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Genprex – Developing Novel Gene Therapies in Cancer with Tumor Suppressor Genes and Diabetes Converting Alpha Cells into Beta Cells to Produce Insulin

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CEOCFO: ***Mr. Confer, Genprex is using gene therapy technology in the areas of cancer and diabetes. What is your approach?***

Mr. Confer: Our team at Genprex is focused on developing novel gene therapies. Historically, our focus has been centered on treatments in cancer and more recently we have expanded to gene therapies to treat diabetes. Our cancer program got started at MD Anderson Cancer Center in Houston. We have been focused on research in collaboration with them since the company was founded, focusing specifically on lung cancer. The research has evolved over the years to look at other types of cancer. Our main focus has been around the use of tumor suppressor genes; these are naturally occurring genes in the human body. What we find is that as cancer develops, these genes get systematically deleted. We are simply reintroducing these tumor suppressor genes back into the body so they can fight cancer the way they were meant to.

As for our diabetes program, diabetes is a global epidemic that has a lot of debilitating factors associated with it including increased risk for heart disease and kidney disease and other ailments. The history of diabetes treatments has not fundamentally changed away from insulin. Insulin was created more than 100 years ago and is still the primary treatment in diabetic patients. While there have been treatments such as synthetic insulin, fast-acting insulin, extended delay insulin, and the usage of pumps and monitoring to assist in the maintenance of the disease, there still has not been a fundamentally disruptive shift in the treatment modality for diabetes. We have a novel gene therapy that we believe could change the course of this disease for many diabetic patients.

CEOCFO: ***Is there a particular synergy between diabetes and oncology in the gene therapy arena or are they just two important targets that you decided to focus on?***

Mr. Confer: Beyond the internal synergies we have developed from our Genprex team managing both programs, there are not necessarily any particular synergies between our diabetes and oncology programs. They happen to be specifically targeted focuses. The oncology program came out of MD Anderson, and our researcher there, Dr. Jack Roth, has been studying lung cancer his entire career. He has more than 1,000 publications to his name. MD Anderson is considered one

of the top cancer institutions in the world. The oncology program was conceived through that research. We deliver our tumor suppressor genes with a non-viral lipid nanoparticle similar to how the COVID-19 vaccine is delivered using a non-viral lipid nanoparticle. We find it is a friendly and safe way to administer our treatment to human patients and the safety profile is strong for us with limited side effects and toxicity.

Our diabetes program is a bit different; we use a viral-based delivery mechanism. However, we do it in a way where it is provided through endoscopic procedure to allow us to have that treatment go directly into the pancreas and the pancreas is the main organ that is responsible for producing insulin and maintaining blood sugar in the body. We can deliver our therapy directly to the pancreas. This is also different from the oncology program because our oncology program is an infusion that is given systemically and can travel throughout the body and attach to cancer cells at a rate of about 30x more than normal cells. Both the delivery mechanism and the treatment method are just different.

CEOCFO: ***On the oncology part, you recently stopped the Acclaim-2 trial and made some changes in your Acclaim-1 clinical trial. Why?***
Mr. Confer: These were two important changes made purely from a business decision point of view and not for any reason related to the technology. The data supports the Acclaim-2 clinical trial that we had initiated. In Acclaim-2, our drug Reqorsa® Gene Therapy (quaratusugene ozeplasmid), was being used in combination with Merck's drug Keytruda®, which is one of the largest-selling cancer drugs in the world, and it is used in several different cancer types. The issue we were seeing primarily is that several pharmaceutical companies have clinical trials designed in combination with Keytruda as well, just because it is such a well-known drug, and we were part of that mix. There are hundreds of lung cancer trials that we are essentially competing with to get patients into our trials, and, as a result, we saw slower than expected enrollment. Therefore, it was a business decision to cut that clinical trial. We could certainly come back to that trial in the future if we wanted to. We have an FDA Fast Track Designation associated with that clinical trial patient population, so there is certainly validation of it being an approach that the FDA thought had potential.

