ISSN 1443-850X

In this edition...
In this edition, we provide a major report on Hexima, an agbiotech company that has placed itself in a central position for developing the world's first fungal resistant biotech crops with its partner DuPont. We also provide further coverage from the BIO conference in Atlanta held earlier this year and some very relevant issues raised at that meeting relating to biotech crop development. It's one the longer reports we've published in the pages of Bioshares but it is well worth taking the time to read.

The Editors
Companies Covered: ACL, ACG, BTA, CMP, HXL, OMI

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - Current)	16.3%
Cumulative Gain	**126%**
Av Annual Gain (8 yrs)	**14.7%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au
David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 321 (24 July 2009)
ISSN 1443-850X

Bioshares

24 July 2009
Edition 321

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

Extract from Bioshares –

Hexima – To Seize Early Position In Nascent Multi Billion Dollar Biotech Seed Industry

The high level of active discussion over the role of genetically modified food crops over the last 10 years could cause one to believe that genetically modified (GM) plant technologies have been around for decades. But the first commercial GM crop reached the market only in 1996. And given it takes around 10 years to get these products through the development path, this is very much a nascent industry, and one that is anticipated to experience very strong growth over the next 15 – 30 years.

The global agriculture industry is worth US$2.2 trillion dollars. The global population is set to increase by three billion people by 2050. However limited land and water and global warming are factors demanding technology improvements to deliver agricultural product output gains. Where agricultural efficiencies and better yields were achieved in the 20th century from mechanical and chemical means, the 21st century will look to scientific means to deliver improved crop outputs.

Growing Acceptance

After a decade of strong debate about genetically modified (GM) or biotech crops, there is a growing acceptance of biotechnology being applied to agriculture, with 8% of the world's farmland growing 'biotech' crops.

Hexima has emerged as a well positioned, early player in the GM seed industry. Its claim to fame so far is that it has been able to successfully introduce fungus resistant traits into cotton for three successive years. This was a significant achievement, with **DuPont** signing a co-development agreement with Hexima last year to use their respective technologies to deliver fungal resistance into two major global crops, soybean and corn.

The GM seed industry is built around a harmonious relationship between seed technology developers, seed growers and distributors, and farmers. This was certainly the message delivered by farmers who presented at the BIO conference in Atlanta earlier this year (see break out on page 6). The relationships work as follows.

Technology developers either license their technologies to a major seed grower and distributor. For an early stage deal the technology developer may receive around a 7.5% royalty according to a Wilson HTM report in 2007. Alternatively the seed distributor may elect to acquire the technology (e.g. **Monsanto**'s acquisition of **Alellyx** last year).

Alternatively, the smaller technology developer may elect for a co-development deal with a major seed distributor, such as that signed between Hexima and DuPont. Under this type of an arrangement the technology developer can achieve in the order of a 25% royalty according to the Wilson HTM report.

Cont'd over

'Future upside' arrangement

The arrangement between farmers and GM seed growers is designed such that both groups profit from the introduction of improved yields from GM seeds. As a general rule, the GM seed companies are paid for their seeds as a percentage of yield improvements in their crops and/or cost savings from the lower use of chemicals, fertilizers and other inputs such as tractor fuel. So the cost of seeds in a region where a yield improvement of 20% is achieved will be considerably higher than in an area where only a marginal 4% improvement in yield is attained.

The benefit from that improved yield and savings is shared with around 40% going to the seed company and 60% going to the farmer. For companies such as Hexima in a co-development arrangement, their share in the upside is a significant 10% (around 25% of 40%) or thereabouts we estimate.

To put this in perspective, as an example the US corn market is worth US$48.5 billion a year. If Hexima's antifungal trait technology was utilised in the entire US corn industry for a 10% yield improvement, Hexima, we estimate, would receive 1% of US$48.5 billion, or US$485 million a year! We are not suggesting it will be used by 100% of corn producers, but even if it is used by 70% of US corn producers and generates a 7% yield improvement on average, it is potentially a very large future profit share to Hexima, for one seed, in only one market, of around US$240 million a year.

Biotech crops are now being accepted more rapidly and more widely. When herbicide resistant sugar beet was released last year, it is forecast to achieve a 95% penetration in 2009 in only its second year. With corn, the problem with fungal disease is that it occurs in the soil, at the roots, the stalk and then the seeds. Fungal disease is only recognised through decreased yields. Fungus also produces toxins that are hazardous to human health, giving fungal resistant crops another benefit.

