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In this edition...
This week, a number of companies provided updates on progress together with their half year results. We summarise the key points from this week's briefings from Nanosonics and Mesoblast. Nanosonics is hoping to make the switch to the profit making class of companies sooner rather than later. Its Trophon unit is emerging as a game changer in the disinfection business. While Mesoblast is a company that has a 'Take Profits' rating while it sustains a hefty capitalisation of $1.9 billion, it nevertheless is one that can surprise. Did you know the company has eight Phase II trials underway or planned for 2013? Bioniche has offered an explanation as to why a Phase III trial of Urocidin, which was being managed by Endo Pharmaceuticals, failed to recruit. The program is now back in the hands of Bioniche.
Companies Covered: BNC, MSB, NAN

	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)	-4.1%
Cumulative Gain	**231%**
Av. annual gain (11 yrs)	**17.8%**

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Bioshares

15 February 2013
Edition 491

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

Nanosonics' Trophon EPR: A "Transformational Product"

Nanosonics (NAN: $0.48) confirmed its expectation of increased sales in this financial year to exceed last year's sales of $12.3 million. The company appears to have reached the tipping point with sales in the US looking to have gained good traction. The company is even mentioning the 'P' word, with CEO Ron Weinberger saying the company will move to profitability as soon as possible.

The driver for Nanosonics is the US market. In the last six months the US business has increased fourfold over a year ago. The company is starting to make some medium sized multiple sales of its Trophon EPR disinfection units, with awareness and enquiries starting to accumulate. The company is receiving about 15 enquiries a week, outside of its direct marketing efforts.

In California, Nanosonics sold 36 Trophon units to one healthcare group, which has the potential to buy up to 300 units if it is fully rolled out within that organisation.

Weinberger said the end user has been a big driver to product take-up. Recently, two sonographers in the US had to make career changes because of sensitivity issues to the chemicals used currently to disinfect ultrasound probes.

The success in the US is being driven by the Nanosonics sales team, which works alongside its distributor in the US, GE Healthcare. Nanosonics has nine staff in the US, with five in sales. That may increase, with Nanosonics looking to drive sales in the US aggressively. In Australia, the company has a 35% penetration of its units in the target markets. At the moment there is no price pressure on the product.

The company is seeking to gain approval in South Korea shortly. In Europe, Weinberger said it will take a while to gain traction. He expects to see an improvement in Europe from the first half of FY2014.

Comments

A positive aspect to the Nanosonics business is the lack of new competition. Nanosonics is seeking to 'own the ultrasound probe reprocessing market'. It sees the Trophon system as a transformational product with no direct competition.

The other appealing aspect of the business is the high quality of sales, whereby 52% comes from consumables. By way of example a single unit, which the company sells to its distributor for $5000, is expected to generate $18,000 of total revenue over four years. There should also become a market for replacing existing units, which have a user-life of around five years.

Nanosonics is capitalised at $125 million.

Bioshares recommendation: **Speculative Buy Class A**

Mesoblast – Eight Phase II Trials Planned or Underway

Mesoblast (MSB: $6.78) has continued to refine its investment message, highlighting the three areas of focus for the company's business activities. The first area is the treatment of systemic diseases, including diabetes, the second is the treatment of orthopedic diseases including early intervention in intervertebral disc damage, and the third area is in the treatment of cardiovascular diseases.

1. Systemic Delivery

What makes the Mesoblast stem cell approach suitable for complex diseases involving inflammation and the immune system is that the stem cells affect multiple pathways involved in these processes in the body. It has the potential advantage over existing therapies that modulate single pathways.

Rheumatoid Arthritis

Mesoblast has received FDA clearance to start a 48 patient trial in rheumatoid arthritis, which will be a double blinded study. It will enrol patients who have had a poor response to the anti-TNF biologic drugs. The trial will follow patients for three months, with patients receiving a once-off IV infusion of one of two doses. Mesoblast will also start a second Phase II trial in RA in Europe this half as a first line therapy.

Type 2 Diabetes

Mesoblast is conducting a Phase II trial in 60 patients with Type 2 diabetes, where the disease is not being managed well using oral glucose. That trial is due to report this year. There has been no evidence of any adverse events. Mesoblast CEO Silviu Itescu said in an investor briefing that the FDA is becoming more comfortable with systemic delivery of its stem cells, given the positive safety profile that supports the diabetes study.

In the second half of this year, the company is planning to start a Phase II trial in patients with end stage kidney disease. Kidney disease is the biggest complication in diabetes, affecting up to 30% of patients. The trial will investigate whether stem cell therapy can stabilise or reverse the kidney damage.

2. Orthopedics

Spinal Fusion

In January Mesoblast reported results from a Phase II study in posterior (from the back) lumbar (lower back) spinal fusion. In the 24 patient trial, spinal fusion was achieved in 62.5% of patients given the highest dose of the Mesoblast stem cells (75 million cells), compared to 75% of patients in the control group achieving spinal fusion (who received a bone autograft). However, the best result was achieved in the lowest stem cell dose (25 million cells), where spinal fusion was achieved in 85.7% of patients.

