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Advancing the Next Generation of Inflammation-Targeting Therapies: AMTX-100 Technology delivers First-in-Class Biologically Active Molecule to Treat Chronic Diseases Mediated by Inflammation

Dr. Matthew A Gonda, Ph.D.
Founder, President & CEO

Amytrx Therapeutics, Inc.
www.amytrx.com

Contact:
Amytrx Contact:
Maya Frutiger, VP of Corporate Affairs
214-668-2916
mfrutiger@amytrx.com

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

CEOCFO: ***Dr. Gonda, the first thing I see on the Amytrx Therapeutics, Inc site is "Transformative anti-inflammatory therapies are on the way." How are you going to do that at Amytrx?***
Dr. Gonda: Amytrx's inflammation-targeting technology is an entirely new therapeutic approach with immense potential to yield safer and more effective therapies for a large array of unmet medical needs. The company's lead program, AMTX-100, is a first-in-class, biologically active peptide capable of targeting a range of inflammatory diseases. Our initial clinical program is focused on inflammatory diseases in dermatology for which we've advanced a potentially best-in-class topical treatment of our lead compound into first in human clinical trials for atopic dermatitis, the company's initial indication. Our peptide technology is breakthrough in that this will be the first time a biological molecule is able to penetrate the skin and treat disease. This is not only true for inflammatory skin conditions like atopic dermatitis but for a whole host of other chronic inflammatory diseases for which AMTX-100 could be specifically formulated to deliver superior treatment. By naturally modulating common and key pathways used to initiate inflammation, we are able to provide broad therapeutic activity without affecting important housekeeping genes essential for cell growth and viability. We believe this approach will drastically minimize side-effects and safety concerns seen with many small molecule and biologic anti-inflammatory drugs.

CEOCFO: ***What is it about what you have developed that allows it to penetrate the cell? What is different about your approach?***
Dr. Gonda: AMTX-100 is a novel chimeric peptide in having dual functions, cell penetration and very specific protein binding to nuclear transporters called importins. The latter binding sequences are also found on inflammatory transcription factors and are essential for their transport to the nucleus by importins. The peptide sequences in AMTX-100 for cell penetration were derived from fibroblast growth factor 4, a transcription factor expressed early in development, and were joined to those for binding that come from the nuclear localization sequences of NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells), a transcription factor and the master regulator of inflammation.

Instead of trying to block key components of inflammatory pathways outside of the cell or on the surface of the cell, AMTX-100 can penetrate cells. Once inside, it functions as a decoy mimicking exactly the function of binding sequences found on some of the most important inflammatory transcription factors, like NF-κB, used to initiate the cascade of

biological responses—all of which start in the nucleus of the cell and lead to inflammation. In order for these large transcription factors to get into the nucleus, however, they need to be transported by importin. AMTX-100 has no other biological function than to bind to the nuclear transporter. The sheer presence of AMTX-100 in the cell creates a competition between native and fully functional inflammatory transcription factors and AMTX-100 for importin that modulates—but does not inhibit—transcription factor nuclear trafficking, effectively controlling inflammation by a natural process already in use by nuclear transport mechanisms of the cell. The competitive mechanism and effectiveness of AMTX-100 has been successfully tested in a number of animal models of human inflammatory disease as a proof-of-concept—where no significant toxicities were observed.

CEOCFO: ***What was involved in getting to where you are today? When will you be ready for the world to know about AMTX-100?***
Dr. Gonda: AMTX-100 has been in development for the past 25 years with $25 million in federal grants in the laboratory of Dr. Jacek Hawiger, a well-known immunologist at Vanderbilt University, who is also a scientific co-founder of Amytrx. He was studying facets of the immune system related to inflammation and wanted to understand the mechanism by which inflammation is initiated and controlled. Inflammation is a natural process in which the body recognizes invading microbes and damaged tissue and attempts to limit the spread of infections and repair the injury. The arm of the immune system responsible for this is called innate immunity. It is the rapid, first responder of the host that initiates production of cytokines, chemokines, and growth factors that defend and help stimulate other cells to participate.

