 | November 2007 |
| Sirtex Medical | $11.61 | $3.90 | October 2007 |
| Clinuvel Pharmaceuticals | $1.88 | $6.60 | September 2007 |
| Pharmaxis | $1.25 | $3.15 | August 2007 |
| Universal Biosensors | $0.90 | $1.23 | June 2007 |
| Alchemia | $0.510 | $0.67 | May 2004 |

### *Portfolio Changes – 30 November 2012*

**IN:**
No changes

**OUT:**
No changes

### Implications:

Starpharma is now unable to proceed with a New Drug Application for Vivagel for the treatment of bacterial vaginosis. Fresh discussions with the FDA must take place before an approval pathway can be decided on, if at all.

The company could seek different labelling claims that encompass the use of Vivagel to treat the symptoms of bacterial vaginosis. The Phase III trials reported statistically significant and highly convincing data on Vivagel's ability to treat symptoms (as identified by Amsel Criteria). Patient reported resolution of symptoms in the treatment group were also highly statistically significant, as were sustained relief of symptoms.

In trial '015' discussed above, 50% of subjects achieved a Clinical Cure at the end of treatment period (not the primary measurement at Test of Cure), compared 17% of subjects receiving the placebo gel. In trial '016' discussed above, 57% of subjects achieved a Clinical Cure at the end of treatment period (not Test of Cure), compared to 21 % of subjects receiving the placebo gel. In both cases again, Vivagel delivered a highly statistically significant result.

Starpharma will also explore commercialisation opportunities in markets outside of the US, where less stringent pharmaceutical product development rules apply.

In our view, the Phase III setback, coupled to the need to seek clarification, will also delay the company's plans to out-license Vivagel, as well as reduce any implied value of the asset in the BV treatment market in the US.

### Vivagel Phase II Trial Underway for Prevention of the Recurrence of BV

Starpharma is currently conducting a Phase II trial of Vivagel for the prevention of the recurrence of BV. This trial has now completed recruitment of more than 200 subjects. Results of the trial are due in 2013 Q1. The Phase II trial involves an efficacy measurement out to 112 days (compared to the Phase III treatment trials which went out 21-30 days). The trial is also comparing a 1% dose and 3% dose of Vivagel.

The BV prevention market is larger than the treatment market and there are no drugs approved for the prevention of BV.

With the Phase III results now available, which although are unsatisfactory from a primary endpoint perspective, Starpharma may have moved to a far better position in managing its future Phase III prevention of recurrence trials from what it has learnt from these treatment trials. It may also be in a much stronger position to map out and plan for the commercial opportunities in the prevention of recurrence market.

### Reporting & Communication Standards

Starpharma's approach to reporting and communication of its Phase III clinical trial results is to be commended because of the level of detail provided and willingness to answer questions posed at the company's recent AGM.

### Summary

Starpharma is a platform technology company with a large number of projects under management, both in house and with collaboration partners. However, the confounding results of the Phase III studies have instigated a phase of uncertainty requiring discovery and elucidation.

A **Hold** is placed on the stock until clarity emerges regarding protocol breaches (or other issues) in the Phase III BV trial and until discussions with the FDA reveal the FDA's response to any new information that may have emerged from the review.

Starpharma is capitalised at $329 million. The company retained cash of $37.6 million at September 30, 2012 and it also expects to receive a $6 million tax refund.

*Bioshares* recommendation: **Hold**

Bioshares

# *A Major Market Opportunity for Uscom*

A major market opportunity and a major need has emerged for the use of Uscom's (UCM: $0.17) non-invasive cardiac output monitor.

Uscom's challenge is that it needs to change global medical practises, a process that takes a very long time and must be supported by publications documenting clinical use and benefits from use of its technology. To date there are over 250 publications that report on the use of the Uscom cardiac monitor. Yet one publication in particular may crystallise the real value and need to use the Uscom technology, in the treatment of sepsis.

### Sepsis and Septic Shock

When a person acquires sepsis, a bacterial infection in the blood, that infection can cause the production of endotoxins in the blood. These endotoxins can have the effect of dilating the arteries and smaller blood vessels in the body, resulting in a dramatic drop in blood pressure. This results in a dangerous drop in perfusion, or the delivery of oxygen to organs in the body.

