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In this edition...
Along the path to revenues for many biotech companies comes the reimbursement hurdle. One of our standout stock picks, Sirtex Medical, secured US reimbursement some years ago, yet it continues to this day to seek reimbursement in new territories. Now diagnostic company Impedimed has secured a US reimbursement code on its way to gaining coverage from US insurers. Its Category III code offers an important layer of commercial protection due to the specific wording used in the code.
Peptide company Phylogica is now focusing on gaining revenues from library services supplied to drug discovery companies. We also update readers on developments at Calzada's Polynovo business.
The Editors
Companies Covered: CZD, IPD, PYC, SRX

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - Current)	71.0%
Cumulative Gain	**232%**
Av Annual Gain (9 yrs)	**20.9%**

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Impedimed Gets US Category III Reimbursement

For healthcare companies, especially the more competitive medical device development companies, reimbursement is a paramount factor in the widespread commercial adoption of an emerging technology. This week Impedimed (IPD: $0.89) received very positive news, that use of its lymphedema detection device would be covered by Category III reimbursement from private health insurers in the US. It is arguably the most ideal outcome for Impedimed at this stage for this technology.

Category III reimbursement is generally assigned to emerging technologies. It means that health insurers in the US can, but are not compelled, to cover certain procedures, such as a test for early signs of lymphedema. Impedimed's CEO, Greg Brown, is aiming for at least 30 million Americans to be covered for use of its technology by the end of 2010. The Category III coding is expected to be published in July this year and applicable from January 2011.

Impedimed now needs to secure coverage and negotiate reimbursement pricing for procedures using its technology.

Other Benefits from Reimbursement Coding for Impedimed

The reimbursement coding also comes with another important benefit. It is completely specific to the use of 'bioimpedance spectroscopy (BS)', which is the patented technology that Impedimed has developed for this application. This places an additional obstacle for competitors.

Other good news was that the coding covers the detection of lymphedema in the arms and legs (not just arms), and covers not just lymphedema but edema as well.

Why Category III is Better than Category I for Impedimed at this Time

A Category I reimbursement means that more private health insurers will cover the particular procedure than for a Category III code procedure. It is applied to more established procedures that are widely performed. However the other key difference, other than increased coverage from insurers, is that the reimbursement rate is set by Medicare under the 'RUC' process (Relative Value Scale Upside Committee). Category III code reimbursement is negotiated with individual insurers. It should be noted that a Category III code is a temporary reimbursement assignment, and procedures can be upgraded to a Category I level after widespread adoption.

Impedimed believes that if the procedure to detect lymphedema using BS was awarded Category I coding, its reimbursement level may have only been around $50 per procedure. This would have limited how much Impedimed could have charged physicians to around $25. The health care reforms underway in the US are placing considerable pressures on reducing health care costs. This pricing pressure is making a Category III coding more attractive than previously considered and with more larger payors now covering Category III code procedures.

– Impedimed...from page 1

Impedimed believes it can negotiate reimbursement of at least $100 per procedure to physicians, and charge the physician around $50 per procedure. Impedimed believes the available health economic data (which could justify up to four times this amount) will allow it to argue its case with payors.

Reimbursement price is a key issue. At a reimbursement rate of around $50 per test, it leaves little to share between Impedimed and the Physician. At between $80-$100 per test, it provides sufficient incentive for physicians and reward for Impedimed. For the physician this is appealing because he or she will be paid for the consultation plus potentially an additional net $50 or so from private health insurers.

Under the miscellaneous code, reimbursement of around $220 has been achieved. However, there is no guarantee of payment under this code with supplementary documentation required to be sent with each reimbursement application, with no guarantee of success, and taking months to be paid. Under the Category III code, doctors will know which insurers reimburse for the procedure.

Awareness of Lymphedema Builds

A bill was introduced last month in the US House of Representatives last month to improve the diagnosis and treatment of lymphedema under the US Medicare program. The bill is under consideration. One of the other benefits of this proposed legislative change is to also reduce costs associated with complications arising from lymphedema.

When Impedimed's technology is assessed for a Category I coding after wider use is adopted, it should be able to achieve a higher reimbursement. This is because it was currently falling under a breast cancer treatment code, where use later should include arms and legs and therefore a more general surgical code.

Business Model

Impedimed's business model is cleverly constructed that the company receives payment from each procedure that uses its devices, through 'L-Dex agreements'. L-Dex, or lymphedema index, is a term the company has coined.

Barriers for Competitors

The company's patents give it protection from competitors using the same bio-impedance spectroscopy technology. The specific reimbursement coding for bio-impedance spectroscopy places another barrier for competitors.