The main benefit of a stem cell approach over an autograft procedure is that a second operation to source the bone graft (generally from the hip) is not required. (Bone graft side effects include infection, bruising and pelvic fracture.)

The reason why the best effect was seen in the lowest dose was explained as being due to the effect of the concentration of cell numbers. If the cell concentration is too high, then there are insufficient nutrients to allow the stem cells to survive.

If this product gets to market, it will compete with Medtronic's Infuse product, which generates US$800 million of sales and is approved only for the treatment of anterior (from the front) lumbar fusion. Posterior lumbar fusion procedures account for 62% of lumbar fusion procedures.

In this Phase II trial, there were no cell related adverse events and also importantly no ectopic bone formation, which has been seen with the Infuse product when used posteriorly. The company said these results warrant progression to a Phase III trial this year, with the correct dose having been found (25 million cells). If successful it will compete with Infuse as the only product approved in this market in the US.

Intervertebral Disc Repair

Mesoblast's 100 patient trial to treat intervertebral disc disease (IDD) has completed enrolment. The final patients will reach the six month endpoint in April and results are expected by mid year. The trial is comparing a single injection of two different doses of the mesoblast stem cells versus saline or hyaluronic acid. If successful, the company will have two programs to move into Phase III trials.

3. Cardiovascular Applications

Itescu said Mesoblasts alliance with Teva is strong. A Phase III trial in patients with congestive heart failure (CHF) is due to begin. However the trial and its timing is controlled by Teva. In answer to a question over the funding these trials, Itescu said that it is the responsibility of Teva to fund Phase III trial development, where the program warrants progression from Phase II to Phase III.

The exception is in the company's Phase II 90 patient heart attack trial, which was to be funded by Mesoblast. However, Teva wanted that trial expanded to 225 patients and is now co-funding the trial. That trial is underway in Europe and Australia.

The Phase III CHF trial will involve 1700 patients, to be divided equally between a control group and the active group. The active arm will receive one injection containing 150 million stem cells via a catheter. The control group will receive a sham angiogram.

According to Itescu, there will be the possibility of two interim data analyses. The first will look at surrogate markers in a blinded fashion. Two thirds of the way through the trial, an interim assessment will look at incidence of heart failure, hospitalisations and deaths.

The company is aiming for approval for CHF treatment in the second half on 2016. The Phase III trial is due to start this year.

Other Clinical Studies

Mesoblast is conducting a Phase II study wet AMD, enrolling patients in Singapore and Australia. It also has an ongoing Phase III study in expansion of cells in cord blood transplantation.

Cont'd on page 4

Bioniche's Urocidin on Pause

Bioniche Life Sciences (BNC: $0.25) has offered an explanation for the lack of clinical progress of Urocidin (EN3348), which had been partnered with Endo Pharmaceuticals. The two companies terminated their partnership in December 2012.

Endo Pharmaceuticals was conducting a Phase III trial of Urocidin, (also known as mycobacterial cell wall-DNA complex). The planned completion date for the 450 patient trial in bladder cancer patients was December 2013.

The problem the trial faced was that rate of recruitment was very slow. In Bioniche's view the reason for the slow rate of recruitment was the intervention in the control arm, mitomycin C. The issue identified by Bioniche was that mitomycin C is chemotherapy *not approved for use in non-muscle-invasive bladder cancer,* although it is used (off label) by some cancer specialists.

Bioniche hypothesised that some specialists would not have been comfortable using two experimental drugs, despite Urocidin showing a 25% disease free survival rate in an earlier Phase III trial and was shown to be well tolerated.

Bioniche has pointed out that Endo Pharmaceuticals changed the original development plan for Urocidin. The initial trial design for the second Phase III trial proposed by Bioniche was to evaluate Urocidin against BCG (an established therapy with a number of drawbacks) in patients with *newly diagnosed* non-muscle-invasive bladder cancer.

However, Endo Pharmaceuticals elected to run the second Phase III trial in patients who were not newly diagnosed with non-muscle-invasive bladder cancer, but had been treated with BCG or were refractory to BCG treatment.

Bioniche has now taken back the rights to Urocidin. However, it must pay a 5% royalty on future net sales to Endo Pharmaceuticals, on future net income for ten years following the launch of the product or until the last valid patent claim expires. Endo had paid Bioniche $38 million in upfront and milestone payments.

Way Forward?

Bioniche is now investigating the possibility of resurrecting its original clinical plan for Urocidin. The company will discuss its options with regulators, including Health Canada. Bioniche will discuss the possibility of early registration in Canada using the Notice of Compliance with Conditions approval route. The pathway supports the approval of medicines for patients with serious or life threatening diseases for which there are no currently available drug.

