



F O R A G E N VISIONS

INDUSTRY PROFILE

Foragen Visions Feature: Chromatin Inc.

Progress has been rapid for GM crops, but there are still problems

Chromatin Inc. is a young Chicago-based company that will create significant value for industries developing valuable products using genetically-modified (GM) plants.

It is the hope of the industry that broader acceptance of GM crops will occur as traits that add more value to the bottom line of the producers than current traits are commercialized. Such enhanced “performance” trait varieties will provide producers with higher yields, even during stressful conditions such as drought or cold, and/or have enhanced nutritional value for consumers. Consumer acceptance of GM plants might also broaden as plant-derived medicines or industrial products hit the market.

Unfortunately, limitations of traditional methods of genetic modification have delayed commercialization of the next generation of valuable plant



Mich Hein
President and CEO of Chromatin Inc.

products. Standard methods cause random integration of genes in the host plant’s chromosome, allowing for unanticipated effects on the plant. As a result, products created using these methods typically require hundreds to thousands of modified plants and as many as twelve years of intensive crop breeding to resolve the genetics for each new commercial variety. These random integrations lead to lengthier development timelines and higher regulatory hurdles, dramatically increasing the time and cost of product development. When multiple genes are required, these problems become magnified, limiting the

number of genes that can be “stacked” in a variety and, hence, the complexity of the plant products that can be produced.

A novel solution is born

To overcome these hurdles, the founders of Chromatin developed a novel platform for introducing genes into plants. Chromatin’s technology focuses on designing plant mini-chromosomes-DNA molecules with the capacity to carry and maintain large sets of genes for plant modification. Chromatin’s founders, Drs. Daphne Preuss, Greg Copenhaver, and Kevin Keith surmounted the major obstacle to the creation of mini-chromosomes. They identified plant centromeres-DNA sequences essential for chromosome inheritance-and assembled mini-chromosomes that can be delivered to plants. Chromatin’s proprietary technology allows the identification and purification

foragen

of centromere DNA from any plant species, the assembly of those sequences into mini-chromosomes, and the use of mini-chromosomes to deliver genes, generating novel plants and commercial products.

“The beauty of Chromatin’s approach is that the mini-chromosomes do not randomly integrate into the genome,” says David Gauthier, Foragen’s Vice-President for Central Canada.

“This allows much finer control of the expression of introduced genes, and eliminates many of the potential negative impacts of random integration inherent in current transformation technologies. As a result, product development times are shorter, particularly in the case where multiple genes are required. It is also not much more difficult to add multiple genes than single genes using this technology, which allows more complex and valuable plant products to be developed.”

Foragen assists in making it happen

The strength of the founders, uniqueness of the scientific approach and potential economic benefits of the technology made it a solid investment opportunity for an early-stage venture fund like Foragen. Along with Burrill and Company (San Francisco) and Venture Investors LLC (Madison), Foragen participated in a US\$4.7 million seed financing of Chromatin Inc. in September 2001. These funds were used to establish an R&D team, establish

operations, and achieve sufficient technical milestones to attract additional investment and partnering opportunities.

“The scientific progress over the past 24 months has been astonishing,” says Gauthier. “The team achieved all technical milestones well ahead of schedule.”

Strengthening the commercial focus of Chromatin

In January 2003, Mich Hein joined Chromatin as President and CEO, bringing with him over 20 years of experience with commercial and technical aspects of plant biotechnology. Dr. Hein began his career as a research chemist at Monsanto and subsequently moved to PPG Industries where he managed their plant molecular biology research effort. Following that, he played a pioneering role in the development of “next generation” plant biotechnology, first at The Scripps Research Institute, and then as a co-founder and President of Epicyte Pharmaceutical, Inc., a plant-based developer of therapeutic antibodies. At Epicyte, he managed the company’s strategic business development, government relations and key commercial alliances, including relationships with the Dow Chemical Company and Dow AgroSciences, Biovation, and the Centocor division of Johnson & Johnson.

The addition of Dr. Hein to the Chromatin team has led to the completion of a full commercial strategy and business plan in preparation for a second financing round.

Chromatin’s strategy is to identify partners with channel-to-market capabilities and the resources to engage in the co-development of high-value products. Chromatin’s near-term objective is to capture value in existing markets by quickly moving preferred combinations of high-value genes into key crop species such as soybean, corn, cotton and canola. Many producers now expect these crops to contain certain herbicide and pesticide resistance traits as a standard, and any new varieties on the market will have to contain these baseline characteristics. Chromatin’s ability to stack these traits with less reliance on breeding will dramatically accelerate the creation of these baseline varieties.

