ISSN 1443-850X

In this edition...
Calzada's Novosorb foam dressing has performed well in a head-to-head trial with the market's leading product, GranuFoam. The results will form the basis for 510(k) application with the FDA.
A pre-clinical study of Circadian's VGX-300 showed that it was good as Elyea, a recently launched and very successfuld drug for wet AMD, in inhibiting blood vessel leakage in the eye.
While the IPO window may appear shut, that has not stopped the re-purposing of at least eight ASX-listed companies with new assets. One of the most recent (yet to be approved) of these is Telesso Technologies's acquisition of acne drug developer Mimetica. The key with backdoor listings is getting assets at a good price.
Companies Covered: CZD, CIR, IMU, NDL (Oncosil Medical), PVA, TEO (Mimetica)

	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%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au

David Blake - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph:(03) 9348 9317
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$400 (Inc.GST)
Edition Number 502 (10 May 2013)

Bioshares

10 May 2013
Edition 502

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

Positive Clinical Trial Results from Calzada – Company to File 510(k)

Calzada (CZD: $0.071) released positive clinical trial results last month for the company's novel wound treatment technology. In an 18 patient trial, the company showed its product outperformed the market's leading product. The current market is worth $400 million a year. Calzada has initiated discussions with partners/distributors and expects to file a 510(k) submission with the FDA in coming months.

The lead product for Calzada is a new foam material used in what is called Topical Negative Pressure (TNP) dressings. TNP dressings incorporate a vacuum negative pressure on wounds such as bed sores to exudate fluid such as puss from wounds, and to remove oxygen, thereby limiting the conditions for bacterial growth. The negative pressure also promotes granulation of tissue to help rebuild deep wounds that often extend to the bone.

In this clinical trial, Calzada's NovoSorb foam dressing was compared to the leading product on the market, GranuFoam, from Kinetic Concepts Inc (KCI). Of interest is that KCI provided the GranuFoam material for the trial to Calzada. KCI has around 80% of the $400 million annual market for these products.

Results

The trial showed that Calzada's NovoSorb dressing was easy to remove on each of the 72 dressings applied. By comparison, while the competing GranuFoam proved easy to change in wounds on the heel and in sacral wounds (shallow wounds at the base of the spine), in the deep wounds on the rear end (these are wounds primarily in patients who are wheelchair bound), the competing GranuFoam product was difficult to remove in 40 of the 50 dressings (80%), causing bleeding in cases.

Cont'd over

On the second measure of retention of foam in the wound, four patients in the competing GranuFoam arm retained foam particles in five separate episodes. Only one patient in the NovoSorb group had retained foam, which was washed out with saline and with no subsequent infection taking place. In the competing GranuFoam group, sharp debridement with scissors was required on four of the five occasions, with infection occurring in three patients.

The third measure was difference in wound size. There was no significant difference between the groups. At 15 days, the competing GranuFoam product was 4.6% better (wound size 59.6% of original size with GranuFoam compared to 64.2% of original wound size for Calzada's NovoSorb). At 50 days this was reversed with Calzada's NovoSorb 10% better (30% of original wound size for Novosorb versus 40% for GranuFoam).

Discussion

Calzada's polyurethane foam was designed as a product that can biodegrade in the skin. This is still a potential advantage with the product, however, is not the primary feature that the company is promoting in this application. It works out that due to the structure of the foam, there is less tissue growth into the foam and thereby less fragmentation of the foam into the wound. That the product is biodegradable should also give it an additional, implied benefit.

In coming months the company will file the product for approval under a 510(k) route, where clinical trials will not be required because a company needs only to demonstrate equivalence to an existing 510(k) cleared device. The company has also initiated discussions with several of the leading commercial players in this market. The NovoSorb assets are housed in the Calzada subsidiary, Polynovo Biomaterials. CEO of Polynovo, Laurent Fossaert, recently visited potential international partners/distributors with plastic surgeon Dr John Greenwood, who is coordinating the company's clinical trials with this product. Fossaert said there is very high interest in the product.

Fossaert is aiming for regulatory approval in the US by year's end, with potentially a partner/distributor signed up by then as well. At this stage the company intends to maintain manufacturing control of the product, which is a very sensible strategy.

One of the drivers for an improved product comes from the FDA itself. The FDA raised concerns regarding bleeding and infection with negative pressure wound therapy (mainly GranuFoam) in 2009 and 2011, with 12 deaths and 174 injuries since 2007 (see Calzada website for scientific presentation). It's easier to see why there might be such strong interest in a safer product.

