THE WALL STREET TRANSCRIPT
Connecting Market Leaders with Investors

Intrexon Corporation (NYSE:XON)

RANDAL J. KIRK is Chairman and Chief Executive Officer of Intrexon Corporation. Randal J. Kirk has served as Intrexon's Chief Executive Officer since April of 2009 and Chairman of the board since February 2008. Mr. Kirk provides a wealth of strategic, operational and management experience. Mr. Kirk currently also serves as the Senior Managing Director and Chief Executive Officer of Third Security, LLC, an investment management firm founded by Mr. Kirk in March 1999. Additionally, Mr. Kirk founded and became Chairman of the board of New River Pharmaceuticals Inc. — previously traded on Nasdaq prior to its acquisition by Shire plc in 2007 — in 1996 and was President and Chief Executive Officer between October 2001 and April 2007. Mr. Kirk currently serves in a number of additional capacities including as a member of the board of directors of Halozyme Therapeutics, Inc. (NASDAQ:HALO) since May 2007 and as a member of the board of directors of ZIOPHARM Oncology, Inc. (NASDAQ:ZIOP) since January 2011. Previously, Mr. Kirk served as a member of the board of directors of Scios, Inc. — previously traded on Nasdaq prior to its acquisition by Johnson & Johnson — between February 2000 and May 2002, and as a member of the board of directors of Clinical Data, Inc. — previously traded on Nasdaq prior to its acquisition by Forest Laboratories, Inc., in April 2011 — from September 2002 to April 2011 and was Chairman of the board of directors from December 2004 to April 2011. Mr. Kirk served on the board of visitors of Radford University from July 2003 to June 2009, was Rector of the board of directors from September 2006 to September 2008 and served on the board of directors of the Radford University Foundation, Inc., from September 1998 to May 2011. He served on the board of visitors of the University of Virginia and Affiliated Schools from July 2009 to October 2012, on the Virginia Advisory Council on Revenue Estimates from July 2006 to October 2012 and on the Governor's Economic Development and Jobs Creation Commission from April 2010 to October 2012. Mr. Kirk received a B.A. in business from Radford University and a J.D. from the University of Virginia.

SECTOR — PHARMACEUTICALS

TWST: How would you characterize Intrexon?

Mr. Kirk: We believe that we are the world's leading synthetic biology company. Our foundational technology is a DNA architecture that gives us inherent advantages in the design and construction of rationally designed complex transgenes, which sounds like a mouthful, but what it really means is that we are capable of building multigenic constructs, meaning large programs that have more than one or two genes, and we add components that allow us to control some of the activities of the gene program in real time.

TWST: How would characterize what you are within the health care space so that we understand that? Where do you fit in amongst all the gene companies, because there is gene sequencing, gene editing, gene testing and gene therapy companies?

Mr. Kirk: We are not involved in sequencing at all as a business. We are customers of sequencing companies. In a previous time in my career, I was involved in gene sequencing services to pharma and biotech, and I sold that business to one of the majors today because I saw that the cost per base pair of sequencing was going to go down probably faster than the market would grow. People are running into that now. I call that the race to the bottom. So we do a lot of gene sequencing, but it is not our business nor what is our unique offering. Considering what I said a few moments ago, obviously, gene therapy in health care would be a primary utility of our technologies, so gene therapy and cell engineering.

TWST: To that point, you are beginning to create something called Precigen to coalesce the health care assets in a more structured manner I believe. What is that exactly?

Mr. Kirk: These are our therapeutic assets in the field of gene and cell therapy. Starting at the first of the year, Precigen is a standalone functioning company that is independent of Intrexon, although it is a wholly owned subsidiary. Helen Sabzevari, Ph.D., leads it. They oversee development of all of our relevant technologies in the field of gene and cell therapy, including those programs in that field that are partnered with other companies, such as Ziopharm Oncology, Merck KGaA and Novartis.

