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INITIATION REPORT

Biotechnology Industry • September 30, 2013

KEITH A. MARKEY, PH.D., M.B.A.
212-514-7914
KMARKEY@GRIFFINSECURITIES.COM

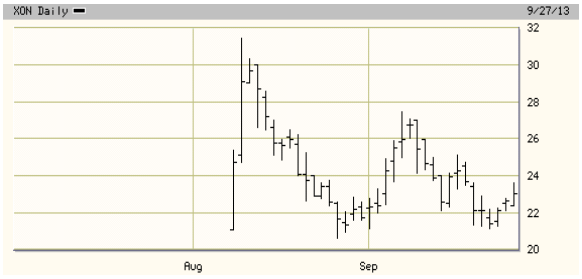
INTREXON CORPORATION (NYSE: XON)

LEADING THE WAY IN INDUSTRIALIZING SYNTHETIC BIOLOGY

- **Intrexon ushers in a new paradigm for a better world.** Synthetic biology is an emerging field of science that offers the promise of new biological molecules and genetically engineered cells, plants, and animals to address the world's challenges. The Company has a highly regarded executive team, a unique portfolio of advanced, proprietary technologies and informatics systems, and franchise business model to rapidly design, build and commercialize novel products in the fields of healthcare, food, energy & chemicals, and environment.
- **Collaboration agreements provide recurring returns and diversify risk** by combining Intrexon's expertise in synthetic biology with partners' knowledge and commercialization skills in specific areas.
- **We like Intrexon's scalable, high-margin business model.** The Company's goal is to ensure the broadest commercial use of its technologies via exclusive channel collaborations (ECCs) with corporations having expertise and development resources to bring new products to market.

We are initiating coverage with a BUY rating and 12-month price target of $36.00.

Share Price (9/26/2013)	$23.01
52-Week Price Low / High	$20.65 - $31.44
Mkt. Capitalization (issued)	$2.23 billion
Shares Outstanding (issued)	97.0 million
12-month Target Price	$36.00
Average Daily Volume (3 mos.)	780,564
Website	www.intrexon.com
Est'd 2013 Earn's (Loss)/shr	($0.71)
Est'd 2013 Adj EBITDA/shr	$0.03
Est'd 2014 Earn's (Loss)/shr	($0.26)
Est'd 2014 Adj EBITDA/shr	$0.82



Source: BigCharts.com

Intrexon Corporation (NYSE: XON) is a leader in synthetic biology, a discipline that applies engineering principles to biological systems. The Company has a proprietary set of complementary technologies that enable the design, construction, and regulation of genes to develop new and/or improved biological products and manufacturing processes. Key technologies include the UltraVector®, which is comprised of modular DNA components, including the clinically-validated RheoSwitch Therapeutic System®, that facilitate genetic engineering, Cell Systems Informatics that includes a database of modules and cellular pathways and simulation programs for *in silico* research with predictive power, the LEAP™ cell selection instrument, and mAbLogix™ platform for antibody production via B-cell libraries.

Intrexon's business model is based on Exclusive Channel Collaborations (ECCs) with companies with expertise in specific areas to ensure the broadest commercial use of its technologies. The four targeted end-user industries are: healthcare, food, energy & chemicals, and environment. The ECC terms provide for technology access fees, reimbursement of R&D costs, milestones, and royalties.

INVESTMENT THESIS

Synthetic biology is an emerging field that has the potential to touch upon virtually every aspect of our lives. Much as advances in chemical synthesis created drugs, industrial materials, and energy sources in the 19th and 20th centuries, new biological molecules and living organisms have the potential to solve many of the challenges of this century as the world's population grows. We believe Intrexon is poised to take the leadership role in capitalizing on the full potential of synthetic biology.

INTREXON'S TECHNOLOGICAL ADVANTAGE. Biotechnology has resembled a cottage industry, with huge successes coming from individual drugs developed in an artisanal manner. But industrialization of the field is beginning now that our knowledge base has expanded and gene sequencing and synthesis can be performed faster and less expensively than ever before. Dr. Thomas Reed, who co-founded the Company, recognized the trends and also realized that genes could be assembled from modules rather than one base pair at a time. Accordingly, he created the patented UltraVector® platform for the synthesis of genes from modules, thereby cutting the time and resources needed to create functional genes, designed for specific purposes. One of those modules, called the RheoSwitch®, adds a level of control that the FDA has been seeking since the first gene therapy was created – it provides a mechanism for adjusting expression in a continuous manner from "off" to fully "on" *in vivo*. Intrexon has created informatics systems to analyze huge quantities of data, store the information in an easily retrievable system, and employ predictive modeling to design genes and proteins. The Company has also added proprietary technologies to rapidly select cells based on different criteria and to create fully human antibodies *in vitro*.

INFRASTRUCTURE IN PLACE TO MEET STRONG DEMAND. Under the direction of Chairman and CEO R.J. Kirk, the Company went through a process over the past few years to ensure that operations were prepared to answer the call for a vast array of synthetic biological products. A variety of industrialization procedures were optimized including work flow mapping to reduce time and resource use; testing the informatics systems for the analysis, storage, and reliable retrieval of huge volumes of data; and a scaling up operations to determine resource needs under different levels of demand. This work was successful and it had another noteworthy outcome – it created new DNA modules and characterized how they may be used together and in various types of cells for optimal gene expression. To date, Intrexon has more than two million DNA modules in its database with information on how each may be used. Moreover, creation of new molecules is now performed within defined timeframes with >90% accuracy, thus minimizing corrections since all products are shipped with 100% accuracy.

A ROBUST BUSINESS MODEL FOR A FIELD WITH FAR-REACHING IMPACT. Intrexon has adopted a collaborative business model to expedite utilization of its extensive capabilities in a science that holds promise in a broad range of applications. We like this approach because it draws upon the Company's expertise in synthetic biology and applies it to projects in which its partners have a strong knowledge base. Also, exclusive channel collaborations (ECCs) compensate Intrexon for use of its technologies, finance the R&D costs, and yield milestones and royalties. As such, Intrexon's risks are mitigated by cost reimbursement, while the large rewards come from commercialization of the final products. The risks have also been limited by careful selection of projects in which there is ample evidence pointing to success. And given the breadth of synthetic biology's potential uses, we find the Company's decision to focus on four areas (healthcare, food, energy & chemicals, and environment) commendable – it should pay off via a greater understanding of the fields and potential applications of the technologies.

WE RECOMMEND INTREXON SHARES FOR MOST PORTFOLIOS. The Company has all the elements that underpin the greatest corporate success stories: a field offering multiple growth opportunities, significant technological advantages, highly regarded executives, and a scalable business model. Moreover, we believe the business risks have been mitigated scientifically and through studies already completed on many projects. In August, Intrexon's IPO was well regarded, resulting in a valuation in excess of $2 billion range for its highly liquid stock. In the months ahead, investors should see more ECCs completed and milestones achieved by both Intrexon and its collaborators. Long term, we expect the current agreements should yield superior profit growth and should drive the share price up markedly. Accordingly, we are initiating coverage of Intrexon (NYSE: XON) with a BUY recommendation and price target of $36.00.

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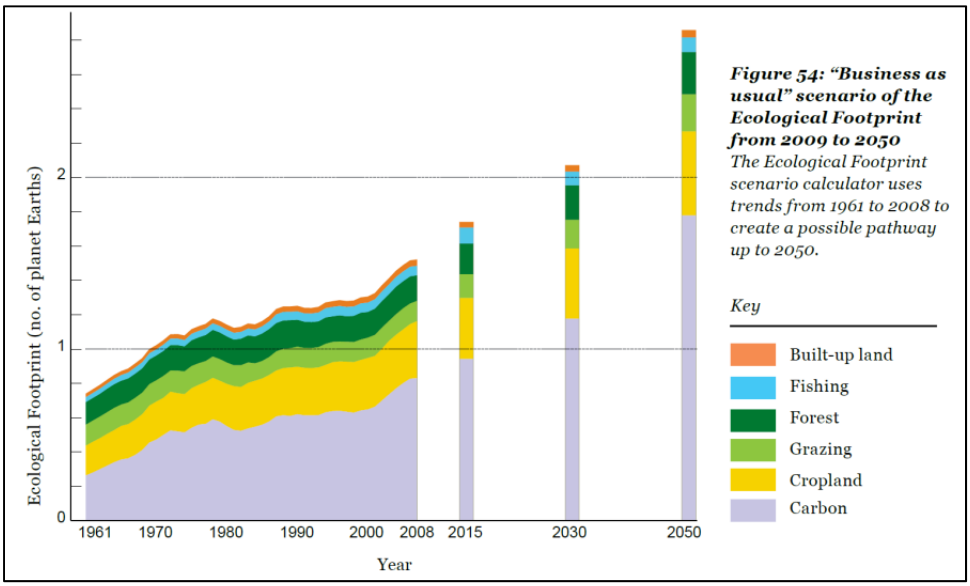
WHAT IS SYNTHETIC BIOLOGY AND HOW WILL IT BE USED?

There are different ways to describe the emerging field of synthetic biology, which blends traditional biology, engineering, and informatics to address problems that mankind and the Earth face today and will face in the future. One way of appreciating the challenges is presented in Figure 1, which provides a view of future demands on Earth's resources for food, feed, and fiber based on recent trends in population growth, land use and productivity, energy use, diets, and climate change.[1] Perhaps the most important driving forces behind these changes will be population growth, projected at 28% between 2005 and 2030, and a 57% increase in per capita income.[2]

Figure 1. Projected Resource Needs Through 2050[1]



Synthetic biology offers a new approach to reducing the demands on the planet through such measures as improved food and forestry production, creating new energy sources, and offering novel solutions to uninhabitable land via bioremediation and altered plant traits. The following are a few descriptions of synthetic biology:

"Opinions on what synthetic biology actually is range from a natural extension of genetic engineering to a new manufacturing paradigm. It offers, for the first time in the life sciences, rational design and engineering standardization. It could address problems across a broad spectrum of human concerns including energy and food security, and health of growing and aging populations."[3]

"Synthetic biology aims to design and engineer biologically based parts, novel devices and systems as well as redesigning existing, natural biological systems."[4]

"Synthetic Biology (SB) is the repurposing of living systems for useful ends. SB, philosophically rooted in the engineering paradigm, aims to reduce complex 'natural' (i.e., evolved) systems to simplified, reliable, quality-controlled modules, or 'parts', that can be mathematically modeled, manipulated by computer aided design (CAD), 'abstracted' (passed between loosely coupled design and production layers), bolted together to achieve predictable results, and fabricated on an industrial scale."[5]

[1] WWF, 2012. Living Planet Report 2012. WWF International, Gland, Switzerland.
[2] OECD International Futures Project. The Bioeconomy to 2030: Designing a Policy Agenda (2009). Paris, France.
[3] Philip, JC, et al. Synthetic biology, the bioeconomy, and a societal quandary. Trends in Biotechnol (2013); 31(5): 269.
[4] The Royal Academy of Engineering. Synthetic Biology: Scope, applications, and implications. London, 2009.
[5] Mitchell, W. Natural products from synthetic biology. Curr Opin Chem Biol (2011); 15(4): 505.

The central theme of these descriptions is the application of engineering principles to biological systems to create new products. One comparison has been made to synthetic chemistry, which underpinned the advances made in the 19th and 20th centuries in such areas as fuels, foods, and drugs. The potential value of synthetic biology may well exceed that of synthetic chemistry, given its utilization of diverse genetic components to create new molecules as well as genetically modified living cells. Shown in Table 1 are the projected types of synthetic biological products in three general areas that are expected to be commercialized by 2030.

Table 1. Applications of Synthetic Biology with a High Probability of Reaching the Market by 2030[2]

Agriculture	Health	Industry
Genetically modified (GM) varieties of major crops and trees with improved starch, oil, and lignin content to improve industrial processing and conversion yields.	New pharmaceuticals and vaccines, based in part on synthetic biological technologies.	Improved enzymes for a growing range so applications in the chemical industry.
GM plants and animals for producing pharmaceuticals and other valuable compounds.	New screens for multiple genetic risk factors for common diseases.	Improved micro-organisms that can produce an increasing number of chemical products.
Improved varieties of major food and feed crops with higher yield, pest resistance, and stress tolerance developed through GM, intragenics or cisgenesis.	Improved drug delivery systems, including GM cells.	Biosensors that provide real-time monitoring of environmental pollutants and biometrics for identifying people.
Major staple crops of developing countries enhanced with vitamins or trace nutrients, using GM technology.	Nutraceuticals produced via GM micro-organisms and/or plants.	Biomaterials, such as bioplastics, that have cost and/or performance advantages.
GM animals and fish with improved growth and/or nutritional qualities.	Regenerative medicine products that repair or replace some types of damaged tissue.	

The potential shares of the gross value added by such biotechnology products in 2030 are as follows: health, 25%; agriculture, 36%; and industry, 39%.[2] At this juncture, health-related research accounts for the lion's share of the R&D dollars at 87%, while agriculture and industry account for 4% and 2% respectively. (Another 7% is categorized as "other".)

WHAT CHALLENGES DOES SYNTHETIC BIOLOGY FACE?

Regulations probably pose the greatest challenge to the development of synthetic biology, but they differ considerably with respect to the nature and use of the new products. Presently, this emerging field of science is governed largely by regulations associated with food/agriculture, medical devices, and drugs. But as the technology is applied to new areas, additional regulations will probably be enacted in the realms of safety and biosecurity. Today's regulations already add to the cost and time needed to commercialize new products, as shown in Table 2.

Table 2. Regulatory Costs to Commercialize a Biotechnology Product[2]

Agriculture	Cost In thousands
Plant	
GM crop[2]	435–13 460
MAS crop[3]	5–11
Animal	
Vaccine[4]	242-469
Therapeutic[5]	176–329
Diagnostic[4]	9-189
Health	
Therapeutics[6]	1 300
In vitro diagnostics[7]	150–600
Industry	
GM open release[8]	1 200–3 000
GM in closed loop	Unknown

The costs in the table, which do not include R&D expenses, were obtained from such agencies as the U.S. Food & Drug Administration, Environmental Protection Agency and Department of Agriculture. We believe they provide a basis for comparing the impact of current regulations.

Intellectual property rights will undoubtedly undergo further changes over time and some will affect the emerging field of synthetic biology. Indeed, the recent U.S. Supreme Court decision that rendered patents on natural genes invalid has already altered the landscape. It exposed some products, notably diagnostic tests, to greater competition. But it probably also created an atmosphere that favors innovation in the field of synthetic biology. Debates will commence, nonetheless, over such issues as what constitutes innovation or how to define "novel" in the field of synthetic biology. (For instance, if a single amino acid in a protein is changed without greatly altering the three-dimensional structure of the molecule or its general physical or therapeutic properties, does that constitute a "new" protein? If not, what kind of change(s) is needed for it to be "novel"?) How these issues are resolved will define the competitive playing field.

Public policies will also shape the use of synthetic biology through R&D funding mechanisms, such as the National Science Foundation, by supporting the development of skilled personnel and by fostering the acceptance of new products that are derived from synthetic biology. It is noteworthy that resistance has emerged to one of the first products created via synthetic biology, the anti-malarial drug artemisinin.

BUILDING LEADERSHIP IN SYNTHETIC BIOLOGY

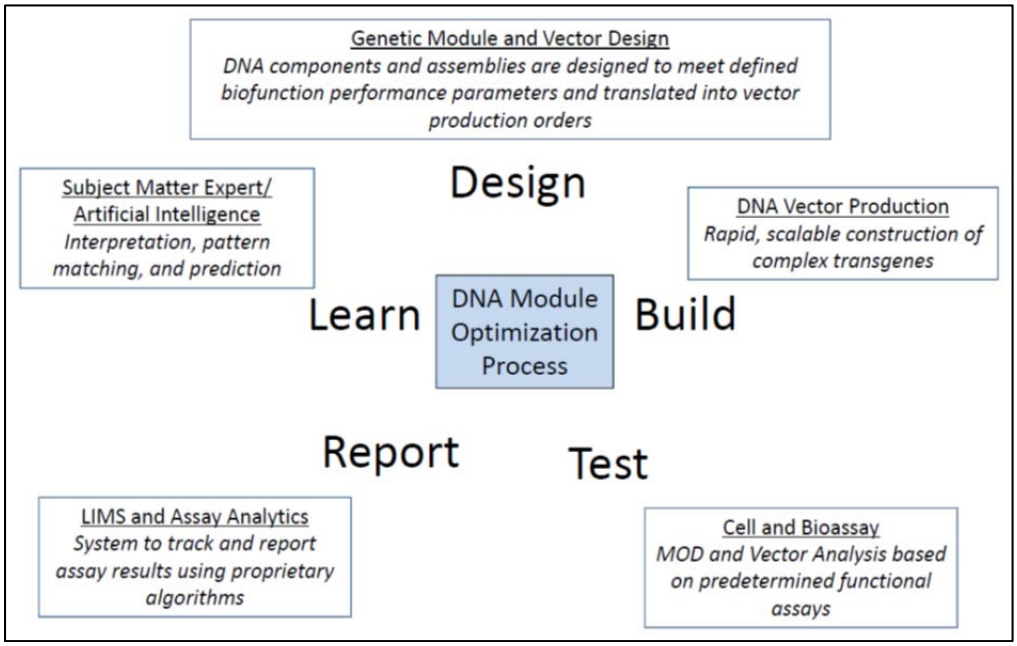
Innovation does not always translate into a successful commercial enterprise. But with the foundation provided by Dr. Thomas Reed, the business model fashioned under Intrexon's Chairman and CEO R.J. Kirk, and the investments in the operations to date, we believe Intrexon is the undisputed leader in synthetic biology with a head start, measured in years, over would-be competitors.

Dr. Thomas Reed co-founded the Company and began building the modules that are the key components of today's transgenes. (Transgenes are artificial genes that include all of the elements required for gene expression, including a promoter that identifies the transcriptional start site; an intron, which is a regulatory signal influencing gene transcription; the protein coding sequence, or reporter; and a transcriptional stop signal.) Among the most important modules is a gene switch, called the RheoSwitch Therapeutic System®, which is designed to control the time and magnitude of a gene's expression *in vivo*.

Under the leadership of R.J. Kirk, Intrexon scaled up its ability to create transgenes and the modules that comprise them over the past few years. Today, the Company has more than 2 million modules in inventory, all annotated in its database on their use in conjunction with annealing enzymes and in different cell types. The targeted peak production capability was tested last year and since then, operations have been returned to a level consistent with demand. (Current capacity is 10 – 15 projects per month with 90% on-time delivery.) Not only did this exercise provide modules and internal confirmation of scale-up parameters, but it was also used to improve product quality. The DNA-assembling platform, called UltraVector, now produces genes with 90%+ accuracy via a robotic process. Nonetheless, the Company tests the protein sequence from each gene to ensure 100% accuracy before supplying it to a client.

The creation of transgenes follows an iterative process to arrive at an optimal outcome. But the time that is required to achieve a final product is considerably less than the biotech industry norm due to the aforementioned experience and the Company's proprietary technologies that include the predictive software of its Cell Informatics division. The iterative process, which is illustrated in Figure 2, has been shortened to three to four weeks for a standard monogenic project.