Hein says’ “In addition to these crop input applications, there is enormous potential for moving beyond herbicide and pest resistance to improving yield by mitigating the impact of such factors as cold weather, drought, salinity, soil erosion, and pathogen attack.”

These targets have clear economic potential; drought and salt stress alone cost the US economy \$1.5 billion per year. The next generation of mini-chromosome crop products will include biopharmaceuticals, industrial chemicals, specialty chemicals, and food products such as modified vegetable oils, food additives, and foods with greater nutritional content.



Towards alleviating concerns with GM plants

Chromatin's mini-chromosome technology will directly address a number of regulatory issues that currently impact the industry. Mini-chromosomes provide the ability to insert transgenes into plants without disrupting the host genome. Current technologies instead introduce DNA randomly into plant genomes, with uncertain outcomes, and unknown sites of insertion, requiring costly genetic characterization prior to regulatory approval of each transgenic event. Because mini-chromosomes are DNA packages separate from the host chromosomes, they can be independently traced, genetically and visually. Mini-chromosomes provide facile methods for monitoring the presence of multiple, linked transgenes for regulatory and quality control purposes.

Mini-chromosomes also allow multiple genes to be introduced in a stable genetic package, and with defined contexts for gene expression. Consequently, Chromatin's mini-chromosome technology permits the simultaneous control of multiple traits that are inherited as a single genetic unit. These advantages could lower regulatory risks and could reduce the costs of evaluating the impact of gene insertion on the host genome. They could also establish a benchmark of tractability and control that could help create a new standard for other technologies.

Ready for Success

Although there has been significant debate concerning the safety, containment and environmental impact of GM foods, over 1/5 of the combined acreage of corn, soybean, cotton, and canola worldwide is currently GM. The reason for the rapid acceptance of this technology since its introduction in 1996 is simple-producers realized that these new crops could increase profit margins by reducing input costs and attenuating losses due to devastating pest infestations. By accelerating the development of even more valuable crops for farmers and making the development of plant-derived pharmaceutical and industrial products feasible, Chromatin hopes to increase acceptance of GM crops much further.

With its innovative approach, solid science base, experienced management team and significant market potential, Chromatin is well positioned for commercial success. The Company is currently seeking a US\$12 million Series B financing to bring its technology to market. For details on the financing or for more information on Chromatin Inc. please contact:

Mich Hein
Chromatin Inc.
2255 West Harrison Street
Chicago, Illinois
60612
US

T: 312-455-1935
Email: hein@chromatininc.com

Dr. Daphne Preuss,
Chair of Chromatin's
Scientific Advisory
Board Professor of
Molecular Genetics
and Cell Biology
at the University
of Chicago
Investigator in the
Howard Hughes
Medical Institute

Dr. Greg Copenhaver
Assistant Professor,
The University of
North Carolina
at Chapel Hill

Dr. Kevin Keith
Postdoctoral Fellow,
University of Chicago

Chromatin's Founders

The logo for 'foragen' features the word in a lowercase, sans-serif font. A green curved line arches over the letters 'o' and 'r', extending from the top of the 'o' to the top of the 'r'.

President's Message



Dr. Murray McLaughlin PhD, P.Ag.

As we go about our business of creating new business opportunities to enhance value in agriculture and food, we receive great gratification from knowing that we are helping to ensure a future for the sector in Canada. The agri-food sector will be going through significant change over the next few years. There are many factors at play -

- aging farm populations
- impact of disease on the cattle industry
- global trade barriers lifting
- increased acceptance of GMOs
- consumers seeking wellness through the food they eat
- higher demand for organic foods
- increasing demand for quality and safety assurances for agricultural products
- lower tolerance for livestock production influences on ambient air and water
- global warming and climate shifts

In spite of buffeting from winds of change, the farmer stands tall. I recently heard an old song that brings back a lot of good memories of my days on the farm, but also carries a message that we need to remember and appreciate. That is a song by Murray MacLauchlan - *Dusty Old Farmer*. I am not sure the image of "straw hats and old dirty hankies moping a face like a shoe"

is right, but it is presented in the spirit of respect. The real message lines are:

"Thanks for the meal and I hope there's no shortage of rain. Can I wave at you just like a friend, these days when everyone is taking so much, there is someone giving back in. Thanks for the meal, here is a song that is real, from the kid from the city to you."

Farmers deserve appreciation and respect. We owe them a great deal. If it weren't for their entrepreneurship; faith in a better day; risk taking every year, and constant ability to produce the base ingredients of grain, oilseeds, livestock and poultry, and fruits and vegetables, our quality of life would be lower and much more expensive. With the help of science, farmers have tripled the world's food output in the last 4 decades. Twice as many people are being fed using the same farm acreage that was in place in 1960.