TWST: I want to get back to the company as a whole a little bit and zoom out a little bit. In 2016, you had about $191 million in revenue, and it was mostly from collaboration licensing, and then, you had the second-largest piece for service, and the last was for product in terms of how the ratios played out. Coming toward the end of this next financial year, and please talk about whatever you'd like to as far as the financial picture is concerned, but can you address whether you think that revenue composition would remain somewhat similar, or is it changing quite a bit?

Mr. Kirk: The revenue composition will be dissimilar because we are, as was always the intention, shifting our business model to focus on partnering late-stage products and platforms to bring to market and have a greater share of products brought to market using our technology.

We began strictly as an early-stage partnering enterprise. We began doing business in January 2011 through a model, which we refer to as Exclusive Channel Collaboration, in which we would make our technology available to our partners within a stated field in exchange for payment upfront and some in milestones, plus regular billings for the work we did — you referred to that a few moments ago as the R&D revenue — and then the economics in the ultimately commercialized product. Over time, however, we have become increasingly confident that we know what we are doing and can deploy capital ourselves. Today, we are focusing on partnering only our mature assets. It has been over a year since we partnered on an early-stage program.

TWST: You are in several different markets from consumer and energy and health and several more. What would you consider to be some of the most significant achievements in 2017 within the health arena?

Mr. Kirk: Within health, the big objective that we have had, for some time, has been the creation of what we call point-of-care CAR-T, as in the ability to do chimeric antigen receptor T-cell therapy in the clinic on a two-day basis from apheresis to dosing of the patient. Theoretically, it could be a same-day basis. This is only possible with the kind of technology that we possess, meaning rather than having a central laboratory facility using a virus to transfect the patients' T cells, doing ex vivo cell expansion and so forth, we design larger gene programs that allow us to proliferate the cells in vivo in the patients, so we don't need as many cells. And we use nonviral transduction technologies.

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We think in consequence we can provide a superior product. We are close to producing clinical data, so we will see, but we think that our technology will produce a safer and more efficacious product and certainly a less costly one. The work we did in 2017 was terrific on that score, but of course, soon we will have clinical data, and we will see how well we did.

TWST: You acquired GenVec in 2017 for what reason?

Mr. Kirk: We acquired it because of its library of gorilla adenoviruses. We don't like the viruses that are typically used by the small gene therapy companies. They are basically 1990-ish technology, as in AAV or lentivirus for example. The bandwidth that is available to install a gene program and transfect the cell with the gene program using either of those two viruses is too small in our opinion to contain and transfect a multigenic construct with gene expression switches and so forth. So everything that we want to do is more complex, and we think what we have is of higher value. It requires a virus with greater bandwidth and may require the ability to redose the patient, so we acquired that library to give us both of those abilities.

TWST: To the last point, that sounds to me like one of the current challenges in gene therapy when you mention about redosing the patient. Can you elaborate on that?

Mr. Kirk: It relates to the immunogenicity of the virus and how rapidly it is to elicit an immune response. In the case of the gorilla adenoviruses, we are engineering those, so we think that we can make them either low- or non-immunogenic.

TWST: You're at so many different levels in different industries from very foundational work to later-stage work, including that which is already commercial. Help us understand what I believe are two of the foundational elements for the company in the health space, as in Ultra Vector and BeyondBio. How would you distinguish those two things from each other?

Mr. Kirk: BeyondBio is the name of one of our informatics programs, while Ultra Vector is the name of the DNA architecture that I mentioned a few moments ago, but we have many other technologies.

TWST: Are those two designed to be complementary in any way or not really?

Mr. Kirk: I am going to give you an example. Our energy program consists of our program to engineer a bacterium called a methanotroph. We engineered this bacterium, which naturally consumes methane, to convert that natural gas to much more valuable and more complex hydrocarbons. So it is natural gas upgrading, which is the opposite of what has been done normally in industrial — "white" — biotech.

In white biotech, normally, they are doing what we call carbon downgrading, so they typically start with a sugar, which is a C6, and they downgrade it to, say, ethanol, which is C2. This doesn't make sense to us because you are literally turning something that is more valuable into something that is less so. Absent government rebate and mandate, it couldn't possibly be a business in our view, so in order to figure out the effects possible in this organism, we had to construct bioinformatic models.