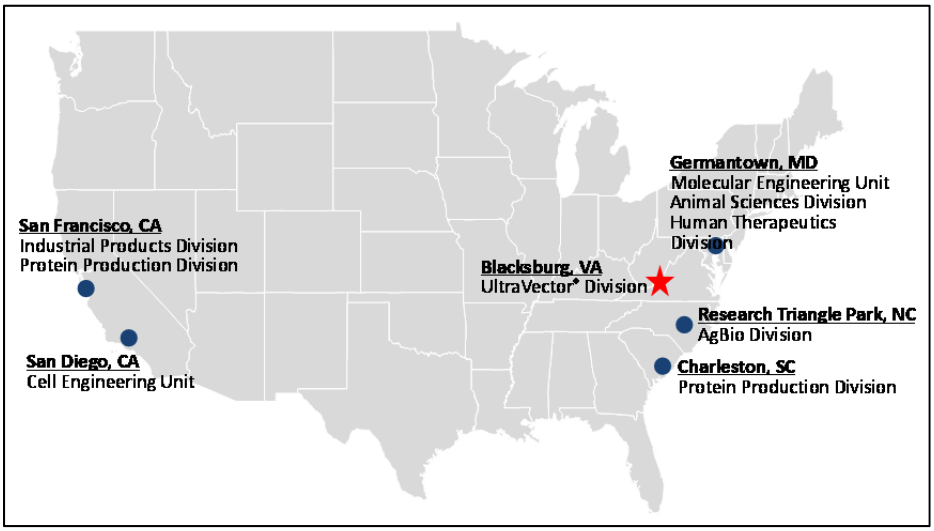
Figure 2. Continuous Information Flow in Gene Assembly



Source: Ziopharm Oncology Investor Day Presentation, dated June 23, 2011

To fully realize the opportunity presented by synthetic biology, Intrexon has facilities dedicated to various endeavors, as illustrated in Figure 3. The core of the Company's business, the UltraVector division, is located in Virginia, and its cell engineering unit, which utilizes a special cell-identification technology (laser-enabled analysis and processing, or LEAP), is located in California. In addition, a center in South Carolina is devoted to protein production. Proteins produced from transgenes are analyzed in Maryland, where molecular designing and veterinary medicine are also based. Energy and chemicals research is being conducted in California, while agriculture opportunities are being pursued in North Carolina.

Figure 3. Intrexon Facilities & Their Areas of Specialization



Source: Intrexon Corporation

We believe the specialization at these sites helps to foster intellectual exchanges on the specific fields of commercial interest. It also avoids duplication of highly technical functions. However, the network of facilities and scientists collaborate on projects. In some cases, for instance, the best cell line to employ is

identified through tests performed at separate locations with different cells, and the final decision is based on such factors as protein expression levels, post-translational modification of the molecule, cell growth characteristics, and purification schemes. The goal of this type of process is to determine the most economical production system possible for a new protein or genetically modified cell in an efficient manner. The various technologies that Intrexon has at its disposal are designed for this very purpose.

EXECUTIVE MANAGEMENT TEAM

The management team and Board of Directors distinguish Intrexon Corporation from other companies in the biotechnology and emerging synthetic biology industries, in our opinion. They have a unique blend of skills and experience to expand the basic science, create viable commercial products, and secure relationships with companies that will market Intrexon's creations.

Randal J. Kirk, J.D., Chief Executive Officer and Chairman of the Board

- Has served as Chairman of the Board since 2008 and CEO since 2009, with deep experience in operational and management experience having founded General Injectables and Vaccines that spun off King Pharmaceuticals and founded New River Pharmaceuticals, as well as Third Security, LLC.
- Serves as the Senior Managing Director and CEO of Third Security and on the board of directors of Halozyme Therapeutics and Ziopharm Oncology.

Thomas D. Reed, Ph.D., Co-Founder and Chief Science Officer

- Co-founded Intrexon in 1998 with more than 20 years of experience in recombinant DNA technology and has multiple patents in the field.
- Developed transgenic model systems for studying the role of gene products in neuronal, cardiovascular, and cancer systems and has numerous scientific publications in the areas of subcellular modulation, gene regulation, and cardiac function.

Krish S. Krishnan, M.S., M.B.A., Chief Operating Officer

- Assumed his current position with extensive senior management experience in the pharmaceutical industry, having served as CEO of Pinnacle Pharmaceuticals and as the CFO and COO of New River Pharmaceuticals. .
- Served as a Senior Managing Director of Third Security and on the board of directors of New River Pharmaceuticals and Biotie Therapies Oyj.

MARKET LEADERS

Samuel Broder, M.D., Senior Vice President – Health Sector

- Joined Intrexon in 2012 with experience that includes Executive Vice President of Medical Affairs and Chief Medical Officer of Celera Corporation and Director of the National Cancer Institute.
- Had an instrumental role in developing the first three drugs approved by the FDA for treating HIV infections.

Thomas R. Kasser, Ph.D., Senior Vice President – Food Sector

- Has served in his current position since May 2013, after joining as the President of the Animal Sciences Division in 2011, with over 25 years of business management experience in the biotechnology and life sciences industry, having held the positions of President and Chief Executive Officer at Angionics and General Manager of Covance Research Products.
- Serves on the Board of Directors for AquaBounty Technologies, a biotechnology company that focuses on enhancing aquaculture.

Robert F. Walsh, III, Sr. Vice Pres. – Energy Sector, & President – Industrial Products Sector

- Joined Intrexon in 2013, with more than 30 years of experience in the global petroleum and chemical industry, including the biofuel segment.
- Held executive positions with four biofuel/industrial biotech companies and senior management positions with Royal Dutch Shell.

Nick Macris, M.E.Sc., M.B.A., Vice President, Environment Sector

- Has held his current position since May 2013, after joining the Company as the Vice President, Business Development – Agricultural Biotechnology Division in 2012.
- Has more than 15 years of business and technical experience in specialty chemical, water treatment, agricultural, chemical, and biopesticide companies including 3M Company, Rohm & Haas, FMC Corporation, and Marrone Bio Innovations.
- Previously was VP of business development at Marrone Bio Innovations, a company that focuses on natural product solutions for disease and pest management in plants and aquatic systems.

CORPORATE EXECUTIVES

Don Lehr, B.A., J.D., Chief Legal Officer

- Assumed his current position in 2011 after joining Intrexon in 2009 as Associate General Counsel with experience in areas of corporate, securities, and general business law.
- Served as an attorney for corporate clients in the public and private sector across such industries as biotechnology, pharmaceutical, healthcare, software, technology, and manufacturing.

Rick Sterling, CPA, Chief Financial Officer

- Joined Intrexon in 2007 in his current capacity, with considerable knowledge about SEC filings and Sarbanes-Oxley compliance regulations.
- Has more than 17 years of audit experience with clients in the healthcare, technology, and manufacturing industries.

Darryl Webster, J.D., Senior Vice President, Intellectual Property

- Has served in his current position since 2010 with extensive experience in corporate and patent law, as well as scientific experience in the areas being targeted by Intrexon.
- Has more than 25 years of legal experience, including serving as Senior Patent Counsel at Wyeth Pharmaceuticals and having had responsibility for overseeing intellectual property related to a $6 billion biological drug, the Asia-Pacific Region, and Wyeth Nutrition business.

BOARD OF DIRECTORS

Cesar L. Alvarez, M.B.A., J.D.

- Has served as a Board member since February 2008.
- Serves as Executive Chairman of the international law firm of Greenberg Traurig, LLP and on the boards of Mednax, Inc., Watsco, Inc., St. Joe Co., and Fairholme Funds.

Steven Frank, M.B.A.

- Joined the Board in February 2008 with experience in investment banking and portfolio management.
- Holds the position of Chairman of Global Healthcare Investment Banking at J.P. Morgan Securities, having played major roles in mergers and acquisitions involving pharmaceutical, medical devices, and biotechnology companies.

Larry Horner

- Joined Intrexon's board in February 2008, having served as Director of Clinical Data and New River Pharmaceuticals.
- Held the positions of Chairman and CEO of KPMG Peat Marwick and Chairman of Pacific USA Holdings and Asia Pacific Wire & Cable, as well as director of Atlantis Plastics, TOUSA, UTStarcom, ConocoPhillips, and American General Company.

Randal J. Kirk, J.D., Chief Executive Officer and Chairman of the Board

Jeffrey Kindler, J.D.

- Joined the Intrexon Board in November 2011, having held the positions of Chairman and Chief Executive Officer of Pfizer and Chairman of Boston Market, and President of the Partner Brands group of McDonald's Corporation.
- Is a venture partner with Lux Capital, director of Starboard Capital Partners, and principal at Paragon Pharmaceuticals, as well as a director of Chipotle Mexican Grill and Siga Technologies.

Dean J. Mitchell

- Has served as a Director of Intrexon since March 2009 and has extensive experience in the pharmaceutical industry, having held the positions of President and CEO of Alpharma, Inc. and Guilford Pharmaceuticals, as well as executive positions with Bristol-Myers Squibb and GlaxoSmithKline.
- Is the .President, CEO, and Director of Lux Biosciences, and a director of ISTA Pharmaceuticals.

Thomas D. Reed, Ph.D., Board Member, Founder, & Chief Science Officer

Robert B. Shapiro

- Appointed to the Board in November 2011, having held several executive positions with Monsanto, including Chairman and CEO, and on the President's Advisory Committee on Trade Policy and on the White House Domestic Policy Review of Industrial Innovation.
- Is also the Co-Founder and Managing Director of Sandbox Industries and on the boards of Chromatin Inc., Elevance Renewable Sciences, and Sapphire Energy.

HISTORICAL MILESTONES

Building the Corporate Infrastructure & Technology Base

Jan,'11	Acquired Agarigen, Inc. to garner expertise in the agriculture sector.
Jun,'11	Entered a collaboration and license agreement with Halozyme Therapeutics for the rHuPH20 enzyme to facilitate uptake of human alpha 1-antitrypsin, a recombinant enzyme for treating an inherited disorder that affects the liver and lungs.
Aug,'11	Acquired LEAP platform technology from Cyntellect, Inc.
Oct,'11	Acquired cell systems informatics technology from GT Life Sciences, Inc.
Oct,'11	Acquired mAbLogix antibody platform from Immunologix.
Nov,'12	Acquired 48.6 million shares of common stock from AquaBounty representing a 47.6% stake.
Mar,'13	Acquired an additional 18.7 million shares of AquaBounty, which raised Intrexon's ownership to 53.8%.
Aug,'13	Completed initial public offering, raising more than $180 million via a sale of 11.5 million shares, and listed on NYSE under the ticker symbol XON.

Exclusive Channel Collaborations

Jan,'11 Entered into an ECC with Ziopharm Oncology to develop and commercialize anticancer therapies.

Nov,'11 Formed an ECC with Eli Lilly's animal health division, Elanco, to address chronic diseases of companion animals and to prevent certain infectious diseases in swine.

Jun,'12 Formed an ECC with Oragenics for the development of lantibiotics, which are a family of broad-spectrum, natural antibiotics to treat various infectious diseases.

Aug,'12 Entered an exclusive research collaboration with BioLife Cell Bank, Inc. that gave BioLife an option to form an ECC to create a treatment for spinal muscular atrophy.

Aug,'12 Formed an ECC with Synthetic Biologics for the development of monoclonal antibody-based therapeutics against infectious agents.

Oct,'12 Entered into an ECC with Fibrocell Science to optimize fibroblast cell culture conditions and to develop engineered autologous fibroblasts for a severe, rare genetic disorder of the skin.

Feb,'13 Entered an ECC with AquaBounty to develop and commercialize genetically modified finfish for human consumption that are more nutritious, have increased muscle mass, and grow quickly to full maturity.

Mar,'13 Completed an ECC with AmpliPhi BioSciences Corp. to develop and commercialize new bacteriophage-based therapies to target specific antibiotic-resistant infections of acute and chronic wounds.

Mar,'13 Entered into an ECC with Genopaver, LLC to develop genetically modified microbes for the fermentative production of pharmaceutical intermediates and/or active ingredients.

Apr,'13 Formed an ECC with Soligenix to create human monoclonal antibody therapies for treating melioidosis, an infection caused by a Gram-negative bacteria, *B. pseudomallei*, that is endemic in Southeast Asia and northern Australia and poses a potential biowarfare threat.

Jun,'13 Expanded the ECC with Fibrocell Science to include three diseases with an autoimmune and/or inflammatory etiology, psoriasis, morphea, and cutaneous eosinophilia.

Sep,'13 Entered into an ECC with Rentokil Initial, LLC for a new pest-control solution.

NEAR-TERM MILESTONES

The following milestones pertain directly to Intrexon and the work that it is performing under existing ECCs. However, the Company's collaborators in ECCs have their own milestones based on the division of responsibilities on each project that in many cases will have a direct bearing on Intrexon's future royalty streams. Nonetheless, those milestones are not included in the following list.

Q4,'13 Receive FDA approval of the first genetically modified animal, AquaBounty's salmon.

Q4,'13 Initiate commercial sales of AquaBounty salmon.

H2,'13 Consummate the first ECC in the Energy & Chemicals field.

H2,'13 Identify a lead lantibiotic compound via preclinical testing under an ECC with Oragenics.

H2,'13 Identify optimal clones of antibodies against the bacterium *Acinetobacter baumanii* under an ECC with Synthetic Biologics.

H2,'13 Collaborate with Fibrocell on the development of genetically modified fibroblasts for treating the severe skin disorder known as recessive dystrophic epidermolysis bullosa.

2014 Expand the number of ECCs in all fields being targeted for business development.

KEY TECHNOLOGIES TO INTREXON'S LEAD IN SYNTHETIC BIOLOGY

Intrexon has four technologies that set it apart from would-be competitors in synthetic biology. Separately, each is on the cutting-edge in its particular field of biology. But combined, they form an unrivaled platform for creating biological solutions to the world's problems.

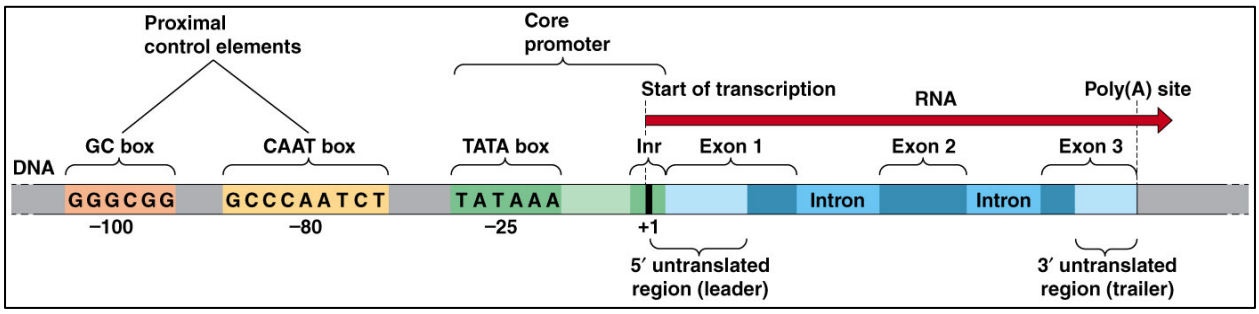
ULTRAVECTOR – THE ULTIMATE GENE MANUFACTURING TOOL

The UltraVector technology was the brainchild of Intrexon's co-founder, Dr. Thomas Reed. He recognized the opportunity to apply standard engineering and information management techniques to biological systems, based on the common "language" and constructs of DNA. This innovative thinking led to the creation of the UltraVector technology and the founding of Intrexon. The system builds genes from DNA modules with seemingly limitless uses. Based on the ECCs already signed in the healthcare sector alone, the UltraVector platform is being used to create recombinant proteins, monoclonal antibodies, and genetically modified cells for therapeutic applications.

The Basic Gene

Genes define the substance that we are, determine our physical appearance, and contribute to our personality and susceptibility to disease. The gene is constructed from DNA, but it is not just a simple double helix. Rather, it is a highly organized structure with multiple regions. As shown in Figure 4, a gene contains a promoter region that basically serves as a starting point for transcription (exon segments) into mRNA. There are also regulatory portions, sections (Introns) with seemingly little information that are not expressed in the final mRNA, and a "stop" signal, along with the poly(A) site.

Figure 4. Basic Components of a Gene



Source: Memorial University of Newfoundland

This basic structure is found in nature, from bacteria to man. As a result, it is possible to utilize nature's own coding system to introduce a human gene into a lower life form (e.g., *E. coli* or Chinese hamster ovary cells) to produce a human protein. This has been accomplished one gene at a time with few attempts to standardize or automate the process, even in companies with more than one biological product under development or on the market. Accordingly, it is reasonable to think that synthetic biology is still in its infancy, with such hurdles to still overcome as different nomenclatures in use making it difficult to share information efficiently.

The Benefits of Modular DNA

Use of DNA modules offers a number of advantages over the genetic research that has been conducted historically in which sections of DNA were linked until the final chain was formed. Historically, gene assembly has been a time- and resource-consuming process, but new technology offers significant improvements. What's more, modular DNA is providing the efficiencies that come from employing standardized parts, and scientists are working to construct online databases such as the MIT Registry of Standard Biological Parts, BioBrick Standard 10.[6] Moreover, new nomenclature is being proposed to

[6] See http://partsregistry.org

facilitate the exchange of information about synthetically created biological molecules. (For instance, see a proposal on ribosomally synthesized natural and modified proteins.[7])

Intrexon has taken DNA synthesis to a higher level of industrialization through investments in modular components, information systems, and standard workflow protocols. Modular DNA facilitates the design of genes for specific functions. For instance, a gene for an enzyme may be altered by exchanging one amino acid for another to increase its affinity for its substrate. Gene construction can follow a logical framework using experience with the components and overall process. Moreover, the design, assembly, and testing is well organized, while risk is lowered by reusing modules that have been utilized previously. This is particularly important in optimizing the regulatory components of a gene for expression in specific cells, because these components are not always compatible with a particular cell type (see below). **In sum, modular gene assembly offers the same advantages that Henry Ford realized with his interchangeable parts, namely high throughput (high-volume production) and low cost. But in biological applications, modularity offers the extra benefit of rapidly building genes for a variety of end products, not just one type of car.**

The importance of using the proper components is exemplified in Figure 5. In that particular experiment, 15 vectors were created with a reporter gene for human interferon-α and different regulatory components, and interferon-α was measured in the cell culture media.[8] The results demonstrate the significant improvement in protein expression that is achieved with optimal vector construction.

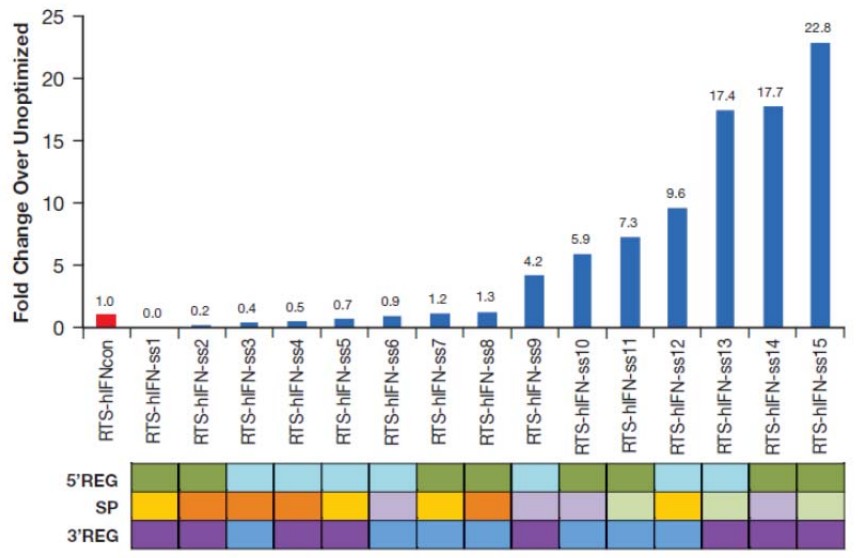


Figure 5. Selection of regulatory elements (color coded in the 5'REG and 3'REG rows) that are located adjacent to the reporter gene for human interferon-α and the choice of a secretory signal (SP) greatly influence the expression/secretion of human interferon-α from a human cell line in culture. The optimal construct produced nearly 23 fold more interferon-α relative to an unoptimized gene (depicted by the red bar).

