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Developing a Novel Preeclampsia Therapy, Advanced Prenatal Therapeutics, Inc. is Using a Device Approach with an Apheresis Column That Filters Out Harmful Factors From the Mother's Blood

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Executive Bio:
Dr. James Smith, Ph.D.
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Dr. Smith has over twenty years of experience in regulatory affairs and the development of novel technologies from concept through commercialization. He is experienced in all aspects of regulatory affairs, quality and data management systems, supervision of R&D, development of new product specifications, and with evaluating and registering medical drug and device product lines. Dr. Smith obtained his Ph.D. in Pharmacology and Toxicology from the University of California, Irvine.

"Our novel preeclampsia therapy will not only treat a woman in crisis; it may also provide a mother with the highest quality time that she will ever have with her child."- Dr. James Smith, Ph.D.

CEOCFO: *Dr. Smith, what is the focus at Advanced Prenatal Therapeutics, APT, today?*
Dr. Smith: We are continuing to develop one of the first direct treatments for preeclampsia, which is a disease that affects about five to eight percent of pregnant women in the US, and even more women outside the US. Preeclampsia is one of the most significant issues in women's healthcare in that it is a leading cause of maternal death, fetal death, and fetal prematurity. In fact, nearly 40% of medically necessary preterm deliveries are due to preeclampsia. Our hope is to create a therapy that will allow doctors to extend pregnancy, thereby helping to avoid life-long complications with the baby like blindness, deafness, asthma, and cerebral palsy that are associated with preterm birth.

CEOCFO: *What is preeclampsia?*
Dr. Smith: Preeclampsia is a very complex disorder that affects pregnant women. It is basically a mis-development of the pregnancy that

is marked by high blood pressure, proteinuria (which is protein in the urine), headaches, dizziness, blurred vision, and potential for seizure. In a small percentage of patients, preeclampsia can also lead to seizures and death. The causes of preeclampsia are still unknown, but we are exploring different therapeutic targets that are likely to contribute to disease progression and the dysfunction of the various body systems involved in the disease.

CEOCFO: ***What have you created so far?***
Dr. Smith: We have been developing a device approach to the treatment or preeclampsia, where we use an apheresis column to physically filter out factors from the mother's blood that may be causing or contributing to the disorder. By doing so, we believe that we will be able to interfere with the progression of the disease and even maybe reverse the effects of the patient's critical state, allowing doctors to safely extend the pregnancy. We are excited to have completed a commercial prototype of our novel device that we hope to further evaluate for clinical use.

Our approach is novel in a couple of ways. First of all, almost all preeclampsia treatment today is palliative in nature. This means that doctors are not currently able to treat the underlying disease, but simply manage the symptoms as best they can. Preeclampsia is often managed by giving blood pressure and anti-seizure medications as long as possible. Doctors may also administer steroids to help advance the baby's lung development before they have to intervene and prematurely deliver the baby. All of these approaches are palliative in nature. Our approach is a direct therapeutic intervention for the underlying disease.

The other thing that makes us novel is that most solutions that have been proposed in the past have been pharmaceutical or nutraceutical in nature, where some factor or medication is added to the mother's system in the hopes that it will interfere with the disease or manage the symptoms. Our approach is to selectively remove factors that are harmful to the pregnancy.

CEOCFO: ***How did the idea develop that this might be an approach?***
Dr. Smith: Back in 2005 my father and I (the co-founders of the company) were looking at a range of diseases that might be able to be treated by focusing on circulating factors in the blood. We saw that there was quite a bit of literature about sFlt-1, a soluble receptor for an important growth hormone that helps with the development of blood vessels in the placenta, and a potential mediator of the progression of preeclampsia.

We initially thought that it could be a therapeutic target for a new drug therapy, in line with work we were doing for other diseases. However, as we discussed more, we concluded that a drug was probably not a viable or desirable approach during pregnancy. Then we recognized that, since the receptor was soluble, meaning it is free in the circulation, it might be something that could be removed in a targeted fashion using apheresis (a blood filtering process, much like dialysis). That is what led us to develop the idea of using "targeted apheresis", as we call it, to remove sFlt-1 from the mother's blood. Since then, we have also begun to recognize that the same approach could be used to remove many other harmful factors from the blood that may be involved in disease progression. Therefore, as our knowledge of preeclampsia grows, we

can extend the number of potential therapeutic targets in our product pipeline.

CEOCFO: ***Would you tell us about your recent FDA Breakthrough Device Designation?***
Dr. Smith: For quite some time, we have been developing binding agents for various therapeutic targets and making sure that we can incorporate them into our platform device, which is basically an extra-corporal column compatible with standard apheresis equipment. Over the last couple of years, we focused our efforts on research, development, prototype exploration, and proof of concept. We are now ready to make a formal run at the commercialization process. This phase of development will require formal non-clinical testing according to certain regulations intended to ensure safety, quality, and efficacy; and clinical studies to get direct evidence to show that our device provides a clinical benefit that outweighs the risk of using the device. We will then pursue market approval from regulatory agencies like the FDA to have the approval to sell the device.

The challenge for any truly novel technology is the lack of a road map to follow. When you are proposing something that has never been done before it presents a big regulatory risk because it can be hard to know exactly what studies and data are required and what data will best assure the FDA that you have a safe and effective device. In our case, we are talking about a situation where we are treating pregnant woman during a time where her system is highly dynamic and it could be very challenging to develop good data. So we are approaching it with a lot of conservativeness and a lot of respect for the patient condition and the risks associated with our treatment.

