

Novel Catheter-Based System for COPD Treatment



Dennis Wahr, M.D.
President & CEO

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About Holaira, Inc.

Holaira, Inc. (formerly Innovative Pulmonary Solutions, Inc.) located in Minneapolis, Minnesota is a privately held lung denervation company developing minimally invasive products to make breathing easier for patients suffering from obstructive lung diseases. Founded in 2008, Holaira is currently working on a novel catheter-based system that has the potential to improve lung function, exercise capacity and quality of life for patients with chronic obstructive pulmonary disease.

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

CEOCFO: Dr. Wahr, what is the concept behind Holaira?

Dr. Wahr: We are developing a novel catheter-based system to treat COPD.

CEOCFO: How does it work?

Dr. Wahr: We have a specialized dual cooled RF energy catheter, introduced through a standard bronchoscope that delivers targeted energy to ablate the parasympathetic nerves in the walls of the right and left main stem bronchi. Consequently, the airways are dilated and air can flow more easily to the lungs, enabling the patient to breathe more easily.

CEOCFO: What are you doing to the nerves when you are disrupting them?

Dr. Wahr: You are ablating the nerve. Nerve tissue, heated above about 65 degrees centigrade, ceases to function.

CEOFCO: *Would this be a one-time procedure?*

Dr. Wahr: We believe it is a one-time procedure. In our first two clinical studies and registries, the effect was sustained through the one-year follow-up. Subsequently, we expect the effect to be permanent. This will be validated with two to three year follow-up data.

CEOFCO: *Has a similar process been tried previously?*

Dr. Wahr: No, this is a completely novel therapy. We are disrupting nerves in the main stem bronchi, and that is like cutting an electrical wire. The effect of this extends throughout the whole lung field. That is where the company name comes from: Hol-air-a, which means air flowing to the whole lung.

CEOFCO: *Why did you think it would work?*

Dr. Wahr: The mechanism of action here is well known. COPD is treated today with pharmacologic therapy. The most common form of pharmacologics for COPD is a class of inhaled drugs called anticholinergics, like Spiriva™. These drugs target the parasympathetic nervous system, which controls the motor function that causes the airways to constrict, making breathing difficult. The drugs work by temporarily blocking the neurotransmitter, called acetylcholine, from reaching the constricted smooth muscle. This causes the smooth muscle in the airway to relax and the airway to open, making breathing easier. The inventor of this technology, Dr. Martin Mayse, is a pulmonologist himself and was aware of this mechanism of action. He had the great idea that if you just disrupt these nerves when they enter the lungs, you might be able to achieve a permanent sustained effect and get away from some of the disadvantages of inhalers.

CEOFCO: *Where are you in the development process today?*

Dr. Wahr: We have completed multiple preclinical studies and two multicenter human feasibility studies. Both of the feasibility trials were conducted outside the United States, and data from those studies were presented at the European Respiratory Society meeting for the first time in September of this year. We expect a comprehensive paper will be coming out shortly in a peer-reviewed journal. We are now moving forward with a phase 2 trial, which we call AIRFLOW-1. AIRFLOW-1 is a two phased randomized trial with a sham control, designed to help us better understand two things. The first goal is to determine the optimal dose of energy to get the best result. The second is to compare results in those who undergo the actual procedure with those who have the sham procedure.

CEOFCO: *How is the procedure done?*

Dr. Wahr: The procedure is done with the patient lying on a standard bronchoscopic examining table. While currently done with general anesthesia, in the future we believe it will be preferable to use conscious sedation. An interventional pulmonologist puts a standard flexible bronchoscope down the patient's airway through the trachea, and once that is placed our catheter is inserted through the working channel of the flexible bronchoscope. It is possible to treat both main stem bronchi in a single procedure. A procedure takes less than an hour to complete.

CEOFCO: *How do you measure the results both immediate and ongoing?*

Dr. Wahr: The clinical endpoints are very well understood for this type of therapy because they have been used for decades in pharmaceutical trials. They consist of three main areas. The first is to measure improvements in lung function using pulmonary function tests. That is where patients breathe into a machine that can precisely measure and quantitate lung function. The second area is exercise capacity or

endurance, where you test the patient's physical abilities in a quantitative way using cycling or walking tests. The third area is quality of life. There are well-validated questionnaires that patients fill out, which allow us to assess whether or not the patient is in fact having a better quality of life compared to before the therapy.

CEOFCO: *What types of patients would be candidates for the procedure?*

Dr. Wahr: Our studies include criteria for patients with moderate to severe COPD. This is a very large patient group. It includes both patients with emphysema and chronic bronchitis. Both types of patients are potentially eligible for the therapy.

CEOFCO: *So almost anyone with COPD?*

Dr. Wahr: Well, all patients in any clinical study have to go through a checklist of inclusion/exclusion criteria. You try to identify patients that do not have other associated diseases that could complicate the ability to study your effect on a disease. I would not say that anybody who shows up gets included in the study, but the potential pool of patients for this study is very large. Globally, there are over 190 million people estimated to have COPD, and at least 15 million of those are in the US. Another 20 million are in Europe. There are a lot of people suffering from this disease.

CEOFCO: *What did you learn from the initial test that may have changed what you are doing?*

Dr. Wahr: In our first two feasibility studies we learned a couple things. We learned that the procedure appears to be safe. That was the first priority. The second was that we have a preliminary signal that we can improve lung function. Those were the two key things. We also learned, like you always do in early stage medical device development, small nuances of the device that we could modify to make it more user friendly and potentially more efficacious. After treatment, we followed up with the patients for one year. We took advantage of that one year to design and develop a second generation device, which is now being used in our AIRFLOW-1 study.

