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In this edition...
Tissue Therapies is another company that has selected an alternative commercialisation plan in Europe, and it's a sound decision that shareholders can be pleased with.
Biota Holdings is still looking for a US M&A deal but difficult capital markets and a falling share price are two impediments.
And Acrux's Axiron sales continue to look strong, with a 10% market penetration possible by year's end and a run up to 25% looking likely without too much difficulty.

The Editors
Companies Covered: ACR, BTA, MSB, TIS

	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 - May'11)	45.4%
Year 11 now commenced	-26.3%
Cumulative Gain	**210%**
Av. annual gain (10 yrs)	**21.2%**

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Bioshares

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

Tissue Therapies Bypasses 'The Pharmocracy' – Appoints Contract Sales Teams in Europe

Tissue Therapies (TIS: $0.42) has signed on **Quintiles** to provide the company with a dedicated sales force in Europe to sell its wound healing product VitroGro in Europe. The company has taken a leaf out of Pharmaxis' sales strategy for Bronchitol in Europe which signed a similar agreement with Quintiles in August 2010. Tissue Therapies adoption of the contractor model (extending from manufacturing, to logistics and sales) in preference to the licensing model is yet another indicator of the declining state of bureaucratic pharmaceutical companies, which could now perhaps be referred as 'The Pharmocracy'.

Tissue Therapies anticipates gaining European regulatory approval for VitroGro in 2012 Q2, with sales to commence in the UK, Germany, Netherlands, Austria, Switzerland and north Italy. However, a VitroGro launch in France and the Nordic countries would not follow until 2013 Q4.

Although Quintiles is better known as a contract clinical trials company, it has diversified into managing regulatory submissions, managing pricing and reimbursement activities as well as providing contract sales staff.

Quintiles will be paid a base fee by Tissue Therapies over a five year term, with a double-digit performance-related component kicking in if certain sales figures are exceeded.

There are several advantages to this form of commercial arrangement for Tissue Therapies, with flexibility a primary consideration. Tissue Therapies could, if it wished to at a later stage, license VitroGro to a pharmaceutical company, potentially generating even stronger commercial terms if VitroGro becomes a recognised product with sizeable market share.

One of the reasons Tissue Therapies has elected to use a Quintiles dedicated sales force is that the partnering process with pharmaceutical companies has become increasingly difficult as these the companies experience corporate stress, as evidenced by waves of layoffs (or re-location of jobs on a geographical basis e.g. from Europe to China) from global pharmaceutical companies over the last few years. According to Tissue Therapies, corporate stress is even more acute in companies operating in the wound care space.

A second advantage is that direct employment of personnel in Europe is costly, with a number of countries possessing rigid and inflexible labour markets. While hiring staff may be relatively easy, termination of employment in some jurisdictions is more costly

Cont'd over

– Tissue Therapies cont'd

and time consuming. For a company such as Tissue Therapies that is seeking to launch a single new product, building flexibility to cover these considerations is of strategic and financial importance.

Other Contractors

Tissue Therapies has signed specialised European logistics company Movianto to manage product warehousing and distribution. Movianto manages 46 warehouses across Europe. Belgium-based Eurogentec and Catalent are used for manufacturing and fill and finish respectively.

Price of VitroGro

Tissue Therapies is currently looking at a selling price for VitroGro of £50 or €60 per weekly treatment unit, applied weekly for ten weeks.

US Clinical Trial – A Consideration

Tissue Therapies expects to commence a US 270 patient clinical trial of VitroGro 2012 Q1 in venous leg ulcer patients, to be completed in 2013 Q2. However, the company is yet to decide if it will make the study double-blinded. VitroGro is one of the few, if not the first wound care product that could be evaluated in a double blinded study.

If the company does make the trial double-blinded, then the trial would be extended by six months (to 2013 Q4). At the same time, Tissue Therapies understands that under the BLA approval pathway it must follow in the US, data generated from diabetic foot ulcer trial (scheduled for start in 2012 Q2 and be completed 2013 Q3) can be included in its submission with the FDA.

