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DioGenix is focused on becoming the "go to" Molecular Testing Company in Neurological Diseases, Identifying New Markers critical to Understanding Diseases Such as Multiple Sclerosis, Neuromyelitis Optica (NMO) and Transverse Myelitis

Healthcare
Molecular Testing

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Larry Tiffany
CEO

BIO:
Prior to co-founding DioGenix, Mr. Tiffany was the SVP & General Manager of Genomics for Gene Logic where he managed a $22M business until he orchestrated its sale to Ocimum Biosolutions, Inc. He has held numerous executive positions leading operations, product development, business development, and marketing & sales. Prior to re-joining Gene Logic to restructure and strategically reorient the Genomics business in 2006, Mr. Tiffany was Chief Business Officer and President of Genetraks, an Australian-based veterinary molecular diagnostics firm. Prior to Genetraks, Mr. Tiffany was instrumental in building Gene Logic's Genomics business from less than $10 million per year in revenue to well over $50 million per annum. He holds a JD from Franklin Pierce Law Center in Concord, New Hampshire; a MS in Biotechnology from The Johns Hopkins University in Baltimore, Maryland; and a BS in Chemistry from Nazareth College in Rochester, New York.

About DioGenix:
DioGenix, Inc. (DGx) is a molecular diagnostics enterprise focused on the rapid development and commercialization of novel, diagnostic, prognostic and treatment response monitoring tests. Headquartered inRockville, MD, DGx was founded to exploit over $250M and hundreds of man-years invested in the development of a unique set of assets and capabilities that are actively being used to develop new clinically and commercially relevant molecular tests. For over eleven years the DGx management team worked with the world's largest pharmaceutical companies to identify and exploit biomarkers that correlate with disease activity and response to therapy, primarily utilizing the tools that are now the core assets of DGx. Over this period, these assets and the well-established methods for their use have been optimized to a performance level and quality required to develop useful new molecular assays. The team's collective scientific, clinical and business experiences have been instrumental in guiding the identification of a series of commercial opportunities, which have significant market appeal, and can be developed on an accelerated schedule.

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

CEOCFO: Mr. Tiffany, what was the vision when you started DioGenix?
Mr. Tiffany: DioGenix is a "spin out" of a publicly traded genomics company called Gene Logic. DGx Management Team had spent over ten years perfecting a set of capabilities and assets used in the identification of new molecular markers that are critical to better understand diseases of interest. When we started DioGenix we saw an opportunity to take those capabilities and assets and be able to now apply them to this new field of developing molecular tests and molecular diagnostics. In particular, we were very excited about the opportunity to do that in the field of neurological medicine, given the number of diseases that are very difficult to identify and manage using currently available tools in combination with a clinicians' intuition and expertise in looking at the symptoms and the feedback that they get from patients.

CEOCFO: Could you explain the molecular concept as opposed to the way it has been looked at for disease treatment or abatement?
Mr. Tiffany: I will give you an example. Multiple Sclerosis is a disease that affects almost half a million people in the United States and over two and a half million people worldwide. Unfortunately, it is a disease, predominantly of mid-career women, that present to their doctor with a diverse

set of clinical symptoms. Sometimes, even within family members, there are different ways in which that disease manifests itself. Today, a neurologist will sit down with a patient, talk to them about their symptoms and family history, and then diagnostically evaluate them using a series of tests. There is no single definitive test to help identify early stage MS patients, so neurologists will order MRI imaging, cerebral spinal fluid analysis and a series of blood test to rule out other diseases like Lyme disease and Lupus. These tests provide certain pieces of information that help the neurologist, but in total, the misdiagnosis rate is still extremely high. In particular, cerebral spinal fluid (CSF) analysis; based on a spinal tap has been in use since the late 1960's. This test does provide an important piece of information to the neurologist as it will detect general immune dysfunction in the Central Nervous System (CNS). It does not, however, look for specific markers or proteins, instead it gauges whether there is a general immune response in their CNS, as compared to a more systemic response resident in their blood. Principally, it makes tremendous sense to look for these types of immune response; unfortunately, the test has low resolution in identifying the specific disease causing the inflammation. DGx is standing on the shoulders of giants, as we believe in this same principal, but instead are using far more sophisticated technology, which provides much higher resolution as it relates to identifying those patients.

CEOCFO: What have you figured out about how to do this that others have not?