An unmeasured but very real upside is also the increase in the

Cont'd over

GM Now 'PC'

In the same way that uranium mining is beginning to be seen as environmentally friendly, in a relative sense – even being supported now by prominent vocal anti-uranium critics in the past such as the Labour Party's Peter Garrett – global warming has made use of GM technology for food crops more socially acceptable, with the ability to deliver drought-resistant crops and decrease carbon emissions.

Unlike the pharmaceutical industry, where drug costs need to be absorbed by payors such as insurers and government health bodies, the GM seed industry is almost a greenfield site that offers fresh development opportunities on a very large scale.

According to a report released by Clive James at the ISAAA (International Service for the Acquisition of Agri-Biotech Applications) for 2008, biotech crops are now being planted in 25 countries with a further 30 countries accepting biotech crop product imports. It took nine years for the first billion acres of biotech crops to be planted up to 2005, then only three years (2005-2008) for the second billion acres of biotech crops to be planted on a cumulative basis. This highlights the growing acceptance and need for improved technologies to increase agricultural output.

In 2008, soy was the dominant biotech crop, with 65 million hectares planted (53% of total biotech crops), with biotech maize crops making up 30%, biotech cotton 12% and biotech canola 5% by hectares. From the same report, the main trait was for herbicide resistance (63%). The only other current trait added from biotechnology at the moment is for insect resistance. The products are now also being stacked with both herbicide and insect resistance.

Drought resistant traits in biotech crops are expected to reach the market by 2012. At the moment there are no fungal resistant traits on the market and no field trials underway in current biotech crops. We believe Hexima's antifungal crop program is the most advanced.

No protests to GM crops at this years BIO, in stark contrast to seven years ago. According to Steve Burrill at this year's BIO conference, it is PC now to apply biotechnology to crops.

Once again, that Hexima has shown its fungal resistance technology to work in field trials for three years running is a major achievementand and is a very appealing feature for seed developers and producers. (The field trial in northern NSW and Queensland showed up to a fourfold increase in a cotton yield from Fusarium fungal resistance and up to a twofold increase in cotton yield from Verticillium fungal resistance with no difference in lint quality. The trial was conducted in a cotton seed variety susceptible to these fungal diseases to emphasize the protective effect. It was these trial results which sparked the interest from DuPont.)

Other future traits are expected to improve product quality, increase yield, flood and salt resilience, and enhanced nutritional attributes such increased Vitamin A in rice.

value of the land to farmers who utilise GM seed technology to generate substantial yield improvements (see BIO coverage breakout on page 6).

Hexima's Core Technology

Hexima has three core technologies. These are the anti-fungal proteins (e.g. the defensin proteins), the insect resistance assets (protease inhibitors), and the MGEV technology (Multi-Gene Expression Vehicle). The defensin proteins are naturally present in a variety of plants and these proteins inserted into cotton seeds generated stunning results in cotton field trials.

To put one gene into a plant is not overly difficult. But to place several genes at the one time and in the right place is extremely difficult, and this is the capability that the MGEV technology brings. This technology will be critical for developing a multiple protein commercial product for fungal resistant corn, where the aim will be to deliver protection against a range of fungal diseases with a durable effect. The trend for increased stacking of traits/proteins into the one crop will also increase demand for Hexima's versatile MGEV technology.

With DuPont and Hexima, the two companies have the full suite of proprietary to tools to develop fungal resistant traits for crops and we believe are leading the way for introducing fungal-disease-resistant crops. Hexima's scientists are acknowledged experts in the anti-fungal field and have arguably made more progress that any other group in the world in developing fungal resistant crops. Professor Adrienne Clarke, Professor Marilyn Anderson and Dr Robyn Heath, founding scientists of Hexima, have written 63 patents (as of March this year).

Biotech Crop Market

In 2008, the biotech crop market generated sales estimated at US$7.5 billion, with biotech seeds being used in only 8% of the world's crops by area. It has the potential to become more than a US$50 billion market by 2025 for the six majors involved in the industry, these being **Monsanto**, **DuPont**, **Syngenta**, **Bayer**, **BASF** and **Dow**.