"One thing we are excited about – as we just recently announced -- is our plan to launch a spin out of our diabetes program into a wholly-owned subsidiary of Genprex. We believe this will allow us to explore potential partnerships with those entities solely focused on the diabetes program and find the right funding, partners, and collaborators that could drive these programs forward, which is important to us in terms of getting these innovative drugs to patients faster and to creating value for our stakeholders." Ryan M. Confer, MS, President, CEO & CFO

In the Acclaim-1 clinical trial, REQORSA is being used in combination with a drug called Tagrisso®, a registered trademark of AstraZeneca, which is an EGFR inhibitor, for a certain subset of non-small cell lung cancer patients. We had two different patient arms. One had previously received Tagrisso and another patient group that had previously received Tagrisso plus chemotherapy. That latter group, of Tagrisso plus chemotherapy, is just a more difficult group of patients to treat. It is a more difficult bar to hit from an efficacy standpoint. We made the business decision there to cut that arm of the trial, just to save on costs. Those were business decisions, and we still feel confident that the technology is fully sound in each one of those clinical settings.

CEOCFO: ***Would you tell us about your program analyzing biomarkers in oncology?***
Mr. Confer: This is an exciting area. We have continued to do research with MD Anderson for a long number of years. One of the areas that we have been focusing on recently is identifying different biomarkers, and it may allow us to identify certain patient population subsets that could have the most benefit from our drug. As further illustrated and explained in our corporate slide presentation, you can see data on how some patients benefit more than other patients in response to our drug.

In our Acclaim-1 clinical trial for example, we have had a few patients that have taken our REQORSA gene therapy in combination with Tagrisso, and their disease has unfortunately progressed after numerous cycles. However, we have other patients in our Acclaim-1 clinical trial that continue to take our REQORSA gene therapy in combination with Tagrisso, and they have stable disease and have had shrinkage in tumors of more than 30% and their disease is not progressing. One of these patients, in particular, has now been on our drug for more than two years without disease progression, which is significant in late-stage non-small cell lung cancer.

What we are trying to get at with our biomarker work is understanding if there are key differences in certain patients that will allow them respond very well or if there are patients that may not respond to our drug. That will allow us to fine-tune our trials to be able to use our drug most effectively based on the patient.

CEOCFO: ***Where are you today in the diabetes program? Does the popularity of Ozempic and similar treatments have an effect on interest in other diabetes treatments?***
Mr. Confer: The technologies that have come out to control insulin in Type-2 diabetes are also controlling weight loss. This has been fantastic for the industry, and it is great to see that we have those new treatments. Unfortunately, there is still a significant unmet medical need in the diabetes space. There are two reasons why and it happens to be with both Type-1 and Type-2 diabetes. Type-1 diabetes is an autoimmune condition in which the body's immune system attacks the beta cells in the pancreas that are responsible for producing insulin. Those beta cells are attacked by the immune system and die out. As a result, the body cannot produce insulin on its own. The body requires insulin to survive. These new treatments related to weight loss have no impact on this autoimmune disease, nor do they have the ability to reproduce beta cells to produce more insulin. Consequently, they have no role in the treatment of Type-1 diabetic patients.

Type-2 diabetes is different in that the beta cells that are producing insulin have essentially just been overworked for such a long time that they no longer function and produce insulin as effectively as they once did. These patients might produce insulin better than others. There is a reason for the delayed reaction or fast-acting glucose and a need for things like insulin pumps or monitoring devices so people understand how their diabetes is affecting them personally. However, even with the new drugs that impact weight loss, they are still not completely restoring the functionality of the beta cells that they originally had, and there is still a significant need to fix that underlying issue.

CEOCFO: ***Do you see partnerships or collaborations ahead for Genprex; what do you see with both of the programs moving forward?***
Mr. Confer: Over the last year, we have put a significant amount of time and effort into getting the word out for both our oncology and diabetes gene therapy programs and have been speaking with several potential collaborators and partners in both spaces. Unless we are talking to big pharma, who may have diversified interests in oncology and diabetes where there could be interest in both programs, typically, potential collaborators have an interest in one area over the other. In oncology, the work we are doing with tumor suppressor genes is unique. Over the past ten years, there have been several drugs that have come to market in oncology that have made a big impact on patient treatment paradigms. So, it's not surprising that we continue to see a lot of deals being done after Phase 2 efficacy data is shown with oncology programs.