The design of the US venous ulcer trial as a double-blinded evaluation has the potential to add significant value to VitroGro in the wound-care market where it can deliver superior label claims.

One important aspect of the US venous ulcer trial is that it will include several clinical trial sites in France. This will allow the company to meet its obligation to gain French payment authorisation by having conducted clinical trials of VitroGro in that country.

Summary

Tissue Therapies has diverted from the traditional licensing model but with good reason. Much like Pharmaxis' Bronchitol product for cystic fibrosis, Tissue Therapies has a specialised product that can be sold by a smaller dedicated sales force. The availability to Tissue Therapies in its first targeted region of high quality third party pharmaceutical contractors, from start to finish, is factor that has not always been an option in the commercialisation plans of biotech companies. The bureaucracy and cost cutting strain within pharmaceutical companies has forced another option to the surface in recent years for drug and medical product developers.

Tissue Therapies has exchanged licensing risk for contractor risk and will need to manage its relationships with these companies extremely diligently. Appropriate resourcing of the company's oversight capabilities should be a priority going forward. However with Quintiles providing dedicated sales teams to sell only the VitroGro product, it removes the risk that its product will lose priority and focus in the hands of a larger multinational licensee.

Tissue Therapies is capitalised at $58 million and held cash of $13.5 million at September 30, 2011

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Mesoblast –Clarification

A correction to last week's piece on Mesoblast: last week we looked at heart failure treatment results using stem cells that were presented at the American Heart Association's annual meeting. We noted that Mesoblast increased left ventricle injection fraction (LVEF) by 7%, in absolute terms, in its best performing cohort, that being its smallest dose of cells at three months.

We compared this with results from an autologous stem cell therapy, whereby cardiac stem cells were taken from cardiac bypass surgery, isolated, grown and readministered six months later. This group showed an increase in LVEF from 30.3% to 38.5% at four months. This represents an 8.2% improvement in absolute terms (from 30.3% to 38.5%) at four months, compared to the 7% absolute increase with Mesoblast's best result. We incorrectly last week compared Mesoblast's absolute increase with the percentage change of the baseline figure in the autologous group.

Mesoblast believes its patient group was a more difficult to treat population, because they were not considered to have reversible ischemia at time of implant and were not eligible for bypass surgery. CEO Silviu Itescu said that by chance all of the patients in their lowest dose group that delivered the best result in fact were found to have reversible ischemia, delivering a comparable result to the autologous study. The difficulty with the autologous therapy is that patients, in this case, had to wait six months after bypass surgery to grow the cardiac stem cells that were implanted. There was also no mortality data released from the autologous trial.

Itescu believes the patient population chosen in the autologous study, those being patients undergoing bypass surgery, is an easier patient population to treat with improvement in ejection fraction to be expected. Mesoblast is positioning its therapy, Revascor, for a different patient population.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Acrux Update

There is good news for Acrux (ACR: $3.07) on two fronts: Axiron continues to build market share in the male testosterone replacement market; and the market for testosterone therapy products continues to display strong growth.

With respect to market share in the US, Axiron had 8.8% of the market at the end of October, after only seven months of selling to specialists and five months to general practitioners. At this rate we expect market share will exceed 10% of the market by year's end and achieving 20% of the market by the end of 2012 is a realistic target.

The other good news is that the testosterone market is growing at just under 16% a year at the moment in unit sales. This compares to 29% growth in 2010, with about 9% of that attributable to price increases and 20% from volume increases. In 2010 the total market was worth around US$1.3 billion in the US, with transdermal products, such as Axiron, making up US$1.2 billion of that figure.

At the moment there are co-pay arrangements for Axiron, until the product achieves widespread reimbursement from payors, which takes around 12 months from product launch. There should be a significant wind back of this rebate by mid 2012, which means the payments to Acrux should increase for three reasons.

The first is that overall sales value will increase. The second is because Acrux's royalty is on a tiered system, where its royalty rates increase with sales. And thirdly, the higher sales should start to trigger some of the remaining US$195 million in potential milestone payments.