Source: Agarwal, P, et al.[8]

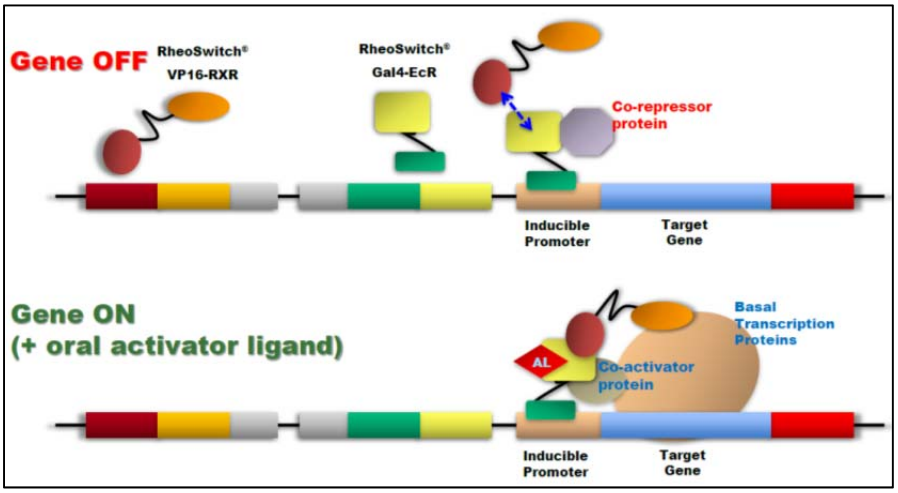
[7] Arnison, PG, et al. Ribosomally synthesized and post-translationally modified peptide natural products: overview and recommendations for universal nomenclature. Nat Prod Rep (2013); 30(1): 108.

[8] Agarwal, P, et al. Intramuscular electroporation of an optimized RheoSwitch-regulated interferonα plasmid transgene shows long term persistence *in vivo*: implications for therapy of cancer. Presented at the International Conference on Molecular Targets & Cancer Therapeutics, November 2012.

Controlling Gene Expression *In Vivo* – The RheoSwitch Therapeutic System

The Company has developed different DNA constructs that influence the expression of transfected genes, but the most significant control mechanism is the RheoSwitch Therapeutic System (RTS). This novel regulator consists of four basic components, two RheoSwitch fused proteins (VP16-RXR and Gal4-EcR) that are constitutively produced, an activator ligand (AL) that is a small, orally available molecule with no biological activity in humans outside of the RheoSwitch; and an inducible promoter that permits transcription of the reporter (also known as the target gene). The switch is typically set in the "off" position, which means the gene it controls is not expressed until the activator is present. (See Figure 6.) In the "off" position, the interaction between the two fused proteins is unstable and any potential activity is limited by a co-repressor protein. As a result, background expression of RheoSwitch-controlled genes is very low. In the "on" position, the two fusion proteins form a stable complex with the activator ligand and bind to both the inducible promoter and a co-activator protein. That stable complex permits the transcription of the target gene, thereby forming the messenger RNA for the related therapeutic protein.

Figure 6. The RheoSwitch "On" and "Off" Positions



Source: Nemunaitis, J.[9]

The RheoSwitch provides a simple system for a patient to use, as it only requires that the activator ligand be taken at the prescribed time and in the proper dose after the gene is administered, as shown below.[10]

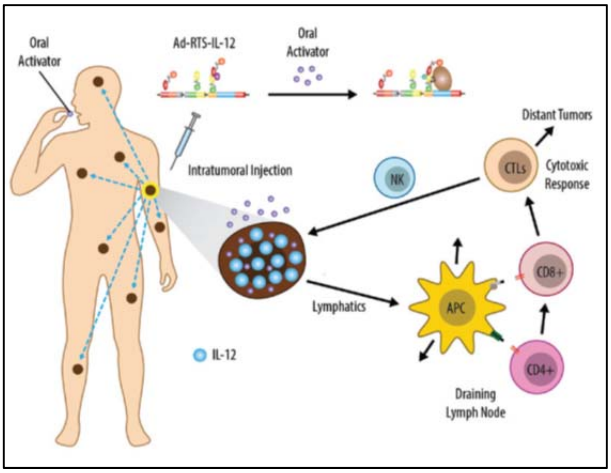


Figure 7. Clinical application of a RheoSwitch-controlled gene therapy for cancer exemplifies the simplicity of this technology. In this diagram, delivery of an RTS-IL-12 gene via an adenovirus (Ad) is injected into a tumor, followed by oral administration of the activator ligand. Expression of the cytokine interleukin-12 (IL-12) within the tumor stimulates the immune system at multiple levels, including natural killer cells (NK), cytotoxic lymphocytes (CTLs), antigen presenting cells (APC), two types of T cells (CD4+ and CD8+) that recognize antigens on malignant cells. This is the approach being taken by Ziopharm Oncology to treat melanoma.

Source: Linette, GP, et al.[10]

[9] Nemunaitis, J. Nonclinical and Phase I clinical studies with a regulated adenoviral gene delivery of IL-12 show promising clinical activity in unresectable stage III/IV melanoma. Presented at the ASGCT Meeting, June 2013.

[10] Linette, GP, et al. A Phase I open-label study of Ad-RTS-hIL-12, an adenoviral vector engineered to express hIL-12, in combination with an oral activator ligand in subjects with unresectable stage III/IV melanoma. ASCO Poster #3022 (2013).

The RheoSwitch also addresses the principal regulatory concern of gene therapy – it permits exquisite control over the therapeutic gene's expression *in vivo* with very low background leakage and a strong dose-response relationship).[9,11] Figure 8 provides results from preclinical studies with a RheoSwitch-controlled gene for interleukin-12 (IL-12), showing that the gene can be turned on and off via the presence of activator ligand in cultured cells and that the gene therapy blocks tumor growth in a ligand dose-dependent manner *in vivo*.

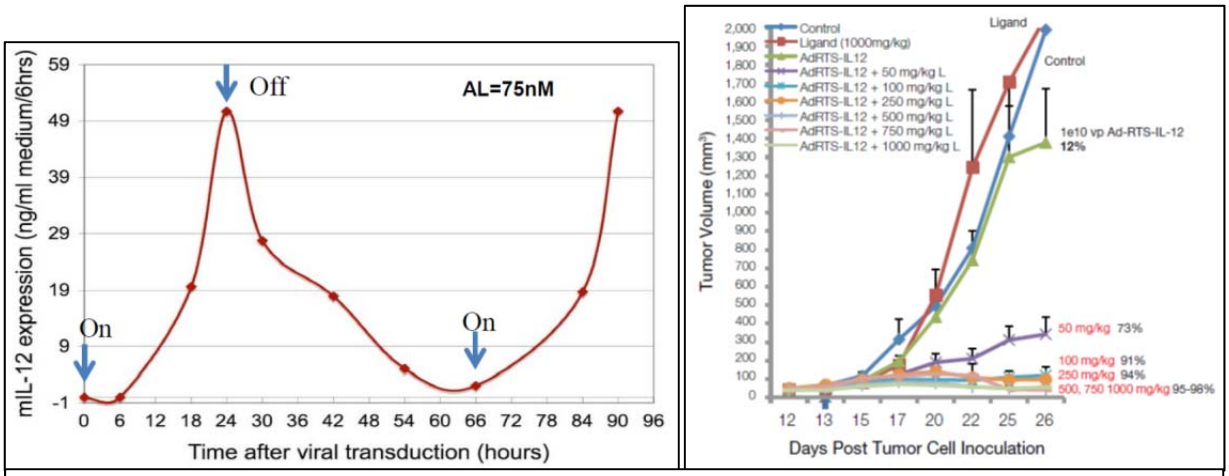


Figure 8. Intrexon's RheoSwitch is able to adjust gene expression from "off" to fully "on" in an activator-ligand dose-dependent manner. Left panel: Expression of interleukin-12 (IL-12) in a human cell line is controlled temporally by the addition and removal of the activator ligand (75 nM) in the culture media. Right panel: A dose-response relationship is observed between the dose of activator ligand administered orally to an animal bearing a tumor and the effect of IL-12 expression on the tumor cell volume. At doses 100 mg/kg and higher, tumor volume was less than 10% of that observed in the animals that did not receive the IL-12 transgene or received only the activator ligand.

Sources: Right panel, Nemunaitis, J.[9]; Left panel, Murugesan, SA, et al. [11]

The importance of Intrexon's UltraVector and RheoSwitch technologies is apparent from the clinical development program at Ziopharm Oncology, one of the healthcare companies with which it has an ECC. The collaborators have tested an adenovirus delivered interleukin-12 DNA therapy for melanoma and breast cancer in clinical trials. The studies have already yielded promising efficacy and favorable safety data.[12] Specifically, patients with unresectable stage 3 or 4 melanoma were treated with ad-RTS-hIL-12 and four different doses of INXN-1001, the activator ligand. The results demonstrated a dose-response relationship between INXN-1001 and serum IL-12, as well as interferon-γ, which is induced by IL-12. Five of the seven patients showed clinical activity with one having a prominent inflammatory reaction and flattening of the injected tumor and another having stable disease for 18 weeks. Side effects, which included fever, chills, and myalgia, resolved within a week.

The stage is set for more advanced, multigenic therapies, including separate vectors regulated by different activator ligands and single vectors with multiple reporter genes under the control of a single activator. The advantage of these two formats is the great flexibility of coordinating expression of the reporter genes, either separately or together. Preclinical research has already demonstrated the feasibility of a single transgene with four reporter genes without a reduction in expression of any of the genes relative to their expression in single-gene vectors (see Figure 9).[13]

[11] Murugesan, SA, et al. RheoSwitch-mediated regulation of IL-12 protein delivered using an adenoviral vector results in anti-tumor effects across a spectrum of tumor types. AGSCT Poster #883 (2011).

[12] Vergara, A, et al. Nonclinical and Phase I clinical studies with a regulated adenoviral gene delivery of IL-12 shows promising clinical activity in unresectable stage III/IV melanoma. AGSCT Abstract #15 (2013).

[13] Ziopharm Oncology Presentation at the Deutsche Bank Healthcare Conference on May 29, 2013.

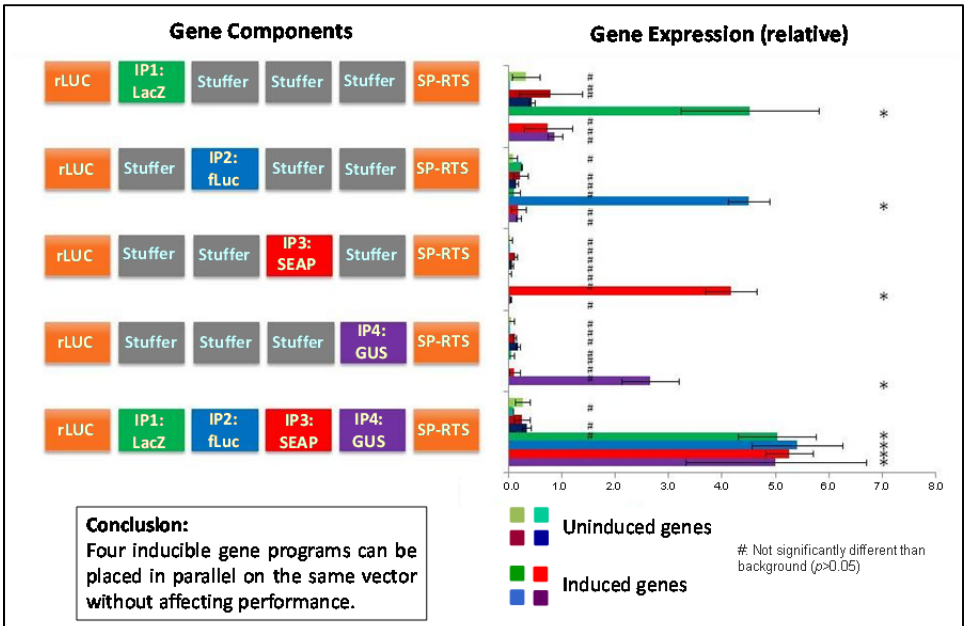
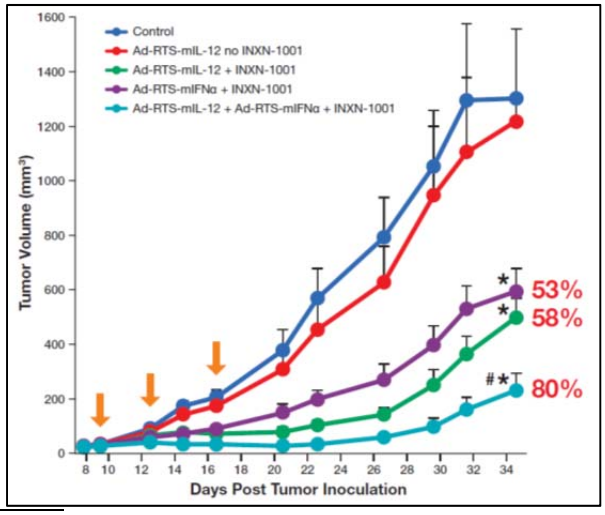


Figure 9. The feasibility of multigenic therapies has been proven possible. Intrexon created five transgenes, four of which carried only one reporter gene (labeled as IP1 – IP4 in the left panel) and placeholders (Stuffer). The fifth transgene carried all four target genes. The right panel shows that expression of the reporter genes in the multigenic construct was comparable to that of the four single-reporter transgenes.

Source: Ziopharm Presentation[13]

The benefit of multigenic therapies is illustrated in Figure 10. Adenoviral vectors carrying genes for the cytokines, interleukin-12 (Ad-RTS-mIL-12) and/or interferon-α (Ad-RTS-mINFα), were injected into breast tumor xenografts at the times indicated by the orange arrows.[14] Daily administration of the activator ligand INXN-1001 resulted in a 53% and 58% inhibition of tumor growth in animals that received treatment with interferon-α or interleukin-2, respectively. In contrast, activation of genes for both cytokines resulted in 96% inhibition, thus showing a synergistic effect of the combination therapy. Note that without the activator ligand, the Ad-RTS-mIL-12 gene therapy had no effect.

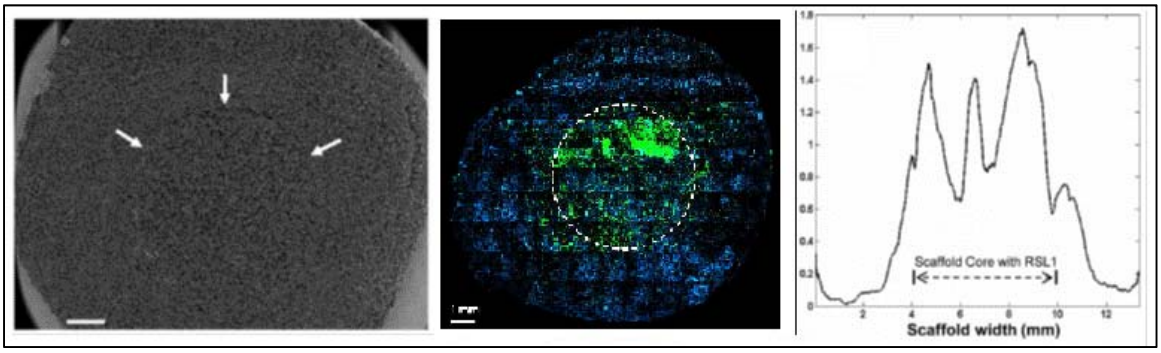
Figure 10. Inhibition of Tumor Growth with Two Gene Therapies[14]



[14] Murugesan, SR, et al. Combined direct intratumoral adenoviral delivery and production of RheoSwitch-regulated mIL-12 and mINF enhances antitumor activity in lung and breast cancer models. Cancer Res (2012); 72(8 suppl 1): Abstract 1546.

Further back in the R&D pipeline are projects that use the RheoSwitch to provide localized gene expression. This type of application may be useful in creating new surfaces for implantable medical devices and in soft tissue repair or regeneration. A simple proof-of-concept study has been completed successfully, yielding the results shown in Figure 11.[15] Scientists incorporated the RheoSwitch ligand into a poly(ester)urethane core (center portion identified by arrows in the left panel) and determined that ligand release followed a linear time course for 300 days. Melanoma cells were allowed to grow onto the poly(ester)urethane for three days before they were stained with a blue fluorescent label and evaluated for expression of a RheoSwitch-related reporter for a green fluorescent protein (center panel). An analysis of the distribution (right panel) of green fluorescence revealed that 87 ± 2.5% of the cells expressing the reporter were within the central core, versus 14 ± 2.6% outside the core containing the RheoSwitch ligand. Hence, it is possible to use artificial scaffolds to cause localized gene expression to facilitate tissue repair, even over prolonged periods of time.

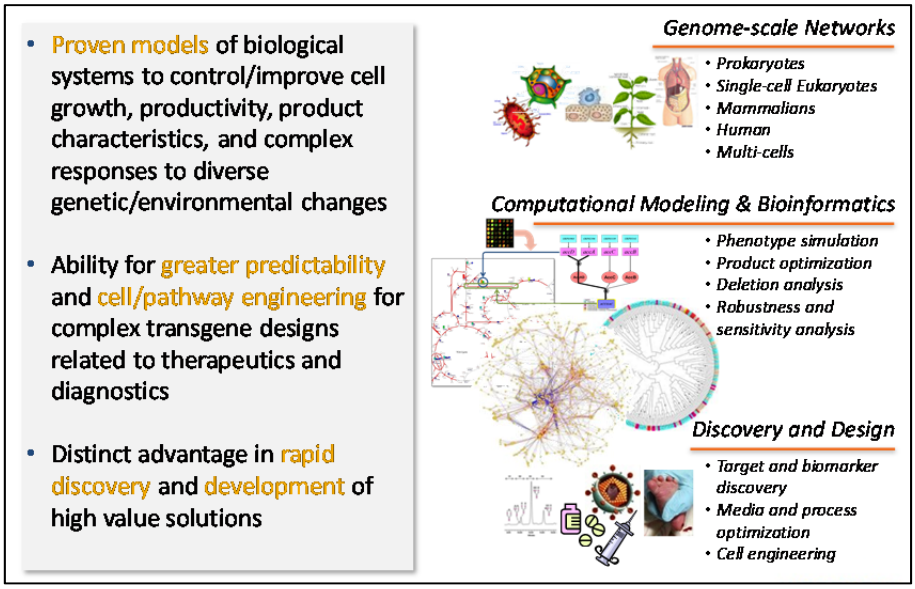
Figure 11. Use of RheoSwitch for Spatial Control of Gene Expression[15]



PROPRIETARY CELLULAR INFORMATICS

Intrexon has invested heavily in computational biology tools for such functions as *in silico* designing (i.e., computer-aided design of new proteins and/or genes), as well as a proprietary database to record and access information on DNA modules, their assembly, and their expression in various cell types. The central role of the bioinformatics software becomes apparent in Figure 12.