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AMTX-100 is the tool that Dr. Hawiger conceived and developed to study inflammation. It is a novel approach, and significantly ahead of its time. Currently, most therapeutic approaches to control inflammation focus on monoclonal antibodies and small molecules. We feel that AMTX-100 uses the best from both of these therapeutic modalities and will be more effective and versatile than either of these approaches alone to controlling inflammation. Most of the anti-inflammatory drugs in development or already commercialized interrupt events prior to the nuclear transport pathway modulated by AMTX-100. We regulate one of the most important and pivotal pathways in the crossroads of inflammation initiation and control.

Amytrx was formed in 2014 to commercialize AMTX-100. The Company obtained an exclusive license from Vanderbilt University for a portfolio of newly filed patents and raised enough capital from investors to execute on our commercialization plans. A considerable amount of pre-clinical activity had to occur to ready AMTX-100 for regulatory approval to start clinical trials. As a prelude to this we had to develop a method to manufacture enough drug for pre-clinical and clinical studies to move the product from bench to bedside. This was key to receiving FDA approval of our IND and Phase 1/2b protocol and initiate first in human studies. In addition, we wanted to make sure our portfolio of patents had matured sufficiently to secure protection for our product. It is not uncommon these days to remain a stealth company until a significant value inflection event like initiation of our Phase 1/2b protocol takes place.

CEOCFO: ***What is happening today?***
Dr. Gonda: We have produced enough GMP drug to enable executing on our FDA approved Phase 1/2b clinical protocol and raised enough capital to support our commercialization plans over the next year or two. There are a large number of diseases caused by inflammation that still represent unmet medical needs. Inflammation causes or is associated with 80% of all diseases worldwide. We wanted to select a disease which represented an unmet medical need and where we could see the results quickly with our new therapeutic. So skin was our target. Of course, there are many skin diseases caused by inflammation, including psoriasis, atopic dermatitis, which is also known as eczema, rosacea, acne, herpes infections and shingles. I said, "Let's target a significant disease of skin with AMTX-100 where we could have safety results and obtain insight into its biological activity to determine if there was sufficient data to move the drug forward." We chose atopic dermatitis, developed proof-of-concept in an animal model, safety testing studies and a clinical protocol for a

topically applied drug to accelerate drug development and submitted it to get regulatory approval from the FDA. The type of protocol we developed is called an adaptive Phase I/IIb, which means we could accelerate the clinical process, simply because we do not have to go back to the FDA with a Phase II after the Phase I protocol for approval. We started our Phase I clinical trial in March of 2020 and have completed two out of five cohorts and have enrolled several patients in the third cohort. The results thus far are very encouraging. Completing the Phase I is a priority. That is basically where we stand today.

CEOCFO: ***Why is it so hard to treat eczema? It seems that by now it should be treatable?***
Dr. Gonda: There are a number of explanations for the difficulty in treating eczema. Eczema is most likely a conglomeration of a number of different disorders; some maybe genetically caused such as in autoimmune disorders and others may just be an overreaction of the immune system to contact with a microorganism, foreign antigen or chemical. Regardless of the underlying cause, eczema represents a disease in which there is a chronic, smoldering skin inflammation caused by immune dysfunction locally and probably made worse by a systemic immune response. It can express itself as a mild to serious disease that is chronic or intermittent. Injected anti-inflammatory antibodies work great for some in the moderate to serious forms of the disease, but they don't come without consequences that are sometimes serious to your health and there is no guarantee that you will get completely clear skin or alleviate all the symptoms that come with eczema. Because of this, there is great room for new treatment options, especially ones that are broad spectrum. We feel AMTX-100 will offer a new way to treat systemic as well as local disease and achieve clear skin for those afflicted due to the peptide's broad-spectrum activity in inflammation and the variety of ways it can be formulated and administered.

CEOCFO: ***Where does COVID come into play here?***
Dr. Gonda: With an infection by COVID, the virus enters the body orally or nasally and initially the infection resides in the lungs where there is extensive virus replication. However, viral receptors for entry into a cell, in addition to lung epithelial cells, are found in a number of cell types throughout the body including endothelial cells of blood vessel walls. That is where you see a lot of the pathogenesis and the damage that is done outside the lung, and since blood vessels reside in all organs, when blood vessels are attacked in weakened organs, significant damage can occur to them. When you have an infection that has not been seen before, the first response to the infection, before you can make antibodies to it, is by the innate immune arm of the immune system. It is the most primitive of immune responses and is represented in all animals. It is rapid in onset and produces cytokines, chemokines, growth factors and activated T-cells to defend against the invader and repair damaged tissues. The mere presence of these small molecules creates a feedback system to produce more cytokines and chemokines leading to an overproduction of these defensive molecules, called the "cytokine storm". Unfortunately, in doing so it has overreacted, and when it overreacts, it can cause collateral damage to otherwise healthy but weakened tissue in blood vessels, heart, lung, kidney, liver, and brain—especially in compromised individuals with a pre-existing condition such as diabetes, or the elderly. Signs of COVID infection can also be found in skin.