Acrux has forecast Axiron related payments this financial year of US$7-$8 million, and around US$40 million in next financial year. The 2013 figure we expect is conservative.

If the company continues to build market share by 1% a month, then Axiron sales in FY2013 could reach US$300 million based on a 20% market share. At a 15% royalty (we believe the top royalty rate will be around 20%), that translates to a royalty flow of $45 million, excluding any milestone payments, which we estimate might be US$20 million in that year.

At the end of October, Axiron was being prescribed to 28% of new patients by specialists and 25% of new patients by GPs. It appears that Eli Lilly is securing about one quarter of the 'low hanging fruit' in this market.

To make further inroads against the leading Androgel products is now going to take some real marketing muscle, something we believe Eli Lily has the capacity and intention to do.

Orion Facility Fire

This week there was a fire in the basement of Orion Corporation in Finland, the contract manufacturer that makes Axiron. The fire was contained to the basement. Whilst production was stopped, it is expected to restart next week. The fire has not interrupted sales of Axiron.

Axiron Outside of the US

Acrux expects Axiron to gain approval in Europe and Australia by mid 2012. The margins are smaller outside the US, with prices around 40% lower in Europe. The price in the US is US$275 per month. The market outside of the US was worth only around US$200 million in 2010. It is expected Eli Lilly will look to grow this market, particularly in the higher priced markets.

A US$2.5 Billion Market Potential

The market for testosterone replacement products is expected to continue to grow. The drivers are an aging population and a more active approach to men's health. Based on the above growth rates, the testosterone replacement market in the US alone should reach US$1.5 billion this year. At current growth rates, this could reach US$2.5 billion in five years time.

It appears there will be two dominant players in this market, those being Abbott (with Androgel 1% and 1.62%) and Eli Lilly. It will become difficult for other groups to compete unless they have a significantly differentiated product. Endo Pharmaceuticals' Fortesta, which was launched at the start of 2011 before Axiron, has only around a 2% share.

And there is the market outside of the US for Eli Lilly to grow, using its existing sales force that also sells the drug Cialis, which competes with Viagra.

Acrux CEO Richard Treagus said Eli Lilly has a substantial marketing budget to support Axiron. The product is being marketed to specialists and GPs however direct-to-patient marketing has yet to commence. Treagus not see any threats emerging to this product at the moment.

Acrux has reduced its expenditure to $6 million a year net of technical service work for Eli Lilly. It had $33 million in cash at the end of June and expects to pay its next dividend in August 2012.

Bioshares recommendation: **Buy**

Bioshares

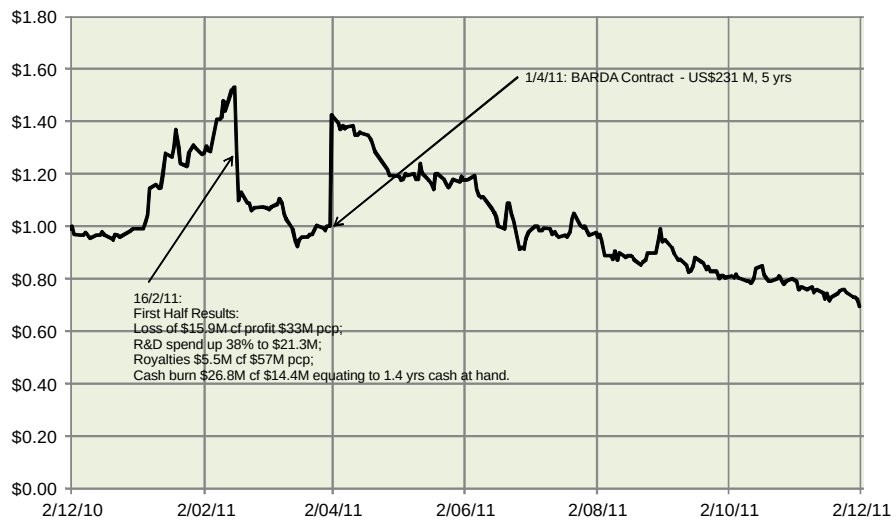
Biota AGM Report – Options for US Corporate Activities Delayed

At the Biota (BTA:$0.72) AGM this week, Chairman Jim Fox said that the company's plan to present a proposal to shareholders regarding the future organisation of the company had been delayed by three months, citing turbulence in global markets as the cause.

