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The Most Powerful Name in Corporate News



Tahir Mahmood, PhD Chief Business Officer & Co-founder

Oral Biopharmaceutical Product Pipeline

CEOCFO: Dr. Mahmood, what is the concept behind AMT?

Dr. Mahmood: Applied Molecular Transport is developing a pipeline of transformative. targeted, next generation oral biopharmaceutical products. These are large molecule drugs that currently must by given to patients by injection during the course of disease or over their lifetime, due to stability challenges and the barrier properties of the intestinal tract that restrict trans-intestinal transport. Our technology platform allows these to be administered orally as pills. The concept behind AMT's core technology is based on new understanding of microbial science and proteomics. Certain pathogenic microbes make us sick by colonizing our intestinal epithelia and secreting proteins into our body that are toxic to immune cells. These microbes have evolved over millennia to very efficiently highjack internal transport mechanisms in our gastrointestinal tract to traffic proteins across the GI in order to target and prevent the immune system from launching a host response against the bugs. Our company's founders and scientists have been able to dissect these transport mechanisms and have built a deep understanding of the structural elements of these proteins mapped to the corresponding transport pathways. AMT's platform utilizes these elements and the natural pathways that are already in our bodies, while maintaining the integrity and functionality of the GI tissue. This allows us to engineer highly effective and safe biological scaffolds based on these firm scientific principles.

CEOCFO: What do you understand about the process as it is happening that was not understood before?

Dr. Mahmood: At a high level, we know what it takes to keep these drugs stable in the intestinal lumen as well as the mechanisms used to transport them across the intestines into the body and target them to specific cell types. At a granular level, we understand that certain receptors are expressed ubiquitously and consistently across the entire length of our GI tract. These are the receptors utilized by this class of microbes to initiate the process of shuttling molecules across the intestinal tract. Our scientists have elucidated the actual pathways that are responsible for this process, which were not known in the past, as well as how to protect and stabilize the therapeutic molecules within these molecular transport pathways. What we have done, which is novel, is to break down the pathways into discrete components and to engineer our biopharmaceuticals with molecular scaffolds that now drive access to these mechanisms and cellular compartments. The essence of our approach is that we are working with nature, not against it.

CEOCFO: Where are you in the process of development and commercialization? What is happening today?

Dr. Mahmood: As a company, we are focused on immune-mediated inflammation and metabolic diseases. The main reason for this is that we are aiming not only for improved compliance and patient or caregiver convenience, which by themselves have significant benefits when it comes to chronic therapies, but most importantly for superior biology and pharmacology. We are concentrating on these two therapeutic areas at this time because the directed presentation of targeted biopharmaceuticals to the immune-rich sub-mucosal GI space, and by extension to the hepatic-portal system, enables the enhancement of existing biology as well as access to new biology that until now has been inaccessible in a pharmaceutically feasible manner. In these areas, we are a pre-clinical stage company. However, we are leveraging the increasing understanding of these classes of protein scaffolds and pathways that have indeed proven to be valid in the clinic. We are very confident that the data, safety profiles and pathway validation from the work in humans can now be applied directly to the pre-clinical programs that we are running on the therapeutics side.

CEOCFO: How are the drugs administered?

Dr. Mahmood: Patients will swallow a pill in the shape of either a tablet or a capsule, depending on the indication and target. The stable formulation contained within the pill is engineered based on the specific drug release profile required for each drug.

CEOCFO: Has the medical community paid attention so far?

Dr. Mahmood: We have received tremendous response from medical key opinion leaders as well as clinical specialists and general practitioners. Of the four members on our Scientific Advisory Board, three are MDs. There has been strong interest from these groups because they are at the front line of interfacing with patients and caregivers. They, perhaps more than anyone, recognize that increasing compliance and adherence to prescribed drug regimens by dosing with pills instead of injections will result in improved treatment outcomes. It's simple and painless, and now, patients can be expected to be taking drugs that they would otherwise not be taking frequently, if at all. Additionally, in terms of advancements in treatment options, the fact that we can open new biology and reach new targets that had not been accessible is very exciting to clinicians who are passionate about expanding their repertoire of therapeutic modalities to more precisely and effectively treat their patients.

"We are aiming not only for improved compliance and patient or caregiver convenience, which by themselves have significant benefits when it comes to chronic therapies, but most importantly for superior biology and pharmacology." - Tahir Mahmood, PhD

CEOCFO: Is there much research in this arena?