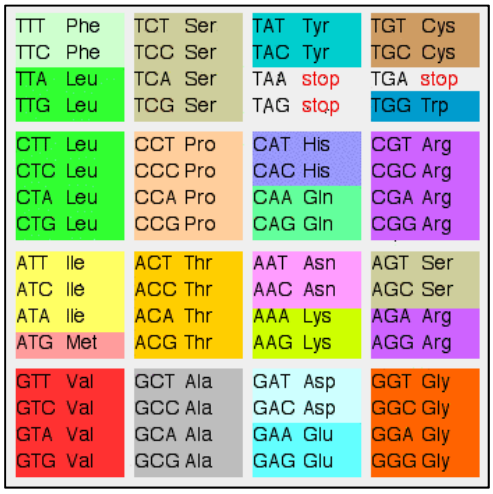
Figure 12. Informatics Contribution to Synthetic Biology



[15] Baraniak, PR, et al. Spatial control of gene expression within a scaffold by localized inducer release. Biomaterials (2011); 32(11): 3062.

But the complexity of building a gene is probably appreciated more by simply considering the huge number of possible DNA coding patterns that may be used for a single protein. As shown in Figure 13, there is more than one code for many amino acids and not all organisms are able to translate all of the codes into a protein. In addition to codes for the amino acids, there are three "stop transcription" codes.

Figure 13. DNA Codes for Amino Acids[16]



Amino Acid Abbreviations	
Ala alanine	Leu leucine
Arg arginine	Lys lysine
Asn asparagine	Met methionine
Asp aspartic acid	Phe phenylalanine
Cys cysteine	Pro proline
Gln glutamine	Ser serine
Glu glutamic acid	Thr threonine
Gly glycine	Trp tryptophan
His histidine	Tyr tyrosine
Ile isoleucine	Val valine

Intrexon's database has more than 2 million entries that include DNA modules, such as promoters, regulatory modules, and other components that enable expression of a reporter gene in a foreign host cell and delivery of the protein to a subcellular location where it will function or be prepared for secretion. Using predictive software tools, designers can rapidly build a gene for a client that, for instance, wants to produce a particular protein in a specific cell type. In this case, the database can be used to identify which of the modules have functioned well in the cell line of interest. The database can also aid in planning the sequence of enzymatic reactions that will assemble DNA modules, as considerable time and resources are often lost when the annealing steps are performed without regard to the requirements of the enzymes involved in that process. Hence, an important aspect of cellular informatics is the intellectual contribution that it provides in the predicting what combination of DNA codes, modular components, and cells has the greatest likelihood of creating a product. The gene design is then sent to a lab information management system for robotic construction of the vector. Similarly, Intrexon's LEAP instrument expedites the selection of cell line candidates to arrive at the final, optimal package of gene and cell.

Intrexon is developing a computer-based terminal system for collaborators that should facilitate communicating the parameters of each project. For instance, a terminal, which will be sited in a collaborator's office, may be used to request variants of a cytokine that will have improved pharmaco-kinetic properties. A simple input screen(s) will enable the collaborator's scientist to enter preferred amino acid sequences of the desired molecule, the cells that will be used to produce the molecule, and the desired yield to make the project economically feasible. That information is then used by an Intrexon scientist to build multiple designs of the gene for testing in the cell line of choice. Beta-testing of the terminal system is scheduled to commence next summer.

The utility of Intrexon's UltraVector platform and cellular informatics expertise is evident from the ECC with Oragenics. That program is developing antibiotics based on a family of naturally occurring compounds called lantibiotics, each of which has a unique spectrum of activity against bacteria. Historically, lantibiotics have not been produced in quantity for pharmaceutical purposes, but with Intrexon's expertise, the Company reported a novel, genetically modified host capable of producing the natural lantibiotic MU1140 and analogs, just 14 months after forming the ECC.

[16] See: www.chemguide.co.uk/organicprops/aminoacids/dna6.html

THE LEAP TECHNOLOGY ADVANTAGE

Purification of cells is a fundamental step in creating synthetic biologic products. Depending on the source, the starting material can be rather heterogeneous. For instance, the creation of a gene therapy delivered via an autologous cell graft would start with harvested tissue/cells, from which the appropriate cells would be extracted for gene modification, and after they were transfected, another cell sorting would be required prior to either expansion in culture and/or administration. Just as important, obtaining FDA approval of such a cell therapy would require tight control over the entire process and a well-defined final product in terms of cell purity and viability. In addition, a commercial enterprise based on such a product would probably want to protect the product from competition with a patent(s) and that would require a definition of the product not unlike the one needed by the FDA. For other applications, such as the manufacture of a novel genetically engineered molecule or simply a common compound through a newly created biological process, cell purity plays a crucial role in the defining production costs.

Several techniques have been developed to sort and purify cells based on various parameters, but the most commonly employed are cell surface biomarkers and the most common technology is fluorescence-activated cell sorting. This technology utilizes fluorescent-labels to identify a specific biomarker(s) and then to separate individual cells based on the presence of the biomarker as they pass through a chamber. The technique has gained wide acceptance, but it has limitations. For instance, fluorescence-activated cell sorting is impractical with small sample sizes, and its ability to accurately sort cells is dependent on the number of biomarkers being used, with accuracy declining as the number of biomarkers used to define the cell population increases.[17]

Cell Purification with LEAP: Intrexon acquired a cell processing instrument based on laser-enabled analysis and processing (LEAP™) technology in 2011 that uses a computer-guided laser to create highly purified cell populations. The instrument incorporates an advanced form of laser scanning technology utilizing fluorescence and/or light scattering in combination with morphometric analyses of the cell and/or subcellular components (i.e., nucleus) to identify cells of interest.[18,19] In addition, it is capable of reproducibly returning to a spatial location in a culture dish for temporal analyses of a specific group of cells or for multiple evaluations with separate probes. The instrument provides real-time images of cells in culture that allow the user to dynamically adjust the selection criteria and observe how the changes would alter the makeup of the final cell population once the laser is activated. Of course, standardized selection criteria may be implemented for automatic cell processing for routine analyses.

The LEAP instrument offers a number of advantages for working with cells. For one, it can be used with culture wells of different sizes without adjusting the optics for visualizing the cells. Indeed, the galvanometric scanning optics, which use mirrors to focus the laser beam, minimize the movement of the staging, thereby permitting the selection of adherent (e.g., fibroblasts) or non-adherent (e.g., T cells) populations for targeting. Three different methods are available for eliminating unwanted cells from a heterogeneous mix: (i) photothermal ablation, which requires an innocuous red dye in the culture medium, results in rapid ablation of the targeted cells, but causes a sudden release of cytoplasm into the culture media; (ii) photochemical ablation induces apoptosis with little necrosis via the formation of reactive oxygen species; and (iii) photomechanical ablation, which utilizes repeated sublethal pulses to disrupt the cells, independent of their composition. Since each of these mechanisms has attributes that are favorable for different applications, they increase the flexibility and effectiveness of the LEAP workstation. Figure 14 presents a basis for choosing one method over the others based on laser power.[18]

In addition, the LEAP technology supports high-throughput cell selection using specific criteria either semi-manually, when the operator sets up the selection criteria, or automatically, when predefined criteria are used. Once the criteria are established, the instrument performs the task rapidly and in a highly

[17] Amos, PJ, et al. Methods of cell purification: a critical juncture for laboratory research and translational science. Cells Tissues Org (2012); 195(1-2): 26.
[18] Koller, MR, et al. High-throughput laser-mediated in situ cell purification with high purity and yield. Cytometry Part A (2004); 61A: 153.
[19] Szaniszlo, P, et al. Scanning cytometry with a LEAP: Laser-Enabled Analysis and Processing of live cells in situ. Cytometry Part A (2006); 69A: 641.

reproducible manner. Numerous reagents have been developed that facilitate the process, including monoclonal antibodies that recognize various cell-surface markers and are used with fluorescence-activated cell sorting. LEAP technology is also compatible with the latest fluorescent compounds that label intracellular and extracellular molecules of living cells.[20,21] These indicators can be used in combination with morphometric properties (e.g., cell and/or nucleus size, and cell shape).

Published results obtained with the LEAP technology underscore the value of the instrument to Intrexon's synthetic biology program. Purification of a select type of cell from a mixture is dependent on the cell density and the percentage of contaminating cells. This relationship is presented in Figure 15.[18]

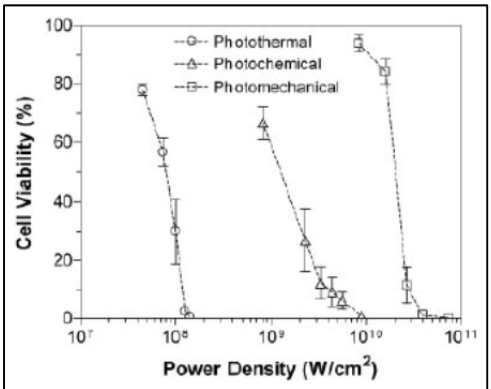


Figure 14. In situ cell purification by the LEAP instrument using three mechanisms, photothermal, photochemical, and photomechanical.

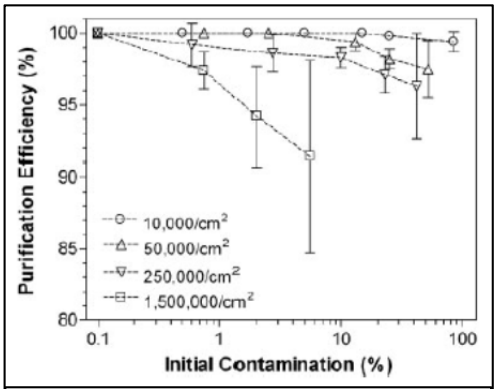


Figure 15. Purification efficiency via photothermal laser treatment at various cell densities and starting contamination percentages.

The results obtained in Figure 15 were comparable across seven cell populations of three different species, although sensitivity (as measured by LD_{50}) between cell types was greater with the photochemical method than with the other two. By taking into consideration the data presented in the two figures above, it is clear that by varying the laser method and cell density, optimal purification efficiencies can be achieved. In automated, closed-loop processing, LEAP routinely achieved 99.5% purity with yields greater than 90% with certain samples ranging from 10 – 100,000,000 cells per cm^2. (Yields vary with both the cell type and starting contamination levels.) Moreover, throughput processing speeds were in the range of 1,000 – 100,000 cells per second when used to purify samples with starting contamination percentages of 99% – 0.1%. Even when the sample size is small, it is possible to achieve 95% purity and greater than 80% cell recovery, even when contamination is near 50%. This is accomplished by plating the cells at a lower density that require slightly more time to process (still done in a matter of minutes). With larger samples, where lower yields are acceptable, the cells can be plated at a higher density and the purification is performed more rapidly with yields greater than 90%.[19]

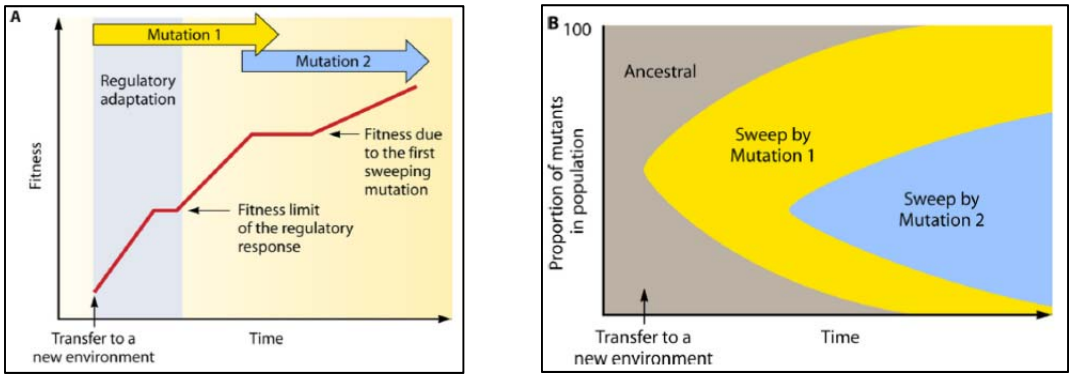
There is a less obvious, but equally important advantage – the LEAP instrument provides the least intrusive method of cell selection that is available. That becomes apparent when one considers the impact of an external stress (e.g., suboptimal availability of an essential nutrient *in vivo* or cell sorting via FACS equipment) on a cell population. This is critical to optimizing cell cultures, because stresses are now known to initiate adaptive responses coordinated through regulatory mechanisms and genetic mutations. When a cell is stressed, it attempts to adapt to the environment and that can give rise to a variety of regulatory and genetic responses. Accordingly, a small subset of the original cell population may gain an advantage, but also lose traits essential to their intended use. Figure 16 illustrates the effect of regulatory changes and two mutations on a cell population after a stressor (i.e., transfer into a new

[20] Chudakov, DM, et al. Fluorescent proteins and their applications in imaging living cells and tissues. Physiol Rev (2010); 90(3): 1103.

[21] Hori, Y, and Kikuchi, K. Protein labeling with fluorogenic probes for no-wash live-cell imaging of proteins. Curr Op Chem Biol (2013); 17: 644.

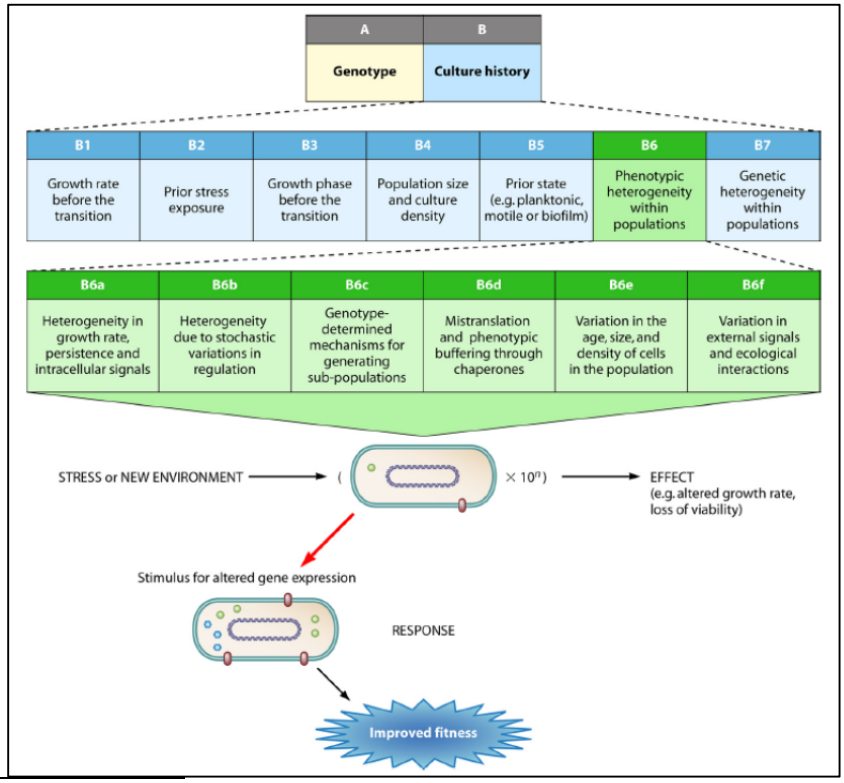
environment) takes place.[22] Briefly, it comes down to "only the fittest survive" when the environment changes.

Figure 16. The Effect Adaptation on a Cell Population[22]



The effects of genetic and environmental factors (i.e., culture conditions) on a cell population are described in greater detail in Figure 17. Exposure to prior stress, growth rate of the cells, cell density, phenotypic variability (i.e., physical and biochemical traits), and genetic variability ultimately define the culture. When a cell population is exposed to a stress or new environment, all of these factors contribute to the response. By way of example, the phenotypic traits that determine a cell population's response include each cell's growth rate and persistence, differences in regulatory systems between cells, variability in genetically defined mechanisms for generating subpopulations, intracellular corrections by chaperone proteins, and differences in the cells' ages, sizes, and microenvironments (i.e., cell densities and extracellular signals).

Figure 17. Effects of Cell Culture Heterogeneity on Adaptation[22]



[22] Ryall, B, et al. Culture history and population heterogeneity as determinants of bacterial adaptation: the adaptomics of a single environmental transition. Microbiol Mol Biol Rev (2012); 76(3): 597.

Figure 17 was originally in a scientific paper discussing bacteria and the interactive effects of regulatory and genetic responses to stress — that necessitated references to biofilm and ecological interactions. But otherwise, the discussion is pertinent to any cell. Hence, investors should understand that Intrexon's tightly controlled cell culture system and LEAP instrument generate high-quality cultures.

Special Cell Purification Applications – Protein Production: This approach has been utilized to automate the selection of cells secreting human antibodies to optimize the cell line for commercial production purposes.[23] This was accomplished with a green fluorescent label for live cells and red fluorescently tagged-monoclonal antibodies that recognized human immunoglobulins. Thus, the LEAP instrument rapidly identified green-labeled cells and those with halos of red. These images were analyzed with the instrument's algorithm to expedite the identification and ablation process. Figure 18 provides photomicrographs of the parental cell line and the derived clone after 50 population doublings post-purification. The improvement in the antibody-producing efficiency of the purified cell culture is portrayed rather clearly in the bar graph.

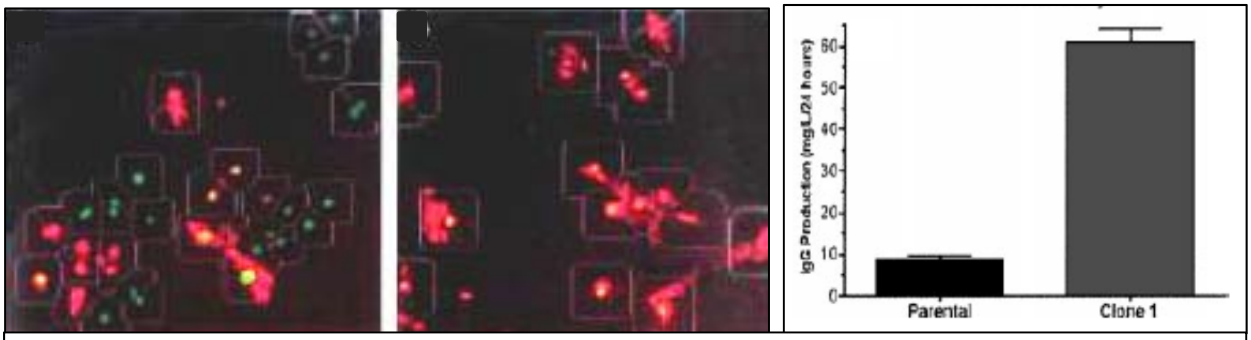


Figure 18. LEAP technology significantly improves the yield of a specific protein produced in cell culture. The left panel is a photomicrograph showing a parental cell culture labeled with a green fluorescent marker and the desired protein labeled by an antibody carrying a red fluorescent tag. The instrument used an algorithm to locate each cell and create a box (white shape) around each for measuring the amount of red fluorescence associated with each cell. The cell that produced the highest quantity of the desired protein in each well was retained, while all other cells were destroyed. The middle panel shows that this procedure results in a culture characterized by stable, homogeneous production of the desired protein. The right panel quantifies the effect of the cell selection process on productivity – it resulted in a roughly 6-fold increase in yield, measured in the milligrams of desired protein produced per liter of culture in 24 hours. (In this example, the protein of interest was an immunoglobulin.)

Source: Hanania, EG, et al.[23]

Isolation of the most productive clone is essential to optimizing commercial protein production. Another is optimizing the cell culture conditions since they may alter not only cell growth, but also the quantity and quality of the protein produced. The LEAP technology has been used successfully to address this issue as evidenced by experiments evaluating the effect of different culture media on charge heterogeneity of monoclonal antibodies.[24] (The charge on antibody molecules can significantly alter their ability to bind to targets and their pharmacokinetic properties.[25]) By standardizing the culture conditions, including the media used, even therapeutic proteins, which require the most rigorous standardization, can be manufactured consistently with high productivity.

