Recombinant Version of the Naturally Occurring Human CC10 Protein Showing Promise as an Anti-Inflammatory Agent for Patients with Respiratory Disease

"While we have seen successful development initiatives for respiratory disease, today's therapeutics primarily address 'signs and symptoms' of disease only. As we look at other therapeutic categories, advancement of the promise of disease modification has been encouraging. The reason I joined Therabron is that I see the potential to move beyond respiratory disease signs and symptoms management and the opportunity to develop a completely new therapeutic platform with the potential to help countless respiratory disease patients."

- Dr. Thomas F. Miller

Dr. Thomas F. Miller
President & CEO
Therabron Therapeutics, Inc.

CEOCFO: Dr. Miller, what is the concept at Therabron?
Dr. Miller: At Therabron we are a development stage Biotechnology Company that is focusing on a category of drug candidates to potentially help respiratory disease. In normal human biology, throughout the respiratory tract, we have a protective layer of cells called epithelial cells and they play a very important role in normal lung physiology. There is a certain type of cell called a Club Cell that you could think of like a progenitor cell, which is much like a stem cell, but naturally occurring. It can change into other types of cells as normal biology or physiology would dictate. These Club Cells secrete a regulatory protein that is colloquially referred to as CC10. CC10 plays a very important role in the respiratory tract by helping Club Cells regenerate and reduce inflammation. Our researchers have created a recombinant version of this naturally occurring protein to evaluate potential use in circumstances where there has been damage to the lungs and there is a deficiency of this respiratory protein. Simply stated, we are exploring the possibility of replacing what nature would otherwise have intended to restore this very important protective function that is necessary for respiratory viability.

CEOCFO: Where are you in the process?
Dr. Miller: We have a tremendous amount of experience in several nonclinical investigative models that have been published and peer reviewed. Additionally, we have already concluded two clinical trials. One clinical study is for our lead indication in preterm infants who have very
severe respiratory disease at birth. Another study is in healthy normal adults to evaluate safety and tolerability in that patient population. Additionally, we are now working hard to complete a very important Phase 2 or mid-stage trial, which we expect to complete enrollment shortly. That would become the basis for determining what our Phase 3 pivotal trial will be. We are now moving towards a later development stage company with eyes on identifying new indications for patient populations that are also deficient in CC10.

CEOCFO: What have you learned so far in the early trials?
Dr. Miller: It is an exciting time for drug development in the pulmonary space today. The pulmonary pharmaceutical market is estimated to be a $50 billion global market by 2018. If you look at the history in development of respiratory therapeutics, it has essentially depended upon similar pharmacology treatments that we have been familiar with for several decades. They have increasingly been combination products of currently available therapies addressing “signs and symptoms” of respiratory disease. At Therabron, we believe that recombinant CC10 has the potential to alter disease progression and change the course of the disease. Science suggests that the drug could play an important role in immunomodulation, and potentially reduce pulmonary inflammation.

CEOCFO: How has Therabron Evolved?
Dr. Miller: We are very fortunate in that the founder of Therabron, Dr. Aprile Pilon, was interested in studying the biology of this naturally occurring protein during her time at the NIH in the mid-90s. I have to say she has done an incredibly impressive job moving from those initial observations towards translational work with the potential to address several respiratory disorders. More recently, we have begun to build a very experienced Executive team to help support this scientific platform. I am in the role now for the better part of 10 months. We recently brought on a Chief Financial Officer, Chief Medical Officer, and experts in Regulatory Affairs. We plan to evolve as a company, to maintain momentum by bringing on complementary competencies that are necessary to help transition from a very well thought through research platform to an integrated company. That is the path we are on right now.

CEOCFO: What have you learned from previously experiences? What is important to do and not to do?
Dr. Miller: My career-long focus has been in respiratory drug and medical device development. What I have learned through the years that it is best to interact with regulatory agencies early and often. If you do so and you are able to understand their perspective, it can significantly help prevent development risk. Our lead program is funded by a little known grant opportunity that comes directly from the FDA. It is a financial funding opportunity through the Office of Orphan Drugs. Our lead program is designated as an orphan product candidate. While the financial resource is always helpful for emerging biotechnology companies, what I think is even more helpful is the opportunity to interact with leadership within the relevant reviewing division, in our case it is the Pulmonary and Allergy Division.