Mr. Tiffany: DGx, in partnership with the University of Texas Southwestern, have found specific DNA changes in certain immune cells in CSF. These changes are very specific for different neurological diseases. We now measure those changes using Next Generation Sequencing technology, that will allow us to provide much more accurate information back to a doctor as to whether a patient has Multiple Sclerosis, Neuromyelitis Optica (NMO), Transverse Myelitis (TM) or a variety of other similar looking but different functioning diseases.

CEOCFO: What is happening scientifically and how are you able to identify it?

Mr. Tiffany: Within CSF, there is a series of immune cells. One of the very important cells is a "B" cell. It has been established that these B cells act as sentinels waiting to be brought into the CSF to engage "foreign invaders" and remove them as threats to the patient. Unfortunately, in the case of patients that have some of these diseases, it is actually their own body that starts to present proteins that the B cells believe are foreign invaders. The B cells job is to mount a defense against these antigens. The B cell is able to do this using a very specific part of its genome that was designed to be able to change very rapidly in order to develop a "library" of antibodies. These soldiers are sent out looking to disable these antigens. The B cell does not know which one of the soldiers is going to be successful, so it makes a vast variety of antibodies that are all slightly different. As certain soldiers become more successful, there is a signaling system back to the B cell that says "hey, that is the kind of soldier that we need to be in this battle." Then the B cell makes more of those antibodies and starts to send them out in mass quantities. Generally speaking, that works really well if it is a foreign invader. Unfortunately, in the case of patients, for example, with Multiple Sclerosis, that process starts to strip the insulation from around your nerves eventually leading to neurodegeneration and permanent disability..

CEOCFO: What is the secret that you understand to make the identification?

Mr. Tiffany: We started working with a group at the University of Texas Southwestern led by Dr. Nancy Monson, who originally had done this on the "bench top" within her lab, looking at this very specific region. What she did that was unique was to look at this certain region within the DNA of these B cells to understand these changes relative to a healthy patients whose B cell had not been challenged resolving which changes are most important. She found a series of "hot spots" that seem to change more rapidly related to, for example, Multiple Sclerosis versus other similar immune-mediated neurological diseases. We saw that as "a fantastic idea, but it needs to now be commercialized." We chose next generation sequencing that would allow us to do this faster, cheaper and more reliably. Therefore, what we have done is utilize this new state of the art sequencing technology to be able to look at these DNA changes that are occurring in patients that are in the early stages of these diseases.

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- Larry Tiffany

CEOCFO: You have started to commercialize. What has happened so far?

Mr. Tiffany: Once we developed the next generation sequencing assay we did a series of studies looking at some of the exact same patients that are part of the differential diagnosis resulting from these symptoms. This allowed us to confirm that the results that Nancy was getting, we were getting. Those studies went extremely well; very similar results as you would expect. Then we went to the next

step. We did an independent study of roughly one hundred individuals where we looked at patients with MS, patients with other neurological diseases, and then some healthy controls. We wanted to make sure that this same next generation sequencing assay that we had developed would allow us to separate out the patients with MS from the patients with other diseases. What we saw was that yes, we could do that with pretty good performance, and we have also started to see that even in some of those other neurological diseases there are, not surprisingly, specific DNA changes that seem to be related to these other immune-mediated neurological diseases. What that means is that downstream, as we look at more and more of these diseases which are controls within our studies; in example patients with NMO, patients with TM, patients with Optic Neuritis, that we might also be able to find signatures for those other neurological diseases just like we have or Multiple Sclerosis.

CEOCFO: That would be quite a breakthrough!

Mr. Tiffany: You are absolutely right! We could beheading towards providing a neurologist with more and more useful tools. It is one thing being able to say, "Yes, you have MS" or "no, fortunately you do not have MS". However, when you say no, it would be great to say, "…however you may have NMO". That is because, of course, every patients wants to get to the root cause of why they are having the symptoms that they are feeling on that day. The next clear step in developing our lead product is a prospective clinical trial; as patients in previous studies were, in general, retrospectively collected. We knew what kind of patients they were going into the study and you need that to be able to check the performance of your new test. What we have just launched; and our current financing announced the other day providing support for us to run, a prospective multi-site clinical trial. That is just as you would imagine it. We are now having patients that are coming through thought-leading neurological clinics and high-volume community practices that are being typically evaluated for these kinds of diseases. We are getting access to their CSF and their blood; looking at both of those biofluids on each patient. Those patients go on to be diagnosed with MS and a variety of diseases. However, we are going to test them in a blinded fashion without having any knowledge of what their eventual diagnosis will be and then we will "break the blind" and determine "The test scored you as an MS patient or another neurological disease patient. Was the test accurate?" That really gives us a much more "real world" sense of how this test is going to perform in the clinic.