Therapy for the "cytokine storm", is where AMTX-100 fits well. The innate immune system when thrown into high gear produces a multitude of inflammatory cytokines and chemokines. AMTX-100 has been shown to have broad spectrum anti-inflammatory properties, being able to quell the expression of at least 26 cytokines/chemokines. It is not a vaccine or an antiviral but an anti-inflammatory defense against inappropriate expression of one's own innate immunity—it does not completely suppress it; it modulates its expression. We have already proven that AMTX-100 can improve survival in animal models of bacterial sepsis in which a "cytokine storm" is the main driver of sickness and death. AMTX-100 treatment alone or in combination with antibiotics improves survival outcomes better than using antibiotics alone.

CEOCFO: ***Are you seeking funding, investment or partnerships for any or all of the things you are working on right now?***
Dr. Gonda: Yes. We are a private entity with stock ownership. We seek out funding from non-dilutive grants and direct investments through the sale of stock. It takes millions of dollars to get to a drug approval. As the CEO, I am always looking for funding from investments or a partnership. As first choice, we would like to have a corporate partner to participate in both risk or returns of commercialization, such as milestones or royalties, in addition to our shareholders to accelerate development. There is also the possibility of raising money for our commercialization plans by becoming a publicly traded stock company through an IPO. The opportunities for providing a therapy for diseases caused by inflammation are huge. We would like to rapidly expand the various disease targets and formulations and are interested

in obtaining an experienced corporate partner who would work with us to commercialize AMTX-100 in dermatology and other unmet medical needs throughout the world. The driving motivation is to see our product benefiting people who have limited options for their affliction.

CEOCFO: ***What has been the interest from the investment and the medical side, who have learned what you have developed so far?***
Dr. Gonda: I would say the breath of the Amytrx opportunity has created excitement from investors that comes from hearing about a technology which can produce transformative drugs for treating a wide array of unmet medical needs. We [the medical field] have become accustomed to treating end-stage disease, like cancer, heart attack, atherosclerosis or diabetes. Inflammation is a word that, 10-15 years ago, you would hear in a doctor's office and not know the real meaning of how it equates to disease. It was almost like having a headache; go home and take some aspirin. The broad implications were not well known. Inflammation eventually made the cover of *Time Magazine*. The cover read "The Fires Within." That is what they called inflammation and the article gave it as the cause of many different diseases. However, a lot has happened since then to change this impression. As mentioned earlier, inflammation is the cause or associated with eighty percent of all diseases. The pathway that we directly target with AMTX-100 is the same pathway for almost all types of diseases caused by inflammation, anywhere in your body, including psoriasis, age-related macular degeneration, heart attacks, atherosclerosis, and type 1 and 2 diabetes. The field of diseases caused by inflammation has expanded to include inflammation in the brain, for example, MS, Parkinson's, Lupus and Alzheimer's. Knowing the role innate immunity plays in inflammation (defined as redness, swelling, heat, pain and loss of function) and the enormous amounts of knowledge that have amassed about how innate immunity causes inflammation is similar to the huge amount of knowledge in immunology that came from studying the AIDS virus. We have engaged physicians in such conversations and they believe such products will have a real impact on both acute and chronic inflammation. With that said, we also have had interest shown in our novel anti-inflammatory peptide by a number of pharmaceutical companies from which we hope to derive a partner.

CEOCFO: ***Could people at some point just be taking this all the time to ward off many problems?***
Dr. Gonda: At this stage in the history of AMTX-100, I do not think that anyone would be prescribed our anti-inflammatory drug prophylactically. However, you bring up an extremely good point! Let me tell you something about inflammation. It really is associated with staying young and healthy. It defends us from invaders and repairs us well enough to keep us healthy to perpetuate the species. It is found in all animals. When you are young, you repair well. However, we live a lot longer today and some of the inflammation stays with us. With that longevity comes diseases from chronic expression of inflammation-—injury-repair—injury-repair. Eventually, you run out of stem cells. Inflammation can be considered your friend when you are young and can be your enemy when you get older. A recent issue of *Scientific American* dedicated an issue to inflammation and its role in aging. The authors imply that we could live for 140 years, if we could control inflammation. However, you would have to start the treatment early in life. This concept is still too far out there to be reality.

