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In this edition...
Biota Holdings has indicated it is not happy with the little value the market is placing on its assets and looks determined to do something about it.
Tissue Therapies appears confident it will hit many major milestones in coming months, including a licensing deal next month. It's a stock readers should consider if they haven't already.
Patrys has clearly articulated what it needs and what it hopes to deliver in the next 15 months. And Pharmaxis is approaching a crucial reassessment of its new drug application for Europe.
The Editors
Companies Covered: BTA, PAB, PXS, 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	-26.6%
Cumulative Gain	**209%**
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.

Biota Holdings – A Takeover Target?

Biota Holdings was holding briefings this week to update investors on the business and its views on the direction the business is heading. The company believes the market is not appreciating the value of its $231 million BARDA contract, and is looking to how that might be corrected, namely through direct access to US capital markets. A merger/acquisition with a US company would facilitate that process.

Relenza Royalties

Relenza royalties in FY2011 were low, only $6.6 million. CEO Peter Cook said the swine flu outbreak in FY2009 and FY2010 caused countries to overload on influenza drugs, and this contributed to the lower sales of Relenza in the last financial year.

Patent Life

Biota will continue to receive Relenza royalties in the US until December 2014 and in Japan until December 2019. Other major regions in the world its royalty rights will expire with patents around the same as the US patent expires. Cook believes it's unlikely there will be generic competition to Relenza because it is an inhaled powder and is not absorbed in the blood stream, meaning competitors will have to conduct their own trials. However this is not completely relevant to Biota, with its royalties ending with patent expiries.

Stockpiling Orders

Stockpiling orders for Relenza are expected to increase for two reasons. Firstly, countries need to replenish old stockpiles of influenza drugs. The shelf life for Relenza is only five years and for Tamiflu is seven years. The second reason is that countries, including the US and the UK, have indicated they will replenish their stockpiles in equal proportions between Tamiflu and Relenza. In 2009, when the US indicated an equal balancing of these two drugs, it held on 15% of its influenza drugs in Relenza.

The US has indicated that there will be a lot of stockpile expiries in 2012

LANI Development

Biota has received a US$231 million contract from BARDA in the US to develop a long acting influenza drug for the US market. It is expected to take five years to complete development, with the company expecting to file an NDA in Q1 2016.

Cook said the BARDA contract is much like a defense contract and that it can be switched off if BARDA is not satisfied with the program or its outcomes.

Biota indicated that it had received some highly conditional offers to license LANI that were not on commercial grounds. Whilst some shareholders are asking the company to license the program now to a major partner, in *Bioshares* view there is little point in doing this now if it has funding to complete development.

Cont'd over

– Biota cont'd

The stockpiling market is a very narrow market to sell into, with only about 20 customers worldwide, something that a small company can easily achieve. Around $2 billion has been spent each year by governments on influenza drug stockpiles since the stockpiling commenced.

Rights to LANI

Biota currently shares the rights to LANI outside of Japan equally with **Daiichi Sankyo**. The company said it is not in any hurry to spell out how the revenue from LANI sales outside of Japan will be distributed.

Cook pointed out that it will be Biota, not Daiichi Sankyo, that will receive the marketing approval for LANI. From there, there will be development costs that will need to be recouped, and marketing and manufacturing costs will need to be paid for, before any profits are distributed equally between Biota and Daiichi Sankyo. Biota does not expect to fine tune this arrangement until it Phase III trials have been completed.

Cook said the key risk for LANI is execution, not technical (given the product's efficacy has already been proven in Japan).

Management Believes Company Undervalued

The view that the company is significantly undervalued by Australian markets appears to be a sticking point for Biota. The company's share price has halved after its US$231 million contract with BARDA in the US was announced. The company is capitalised now at only $145 million with $70 million in cash at June 30.

The Siga Comparison

At its briefing this week, the company cited the example of another company that had received a BARDA contract. **Siga Technologies** was awarded a BARDA contract in 2008 for US$55 million to develop an antiviral drug for Smallpox. Its market value increased from $43 million in 2006 to $122 million in 2008 when it was awarded the grant. The company's value then doubled to $241 million the following year when BARDA indicated it would order material from the company, and then to $716 million when it was given a five year order from BARDA worth $2.8 billion in 2011.

Biota has indicated that it will seek value recognition in other markets if it does not occur in Australia. Direct access to US capital markets will also better facilitate funding for the company's other late stage programs other than LANI. Biota has also indicated that it is open to exploring acquisitions/mergers with other companies. Does this mean the company is potentially a takeover target from a US listed biotech company? We believe that is a strong possibility. Other options such as a backdoor listing is also open, said Cook. A dual listing is also a possibility but not a preferred option. In *Bioshares* view, the most preferred option would be a merger with a slightly larger antiviral biotech company, on terms that would value Biota at a premium.