Where in drug discovery the key hurdles are safety and efficacy, in diagnostics the main commercial objectives are awareness and reimbursement. It is a long and complicated path to achieve reimbursement coverage for a diagnostic technology. However, once established, it secures a strong competitive advantage and provides a mechanism to encourage users (physicians) at a time where reduction or capping of healthcare costs has become a major issue.

Summary

Lymphedema, which is often preventable if diagnosed early enough, is becoming more widely seen as a medical issue that is poorly addressed and Impedimed is at the forefront in offering products that can aid it its early diagnosis. The Category III coding for procedures utilising the Impedimed devices is a major stepping-stone for building a successful medical device business for Impedimed.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Phylogica Refocuses

Over the last 12 months, Phylogica (PYC: 9 cents) has changed its business model and believes it is about to hit the sweet spot with its peptide drug discovery engine. In December last year Phylogica signed a collaborative deal with **Roche** and believes that was the start of what should be a series of discovery deals to access Phylogica's unique peptide library.

Phylogica's previous business model was to out-license but also to build its own clinical drug pipeline. However, the company will now concentrate on becoming a drug discovery research engine for larger biotech and pharmaceutical partners.

Phylogica has continued to build and improve its peptide libraries, having made eight new libraries over the last year. Most peptide drugs are variations of existing drugs or are analogues of natural peptides. Phylogica's library is unique because of its diverse range of peptide libraries which are derived from ancient bacterial genomes. Some of these peptides have rare properties, such as an ability to survive in extreme conditions, and the expectation is that some unique drug-like properties may also be detected.

The deal with Roche saw an upfront payment of $433,000 which will be received this quarter. Under the collaboration, Phylogica will use its library to find peptides that can transport large molecules into cells to interrupt disease. If this program is successful, there is the possibility of moving to a more comprehensive relationship with Roche.

Pharmaceutical companies continue to rely on external drug discovery from biotech companies, with 88% of active preclinical programs being developed by biotech companies according to Pharmaprojects. Phylogica wants to build a business that can service this market, with the aim of generating a healthy revenue stream whilst maintaining further upside from downstream royalties should any of the compounds reach the market.

Phylogica is seeking to emulate drug discovery library companies such as **Morphosys** (antibodies), **Evotec** (small molecule with genetic-based library), **Evolva** (small molecule) and **Galapagos** (small

– Cont'd on page 5

Sirtex Medical – Briefing Update

Sirtex Medical (SRX: $6.20) held an investor briefing this week. Sirtex management was very optimistic about the future growth potential for the company, despite of the short term slower growth. Of interest, is that the 17% growth in unit sales seen in the six months to December over the previous corresponding period is viewed as slow growth for the company. The company believes it should see more significant growth in the future for a number of reasons.

The company observed that if sales growth was strong in a particular year, then the following year has seen more subdued growth before that strong growth returns in year three, such is the dynamics of this business. (In this is the case, then FY2011 should see high growth in unit sales). In the first half of this financial year, Sirtex achieved sales of $32.2 million. However due to adverse currency movements, sales increased only by 6% over the previous corresponding period.

Sirtex is building a strong position with its radioisotope liver cancer treatment. The procedure has been conducted now in almost 300 centres worldwide, and not just in the major countries. In Europe, Turkey has become the third largest market for the company. The company is currently not selling into France because there is no reimbursement available for the treatment. Sirtex is aiming to achieve French reimbursement by July 2010.

The treatment is currently reimbursed in the USA, Germany, Belgium, Turkey, Switzerland and The Netherlands, Australia (through private insurers), in Spain and Italy in certain regions, and only limited funding through primary care trusts in the UK. The treatment is approved for use in South Korea but is not reimbursed. And the company is seeking to introduce the product in Canada and Latin America.

US Insurance Coverage – 200 Million People

In the US, 16 of the major heath insurers cover the Sirtex treatment providing coverage to 200 million people. The company has achieved all the reimbursement coverage it has sought to date. Reimbursement in the US is expected to increased to US$15,799.

Singapore Facility

Its new processing facility in Singapore, which combines the bulk isotope with the spheres into treatment doses, is expected to be operational by August with first dose sales commencing by May 2011. This will give the company three manufacturing facilities, the other two being in the USA and Australia. The Singapore facility will allow delivery anywhere in the world, and will be close to the Asian markets, including India and China.

Sirtex is exposed to foreign currency differential changes. The company has around a 60% natural hedge from local direct operation costs. Around 50% of free cash flow is hedged using a derivative collar arrangement six months ahead.

