

Utilizing Pluripotent Cells that Can Become Any Type of Cell in the Body, Regenerative Medicine Company BioTime Inc. is developing treatments for Dry-Age-Related Macular Degeneration and Facial Aesthetics



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CEOCFO: *Mr. Mohanty, according to your website, BioTime is leading the next revolution in regenerative medicine. How so?*

Mr. Mohanty: Regenerative medicine is a big word. There are many ways to approach regenerative medicine and we have a couple. When you look at different ways diseases are typically treated, most of them try to help reduce the effects of the disease, whereas what we are trying to do is something that we see as more of a cure. So, aspiring towards cures, rather than alleviating symptoms and/or reducing the effect of the disease is one of our top priorities. One of BioTime's primary approaches utilizes pluripotent cells, which can become any type of cell in the body. We have lots of technology and ways that we can differentiate human cells. BioTime can make almost any cell in the human body and we have made about 200 types of cells. One of the most fascinating derived cells that BioTime has identified potentially addresses Dry-Age-Related Macular Degeneration or Dry-AMD. Dry-AMD is a devastating and debilitating disease of the eye, where as you get older, you start to lose the retinal pigment epithelium (RPE) cells in the back of the eye. Despite the clinical research encompassing various modalities, there is currently no cure for this disease and it is the leading cause of blindness in people over the age of 60, affecting more than 20 million people in the western world. Here at BioTime we have taken a different approach to Dry-AMD. Our cell transplant therapy, replaces the missing and/or damaged RPE cells through a sub-retinal injection into the eye. We see parallels in our cell transplant therapy to organ transplants, like the liver or kidney. Transplants performed today have very high success rates of approximately 80 to 90 percent, even if the disease mechanism is not fully understood. This gets back to what I said at the beginning: that instead of focusing on the disease pathway, which has resulted in no approved therapies to date, we are focused on replacing the layer of damaged and/or missing RPE cells with the hope that we can potentially address this debilitating disease.

“Our two lead programs target multibillion dollar markets. We are filing for approval for a medical aesthetics product for facial aesthetics and we are expecting game changing data from our ophthalmology product for dry AMD in the coming months. We are looking forward to a data and milestone rich 2018 which will transform BioTime.”- Adi Mohanty

CEOCFO: Did you decide you were going to look at macular degeneration and find a cell to fit that or did you develop a technology and say AMD is a good place to start?

Mr. Mohanty: It is a little of both. We were building the core technology and focusing on the differentiation of different types of cells. As we were working on these cell types, we were able to make some robust RPE cells along with other types of cells. At the same time, we were looking at what application to utilize for the different cell lines we were creating. One of the things about cells that are made in a factory that are transplanted into the body, in a similar fashion to that of organ transplants, is whether or not the body will accept or reject the cells, and whether or not there may be rejection issues. Having said that, the eye is a great place to start because the eye is immune privileged. While it is not completely immune protected, it is immune privileged in the sense that there is not a lot back and forth in the body, the blood and the eye. Therefore, given the big need for a Dry AMD product and the immune privileges of the eye, starting with an RPE cell transplant therapy made a lot of sense. It matched our ability to manufacture it, it matched the need and it matched where this technology was likely to have early success, compared to other locations.

CEOCFO: Where are you with OpRegen® today?

Mr. Mohanty: We have performed years of work, conducting huge numbers of preclinical studies in the lab and animal studies. We have some great data and the early data in animals suggested that we could see the transplanted cells for the life of the animal. We could see that cells survived and proliferated. We could also see that it helped their vision. It was a great data set and we filed this data with the FDA. The FDA liked the data so much that we received a fast track designation. We started human studies a while ago and OpRegen® is in a Phase I/II A clinical study. We finished enrolling the Phase I portion of this study, which included three cohorts and three patients per each cohort. We shared some data last year and will continue to do so when it becomes available. There were signals of biological activity that the cells transplanted were present, alive and growing. These are great indicators and we are encouraged by it. As a reminder, the patients in these first 3 cohorts were at the end of the disease spectrum and legally blind. Further, this study is mainly about the safety of our cell transplant therapy, and to date there have been no related serious adverse events reported. Given the patients extremely poor vision, we do not expect to see a lot of functional data from these patients. The next step in the process is to begin looking at functional data in a less severe patient population. In the coming month or so, we expect to receive approval to proceed to the next step, where we plan to have less severe patients, patients that still have functional eye sight and it's in this patient population where we hope to see functional data. So, the next six months looks exciting. We have the initial proof and now we are hoping to share, later this year, some functional data with these additional patients. Our expectation is to receive DSMB approval of the next phase of this trial later this quarter and immediately begin enrollment of another six to twelve patients. Sometime later this year, probably the second half of 2018, we plan to see functional data from these additional patients. Given there are currently no approved therapies for Dry-AMD, if the functional data from our trial is positive, it will be a game changer for BioTime. So needless to say, we are excited about where we are and are looking forward to the rest of 2018. If we are accepted, we are targeting to present some data at the largest ophthalmology conference in May at ARVO (Association for Research in Vision and Ophthalmology), and then hopefully some good functional data later in the year.

CEOCFO: What else are you working on today?