There are about 12 small technology developers along with numerous academic and government supported institutes

Cont'd over

Severe soil erosion. Biotech crops can allow zero or reduced tilling and prevent such soil erosion. (Photo: BIO presentation, 'Ag Biotech – Improving Farmers' Lives')

A farm on Portugal where tilling of non-biotech crops causes severe soil erosion. (Photo: BIO presentation, Gabriela Cruz, 'Ag Biotech – Improving Farmers' Lives'

Environmental Appeal of Biotech Seed Technologies

Less soil erosion and lower carbon emissions

GM crops have allowed plants to be modified that are resistant to herbicides. GM crops can be grown with a no till (no plough) approach or with reduced tilling. Tilling is conducted to not only break up the soil but also to disturb the soil environment for weeds. The tilling releases carbon into the atmosphere from decaying matter in the soil, increasing carbon gas emissions. Tilling also causes land erosion and pollution of waterways. Carbon dioxide emissions have also been reduced by lower herbicide and insecticide sprays, estimated at 1.1 billion kg of carbon dioxide in the ISAAA report.

It is estimated that in 2007 the reduction in carbon dioxide emissions as a result of reduced fuel use on biotech crop farms and probable carbon sequestration gains would be equivalent in carbon dioxide emission reduction to removing 24% of all registered cars in the UK, according to the PG Economics report.

Reduced pesticide use

Insect resistant GM crops have caused a massive reduction in the use of pesticides on crops. India has seen a huge increase in productivity in its cotton crops using GM technology to reduce insect damage. But the lower pesticide use has also come with a sharp reduction in human deaths from toxic insecticide exposure.

From 1996 to 2007, it is estimated that 359,000 tonnes less pesticide was used globally as a result of biotech crop technologies.

Drought tolerance for warmer conditions

GM seeds have the potential to deliver drought resistant properties to crops to adapt to drier and warmer conditions. With 70% of fresh water used throughout the world for agriculture, reducing agricultural water usage as the world population grows will be essential.

Cont'd over

conducting gene discovery and basic research in the field.

An organised industry

Major agricultural and chemical companies have been buying up seed distribution companies. The market is relatively better organised compared to the pharmaceutical sector because there are no payors such as insurers or government reimbursement bodies in the middle. This is a market where there is plenty of upside for all involved and where the customer is the end user. If a deal offered by a seed company is not favourable to a farmer, then he or she will not buy the seeds. The seed developers had already been in this market and established relationships with customers. And seed developers have been prepared to work together, with sub-licensing arrangements and stacking of two or three traits into the one plant.

Product Development Progress

The fungus resistant corn program has become the lead for Hexima following the deal with DuPont. Hexima is currently selecting the antifungal proteins and protein combinations (and genes that code for those proteins) that will be present in the biotech corn product candidates that it will grow in its glass houses. Once the optimum product and back-up products are chosen, and the glass house trials have been completed, then Hexima will hand the program over to DuPont to conduct field trials with a few of lead candidates. It is expected to take approximately four years to reach the handover point, and another five years after that to get the seed products to market.

The Catch – Long Product Lead Time

The potential value in the Hexima assets would suggests there is exceptional value in the current Hexima stock price. The downside from an investment perspective is that it will take up to 10 years to see the first product reach the market.

However this does not stop value from being recognised by the market before profit share revenue from seed sales are achieved. Last year Monsanto acquired two Brazilian sugar cane breeding technology companies, CanaVialis and Alellyx, for US$290 million. Those acquisitions are not expected to generate products until around 2025.

Once the project has been largely de-risked – once the glass house trials have been completed for corn and the project is handed over

Cont'd over

Other Benefits from Biotech Seed Technologies

Increased food production

Over the last sixty years, the world's population has tripled but the available arable land has remained largely constant. Improved yield efficiencies are part of a solution to solve anticipated food shortage conditions over the next 40 years, as the world's population is expected to increase by almost 50% to 9.2 billion people.

Improved nutritional properties

GM crop technology also has the potential to improve nutritional properties of foods, such as increased Vitamin A in rice and higher omega-3 levels in soybean.

Reducing the poverty of small farmers in developing countries

In 2008, 13.3 million farmers used biotech crops in their fields, an increase of 1.3 million farmers over the previous year. Of this 1.2 million additional farmers starting using biotech crops in India, which now produces 82% of the world's cotton. This is because insect damage has been a major problem in India. But insect resistant cotton strains has allowed a massive productivity capability for growing cotton in India, with now five million farmers using biotech crops in that country. In China 7.1 million farmers use biotechnology crops, and 200,000 in the Philippines.The availability and use of biotech seeds has not been a factor of the farm size, with over 90% of farmers (12.3 million) using biotechnology being resource-poor farmers in developing countries according to the ISAAA report.

Improving the yields and outputs for small farmers has the potential to significantly reduce poverty. Once again farmers will benefit not only from higher outputs, but also from increased farmland values.