The first thing we had to do, which no one had ever done before apparently, was to elucidate the metabolic network of our methanotroph in order to create the bioinformatic models. This would allow us to interrogate it in order to determine what is possible and at what theoretical yield, how many carbon atoms are coming in versus how many carbon atoms are coming out in the form of, say, isobutanol. We worked on that model about one year, and now it is done and in fermenters of various sizes for about 4.5 years following that work, and the original model is holding up very well. That is an example of the use of bioinformatics to inform what is possible and to what degree of possibility. Our bioinformatics team is first-rate.

TWST: You talked about when the company began, and you focused just on this model called exclusive channel collaboration. Are you still committed to very tight relationships with certain companies for certain purposes that are very long-term? Are you still committed to that way of operating, or do you see the company doing more licensing deals that are more, to use a word, transactional in nature? As you go forward, how are you deploying?

Mr. Kirk: We didn't build Intrexon to be a buyer and seller of assets. It is not a hedge fund or a private equity firm. We think Intrexon can be one of the greatest companies on the planet, while enabling many enterprises. Always, we are seeking and open to partnership, but today that is mostly true only if the other partner brings strategic value. With regard to any partnering exercise that we have going on now, in each case, the ideal partnership would be a 50-50 JV with a partner or a set of partners who bring value other than money to the project and enable it to succeed maximally. We are still committed to long-term relationships with our legacy partners beyond question, however. It is one of the foundations of the company that we should enable great businesses.

TWST: What is the AttSite Recombinase technology, and how is it different from gene editing?

Mr. Kirk: It depends on how it is employed. We can employ it to do portions of gene editing, but not always. The AttSite technology is, in the first instance, a library of large serine recombinases, and we use them for multiple purposes. For example, we can establish a landing pad in a genome and then land a gene program with extremely high fidelity

in exactly the location that we have specified. This is, of course, part of the incision part of gene editing. In gene editing, there are basically two aspects: excision and incision. There is an example of an incision.

TWST: I also wanted to talk about your proprietary technology called the RheoSwitch Therapeutic System that you are using in collaboration with ZIOPHARM Oncology. Can you elaborate on the collaboration and the proprietary system first?

Mr. Kirk: We have done a lot of work in switches, and so while there was an original switch and an improvement on that switch, there are several other variations on that switch too. We now have a switch that we use in plants that we call Florian. So we have a number of switches now. In general, what this class of switch enables us to do is to induce and then regulate the amount of transcription that is coming off of an open reading frame.

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As a practical matter, it means that we can use, in the case of therapeutics, an oral pill, which we refer to as the activator, to control through dosing the amount of expression of, say, a protein or a number of proteins by altering the dose of the activator that the patient is taking. With regard to ZIOPHARM, they have demonstrated in the clinic that this switch works very well in humans. They use it to induce and regulate the expression of interleukin-12, which is a very powerful cytokine that when simply injected into patients is too dangerous for therapeutic use. They have shown that the RheoSwitch can provide the right amount of IL-12 to obtain the therapeutic benefit of that cytokine while keeping it from reaching toxic levels.

TWST: That is actually in a Phase II clinical trial currently, right? Can you tell us the status of that and when you think it might go to the market, if that trial were to be successful?

Mr. Kirk: I cannot get out ahead of our partners. One of the advantages and disadvantages of these partnerships is I cannot speak for our partners. They are responsible for conducting Phase III trials and marketing. But we are very close to this program and very collaborative with ZIOPHARM, which we refer to as Ad-RTS-hIL-12. You are right that they have been greenlighted to do a Phase III trial in recurrent glioblastoma. We are fully supportive and think the data produced clinically thus far is extremely encouraging.

TWST: Is the data so far showing that it can extend survival in brain cancer patients?

Mr. Kirk: Yes.

TWST: You have at least 14 indications that perhaps represent separate programs within the company for developing candidates for use as therapeutics. What are you most excited about and why within this set of programs?