The company has previously flagged its direction with major decisions well in advance to investors. CEO Peter Cook this week said the company is continuing with its strategy outlined at its AGM last year. This included the following:

1. License LANI to a partner. (It has indicated this will now not occur until the end of development of LANI.)
2. Secure non-dilutive funding for LANI. (Achieved, with a US$231 million BARDA grant.)
3. Secure commercial funding for LANI and license on marketing approval (has secured funding and will now license on marketing approval.)
4. **Consider restructuring of the company in some way to facilitate a significant re-rating of the company and/or its assets.**
5. Any appropriate combination of the above.

Item four is the only remaining item to be addressed. The company indicated at last year's AGM that it would take a year for these steps to play out. That leaves about one month, and the company appears very determined to see better asset value recognition.

A merger with another US biotech company would turn Biota into more of a global biotech business. Last year it acquired early stage drug development assets from the US and UK. The merged business into a US traded company may also make sense, given the company's very large contract with the US Government (BARDA). However, a merger could only be supported by management presumably if the merger price was at a significant premium to Biota's current market value.

We believe an acquisition/merger of Biota is a strong possibility in the short term.

Bioshares recommendation: **Strong Speculative Buy Class A**

Bioshares

Tissue Therapies Approaches Major Inflexion Points

Everything is falling into place for Tissue Therapies (TIS: 44 cents). Results from the company's wound healing study in around 40 patients are due this month. The company is confident of signing a global licensing deal next month for its wound healing technology, VitroGro. It expects to file VitroGro for approval around the end of the year, with a decision expected 45 days later, then start selling the product into Europe in the second quarter of 2012.

CEO Steven Mercer is very confident about the company's prospects and said he will be very disappointed if the company's wound healing product, called VitroGro, does not eventually generate sales well in excess of $100 million a year.

VitroGro is a combination of a number of naturally occurring growth factors that promote skin growth and cell migration. Previous trials have shown the product delivers excellent results in even very difficult to heal wounds. In a trial in 30 patients with venous leg ulcers who's ulcers had not healed even after nine months of best practice compression therapy, VitroGro delivered complete heal-

Cont'd over

– TIS from page 1

ing in one in six patients in just 24 days, with an average ulcer healing of 43% over the 24 day treatment.

Tissue Therapies, through a licensee, expects to start selling the product into Europe into hospitals and wound care clinics where reimbursement approval is not required.

The trial just completed was conducted with a new re-engineered protein which will allow manufacturing costs to be reduced. Previous trials involved a combined number of proteins, but through re-engineering, the same actives have now been incorporated into the one synthetic protein.

That protein is manufactured by Eurogentec in Liege (Belgium) and the syringe filling and finishing is outsourced to Catalent in Brussels, one hour away from the first facility. Mercer is confident the results from the current trial using the newly re-engineered protein will match those, if not improve, the results from earlier trials.

Licensing Deal

Mercer is very confident that a global licensing deal will be completed next month, with discussions down to the final potential partners. A large upfront fee should not be expected by investors, and which is often not the case for device-like products, which is the classification that VitroGro will likely fall into. Tissue Therapies expects to maintain manufacturing. Net royalties to Tissue Therapies we would estimate to be between 20%-25%.

USA – FDA Classification

Approval into the US will become the next priority. In the US the company expects its product will be assessed as a device by the FDA. A decision by the FDA regarding this designation of VitroGro will occur this month.

From there, the company will file an IDE (Investigational Device Exemption) application with the FDA, the documentation which Mercer says is largely complete. The company expects to start recruiting by the end of December, with a CRO already in place and a chief clinician selected for the trial.

What is unknown at this stage is whether there will be a placebo arm, which if there is, will increase the size of the trial. The company will also recruit in France, which is required to achieve reimbursement in that country. It is not expected to be a very expensive trial, costing around $2 million.

Tissue Therapies is capitalised at $74 million. The company runs a virtual biotech company model, although it has doubled its full time employees in recent months from two to four staff. The company had $15.4 million in cash at the end of June. Tissue Therapies has $22.8 million in accumulated losses.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Patrys Sets Funding Agenda to Broaden Clinical Program

Patrys (PAB: 5.6 cents) is now a clinical stage oncology company. Its lead candidate, PAT-SM6, is being tested in a Phase I study in patients with recurrent, in-transit, cutaneous melanoma. A lot of the hard work has been done at Patrys, that being isolating the antibodies and working out how to manufacture them. The next stage, which is a major value creation stage, is testing those antibodies in patients with cancer. Finding funding those additional trials is now the immediate focus for Patrys.

The current Phase I trial is fully funded and is expected to be completed by year's end. It involves nine patients with a single, low dose of PAT-SM6. The company has now completed multiple dose preclinical toxicology, which means the company can move into multiple doses with other trials next year.

Surprising Positive Early Results

The Patrys antibodies have very specific cancer tissue targeting capabilities. In a surprising result – surprising because the current trial is using such low doses – PAT-SM6 was clearly detected in biopsies from two patients in the trial, one in the lowest dose group (0.15mg/kg) and one in the second lowest dose group (0.3mg/kg). Standard cancer antibody drugs on the market use doses 30-60 times as great as that used in these first two cohorts. It's a very promising result, indicating PAT-SM6 is doing just what it should, even at very, very low doses, that is to attack melanoma cells.