Biota appointed US life science investment bank Piper Jaffray in March 2011 to assist with exploring options for recognizing value in the company. Options being considered include the costs and benefits of a Nasdaq listing, either through an existing cash box company or through the formation of a US entity and working with a similar and like minded US company with a view to a combination of businesses but also coupled to a US listing.

Biota's share price has languished this year, falling 52% from $1.53 to $0.72 today (see chart). This is despite the company being awarded a five year contract to the value of US$231 million by BARDA (Biomedical Advanced Research and Development Authority) to develop laninamivir (called Inavir in Japan), the long acting neuraminidase inhibitor for the treatment of influenza for the US market. BARDA is a US government agency within the Department of Health and Humans Services responsible for the advanced development, acquisition and stockpiling of biodefense materials. Biota retains the rights to laninamivir outside of Japan (ROW).

Price Chart – Biota Holdings



The details of potential entitlements to laninamivir for the ROW have not been fully resolved with Biota's partner Daiichi Sankyo. However, with the product being at the Phase I stage of development for ROW commercialisation, commercial licensing royalty rates back to Daiichi Sankyo would possibly be about 4% if the product is co-owned and Biota facilitates full commercialisation past Phase I. It should be noted that the BARDA contract is with Biota, not Biota *and* Daiichi Sankyo together, and Biota will own the marketing rights to the drug if it completes the development.

The Biota share price experienced a dramatic slump when the company released its half yearly results in February, posting a $15.9 million loss. One explanation of the share price slump is that investors reacted to the calculation that Biota's cash at hand of $77.5 million (as of December 31, 2010) supported 1.5 years of operations of annualised net operational cash flows (cash burn) of $53.6 million with potentially no significant royalty income to offset clinical development costs based on last year's Relenza sales.

However, by June 30, (annual) net operational cash flows had fallen to $34 million with cash at hand of $70 million, covering net operational cash flows for 2 years of operations. While Relenza royalties are dependent on the vagaries of the northern hemisphere flu season and stockpiling demands, the prospects for seasonal sales of Inavir in the more mature Japanese flu drug market are different. Inavir recorded sales of $75 million in its first (winter) season. At the AGM, Chairman Jim Fox noted that Biota may receive sales related milestones of up to US$18 million (separate to the 4% royalty Biota receives on sales of Inavir in Japan by Daiichi Sankyo), including a US$3 million payment for when Inavir sales exceed $110 million. Daiichi Sankyo expects Inavir to capture one third of the flu drug market (in the immediate winter season) and Biota expects this first milestone payment to be triggered this financial year or next.

The BARDA program is now the principle activity of Biota, although the company is nearing completion of a Phase II trial with BIT798 for human rhinovirus infection. BIT798 is being evaluated in 300 subjects with confirmed stable asthma and the last patient has now been enrolled. Biota expects results to be available in three to four months. BIT798 targets the virus that causes the common cold. However, the commercial opportunity for such a drug is with asthmatics and patients with lung problems such as Chronic Obstructive Pulmonary Disease, for whom a 'common cold' infection is more debilitating.

Biota CEO Peter Cook said that the early stage projects are of less significance now that the BARDA contract is in place, but also because of shifts in the licensing preferences of large pharmaceutical companies which are more likely to license later stage products, and not the early stage products championed by Biota.

BARDA Laninamivir Milestones

At the Biota AGM, Biota's Vice President of Product Development and Strategic Marketing, Jane Ryan gave an overview of the BARDA-laninamivir program.

