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In this edition...
Investment opportunities in the Australian biotech sector continue to offer increasing appeal as global credit market weakness continues. In recent editions we have highlighted some core biotech holdings investors should consider closely. This week we look at a profitable biotech company (IDT) paying a 5% dividend yield with expectations of strong growth ahead and arguably Australia's strongest drug discovery engine (Cytopia) that has fallen to extraordinary low share price levels that in no way reflects progress at the company. We also update readers on BioMD, which is ready to move into Phase II studies for the testing of its tissue processing technology.

The editors
Companies covered: BOD, CYT, IDT

	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 (from 4 May '07)	-40%
Cumulative Gain	**94.7%**
Av Annual Gain (6 yrs)	**26.8%**

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Bioshares

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

IDT Begins Next Phase With Strong Growth Prospects Ahead

Institute of Drug Technology Australia (IDT: $1.90) is primarily a manufacturer of active pharmaceutical ingredients (APIs) for local and international biotech and pharmaceutical companies. It makes both APIs for drugs in development and for drugs on the market and specialises in high containment manufacture, particularly of oncology drugs. IDT Australia is a profitable business that pays dividends. However, over the last four years the company has had to broaden its business base to counter competition from low cost manufacturers. With that process successfully completed, the company is set to deliver strong growth moving forward, with an important change of CEO who is determined to aggressively grow and expand this successful business.

New CEO, fresh mandate

IDT was founded in 1975 and was privatised through a management buyout from the VCP by IDT's current Chairman Dr Graeme Blackman in 1985. Blackman recently stepped down from his position as CEO. He has been replaced through an internal appointment of Dr Robyn Elliott, who was effectively the Chief Operating Officer of the company prior to the promotion. Blackman has significantly wound back his involvement with the business to allow the new CEO full reign within that role. It's an important and good appointment.

It would appear that Elliott has been given authority to run the business in her own style. This is important as investors and shareholders can expect more open communication with the market which may increase interest in this stock. For a company currently trading on a PE ratio of 13.4 times with strong growth anticipated to continue, this stock appears well undervalued.

IDT makes bulk active pharmaceutical ingredients (APIs) for pharmaceutical companies and in recent years (2005/2006) expanded to making finished drugs (mainly in tablet and capsule form). This would contribute to between 40% - 50% of its revenue stream. The remaining 50% - 60% of revenue is derived from assisting with the development of new drugs, either from assisting with making APIs and finished product for clinical trials, or from its Phase I clinical trial testing business, CMAX in Adelaide, acquired in 2002.

The CMAX acquisition was a surprising one for the company, although it's believed the purchase price was attractive. The business was also acquired to ensure the continuity of services to many of IDTs customers.

IDT began making its first cytotoxic API for the US market in 1998. In fact, most of IDTs business continues to be based in the US. Problems occurred with the business back in 2003 when two of the drugs the company made, cisplatin and carboplatin, came off patent. These two products generated around 50% of IDT's revenue and all of a sudden the manufacture of these APIs came under strong pricing pressure from low cost generic

Cont'd over

manufacturers in India and China. In 2006 the company stopped manufacturing these drugs.

Today IDT manufactures about six or seven different drugs with none of its APIs expected to come off patent in the medium term. It concentrates on making API's for branded pharmaceuticals and recently approved new chemical entities.

Growth in IDT's business is expected to be driven by several factors.

1. The Pfizer contract

In January 2007, IDT announced that it was expanding its business relationship with its most important client **Pfizer**. The importance of this new development project has now become clearer. Pfizer has paid for the installation of a $20 million facility at IDT to make sufficient material for Pfizer's forthcoming Phase III oncology study. The 4000 litre facility is expected to be commissioned by mid year. Being a smaller company, IDT believes it has the capacity to build a new manufacturing facility significantly more quickly than a larger pharmaceutical company.