Long-term Implant Trial

Under John Greenwood, Calzada is also conducting trials with its NovoSorb technology as a long-term, biodegradable implant. To date at least six patients have been successfully implanted with the NovoSorb Biodegradable Temporising Matrix (BTM). Made from similar polyurethane material, the product can be used to fill full thickness burns. Results to date have been brilliant said Fossaert. With this product, you don't see any muscle fibres, which is often seen with thin skin grafts, the wounds are flush with the tissue, and final healing of the wounds appears excellent.

The NovoSorb BTM is applied to full thickness wounds (in this trial the tissue was removed to be used for reconstruction surgery to other parts of the body), the area is sealed for 21 days, after which the seal is removed and a final skin graft is placed on the wound to complete the procedure. Greenwood said the product integrates quickly well with the surrounding tissue.

Greenwood has ethics approval to conduct a pilot burns trial in patients with 20%-50% body wounds once this current trial is completed. Calzada plans to submit the BTM product for 510(k) approval for the treatment of surgical wounds either in last quarter of 2013 or the first quarter of 2014.

Calzada also has existing assets in the form of the the failed obesity drug candidate AOD9604. This unapproved compound has received significant exposure from off-label and inappropriate use by sporting clubs, with the drug sourced from off-shore manufacturers in many cases. However, the core asset for the company in *Bioshares* view is the NovoSorb wound healing technology.

Calzada is capitalised at $25 million. The company had $4.0 million in cash at the end of January this year.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Positive Pre-Clinical Data for Circadian's Wet AMD Drug Candidate

Circadian Technologies (CIR: $0.22) has received some positive preclinical data on its drug candidate VGX-300. Data was presented at an ophthalmology conference in the US by a researcher collaborating with the company, Dr Kameran Lashkari from The Schepens Eye Research Institute at Harvard Medical School.

Data from a mouse model showed that VGX-300 successfully inhibited blood vessel growth in the eye and vascular leakage in the eye as effectively as the wet AMD drug Eylea. In the first year on the market, Eylea generated sales of US$838 million and is expected to achieve sales this year in the order of $1.3 billion.

Dr Lashkari also showed for the first time that VEGF-C levels are elevated in people with AMD compared to healthy volunteers.

Eylea and Avastin both block the VEGF-A pathway for making new blood vessels. However, VGX-300 blocks also the VEFG-C and VEGF-D pathways. The theory is that blocking all three pathways will deliver a comprehensive approach to shutting down unwanted new blood vessel formation in the eye.

According to Dr Lashkari, at least 40% of patients with wet AMD taking VEGF-A inhibitors experience some form of resistance to therapy. According to Circadian, anecdotal feedback from ophthalmologists is that vision gain is achieved in only around 30% of patients in the real life setting.

Another problem with these drugs is delivery. They need to be injected monthly (Avastin) or every two months (Eylea). Combining the therapy with a compound such as VGX-300 many mean that therapy may be sustained for longer, thereby requiring less frequent injections.

Circadian intends to move the program into Phase I trials in the second half of 2014.

Summary

Circadian is capitalised at $11 million. It had $12.1 million in cash at the end of last year, plus $2.7 million in equity in other companies (including Optiscan Imaging and Antisense Therapeutics). The company also received a tax rebate of $1.3 million in February this year.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

pSivida's Iluvien Launched by Alimera in Germany

pSivida's licencee Alimera Sciences has launched the drug Iluvien in Germany. Iluvien is a three year depot injection for the treatment of diabetic macular edema (DME).

pSivida is entitled to a 20% profit shares, which results in a net royalty of around 15% from sales. The product is also on the market in the UK under the private healthcare system.

Alimera recently refiled the drug with the FDA in an amended marketing application. In Europe, the drug is approved for use in patients with chronic DME. Alimera has been knocked back by the FDA twice. This third attempt will mirror the European indication for chronic patients. If Alimera gets approval in the US, then pSivida will receive a payment of US$25 million under the license arrangement. The PDUFA date for Iluvien with the FDA is October 17, 2013.

pSivida is capitalised at US$65 million. The company had $15.7 million in cash assets at the end of last year.

pSivida's share price is up 123% from its 12 month low and is up 74% since it was added to the *Bioshares* Model Portfolio in November last year.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Backdoor Listings Rollcall – Eight Companies Repurposed

At least eight companies have entered, or are in the process of entering, the ASX list of biotech stocks through a process that is better known as a back door listing. This process typically sees a company (the shell) containing cash assets acquiring a private company with assets or more simply acquiring the assets directly. The process is also referred to as a reverse take-over (RTO).