Sepsis is a very dangerous condition with a 25%-30% fatality rate. The risk to life increases if this condition progresses to septic shock, when a highly dangerous low blood pressure starts to shut down body function. About half of patients who progress to septic shock die.

The danger point in sepsis is measured by blood pressure. However there are three variables that make up the blood pressure reading. Blood pressure is a factor of heart rate, the stroke volume, and the systemic vascular resistance. The latter two determine the correct treatment of sepsis

After ensuring airways are open and additional oxygen is supplied if required, the first line of drug treatment of sepsis is the delivery of intravenous fluids to increase blood volume (to counter the low blood pressure). About five litres is added over the first six hours.

The second line of treatment of sepsis is the use of vasopressors, which stimulate the contraction of blood vessels. The third line of therapy is the use of inotropes to stimulate contraction of the heart.

The problem with this approach to treatment is that if the patient is given IV fluids to increase the vascular resistance when the reason for the low blood pressure is cardiac function (low stroke volume), then they may be receiving the wrong treatment while they progress to the highly dangerous condition of septic shock.

### Bathurst Hospital Study

Assoc. Professor Brendan Smith's team at the Bathurst Hospital have used a Uscom monitor for the last six years with some astounding results. Results of his study are expected to be published in coming months with some of the key outcomes as follows.

The study looked at the mortality rate of people admitted to hospital with sepsis. The condition has a very high mortality rate. Independently sourced data shows that in the US each year, over 750,000 people contract sepsis with approximately 200,000 fatalities (26%). Using the Uscom device in Bathurst, mortality rates from sepsis have been reduced to an astonishingly low 4.4%.

In other measures in these patients, renal failure as a result of sepsis has been reduced to 2.6% at Bathurst Hospital, and emergency transport of sepsis patients (to other larger hospitals) has been reduced by 87%. According to Uscom's CEO, Rob Phillips, Professor Smith optimses patients with sepsis within one hour, when seven to eight hours is the normal time taken to optimise patients.

The issues with patients is that if they are not treated quickly enough, and not treated with the correct therapy, they can reach a point of no return. Each hour a patient with sepsis progresses with the infection, their of dying risk of increases considerably.

### The Uscom Solution

The Uscom cardiac output monitor facilitates correct treatment of sepsis before disease escalation. Standard treatment protocols suggest that pharmaceutical treatment of sepsis to use firstly IV fluids, if there is no evidence of heart failure, either clinical or radiographic. What the Uscom device brings to this solution is a portable, non-invasive approach to measuring cardiac output quickly.

### Other Uses

The Uscom device sells for around $30,000. It is made in Sydney and the company can make 80 units per month. Other applications of the technology are in patients with hypertension, congestive heart failure, pregnancy hypertension, and for use in anesthesia.

The company generated sales of $800,000 in FY2012 and is burning around $300,000 a quarter. The company holds $1.2 million in cash with a further $500,000 expected from an R&D tax rebate.

Currently there are between 500-600 systems installed worldwide, all bought without reimbursement. Uscom expects clinical data will now drive sales. The company is also looking to partner with major hospital instrumentation companies to have its product added to existing critical care instruments.

### Summary

The challenge for Uscom is firstly that it sells a capital equipment item to hospitals where the sales process takes time.

Secondly, the company needs to convince medical practitioners around the world to integrate its device into the critical care/ emergency care setting. The Bathurst Hospital study should help raise considerable awareness.

Uscom is capitalised at $11 million.

*Bioshares* recommendation: **Speculative Buy Class B**

**Bioshares**

# *Bluechiip's Next Phase: Sales, Sales, Sales!*

Bluechiip (BCT: $0.21) recently completed a $1.5 million placement and announced a Share Purchase Plan for shareholders. The SPP is underwritten by Baillieu Holst to a maximum of $500,000. The company had raised $5.7 million to date,since and including funds raised at listing in June 2011. It should be noted that $1.2 million of those funds was spent on acquiring specialised laser equipment used to program Bluechiip's unique tracking chips.* *[See note on next page]*

Together with the recent receipt of an R&D Tax Refund of $0.9 million, the company is now in a stronger position to meet its primary challenge of building commercial sales of its tracking technology.