CEOCFO: What are the delivery methods for your programs?
Dr. Miller: That is a very important part of our strategy. The initial program is for preterm infants, who are very sick babies that often require significant respiratory support. They have a special breathing tube called an endotracheal tube (ETT) inserted through their mouths
and into their tracheas so that there is a conduit into the lungs to help support respiration. While that is necessary for many of these high risk premature children, it is an invasive process that often comes with risks. Our lead product candidate, which we refer to as CG100, is administered to preterm infants through the endotracheal breathing tube and the pressure from the mechanical ventilator facilitates distribution of the drug throughout the respiratory tract. Although this helps to deliver CC10 efficiently to this particular patient population, it is not an appropriate way to deliver our medication into other respiratory disease populations that are ambulatory. Therefore, in addition to ETT delivery, we are developing intravenous dosage forms for more stable patient populations where CC10 and Club cells are compromised such as in COPD, certain phenotypes of asthma and chronic rhinosinusitis. We are also exploring other delivery methods such as via inhalation (aerosolized delivery) to provide flexibility in the delivery routes of administration.

CEOCFO: Why has it been so hard to address the problem of COPD effectively?
Dr. Miller: I think there are a number of groups around the world including academicians, regulators, and industry executives that recognize what a complex medical problem and incredible cost driver COPD is from a health care utilization perspective. This is important not only in developed markets but it is also important to consider for emerging markets with China being a good example. The focus for drug development in the broader respiratory care space, COPD included, has been in an effort to address inflammation and airway reactivity. The complexity of COPD and the aggressive decay of the disease at end of life leaves limited options available for patients. I think that various teams that are now trying to look at COPD more holistically with the idea that perhaps the way that we have developed medications for this particular problem can be improved upon. For example, a large area of focused interest in COPD disease management is biomarkers. There have been a number of biomarkers that have been correlated with either baseline disease severity at time of diagnosis or predicted decline of disease until demise, including cytokines like Interleukin 6 or Interleukin 8. There are other inflammatory expressing agents such as Tumor Necrosis Factor and C-reactive Protein as well. However, at this time there is only one identified biomarker that has been associated with both the establishment of baseline disease severity in COPD and predictive of the subsequent decline in respiratory function ultimately leading to the patient’s death. The biomarker happens to be CC10 -- the endogenous protein for which we have a recombinant version. We think that there is an opportunity for our lead molecule as well as modified versions of CC10 to play a role in the next generation of therapeutics to address this debilitating problem.

CEOCFO: How far will your current funding take you?
Dr. Miller: We are a small biotech company. However, we have managed to get relatively deep into Phase 2 clinical development with a total investment thus far of only about $14 million, which I think represents an extraordinary capital efficiency. We are very active on the fundraising front. We are also very active on the strategic and business development front where we believe that part of the solution in addressing our capital needs can come through collaborations with strategic alliances. Larger companies have the funding to help advance early stage ambulatory respiratory problems such as COPD, certain phenotypes of asthma, and so on. In our lead program, we are very
active in the pursuit of regional licenses and transactions while keeping U.S. rights for that program. We recognize that it is unlikely that we would commercialize those assets outside of the United States by ourselves. If a company has a hospital sales force in place with compounds that are synergistic to the ones that we are developing, there is a strong rationale for a regional deal. We are looking at a multi-prong financial access strategy, which includes traditional financing as well as strategic collaboration.

**CEOCFO: Why pay attention to Therabron today?**
**Dr. Miller:** While we have seen successful development initiatives for respiratory disease, today’s therapeutics primarily address “signs and symptoms” of disease only. As we look at other therapeutic categories, advancement of the promise of disease modification has been encouraging. The reason I joined Therabron is that I see the potential to move beyond respiratory disease signs and symptoms management and the opportunity to develop a completely new therapeutic platform with the potential to help countless respiratory disease patients. I think Therabron has a special program with a tremendous promise to millions of patients with respiratory disease.

*Interview conducted by: Lynn Fosse, Senior Editor, CEOCFO Magazine*