There has even been knock-on benefits in India where the dramatic reduction in insecticide use has even meant fewer bees lost from insecticide spraying.

A report from PG Economics released in May this year states that the global benefit to farmers in 2007 from the use of biotech crops totaled US$10.1 billion, and a cumulative total benefit from 1996, when biotech crops were first introduced, to 2007 of US$44 billion. This figure in 2007 represents an average 4.4% increase in production value output for farmers for the four main crops of soybeans, maize, canola and cotton which use biotechnology.

The cost for developing countries of biotech seeds has also been substantially lower, with developing country farmers paying 14% of total technology gains to seed producers, compared to 34% for developed countries (PG Economics report 2009). And developing countries look to be benefiting more from biotechnology crops. In 2007, developing countries' biotech crops increased total farm income by US$5.8 billion compared to US$4.2 billion in developed countries.

More time for farmers

The less work involved in tilling the soil and spraying against pests makes farming more efficient and gives farmers more spare time. This is not just biotech seed company rhetoric but feedback from farmers themselves (see BIO coverage). In India there are cases of cotton farmers having more time to grow chickens as well, and even to grow second crop. In Argentina because of the reduced or no tillage, farmers have been able to grow a crop of soybeans immediately after a wheat crop in the same season according to the PG Economics report.

Bioshares

Hexima's Deal with Dupont – From a Position of Strength

The deal Hexima negotiated with DuPont last year suggests it was negotiated from a position of relative strength following achievment of stunning results in fungal resistant field trials completed in cotton. Although cotton is not the main game, the results showed that Hexima has the skills to successfully incorporate fungal resistant traits into commercial crops in field trials, which no other group has shown to date. The deal puts Hexima on a very solid footing, with both companies to benefit considerably should the technology become commercially successful.

Under the terms of the deal:

- Hexima will share in the profits from future yield improvements in any crops that utilise the Hexima technology, and will not be based on the selling price of the seeds. Our estimate is around 10% of any yield improvement will potentially be received by Hexima.
- The deal sees the two companies sharing respective technologies to deliver anti-fungal properties in corn and soy. Regardless of which company's technology is eventually used, Hexima's commercial outcome will not differ. Hexima is trialing both its own and DuPonts proteins, and DuPont has sent Hexima its corn germ plasm.
- Hexima will co-develop the first application for fungal resistant corn, which is currently in glass house trials by Hexima, and the second application for fungal resistant Soybean, where we estimate future royalties to be in the order of 25% for both applications.
- Hexima controls outcomes from this antifungal technology collaboration for application in other crops such as canola, sugar cane, cotton and cereals such as wheat, and can partner these developments with another company, although will be required to pay DuPont a royalty in such an arrangement.
- DuPont has taken a 5% shareholding in Hexima.
- DuPont is not allowed to partner with any other groups to develop fungal resistant crops for five years while working on this program with Hexima.
- There is a clause in the agreement whereby DuPont is required to sublicense any fungal resistant seeds to other seed companies, to encourage any product is taken up as widely as possible by the market.

to Dupont for field trials – there is the potential for Hexima to monetise its future income stream. This could occur within four to five years time, where future revenues could be predicted with a reasonable level of accuracy.

There are also value creation events that we expect to occur over the next two years, which might include commercial deals for the technology for other plant varieties outside of corn and soy, and progress with the insect resistant trait technology which is at an earlier stage of development. We expect several access deals to occur for Hexima's MGEV technology for stacking or protein expression applications.

And increased awareness of this stock by the market, as a result of additional commercialization deals and achievement of product development milestones, may correct mispricing of this asset independent of product release timelines.

Risks

Technology risks

Although Hexima has successfully delivered fungal resistance traits into cotton, corn is more complicated to work with than cotton. The plant also needs to show durable fungal resistance and target a range of different fungal diseases. This is why several proteins are selected, to prevent fungus adapting to one specific antifungal protein and to provide a broad range of fungal disease control.

The expertise in delivering fungal resistance traits to plants has certainly sparked the interest from DuPont, suggesting strong research capabilities and expertise at Hexima. The technology risk is lowered with the potential to utilise the fungal resistance capability against a number of plant varieties.

Hexima's defensin proteins are natural proteins that come from other plants, so the genetic modifications are subtle. Most of their defensin proteins come from regions in flowers that have evolved highly specialised systems to protect against damage from fungi or insects. For centuries genes have been added to crops through conventional cross breeding of plants. Biotechnology accelerates this process in a controlled, targeted and more accurate manner to deliver improved plant properties. In the words of one of the founding scientists, Professor Marilyn Anderson, 'it is not about putting genes from fish into tomatoes'.