These funds give Bluechiip cash sufficient to cover at least two years of net operational cash flows based on recent spending patterns.* However, two variables that could effect this position is growth in sales, which could be offset by increased spending on marketing and other sales related investments.

Bluechiip has developed a wireless technology that can be used to track biological samples stored at very low temperatures, for example in liquid nitrogen (-196°C). The commercially competitive and distinguishing feature of the technology is that it enables temperature tracking of samples to occur, in addition to sample identification.

### Commercial Drivers

The drivers to the commercial success of Bluechiip's technology in the biological samples storage market are powerful. They include the demand for superior sample identification which matters, for example, in the case of the storage of human embryos or sperm intended for fertility programs or with cord blood stored for personalised therapeutics. Storage systems that use barcoding may not work when bar codes are obscured by frost or labels detach.

A more important consideration is that of sample integrity. Bluechiip's chip based system uses a wand to identify and locate a sample which reduces the number of physical steps involved in the process.

The Bluechiip system can minimise the subtle degrading effects of thawing that can take place with existing approaches. Sample integrity is supported by Bluechiip's ability to track temperature, which is a distinct advantage in verifying 'chain of custody' temperature status (and changes). Other radio frequency based approaches do not offer temperature tracking.

Biological samples requiring storage range from plasma, serum, blood, cells and tissue obtained from humans and animals to micro-organisms, including bacteria, viruses and protozoa. Pharmaceutical companies, hospitals, medical research institutes and public health bodies are among those organisations which are dependent on high quality storage systems.

### Sales Strategy – Early Adopters Program

Bluechiip's marketing strategy to date has been to employ an Early Adopters Program (EAP). The company signed on the ATCC (the American Tissue Culture Collection) and Corning Inc's Life Sciences Division as a collaborative evaluation partners in November 2011.

In June 2012, Bluechiip received its first sales order from the ATCC (American Type Culture Collection). This first sales order from the ATCC is noteworthy and significant because of ATCC's global and leading status in the world of biobanking. The ATCC was founded in 1925 and is a not-for-profit biological resources business. The ATCC collection includes 3,400 human, animal and plant cell lines as well as 8 million cloned genes from many species. Its collection includes 18,000 strains of bacteria, 2,000 types of animal virus and 1,000 plant virus.

### Sales Director Appointment

Bluechiip appointed Brett Roberts as the company's Commercial Director in September. Roberts brings extensive sales experience gained at Pfizer Australia, Cell Care Australia and Hi-Fert to Bluechiip. His skills complement those of the company's management team.

### Sponsorship of the ISBER

Bluechiip has become a Platinum Corporate Sponsor of the International Society of Biological and Environmental Repositories (ISBER). The ISBER is a division of the American Society of Investigate Pathology and it is the global industry body which groups together participants in the biobanking business. The ISBER will hold its annual conference in Sydney in May 2013. A Platinum Sponsorship costs US$15,914 per annum and entitles the sponsor to premium logo positioning on the ISBER website and conference presentation and exhibition benefits.

This sponsorship commitment has the potential to significantly raise the visibility of the Bluechiip's product offering in front of a primary stakeholder group.

### Risks and Challenges

Bluechiip is now moving into a marketing and sales phase of business, after investing in capital equipment to manufacture chips*, sign on a manufacturer, complete final testing of chips and appoint a manufacturer for its reader.

A risk ahead for the company is how well it can convert sales opportunities into sales and then to build and entrench those customer relationships. The Bluechiip system is commercially unvalidated (outside of the EAP) and it will take time to persuade new customers to take on a system for use with high-value stored items despite the benefits inherent in the Bluechiip system.

What could greatly aid the uptake of Bluechiip's technology is that its use is incorporated in policies and guidelines that cover best practice, especially where data is available to support such claims.

The use of distributors always carries the risk that a distributor will fail to sell product or sell product in a vigorous and timely manner.