In the next 50 years the United Nation's projections estimate that global population will grow by 40%. That's an increase from 6.9 billion people to 8.9 billion in 2050. Feeding those people and providing for increased protein rich diets will require food output to double or even triple.

This food supply can be produced even as we return marginal land to wilderness, repair soil, rehabilitate water supplies and restore ecosystems. How can this be done? It can be accomplished through the use of biotechnology tools. Whether they use biotechnology tools, conventional or organic systems, first and foremost with every farmer is environmental stewardship. They have a vested

interest in ensuring quality of land, air and water - it is their future. Perhaps this awareness is what has led North farmers to accept biotechnology so fully and adapt it to their needs so quickly.

Far sighted farmers are the reason that we at Foragen are able to make excellent investments in companies like Chromatin, Inc. the corporation is profiled in this issue. Chromatin uses mini-chromosome technology to accelerate the pace of crop improvement that allows the rapid delivery of large numbers of genes. We are confident that with investments like these we are giving a little back to the men and women who work the land.

I have spent over 40 years in the agricultural industry and can honestly state that farmers are dedicated, entrepreneurial, risk taking business people. It has been a privilege to be associated with such a dedicated group of people. Thanks to our farmers for responding to the highest calling. Thanks for their effort and commitment to provide healthy, nutritious and safe food!

"Your life is the sum result of all the choices you make, both consciously and unconsciously. If you can control the process of choosing, you can take control of all aspects of you life. You can find the freedom that comes from being in charge of yourself."

Robert Bennett, U.S. Senator

Interns offer promise for the future



*From left to right:
Diane Harms, Intern, Armand Lavoie
Foragen VP for Western Canada and
Carla Meyer, Intern.*

Foragen's commitment to advancement of technology takes many forms and one of the most satisfying is the helping young people develop their business capabilities. Members of the Foragen team have had many opportunities to work with bright young talents. "When I look at the young people emerging from our Universities, I feel a great surge of pride. Our academic institutions are offering excellent programs and are producing graduates who are far advanced." says Dr. McLaughlin, President and CEO of Foragen Technologies Management Inc. "We are aware that in North America there is a human resource pool with unlimited potential. We are also aware that potential cannot be realised without suitable experience and support. At Foragen we work hard to ensure that talent is developed and potential is fully realised. We do that for our investees and now we are also doing it with our future investees - the graduates who are entering the world of technology based business."

Two and a half decades ago North America was experiencing the emergence of a biotechnology industry that was led by scientists who were rolling out innovations the like of which had never been seen before. As time progressed it became apparent

that many of these brilliantly talented people were not equipped to deal with commercialisation and the demanding complexities of the corporate world. One of the key scenarios that McLaughlin saw in play was the launch of very promising technology-based companies that could not be sustained over the long term. He says, "It was painfully apparent that although we were strong on science we were lacking managers. We were also lacking the ability to link science with corporations in a meaningful way. Great progress has been made but there is still a need to build co-operative programs that will help individuals bridge the distance between science and business."

"At Foragen we are enthusiastic participants in a project that offers recent graduates an opportunity to experience the dynamics of technology transfer and commercialisation first hand." says Armand Lavoie, Foragen Vice President for the Western Region. For the last two years Foragen has hosted interns from the WestLink Technology Commercialization Internship Program (TCIP). "This program is a premiere vehicle for early stage training for potential technology managers in Western Canada." says Lavoie.

Foragen's Western Canadian office has hosted an intern in every rotation of the program since its inception.

The TCIP was launched in 2001 with 19 interns. Over a 2-year period, the participants work in a technology transfer office, a small to medium enterprise (SME) and a venture capital firm. They spend 8 months at each location. This allows time to become familiar with the



organizations' operations, develop basic skills and experience the varying cultures and dynamics at work in each environment.

Before they are sent on-site, the interns take part in a 'Boot Camp', a five day workshop that is focussed on team building, networking and teaching the interns basic technology transfer skills to use in each of their placements. They also participate in a number of other training events, such as the Association of University Technology Managers (AUTM) Basic Licensing Course, and seminars at each of the rotation changeovers.

McLaughlin says, "The TCIP offers the interns a unique perspective of the innovation chain. The ability to add value to technologies from these diverse viewpoints will help build better business opportunities in the future. Foragen believes strongly in supporting internship programs and technology transfer in Canada. These programs are an excellent opportunity to develop management capacity in Canada."

Foragen hosted Lorraine Barker, Craig Urton, and Diane Harms during the first round of the internship from 2001-2003. Barker is now with Bioriginal Food and Science Corporation in Saskatoon, SK;



is working with Cevena Bioproducts Inc. (a Foragen Investee) in Edmonton, AB; and Harms is working in the Foragen Saskatoon office offering management assistance to Foragen investee companies.

