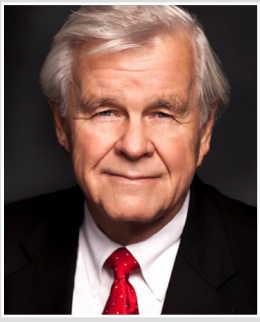
THE WALL STREET TRANSCRIPT
Connecting Market Leaders with Investors

Hemispherx Biopharma, Inc. (NYSEMKT:HEB)

THOMAS K. EQUELS, M.S., J.D., was named Chief Executive Officer in February 2016, served as President since August 2015, has been a director since 2008 and presently serves as our Executive Vice Chairman, Secretary, and General Counsel and Litigation Counsel of Hemispherx Biopharma, Inc. Mr. Equels previously served as Chief Financial Officer from December 2013 to February 2016. Also, for over a quarter century, Mr. Equels has represented national and state governments as well as companies in the banking, insurance, aviation, pharmaceutical and construction industries. He has extensive experience in international business matters. On numerous occasions, Mr. Equels has served as a court-appointed receiver/chief executive for distressed businesses. Mr. Equels received his Juris Doctor degree with high honors from Florida State University. He is a summa cum laude graduate of Troy University and also obtained his Master of Science degree from Troy. He is a member of the Florida Bar Association and the American Bar Association.



WILLIAM M. MITCHELL, M.D., PH.D., was appointed Chairman of the board of Hemispherx Biopharma, Inc., in February 2016 after serving as a director since July 1998. Dr. Mitchell is a professor of pathology, microbiology and immunology at Vanderbilt University School of Medicine and is a board-certified physician. Dr. Mitchell earned an M.D. from Vanderbilt and a Ph.D. from Johns Hopkins University, where he served as House Officer in Internal Medicine — Osler Service — followed by a fellowship at its School of Medicine. Dr. Mitchell has published over 200 papers, reviews and abstracts that relate to the pathogenesis of obligate intracellular pathogens, innate and adaptive immune responses, and liquid biopsy cancer — chromosomal instability — diagnostics. He is the inventor or co-inventor of 14 issued U.S. patents as well as derivative foreign patents. Dr. Mitchell has worked with many professional societies that have included the American Society of Investigative Pathology, or ASIP; the International Society for Antiviral Research, or ISAR; the American Society of Biochemistry and Molecular Biology, or ASBMB; the American Society of Microbiology, or ASM; the American Chemical Society, or ACS; and the American Society of Clinical Oncology, or ASCO. Dr. Mitchell is a member of the American Medical Association, or AMA. He has served on numerous review committees for the National Institutes of Health, or NIH; the Centers for Disease Control, or CDC; the European Union, or EU; and the College of American Pathology, or CAP. He is an independent director of Chronix Biomedical, a genetics-based cancer diagnostic company.

SECTOR — PHARMACEUTICALS

TWST: Can you offer a brief overview of the company, and your core technology and how that technology would differ generally from the standard of care today?

Mr. Equels: We have two platform products. One is our experimental drug, Ampligen. The other is our FDA-approved drug, Alferon. First and foremost, we have a great deal of clinical work that has been done with regard to chronic fatigue syndrome, which is also known in Europe as myalgic encephalomyelitis. I will refer to this as ME/CFS.

With regard to the ME/CFS application, we are moving as quickly as we can to seek a commercial approval. There have been nearly 100,000 doses of Ampligen administered to humans, and it is generally well-tolerated as demonstrated in two placebo-controlled trials. Our pursuit of commercial approval is not just in the United States, but we also have an application pending in Argentina and are opening up early access programs, known as EAPs, throughout Europe.

Now, the standard-of-care issue with regard to ME/CFS is fairly easy to address because there is currently no approved treatment for this disease. In its severe form, it is an extremely serious and disabling disease. The CDC and National Institutes of Health have both put an emphasis on finding therapies that can be used to treat it. NIH has publicly addressed Ampligen, and Ampligen is the only late-stage drug in the pipeline.

Because there are no approved treatments, the current standard of care is treating the symptoms of the disease. An approval of Ampligen would provide the first and only therapeutic aiming to address the disease itself.

Dr. Mitchell: Ampligen, for the FDA, is a new class of drug. To my knowledge, there are no double-stranded RNA drugs that have been approved. There are some small regulatory double-stranded RNAs referred to as microRNAs that may be approved in the future, but they are early development, and none are like Ampligen.

Mr. Equels: Another important point with regard to ME/CFS is that we have an orphan drug designation for Ampligen for ME/CFS. Now, the second area where Ampligen has been tested clinically is cancer, where it appears to have activity against melanoma and kidney cancer, cancers where we also have orphan drug status. We believe it is especially well-positioned for possible use in combination with other drugs in the immuno-oncology space due to its activity as a driver of the immune response.