Bioniche argues that this could apply to Urocidin because the only alternative treatment for non-muscle-invasive bladder cancer patients who don't respond to BCG treatment is a cystectomy.

If Health Canada is supportive, Bioniche believes that Urocidin could be on sale in Canada in 2014.

Bioniche will consider re-partnering Urocidin.

Another consequence of the termination of the agreement is that Bioniche must now receive at least US$5 million by June 20, 2013, either through a capital raising, product development milestones or from licensing activities.

This obligation arises from the consent to the termination of the (Endo) agreement by Capital Royalty LP, a finance group which lent Bioniche US$20 million in May 2012.

Lessons for Biotech Investors?

Bioniche's experience with Endo Pharmaceuticals offers several lessons for biotech investors.

The first is that rates of recruitment in clinical trials can serve as a guide to the potential acceptability of a drug candidate. In this case, the issue appears not to have been with Urocidin itself but with a comparator intervention.

The other consideration for investors relates to the skill and experience offered by a licensee. For example, Endo Pharmaceuticals strengths are in urology and pain management. While a focus on urology appears relevant for a drug candidate such as Urocidin, it is possible that Endo Pharmaceuticals lacked more comprehensive expertise in the area of cancer drug development.

Of 234 studies that appear on ClinicalTrials.gov under the search term 'Endo Pharmaceuticals', including completed, current and withdrawn, only 19 relate to cancer treatments. For Endo Pharmaceuticals to design a trial which included a non-approved treatment (mitomycin C), in hindsight, does not make sense.

Financials

Bioniche has reported its half-yearly results for the period ending December 31, 2012. The company posted a loss for the half year of C$11.7 million, compared to an C$8.5 million loss for the previous corresponding period.

Revenue for the half year was C$15.5 million, up 4% for the same period a year ago. Animal Health revenues rose 14% to C$13.5 million. A decrease in Canadian sales of 19% and European sales of 23% were offset by increases in Australia of 45% and the USA of 29%.

The drag on the company's financial performance is that more than half of its R&D spend of C$8.5 million is committed to the maintenance of manufacturing facilities for Urocidin. Annualised, the expenditure is approximately C$9 million. The company is also spending in the order of C$3 million a year on its food safety product, Econiche, a vaccine designed to limit the incidence of *E. coli* infections in the cattle-to-human food chain.

Summary

Bioniche has issues of funding coupled to business organisation and purpose to resolve before investors can be in a position to contemplate an investment in this stock.

Bioniche is capitalised at $26 million.

Bioshares recommendation: **Sell**

Bioshares Model Portfolio (15 February 2013)

Company	Price (current)	Price added to portfolio	Date added
Psivida	$1.43	$1.550	November 2012
Benitec	$0.015	$0.016	November 2012
Nanosonics	$0.480	$0.495	June 2012
Osprey Medical	$0.57	$0.40	April 2012
QRxPharma	$0.95	$1.66	October 2011
Somnomed	$1.08	$0.94	January 2011
Cogstate	$0.350	$0.13	November 2007
Clinuvel Pharmaceuticals	$2.39	$6.60	September 2007
Universal Biosensors	$0.87	$1.23	June 2007
Alchemia	$0.320	$0.67	May 2004

Portfolio Changes – 15 February 2013

IN:
No changes

OUT:
No changes

– *Mesoblast cont'd*

Patents

Mesoblast has been granted additional patents over its technology in the US and China. This represents a third level of patent protection.

Partnering Objective for 2013

This year the company will be exploring partnering options. The company will look to partner one or both of the orthopedic programs, or conduct both Phase III trials independently.

Comments

The treatment of diseases using a systemic stem cell therapy opens up several major markets for Mesoblast. Results from early proof-of-principal clinical studies, the first being in Type 2 diabetes, has the potential to be a big driver for this stock. However, the unknowns are significant, and the level of difficulty is higher compared to localised delivery of the stem cells, which is the case in orthopedic and cardiovascular applications.

Given this high hurdle, it's a sensible approach to gain clinical data from several Phase II studies within a short time frame. Results from Mesoblast's Phase II trial in type 2 diabetes are expected this year. It has just received approval from the FDA to proceed in a Phase II trial in patients with rheumatoid arthritis. And it expects to start Phase II studies in the next 12 months in patients with diabetic kidney disease and in patients with lung diseases. That will bring the total to eight Phase II trials being, or expected to be managed, by Mesoblast.

In the spinal fusion market opportunity, the incumbent product Infuse is a controversial product, with reports that several thousand people have been injured using the product. That product is only approved for anterior lumbar procedures. With shortcomings in existing therapies, there exists a major market opportunity for a safe and effective product.

Mesoblast is capitalised at $1.9 billion.

Bioshares recommendation: **Take Profits**

Bioshares

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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: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion

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