Special Cell Purification Applications – Cell Therapeutics: Cell therapies offer a unique opportunity to address medical conditions that have proven resistant to pharmaceutical intervention. In some cases, autologous cells (i.e., those from the patient) have proven essential to avoid stimulating an immune attack on the grafted cells. In other cases, allogeneic cells (i.e., from a donor) offer a suitable alternative. Key to the success of these treatments is the purity of the cells and expansion of the cells without altering their genetic and phenotypic traits.

[23] Hanania, EG, et al. Automated in situ measurement of cell-specific antibody-secretion and laser-mediated purification for rapid cloning of highly-secreting producers. Biotechnol Bioengin (2005); 91(7): 872.

[24] Gerber, MA, et al. Integrated strategies for clone and media formulation selection. BioProcess Int (2008); 6(1): 58.

[25] Bumbaca, D, et al. Physiochemical and biochemical factors influencing the pharmacokinetics of antibody therapeutics. AAPS J (2012); 14(3): 554.

The ECC between Intrexon and Fibrocell Science is largely related to the development of genetically modified cell therapies for diseases with a genetic basis. These include four skin disorders: recessive dystrophic epidermolysis bullosa, which is a rare, but extremely painful condition that afflicts the individual from birth (U.S. patient population: 30,000); morphea, which is a localized form of the autoimmune disease scleroderma (patient population: 8,000); eosinophilic fasciitis, which is akin to scleroderma, but affects connective tissues of muscles, blood vessels, and nerves (patient population: 4,000); and psoriasis that afflicts about 4.5 million individuals.

Perhaps the most challenging to work with are pluripotent stem cells, given the difficulties of defining distinct cell populations and maintaining their pluripotency, quality, and genetic stability in culture. The LEAP instrument has already been compared with common, alternative methods (e.g., enzymatic and manual dissociation) for its ability to support propagation of these cells in a consistent manner that maintains their genetic and phenotypic traits. The results demonstrate a distinct advantage in using laser-mediated propagation, represented by more uniform colony sizes based on colony diameters and number of cells in each colony.[26] (See Figure 19.) This is important because it facilitates cell culture methods, but it also eliminates the effect of colony size, variability in differentiation, and gene expression on the quality of the therapeutic cells.

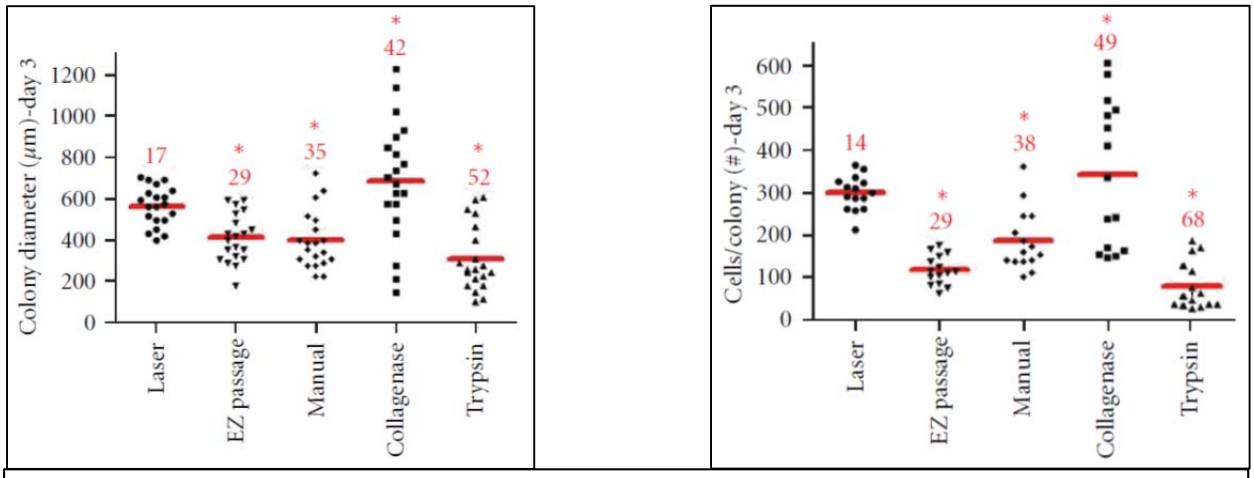


Figure 19. Passage of induced pluripotent stem cells shows the improved uniformity achieved with LEAP technology 3 days after passage. Left panel: Laser-mediated passage was compared with two manual methods, involving a commercial tool (EZ passage) and pipette (Manual), and with two enzymatic methods utilizing collagenase and trypsin. The scatter plots show the colony diameters, with the mean as a red bar and the coefficient of variation is provided numerically in red. Significant differences between results obtained with LEAP and the other methods are identified by a red asterisk. Right panel: The number of cells per colony exhibited significantly greater variability with the alternative methods than with laser-mediated propagation.

Source: Elliott, KAH, et al.[26]

Since manual methods of cell propagation are not feasible for large-scale production, further experiments focused on the enzymatic treatment alternatives. When induced pluripotent stem cells were cultured under conditions that favor differentiation into cardiomyocytes (heart muscle cells), laser-mediated propagation once again proved superior, as portrayed in Figure 20.

[26] Elliott, KAH, et al. Laser-based propagation of human iPS and ES cells generates reproducible cultures with enhanced differentiation potential. Stem Cells Int (2012); Article #926463.

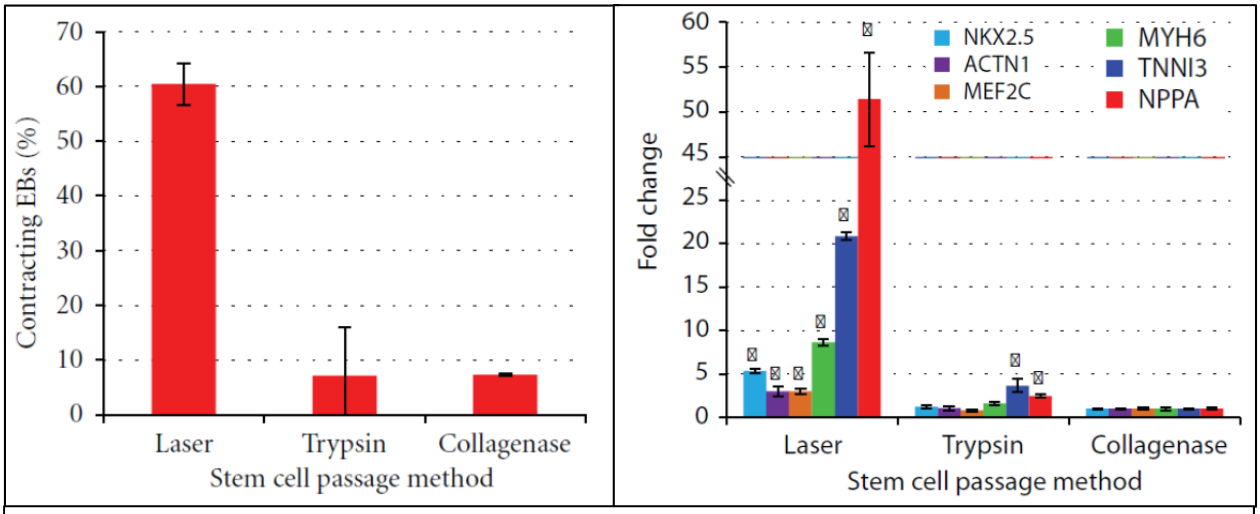


Figure 20. Laser-mediated cell propagation results in better cell differentiation and gene expression than two enzymatic methods. Left panel: Induced pluripotent stem cells grown in culture and passaged with LEAP, trypsin, or collagenase differ significantly in their ability to differentiate into beating cardiac cells (cardiomycytes), with significantly more laser-passaged cells differentiating. Right panel: Gene expression varied in parallel with cardiomycyte differentiation, as noted by significantly greater expression of 6 genes by laser-passaged cells than the enzymatically passaged cells.

Source: Elliott, KAH, et al.[26]

Results similar to those depicted in Figure 20 were achieved when induced pluripotent stem cells were stimulated to differentiate into neurons. Hence, two entirely different sets of genes respond better when the cells are passaged with the LEAP instrument, which suggests that the technology has a universal benefit when employed for stem cell applications.

We note that Intrexon is collaborating with the Sanford-Burnham Medical Research Institute, which is one of the largest generators of induced pluripotent stem cells in the world, to accelerate stem cell research. The Institute is gaining access to the LEAP technology and to the RheoSwitch in exchange for commercial and intellectual property related to stem cells.

Supporting Cellular Research – the Optoinjection Technique: The LEAP technology also offers an approach to studying cellular biology by facilitating the uptake of molecules of interest to perturb cell metabolism and/or gene expression. The sizes and physical properties of the molecules cover broad ranges, from small ions to large, charged macromolecules.[27] There does not appear to be a restriction on the types of cells amenable to this type of intervention.

Laser-induced permeabilization is optimally achieved with multiple, sequential low-radiant exposures rather than a single, high-intensity exposure. The technique may be used on single cells selectively or on 2,000 – 5,000 cells per second with a grid and wide-angle laser beam. Targeting multiple cells is possible, because optoinjection probably causes a temporary pore(s) to form in the membrane that closes exponentially within 30 seconds. A useful aspect of the LEAP instrument is the imaging and targeting software that enable identification of the cells and control the laser. Thus, it is possible to selectively deliver molecules even to traditionally refractory cells with 79%-91% efficiency and with cell viability of 81%-93%.

[27] Clark, IB, et al. Optoinjection for efficient targeted delivery of a broad range of compounds and macromolecules into diverse cell types. J Biomed Opt (2006); 11(1): 014034.

mAbLogix – For Fully Human Monoclonal Antibodies

Intrexon acquired Immunologix in 2011, garnering a patented technology, called mAbLogix, for producing fully human monoclonal antibodies *in vitro*.[28] Unlike prior approaches to preparing therapeutic antibodies, this platform utilizes naïve human B cells isolated from tonsil tissue and transformed through a patented, immortalizing process involving viral exposure under low-speed centrifugation.[29] The key element of this platform rests in the high transformation rate (about 85%), which means that a substantial portion of the antibody-designing capability of the human immune system is represented by the immortalized cells. *Ex vivo* stimulation is then used to produce a library of different immunoglobulins for subsequent screening against the target antigen. Intrexon's LEAP technology is then used to isolate the antibody-producing cells of interest.

The mAbLogix platform saves time and resources by avoiding the immunization and humanization steps that are required with antibodies produced in animals. It also expedites the task of isolating a suitable clone(s), by starting with a larger pool of antibody-producing cells than is possible from alternative techniques.

The novelty of the mAbLogix platform today resides in Intrexon's vast library of human B cell clones that produce antibodies. This enables the Company to screen the library for antibodies that recognize a particular antigen(s) for further testing and development. Subsequent engineering is possible with the UltraVector platform. Similar approaches have been attempted on a much smaller scale with synthetic antibodies.[30,31]

Intrexon is developing monoclonal antibody therapies for two life-threatening infectious diseases via an ECC with Synthetic Biologics. The targets are *Bordetella pertussis,* which causes pertussis (i.e., whooping cough), and *Acinetobacter baumanii*, which is the cause of many serious hospital-acquired infections and has a unique ability to rapidly develop resistance to traditional antibiotics. Molecular targets for antibody therapeutics have already been characterized and antibodies have been created against *A. baumanii* and the pertussis toxin.[32,33]

Another ECC, with Soligenix, is developing a monoclonal antibody therapy against a biological warfare threat, *Burkholderia pseudomallei.* Here, too, the bacterium and has been well studied and initial research into immunizations has been conducted.[34,35]

[28] Duvall, M, et al. A novel platform to produce human monoclonal antibodies. mAbs (2011); 3(2): 203.

[29] O'Doherty, U, et al. Human immunodeficiency virus type 1 spinoculation enhances infection through virus binding. J Virol (2000); 74(21): 10074.

[30] Cobaugh, CW, et al. Synthetic antibody libraries focused towards peptide ligands. J Mol Biol (2008); 378(3): 622.

[31] Pantazes, RJ and Maranas, CD. MAPs: a database of modular antibody parts for predicting tertiary structures and designing affinity matured antibodies. BMC Bioinformatics (2013); 14(1): 168.

[32] Luo, G, et al. Active and passive immunization protects against lethal, extreme drug resistant-*Acinetobacter baumanii* infection. PLoS One (2012); 7(1): e29446.

[33] Sato, H, et al. Monoclonal antibody against pertussis toxin: Effect on toxin activity and pertussis infections. Infect Immun (1984); 46(2): 422.

[34] Breitbach, K, et al. Induction of protective immunity against *Burkholderia pseudomallei* using attenuated mutants with defects in the intracellular life cycle. Trans R Soc Med Hyg (2008); 102 (suppl 1): s89.

[35] Larsen, JC, et al. Pathogenesis of *Burkholderia pseudomallei* and *Burkholderia mallei.* Mil Med (2009); 174(6): 647.

AN IDEAL BUSINESS MODEL: EXCLUSIVE CHANNEL COLLABORATIONS

Intrexon has adopted a franchise-based business model to maximize the utilization of its technological expertise. This is executed through exclusive channel collaborations (ECCs) with companies that have expertise in specific areas that stand to benefit from synthetic biology. The deals are being signed in four general fields of commercialization, healthcare, food, energy & chemicals, and environment.

Each ECC is negotiated separately, but the template that is being used includes a technology access fee, R&D cost reimbursement for work performed by Intrexon, milestones based on product development and/or commercial achievements, and royalties. This framework should help to support Intrexon's operations over the next few years as ECCs are signed and royalty streams grow in size and number.

An ECC is managed by a Joint Steering Committee comprised of representatives from Intrexon and its partner. The group coordinates the collaboration, including use of in-house and third-party (e.g., clinical research organization) skill sets as needed. Indeed, it is there that decisions are made regarding which partner in the collaboration is better suited to perform a particular function in the project. Other decisions, such as which cell type should be used for synthesis of a protein, are taken up by the committee and reached through a review of various factors including economics, protein expression levels, and the ability to scale production for commercial applications.

HEALTHCARE

Intrexon has focused a large proportion of its early business development efforts on the healthcare field. Thus far, four ECCs have been signed with companies targeting bacterial infections, two are with firms that are developing cellular therapeutics, one is developing genetic therapies for cancer, and another is working to improve the production of alkaloid compounds that are active pharmaceutical ingredients.

Ziopharm Oncology

Ziopharm Oncology Inc. is developing therapeutic agents to treat various types of cancer. An ECC was formed in January 2011 that granted Ziopharm rights to Intrexon's technologies for the field of oncology. The collaboration has developed two clinical-stage therapies involving the powerful immune regulator interleukin-12. The lead candidate is a gene therapy delivered via an adenovirus and designated as Ad-RTS-hIL-12 that is in Phase 2 trials for advanced melanoma and recurrent or metastatic breast cancer. The other therapy consists of genetically modified dendritic cells of the immune system that carry a RheoSwitch-controlled gene for IL-12. That therapy is being developed to treat glioblastoma. More advanced, multigenic therapies are at an earlier stage of development.

Oragenics

Oragenics is a biotechnology company with oral probiotics on the market and novel therapeutics for the treatment of antibiotic-resistant infections under development through an ECC. The development program is focused on a family of naturally occurring, broad-spectrum antibacterial compounds called lantibiotics. These molecules include unusual amino acids that render chemical synthesis of the small peptides very difficult. Attempts to harvest them from bacteria growing in culture have met with limited success because the lantibiotics kill the cells before the concentration increases sufficiently to permit large-scale purification. Intrexon has already succeeded in purifying Oragenics' lead lantibiotic called MU1140 in sufficient quantity to support clinical development. Tests have shown that this molecule is active against a wide variety of disease-causing Gram positive bacteria, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococci*, *Clostridium difficile, Mycobacterium tuberculosis,* and anthrax. Intrexon succeeded recently in creating variants of MU1140 and structure-activity studies will soon commence to assess which molecule to take into IND-enabling studies.

Synthetic Biologics

Synthetic Biologics is developing drugs to prevent and treat infectious diseases. Its ECC grants it access to Intrexon's technologies for three programs, two of which have been selected and the third is presently undecided. The two programs utilize the mAbLogix platform and LEAP instrument for developing

monoclonal antibodies against *Bordetella pertussis*, which is the causative agent of whooping cough (pertussis), and *Acinetobacter baumanii*, which causes a serious hospital acquired infection. Use of monoclonal antibodies against these Gram negative bacteria makes sense – *Bordetella pertussis* is readily eliminated by antibiotics, but its toxin persists in a patient's blood and can ultimately kill. Monoclonal antibodies against the toxin should rapidly attack the bacteria and remove the toxin. In contrast, *Acinetobacter baumannii* infections are very difficult to treat with antibiotics because this bacterium readily develops resistance to drugs and some strains are pan-drug resistant. Monoclonal antibodies offer a different approach to the microbe, one that may prove less likely to permit development of resistance.

Fibrocell Science

Fibrocell is a cell therapy company with the first such treatment approved for aesthetics on the market and a long-range strategic plan that will take it into the field of medicine. LAVIV® is presently sold for the improvement of nasolabial fold wrinkles to dermatologists in the United States directly and in China through a partially-owned subsidiary. The R&D pipeline has one product for the aesthetics market, an Autologous Crème that will be sold to patients who are treated with fibroblast injections. It also includes autologous fibroblasts (called azficel-T) for two therapeutic applications, improving the voice of individuals with scarred vocal cords and treating restrictive burn scars (i.e., scars that prevent freedom of joint motion). Fibrocell entered into an ECC to gain Intrexon's assistance in creating a genetically modified fibroblast to treat a rare, inherited skin condition called recessive dystrophic epidermolysis bullosa. The originally ECC was subsequently amended to include dermatological conditions with an autoimmune or inflammatory basis – morphea (a localized form of scleroderma), cutaneous eosinophilia, and moderate-to-severe psoriasis.

AmpliPhi Biosciences

AmpliPhi Biosciences is the leading developer of bacteriophage therapies for antibiotic resistant bacterial infections. These viruses, which specifically attack bacteria, have been considered attractive candidates for therapeutic applications, but development attempts have been thwarted by bacteriophages' extremely high mutation rates. The ECC was formed to apply Intrexon's technology platforms to construct a reliable and stable source of phages for antibiotic resistant bacterial infections associated with acute and chronic wounds, including treatment of acute and chronic *Pseudomonas aeruginosa* lung infections that are common in burn units and *Clostridium difficile* infections. The most advanced products in AmpliPhi's R&D pipeline are for acute and chronic lung infections, methicillin-resistant *Staphylococcus aureus*, and equine endometreitis. The company recently entered into a Collaborative Research and Development Agreement with the U.S. Army for the development of bacteriophage therapeutics to treat *P. aeruginosa*, *S. aureus*, and *E. coli* infections. In addition, AmpliPhi has reported preclinical data showing that its bacteriophage is effective in eliminating *P. aeruginosa* from the lungs within 24 hours and with a lower level of lung inflammation at 48 hours than control.[36] The results have bearing on the use of bacteriophage to treat cystic fibrosis patients who are susceptible to *P. aeruginosa* infections.

Genopaver, LLC

Genopaver is a privately owned company formed as an affiliate of Third Security, which is an R.J. Kirk company. The goal of the ECC, which was consummated in March 2013, is to expedite the development and commercialization of alkaloids from genetically modified cell lines for use in pharmaceutical production. Genopaver paid Intrexon $3 million as a technology access fee and agreed to pay royalties at a low double-digit rate on gross profits of products developed via the collaboration. Alkaloids, which are often produced via fermentation, are found in a wide range of therapeutic families with a variety of clinical uses. The first product being developed is an active ingredient in pain killers.

