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In this edition...
Over the recent past Biota has received much attention because of royalty revenues from the sale of the flu drug Relenza. With this income stream weakening for the time being, the focus for investors is on the company's drug development pipeline, which it has broadened considerably. It plans to spend about $25 million to complete a Phase IIb trial of its HRV drug candidate in patients with chronic asthma. Clinuvel Pharmacueticals has expanded its clinical studies of Scenesse into patients with Vitiligo. Impedimed continues to move the market acceptance of its L-Dex diagnostic through CME programs.
We also update readers on four more companies reporting profits for FY2010.

The Editors
Companies Covered: BTA, CBB, CMP, CUV , HGN, IPD, MVP, TDX

	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 - May '10)	49.2%
Year 10 (May '10 - Current)	-7.0%
Cumulative Gain	**169%**
Av Annual Gain (9 yrs)	**18.5%**

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Bioshares

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

Biota Invests $25 Million in Phase II HRV Program

The volatility and heady share market swings of the last 18 months, caused by the influenza pandemic threat in 2008-2009, appears to be over for Biota Holdings. However, Biota is now in a very secure position financial position with a well structured pipeline.

At June 30, 2010 Biota had just under $105 million in cash, after making a $20 million distribution to shareholders in December. The company generated revenue from operations of $67 million which included Relenza royalties of $63 million, up from $45 million in Relenza royalties in the previous year. The net profit for the year was $16.2 million, with an R&D expenditure of just under $22 million.

Biota last year elected a new chairman, Jim Fox, who helped build and then sell the very successful Vision Systems for around $800 million. Under the new chairman, one of the key focuses is on accountability for any investments made into new development programs.

Biota is approaching a stage where it has a full complement of development programs and products on the market. Its two acquisitions from 2009 give the company a suite of discovery assets in the area of antibiotic drug development. Over the next two to five years these programs should move into preclinical and clinical development.

The company's RSV (respiratory syncytial virus) program was returned from **AstraZeneca** last year. However, Biota is redesigning its potential drug candidates to deliver a compound with a wider therapeutic window. This program may soon be ready once again to move into Phase I testing. The company's human rhinovirus (HRV) program has commenced Phase IIb studies in the US. The company's long acting flu drug candidate (LANI) with **Daiichi Sankyo** has been filed for registration in Japan. And Biota continues to enjoy a royalty stream from global Relenza sales.

HRV Program Focus

The largest focus for the company at the moment is on the Phase IIb HRV program. This trial will seek to enroll around 400 patients and will cost approximately $25 million. The trial will enroll patients with chronic asthma who have been infected with HRV, the virus which is associated with the common cold.

The primary endpoint will include changes in symptoms. Secondary endpoints will include duration and intensity of viral shedding. The company is aiming to complete recruitment by March next year, however this will depend on the incidence of HRV in the US cities where the trial is being conducted (in 57 centres). If full recruitment is not achieved in coming northern hemisphere autumn/winter, it may take an additional 12 months to complete.

It will not be an easy trial to recruit for, having to prescreen participants with existing asthma first, then to enroll those people once they are deemed to have symptomatic HRV

infection. The participants will then be dosed twice daily either with Biota's drug candidate BTA798 or with a placebo. Of particular interest will be the changes in viral shedding between the two trial groups.

The upside for Biota is that if it can deliver a positive result, it will have a drug program that could move into Phase III testing. At that point it may be in a position to partner the program for final Phase III testing. The aim from such a licensing deal would be for an upfront payment and the first milestone payment to recover all development work conducted by Biota, but also leaving Biota with the upside from a potential blockbuster product (over a billion dollars in annual sales) and enjoy a good double digit royalty stream, which we would estimate at between 15-20% of sales.

