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New Stress Response Modulation Drug Showing Promise in the Treatment of Addiction

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"Over the last decade we have seen a significant shift in the understanding that addiction is a mental health disorder, a chronic disease that needs to be treated the same way we treat cardiovascular disease or diabetes... For all addictions, medical care and productivity losses exceed half a trillion dollars per year in the U.S. alone, so there is opportunity to make a significant positive impact on society and the economy and while building a successful biopharmaceutical business."- Robert B. Linke

CEOCFO: ***Mr. Linke, what is the concept behind Embera NeuroTherapeutics?***
Mr. Linke: Embera is a specialty pharma company focused on developing new treatments for a broad range of addictions. The company's products are based on technology that was licensed from Louisiana State University's medical school in Shreveport, Louisiana. The founding scientist and inventor, Dr. Nicholas Goeders, is a professor at the University. His entire career has focused on searching for treatments that could address the unmet needs in addiction. His concept and our technology is based on modulating the stress response that drives craving and relapse associated with addiction.

CEOCFO: ***How does it work?***
Mr. Linke: Our drug, EMB-001, is being developed to address stress and its role in addiction. For example; you are a smoker. You quit last week. You are in an environment where you are accustomed to stepping out to have a cigarette, say after dinner. When you do not have that cigarette your brain says, "Where is my nicotine reward after my dinner?" When the brain does not receive its nicotine reward because you quit, your stress response system is activated and you begin to seek nicotine. What EMB-001 is designed to do is modulate that stress response, which reduces the underlying craving causing you to seek the drug, nicotine in this case, and to help you avoid relapse.

CEOCFO: ***Would this be for someone that has already stopped the drug for a while or would it be at the beginning when they are trying to stop? At what point do you come in to play?***
Mr. Linke: We anticipate that EMB-001 would be utilized in a manner similar to other approved addiction treatments. Studies have shown that

the best results treating addictions are achieved taking a three-pronged approach to treatment. When you make the decision that you want to quit, you would 1.) see your doctor to develop a treatment plan, 2.) receive a pharmaceutical treatment that can help you quit and remain abstinent and 3.) undergo counseling as part of the treatment plan.

CEOCFO: ***What is happening in the brain or the body while someone is using your drug?***
Mr. Linke: That is a very good question, Lynn. If you think about the brain, it is a very powerful organ. The reward system in the brain which drives us to seek food when we are hungry as well as to reproduce are all very powerful drives. Addiction starts when you stimulate the brain's reward system with a drug, and after repeated exposures, your brain comes to expect that reward. It is when you deny the brain that reward that the brain responds, activating the body's stress response system to pursue the reward it seeks in a similar way to how the brain signals the body to seek food by making you feel hungry. With respect to addiction, when that stress response system is activated to seek your drug, cortisol, which is part of your fight-or-flight mechanism, increases. The natural braking mechanism in the brain, the GABA system, gets downregulated. EMB-001, a low-dose combination of two previously FDA approved drugs, acts by modulating the cortisol response and the GABA system, bringing that stress response back into balance so that the patient does not feel the craving that could cause relapse.

CEOCFO: ***You suggested that counseling should go along with it. How much is physical, how much is psychological, do we know and does it matter?***
Mr. Linke: They are both very, very important parts of overcoming addiction. The addiction field has come to accept both therapy and medication assisted therapy (MAT; like suboxone, varenicline, etc.) as important tools for the millions who suffer from addictions. The brain suffering from addiction has been altered to a point where it is expecting that reward both physically and psychologically. What treatment is trying to do is return the brain to a more normal state, where the individual can eventually maintain abstinence on their own without drug therapy and without counseling, but this is not an easy task and takes time.