[36] Pabary, R, et al. S103 Anti-pseudomonal bacteriophage cocktail reduces inflammatory responses in the murine lung. Thorax (2012); 67(suppl 2): A50.

Soligenix, Inc.

Soligenix is developing drugs for inflammatory diseases and for biodefense, with products in clinical development ranging from oral mucositis to an anthrax vaccine. The ECC was formed to capitalize on Intrexon's proprietary technologies for human monoclonal antibodies as a treatment for melioidosis, an infection by the Gram-negative bacterium *Burkholderia pseudomallei*. This infectious agent is found in the soil of northern Australia and Southeast Asia, and it is listed as a high priority threat to U.S. national security.[37] There are several reasons that this bacterium is considered a serious threat – transmission occurs through percutaneous inoculation, inhalation, ingestion, or aspiration following environmental exposure to soil, water, or aerosols; it is a rapidly progressive infection that is often deadly (up to 40% of the time); and treatment requires multiple drugs over a prolonged period and even then, relapse is not uncommon.

FOOD

Intrexon is working in this field to address an issue stemming from the projected increase in the world's population (see Figure 1), namely improving the efficiency in food production. At the farm level, this has been behind a major shift from smaller to larger farms. The trend has been pervasive throughout the farming industry, but Figure 21 makes the point by showing the changes in dairy farm sizes and identifying profitability as the driving force.[38]

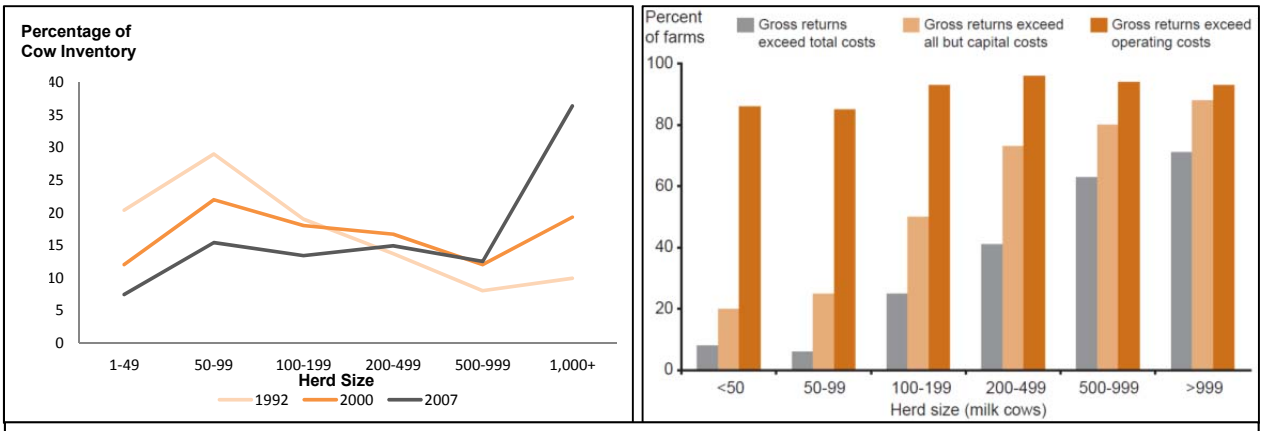


Figure 21. Industrialization of livestock agriculture in the United States has shifted production to large farms to realize efficiencies and maximize profits. Left panel: The proportion of dairy cows in large herds (500 – 1,000+) increased between 1992, 2000, and 2007, while the proportion in small herds (1 – 199) declined. Right panel: The driving force behind the industrialization of dairy farming was economic in nature, as fewer farms with smaller herds were able to cover their total costs than those with larger herds in 2005.

Source: MacDonald, JM [38]

Industrialization of farming in the United States has resulted in efficiencies, but it has also created new risks and challenges. Livestock are now fed in confined conditions and animals are bred to gain weight or produce milk efficiently and with specific meat, milk, or egg characteristics. Yet, breeding is a slow process to achieve a desired effect, if it is reached at all.

In addition, sub-therapeutic doses of antibiotics continue to be used to promote growth, particularly of poultry and swine, despite calls for a halt to the practice. The concern is that use of antibiotics similar to those administered to humans favors the development of drug-resistant bacteria that threaten mankind today.

[37] 2012 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy. U.S. Dept Health and Human Services.

[38] MacDonald, JM and McBride, WD. The transformation of U.S. Livestock Agriculture: Scale Efficiency, and Risks. Economic Information Bulletin #43, U.S. Dept. of Agriculture (2009).

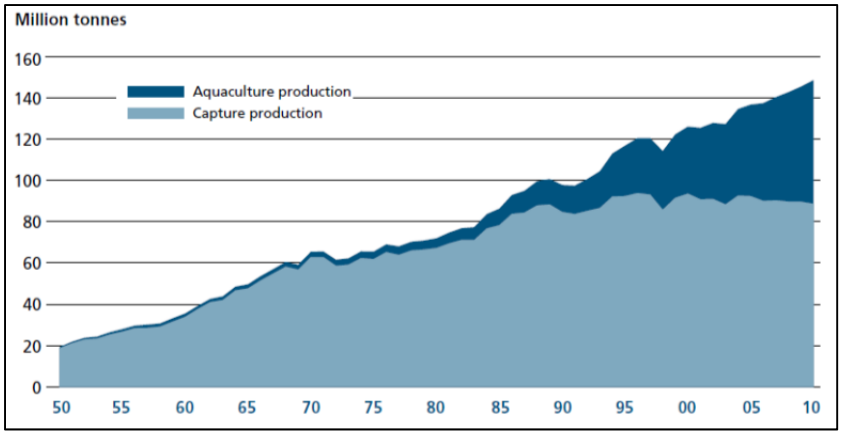
Intrexon's goal is to use its suite of technologies to more rapidly develop livestock and crops than possible through breeding and to increase disease resistance, enhance growth, and raise the nutritional value of agricultural products. The Company's first ECC in this field provides a good example of how this can be accomplished with minimal risk to humans and the environment.

AquaBounty

This partially owned subsidiary of Intrexon is breaking new ground in seeking FDA approval of the first genetically-modified "animal" for human consumption. In actuality, the fish is an Atlantic salmon with only a single gene altered via a transgene. The synthetic gene consists of a promoter for constitutive reporter expression combined with a growth hormone gene from a related species, the Chinook salmon.[39] That small modification results in a fish that is able to grow throughout the year, rather than in the normal, seasonal nature of the wild-type Atlantic salmon. The result is a 40% reduction in the time required to reach its normal mature size, which means that the AquAdvantage® salmon can be harvested that much sooner and consumes 25% less food than its wild-type counterpart.[40] There is another distinct difference between genetically-modified and the wild-type fish – the eggs are treated to yield only sterile AquAdvantage salmon. Indeed, the very success of the company's business model hinges on sales of the eggs of sterile female salmon to commercial fish farms, thereby preventing unsanctioned breeding as a source of competition or as a threat to the environment. (Female salmon eggs will be sold because their reproductive organs will not mature as they may in sterile male salmon.)

Over the past six decades, aquaculture has grown rapidly to become a meaningful source of food worldwide, reaching 60 million tons with a value of $119 billion in 2010.[41] (See Figure 22.) This industry should account for an even greater proportion of the world's future source of fish, given the over-fishing of our oceans, and farmed salmon will likely figure in that growth, as Atlantic salmon accounted for more than 1.4 million tons of production in 2010.

Figure 22. World Capture Fisheries and Aquaculture Production[41]



The road to approval has been extremely long, as AquaBounty submitted an investigational New Animal Drug Application in 1995 and began tests to gain regulatory approval. The data was provided to the FDA in 2001 and then eight years passed until the agency finally issued guidance on evaluating genetically engineered animals as veterinary drugs. AquaBounty responded to the guidance within months and since then, the agency has said the fish is safe to eat, completed a draft environmental assessment of the sterile fish, and the public comment period ended in April of this year. Intrexon and AquaBounty are anticipating final approval of the salmon in the near future. It seems likely that the decision will open the

[39] Yaskowiak, ES, et al. Characterization and multi-generational stability of the growth hormone transgene (EO-1alpha) responsible for enhanced growth rates in Atlantic salmon. Transgenic Res (2006); 15(4): 465. (Erratum: Transgenic Res (2007); 16(2): 253.)

[40] Tibbetts, SM, et al. Effects of combined 'al-fish' growth hormone transgenics and triploidy on growth and nutrient utilization of Atlantic salmon (*Salmo salar L.*) fed a practical grower diet of known composition. Aquaculture (2013); 406-407: 141.

[41] Food and Agriculture Organization of the United Nations. State of the World Fisheries and Aquaculture 2012. Rome, Italy.

regulatory door to additional genetically modified animals that are the subject of an ECC signed on February 14, 2013. The collaborators are focusing on the development and commercialization of genetically modified fish for human consumption that are more nutritious, have greater muscle mass, and grow quickly to maturity.

Eli Lilly's Animal Health Division, Elanco

The ECC with Eli Lilly's animal health subsidiary, Elanco, has two primary objectives: (i) to develop products to prevent certain infections in pigs and (ii) to create therapies for chronic diseases associated with aging in companion animals.

The first project may address a concern that gained considerable attention as industrialization of farming progressed, namely the possibility that use of sub-therapeutic doses of antibiotics contributes to the selection of drug-resistant bacteria in the general environment. Farms have begun to reduce their use of antibiotics to promote growth, but the practice is still commonplace in the swine industry, in which the largest quantities of antibiotics are consumed based on a per animal-mass basis.[42] Indeed, such bacteria as *E. coli* and *Clostridium difficile* pose a threat to livestock health and consumers of pork products. Yet, with industrialization of farming, the risk of epidemic infections has increased.[38] A novel preventive treatment that bears little relationship to human antibiotics would address both concerns and probably gain wide acceptance.

The second project has not been discussed in detail, and the chronic diseases associated with aging in companion animals are too many to guess which is (are) involved in the agreement. However, we think it is worth mentioning that historically drug development has often proceeded from animal to man, and so, the collaboration with Eli Lilly's animal health division may eventually extend to human therapies that are based on the work being performed under the current ECC.

ENERGY & CHEMICALS

Synthetic biology offers a means to potentially increase the availability and lower the cost of chemicals in common use today, while providing an avenue to new compounds. The headline grabber in the area of energy and chemicals has been the production of ethanol from a variety of organic materials, including corn, sugar cane, and algae. But synthetic biology has been used for years for less obvious applications. Enzymes replaced chemical processes used by the textile industry resulting in less water consumption, while specialty chemicals have been created for incorporation into such products as adhesives, paper, wood, and paints.

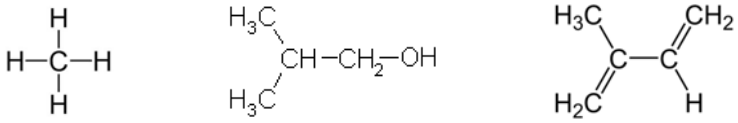
Intrexon's lead program in the energy and chemicals field is devoted to the conversion of natural gas (methane) into larger molecules that can serve as gasoline additives, much like ethanol, or into basic chemicals for conversion into more specialized compounds. This approach clearly deviates from the biofuel programs that have been pursued by a myriad of companies, but there is a good rationale behind this strategy. An important difficulty faced by biofuel producers is the trade-off between using feedstock for ethanol production and using food crops for food. (An alternative consideration is the tradeoff in land use – should land be used for food or fuel?) Several provinces in China, which is the largest ethanol producer in Asia, have implemented regulations that prevent the use of food crops for fuel production.[43] There are other valid reasons for Intrexon's approach too. For one, today's production of biofuels is subject to weather conditions, as evidenced by a recent downward revision in global production estimates because of the impact of last year's drought on the U.S. corn crop and on corn prices.[43] In addition, ethanol is hygroscopic; that is, it readily absorbs water, which poses a challenge in its handling as a fuel additive. The compound is also more corrosive than gasoline and as a result, it cannot be transported in pipelines used for oil, but must be transported by truck prior to blending.

[42] DANMAP – The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme. DANMAP 2011 - Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark.

[43] International Energy Agency. Medium-Term Oil Market Report 2013. Paris, France.

The Company has reported that its energy and chemicals initiative has already created a genetically modified bacterium (perhaps, one related to the anaerobe *Clostridium acetobutylicum*, which showed promise[44]) that converts methane into isobutanol and that it is well along in using methane as a starting material to produce isoprene. (We have provided the chemical structures of these compounds in Figure 23 for a comparison, but we do not have the exact chemical reactions that are used by Intrexon's bacteria in the conversions.) Moreover, isobutanol has a 30% greater energy content than ethanol and about 82% of the energy value of gasoline, which means that isobutanol gasoline would have a competitive advantage over today's ethanol gasoline in the form of greater fuel economy.

Figure 23. The Structures of Chemicals in Intrexon's Energy & Chemicals Project



Methane Isobutanol Isoprene

We consider Intrexon's strategy for its energy and chemicals division meritorious. While it does not constitute a "green" technology in its own right, it does offer the world greater flexibility in the use of fossil fuels and it does so very cost-effectively. But then, there is no reason that methane generated from biomass (i.e., biomethane) could not be fed to the Company's genetically modified microbes to create more valuable end products. (Presently, biomethane is derived from biogas and is often used as a biofuel.) Based on the current bacterial process, the Company estimates that natural gas prices would have to increase multiple folds for its isobutanol to be priced on parity with oil. The bacterial process for producing isobutanol has already been tested for a proof-of-concept and scalability. The next phase will scale the production to a pilot plant size under a collaboration agreement.

Framework for ECCs: The terms that the Energy & Chemicals division is offering differ from the ECCs that have been signed with healthcare companies. Intrexon is negotiating with corporations in the chemical, oil and gas, and utility industries to join a consortium that will support the development of its methane conversion project and pilot plant construction. The actual structure of these agreements may be a joint venture. The goal is to attract a small number of companies that will provide $25 million access fee to defray costs during the scale-up process and for the actual plant. Intrexon will also receive royalties on sales of isobutanol and isoprene, but they are not expected to contribute materially until late decade.

Alternative synthetic biology approaches are under development for isobutanol production, including conversion of biomass-derived sugars with genetically engineered microbes and cell-free processes.[45,46] But these face the same challenge as bioethanol, use of land and food crops for food or fuel. Also the state of the art is inadequate – bio-production is not economically competitive with petrochemical-based production due to the high cost of feedstock, low butanol yields, concomitant production of low-value by-products (i.e., acetone and ethanol), and toxicity of acetone, butanol, and ethanol at high concentrations.

The markets for isobutanol and isoprene include gasoline refiners/blenders and chemical companies. Intrexon will face competition from biofuels, despite the aforementioned drawbacks, in part because the U.S. and other governments are providing incentives to produce and consume renewable energy sources. A significant end-user industry for isoprene, consisting of tire manufacturers, is already investing in renewable sources via collaborations with biotechnology companies. Nonetheless, fossil fuels comprise an enormous segment of the world's economy and we believe the flexibility afforded by the methane to isobutanol or isoprene program will be an attractive investment for natural gas producers, chemical companies and oil refiners. Even biomethane producers may have an interest.

[44] Lee, SY, et al. Fermentative butanol production by clostridia. Biotechnol Bioeng (2008); 101(2): 209.

[45] Atsumi, S, et al. Non-fermentative pathways for synthesis of of branched-chain higher alcohols as biofuels. Nature (2008); 451(7174): 86.

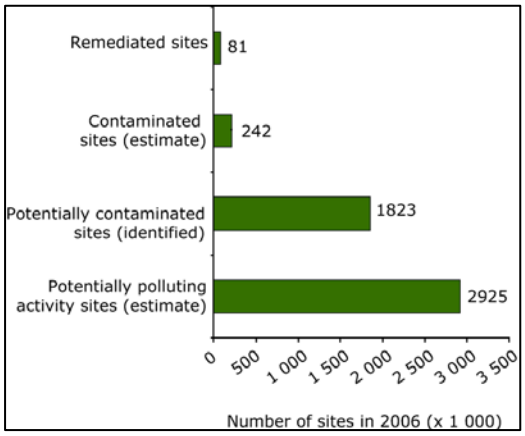
[46] Gonzalez-Ramos, et al. Genome-scale analyses of butanol tolerance in Saccharomyces cerevisiae reveal an essential role of protein degradation. Biotechnol Biofuels (2013); 6(1): 48.

An unexpected by-product of the energy and chemicals project is bacterial matter that is suitable as a fish food. This may seem inconsequential, but in 2008 externally fed aquaculture accounted for 81.6% of the world's farmed fish and crustacean production and to meet the future demand for aquatic animal feed, annual production will have to increase from 29.2 million tons in 2008 to 71 million tons by 2020.[41]

ENVIRONMENT

There are areas in which synthetic biology may be applied to environmental issues. By way of example, we have included Figure 24, which provides the most recent assessment of soil status by the European Environment Agency. [47] Clearly, there is a need to address contaminated sites, assess the status of others, and monitor for polluting activity.

Figure 24. Soil Contamination in Europe[47]



The areas identified in Figure 24 constitute markets for products derived from synthetic biology. For instance, living biosensors (i.e., microbes capable of sensing certain compounds) would permit monitoring of hazards to humans and animals. Indeed, a sensor based on a microbe's natural sensitivity to a pollutant has provided a proof-of-concept for such a design by demonstrating a workable sensitivity and real-time measurement capability.[48] Locations in which these sensors would likely have an important role are in industrial effluents before they enter natural waterways and waste water treatment centers. The market for biosensor use in environmental applications is projected to expand 12.4% annually to $2.2 billion in 2016.[49]

Intrexon's UltraVector and gene switch expertise may be used to create a sensor in a suitable microbe. The switch's recognition of an activator molecule may be used to produce an easily measurable indicator. Indeed, if a gene switch using a pollutant as the activator ligand induced the production of an enzyme that created a readily detectable molecule, the enzyme would serve as a multiplier, enabling measurement of even minute quantities of a pollutant. This concept is illustrated in Figure 25.[50]

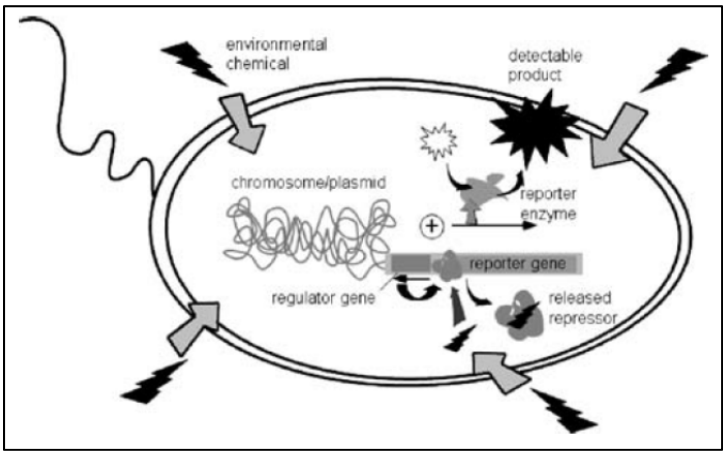
[47] European Environment Agency. The European Environment: State and Outlook 2010 – Soil. Copenhagen, Denmark.

[48] Zhang, Q, et al. A potentiometric flow biosensor based on ammonia-oxidizing bacteria for the detection of toxicity in water. Sensors (2013); 13(6): 6936.