However, this classification can be broadened to include companies that may also have existing life science assets of some value, to which are added other assets to both strengthen as well as provide a new focus for the company.

Companies that have repurposed with new assets include **Invion** (IVX: $0.05) (through **CBio**), **Imugene** (IMU: $0.009), which acquired the Linguet assets of **Consegna**, and **Novogen** (NRT: $0.165), which acquired **Triaxial Pharmaceuticals** in late 2012.

Bioxyne (BXN: $0.015) acquired **Vitality Devices**, a medical device distribution business focused on Asian territories.

Neurodiscovery (NDL: $0.033) acquired the brachytherapy assets of **pSivida** subsidiary **pSiMedica**, which had previously been assigned to the UK entity **Enigma Therapeutics**.

Acuvax (ACU:$0.001) shareholders approved the acquisition of **Biolife** and rebadging as Biolife in March. Biolife's chief asset is a vaccine (HER-Vaxx) for patients with cancer who test positive for the Her2 gene. Biolife is yet to complete a $5 million capital raising and has extended the acceptance date to June 22, while it seeks to secure cornerstone investors.

Telesso Technologies (TEO: $0.10) announced it will acquire the privately held **Mimetica**, a company which is developing an acne treatment.

In a recent, related development, **Pharmaust** (PAA: $0.012) announced it would acquire **Pitney Pharmaceuticals**, an oncology company based in Sydney. The Pitney assets will sit alongside Pharmaust's Epichem business.

Neurodiscovery (Oncosil Medical)

Neurodiscovery is set to be rebadged as Oncosil Medical, following its acquisition of the brachytherapy assets of pSivida (as contained in its pSiMedica subsidiary). These assets relate to the original bio-silicon technology assets that pSivida obtained from the British defence research group QinetiQ.

pSivida continued with the development of ophthalmic uses of biosilicon. However, following the merger of pSivida with Controlled Delivery Systems in 2006, the brachytherapy assets fell into a state of dormancy despite the completion of four clinical trials in patients with liver and pancreatic cancer.

The acquisition was approved by shareholders in April 2013. A $1.5 million capital raising preceded the acquisition. Neurodiscovery issued 75 million shares in consideration for Enigma Therapeutics, equating to $2.85 million at the date of the announcement.

The terms of the licence Enigma held from pSiMedica for the biosilicon assets, which through the acquisition became assigned to Neurodiscovery (Oncosil Medical), included an 8% royalty on future net sales and 20% of any other payments or royalties from third party deals. Commercial milestones include milestone payments that range from US$1 million to US$5 million, commencing when sales first reach US$5 million in a calendar year and later reach US$100 million in a calendar year.

The investment appeal with Oncosil Medical stems from its Phase III ready status. A open label 150 patient Phase III trial in patients with pancreatic cancer could commence as soon as 2013 Q3. But perhaps even more appealing is that, depending on discussions with regulators, a CE Mark application could be lodged in CY 2013.

Oncosil is medical device made of 30 micron particles which contain radioactive phosphorus. The product is implanted into tumours, which then emit radiation that destroys cancerous cells.

The appointment of an experienced CEO is expected to take place in the near future.

Bioshares recommendation: **Speculative Buy Class B**

Telesso Technologies (Mimetica)

Telesso Technology shares have been suspended since December 17, 2012. Telesso held net assets of $0.8 million at December 31, 2012.

Telesso Technology intends to acquire Mimetica, a company which is developing MTC896 for the treatment of acne. An IND for MTC896 has been filed with the FDA. However, it would appear that a Phase II trial for MTC896 is incomplete due to lack of funding, hence the plan by Telesso Technologies to raise $6 million in conjunction with the acquisition, which is valuing Mimetica at ~$16 million.

Telesso has 60 million shares on issue and would be issuing 63 million shares at $0.25 and 3 million options to acquire Mimetica.

Phillip Capital is managing the capital raising.

Bioshares recommendation: **No Rating**

Imugene (Linguet) Update

Imugene acquired the Linguet assets of Consegna in July 2012. Linguet is a drug delivery technology which delivers drugs across mucosal membranes. Termed buccal drug delivery, the approach benefits from the high density of blood vessels that are found in the mucosa (inside the mouth). An advantage of buccal delivery is that drugs can be more quickly absorbed into the body.