This contract is important for several reasons to IDT. Firstly it provides significant current revenue to IDT. Secondly it's a major achievement for IDT that signals to other major pharmaceutical companies IDT's specialty contract manufacturing capabilities. The greatest upside comes if the drug is approved for sale, with IDT being a logical candidate to manufacture the API and even the finished product on behalf of Pfizer. Such a contract would need to be negotiated and IDT may or may not be the sole supplier. It would add considerable and long-term revenue to IDT if the product gets to market.

2. Expansion into Europe

IDT currently conducts the majority of its business in the US. Moving forward, the company will seek to expand its presence in Europe. The company has previously operated by way of word-of-mouth and will launch a marketing campaign to help grow sales.

3. NCE launches

Aside from the large potential upside if the Pfizer drug makes it to market, there are a growing number of drugs moving to later stage clinical development globally, called 'greening', that IDT could manufacture should they pass clinical development.

In 2006, the global API market was worth US$65 billion with a trend to further outsourcing. Of that amount US$27 billion (42%) is currently outsourced, growing at around 7% a year. In the US the outsourcing is higher with 47% outsourced (US$15 billion). India and China capture much of the generic API manufacture. But the IP control in those countries is poor and there is a preference to make NCEs outside of those countries.

The company's major clients are **Pfizer**, **Wyeth**, **Amgen**, **Johnson & Johnson**, **Merck**, **Celgene** and **GlaxoSmithKline**. For Celgene the company makes the finished oncology product Thalomid. Late last year Wyeth had an oncology product approved for which IDT is the sole supplier. There are currently two to three clinical programs underway by IDT's customers that look like they might move into Phase III trials. If these products get to market in around three years time, IDT may well win the manufacturing contract, potentially as a sole supplier.

The company has recently bought two adjacent properties to expand its manufacturing activities, doubling its API manufacturing capability by the end of FY2009.

4. Move up value chain

An additional growth strategy for the company involves moving up the value chain with the products it helps develop and manufacture. IDT is considering working in partnerships with drug developers, to retain some intellectual property over its any internally developed manufacturing processes with a view of receiving a profit share or royalty from sales of drugs it helps develop.

This approach will only be suitable for some companies that would prefer to form an alliance with IDT, where presumably costs as

well as upside would be shared. The end product could be sold to a company such as a mid-sized generics company. IDT is currently in discussions with several companies to form such development alliances.

Financials

IDT is currently capitalised at $82 million. In CY 2007, the company generated a net profit of $6.1 million, representing a PE ratio of 13.4 times.

In the last half year, sales increased by 16% and net profit by 31%. In FY2007, sales increased by 6.6% but net profit soared by 51% over the previous corresponding period. The company has flagged 'continued strong double digit growth. The performance in the second half of the financial year is always stronger than the first because pharmaceutical companies generally place their orders around September each year with the manufacturing being undertaken in the second half (raw ingredients take up to six months to ship over to IDT). The stock is paying a 5% dividend yield (based on last 12 months) which is 30% franked.

Summary

The change in the helm at IDT brings with it a new openness about the growth strategy for the company. The new CEO has an excellent understanding of the intricacies of the IDT business having worked with the company for 10 years and most recently as its COO. Even a name change is anticipated (to the more commercial 'IDT' as distinct from Institute of Drug Technology Australia) and a new logo is planned for the company.

IDT has overcome challenges of the past thrown at it by the emergence of low cost drug manufacturers from India and China. Having secured the core business, it's a very suitable time to launch a more aggressive growth path for the company.

Bioshares recommendation: **Strong Buy**
IDT has been added to the Bioshares Model Portfolio

Bioshares

BioMD Readies for Phase II Trial

BioMD (BOD: 9.1 cents) has shipped its first batch of material to South Africa for its Phase II trial to repair tissue damage in 50 patients with congenital heart defects. BioMD is commercialising a multiple application technology, called the ADAPT tissue engineering process, which is being applied to the processing of bovine tissue for human implant. There are several applications of this technology, with BioMD concentrating on five core uses. The forthcoming clinical trial is a major milestone for this company.