Biota is not the only Australian biotech that is moving up in the value stakes by placing larger bets on distinct drug development plays. **Acrux** did this very successfully when it raised $22.5 million in 2007 for its Axiron program and delivered a US$330 million licensing deal this year. **Starpharma** followed suit last year raising $15 million to fund pivotal studies with Vivagel for treating the condition bacterial vaginosis. And **Alchemia** is getting ready to invest $20 million in a Phase III trial with its Phase III HA-Irinotecan program as soon as its generic fondaparinux product receives US approval to market.

LANI Progress

The Biota/**Daiichi Sankyo** LANI drug candidate has been filed for approval with Japanese regulators. Approval may come as early as this year, ready for the next northern hemisphere flu season, but more likely in 2011. The market for flu drugs in Japan outside of flu pandemic threats we estimate is around US$100 million a year. The potential royalty flow to Biota is comparatively small, and we would estimate at between $2-3 million a year (our assumption is that Biota stands to receive around a 7% royalty from sales in Japan).

There is further upside if Daiichi Sankyo can grab more than 30% market share, if the market increases during a virulent flu season, if another serious flu threat arises, and if Biota can license the program outside of Japan. In financial year 2009, the flu drug market was worth approximately US$250 million due to the pandemic flu threat.

LANI is a once only flu treatment compared to Relenza and Tamiflu which need to be taken twice daily for five days. It should have significant appeal over incumbent products.

Biota is seeking to license out rest-of-world rights for LANI. However with the interest in flu drugs subsiding post pandemic fears, it's likely to have become more difficult to negotiate a licensing transaction. Our expectation is that a licensing deal with not be concluded in the short term. However, the potential demand for this drug candidate may change once it is in commercial use in Japan and it is understood how the product's advantages allow it take market share from existing products, and once the post pandemic global flu drug market becomes clearer. Better licensing terms may be achieved in 12 -24 months time, although the down side is that patent life is lost in delays.

Relenza Royalties

Relenza royalties in the last financial year were $63.7 million for Biota. This was up from $45 million the previous year and $20.5 million in 2008. Over the last five years the average royalty payment to Biota for Relenza sales has been just under $35 million.

The global seasonal flu market (which excludes stockpiling) is worth an estimated US$750 million a year and we estimate that Relenza holds around a 20% market share (and around 50% in Japan). Government stockpiling of influenza drugs Tamiflu and Relenza appear to have halted for the moment.

Ongoing royalties from seasonal Relenza sales we estimate at $12 million, although this figure could increase as Relenza gains more market share and as the seasonal market grows. With continued stockpiling or replenishment of stockpiles, royalties should be maintained around $35-40 million, however it is unclear as to whether the stockpiling market will continue following abatement of the pandemic threat and widespread goals to curtail healthcare budgets. Relenza patents expire in 2014 in major markets and in Japan in 2017. Extended patent protection could occur from patents around the inhaler device.

Summary

Biota is capitalized at $161 million with just under $105 million in cash at the end of June. The fortunes of the company are in the short term linked to Relenza sales. Relenza sales are tied to the seasonal incidence of influenza and the threat of pandemic strains emerging. In the medium-to-long term it is tied to the success of new product development such as LANI and the HRV program.

Biota shares are currently trading at attractive levels and the stock may suit investors with a medium to long term investment horizon.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Clinuvel Targets Vitiligo

Genzyme built its business around developing drugs to treat orphan drug diseases, which are diseases that affect small populations and generally thought to offer only niche financial opportunities. Not so as Genzyme has proven.

Genzyme is currently seeking to defend an unsolicited bid for its specialty pharmaceutical business from **Sanofi-Aventis**, which is willing to pay US$18.5 billion in cash for the company.

In Australia there are at least five companies targeting orphan drug diseases. These are Pharmaxis, Mesoblast, Chemgenex Pharmaceuticals, Antisense Therapeutics and Clinuvel Pharmaceuticals.

The appeal of developing drugs to treat orphan diseases is that smaller pivotal trials are required to bring the drug to market, involving hundreds of patients not the thousands that may be the case for say a novel anti-hypertensive drug.