Mr. Mohanty: We have focused the company on two areas and one is ophthalmology. I tell people that Dry AMD is great, and we will continue progressing, but right behind that we have a couple other products in ophthalmology. For one of them, we have shown some initial animal data where we are making the entire retina. It is like an organoid. In the lab, we have been able to combine RPE cells, photo receptors, and neurons, as a retinoid. If this continues to work, then it does not matter why you are blind because we will be able to just replace the back of your eye, even if you were born blind. This to me is one of the reasons why I say we are leading the revolution and focusing on new ways of addressing diseases. We are pretty excited and so was the NIH, they gave us a big grant last year. We will continue to build on the ophthalmology platform. The other area of focus for us is medical Aesthetics and that came from a technology that we have that no other cell technology company has. One of the biggest challenges in cell therapy is being able to deliver the cells in a manner that will allow them to survive and thrive. As you know, the body sloughs off cells, such as liver cells and skin cells. After the cells slough off, they float around and self-destruct. This is how the body protects itself. So, if you want to deliver new cells you have to attach them because if they are floating around they will eventually die. At BioTime, we have discovered a way to deliver cells, via a hydrogel or an extracellular matrix, that allows them to attach, survive and thrive. Over a few months most of that hydrogel gets absorbed by the body and what is left is a thriving tissue.

CEOCFO: How will this technology be used?

Mr. Mohanty: We intend to use this platform for many different types of cells. We started out with fat based cells because fat extraction is a commonly used procedure. Many use dermal fillers or fat transfers. In the case of a fat transfer, a liposuction is performed, the fat cells are removed and the fat is injected into the face. While fat transfers offer a "natural"

look and feel, fat transfers have a short duration and cost a lot of money. There is a lot of published data that shows that fat drops down to about 50% of the engrafted volume in three to six months. Now if you have gone in and spent about \$8 thousand dollars for this procedure and three to six months later you only have half of what you engrafted, you might be rather disappointed with the results given the cost of the procedure. What we are doing is taking your fat, mixing it with Renevia® and then injecting it into the face. We shared some data from our pivotal trial of patients who suffer from HIV-associated lipoatrophy. This is a pretty extreme patient population, and in those patients, we started with about five cc's in each cheek. At the end of six months, we still had 5 cc's of measured volume in each cheek. We are impressed by this. We have also shown some data at twelve months that shows 70% retention so you could spend \$8 thousand dollars and end up with 50% in three to six months or you could use Renevia and end up at 70% or greater at twelve months. We think this is pretty impressive and with this data we are working towards approval in Europe. The reason we are seeking approval in Europe is because the trial was conducted in Europe. We are getting ready to submit Renevia for CE mark in the next month or so, with approval expected later this year. We believe that Renevia will be much more than just aesthetics product that people use for cosmetic reasons or for facial lipoatrophy. We believe Renevia will have utility well beyond the face; in particular, the hand or the breast as a result of a lumpectomy and the need for reconstructive surgery. We are starting to generate data in the US. The data being generated is from an investigator led trial in non-HIV patients, for aesthetic use and that data will help us with a US trial of Renevia. We also filed with the FDA a request to guide us on what it would take to get approval in the US for anyone who has facial fat loss. We expect to have that meeting with the FDA in the first quarter. Provided we receive a positive response from the meeting with the FDA, we would plan to start the trial later this year. Overall hopefully, approval in Europe, conversation with the FDA, expansion of the label beyond HIV and aesthetic use, and even beyond that, for use in the hand and reconstructive surgery. So, a pretty extensive expansion plan for that product.

CEOCFO: *Do you see partnerships or licensing of any of your technology?*

Mr. Mohanty: I think there are areas, for example in Europe, where there is a country by country market that makes more strategic sense for us at this time to explore having a partner. Certainly Asia, places like South Korea, which per capita is the largest users of these products in the world, is another geographic area we would look for a potential partner. China and South Korea are very interested in what we are doing so we will continue to have these conversations. We think that the market is concentrated in places like the US and we plan handle these markets ourselves. We are open to partnership conversations and we are looking towards partners in Europe and Asia, but we are exploring being able to do it ourselves in places like the US. For example, there are about five thousand plastic surgeons who account for 80% of the procedures in the US, which is a small concentrated market. It would not take a lot of sales reps to call on this small and concentrated market, so certainly we could do something like that ourselves.

CEOCFO: *How do you focus your time as Co-CEO?*

Mr. Mohanty: My job is a lot of fun. I make sure that the strategic direction of the company is headed in the right direction and that everyone is focused on our priorities: clinical progress, simplification and unlocking value for shareholders. I make sure that the strategy is something people are following and then the rest of the time, which is the majority of my time, is spent telling people our story. I think a big thing for me is to let people know what we are working on, because there are a lot of people who do not know our story and do not know what we are trying to do. I think we are doing such exciting wonderful things that more people should know what we are working on.

CEOCFO: *Why pay attention to BioTime right now?*

Mr. Mohanty: We are absolutely leading the way in regenerative medicine, in particular, the area of cell therapies. We are at a stage where we are generating significant data and in the very near term, we are going to have an approved product. Our two lead programs target multibillion dollar markets. We are filing for approval for a medical aesthetics product for facial aesthetics and we are expecting game changing data from our ophthalmology product for dry AMD in the coming months. We are looking forward to a data and milestone rich 2018 which will transform BioTime. Therefore, this is where all those data points will change how the world views and accepts the programs we have. With any success we can add a huge cell therapy pipeline and we could have a large number of programs. These are platform technologies that allow us to do a lot of other things as we get more success.