"Another important point with regard to ME/CFS is that we have an orphan drug designation for Ampligen for ME/CFS. Now, the second area where Ampligen has been tested clinically is cancer, where it appears to have activity against melanoma and kidney cancer, cancers where we also have orphan drug status."

TWST: How can you have this drug candidate work on both chronic fatigue and cancer? What is the underlying mechanism of action that might make it work on both?

Dr. Mitchell: Let me give you a short answer to that, which is more detailed in my *American Journal of Pathology* publication entitled "Discordant biological and toxicological species responses to TLR3 activation." It is available at no cost on PubMed. The double-stranded RNA activates one of the 10 toll-like receptors that are the initial inhibitory molecules for invading microorganisms that recognize structural patterns within microbes and respond by transiently activating hundreds of genes, producing a variety of biological responses. There have been attempts, with other toll-like receptors, to bring pharmaceutical products forward, but one of the problems has been the induction of systemic inflammatory cytokines with toxic effects. Ampligen is unique in that it activates toll-like receptor 3 that, among the 10 human toll-like receptors, uses a unique pathway that minimizes systemic inflammatory cytokine induction.

Mr. Equels: Dr. Mitchell is saying it does not activate any of the other TLRs, and unlike other TLR3 agonists, it does not activate the inflammatory helicases.

Dr. Mitchell: The parent compound is something called Poly I Poly C, and it is more toxic than Ampligen. The reason for that is that it, similar to Ampligen, activates toll-like receptor 3, but it also activates the cytosolic helicases by an inflammatory pathway similar to the other toll-like receptors. For whatever reason, it is unclear why Ampligen, with its unique double-stranded RNA structure, does not activate the cytosolic helicases. So that's the reason it's been given so many times in the clinic and is so well-tolerated. It is ready, I believe, to be studied in clinical trials with the checkpoint inhibitors in advanced cancers.

The immune system generally recognizes cancers as foreign. Cancers, however, are protected by surface molecules that block immune rejection, thus the origin of the term "checkpoint." The checkpoint inhibitors are large protein molecules that bind to these checkpoint molecules, inhibiting their function. Checkpoint inhibitors are an important new class of anti-cancer drugs. Allowing the immune system to reject cancers has resulted in longer periods of disease-free intervals.

There are a small number of people that appear to have had long-term remissions, which may prove to be curative in stage 4 end-stage cancers. The majority of cancer patients, however, do not show these dramatic responses. You can combine two of these checkpoint inhibitors with an increase in survival time, but they are associated with dramatic increases in toxicity. Resistance to the checkpoint inhibitors may be due to other mediators that block immune rejection or by a dysfunctional immune system.

There are animal model systems that indicate that double-stranded RNA in combination with a checkpoint inhibitor provides dramatic improvement over the checkpoint inhibitor alone, suggesting that lack of immune activity is the major reason for resistance to the checkpoint inhibitors. We believe Ampligen can serve as an immune driver in combination with a checkpoint inhibitor.

Mr. Equels: It may also allow a correspondingly lower dose of the checkpoint inhibitor, thereby reducing the toxicity associated with higher doses of the checkpoint inhibitor.

TWST: Ampligen is in Phase I/II in a couple of different types of cancers. Is that correct?

Dr. Mitchell: Yes, Ampligen is currently in Phase I/II studies for ovarian and colorectal carcinoma. In addition, years ago, Ampligen was studied in two other carcinomas. One was renal cell carcinoma, and the other was stage 4 melanoma. There were small numbers of patients with melanoma, but the survivor results that were obtained are equal or similar to that currently seen with the checkpoint inhibitors. Far more patients will need to be studied to make sure that this was not a statistical aberration. Increased survival rates were also seen in renal cancer.

Mr. Equels: Now, there's a third potential application of Ampligen, which is also very significant. Again, because of its function as a host-based innate immune system driver, we are seeing activity in this third area, which is as a broad-spectrum anti-viral. The most lethal viruses are not subject to clinical viral challenge testing. However, the United States Army Lab, USAMRIID, funded a study utilizing rodents with regard to testing Ampligen against the Ebola virus. Animal studies, of course, are not necessarily predictive of the response in humans.

In the USAMRIID study, there were three cohorts. One was a control group, which were mice that were infected with the Ebola virus but did not receive Ampligen. In that group, there was 100% mortality after approximately seven days. There were two other groups infected with Ebola, where a low dose and a higher dose of Ampligen were administered. In the low-dose Ampligen group, there was 100% survival and virtually no weight loss. In the higher-dose group, there was 90% survival, again with no weight loss in the surviving animals.