Clinuvel Pharmaceuticals (CUV: $0.21) is developing a pharmaceutical product, called Scenesse, that increases the melanin density of the skin. The first application is for the treatment of EPP, which is a condition defined by an absolute intolerance to direct sunlight. This indication is classified as an orphan disease and the company may be in a position to file for approval by year's end in Europe although 2011 may be a more realistic expectation.

Last week the company announced a fourth application that it will pursue (six indications have now been identified), that being the treatment of vitiligo. Vitiligo is characterised by an inconsistent colouring of the skin which occurs due to lack of melanin in parts of the skin. In the USA, it is estimated that just under 1% of the population suffer from nonsegmental vitiligo, the particular condition that Clinuvel's product may have an application in treating.

In October, Clinuvel will start four clinical trials in vitiligo, two in the USA and two in Europe. According to the company, it has prepared the trial design in consultation with four of the world's leading vitiligo centers that specialise in this condition.

The existing treatment for vitiligo is UVB phototherapy. The treatment first started in the 1980s. However up to 20 treatments are required and it delivers only a temporary effect. In contrast, the Scenesse therapy consists of a small depot injection that lasts for two months.

The success in developing an orphan drug candidate is about bringing that product to market as quickly as possible, using the regulatory assistance that is offered by orphan drug designation. A high price can be commanded from delivering a product for niche patient markets. Step two is to expand the indication into other orphan or non-orphan disease indications. Clinuvel seems very clear about the path to success, with its product already approved by Italian regulators under a special access system, called Law 648/96, and now its sixth potential indication identified.

Bioshares recommendation: **Speculative Buy Class A**

CME Supports Impedimed's L-Dex

The success of a new diagnostic product launched in the US is more often than not governed by gaining reimbursement and coverage from healthcare insurers.

Impedimed (IPD: $0.78) has developed a technology (L-Dex) to assist in the early detection of lymphedema, with the first target market being breast cancer survivors following a mastectomy procedure. In the last financial year the company generated sales of $3.6 million, up 22% over the previous year, with a net loss of $11.4 million.

In March this year the American Medical Association granted reimbursement for procedures using the Impedimed patented technology under a Category III code. This means that health insurers can but are not compelled to reimburse for procures using the Impedimed technology. Reimbursement under that code will start at the beginning of January next year.

From here the next task for Impedimed is to negotiate coverage with insurers and employee groups, of which there could be 1,000 different groups, to cover their members for the procedure under the specific code. This means people covered by those insurance plans will then be guaranteed of reimbursement for procedures using the Impedimed device.

Helping to coordinate this reimbursement process between the insurer and the doctor are managed care organisations. Impedimed has now signed contracts with four managed care groups that represent 23.5 million members in the US. Whilst this does not classify directly as covered lives by insurance groups - Impedimed is seeking to have 20-30 million Americans covered by years end - around three quarters of those members should be successful in getting their procedures reimbursed.

Continued Medical Education

Impedimed also continues to build awareness of its product in the US. Doctors in the US are required to undertake Continued Medical Education. In the first six weeks of a Medscape online medical accreditation session involving the Impedimed technology, almost 4,000 physicians accessed the session including over 2,000 surgeons. A survey from these surgeons indicated that 70% viewed bioimpedance measurement (Impedimed's technology) as the best way to detect subclinical lymphedema and prevent lymphedema at an early stage following breast cancer surgery.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Profit Reporting Companies FY2010 – Part 3

Halcygen Pharmaceuticals			CMP	$0.55
HGN	Cap'n ($M)	$82	PE	25
	FY2007	FY2008	FY2009	FY2010
Sales ($M)	$0.0	$0.0	$0.4	$36.7
Change				8438%
EBIT ($M)	-$1.96	-$2.64	-$4.13	$2.08
Change	20272%	35%	56%	-151%
Net Profit ($M)	-$1.82	-$3.47	-$3.76	$3.25
Change	20401%	90%	8%	-186%

Halcygen Pharmaceuticals – To Pay Dividend

Halcygen Pharmaceuticals reported sales of $36.7 million, which takes into account eight months of sales from the Mayne Pharma International business it acquired from Hospira in 2009. The company posted a net profit of $3.25 million. The result benefited in part (from March onwards) by Halcygen obtaining marketing and distribution rights from Hospira to products sold into the Australian and Asian markets. Halcygen intends to pay a fully franked 2 cent dividend and may pay a special 1 cent dividend following the release of results for the next half year period.