Phase II study to begin in April

The Phase II study is due to begin in April. The bovine tissue treated with the ADAPT process will be implanted into 50 young adults with heart deformities over a six month period. The tissue was processed at the **Royal Perth Hospital**, taking about two weeks to complete. This will be the first human trial using this technology.

Results from this trial are expected in the second half of 2009. The trial will measure blood markers and will use several imaging techniques (ultrasound and MRI scans) to assess the durability of the implanted tissue.

BioMD believes it has developed the next generation tissue processing technology. Synthetic implants harden over time, reducing functionality, and other animal tissue processing techniques are prone to cause calcification. Previous preclinical studies have shown there are no signs of calcification of the tissue after 200 days using the ADAPT process with even evidence of endothelial cell and capillary formation within the implanted tissue matrix.

Strong growth anticipated in tissue repair market

According to a market research report, demographics such as rising obesity levels are expected to contribute to strong growth in soft tissue meshes over the next three to four years. In 2007, the market in France, Germany, Italy and the UK for soft tissue repair products was US$175 million, and combined with the US market was worth over US$1 billion. The market in the US alone is anticipated to grow to over US$1.5 billion in over this period.

Other evidence of growing interest in this market is the takeover bid earlier this month launched by Covidien for UK-based **Tissue Science Laboratories** for US$80 million. TSL's core technology is a collagen-derived porcine tissue implant used in hernia repair.

Five core applications for BioMD

BioMD will concentrate on developing the technology for five core applications. These are for use in heart repair (moving into Phase II studies next month), treatment of biological heart valve tissue, hernia repair, orthopedic applications such as repair of ligaments, and in plastic surgery for instance in mastectomy procedures.

The company will be seeking to form licensing or collaborative deals with partners for different applications. Whilst data from the current Phase II trial will be very useful, there may be sufficient preclinical data to complete a licensing deal in some applications before the completion of this trial.

Summary

Strong growth is anticipated in the soft tissue repair market. Lifestyle factors are contributing to this growing market and BioMD potentially offers a next generation product. To commercialise its applications successfully BioMD will need to form collaborative partnerships or licensing arrangements, which will be major validation of the commercial potential of the technology.

BioMD is capitalised at $8 million with $1.8 million in cash at the end of last year, which should give the company at least 12 months funding.
Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Cytopia Builds its Pipeline

Cytopia (CYT: 29 cents) is a developer of small molecule drug candidates. The company has made steady progress in building a pipeline of drug candidates that target a class of proteins called kinases. However, it should be noted that Cytopia's lead compound, CYT997, has a different mechanism of action. CYT997 is a vascular disruption agent that works by disrupting tubulin polymerisation. Tubulin is a component of cellular architecture. CYT997 is also thought to be capable of initiating cell death in cancer cells.

Cytopia recently announced that it had selected a compound, CYT387, for formal pre-clinical development. CYT387 is a potential treatment for myeloproliferative diseases (MPDs), a group of diseases of the blood in which the over-production of blood cells occurs. In turn, the prospects for arterial or venous clotting or severe bleeding increase, as does the likelihood for strokes and heart attacks.

There are two main groups of MPDs, those termed 'Philadelphia chromosome positive' (Ph. +), which include chronic myeloid leukemia (CML), and are distinguished by the causative effects of the bcr-abl fusion gene. The other group of MPDs is termed 'Philadelphia chromosome negative'.

The most common Ph. negative MPDs include polycythemia vera, essential thrombocythemia and idiopathic myelofibrosis. These in turn are characterised by the presence of a mutation on the JAK2 kinase, termed the V617F mutation. (A mutation on the JAK2 gene causes the substitution of phenylalanine for valine at position 617 in the JAK2 protein.)