Now, the Ampligen in this experiment was administered shortly after infection. So it shows potential efficacy as an early-onset therapeutic or potential prophylactic. The results also indicate a high level of bioactivity in this experimental setting. Similar bioactivity has been seen in a number of other animal model experiments with other viruses that are highly lethal, such as Venezuelan equine encephalitis and the SARS virus. We believe that Ampligen may have utility against a variety of emerging viruses with lethal pandemic potential. Animal testing has also suggested similar bioactivity in mosquito-borne viruses similar to West Nile and Zika.

A final important component of the Ampligen portfolio is as an immune driver for viral vaccines, such as influenza. We have in an experimental setting demonstrated epitope-spreading properties with seasonal influenza vaccines with protection against highly pathogenic avian influenza as demonstrated by extensive studies conducted at the Japanese National Institute of Infectious Diseases by Dr. Hasegawa. These animal experiments, in a nutshell, indicate the potential for cross-protection against differing forms of the virus. Based on Professor Hasegawa's experimental work, we have designed a formulation of Ampligen for nasal administration, as a potential immune driver for vaccines.

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Based on these important results in influenza, we believe that similar results might be achievable as a vaccine enhancer for Zika virus infections. The potential importance is clear since effects of the Zika virus are dramatically different between Brazil and Columbia, suggesting possible clade differences.

TWST: Can you tell me which is likely to be commercialized first, and when would it be commercialized do you think?

Mr. Equels: We are seeking co-development partners in the I-O space because there are a number of companies that have checkpoint inhibitors that may benefit from the utilization of an immune driver such as Ampligen. In ME/CFS, we are making every effort to go through the approval process as quickly as we can afford to in the United States. We also have pending a new drug application in Argentina. We are currently awaiting a ruling from the ANMAT, which is the Argentine version of the FDA.

TWST: What's the estimated patient population for chronic fatigue syndrome?

Mr. Equels: Our focus is on the severe and disabling form of ME/CFS. The number of patients with ME/CFS is estimated to be over 3 million worldwide; however, only a portion of these have this severe and disabling form of the disease that we are targeting with Ampligen.

TWST: Is ME/CFS believed to have a diverse etiology? Is it believed to have different causes?

Dr. Mitchell: Yes, you can refer to a recent publication of mine found in *Expert Review of Clinical Pharmacology* entitled "Efficacy of rintatolimod in the treatment of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME)" — that also can be obtained without cost from the internet site PubMed — which I can sum up. About two-thirds of patients will have symptoms compatible with an acute infectious process. The remainder have an insidious onset. It is apparent now that there can be a multiplicity of invading microorganisms, which replicate within the cell. There appears to be a genetic subset of people that are incapable or inefficient in clearing the pathogen. So ME/CFS is a complex disease process of unknown origin combined with one or more genetic elements and immune dysfunction.

Mr. Equels: We have to remember that this is a disease for which assessments continue to be developed with respect to its nature, origin and designation as a serious debilitating disease. A formal redefinition in the past year and a half has been recommended by the National Academy of Medicine.

When you look at this disease, one of the things we've discovered is that, in the first two years, there is a significant rate of spontaneous remission. For some with ME/CFS, the body is slowly recovering itself, and the immune system is addressing it successfully over a period of time. Ampligen may be most helpful for those cases where the body doesn't recover on its own and where the disease gets worse to the point where many people are bedridden 24/7, unable to work, unable to function in their family and barely able to walk to the bathroom.

TWST: Do they need to have a diagnostic test that comes up with a certain result to make them a candidate, or do you rule out everything else?

Mr. Equels: The problem is that there are currently no clear diagnostics. The disease and its diagnosis currently are based on a constellation of symptoms and exclusion of other possible causes of the debilitating fatigue.

Dr. Mitchell: You rule out cancer, anemia, multiple sclerosis, thyroid disease and other causes to diagnose it. There would be clear benefit of a diagnostic test, and there are some known biochemical and molecular dysfunction associated with the syndrome that I believe, properly studied, may prove to provide that additional diagnostic capability.

Mr. Equels: But that's not our area of expertise here. We are dealing with the experimental therapeutic.

TWST: You can launch this without a companion diagnostic in the market?

Mr. Equels: Absolutely. That's exactly what we intend to do. However, we are not currently in a position to anticipate the percentage of the total ME/CFS patient population that may be included within any approved indication for Ampligen. ME/CFS is a disease syndrome that demands a therapy. We are going to work as hard as we can to push Ampligen across that goal.

TWST: You've already commercialized Alferon. Have you provided any public disclosure of sales and guidance on future sales for that?

Mr. Equels: Let me explain what we're doing with Alferon. Alferon is commercially approved in the United States for refractory or recurring external genital warts — HPV — in patients 18 and older. In Argentina, we've gotten an approval for Alferon for broader use in patients refractory to recombinant interferon.