*Cont'd over*

## *Genetic Technologies AGM – Members Voted Off Board; CEO Resigns*

At the Genetic Technologies AGM (GTG: $0.072), which was held on Tuesday, the Chairman Mel Bridges and director Huw Jones were not re-elected.

Following the voting, another director, Greg Brown (formerly the CEO of Impedimed and a current director of that company) resigned.

Genetic Technologies CEO Paul Macleman and a senior executive, David Sparling also resigned, effective immediately.

The actions by shareholders to not support two directors and to trigger another board member departure meant that the CEO would in all likelihood not have been supported in implementing the company's current business strategy.

Genetic Technologies' principal business focus has been to commercialise a breast cancer risk assessment tool, Brevagen, firstly in the USA. What will happen to this asset is now, in our view, a matter of uncertainty, given that the company has yet to appoint a permanent CEO. (COO Alison Mew was appointed Acting CEO.)

The company's patent assertion program is a mature source of revenue and could well become the company's main focus going foward.

While uncertainty prevails at Genetic Technologies, investors are recommended to evaluate investment opportunities elsewhere where the business strategy is clear and the goals and objectives are well communicated.

Genetic Technologies is capitalised at $34 million.

*Bioshares* recommendation: **Sell**

**Bioshares**

*– Bluechiip cont'd*

**Summary**

Bluechiip deserves attention by investors because of its impending transition from an R&D stage company to a sales and marketing grade company, thus opening up the stock to a larger set of investors.

Milestones to monitor in 2013 include the signing of a distributor for North, Central and South America and for several other organizations to join the Early Adopters Program.

Bluechiip is capitalised at $21 million.

*Bioshares* recommendation: **Speculative Buy Class B**

**Bioshares**

**Company advises post-publication that the laser has yet to be acquired and that alternative methods and approaches have been used for initial high volume runs; company also advises that it has raised ~$12.5 million since 2005 and that its prospective cash runway is in the order of 1 year :- Ed*

## *The Bioshares Book Review – The Psychopath Test*

After this year's Bioshares Biotech Summit, Bell Potter analyst Stuart Roberts asked delegates to recommend books that investors should consider reading. Pete Smith from Alchemia recommended 'The Psychopath Test', by Jon Ronson, who also wrote 'The Men Who Stare At Goats'. It's well worth a read and below is a brief summary.

In this book Ronson examines the impact psychopaths have on society and whether psychopaths have a significant and disproportionate effect on the problems caused in the world.

Psychopaths are not just restricted to violent, physical psychopaths. In the book, Ronson asks the famous psychopath-spotting expert, Bob Hare, "But surely stock-market psychopaths can't be as bad as serial killer psychopaths?"

"Serial killers ruin families. Corporate and political and religious psychopaths ruin economies. They ruin societies," answered Hare. Hare believes that psychopaths are to blame for our "brutal, misshapen society".

In 1975 Hare and a large group of psychiatrists at a conference put together the Hare PCL-R checklist on how to pick a psychopath. Presumably each item scores two points and if a person fits at least 15 of the points, then there's a good chance they are a psychopath.

These character traits include: glibness/superficial charm, a grandiose sense of self worth, a need for stimulation or a proneness to boredom, pathological lying, cunning/manipulative, lack of remorse, lack of empathy, parasitic lifestyle, poor behaviour controls, promiscuous sexual behaviour, early behavioural problems, lack of realistic long term goals, impulsivity, irresponsibility, failure to accept responsibility for own actions, many short term marital relationships, juvenile delinquency and criminal versatility.

Ronson went on to interview some well known potential psychopaths to apply Hare's 20-point psychopath test. His interviewees include the former leader of a Haitian death squad, the infamous corporate cost-cutter, Al 'Chainsaw' Dunlap, and even television executives. It also followed the efforts of a person who faked being a psychopath and subsequently spent 13 years in psychiatric detention with some of the UK's worst criminal psychopaths

In short, psychopaths are charming, dangerous and very clever, with a very good ability to adapt. They re-offend. And they see the world as having predators and prey, with images of predators such as eagles, bears, panthers and tigers often found close by.

Well worth the read!

## 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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