To its credit, the company clearly acknowledges its funding requirements for 2012 and beyond, and that anticipated fund raising perhaps explains the weakness of the company's share price. The company had $6.2 million at the end of June. It will need to raise a minimum of $5 million.

What gets many biotechs in trouble is the issue of dilution to major shareholders. CEO Marie Roskrow said the company is not concerned about dilution, with its priority to raise funds and to expand clinical programs. Acknowledging the volatile financial markets, Patrys has a very capable management team that should be able to deliver the funding tp expand its clinical trials program. Roskrow was formerly an oncologist and also an investment banker in the life sciences sector (with Lazard).

PAT-SCI

Last year Patrys licensed back the rights from Astrazeneca to PAT-SCI. This naturally occurring antibody had previously been tested in 51 patients with gastric cancer. Ten year survival data from that trial has become available, that shows a 55% survival versus only 30% in a historic control group that did not receive that antibody. The historic control group should be quite accurate, given it is data that comes from the same clinic where the patients in the active (PAT-SCI) group were treated.

Patrys is seeking to out-license PAT-SCI in 2012, with a full data package to be available by year's end. It has converted the manufacturing of PAT-SCI to Patrys' cell-based manufacturing system. A license agreement could see a $5 million payment to Patrys.

Cont'd over

– Patrys cont'd

PAT-SM6

Next year the company would like to conduct two trials with PAT-SM6. The first would be a trial in multiple myeloma in Germany, in about 10-12 patients. It would not be an expensive trial to run, costing around $1 million. The appeal of this study is that after each cohort involving three to four patients, the company could very quickly get an idea of efficacy in treating this blood-based cancer. And if it works early, Roskrow said there will be a lot of interest in this program immediately

The company would also like to expand the current melanoma study into a multiple dose Phase I/II trial, adding also other solid cancers. This trial would cost around $3 million and would take up to 18 months to complete.

Both trials are expected to start in the first half of 2012.

PAT-LM1

PAT-LM1 may enter into clinical studies towards the end of next year, however it will be dependent on funding. It is a more expensive clinical program to run, because the company needs to pay for the completion of manufacturing process for this antibody. This program would cost $5 million for a Phase I/II solid tumour study. The importance of moving this program forward is that it diversifies the company's focus away from PAT-SM6. This trial will take 12 months to conduct.

Summary

Patrys has an arsenal of naturally occurring antibodies that very selectively attack cancers in the body. Its first trial has shown that at even an incredibly low doses, its lead drug candidate hones in on melanoma cells in the body, just as it is supposed to.

The company has clearly spelt out its objectives for the next 15 months together with the additional funds the company will require. With an experienced management team, a potentially very powerful suite of cancer drug candidates, and an expansion of clinical programs next year, this stock should be getting close to the end of its down trend.

Patrys is capitalised at $14 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Pharmaxis – Six Trading Days to EMA Decision

Pharmaxis (PXS: $0.81) had its meeting with the European Medicines Agency's scientific advisory group last Monday. We expect the stock will be suspended from trading from Tuesday 18 October, when the Committee for Medical Products for Human Use (CHMP) meets to review the report from the scientific advisory group. A decision will be posted on the Agency's website at the end of that week. Pharmaxis will have two days to negotiate any label claims, should the CHMP reverse its earlier decision.

That leaves probably six trading days in PXS stock before a decision is received. PXS has gained 19% in the last two trading days.

Bioshares recommendation: **Speculative Buy Class B** ; Investors with a lower risk exposure appetite may want to trim their holdings in the next few days.

Bioshares

Bioshares Model Portfolio (7 October 2011)

Company	Price (current)	Price added to portfolio	Date added
Mayne Pharma Group	$0.385	$0.435	September 2011
Genetic Technologies	$0.16	$0.18	August 2011
Acrux	$3.35	$3.37	June 2011
Psivida	$4.40	$3.95	May 2011
Bioniche	$0.70	$1.35	March 2011
Somnomed	$1.08	$0.94	January 2011
Phylogica	$0.057	$0.053	September 2010
Biota Holdings	$0.80	$1.09	May 2010
Tissue Therapies	$0.44	$0.21	January 2010
Atcor Medical	$0.06	$0.10	October 2008
Impedimed	$0.50	$0.70	August 2008
Bionomics	$0.45	$0.42	December 2007
Cogstate	$0.16	$0.13	November 2007
Sirtex Medical	$4.60	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.50	$6.60	September 2007
Pharmaxis	$0.81	$3.15	August 2007
Universal Biosensors	$0.90	$1.23	June 2007
Alchemia	$0.34	$0.67	May 2004

Portfolio Changes – 7 October 2011

IN:
No changes.

OUT:
No changes

How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

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

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

(CMP–Current Market Price)

Group B

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

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

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

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

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Circadian Technologies, Biota Holdings, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Mesoblast, Atcor Medical, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec, Allied Healthcare Group

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