[49] Thusu, R. Strong growth predicted for biosensors market. Sensors Magazine(October 1, 2010);

[50] Harms, H, et al. Whole-cell living biosensors: are they ready for environmental application? Appl Microbiol Biotechnol (2006); 70(3): 273.

Figure 25. Use of a Gene Switch for the Detection of Environmental Chemicals[50]



Another obvious area in which synthetic biology will likely contribute is in the field of bioremediation. Genetically modified bacteria or plants will likely offer new approaches to environmental clean-up projects, partly because of the cost/impracticality of existing technologies and partly because special capabilities can be incorporated into them to address the needs of each site. Bioremediation offers the opportunity to treat the contamination in place, which means that the cost of soil removal is avoided and the remediation process causes as little disturbance to the site as possible. Some cases have involved natural microbes to remove or contain contaminants without human intervention. The first evidence of intrinsic bioremediation was recorded in Bemidji, Minnesota where a pipeline carrying crude oil burst and contaminated an aquifer in 1979. Scientists from the U.S. Geological Survey found that after a few years, the plume of contaminated ground water stopped enlarging when the rate of microbial degradation of the oil came into balance with the rate of leaching.[51] Similar observations have been made with respect to contamination from chlorinated solvents, pesticides, gasoline, and creosote. It is apparent from these instances that microbes are capable of chemically modifying some contaminant(s), rendering them harmless to the environment. In other cases, bioremediation results in a concentration of pollutants, such as heavy metals, followed by their return to the soil in a safe, insoluble form.

Still, there are ample opportunities worldwide fore genetically modified microbes to address challenging situations. One example is the contamination caused by the 500 billion – 1 trillion low-density polyethylene bags disposed of each year in landfills. Various bacteria including *Pseudomonas* species (an aerobic bacterium) and fungi can breakdown this material under proper conditions, but they have little impact under the oxygen-limited conditions in landfills.[52]

Such situations beg for a new approach to the problem, and Intrexon has the right technologies for that type of job, in our opinion. One aspect of research in synthetic biologics is to utilize Nature wherever possible to address a need. As a result, the answer to the plastic bag problem may start with anaerobic bacteria that can be modified to utilize plastic as a carbon source, perhaps with genes from a *Pseudomonas* bacterium. Alternatively, the Company may employ its LEAP technology to facilitate a screen for natural, anaerobic bacteria with the ability to digest plastic and then increase the appropriate genes' expressions. A gene switch might even be included to prevent the spread of the genetically modified bacteria into the general environment by incorporating a "death" signal as the reporter gene. Thus, the activator ligand could be applied initially at the border of the landfill to contain the bacteria and later on to eliminate them entirely from the environment.

The market for remediation solutions in general is proportional to the surface of land occupied by highly polluting material, the amount of waste, and the volume of polluted water. And there is a considerable

[51] U.S. Geological Survey website: water.usgs.gov/wid/html/bioremed.html
[52] Kyaw, BM, et al. Biodegradation of low density polythene (LDPE) by *Pseudomonas* species. Indian J Microbiol (2012); 52(3): 411.

opportunity for new technologies to participate, since Mother Nature doesn't often solve our problems (see Table 3) and the common solutions available today are not ideal.[53]

Table 3. Common Remediation Solutions Currently in Use[53]

Remediation method	Positive factors	Negative factors
Reactive barrier	Generally no need for removal of the barrier	Long-term operating costs, suitable only for some contaminants
Soil stabilisation, isolation	No need for soil removal; quick; can be economical	No removal of contaminants from environment; can be energy-intensive
Soil vapour extraction (SVE)	Generally cost-effective; low uncertainties in risk reduction	Suitable only for volatile contaminants; exhaust air needs to be treated
Incineration (mobile)	Effective contaminant removal	Flue gas treatment needed; energy-intensive; often needs fuel
Composting	Low cost; treated soil may be used for landscaping; no emissions requiring treatment	Suitable only for some organic contaminants; can be long duration; depends on contaminant concentrations
Landfill	Effective control of risks; soil can be used in daily cover	Not treatment; not suitable for re-use; becoming more expensive; not efficient use of landfill sites

The global remediation market is estimated to generate $35 billion of business annually. Of that, bioremediation accounts for about $1.5 billion.[54] But these figures do not represent such emerging markets as Latin America, Eastern Europe, and Asia adequately, since the inventories of local contaminated sites have not been prepared. Even within the more developed countries, bioremediation is an evolving technology whose greatest contributions have yet to be discovered.

Rentokil Initial, LLC

Intrexon recently formed its first ECC in the environment sector with the international pest-control company Rentokil. The collaborators will employ synthetic biology to create a specific, unidentified pest-control product. Terms of the agreement have not been disclosed at this time, but we would not be surprised if this project is just the first between the two companies.

INDUSTRIALIZATION OF SYNTHETIC BIOLOGY

Intrexon combines platform technologies in biology, engineering, and informatics to facilitate the rational design and programming of DNA, proteins, and cells to rapidly produce desired bio-functions in high-value applications for end-to-end solutions. The Company is leading the way to redefining biotechnology with its industrial approach that can create multigenic biological and cellular products at an unprecedented scale. Behind these feats are the following attributes:

- Proprietary & complementary technologies consisting of the UltraVector platform, Cell Informatics, LEAP instrument, and mAbLogix monoclonal antibody technology.
- Design-build-test-learn continuum that expedites the creation of new products, while expanding the foundation for future advances.
- A head start in the industrialization of biotechnology that will translate into years of limited competition during the emergence of synthetic biology.
- Large & diverse end markets with high demand for new and/or improved products that address the world's needs in food, healthcare, energy & chemicals, and the environment.

[53] OECD (2013). Biotechnology for the environment in the future: science, technology, and policy. OECD Science, Technology, and Industry Policy Papers, No. 3. Paris, France.

[54] Singh, A, et al (eds.) Advances in Applied Bioremediation, Soil Biology 17. Publ. Springer-Verlag, 2009.

- A scalable business model that leverages Intrexon's expertise in synthetic biology with the capabilities of its collaborators to maximize the use of its technologies across all targeted markets rapidly.
- Experienced management with proven track records in research-driven corporations and with the key technologies that underpin Intrexon's competitive advantages.

COMPETITIVE ADVANTAGES & STRENGTHS

Based on its integrated, cutting-edge technologies, we believe Intrexon is the corporate leader in synthetic biology. A number of companies have created novel genes, employed various cell culture systems, plants and animals to produce proteins, and designed such therapeutic molecules as monoclonal antibodies with various levels of humanization, but their involvement in synthetic biology has been limited to only a few projects. Intrexon stands apart with the multi-faceted approach to the field and its collaborative business model.

The Company's business model, which is designed to foster rapid adoption of its technologies, should serve it and investors well, particularly over the long term since the profit centers of its ECCs reside in the royalties derived from commercialized products developed with its assistance.

PATENTS AND OTHER INTELLECTUAL PROPERTY

Intrexon holds patents on the basic innovations associated with at least three of its four fundamental areas of competitive advantage: the UltraVector platform, LEAP instrument, and mAbLogix platform. As of July 15th, the Company had at least 50 patents issued in the United States and 60 pending U.S. applications. These establish protection for such technologies as gene switches (including the RheoSwitch), gene modulation systems, vectors, cells and organisms containing the switches, activator ligands, cell identification, and selection technology for purification, isolation and characterization. Patents have been granted and/or filed in 19 other jurisdictions worldwide. Overall, the Company has more than 700 patents and applications pending worldwide, which will expire from 2017 to 2034.

The Company has decided not to seek patents on some of its technologies, but to treat them as trade secrets, protected internally through confidentiality agreements with employees and granting limited access. Informatics expertise embodied in its database and analytical/predictive software probably constitutes the largest intellectual property that is not patented. That's partly because of the disclosures required to obtain patent coverage and partly because of the ever-changing nature of the information and computational systems.

Besides the existing patents, Intrexon and its collaborators will be able to seek patents on the novel genes and probably most, if not all, of the related therapies derived from them. The recent U.S. Supreme Court ruling did not hold patents on natural genes to be valid. But the unique genes and genetically modified cells created by Intrexon should be patentable, since they are not merely copies of nature.

CREATING A FAVORABLE RISK-REWARD BALANCE

The ECCs signed thus far include projects that have high reward potential and have been de-risked considerably via the progress that has been made already through a careful selection of projects that have sound scientific bases and stand to benefit from the combined skills of Intrexon and its partners:

- Ziopharm Oncology's most advanced gene therapy, which generates interleukin-12 in the vicinity of a tumor, is based on research showing the potent anticancer signal of the cytokine. Indeed, early attempts to use interleukin-12 therapeutically ended in failure due to serious side effects.[55] Similarly, the combination therapy of interleukin-12 and interferon-α is consistent with a general trend in oncology research toward the use of multiple cytokines to arm the immune system

[55] Car, BD, et al. The toxicology of Interleukin-12: A review. Toxicol Pathol (1999); 27(1): 58.

against malignant cells. Moreover, single-gene and multigenic approaches against cancer have yielded favorable preclinical data supporting further investigation.

- The lantibiotic ECC with Oragenics is based on the development of lantibiotic antibiotics, which are naturally occurring compounds used by bacteria against competitors. As such, they are already known to be effective. Moreover, the lead compound has exhibited a good safety profile in preclinical testing.[56]

- Monoclonal antibody programs with Synthetic Biologics and Soligenix have a low risk, in our opinion. Intrexon's mAbLogix human antibodies virtually obviate the risk of an immune reaction to the therapies, and considerable work has been done by independent scientists to characterize molecular targets of those programs.[57,58,59,60]

- Cell therapies included in the ECC with Fibrocell Science have different levels of risk and returns for Intrexon associated with them. It seems highly likely that the work Intrexon is doing to improve its partner's cell culture system is a low risk endeavor that comes with a lower reward than the cutting-edge, genetically modified cell therapies for RDEB, morphea, cutaneous eosinophilia, and psoriasis. Nonetheless, the even those programs, which are well characterized scientifically, should benefit from expertise in both synthetic biology and fibroblast cells.

- AquaBounty's lead program appears close to winning regulatory approval by the FDA, which should help to lower the hurdles for approval of other genetically modified fish in the ECC.

- The energy program has already been de-risked by virtue of the work performed in creating the microbe and scaling up production to a 50 liter vat. Much of the risk in this program is in the uncertainty over the consortium formation that will finance the next stage, which is scaling up production to a pilot plant.

In sum, we believe the programs that currently define Intrexon's 5-year prospects have a favorable risk-reward balance.

[56] Ghobrial, O, et al. Pharmacokinetic and pharmacodynamic evaluation of the lantibiotic MU1140. J Pharm Sci (2010); 99(5): 2521.

[57] Ellis, TN and Kuehn, MJ. Virulence and immunomodulatory roles of bacterial outer membrane vesicles. Microbiol Mol Biol Rev (2010); 74(1): 81.

[58] Roca, I, et al. The *Acinetobacter baumanii* oxymoron: commensal hospital dweller turned pan-drug-resistant menace. Front Med (2012); 3: Article # 148.

[59] Zhang, S, et al. *In vitro* and *in vivo* studies of monoclonal antibodies with prominent bactericidal activity against *Burkholderia pseudomallei* and *Burkholderia mallei*. Clin Vaccine Immunol (2012); 18(5): 825.

[60] Silva, EB and Dow, SW. Development of *Burkholderia mallei* and *pseudomallei* vaccines. Front Cell Infect Microbiol (2013); 3: 10.

INVESTMENT CONSIDERATIONS

For a complete description of risks and uncertainties related to Intrexon Corporation's business, see the "Risk Factors" section in Intrexon's SEC filings, which can be accessed directly from the SEC Edgar filings at www.sec.gov. Potential risks include:

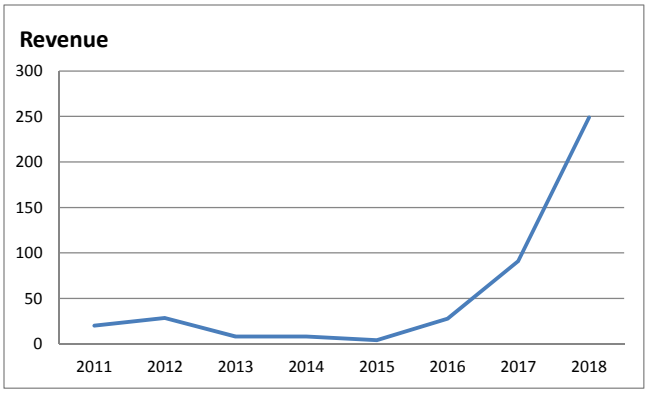
- **Stock risk and market risk:** Trading of the Company's common stock only recently began trading and its valuation can vary widely on a daily basis. There can be no assurance that an active and liquid trading market will be sustained, which could limit one's ability to buy or sell the Company's common stock at a desired price. Investors should also consider technical risks, such as float, risk of dilution, and dependence upon key personnel.
- **Competitive risk:** The markets for some products derived from synthetic biology are already well established with competition based on product characteristics, pricing, and marketing support. Other markets will likely emerge as synthetic biology gains broader acceptance. It is unknown whether other companies are actively engaged in the development/commercialization of products to directly or indirectly address the areas being pursued by Intrexon and its collaborators. These companies may have substantially greater capabilities, as well as significantly greater marketing, financial, and human resources than Intrexon and/or its collaborators.
- **Products still in development phases:** The Company's products may appear to be promising, but they may not reach commercialization for various reasons, including a lack of efficacy in clinical trials, failure to achieve regulatory approvals, safety concerns, and/or the inability to be manufactured at a reasonable cost. And even if the products are commercialized, there can be no assurance that they will be accepted, which may prevent the Company from becoming profitable.
- **Funding requirements:** It is difficult to predict Intrexon's future capital requirements. The Company may need additional financing to continue to fund operations and expand its business. There is no guarantee that it can secure the desired future capital or, if sufficient capital is secured, that current shareholders will not suffer significant dilution.
- **Regulatory risk:** There is no guarantee that products under development with the Company's technologies will be approved by U.S. and/or international regulatory bodies for marketing in the U.S. or abroad. In addition, regulations pertaining to synthetic biologics may undergo further changes, which may affect the Company's ability to gain regulatory approvals and/or labeling that supports its collaborators' marketing strategies.
- **Reimbursement risk:** Healthcare reimbursement decisions have undergone significant changes and may continue to do so. There is no guarantee that the Company's therapeutic agents will receive adequate insurance coverage for them to be commercially viable.
- **Patent risk:** Synthetic biologics is an emerging field, and although Intrexon has licensed and/or filed for numerous patents to secure its right to commercialize products based on its technologies, these patents may not protect the advantages that its technologies currently provide or the products developed with its expertise in the marketplace.

FINANCIAL FORECASTS & VALUATION

Since our financial projections are derived from Intrexon's business model, it is appropriate to review the basic elements. Franchising via the ECCs is expected to facilitate utilization of the Company's expertise in synthetic biology without over-taxing corporate resources and without undue exposure to risk. The mechanics of the model reside in four types of revenue sources: a technology access fee that we believe is related to the technologies needed for a project, R&D reimbursement that limits Intrexon's financial investments in project development, milestones that are relatively small but provide evidence of progress, and royalties based on sales or other financial metrics associated with a project. Of these, we have included the access fees, R&D reimbursements, and royalties in our projections. Milestones were excluded since they are fairly small relative to other revenue sources and because some are not disclosed or will be paid in stock with a future value. We note, too, that smaller collaborators have the option of granting Intrexon stock in lieu of cash for the technology access fee and milestones. (Providing financial support to franchisees is common, as evidenced by terms offered by major restaurant chains, since the practice expedites market penetration and the capture of downstream value.) The other major ingredient in Intrexon's business model is its own expenditures. The corporate goal is to eventually reach a level where its R&D reimbursements approximate 50% of operating expenses In other words, the Company's strategy is to invest in its future at a rate that is equal to the services being utilized by collaborators. It will likely take a few years to reach that steady-state, and in the meantime, we look for operating expenses to exceed the R&D reimbursements.

The implications of the business model are illustrated in Figure 26, which diagrams the actual and estimated cash flows to Intrexon from four ECCs signed in 2011 and 2012, specifically Ziopharm Oncology, Oragenics, Synthetic Biologics, and Fibrocell Science. The payment in the initial year of each ECC is largely the technology access fee, but it also includes a small sum for R&D reimbursement. We assumed that the expense reimbursement related to each ECC was $3 million and that it was paid over 36 months, with a 6-month portion paid in the first and last years. The royalty streams that we expect will be generated from the ECCs with the four companies have been combined. We project that Fibrocell will generate the first royalties for Intrexon from work performed to optimize fibroblast cell cultures. However, the initial payments will likely remain low until 2016, when three of the four companies are expected to pay royalties to Intrexon. By combining the revenues from these ECCs, we believe the chart provides a general approximation of what annual revenues from other agreements will look like, though the time for product development and the rate of product acceptance will vary.

Figure 26. Estimated Revenues from Four Healthcare ECCs

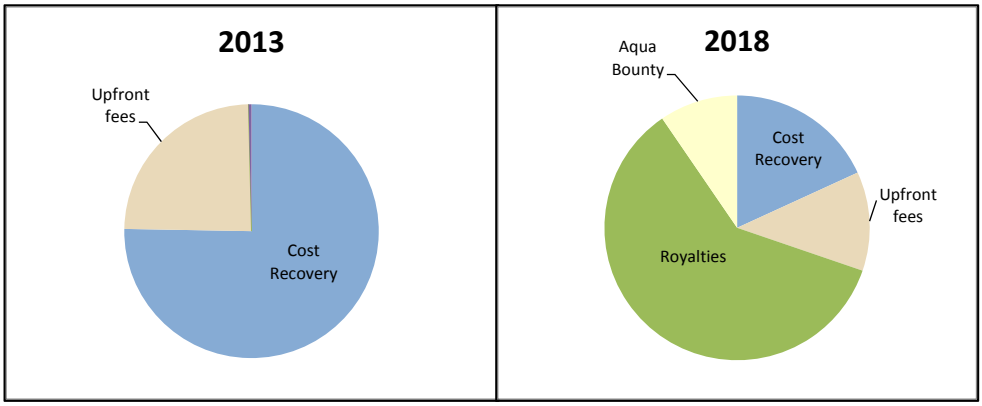


Over the next five years, the composition of the annual revenues will change as new agreements are signed and products are commercialized. For instance, we have assumed that ECCs in the food and environment fields have somewhat lower terms than the standard healthcare ECCs. Specifically, our projections reflect upfront fees of $1 million in both fields and $2.5 million in R&D cost recovery payments.

Additional variance will likely reflect the types of ECCs that are completed. In the healthcare field, the two areas in which the Company has invested significantly in preparation for platform collaborations are miRNA therapeutics and cancer therapeutics consisting of T-cells genetically modified to express

chimeric antigen receptors. We estimate that these two areas will command premium deal terms, each generating upfront fees of $50 million from multiple collaborators. In the energy field, the company is promoting its methane-to-isobutanol program. The collaboration format may be a joint venture that pays Intrexon for scale-up work and relies on the collaborators' expertise for the plant operation. Our financial projections are based on an upfront fee of $25 million from each collaborator in the energy project. We have further assumed that $10 million will be paid to Intrexon as a R&D reimbursement in the year following the formation of the collaboration. Two healthcare platform agreements are included in our projections, one each in 2014 and 2015, as well as four energy agreements, in 2013, 2015, 2016, and 2017. Overall, these changes will result in a significant shift in importance from technology access (upfront) fees and cost reimbursement to royalties, as shown in Figure 27.