CEOCFO: ***You have a long history involved in this arena. How do you deal with the frustration of knowing you have something that could be such a potential game changer in so many ways and it is hard to get it anywhere, let alone everywhere it should be?***
Dr. Gonda: Yes, you bring up another good point and this is what we struggle with in conversations when we describe our technology. It is very new. We show people the data and say, "You know, this is a common pathway. Almost all of the anti-inflammatory biological and small molecule therapies that are out there, are processed through us. AMTX-100 is able to provide broad-spectrum modulation of key inflammatory pathways, reducing inflammation." Our therapy could cover most of the other treatments available that are prenuclear in activation. We need to be persistent in telling our story over and over, and continue to generate plausible data in animal models of human disease and in human clinical trials to back it up. There are always concerns about safety with new drugs. We have safety data on literally hundreds of animals and are now garnering it in human trials.

We have incurred queries pertaining to collaborating on our drug. It takes a long time to initiate collaborators to your therapeutic concept when a molecule is first-in-class and has a novel mechanism-of-action. Having strong, substantial and peer-reviewed data on the mechanism-of-action puts you way ahead of the game. It is simply hard for pharmaceutical companies to move on from their own developed products to something new that may replace their current product for

which they still have patent life and have invested billions of dollars in knowledge, research, and marketing. It is natural to weigh novelty and costs of commercialization with the potential to cannibalize their own marketed product.

CEOCFO: ***Why should people take a look at Amytrx Therapeutics, Inc?***
Dr. Gonda: Several factors play into this: 1) the demonstrated safety of the drug, 2) a thorough understanding of a common, anti-inflammatory, mechanism-of-action, 3) proof-of-concept in numerous animal models of human disease, 4) a newly issued and strong patent portfolio, 5) regulatory approval to use AMTX-100 in human clinical trials through Amytrx's IND and adaptive Phase I/IIb protocol, 6) execution on our drug development plan that to date has yielded very encouraging safety and biological activity data in mild to moderate atopic dermatitis, 7) the breadth of disease targets that this data opens up for us, and lastly 8) a competitive if not less expensive cost of goods in a best-in-class drug. With all of these points going for us, all it takes is for the one light bulb to come on and see the breath of the opportunity in treating arthrosclerosis, rheumatoid arthritis, psoriasis, heart, kidney, liver, lung and neurological diseases.

Pharma have spent twenty+ years researching and commercializing anti-inflammatory monoclonal antibodies and small molecules. It took quite a while to gain their acceptance and clinical use. When one looks at the products on the market and in development, there seems to be quite a few "me too also's in the mix." Naturally this is only until people realize it and see that you can harvest the power of this novel anti-inflammatory peptide which will enable advancement of breakthrough medicines that were considered impossible or unworkable before.

CEOCFO: ***It is very exciting!***
Dr. Gonda: It is a difficult road for a small company, but we are all very dedicated and excited to see this remarkable peptide technology evolve! You have to raise money; do the business development; execute on the regulatory and clinical development, etc. I have surrounded myself with a group of really talented people that have worked with me off and on for over fifteen to twenty years and have come back to work with Amytrx because of the belief in what they are doing. It has been pretty easy to get experienced people excited and foresee the potential, especially when you have a lot of animal data that shows how well it works. It is not just one experiment. It is ten or fifteen experiments in models of human disease. It works in every case, because it is all the same mechanism of action and pathway.

This will be the first time that a biological molecule is able to penetrate the skin and treat disease, because antibodies are way too big to do that and we are only twenty-eight amino acids. This is a really exciting therapeutic pathway, with many challenges along the way, but all resolvable. I have to say, the people who have invested in us are super excited! The technology came out of Vanderbilt University and so people in the Nashville area (there are many entrepreneurs in Nashville) were exposed to it early. They saw the story and it was not hard to convince them. They said, "This is really good, because you know what? I just went to my doctor and he said I have inflammation," and all of a sudden the light bulb comes on and brings them out of the darkness. Once they have heard inflammation, they see it in everything they read.