CEOCFO: You mentioned blood and spinal fluid. What is the differentiation in what you are looking for in each and how does it work?

Mr. Tiffany: We are going to use the same next-generation sequencing approach on all biofluids. Even though access to and testing of CSF is part of the standard of care for these diseases today, all of the market research that we have done and common sense would suggest that a patient would prefer a blood test than have someone do a lumbar puncture, even though lumbar punctures are very safe and reliable. For each one of the patients in our study we are going to have both biofluids, as the National MS society has provided us with a grant to support the collection and analysis of the blood. Because we have not looked at blood on a lot of patients in the past, we do not know yet if the same kind of DNA mutations that we see in cerebral spinal fluid will be resident in blood, or will we see a slightly different set of mutations that pass the blood brain barrier and can be measured in the blood. Either way we are going to get a really great opportunity to see if we can use blood as a biosample as compared to using cerebral spinal fluid. That may certainly be a second-generation product for DioGenix, but very importantly, what that allows us to do is look at and expand out our potential portfolio of products.

CEOCFO: The Multiple Sclerosis Society had provided some funding for DioGenix. How well is DioGenix funded and will you need to look for additional funds?

Mr. Tiffany: We just raised some money over the last few weeks. We are in very good shape to complete this clinical trial. We are going to break the clinical trial in to two pieces. We are going to do an Interim Analysis on about half of the patients and then we are going to complete the trial when we have all of the patients enrolled. As we are going through the trial, we are going to be seeking some additional funding which primarily will be used to commercialize our lead product. Although current investors have committed to fund the entire clinical trial we also believe that it is the right time to start looking for a variety of different partners; partners that can help us commercialize the product as well as qualified venture partners that can help us to further financially support the company.

CEOCFO: Has the neurological community, in general, been paying attention or is it too early?

Mr. Tiffany: They have, but as you know, with most medical communities it is really thought leading groups that are our looking at these new innovative technologies. If you go down to your local neurologist, he may or may not have heard of us. However, we have been able to present at the American Academy of Neurology. We presented some of our results there last year. We are hoping to present there again this year. That is the largest meeting of neurologists in the United States, and I believe actually in the world. We are starting to do that as we have just completed this independent study of one hundred patients. We are drafting a publication right now, and hope to have that out in the first part of 2013.

CEOCFO: You have considerable experience in the industry. What have you learned in past ventures that you can bring to the table to help make DioGenix successful?

Mr. Tiffany: It really came down to the core vision that we have for the company. What we have been doing for almost ten years as a senior management team within Gene Logic is that we know how to find clear clinical

needs. It is all of the pieces that you have to bring to bear to develop a product. You have to have good clinical sites. You have to have really high quality sample collection. You have to have high quality data that is generated from those samples. Although all of those steps, when you look from the outside, all seem slightly trivial, the effort and the detail that goes into recruiting the right clinics and recruiting the right doctors to be involved and making sure that as they start collecting patient samples you are continually monitoring the quality of those samples and then the quality of the resulting data; that is really a lot of the "secret sauce" that makes it work; because if you can do that well then you can believe in the results of the test that you have developed. In the end, that is what the doctors want. They want something that they know they can rely on and that they can use when they are looking at a patient who is certainly going through an anxiety provoking, very difficult time, and even if it is sometimes bad news, they want to provide news that they are confident about. That is really our goal.

CEOCFO: Why does DioGenix stand out for investors and people in the business community?

Mr. Tiffany: Given our expertise, the expertise of the core management team, what we are the best in the world at is looking at clinical problems and finding the right technology to fit those clinical problems, and then understanding, which technologies are ready for commercial application and which ones are a little bit early in the process. Unlike many other companies, which are just headed for the largest market opportunities possible, when you look at DioGenix, what we have found is a very sizable market opportunity, but one where the current competitive landscape is much more barren. The opportunity that DioGenix has is to be the "go to" molecular testing company in neurological diseases. That is our goal. When you look across the landscape, there are very few companies that are trying to do that in comparison to the companies working in oncology and cardiovascular and metabolic diseases and some of the others. We are pretty excited about our capability to do that and the vision of what we want to become.