Figure 27. A Comparison of the Revenue Composition between 2013 and 2018



Based on our projections, technology access fees will diminish in importance as a source of revenues over the next 5 years, despite an increase in the annual number of ECCs completed, as presented in Table 4.

Table 4. ECCs at Year End by Field of Interest

	2013	2014	2015	2016	2017	2018
Healthcare	16	29	45	55	62	68
Food	2	3	6	8	11	12
Energy	1	2	2	4	6	6
Environment	1	3	8	12	15	17
Year-End Total	20	37	61	79	94	103

Our estimates include one new platform EEC per annum, starting in 2013, and one additional ECC this year in the food sector. We are also looking for eight more ECCs in the healthcare area. Over the pull to 2018, the relative distribution of collaborations probably won't change that much between these fields, but those signed in 2011 and 2012 should be generating recurring revenues that are increasing rapidly. Moreover, our projections are based on an assumption that the number of new collaborations gradually eases in the 2015 – 2018 timeframe.

ANNUAL INCOME STATEMENTS[♯] (Fiscal year ends December 31st.)

[♯] Data are in thousands, except for per-share figures. *Estimates are in italics.*

Revenues	**2012**	***2013***	***2014***	***2015***	***2016***	***2017***	***2018***
Collaboration Revenues	$ 13,706	*$ 26,440*	*$ 48,786*	*$ 79,460*	*$ 140,455*	*$ 237,961*	*$ 418,887*
Other revenues	219	*400*	*400*	*400*	*400*	*400*	*400*
Total Revenues	$ 13,925	*$ 26,840*	*$ 49,186*	*$ 79,860*	*$ 140,855*	*$ 238,361*	*$ 419,287*
Operating expenses							
Cost of products sold	-	*150*	*1,250*	*1,300*	*3,100*	*6,300*	*10,000*
Research & development	$ 64,185	*47,000*	*48,000*	*55,000*	*70,000*	*68,000*	*61,000*
General & administrative	24,897	*27,750*	*27,000*	*28,000*	*29,000*	*30,000*	*31,000*
Total operating costs	89,082	*74,900*	*75,000*	*83,000*	*99,000*	*98,000*	*92,000*
Operating profit/(loss)	$ (75,157)	*$ (48,060)*	*$ (25,814)*	*$ (3,140)*	*$ 41,855*	*$ 140,361*	*$ 327,287*
Other Income (Expense)							
Unrealized increase (decrease) in fair value of equity securities	$ (6,290)	*$ (21,635)*					
Realized gain on equity investments	-	*7,415*					
Interest expense	(57)	*(30)*					
Other	(96)	*26*					
Total other income (expense)	(6,443)	*(14,224)*	-	-	-	-	-
Equity in net loss of affiliate	$ (274)	*$ (390)*					
Pretax profit/(loss)	$ (81,874)	*$ (62,674)*	*$ (25,814)*	*$ (3,140)*	*$ 41,855*	*$ 140,361*	*$ 327,287*
Income taxes	-	*-*	*-*	*-*	*15,905*	*53,337*	*124,369*
Net profit/(loss)	$ (82,148)	*$ (63,064)*	*$ (25,814)*	*$ (3,140)*	*$ 25,950*	*$ 87,024*	*$ 202,918*
Net loss (profit) attributable to non-controlling interest	-	*1,685*	*1,800*	*1,760*	*-*	*(2,000)*	*(4,875)*
Net profit/(loss) to Common	$ (82,148)	*$ (61,379)*	*$ (24,014)*	*$ (1,380)*	*$ 25,950*	*$ 85,024*	*$ 198,043*
Earnings/(loss) per share	*$ (1.17)*	*$ (0.71)*	*$ (0.26)*	*$ (0.03)*	*$ 0.26*	*$ 0.86*	*$ 2.00*
Shares outstanding	70,266	*88,380*	*98,000*	*99,000*	*100,000*	*101,000*	*101,500*

Assumptions:

- Revenue estimates are based on two sources largely, ECC-related fees and royalties. The ECC fees reflect the timing of new agreements, while the projected royalties are limited to those generated by four companies, Ziopharm Oncology, Synthetic Biologics, Fibrocell Science, and Oragenics. Our revenue presentation recognizes technology access fees amortized over periods of 10 – 12 years.

- AquaBounty is treated as a consolidated subsidiary that does not turn profitable until 2017, and the proportion of the loss or profit attributable to non-controlling investors is broken out below the "Net profit/(loss)" line.

- R&D expenses reflect work conducted on behalf of ECCs and for internal development purposes. Over time, R&D cost reimbursement is approximately 50% of Intrexon's operating costs.

- SG&A costs increase gradually through 2018 as the corporate infrastructure expands.

- No estimates are included for non-operating items other than interest expense and interest income, which is included in "Other". All other figures reflect results reported for the first half of 2013.

- Tax liabilities are recognized for all years in which operations are profitable, although Intrexon will be able to minimize its cash outlays since net operating loss carryforwards amounted to $225 million as of December 31, 2012 and the Company had R&D tax credits of $6 million.

- Common shares outstanding reflect Intrexon's initial public offering with subsequent adjustments for stock-based compensation. The estimated number of shares for 2013 is an average number of shares calculated on a *pro forma* basis. Basic shares are used for years in which there is a loss and fully diluted shares for profitable years.

- Our presentations for 2012 and 2013 do not include dividends accreted, but not declared on convertible preferred stock that was converted to common at the time of the IPO.

ADJUSTED EBITDA

GAAP requires amortization of technology access fees, but that does not provide an adequate assessment of the timing of payments to the Company. Indeed, Intrexon has largely used a 12-year amortization period for the healthcare ECCs formed thus far. (We have used a 10-year schedule in preparing our estimates, since the actual period may vary depending on the field.) A better mechanism for evaluating the progress of the Company's efforts to engage in new business development and commercialize its technology is based on an adjusted EBITDA that recognizes the upfront and milestone payments in the period in which they are received. The following table provides the related adjustments, based on actual results for 2012 and the aforementioned assumptions underpinning our estimates.

	2012	2013	2014	2015	2016	2017	2018
EBT	$ (81,874)	$ (62,674)	$ (25,814)	$ (3,140)	$ 41,855	$ 140,361	$ 327,287
Interest expense	-	30					
Depreciation	7,984	7,400	7,500	7,700	7,800	8,000	8,000
Stock-based compensation	3,008	2,500	2,500	2,750	2,750	3,000	3,000
Unrealized (increase) decrease in fair value of equity securities	-	21,635	-	-	-	-	-
Realized gain on equity securities	3,591	(7,415)	-	-	-	-	-
Other		2,400	1,550	1,550	1,550	1,550	1,550
Change in deferred revenue from upfront and milestones	(7,491)	38,495	94,375	116,950	84,850	76,700	47,600
Adjusted EBITDA	$ (74,782)	$ 2,371	$ 80,111	$ 125,810	$ 138,805	$ 229,611	$ 387,437
Adjusted EBITDA/share	$ (1.06)	$ 0.03	$ 0.82	$ 1.27	$ 1.39	$ 2.27	$ 3.82

We have made adjustments for interest expense in 2013, which is related to an AquaBounty debt, and the unrealized increase/decrease in the fair value of equity securities of collaborators through the June quarter of this year. (No attempt has been made to estimate the future appreciation or decline in value of such securities.) In addition, we have included other expenses that did not consume cash, notably a contribution of services by a shareholder. However the most important adjustment is reflected by the line "Change in deferred revenue from upfront and milestones", which corrects for fees that are amortized for financial reporting purposes. (The adjustment recognizes payments upon receipt, while GAAP requires amortization.) The result is an adjusted EBITDA that provides a comprehensive measure of cash generated by operations.

QUARTERLY INCOME STATEMENTS♯ (Fiscal year ends December 31st.)

♯ Data are in thousands, except for per-share figures. *Estimates are in italics.*

	2013			
	Q1A	Q2A	Q3E	Q4E
Revenues				
Collaboration revenues	$ 3,864	$ 6,674	*$ 7,862*	*$ 8,000*
Other	112	107	*111*	*110*
Total Revenues	$ 3,976	$ 6,781	*$ 7,973*	*$ 8,110*
Operating expenses				
Cost of products sold	$ -	$ -	*$ -*	*$ 150*
Research & development	11,502	13,602	*11,000*	*10,896*
General & administrative	6,480	7,433	*7,000*	*6,837*
Total operating costs	17,982	21,035	*18,000*	*17,883*
Operating profit/(loss)	$ (14,006)	$ (14,254)	*$ (10,027)*	*$ (9,773)*
Other Income (Expense)				
Unrealized increase (decrease) in fair value of equity securities	(29,369)	7,734	-	-
Realized gain on equity investments	7,415	-	-	-
Interest (expense)	(14)	(11)	*(5)*	
Other	2	12	*6*	*6*
Total other income (expense)	(21,966)	7,735	*1*	*6*
Equity in net loss of affiliate	(390)	-		
Pretax profit/(loss)	$ (35,972)	$ (6,519)	*$ (10,026)*	*$ (9,767)*
Income taxes	-	-	-	-
Net profit/(loss)	$ (35,972)	$ (6,519)	*$ (10,026)*	*$ (9,767)*
Net loss attributable to non-controlling interst	51	507	527	600
Net profit/(loss) to common	$ (35,921)	$ (6,012)	*$ (9,499)*	*$ (9,167)*
Earnings/(loss) per share	$ (0.47)	$ (0.07)	*$ (0.10)*	*$ (0.09)*
Shares outstanding	75,879	83,141	*97,000*	*97,500*

The quarterly income statements include actual results for the first half, based on *pro forma* shares outstanding. Our estimates reflect the assumptions discussed at the introduction to this section of the report and associated with the annual income statements.

BALANCE SHEET♯ (Fiscal year ends December 31st.)

♯ Data are in thousands.

ASSETS	6/30/2013	12/31/2012
Current Assets		
Cash & equivalents	298,215	10,403
Accounts Receivable	1,305	707
Other	3,098	2,423
Total Current Assets	$ 302,618	$ 13,533
Equity securities	$ 65,213	$ 83,116
Property & equipment	18,410	18,687
Intangible assets	42,972	29,506
Goodwill	13,846	-
Other	8,692	6,804
Total Assets	$ 451,751	$ 151,646

LIABILITIES		
Current Liabilities	6/30/2013	12/31/2012
Accounts payable	$ 1,486	$ 632
Debt due	255	49
Deferred revenue	8,270	9,963
Accruals	7,490	5,974
Other	10	99
Total Current Liabilities	$ 17,511	$ 16,717
Long-term debt	$ 2,099	$ 42
Deferred revenue	56,409	48,673
Other	1,098	1,108
Total Long-Term Liabilities	$ 59,606	$ 49,823
Shareholders Equity		
Preferred Equity	$ -	$ 406,659
Common Stock, par value	-	-
Additional Paid-In Capital	736,158	-
Accumulated Deficit	(376,163)	(321,553)
Accum. Comprehensive Loss	14	-
Total Shareholders Equity	$ 360,009	$ (321,553)
Non-controlling interest	14,625	-
Total liabilities & equity	$ 451,751	$ 151,646

Considerations:

- The June 30th balance sheet is *pro forma,* reflecting the initial public offering on August 8th that involved the issuance of 11.5 million shares and raised $168.3 million. That event was accompanied by a conversion of all preferred stock to common.

- A noteworthy item on the balance sheet is the equity securities held by Intrexon in its collaborators. As existing projects advance to commercial status and more deals are completed with small companies, this figure will increase, subject to market conditions.

VALUATION ANALYSES

We used two methods to value Intrexon Corporation. The first method is a discounted future price model and the second is a comparative analysis.

Discounted Future Price Model

For this valuation model, we multiplied the earnings projected for 2018, $2.00 per share, by an appropriate price-earnings multiple (42x), which yielded a future price of $84.00 per share. That price was then discounted back four years to 2014 at an annual rate of 24%, which we believe is consistent with the level of risk associated with the current portfolio of ECCs and the uncertainty of the timing of future collaborations. The final result was a price of $35.53 per share.

Comparative Analysis

This analysis was conducted by searching databases for public companies in areas akin to those being targeted by Intrexon's strategic development plan. Search criteria included the terms gene therapy, genetic engineering, DNA, RNA, cell therapy, stem cells, monoclonal antibody, biofuel, biocide, and bioethanol, as well as a market capitalization between $700 million to $6 billion and sales in the past 12 months of approximately $100 million or more. The results were not limited to a specific industry or geographic area nor was there a limit on profits. Nine companies were identified with positive EBITDA, as shown in Table 5.

Table 5. Valuation Comparators for Intrexon

Company	Business	Domicile	Market Capitalization	EBITDA	MC/EBITDA
Cipla Ltd.	Active Pharmaceutical Ingredients	India	$5,563	$377.2	14.75
Chr. Hansen Hldgs.	Bioscience products for food, drug, agbio	Denmark	$4,542	$321.4	14.13
Techne Corp.	Test kits, proteins, antibodies	U.S.A.	$2,953	$210.3	14.04
Cepheid	Molecular diagnostics	U.S.A.	$2,635	$16.5	159.70
Takara Bio	Genetic engineering, gene med, agbio	Japan	$2,750	$26.7	103.00
WuXi Pharma Technology	Active Pharmaceutical Ingredients	China	$1,983	$139.2	14.25
Morphosys AG	Antibody therapeutics	Germany	$1,970	$34.2	57.60
Abcam plc	Antibodies & research tools	United Kingdom	$1,625	$77.9	20.86
FutureFuel Corp.	Biofuels	U.S.A.	$787	$78.5	10.03
		Average MC:	$2,967		
				Average MC/EBITDA:	**45.4**

The comparative analysis yielded an average market capitalization-to-EBITDA ratio of 45.4x. We then estimated the market capitalization of Intrexon in 2014 by multiplying our estimate for the adjusted EBITDA, $80.11 million, for that year by the average MC/EBITDA ratio. The result was $3.64 billion, or $37.11 per share.

Based on the two analyses, we have set our 12-month price target near the mean, at $36.00.

DISCLOSURES

ANALYST(s) CERTIFICATION: The analyst(s) responsible for covering the securities in this report certify that the views expressed in this research report accurately reflect their personal views about Intrexon Corporation (the "Company") and its securities. The analyst(s) responsible for covering the securities in this report certify that no part of their compensation was, is, or will be directly or indirectly related to the specific recommendation or view contained in this research report.

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Fibrocell Science is currently a client of Griffin Securities, Inc. Griffin Securities' services for Fibrocell Science consist of non-investment banking securities-related services and non-securities services. Griffin Securities has received compensation from Fibrocell Science in the past 12 months for non-investment banking services.

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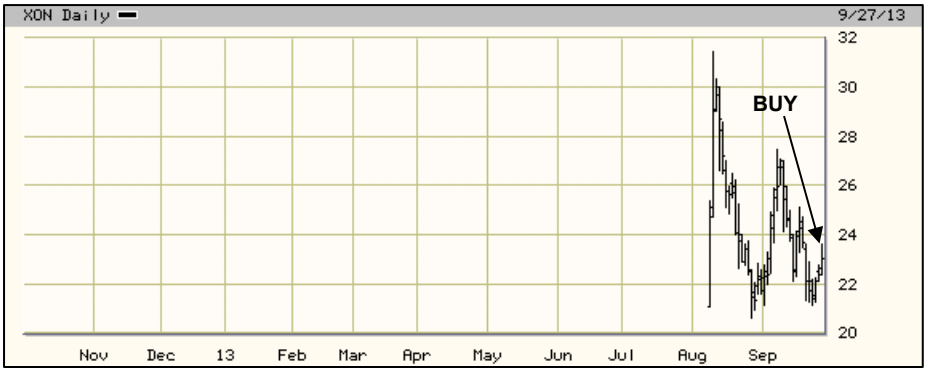
Griffin Securities expects to receive, or intends to seek, compensation for investment banking and non-investment banking services from the Company in the next three months.

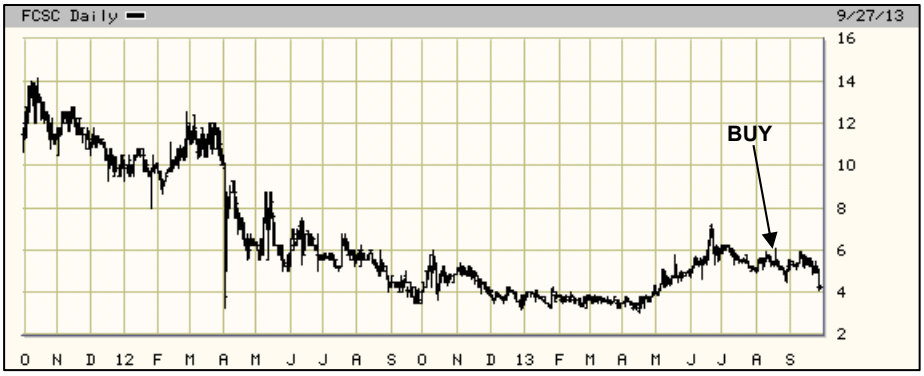
INTREXON PRICE CHART



Source: BigCharts.com

9/30/13 – Initiating Coverage: share price, $23.01; rating, BUY; 12-month price target, $36.00.

FIBROCELL SCIENCE 2-YR. PRICE CHART



Source: BigCharts.com

8/14/13 – Initiating Coverage: share price, $5.65; rating, BUY; 12-month price target, $14.00.

ORAGENICS 2-YR. PRICE CHART

Source: BigCharts.com

11/27/12 – Initiating Coverage: share price, $1.80; rating, BUY; 12-month price target, $5.00; **2/19/13 –** Research update: share price, $3.85; rating, BUY; 12-month price target, $6.00.

SYNTHETIC BIOLOGICS 2-YR. PRICE CHART

Source: BigCharts.com

2/5/13 – Initiating Coverage: share price, $1.82; rating, BUY; 12-month price target, $4.00. **6/26/13 –** Research update: share price, $1.70; rating, BUY; 12-month price target, $4.00; **8/19/13 -** Research update: share price, $1.45; rating, BUY; 12-month price target, $4.00.

ZIOPHARM ONCOLOGY 2-YR. PRICE CHART

Source: BigCharts.com

6/26/06 – Initiating coverage: share price: $5.05; rating: BUY; 12-month price target: $18.00. **12/07/06 –** Research update: share price $6.36; rating: BUY; 12-month price target: $20. **5/03/07 –** Research update: share price $5.80; rating: BUY; 12-month price target: $20.00. **3/13/08 –** Research update: share price: $2.52; rating: BUY; 12-month price target: $15.00. **7/02/08 –** Research update: share price: $1.87; rating: BUY; 12-month price target: $15.00. **5/18/09 –** Research update: share price: $0.77; rating: BUY; 12-month price target: $3.00. **6/09/09 –** Research update: share price: $1.87; rating: BUY; 12-month price target: $3.00. **3/4/10 –** Research update: share price: $3.53; rating: BUY; 12-month price target: $8.00. **1/20/11 –** Research update: share price: $5.60; rating: BUY; 12-month price target: $11.00. **4/25/11 –** Research update: share price: $6.36; rating: BUY; 12-month price target: $11.00. **5/18/11 –** Research update: share price: $6.85; rating: BUY; 12-month price target: $11.00. **9/21/11 –** Research update: share price: $4.57; rating: BUY; 12-month price target: $11.00. **3/30/12 –** Research update: share price: $5.40; rating: BUY; 12-month price target: $12.00. **12/12/12 –** Research update: share price: $4.44; rating: BUY; 12-month price target: $12.00.

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