Partnering risk

As with many biotechs, a major risk is partnering. That a major organization may have different internal objectives to a smaller biotech can not be controlled. However Hexima would appear to have negotiated a very solid contract DuPont that will give it some protection from a potential future souring of relationships between the two companies (see breakout above).

Cont'd over

BIO 2008 Coverage
'Ag Biotech – Improving Farmers' Lives'

At the BIO convention held in Atlanta in May this year, one relevant session to Hexima was titled "Ag Biotech – Improving Farmers' Lives". In this session, three farmers, one from the Philippines, one from Portugal and one from North Dakota, gave insights into their experiences with growing biotech crops. There were some surprising outcomes.

Perhaps the most interesting perspective was that from Terry Wanzek, who's family for several generations has worked a large farm in North Dakota. Wanzek, who is also a State Senator, prefaced his comments with the fact that he is a busy, independently wealthy person who was there to convey first hand experiences from the benefits of biotech crops. There were two key benefits (after increased product yield).

Increase in land value; time benefit

The first was the increased value of his land, which had increased potential due to biotech crops. Land that he had previously purchased for $200-$300 per acre was now worth $15,000 an acre. The second benefit was that "we have more time and can work more land". Wanzek recalled a discussion with his wife one evening asking her what was different as they were enjoying an evening barbeque. What was different was that Wanzek and his family now had more time because of the efficiencies that biotech crops deliver.

Rosalie Ellasus gave a small farmer's perspective in growing biotech crops in the Philippines. Pest resistant corn crops provide protection against the Asian corn borer and army worms. Biotechnology has increase yield from 3.3 to 7.3 metric tones per hectare. It requires less insect monitoring and reduces spraying with pesticides. The Philippines was the first country to use biotech seeds for food crops.

Gabriela Cruz, a farmer from Portugal, highlighted the high risk of soil erosion in Portugal, which can be a consequence of intensive tillage. In one example, she presented a photo of extreme soil erosion (see page 3) where non-biotech crops were used, yet farmland adjacent where biotech crops were planted with no tillage remained intact. Another benefit is less cleaning of rivers where there is less soil erosion.

There is a move to what's termed Conservation Agriculture in Portugal, making sure a crop is planted during winter to reduce soil erosion. But Cruz said Conservation Agriculture, with no or little tillage, was not possible without biotech.

The conclusion – "In Europe we know how this story ends, but how long it will take to move to a more sustainable and environmentally friendly paradigm that biotech provides is unknown."

– Hexima cont'd

Summary

Hexima is capitalized at $42 million. It is extremely well funded with $32 million in cash at the end of March or four years funding. Biotech crops are becoming more acceptable and the US$7.5 billion biotech seed market is expected to become a US$50 billion market by 2025 from the adoption of the technology by more countries, from use in additional crop varieties, and from the inclusion of new traits.

Concerns in the past have been raised that farmers will be forced adopt biotech crops and will be at the mercy of the major seed producers. However the pricing model of this industry ensures that farmers and seed developers share in the upside. Farmers also stand to benefit, sometimes substantially, from increased land values where improved output can be achieved. Over 90% of farmers using biotech crops are based in developing countries where the total cost of biotech seeds represents only 14% of total technology gains in those countries (i.e. 85% of the uplift goes to the farmer).

The Hexima technology was discovered and is being developed at the **University of Melbourne** by Professor Adrienne Clarke's research team that includes Professor Marilyn Anderson and Dr Robyn Health. It's a stones throw from **WEHI**, where discovery of the G-CSF protein in the 1980s ended up being commercialised by **Amgen** as Neupogen, which last year generated sales of US$4.6 billion for Amgen with no entitlements ever flowing WEHI. It is a slightly further stones throw from where the Relenza discoveries was made at the former **Biomolecular Research Institute** and the **Victorian College of Pharmacy**. Relenza sales, from which Biota Holdings receives a royalty, remain a fraction of that achieved by similar acting product, Tamiflu, although they may start to escalate in the next 12 months (see update on page 7).

This time around you get the feeling the Parkville Precinct will finally get biotech commercialisation right. If it does, Hexima shareholders stand to make an exceptional return on their investment.

Bioshares recommendation: **Speculative Buy Class A**

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: Phylogica, Pharmaxis, Cytopia, Arana Therapeutics, Starpharma Holdings, Cogstate, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical, CathRx