Diabetes is a bit different. For example, Vertex Pharmaceuticals started acquiring various early-stage disruptive technologies in the diabetes space, and these technologies specifically worked by converting stem cells into new beta cells usually in the lab in order to produce insulin. These beta cells were then delivered back into the patients using an implantable device. Vertex's very early-stage company acquisition has resulted in increased M&A activity from the three insulin manufacturers in the U.S. market: Eli Lilly, Novo Nordisk, and Sanofi. We have seen a lot more interest from these three companies in much earlier stages of the R&D lifecycle at preclinical levels even when you are talking about doing animal studies. Consequently, we have seen a lot more interest in early-stage diabetes programs, which is exactly where we are with our preclinical trials in our diabetes program.

One thing we are excited about – as we just recently announced -- is our plan to launch a spin out of our diabetes program into a wholly-owned subsidiary of Genprex. We believe this will allow us to explore potential partnerships with those entities solely focused on the diabetes program and find the right funding, partners, and collaborators that could drive these programs forward, which is important to us in terms of getting these innovative drugs to patients faster and to creating value for our stakeholders. We do not want to reinvent the wheel. We believe we can leverage the expertise of other companies -- whether it's their manufacturing capabilities or their economies of scale -- to help take our programs to the next level.

CEOCFO: ***Do both the medical and investment community understand the potential value of gene therapy for diabetes or is it fairly new?***
Mr. Confer: I think gene therapy has evolved quite a bit over the last decade, and it certainly is a lot better understood and getting more attention now than ever before. Diabetes has received more interest, at least with the M&A activity that

has been more focused on the stem cell-based approach over the last five years as I noted earlier with the original Vertex transactions. While not entirely gene therapy-focused, they are moving in the direction of disruptive technologies. I think gene therapy is the next forefront beyond the stem cell-based approaches.

We know of other companies that are looking at gene therapy approaches too that have raised considerable amounts of money, and that capital has come from large institutional investment funds as well as large pharmaceutical companies. It is an emerging area that hopefully will get more and more attention. There is a competitive advantage to what we are attempting to do with diabetes. Unlike the stem cell-based approaches that require some type of implantable device, which require maintenance and additional stem cells, our approach is through an endoscopic procedure, where we deliver the gene therapy directly to the pancreas. The goal of our diabetes gene therapy is to convert alpha cells, the cells that regulate glucagon or blood sugar levels in the body, into beta cells that can produce insulin. We call them "beta-like" cells because they are not quite beta cells and they can evade the immune response to some degree. We are working to further refine this technology, and we believe it will be a treatment approach that can provide long-term glucose stabilization for the patient, which would represent a considerable improvement over an implantable device or the daily finger pricks for monitoring insulin levels and the need for insulin shots. That is the future we hope to provide for diabetic patients.

CEOCFO: ***With so much going on at Genprex, what might be overlooked that people should recognize?***
Mr. Confer: On the diabetes side of things, what we are doing is in my opinion is disruptive compared to where the market is at currently, and I think that is why it makes the diabetes program so exciting and people are so interested in it. On the oncology side of things, I would say the typical investor likely overlooks the safety profile of our drug, REQORSA.

Because we are using a non-viral approach of lipid nanoparticles in oncology, what we have seen in our clinical trials tested in more than 60 patients, is their side-effect profiles are limited to a post-infusion syndrome like fever, chills, and muscle aches, for a limited period. That is something that can be controlled with over-the-counter drugs. That is a very favorable safety profile for a cancer drug where other drugs, like chemotherapy, can destroy the body and your muscles. The immunotherapy drugs out there can ramp up the immune system too much and that can cause all sorts of issues in the human body.

We believe our drug REQORSA is a friendly option for patients. The fact that some of our patients can continue their daily lives, work and do their physical activities, we think that is a game-changer in how people manage cancer therapy. I think that is just one area in the oncology program that is overlooked. You want to try to cure the disease and that is tricky because cancer affects everybody differently, but we are moving toward an area of personalized medicine where combinations of various therapies are very important. We are striving to do that with each of our Acclaim clinical trials but I think it is the safety element of the drug that is such an important factor that people often overlook.