Now, you're probably familiar with alpha interferon. Alpha interferon is a very large market. With the exception of Alferon, all commercial interferons are a recombinant or, in layman's terms, a synthetic product. With the use of recombinant alpha interferon, there are a significant percentage of cases, and it depends on the disease, that produce neutralizing antibodies to recombinant interferon, which makes it ineffective for those patients. Alferon does not produce these neutralizing antibodies due to it being a highly purified natural product. Alferon is bio-identical to the alpha interferons produced in response to viral infections and, therefore, does not create neutralizing antibodies.

Now, in both the United States with refractory HPV and in Argentina for all refractory applications, our natural alpha interferon is not subject to these neutralizing antibodies. Moreover, Alferon has been demonstrated in various assays to have higher activity against a range of viruses than recombinant forms of interferon.

Dr. Mitchell: In vitro testing has shown it is 10 to 100 times more effective than recombinant interferons.

Mr. Equels: You asked the question about production. The production method utilized to get the commercial approval was a production method that was highly manually intensive and based upon the use of 6-liter flasks for processing the interferon. What we have done or are in the process of doing is to create a more sophisticated and efficient process that is highly sophisticated and utilizes a 600-liter bioreactor.

Now, the reason that we are doing this is because the cost of Alferon. If you were to use the 6-liter flask in the manually intensive process, it would be so expensive that it would be out of reach as a substitute therapy for those situations where you have people refractory to the recombinant interferons. However, with the bioreactor, we hope to get preapproval inspection and FDA approval of the system. Once, God-willing, we get that done, the cost of production of the Alferon will drop significantly from the prior process, and that will allow us to be, though somewhat more expensive, still at a price point to be available to patients. The potential market is substantial.

TWST: Do you have sales of that now, and can you talk about what your previous annual sales were?

Mr. Equels: We haven't engaged in sales of Alferon in probably four years. We had to basically shut down and invest in this new production system with over $8 million in equipment upgrades. When we would be able to provide Alferon is all subject to governmental approvals. I'm not in a position to even guarantee that we will get the governmental approval of the new system, though we believe we will be able to obtain that goal. We are trying to work out the final funding requirements necessary to take this to completion. All the equipment has been installed, and we are ready to take those next steps once funding is obtained.

TWST: What do you think is the market potential?

Mr. Equels: I can tell you almost precisely what the market potential is because the market vastly exceeds our production capability with one bioreactor. So assuming a reasonable amount of time for market penetration, probably the entire capacity of the bioreactor system would be available for sale, and there would be a demand I believe, and this is a rough estimate, but probably $90 million-a-year gross. We have the ability to add an additional bioreactor, but obviously, we need to get this first one up and running, and get sales started, and then, we can look at expanding the market from there.

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TWST: For strategic objectives for 2016, you talked about looking for licensing opportunities. What do you mean by that, and can you talk about any changes to your business model?

Mr. Equels: We have clearly articulated a new business model, and if I may, I will give you just an example. With regard to ME/CFS, for example, we have an experimental drug that is very late-stage in its development, as it has gone through a Phase III placebo-controlled study with a large number of subjects. We have a market in which the course of treatment is probably $60,000 to $70,000, roughly. Worldwide, severe ME/CFS is a huge market, where there is absolutely no competition because there is no other approved therapeutic. In fact, there is no other drug specifically directed against ME/CFS that I'm aware of that's even in the pipeline.

So one would think that finding a co-development partner would be something that could be mutually attractive by taking our expertise and what we've done to date to develop the drug and working with a company that would be prepared to move it into that large market. Those are the kinds of partners that we are looking for and the kind of opportunity that we're trying to develop.

TWST: Do you have the financing to get through your next set of milestones? I know you've just announced a partnership with a company to expand manufacturing capacity, but do you have the financing or the partnerships to get you to where you need to go over the next year or two?

Mr. Equels: We do not have all of that in place, and that is one of the reasons we are working on these co-development deals. Fundraising of one form or another will be important to accomplishing these goals. We are striving to raise funds in a nondilutive manner.

TWST: What do you want a potential investor in Hemispherx Biopharma to know today?

Mr. Equels: It is very important to me that they know that we have worked diligently, over a long period of time, to develop this experimental drug, Ampligen, because we believe it has a multifaceted

important role to play in the future of medicine in ME/CFS, immuno-oncology, as a viral-vaccine enhancer, and as a broad-spectrum prophylactic and early-onset viral therapy. At Hemispherx, our team has the dedication to accomplishing those goals in large part based upon the fact that we have a strong and unrelenting belief that we are doing something that is very important for people who suffer from these diseases, many with clearly unmet medical needs. We are going to do our best to work, with what we have, to accelerate the process — in part by acquiring partners — so that we accomplish those goals.

TWST: Is there anything else that you wanted to add before we end?

Mr. Equels: Nothing I can think of.

TWST: Thank you. (KJL)

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