Mr. Kirk: I get asked this question a lot. I am very excited by each project that we are involved with. So it really depends. I like the programs that we have that really emphasize the core capability of Intrexon, whereby we are relying on the sophistication and complexity of the gene program more than anything else.

So one program that I find particularly interesting and exciting is our program, which is partnered with Xogenex, a company in which we own 75%, in heart failure, on which we actually are waiting to receive word on when the first patient will be dosed. That is definitely coming very soon. To our knowledge, it is the only multigene gene therapy ever greenlighted for a clinical trial by the FDA. It employs three genes, and we think that, combined, the effect of these three effectors could really make a big difference in the outcomes of heart failure patients. As you may know, heart failure is the number-one cause of death for our species.

Another reason I like it is because the cost is quite reasonable. You will have noticed that many companies are using very expensive manufacturing approaches, and so they're focusing on rare and ultra-rare indications because they believe the payers will pay a lot per patient in the case of an ultra-rare indication.

For this heart failure therapy unmet need that we want to solve, it is too soon for me to claim success. We will have clinical data soon enough, but if we are successful in the program, realize, this is a gene therapy for the number-one cause of death. Our cost of doing it will allow us to price it where it should be priced in relation to a market of that size, which would not really be possible if we had approached the problem in a different way.

TWST: Help us understand. If this therapy were to work, what would occur in the heart muscle?

Mr. Kirk: I'm not really at liberty to discuss what the effectors are, but I can state the obvious. Many people have tried cardiac gene therapies over the 20 years. They have worked in one axis only because, typically, they are using AAV, adeno-associated virus, which only has enough bandwidth to have a constitutive promoter, which means the gas pedal always goes all the way to the floor. It means that there is only enough room for one open reading frame, and therefore, it can only express one protein.

The main problem in addressing heart failure is it is complex. There may be more things one must do to move the dial on the ejection fractions and improve how well your heart pumps blood. At a minimum, you have to get rid of scar tissue, and you need to regenerate some cardiomyocytes as in some healthy heart cells. We do each of those and also a third thing with this, at least according to our preclinical data. It looks very promising. By combining these effectors, we are addressing a much more pressing and widely shared unmet health care need. And we shall be able to do so at a cost that I think will be very reasonable.

TWST: That is amazing. What do you think are the top challenges within safe gene technologies and health care that the company is uniquely addressing? Where is the technology truly differentiated within health care?

Mr. Kirk: Two areas we already mentioned, and one is the ability to have multiple effectors in a gene program, meaning you can express multiple proteins and/or multiple bioactive RNAs at the same time. The second one is to be able to control and regulate that gene program in real time, so dial it up, dial it down and turn it off. We think each of these is absolutely critical. We start with that and add to that two more elements that I will introduce now. I alluded to it, I think, twice already, and that is the cost.

It really needs to be a reasonable cost. Therapeutics is clearly an industry that needs regeneration. I don't know if you've seen the studies, but there is some pretty good scholarship out there to the effect that the IRR on R&D in pharma and biotech today is globally zero. That is not a good sign for an industry, and the industry's response so far has been to answer, "Let's see how many $150,000 cancer therapies we have to stack on top of each other." It just can't go on forever, and we are focused on combination therapeutics that don't have combination price tags.

We don't think that's the appropriate response. The industry's response so far has been to continue to raise prices and to develop therapeutics

that cost more and more. We think that the engineering of biology gives us an ability to produce higher-quality product at lower cost.

Then, the last thing I will mention is that, at least judging form market capitalizations and recent M&A activity, others are beginning to appreciate that the age of engineered biology has arrived. But this industry, meaning life science, is probably the last major industry to adopt engineering for the basis of the construction of its new products, so it has not yet fully grasped the industrial and organizational implications. I'm speaking to you on an iPhone X; it is made by the largest market cap company ever in the history of the world. But if they don't give me a new one of these every so often, they won't hold that status.