Although Sirtex understands the importance of continuing R&D, it uses collaborations with universities and institutes to keep these costs relatively low (around 13% of revenue). One example is a radioprotective pharmaceutical product. The Peter Maccallum Research Institute has spent 12 years developing this product. There are now five resrach groups working on this product and Sirtex has the commercialization rights to the technology

Growth in sales will come from increased awareness of the treatment, further expansion into the larger primary liver cancer market (rather than use in treating cancer metastases in the liver from the colon), and from use as a first and second line therapy in combination with existing liver cancer drugs (currently the treatment is used as a third line salvage treatment). Three major studies are currently underway or in the planning to confirm the use of the Sirtex Sir-Spheres in these applications. Sirtex CEO Gilman Wong highlighted the enthusiasm of **Bayer Schering** has for evaluating the combining its Sorafenib product with the Sir-Spheres treatment. These three trials will recruit just under 1,300 patients and it will take up to five years before results are published.

One region that underperformed was the USA. Sirtex has put on a new head of operations in the US, who has more of a marketing background than the science background of the previous head of US operations. The company is planning on adding many more staff to the US operations to ensure 'accelerated growth' growth in that region is achieved. This 'accelerated growth' is not anticipated to be limited to the US region alone.

Gilman Wong says the company has been around for a while but is still in its infancy. Clinicians are starting to see anecdotal evidence growing so much that they can't ignore it.

Hunter Hall's Views on Sirtex

Worth watching is a short presentation from PeterHall from Hunter Hall, which owns 32% of Sirtex (http://www.hunterhall.com.au/media/company-outlooks). Hall says the company has achieved only 0.2% market penetration into the 1.5 million people who are diagnosed worldwide each year with primary or secondary liver cancer. According to Hall, the real value comes from moving up the chain to a second and first line therapy with existing drugs. The company could potentially achieve at least 2% or 4% market penetration, representing a 10 to 20 times increase from current dose sales (which this year we estimate should reach $70 million). Hall believes that once the major trials are completed, if they are positive there will be a 'rollover in the oncology community' that will have to include Sir-Spheres in the liver cancer treatment regime.

Bioshares recommendation: **Strong Buy**

Bioshares

Calzada – Update on the Polynovo Business

Calzada (CZD: 3.7 cents) is the entity that retains the assets of **Metabolic Pharmaceuticals** and following a recent equity exchange with the **CSIRO** and **Xceed Capital**, the assets of **PolyNovo**. The largest shareholder in CZD is Entrust (17.5%), followed by Xceed Capital (8%) and the CSIRO (4.5%).

The company is looking to realise whatever value it can from the AOD9604 assets, including the drug and collected data packages, a task enlivened by recently exposed illegal manufacturing and sale of AOD9604 is China and in other parts of the world. (see *Bioshares* 350).

The Polynovo Business

The company is also to looking to move rapidly on the Polynovo portfolio of projects to determine in a the space of 12-24 months which ones warrant further development or investment cessation

After the decision was made to cease the development of AOD9604 as an obesity treatment, Metabolic elected to invest in Polynovo Biomaterials, a Melbourne-based bio-polymers company, which was owned by Xceed Biotech (now Xceed Capital) and the CSIRO. Polynovo has been developing applications of novel biodegradable polymers for use in a wide range medical settings including bone fixation, bone void filler and burns treatment among others. Polynovo biopolymers can be controlled to give effect to different rates of curing or setting, hardness and rates of degradation.

Smith & Nephew Collaboration

An important collaboration underway is that with **Smith & Nephew** for both a fracture fixation product and a bone void filler. S&N has recently received a US DARPA grant to develop a 'bone putty'. It is understood this product utilises Polynovo polymer technology in a minimally invasive way and the product is targeted at load bearing fractures.

Novoskin Joint Venture

The Novoskin joint venture between Polynovo and Adelaide burns surgeon, Dr John Greenwood, is developing a biodegradable temporizing matrix, BTM, for use in the treatment of severe burns.

There are several approaches to treating severe burns. Skins grafts are an established approach but depend on sufficient skin to be available for donation from another part of the body. In the case of very badly burnt patients there is usually not enough skin available for grafting.

Skin substitutes that serve as temporary matrices currently come in two types. Nylon mesh products are must be left in place for three or four weeks but then must be removed presenting a pain and discomfort challenge. Collagen matrix products such as Integra are effective but are also very expensive and treating an extensively burned patient could cost in the order of $250,000.

The potential benefit with Novoskin is that it can degrade and hence overcome the problem that nylon mesh products face. The joint venture team has evaluated three different scaffolds, BTM-1, -2 and -3, with BTM-1 losing 50% of its mass over 7 days, BTM-2 losing 50% of its mass over 90 days and BTM-3 lost 30% at the end of six months. BTM-2 offers the degradation range suitable for burns treatment.

