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Todd Krueger discusses AOBiome's positive results from its Phase 2b trial for both Pruritus (Itch) and Appearance of Atopic Dermatitis (Eczema)

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CEOCFO: ***Mr. Krueger, one of the first things that I see on the AOBiome Therapeutics, Inc site is, "An evolutionary approach to restoring health." How are you going about that? What is the approach?***
Mr. Krueger: Our approach is to reintroduce a key bacteria that we have evolved with, that we no longer have as part of the population of our microbiome. Anywhere on the planet that you find ammonia, you will find Ammonia Oxidizing Bacteria (AOB), it is part of the nitrogen cycle, the same way you think about trees and oxygen. The issue is that this particular type of bacteria, which is a soil bacteria, is very sensitive to soap and preservatives. The only humans that have been found to naturally have this bacteria on their skin live in environments close to nature, such as tribes in the Amazon. You and I take showers in the morning, use soaps and other skin care products, and we live in a house without dirt.

Over time this class of bacteria has been stripped out of skin and out of our microbiome. This leaves our skin with no way to process the ammonia that our body naturally secretes. This is a problem because this ammonia is an irritant to the skin. More importantly we believe that the byproducts of particular bacteria are very helpful. It produces both nitric oxide and nitrite. Nitric oxide being a vasodilator and anti-inflammatory and nitrite being an anti-infective. More importantly it actually has a relationship with your immune system, the bacteria down regulate interleukins 4, 5, 13 & 31, which are typical targets of drugs associated with atopic dermatitis, itch, acne, rosacea, and a longer list of things where you essentially have an inflammatory response that your body should not be having.

CEOCFO: ***How did you know to look for this? How did you know what was missing?***
Mr. Krueger: The founder of this company, a gentleman named David Whitlock, was actually out on a date on a farm and saw a horse roll around in the dirt. The woman asked, "Why do horses roll around in the dirt," and David said, "Well, it must be mosquitoes." The woman said, "Well, it is March, that is probably not the case." Therefore, David took some time alone to think about this question, which was a good one. He was an MIT chemist, and he was able to mix farm dirt and artificial sweat together, and left it in a jar for 3 months. This particular class of bacteria proliferated, because in sweat, there is a lot of ammonia. He isolated the specific bacteria and then he actually cultured it on himself and stopped showering just to preserve the bacteria to live a more natural life.

We believe, although I cannot attest to it, that there were many different varieties of ammonia oxidizing bacteria on David's skin, and this particular bacteria out competed all of the other bacteria in this class. Due to the known mechanism of action of AOB, there were clear medical indications that could create potential benefit. That was the basis for the beginning of the company.

CEOCFO: ***Where are you today in going from theory to, "We are sure it is good?"***
Mr. Krueger: We have done extensive R&D, which has guided us in areas such as dosage, formulation, delivery, regimen and manufacturing. We think of our drug, which is named B244, as more of a topical biologic than a microbiome drug. It delivers a very well understood set of things, and we have then taken that information and that knowledge and entered the clinic.

We view B244 as an important topical biologic addressing issues ranging from inflammation to inappropriate immune response. We have run a number of FDA Phase 2 trials with positive and promising results in indications such as Eczema, Pruritus, Acne & Rosacea. Our most recent Phase 2B trial had positive results in both appearance and itch of atopic dermatitis. We are now in the process of going to the FDA for an end of Phase 2 meeting, with an eye on starting a Phase 3 trial, somewhere in the end of this year or beginning of next.

CEOCFO: ***How does what you have learned so far stack up against current treatments?***
Mr. Krueger: Current treatments for Atopic Dermatitis, and there are quite a few, are mostly for moderate to severe cases. They do not work particularly well for itch, in some cases actually cause itch, and have all sorts of adverse events associated with them. For example, injections of DUPIXENT® or JAK inhibitors, which are some of the primary products that are available at this point in time, have black box warnings, which basically say that it has a high risk of side effects that, generally speaking, you do not want. Some also take a long time to work. Most of these drugs are not able to be prescribed for children, or even the elderly. The elderly, in some cases, may just fail out because they have too many risk factors to take the drug in the first place.

"What I think sets us apart is that we have a scalable drug platform that can be applied to across multiple indications, that leverages the immune response across multiple dermatological opportunities. It is first line therapy, because of its safety and ease of delivery. It can be used in children and the elderly, and this is a massive untapped market." Todd Krueger

We see our topical biologic B244 as first line therapy. It has virtually no safety issues whatsoever, as the body expects it be on the skin to begin with. We have run over 1,500 patients in clinical trials, and we have yet to have a serious adverse event. Generally speaking, the adverse event profile of B244 is that of the placebo, which in this case, is just salt water without our drug. Therefore, we see this as being a very safe, offering a quick response to treat patients before they need to essentially enroll in something more drastic.

CEOCFO: ***Why do children, as indicated on your site, have a greater occurrence of atopic dermatitis than adults?***
Mr. Krueger: That is a great question. The causes of Atopic Dermatitis are not well understood. High levels of *Staph aureus* on the skin, have been shown to be correlative, not causative of the disease. Children and adults have different immune systems and therefore respond differently over time. Children do not get diseases that show up later in life – rheumatoid arthritis for example. The same way that children tend to fight off Covid more easily than older patients. In this particular case, children's immune system overreacts to the drivers of atopic dermatitis – the causes are not well understood. To be clear, some people grow out of their bouts with eczema where others continue in adulthood, or in some cases, develop the disease later in life. The pediatric population is a particularly underserved group, especially when it comes to the more irritating symptom of the disease, which is itch.