Dr. Mahmood: There have been research efforts to develop orally administered peptides and proteins for at least twenty vears. Unfortunately for patients, these efforts have been mostly very unsuccessful, while some have been moderately successful, as evidenced by the lack of marketed products and thin pipelines. The majority of groups working in this area have been trying to formulate the peptide or protein in order to keep it stable in the GI tract with the hope that some of it will come across the intestinal epithelia. However, the intestinal epithelia is a barrier that is designed to keep materials out of the body, including proteins. So even if a drug can be kept temporarily stable inside our intestines, it is highly improbable that any significant amount will actually traverse a healthy, intact GI tract. Other efforts in this space have focused around opening tight junctions, which are like the 'cement' between the cellular 'bricks' in our GI. When these are opened, channels are formed, allowing the drug to come across. Unfortunately, that is less than optimal because in addition to the drug, everything else in that region of the GI tract, including potentially harmful content, will also enter the body. Therefore, for chronic therapies, the toxicity liability and safety concerns are paramount, even for approaches that transiently open GI tissue, and have greatly held back the development of products in this area. These comprise the bulk of the efforts in this space. There have been additional orthogonal strategies employed by some other groups, but these are few in number. At AMT, we are not only stabilizing proteins in the GI tract, which is an absolute necessity, but more specifically have designed technologies to overcome these intestinal barriers in a way that does not cause damage or change intestinal epithelium functionality, since we are leveraging endogenous transport mechanisms. That is how we would differentiate ourselves from the majority of the groups in this arena.

CEOCFO: Explain about metabolic diseases and how does that fit in with what you are doing?

Dr. Mahmood: Metabolic diseases are of particular interest because many of them are regulated in the anatomical region between the intestinal epithelium and liver, which is where our technology can directly present therapeutic molecules. In short, our products can closely mimic endogenous endocrine regulation and release, by targeting the very nexus of endocrine and exocrine systems. This is due to the local physiology because when we take any oral medication, it exits the GI tract and heads to the liver. It is only after it has moved through this region that it is then sent to the rest of the body. This makes for a very interesting situation because we can now directly aim for any target along or on the other side of the GI tract, through to the liver. If you think about some of the key molecules that are produced, regulated or act on this area, the list includes GLP-1, insulin and growth hormone, to name just a few. Their sites of action are in that compartment and we can directly target those tissues and cells without systemic exposure. What we are leveraging is the clear biological benefit of the oral route versus other routes of administration. Most of us know people who take medication for diabetes with many of them taking daily injections, and we can understand that their lives could be considerably different if they did not have to get shots. But just think if they can not only avoid the shots, but their diabetes-associated symptoms improve as well. Pharma researchers have already started exploring these remarkable phenomena and we are very excited because if you look at all the disparate data sets out there, they point toward reduced side effects and improved pharmacology. That is why the metabolic disease space is so exciting for us.

CEOCFO: Are you funded for the next steps? Will you be seeking partnerships or additional funding?

Dr. Mahmood: We have sufficient funding to move forward with some our key programs. However, we are working towards additional partnerships and are in discussions right now with several parties. We are also looking to reinforce our balance sheet by raising a venture-backed private placement financing this year. This would allow us to accelerate and drive our internal development programs to the clinic, as well as enter exciting new areas where our technology can be applied in novel ways.

CEOCFO: What have you learned in your previous experiences that helps in the process of development, going to market, commercialization and funding? What do you recognize that others might not?

Dr. Mahmood: I am not sure there are any specific insights that others will not have known, but there are certainly many things that we have learned along the way. One of the most important is an internal mantra at our company - if you cannot make it, you cannot sell it. Being able to simplify the process of protein design and biologics manufacturing is extremely important, and is a feature that we factor into our programs very early on. We do not simply leave it up to our partners or others down the road to deal with the challenges of scaling up. This is technical insight derived from our leadership's experience at companies like Amgen and Genentech. Also, the drug reimbursement landscape in the United States and internationally has changed significantly over the past few years. Being able to clearly articulate the economic benefits of our approach versus the standard of care is a critical element of our products' value proposition and development strategy, and one that we have incorporated into our thinking at the very earliest of stages. In terms of corporate strategy, we see that interests and areas of focus within the large pharma companies and investment community can shift over time, often driven by what their competitors are doing in the market. While we certainly must be cognizant of what potential investors, partners or buyers are looking for, we defined a clear strategy and have stuck with it. We certainly had to refine our plans over time, but overall, we have been on track with what we started out to do. This has been validated by the intense interest from across the pharmaceutical industry, medical community and patient advocacy groups, with support from the latter being incredibly gratifying. As long as the fundamentals are strong and our programs and pipeline have solid scientific foundation, we remain confident in our ability to forge a path forward. Even though industry winds may shift every now and then, many medical needs remain inadequately addressed, and the data and science behind overcoming these challenges will speak for themselves. We have stayed with that philosophy, and we have been successful.

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