The company is currently conducting an SPP. It retained cash of $0.5 million at March 31, 2013. The goal of sourcing capital for the company's development plans is an urgent and high priority and Peloton Capital has been engaged to support the SPP.

Cont'd over

Bioshares Model Portfolio (10 May 2013)

Company	Price (current)	Price added to portfolio	Date added
Atcor Medical	$0.075	$0.082	May 2013
Circadian Technologies	$0.240	$0.270	March 2013
Tissue Therapies	$0.125	$0.255	March 2013
Allied Healthcare	$0.036	$0.026	February 2013
Psivida	$2.70	$1.550	November 2012
Benitec	$0.015	$0.016	November 2012
Nanosonics	$0.470	$0.495	June 2012
QRxPharma	$1.16	$1.66	October 2011
Somnomed	$0.92	$0.94	January 2011
Cogstate	$0.360	$0.13	November 2007
Clinuvel Pharmaceuticals	$2.07	$6.60	September 2007
Universal Biosensors	$0.65	$1.23	June 2007

Portfolio Changes – 10 May 2013

IN:
No changes

OUT:
No changes

Imugene has now settled on a development plan for its Linguet assets.

The company's lead program is a Vitamin D product , for which it has completed formulation development for two forms – cholcalciferol and calcifediol (25-hydroxyvitamin D3).

Vitamin D deficiency is a problem for patients with Chronic Kidney Disease (CKD) because of excess production of an enzyme which destroys Vitamin D. This drug segment achieved important validation when Cytochroma acquired OPKO Health for US$100 million up front and for US$190 million in milestone payments. OPKO has developed a controlled release form of an analogue of Vitamin D, with its programs at the Phase III stage.

Imugene is aiming to get a calcifediol formulation registered as a prescription product in Europe in early 2014. It also is aiming to lock in a license and distribution agreement also by 2014 Q1.

It may also develop cholcalciferol for the supplements market.

Imugene knows that its Vitamin D formulations meet the criteria of acceptable mouth feel, acceptable dissolution in the mouth, ease of swallow and acceptable taste.

It is now subjecting the Vitamin D formulations to stability testing and will also arrange for *in vitro* buccal testing in the US to compare penetration differences between the cholcalciferol and calcifediol formulations.

Once that is complete it can then start on bio-equivalence studies in 20-30 patients in Europe, a study which should cost approximately $70,000 to complete.

Imugene's second product is a buccal formulation of ibuprofen, a well known pain and anti-inflammatory drug. While this is available in many dose strengths and formulations, it must have a protecting layer so that it doesn't generate throat burn. Recket Benckiser currently market an orally disintegrating tablet (Nurofen Meltlets Lemon) which points to a market opportunity for a buccal form of ibuprofen.

The company possesses clinical data from a trial in 2010/11 which showed that the taste and burn sensation with a buccal formulation of ibuprofen did not occur.

The commercial rationale for pursuing an improved formulation of a drug that is established as a generic is that branded producers will access improved formulations to sustain and command price premiums.

Blue Sky – Parkinson's Disease Drug

The company's blue sky opportunity is a buccal formulation of a drug used to manage Parkinson's Disease, apomorphine. This drug is injected on average 12 times a day. In other words, the route and frequency of delivery is a source of significant non-compliance or even lack of take-up. There are also injection site reaction issues because of the drug's high acidity, as well as nausea and vomiting.

The development of a buccal formulation of apomorphine would necessitate that Imugene conduct a reasonably large (200 patient) bioequivalence study. However, until the company proves that it can commercialise simpler, less ambitious formulations, then it will not be able to attract the funds needed to attack the blue sky opportunity in Parkinson's disease.

Imugene is now clearly defined as pharmaceutical company with a drug delivery company as its core asset. A change of name to reflect this status would be a positive move at the right time.

Bioshares recommendation: **Speculative Buy Class C**

Summary

The entry onto the ASX of so many assets by means of backdoor listing (reverse take over) is a sign that the underlying world of medical product development is rich with investable opportunities.

Perhaps what the level of activity really shows is that backdoor listings become feasible when the vendors of assets submit more realistic prices for their assets and map out more realistic spending and development plans .

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, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion, Circadian Technologies

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$400**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$630	2-3 email addresses
	$855	4-5 email addresses
	$1090	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____