CEOCFO: ***What have you learned from the trials so far?***
Mr. Krueger: I would have to say that the biggest learnings have been around dosage, delivery and regiment. When we originally started out, I think we under-dosed patients in the early trials. We also took those patients off of their everyday hygiene routine, and it turns out that in many cases when you take people off of the soaps and the creams that they use, their skin actually improves. Therefore, we ended up with very high placebo rates.

We have extended the time for wash-out periods before putting patients on trial. We screen someone, and then 3 weeks later we enroll them, and during those 3 weeks we allow them to use whatever sort of hygiene routine they are using, and if they get better, that is great for them, but they do not end up on our trial. This is why we did not have artificially high placebo rates in our latest trial.

We have also learned that after a number of months our bacteria settles at the bottom of the bottle and that it needs to be re-mixed, right at the time of when we give it to patients. That increased the dose that the person was getting, even if we didn't put more bacteria in the bottle. We now vortex the bottle before delivering to a patient which resolves this issue.

CEOCFO: *In addition to topical, how else might B244 be used?*
Mr. Krueger: We have done several studies intranasally, which are looking at things like migraines and allergic rhinitis. We have studied and done some work looking at the eye. Obviously, the Holy Grail of glaucoma is to deliver nitric oxide to the eye, so this is one of the areas that we have been interested in. There are many diseases that are related to inadequate processing of nitrogen and nitric oxide in the lungs, so we have also looked at inhaling B244 into the lungs as well.

CEOCFO: *Have similar approaches been tried in the past?*
Mr. Krueger: The answer to the question is no. This is a first-in-class drug. The idea of replacing bacteria that should be there and is not, is the very basis of much of the work that Seres Therapeutics has done in the area of *C. difficile* in your stomach. The idea of restorative bacteria on the skin is fairly new. Due to our know mechanism of action, our approach, although very new, is actually more mature and better understood than similar technologies being studied in the gut.

CEOCFO: *What have you learned about rosacea?*
Mr. Krueger: We ran a trial in rosacea, about 3 years ago, and that the product performed better than the placebo. The placebo rates were quite high, but the efficacy was actually also quite high. I think that if we re-ran this, we would definitely want to put the higher dose and the new regiment in place.

I believe that rosacea is an inflammatory disorder, although when you ask someone, they are not really sure what causes rosacea. However, in virtually every trial that we have run we have seen B244 ability to reduce inflammation on the skin. We think B244 would be relevant for this. Therefore, we are excited about rosacea. We think it is a great target, and there are very few good drug therapies available in the area of rosacea.

CEOCFO: *What has been the reaction from the medical community? Is the awareness high in the medical community?*
Mr. Krueger: I would say that in the medical community, the awareness is actually fairly high. I think that obviously anything new is difficult for people to understand the first time that they see it. I think that in principle, most people feel that the microbiome is an important thing. What is complicated is that we have confused clean and sterile. Our modern approach to hygiene causes us to regularly sterilize our skin. We have not grown to think yet about modifying that behavior or layering in restorative bacteria, as we have learned to do in the gut. I will say that the interest and excitement that we have seen since we have had positive results on our trials has been quite high. People are very interested in B244 to address the unmet need of itch, especially in a safe first line therapy.

CEOCFO: *Are you seeking funding, investment, or partnerships as you move forward?*
Mr. Krueger: Always. We are currently not in a position to fund Phase 3 ourselves, so we are looking at a variety of strategic, and financing options.

CEOCFO: *Does the investment community understand?*
Mr. Krueger: I believe that they do understand both our approach and market opportunity.

CEOCFO: *What is the plan for the next year or so?*
Mr. Krueger: The next year is all about getting ready for Phase 3. It requires scale up of manufacturing and a design of our Phase 3 trial. We are also obviously looking to figure out the best way to fund this trial. Therefore, we are exploring all options available to us.

CEOCFO: ***What is the reaction when you are at a conference? With many other people and ideas that they would like to show, how does AOBiome you standout?***
Mr. Krueger: First of all, we are a first in class drug, so there are very few, if anyone, talking about the disease states and related therapy the way we do. It is a unique option. We don't have the safety issues that other treatments have. We don't have to make the excuses that other do as to why these black box warnings really are not something that needs to be heeded.

I think it is just the sheer elegance of restoring a particular bacteria back onto skin, especially since that particular bacteria is understood in terms of what is delivers. I think the idea that something that naturally occurs and down regulates IL-4, IL-5, IL-13 and IL-31, where most of the other drugs that you see in the marketplace target only one of those interleukins, I think is also quite unique. The other unique part of this is to have a drug this safe get this far forward in clinical trials is a game changer.

CEOCFO: ***Why pay attention to AOBiome Therapeutics, Inc?***
Mr. Krueger: What I think sets us apart is that we have a scalable drug platform that can be applied to across multiple indications, that leverages the immune response across multiple dermatological opportunities. It is first line therapy, because of its safety and ease of delivery. It can be used in children and the elderly, and this is a massive untapped market.