CEOCFO: ***Where are you right now in the development process?***
Mr. Linke: We are now testing EMB-001 in clinical trials. Last year we completed a Phase 1 safety and pharmacokinetics study where we found that the drug was well tolerated and the pharmacokinetics, meaning how the drug is metabolized in the blood stream, support twice daily dosing of our drug. This has now allowed us to proceed into the next phase of clinical testing, Phase 1b and Phase 2 clinical studies. We have two indications of EMB-001 in development; one for cocaine addiction and the other for smoking cessation. For the cocaine addiction indication, we expect to complete a cocaine interaction study in early 2017. This is a study, called a drug-drug interaction study, that is required by the FDA to demonstrate that if a patient were to simultaneously take our drug, EMB-001 while using cocaine, to which they are still addicted, there would be no dangerous interactions between cocaine and EMB-001. The next study in smoking cessation will be a Phase 1b/2a study in which we will test the efficacy of EMB-001 in a smoking population, and the next study in cocaine addiction will be a Phase 2 study evaluating the efficacy of EMB-001 in a population of cocaine addicts.

CEOCFO: ***What have you found so far that might have surprised you, might have led you in one direction more than another? What have you seen as you have started to work with the drug?***
Mr. Linke: The drug development process is preceded by research in animal models that might provide some evidence of efficacy. In the case of drugs for various addictions there is a standard preclinical research model with rats that are addicted to the drug of interest. They are trained to get their drug by pressing a lever. You compare a group of rats treated with your investigational drug to a group of untreated rats and see if there is a difference in the number of times they press the lever. The surprising result is that we saw significant reductions in this self-administration model in three different addictions, cocaine, nicotine and methamphetamine, after treatment with EMB-001, providing initial validation of the general mechanism of our drug. It was those studies that led to our ongoing clinical development program that began with a small pilot study in cocaine dependent subjects and progressed through a Phase 1 safety study and the Phase 1b drug-drug interaction study that is nearing completion. We are now preparing for Phase 2, the second of the three phases of clinical testing required for submission to the FDA for review and potential approval of the drug.

CEOCFO: ***Is it accepted in the medical community that the stress factor and that what you are attempting to moderate or overcome is involved or is it something that most people do not agree with yet?***
Mr. Linke: That is another very good question, Lynn. We have known for decades that stress plays an important role in addiction, but addressing the role of stress is a new approach to addiction *treatment*. Looking at approved treatments, the majority either substitute what you are addicted to; for example, nicotine replacement therapy, where instead of inhaling nicotine with carcinogenic smoke, you chew your nicotine with gum or a lozenge or you wear a patch. Suboxone®, the treatment for opioid dependence, is also substitution therapy in which the patient is provided with a safer form of an opioid in place of oxycontin or heroin to manage the addiction. Other approved treatments utilize the approach of blocking the effect of the drug; for example, Alkermes has a drug called Vivitrol® that is approved for alcohol dependence and, more recently, opioid dependence. With this approach patients take the drug and if they were to use alcohol, for example, the drug blocks the euphoric affect. In contrast, Embera's approach to modulate stress response is a very different path to treat the disease and is the first company to advance this approach into clinical testing.

CEOCFO: ***As you explain it, it makes a great deal of sense. Why has it been overlooked?***
Mr. Linke: Historically, treatment of addictions has not been a significant focus in the pharmaceutical industry; nor has the combination-drug approach. Thanks to Dr. Goeders, who has devoted much of his 30-year career to exploring this mechanism and its potential as a new approach to treating addiction, we have a product that is advancing through clinical testing.

CEOCFO: ***How are you funded?***
Mr. Linke: We are a development stage company financed primarily by two sources: private investors and grants from the National Institutes of Health, specifically the National Institute on Drug Abuse (NIDA). Our first $3.9 million grant with Dr. Goeders and Louisiana State University Health Sciences Center -Shreveport funded the majority of our preclinical work

required by the FDA to begin clinical trials. This past summer Embera was awarded an $11 million grant from NIDA that will fund the majority of Phase 1b and Phase 2 clinical trial costs for the EMB-001 cocaine addiction product. With respect to funding from private investors these include two venture capital funds, a family office and angel groups. We are raising a Series B financing that will fund the company through the Phase 2 testing process for EMB-001's indications in clinical development.