The breakthrough device designation is a program that the FDA implemented in recent years to help make sure that companies with novel treatments for a life-threatening disease, and that may represent an enhancement over current approaches, can reach the market as efficiently as possible. Very importantly, the FDA is not providing a quicker or easier path to market. Instead, what they are trying to do is make sure that companies can work with them in a highly interactive manner to provide regulatory clarity. This includes support from their dedicated, multidisciplinary team to ensure that efficient nonclinical and clinical testing plans are possible.
Having access to that kind of support enables what I call “first-pass success” for our regulatory filings. When we approach the FDA we expect to be able to efficiently meet all their requirements because they have been fully discussed in advance. The FDA breakthrough device designation also gives us something called expedited review. That means that the FDA prioritizes the review of our application when they receive it, which can dramatically shorten the overall review time to reach a final decision. The Breakthrough Device Designation doesn’t guarantee approval, but it certainly expedites the development and regulatory review processes, and that is the goal.

CEOCFO: ***How does it work? How often would a woman have the treatment? What would be the process in using this device?***
Dr. Smith: That is a very good question! We expect that our initial target population will be somewhere between twenty-five to thirty-two weeks into their pregnancy. The goal is to mitigate the development of preeclampsia and its clinical symptoms, such as high blood pressure and

organ damage, or any other risk factors that force a clinician to intervene. We contemplate that you may be able to do one or more treatments as needed until the baby is delivered at full term. While one treatment may be enough, the patient may need a treatment every few days, or maybe every week or potentially every couple of weeks. The idea is that the apheresis process can be repeated in order to maintain the pregnancy for an extended period of time; maybe a few weeks, maybe a month or more. We will not know until we do clinical testing. However, there is preliminary evidence out there, from other teams using a non-specific column, that an apheresis process can successfully extended pregnancy by as much as fifteen to twenty days. Therefore, we are hopeful that our targeted device will have a much more profound effect.

CEOCFO: ***Does it hurt?***
Dr. Smith: The apheresis process is similar to dialysis or donating blood or platelets. The patient's blood is drawn from a vein in the arm, processed through our device, and then returned to the patient through the other arm. So there are a couple of needle sticks to put in the IV catheters, which is mildly uncomfortable but very tolerable. The mild discomfort, along with the modest anxiety or apprehension that would be normal to experience during a treatment, is well-worth enduring for the potential benefit of avoiding loss of life and extending pregnancy, which would reduce the need for neonatal intensive care units for an extended period of time, or potentially at all.

CEOCFO: ***Is there a potential downside? Would this be appropriate for every patient?***
Dr. Smith: There are always risks associated with any medical procedure and apheresis is no exception. Therefore, it is going to be important for doctors and patients to weigh the risks with the potential benefits. The purpose of our planned clinical work is to help identify and quantify what those risks are, what the likelihood of them are, and be able to allow comparison to potential benefits. Obviously, the less risk you see, the more safe the device, compared to the more dramatic the benefit, the more obvious that consideration becomes. Not every patient with preeclampsia will be amenable to the treatment. We will have to identify patients that exhibit a high level of the specific factor or factors that we are removing. Where you can identify that a patient has an excessively high level of a harmful material, it does make good sense to remove it.

CEOCFO: ***What are your next steps?***
Dr. Smith: We are in the process of completing our nonclinical development. Again, we are hoping to work with the FDA in order to make sure we do that with a high level of compliance and quality. We are hoping to be able to enter into initial clinical studies by the end of the year and we are excited to transition from kind of a virtual company into an emergent player in the industry.

CEOCFO: ***Are you seeking financing, partnerships or investment? Where are you or where will you be by the end of the year?***
Dr. Smith: We have worked on a very modest amount of funding, which demonstrates how much we can accomplish on very thin resources! We are proud to say that we have been very efficient with our resources and that we plan to continue to do so. As with any developing company, we are always exploring our network for financial, administrative, and intellectual support in order to effectively execute our strategic plans and

ultimately commercialize our device. We are interested in having conversations with any groups with an interest in technologies that address women's health or infant health and that are aligned with APT's mission of providing new and improved healthcare options in the perinatal space. We truly believe that APT's technology has potential to very positively impact an unmet need, significantly reduce maternal risks, and improve fetal outcomes, as well as dramatically reduce the very high healthcare costs associated with preterm births.

CEOCFO: ***What is the interest from the investment community? Is it a topic that people think is important or getting little attention?***
Dr. Smith: We are developing a solution for a global issue in women's health that is also an unmet need. For investors, this means that they have the opportunity to support the commercialization of a life-saving product for a large patient base that has virtually zero competition. Investors are naturally excited about such opportunities, but they are also understandably hesitant about any project that deals with a disorder of pregnancy and the implications for risk and clinical testing. Since there are no other commercialized direct treatments for preeclampsia, we aren't able to tell our potential supporters "This will work because look at the last group that did it". This is one of the reasons that the Breakthrough Device Designation was so exciting for us. It helps that the FDA is committed to working closely with us to provide a well-defined road map, including a clear clinical study strategy, and to ultimately help us bring our product to the patients that need it most.

CEOCFO: ***How do you stay positive when it is such a long process just to get where you are today?***
Dr. Smith: We are trying to make an impact on one of the most significant issues in women's health. At the end of the day, it is all about helping mothers and babies. Our novel preeclampsia therapy will not only treat a woman in crisis; it may also provide a mother with the highest quality time that she will ever have with her child. Helping the baby to be born on time means higher birth weight, better lung function, better immune function, less congenital defects, and less risk of mortality right from the get-go -- and that is exciting! If you are going to work in medical devices and hope to make an impact, I can't think of a better place to make a bigger or more significant one! That is what drives us.