Largely unappreciated by people who are participating and spending M&A dollars and so forth is that, until very recently, the buy-side analysts treated all players, all comers, as if they were contestants in a lottery for government monopoly. That is clearly changing. It is clearly changing because, to win in this engineered field going forward, you need to constantly improve your product. You need to add features. You need to make it more complex and provide more and more benefit with each generational change. At Intrexon, we have the discipline to be committed to everything we are working on and so are often working on the second and third generation of the first instance product at the same time.

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TWST: What do you want an investor to know today about Intrexon Corporation, if you had to summarize that for the investor community? You made a case for why the company has thought leadership that extends well-beyond generic technology in the health space and setting a new standard in the economics of science and health care too.

Mr. Kirk: What is it that investors aren't getting about Intrexon? What is interesting, what they are not getting is, in some ways illustrated in this conversation when you began somewhat complaining about Intrexon's complexity, but in actuality, we are not really that complex. We may indeed be active in food and energy and health, but we are doing the same kinds of things in each of these areas. In other words, all of these relate to living organisms, and they all run on the same software language. Our foundational basis is in that software language.

Sometimes when I have spoken publicly, I'll make a joke of it. I'll say, "You may not know this, but the homology between man and banana is 50%," and then I'll pause for the punch line, and I'll say, "For some of us, it may be more!" My point is this: We tend to use the prevailing taxonomy to classify the world. Every generation does that. Even though we know the prevailing taxonomy is artificial and transient, meaning we made it up, and we are going to keep changing it. Even though we know all that, we insist that everything that we hear about, every new thing, maps to that. History is replete with examples to show that this attitude is always wrong.

Intrexon may seem complex because people are thinking in terms of standard industrial code. How could food be the same as health, and how could that be the same as energy? Think about my man-banana example however. I can assure you, however, that our genome engineers don't care if they're working on an avocado genome or a human primary T cell. Put it this way: It means that if you think that a company working in both man and bananas is diverse, then — just to use a standard industrial code metaphor — it means that you might have trouble wrapping your mind around a company that is in both banking and insurance. Berkshire Hathaway and others show that it's really easy to be in both because the analytical tools and essential objects of these two industries are the same.

The real question has to deal with: What is the underlying architecture on which an industry is built? We, as consumers, of course, see insurance and banking as very different, but underlying those in terms of the analytics and what it takes to run either of those kinds of enterprises, it is all about turning stock to flow and flow to stock, to use some quaint business language, meaning it's about money movement. You are adjusting money through time from a sum to a flow and back.

So what I want investors to know is that Intrexon is a very focused company. Our teams, and we have about 660 scientists, don't have any difficulty speaking to one another, and their cross-pollination has really been quite dramatic and produced some profound results. They are all working in the same language and with very similar tools.

TWST: Is there anything you wanted to say in terms of the operational complexity of the company? You mentioned the complexity in talking about the science, but obviously, you have to be a gifted executive team enabled to handle all these moving parts?

Mr. Kirk: We do. We have a very deep bench. We have a lot of talent on this team, and they are a lot of fun to work with. And you are right to wonder then about how we manage a diverse set of opportunities, once it's understood that they are more closely related than many might have supposed.

It actually begs the question: Well, then, how do you choose among various potential projects? There is a consistent thing we have done, and that is almost without exception. The projects that we embark on have huge value gains if we are successful. We are not hunting mice.

Consider the methane bioconversion platform that I was alluding to a little while ago. So far, we have publicly announced that we are in the money on two molecules and have proven that we can make, I think, six complex hydrocarbons so far. But the totality of that industry, meaning what I refer to as the petrochemical complex, as in everything that comes from oil to natural gas and everything in between and those that derive from either oil or gas, probably represents 15% of the gross world product. One of the molecules that we declared ourselves to be very much in the money on is 1,3 butadiene. That's not a product that a lot of health care people know about, but it's $22 billion a year and a commodity. If we're right, and we think we are, we just figured out how to turn that into a biotech product with biotech margins.

TWST: I'm assuming you're entering different markets with different technologies and at different angles, and you have to think about how all of those things can and could fit together.

Mr. Kirk: And how they fit together with what we already have, and we are doing all of this.

TWST: Thank you. (KJL)

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