CEOCFO: ***You have a long history in the field. What do you understand about testing, development, and ultimately about commercialization that perhaps less experienced people do not recognize?***
Mr. Linke: We have been very fortunate to recruit a very experienced team of drug developers at Embera. If you look at our senior management team comprised of 5 people we have over one hundred years of drug development and commercialization experience with both large and small pharma companies. The Embera team works with leading drug developers throughout the US to develop and manufacture EMB-001, and to conduct the specific preclinical and clinical studies to pursue approval for our drug with the FDA. We also have dedicated advisory boards made up of some of the top academic and pharmaceutical drug development experts in addiction. Thanks to the Embera team and our development partners, EMB-001 has advanced to the next stage of clinical testing with the experience and resources in place to execute a plan to advance EMB-001 through clinical testing and submission to the FDA for review.

CEOCFO: ***What is different about working in the addiction arena?***
Mr. Linke: I have been in the healthcare field and biopharmaceutical field for thirty years, developing and commercializing drugs. One of the reasons I am here is because we are trying to find answers for problems that do not have adequate treatments for patients. Addiction has historically been an overlooked area unlike cardiovascular disease or cancer. This is the result of a historical stigma associated with addiction, with many people questioning whether addiction is really a disease or a character flaw. Over the last decade we have seen a significant shift in the understanding that addiction is a mental health disorder, a chronic disease that needs to be treated the same way we treat cardiovascular disease or diabetes. I began my work in the addiction field seven years ago. Since that time, there has been a big change in people's understanding of addiction, particularly lay people's understanding. Unfortunately, it took the opioid crisis to cause many people to take a different look at addiction, given it has touched people from every walk of life, including our colleagues, our friends, and our children. As a result, much more attention is being paid to the area and we are seeing a shift in the attitudes towards addiction and a greater understanding of the need to treat the disease by the general public. Because of the historical lack of attention to the treatment aspect of addictions, there is enormous unmet medical need and cost to society. The direct cost of medical care due to smoking alone is $132B/year in the United States. For all addictions, medical care and productivity losses exceed half a trillion dollars per year in the U.S. alone, so there is opportunity to make a significant positive impact on society and the economy and while building a successful biopharmaceutical business.

CEOCFO: ***There are certainly many people working on new ideas in healthcare. Why is Embera NeuroTherapeutics important and unique?***

Mr. Linke: We are working on a new way to address big medical problems at Embera. Cocaine addiction is probably the best example. The primary reason it is our lead development program is that there are *no* approved treatments for cocaine dependence. Today the only option for patients suffering from cocaine addiction is a 30-90 day rehabilitation program followed by a twelve-step program, which historically have been shown to have very limited effectiveness. We have over one million people in the United States addicted to cocaine. Seven hundred and fifty thousand of those people seek treatment every year, but there are no approved pharmaceutical treatments today to help these people. Nicotine addiction, or smoking, is the most significant addiction, with over one billion smokers worldwide. In the U.S. forty six million people still smoke, and half of them try to quit every year. However, even though there are three approved treatments available, only twelve percent successfully quit and are abstinent one year later. We need better treatments to help these people quit for good.

CEOCFO: ***What might someone miss when they first take a look at Embera NeuroTherapeutics?***

Mr. Linke: Again, I think it is the fact that we work in the addiction field, an area that has not experienced significant drug development historically. As a result, we do not attract the attention a cancer, cardiovascular, or Alzheimer's company might. However, the needs here are just as great and impact greater numbers of people; that is what people might overlook. We are a small company, but one with a very experienced management team with a promising technology and product. If we can show that it is effective in future clinical studies that we are moving forward, we could bring a new approach to treating addiction to the world.