As of June 30, 2010, Halcygen retained cash of $19.7 million, against debt of $14.1 million of borrowings and other financial liabilities. The company expects to pay down its debt in FY2011.

Bioshares recommendation: **Buy**

Cordlife			CMP	$0.36
CBB	Cap'n ($M)	$39	PE	21
	FY2007	FY2008	FY2009	FY2010
Sales ($M)	$9.2	$14.1	$22.9	$24.6
Change	48%	53%	63%	7%
EBIT ($M)	-$3.11	-$0.01	$4.84	$2.78
Change	-61%	-100%	-40408%	-43%
Net Profit ($M)	-$17.94	-$0.26	$6.22	$1.82
Change	172%	-99%	-2502%	-71%

Cordlife – Growth in Costs Impact Bottom-line

Cord blood banking operator Cordlife posted sales of $24.6 million for FY2010, an increase of 7% from the previous year. On a functional currency basis, revenues increased by 29% for FY2010. This is consistent with a 28% increase in new clients for FY2010.

Cordlife recorded a net profit for FY2010 of $1.8 million, 71% less the figure recorded for the previous year. Cordlife's bottom-line was impacted by increased distribution and marketing expenses (+ 32%) and administrative costs (+12%).

Bioshares recommendation: **Not Formally Covered**

Medical Developments Int.			CMP	$0.24
MVP	Cap'n ($M)	$12	PE	14
	FY2007	FY2008	FY2009	FY2010
Sales ($M)	$7.4	$9.2	$8.7	$8.3
Change	13%	25%	-5%	-5%
EBIT ($M)	$1.66	$1.27	$1.19	$1.27
Change	28%	-24%	-6%	7%
Net Profit ($M)	$1.21	$0.89	$0.81	$0.88
Change	51%	-26%	-9%	9%

Medical Developments Int. – To Focus on Europe

Medical Developments International (MDI) markets the Penthrox acute pain management product, in addition to a range of respiratory medicine products. Sales of $8.3 million were 5% less than the previous year's figure. However, the company recorded a small lift of 9% in NPAT, which was $0.88 million for FY2010.

MDI closed the year with cash of $1.78 million at hand, which is being conserved while it waits to complete a tender for conducting a clinical trial that would lead to a European marketing approval for Penthrox. Penthrox accounts for about 60% of MDI's revenues.

Bioshares recommendation: **Hold**

Compumedics			CMP	$0.15
CMP	Cap'n ($M)	$24	PE	54
	FY2007	FY2008	FY2009	FY2010
Sales ($M)	$36.7	$38.6	$38.4	$32.4
Change	-3%	5%	-1%	-16%
EBIT ($M)	$0.99	$1.40	$3.29	$0.98
Change	NA	41%	135%	-70%
Net Profit ($M)	$0.12	$0.76	$2.73	$0.45
Change	NA	515%	261%	-83%

Compumedics – A Weak Result

Compumedics develops and sells diagnostic equipment for use in the areas of sleep disorders, neurophysiology and cardiology. Sales decreased by 16% in FY2010, from the previous year. On a constant currency basis, FY2010 sales declined by 3.6%.

Revenues in the US fell by 26%, in Australia and Asia-Pacific by 2% and in Europe by 15%.

The company reported a net profit of $0.45 million, 83% less than the figure reported a year ago.