The interns placed with Foragen share the sentiment expressed by Lorraine Barker. "My time at Foragen was a wonderful learning experience. I know that it will assist in the development of my career." says Barker. "I really enjoy working with early stage companies; and my internship at Foragen gave me the opportunity to experience the challenges and rewards of company creation."

Foragen is currently hosting Carla Meyer, their first intern from the 2003-2005 internship program.

Pxyis Genomics Canada, another Foragen investee, has also hired a graduate Tyler Bradley who was a participant in the 2001-2003 TCIP.

Foragen's Lavoie says, "I have been impressed with the calibre of individuals who have come to us through TCIP. Each intern brings a unique skill set developed in both science and business activities. They have had experience in technology transfer, start-ups and venture capital. They have been pivotal in evaluating technologies as well as providing support for existing investments. The intern's diverse skills sets make them ideal team members for Foragen."

McLaughlin agrees, "These young people are our first, best hope for the future. As they realise their potential

they will create ongoing success for their chosen employers.

"WestLink Innovation Network Ltd. is the not-for-profit organisation that manages the TCIP. The agency was formed to increase academic and industry collaboration for improved technology transfer.

WestLink's members represent 25 western Canadian universities, colleges, and research institutes. WestLink is supported by the government of Canada's Office of Western Economic Diversification (WD) and the Natural Sciences and Engineering Research Council (NSERC).

For more information on WestLink visit <http://www.westlink.ca>.

Looking ahead with RBC Technology Ventures Inc.

*René Douville, Vice President,
Life Science Ventures*

It is with immense pleasure that I accepted Dr. McLaughlin's invitation to collaborate on Foragen's newsletter *Visions*. The simple fact that the Foragen team produces this widely distributed - but more importantly widely read - newsletter is a real tribute to the progress achieved by Murray and his colleagues. In less than four years, Foragen has built a strong portfolio of investments. It has a reputation as a premier added-value venture capitalist, recognized not only in Canada, but increasingly in North America.

This progress is remarkable when one looks at the difficulty of investing at the seed and early stage development



of technology companies, let alone in agriscience. Very few venture capitalists have an appetite for investing at a stage where companies are being formed or technologies are not yet proven. As well, agriscience is generally not perceived by investors as providing the same rewards as other sectors such as advanced technologies or health.

In 1999 Foragen was the third seed and early-stage venture fund (or what we called internally our company creation vehicles) launched by RBC Ventures. It was build on the premise

that excellent science combined with a deep knowledge of market needs and a strong dose of entrepreneurship could turn premier Canadian sciences into sustainable and profitable businesses. Indeed, RBC created RBC Ventures in 1997 on the basis that if done wisely, with the right management team and the right global partners, it was possible to address gaps in Canadian science and technology development and commercialising.

With \$160 million under management, RBC Ventures has just announced the launch of a



new life science fund, its fifth sponsored or affiliated fund, and is working on successor funds for its advanced technology and IT business, and of course the next Foragen generation.

In all cases, RBC Ventures is working with global strategic partners who bring a lot more than money to the table. In the case of Foragen,

SGF Soquia in Quebec and CIC in Saskatchewan bring their full expertise and networks to help Foragen's management add value to their investee companies. More importantly, Foragen operates like a true general partner, making investment on behalf of its limited partners with no interference from its sponsors. We feel this is the only

way to deploy this type of investment strategy efficiently.

Foragen's team and investment strategy are, as far as we are concerned, unique. Foragen is breaking new ground, which will make its success that much more rewarding. We wish them well and look forward to pursuing this amazing adventure.

About Foragen:

Foragen Technology Management Inc. and its team manage investments in advanced agricultural technologies and provide a complete development package to move technology from concept to successful commercialization.

The company seeks out innovative ideas in such areas as human and animal wellness, food and fibre quality and trait enhancement, food safety, and alternative bio-based products, materials and processes.

Foragen is committed to building long-term productive partnerships with technology innovators. Future issues of *Visions* will feature Foragen clients and members of the Foragen Management Team.

For more information, visit our Web site at www.foragen.com, or e-mail Dr. Murray McLaughlin at murray.mclaughlin@foragen.com.

Foragen is a bilingual company, offering services in English and French. For service in French, in Eastern Canada contact Dr. Roger Bernier at roger.bernier@foragen.com, or in Western Canada, Armand Lavoie at armand.lavoie@foragen.com.

Published on behalf of:
Foragen Technologies Management Inc.
by The Signature Group
489 2nd Ave. N. Saskatoon SK
S7K 2C1