The first iteration of the BTM product is as a wound stabilising mesh that is also designed to deal with wound contraction. BTMs will likely be devices that incorporate cells that are essential for the development and growth of skin – fibroblasts, endothelials and keratinocytes. Various experiments have been performed to study the proliferation and behaviour of these cells on BTM matrices. A challenge has been to work out how to construct the matrix so that epithelial cells do not crowd out fibroblast cells and also allow vascularisation to take place.

A second development goal with the BTM product is to develop it as a bi-layer skin substitute. The joint venture has experimented with seeding keratinocytes over a BTM construct seeded with fibroblast cells. In some areas, keratinocytes were observed to be forming a monolayer, similar to that observed in normal skin and with vascularization beginning to take place, according to the company. The next goal of the joint venture is to further optimize the BTM constructs and work on manufacturing development.

NovoCosmetica

Polynovo is also working on dermal filler applications of its technology in conjunction with a group of South Australian cosmetic surgeons. The challenge here is to create and manufacture particles that can be injected through very fine 32 gauge needles.

Collaborations Dead or in Doubt

In February 2007, the company signed with **Biomet** to develop cartilage and cranial and facial bone repair products. However, Calzada says little progress has been made with this license agreement and it will look to terminate or reshape the agreement.

Polynovo signed an agreement with **Medtronic** in January 2006 to develop a biodegradable stent. The stent market is very large and a biodegradable polymer stent could offer significant advantages over metal stents. While significant progress was made towards the development of the product, it appears that several other factors were at play in seeing Meditronic cool on the development plan. Following a ten year battle, in 2009 Medtronic paid US$400 million to settle litigation initiated by **Abbott Laboratories** covering stent design and stent delivery systems. With Medtronic holding a seemingly weaker IP position and smaller market share (12%) than **Boston Scientific** (50%) and Abbott Laboratories (25%), the challenge of taking a new product into this market looks to have become too hard for Medtronic, and hence underscores the disinterest in what now appears to a dead agreement with Polynovo.

Summary

Calzada is capitalised at $12.8 million and held $12 million cash at December 31, 2009. Calzada has the potential to generate returns for shareholders over the next 12 months if meaningful progress is made in the burns joint venture and the collaboration with Smith & Nephew.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares Model Portfolio (12 March 2010)

Company	Price (current)	Price added to portfolio	Date added
Tissue Therapies	$0.23	$0.21	January 2010
Biodiem	$0.20	$0.15	October 2009
QRxPharma	$0.89	$0.25	December 2008
Hexima	$0.44	$0.60	October 2008
Atcor Medical	$0.15	$0.10	October 2008
CathRx	$0.25	$0.70	October 2008
Impedimed	$0.89	$0.70	August 2008
Mesoblast	$1.92	$1.25	August 2008
Circadian Technologies	$0.67	$1.03	February 2008
Patrys	$0.15	$0.50	December 2007
Bionomics	$0.33	$0.42	December 2007
Cogstate	$0.29	$0.13	November 2007
Sirtex Medical	$6.20	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.25	$0.66	September 2007
Starpharma Holdings	$0.72	$0.37	August 2007
Pharmaxis	$2.69	$3.15	August 2007
Universal Biosensors	$1.61	$1.23	June 2007
Probiotec	$1.73	$1.12	February 2007
Acrux	$2.28	$0.83	November 2004
Alchemia	$0.69	$0.67	May 2004

Portfolio Changes – 12 March 2010

IN:
No changes.

OUT:
No changes.

– Phylogica from page 2

molecule with genetic-based library), which generated revenues of in the tens of millions of dollars in 2009.

The game plan in many of these library companies is to generate enough interest across multiple partners to execute a very lucrative trade sale. Perhaps the most successful of such exits was from C**ambridge Antibody Technology** which was sold to **AstraZeneca** in 2006 for US$1.3 billion. Other biologic library company acquisitions include **Domantis** (by **GlaxoSmithKline** for US$450 million) also in 2006, and the acquisitions of **Avidia** (by **Amgen** for US$290 million) in 2006, and **Adnexus** (by **Bristol-Myers Squibb** for US$415 million) in 2007.

Summary

Phylogica says it has several negotiations underway for discovery collaborations with major pharmaceutical companies. The company's goal is to form three to four partnerships per year. The company's progress can be judged over the next 12 months by its success in signing further discovery deals with major drug developers.

Phylogica is capitalised at $21 million with $3 million in cash at the end of last year and has 21 staff.

Bioshares recommendation: **Speculative Buy Class C**

Bioshares

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

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