The mutation is found in about 95% of polycythemia vera cases, 50%-60% of essential thrombocythemia cases and idiopathic myelofibrosis cases. In fact the discovery of the V617F mutation has now shifted the definition of the disease so that an MPD (excluding CML) is now V617+ or V617- , with V617+ polycythemia vera and V617+ thrombocythemia regarded as the chronic phase myelofibrosis seen as an accelerated phase of the disease. This is similar to how CML is broken down into chronic, accelerated and blast phases.

The very strong correlation of the mutation to the disease marks the MPDs out as an attractive drug opportunity because treatment of the disease is arguably mechanistically simple. Blocking the effect of the mutation should theoretically result in disease remission in a clear-cut way. The more specifically it is addressed or blocked by a drug, then the more likely the side effects are contained.

The development pathway for CYT387 is extremely attractive because once satisfactory dosing information is obtained in Phase I studies, then efficacy studies will fairly rapidly reveal the effectiveness of the drug candidate because the effectiveness of disease treatment can be measured simply and quickly by blood analysis. Cytopia expects to lodge a US IND in by Q4 2008.

CYT387– Competitive Opportunity

Current treatments for MPD's are limited. They include phlebotomy (the centuries old practice of therapeutic bleeding) and the use of myelosuppresive agents such as radioactive phosphorus and hydroxyurea.

Currently there are at least five other companies that have initiated JAK2 programs targeting MPDs (see table below). **Incyte**, a genomics company that morphed into a drug developer in 2002, has the most advanced candidate in clinical trials, INCB18424. Incyte is testing the compound not only in myelofibrosis, but also in rheumatoid arthritis, psoriasis, multiple myeloma and prostate cancer. The strategy to test the drug in so many non-MPD indications as well as myelofibrosis (which is an advanced stage MPD disease) suggests that company has developed a less specific agent, compared to Cytopia's CYT387 or indeed even others in development by other companies.

The competition objective being addressed by Cytopia is to develop a highly specific drug that delivers a more favourable safety profile than its competitors.

Although Cytopia is not a current leader in the JAK2 MPD drug development group of companies, in reality the numbers of competitors are few, with as far as *Bioshares* can ascertain, no significant involvement to date by large pharmaceutical firms. This fact lends support to Cytopia's strategy to license out CYT387, when sufficient and appropriate data has been gathered, to a pharmaceutical partner.

Update on CYT997

Cytopia has moved CYT997 into a Phase II trial with multiple myeloma patients. Multiple myeloma is a cancer of the platelet blood cells. This indication (as a blood-based cancer) is outside the original focus on solid tumours. Cytopia has selected this development option because of data gained in pre-clinical studies of the compound. An opportunity exists for drug developers to find compounds that can treat multiple myeloma once other options have been exhausted and also because current treatments such as Velcade, Revlimid and Thalomid exhibit certain toxicities.

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JAK2 Drug Developers - Myeloproliferative Disorders

Company	Num. Drug Cand. (all indications)	INDs filed (all indications)	Founded	Employees	Cap'n ($M)	JAK2 Candidate	Status
Cytopia	3	1	1998	46	$25	CYT387	Pre-clinical
Exelexis	11	14	1994	735	US$710	XL019	Phase I ongoing
Incyte	11	12	1991*/2002	196	US$866	INCB18424	Phase II
TargeGen	3	2	2002	~60	Private	TG101348	Phase I/II
Astex	8	?	1999	~100	Private	AT9283	Discovery
S*Bio (Singapore)	5	?	2000	~50	Private	SB1518	Pre-clinical

*Founded as a genomics company; refocused as a drug developer in 2002

Recent research has revealed that aberrant signalling in the NF-kappa B pathway is implicated in multiple myeloma. It would be of no surprise if researchers ascertain that point mutations are involved in multiple myeloma, and in fact patients who respond to Velcade are thought to be respond positively because of mutations in proteins in the NF-kappa B pathway.