Bioshares recommendation: **Sell**

Bioshares Model Portfolio (3 Sept 2010)

Company	Price (current)	Price added to portfolio	Date added
Sunshine Heart	$0.029	$0.036	June 2010
Biota Holdings	$0.90	$1.09	May 2010
Tissue Therapies	$0.21	$0.21	January 2010
QRxPharma	$0.92	$0.25	December 2008
Hexima	$0.30	$0.60	October 2008
Atcor Medical	$0.12	$0.10	October 2008
CathRx	$0.18	$0.70	October 2008
Impedimed	$0.78	$0.70	August 2008
Mesoblast	$1.95	$1.25	August 2008
Circadian Technologies	$0.58	$1.03	February 2008
Patrys	$0.09	$0.50	December 2007
Bionomics	$0.28	$0.42	December 2007
Cogstate	$0.25	$0.13	November 2007
Sirtex Medical	$4.86	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.21	$0.66	September 2007
Starpharma Holdings	$0.48	$0.37	August 2007
Pharmaxis	$1.95	$3.15	August 2007
Universal Biosensors	$1.52	$1.23	June 2007
Acrux	$2.09	$0.83	November 2004
Alchemia	$0.49	$0.67	May 2004

Portfolio Changes – 3 September

IN:
No changes.

OUT:
No changes.

Tyrian Diagnostics Validates Lead RNA Marker for Active TB Test

Tyrian Diagnostics (TDX: $0.013) has announced that it has successfully validated a lead RNA marker for active *Mycobacterium tuberculosis* (TB) infection. The RNA marker is associated with a protein marker drawn from a panel of approximately 70 biomarkers it has identified over several years of research.

Previously Tyrian had collaborated with **Becton Dickinson** on the development of a protein based point-of-care diagnostic using the protein expression of the lead (RNA) marker. However, the program was discontinued due to an inability to achieve a desired level of sensitivity.

Tyrian contracted with the US-based **Public Health Research Institute** TB Centre to perform the validation of the molecular (i.e. RNA) test. The Tyrian RNA TB biomarker was evaluated alongside the current gold standard used for the diagnosis of active TB, which is 16S RNA. However, this is a gene sequence that is highly conserved across (or is very common to) other bacteria, which limits the usefulness of the gene as a specific identifier of TB, let alone sub-types of the bacteria.

The lead marker was selected for development because it appears to be present in high levels for most strains of TB.

Tyrian's reason for developing an RNA-based diagnostic is because RNA is detectable at much lower levels than protein matter. Furthermore, RNA is only detectable when there is active virus because RNA is required for cell replication.

In contrast, DNA-based molecular diagnostics do not distinguish between nucleic acid material originating from either dead or living cells, and as such could contribute to a greater number of false-positive test results. The US company **Cepheid** has developed a DNA-based test for TB. In March 2009, it released the Xpert MTB/RF (Mycobacterium tuberculosis/rifampicin) test which can detect for TB infection and rifampicin resistance at the same time. Rifampicin is an antibiotic used to treat TB.

Partnering Goal

The next step that Tyrian intends to take with the RNA diagnostic is to seek a development partner. Such a partner would likely have the ability to develop a fully integrated molecular diagnostic (MDx) product that could be deployed in a field situation, would have strengths in respiratory or infectious disease testing and would also be capable of defining a clear market strategy for a TB test.

The TB testing market comprises two parts. Latent TB is tested using the tuberculin skin test or interferon-gamma release assays (IGRA) such as Quantiferon Gold, which is sold by Cellestis. However, IGRAs only measure an immune response, but not the presence of the *Mycobacterium tuberculosis*, which means that false negatives can be produced in the early stages of infection. Active TB can diagnosed using smear microscopy, but this lacks sensitivity. Culture-based testing is more sensitive, but takes days to complete. A highly sensitive rapid RNA test, if developed to fit the economic and logistical demands of third world settings where TB is most prevalent, could gain the commercial support of global public health agencies and consortia.

Tyrian Diagnostics is capitalised at $6.5 million and held cash of $3.2 million at June 30, 2010.

Bioshares recommendation: **Speculative Buy Class B**

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
Sell

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical, CathRx, BioMD, Tissue Therapies, Viralytics, Phosphagenics

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