Biota has five milestones under the BARDA contract, the first two of which have been submitted. Milestone 1 concerned a Product Development Plan and Milestone 2 related to a Clinical Development Plan and Regulatory License Plan (including the submission

Cont'd over

Bioshares Model Portfolio (25 November 2011)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.35	$1.66	October 2011
Mayne Pharma Group	$0.470	$0.435	September 2011
Genetic Technologies	$0.13	$0.18	August 2011
Acrux	$3.07	$3.37	June 2011
Bioniche	$0.69	$1.35	March 2011
Somnomed	$1.08	$0.94	January 2011
Phylogica	$0.056	$0.053	September 2010
Biota Holdings	$0.72	$1.09	May 2010
Tissue Therapies	$0.42	$0.21	January 2010
Atcor Medical	$0.08	$0.10	October 2008
Impedimed	$0.52	$0.70	August 2008
Bionomics	$0.53	$0.42	December 2007
Cogstate	$0.23	$0.13	November 2007
Sirtex Medical	$4.20	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.44	$6.60	September 2007
Pharmaxis	$1.07	$3.15	August 2007
Universal Biosensors	$0.80	$1.23	June 2007
Alchemia	$0.290	$0.67	May 2004

Portfolio Changes – 2 December 2011

IN:
No changes

OUT:
No Changes

– Biota cont'd

of an IND with the FDA). Milestone 3 is based on developing a manufacturing facility plan and Milestone 4 is based on developing a manufacturing feasibility plan. Milestone 5, an 'implementation step' covers all aspects of a submission of a New Drug Application with the US FDA.

Biota envisages a clinical development program to include three Phase I trials (one exploring cardiac safety, one drug profiling and one in asthmatic patients), three Phase II trials (in adults, the elderly and in children patient groups), three Phase III trials (a US adults study and an EU adults study, and a pediatric study), and finally device handling studies. An FDA submission is expected to occur in 2016.

In 2012, Biota expects to transfer laninamivir from Japan to the US, meaning that drug product and inhaler device manufacture and development processes will be set up in the US.

Comments

Biota has now shifted its priorities to make the BARDA contract its number one priority. The company's employment of Piper Jaffray to 'solve' the company's valuation crisis is not guaranteed given that developments in global finance and equity markets may overtake the plan once more.

Biota has the ability to continue with its plan to fulfil the BARDA contract, without necessarily merging with a US company or list on a US exchange. A merger will not necessarily add any professional skills or synergies with Biota's operations, merely creating a new object of investment interest for investors based in the US.

The chief uncertainties for investors is firstly that the BARDA program is being undertaken without a drug supply contract in place, although the likelihood that a contract will ensue is reasonably high and secondly that terms with Daiichi Sankyo have not been resolved.

The profile of laninamivir is well established so the technical risk is low. The second important point is that the program has been fully funded by a US agency which may at the end of the contract become the buyer of the drug (on a stockpiling basis). The upside is that this buyer would potentially commit to hundreds of millions of dollars of product. For the US, Biota can aim to capture pharmaceutical gross margins. Added to that is the potential for Biota to also sell laninamivir directly to other governments including Australia, the UK and in Europe.

We expect Biota will need to obtain bridging finance, to cover costs of the BARDA contract, which are recoverable. There is now a track record of US investors investing directly into Australian biotech company, and a Nasdaq listing or merger with a US entity may not be necessary. In fact, one US hedge fund now has a 10% stake in Biota. This is proof enough that the company, with its BARDA contract, is on the radar of US investors. One of the reasons to merge with a US company is to increase its size and potentially prevent being acquired at a low value. However a falling share price reduces Biota's M&A purchasing power.

Biota's strength is it weakness. It has specialised in developing flu drugs, for which the demand cycle is lumpy and volatile, with a market worth billions of dollars and with only a handful of companies active in the space.

In the words of Chairman Jim Fox, Biota is seeking to shift from being a royalty income business to a gross margin business. When an Australian biotech has the opportunity to do this, it's a positive move for investors. The chance is that it gets acquired in the process.

Biota is capitalised at $131 million and retained cash of $70 million at June 30, 2011

Bioshares recommendation: **Speculative Buy Class A**

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

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