Cytopia intends to commence a Phase I/II trial of CYT997 in glioblastoma multiforme, a cancer of the brain. Glioma's are currently treated with surgery, radiotherapy and drugs including Temodar and platin class cancer agents. These tumours are highly vascularised, which means they may be amenable to treatment with vascular disruption agent such as CYT997. The Phase Ib dosing component to determine the optimal dose will see CYT997 administered in combination with carboplatin and one other chemotherapeutic on a 21 day cycle, with CYT997 being administered by infusion for 24 hrs on day 2 of the cycle. A two-stage phase II part of the trial will follow. Between 25 and 30 patients will be enrolled overall in the trial.

Commentary

Cytopia has been focusing on building a drug development pipeline with both breadth and depth. The company's strategy has been to harness a drug discovery engine that is based on understanding of a special class of proteins called kinases, which are involved in cell signalling.

Cytopia's objective is to develop a steady stream of drug candidates, and with the selection of CYT387 for advanced pre-clinical studies, the company has demonstrated its comprehensive drug discovery skills.

What makes Cytopia attractive, and even more so at its current valuation of $25 million, is that it is structured to accommodate the high risk of failure in drug development, by building the capacity to develop many compounds. It has partnered out drug development pertaining to the JAK3 kinase for transplant-rejection with **Novartis**, and now has two compounds in development, over which it holds 100% ownership. The company has the capacity to bring forward more compounds, although development is constrained by funding. Our expectations are that the company will bring forward into pre-clinical development a JAK2 targeted candidate for the condition of pulmonary arterial hypertension and a second generation follow-up to the FMS inhibitor CYT645 in the near future.

The very poor state of equity markets has seen many biotech stocks driven to very, very low prices. In the case of Cytopia, its share price is offering exceptional value at present and the stock sits well under the value range that biotech investors have regularly awarded companies that have drug candidates at the Phase II stage of development.

Milestones to monitor

- Commence glioma trial Q2 2008
- Conclusion of CYT997 Phase I Oral H1 2008
- Interim analysis multiple myeloma trial Q3 2008
- Filing of IND for CYT387 Q4 2008

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bioshares Model Portfolio (28 March 2008)

Company	Price (current)	Price added to portfolio	Date added
IDT	$1.90	$1.90	March 2008
Circadian Technologies	$1.03	$1.03	February 2008
Patrys	$0.37	$0.50	December 2007
NeuroDiscovery	$0.13	$0.16	December 2007
Bionomics	$0.36	$0.42	December 2007
Cogstate	$0.10	$0.13	November 2007
Ventracor	$0.32	$0.625	October 2007
Sirtex Medical	$3.32	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.37	$0.66	September 2007
Starpharma Holdings	$0.32	$0.37	August 2007
Pharmaxis	$2.24	$3.15	August 2007
Universal Biosensors	$0.90	$1.23	June 2007
Biota Holdings	$1.24	$1.55	March 2007
Probiotec	$1.19	$1.12	February 2007
Peplin Inc	$0.52	$0.83	January 2007
Arana Therapeutics	$0.92	$1.31	October 2006
Chemgenex Pharma.	$0.78	$0.38	June 2006
Cytopia	$0.29	$0.46	June 2005
Optiscan Imaging	$0.25	$0.35	March 2005
Acrux	$1.00	$0.83	November 2004
Alchemia	$0.43	$0.67	May 2004

Portfolio Changes – 28 Mar 2008

IN:

IDT has been added to the portfolio (see article on page 1)

OUT:

Tissue Therapies and Phylogica have been removed from the Bioshares portfolio due to short and medium term funding issues respectively. Tissue Therapies wound trial has yet to begin and at the end of last year had access to $1.4 million. Phylogica has sufficient funds for at the next 12 months however the portfolio is being weighted towards companies with more secure funding positions.

How Bioshares Rates Stocks

For the purpose of valuation, *Bioshares* divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, *Bioshares* grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

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

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