CEOFCO: *What attracted you to Holaira?*

Dr. Wahr: When I was called by the company to solicit my potential interest in becoming the CEO, I went in with no preconceptions. I had not been in the pulmonary field before, but when I look at medical technology I always start with how big is the problem being solved, the unmet clinical need. COPD is actually one of the larger and more serious unmet clinical needs in medicine today. The benefits that patients get from pharmaceutical therapy are temporary. There exists a stunningly huge opportunity to help millions of people. That was the first thing. The second thing that attracted me was the realization that the mechanism of action was very clear. The Holaira technology appeared to be an elegant solution and I could easily understand how this therapy might work. Realizing how much potential benefit could come from this type of therapy and the fact that I could understand the mechanism of action, I could not resist jumping in to help bring this to life.

CEOFCO: *Are you funded for the next steps you would like to take?*

Dr. Wahr: Yes. In April of this year we closed a \$42 million Series D financing round, which will fund AIRFLOW-1, our phase 2 clinical trial, and continued development of our technology platform. This should carry the company through the end of 2016 and into the first part of 2017. At that point, we should have one year follow-up on our AIRFLOW-1 patients. One-year follow-up data for a randomized trial will be a key milestone. Additionally, we anticipate obtaining our CE mark during this

time period, which will provide us the potential to commercialize should we choose to.

CEOCFO: *Has the medical community been paying attention or is it too early?*

Dr. Wahr: I believe that you should not raise hype, and that's why we held off doing any type of public introduction of our technology until last month's scientific presentations at the European Respiratory Society Congress in Munich. That was really our first coming-out. We held off until we had at least one year follow up on all the patients in the feasibility studies. I believe that the data was well received by the pulmonologists who attended the meeting.

CEOCFO: *What else have you learned through past experience that is helpful in going from creation or development to commercialization?*

Dr. Wahr: I believe that in the medical device industry you need to make sure you have a profound understanding of your device, its safety profile, and how to optimize its treatment effect before jumping into a pivotal trial. For this reason, we are taking a little bit different approach than what medical device companies have typically done in the past where they have jumped from small feasibility trials straight to the pivotal trial and then learned things in the pivotal trial that they wished they had known sooner. I actually believe the device industry should do product development more like the pharmaceutical industry does with a three-phase clinical development program. It takes a little bit longer, and it probably adds a year-and-a-half to two years to the overall timeline, but I think it is safer for the patients and it greatly enhances the potential for developing a product that has meaningful benefits for the patients.

CEOCFO: *Are there any potential side effects that you have seen so far?*

Dr. Wahr: No, we have been very happy with the safety profile of our product so far. This is not by chance. We have conducted a large pre-clinical animal program to make sure we understood the treatment effect of our specialized RF ablation technique and the optimal energy dose. If you under-dose it, you might not get a treatment effect. On the other hand, you do not want to use too much energy because, similar to ablation techniques anywhere in the body, safety can be compromised. We have been very careful about that.

CEOCFO: *Will you be looking at potential partnerships?*

Dr. Wahr: I believe companies need to develop their products from the perspective that they are going it alone. The practical reason is that you do not get to choose when to sell the company. The buyers are the ones who get to make that choice. The practical way to manage a company and product development is to expect that you will need to be self-reliant. Avoid the temptation to cut corners and, instead, build a strong foundation that will both enhance your chances of success and make you more attractive to potential acquirers. Sometimes partnerships can be very helpful, but we are not making that an essential part of the business plan.

CEOCFO: *Put it all together for our readers. Why does Holaira stand out?*

Dr. Wahr: I think it is the most exciting opportunity in medical devices today because the therapy has the potential to have a very clinically significant treatment effect for a huge number of patients. On top of that, we have the potential to lower the overall costs for their medical care worldwide. COPD patients are very expensive patients. In fact, the US alone spends about 50 billion dollars annually on the treatment of COPD,

with similar numbers in Europe. Worldwide, of course, it is even bigger. The most expensive part of the care of COPD patients is treating exacerbations, where they suddenly have a flare-up in their lung function and wind up being seen in the emergency room or admitted to the hospital. These are extremely expensive readmissions, and a truly effective therapy for COPD has the promise or the potential to lower the readmission rates to hospitals. If that is the case, this is that perfect situation where you could deliver a great clinical benefit to the patients while saving the health care system money, which I think is something that is very exciting.

BIO: Dennis Wahr, M.D. joined Holaira in September 2012, with a unique background in serial medical device development, clinical evaluation and commercialization experience.

Prior to joining Holaira, Dr. Wahr co-founded Lutonix in 2007 and served as its President and CEO until CR Bard acquired the company in December 2011. Preceding its acquisition, Lutonix developed a unique drug coated balloon angioplasty technology for the treatment and prevention of vascular stenosis caused by atherosclerosis. Prior to Lutonix, Dr. Wahr co-founded Velocimed in 2001, and served as its President and CEO until its acquisition by St. Jude Medical in 2005.

As a company CEO, Dr. Wahr has wide-ranging experience with both the European regulatory authorities and the US FDA. His companies have sponsored 9 clinical trials involving more than 1500 patients leading to approvals for 4 unique and innovative medical products.

Dr. Wahr has served on the board of directors of several medical device companies including Accumetrics, IDev, Velocimed, and Lutonix, and he currently serves as chairman of the board for Intact Vascular. Additionally, Dr. Wahr spent two years as a Managing Director with RiverVest Ventures focusing on capital investments in emerging medical technology companies.

Dr. Wahr received a Bachelor of Arts from Albion College and his Medical Degree from Wayne State University School of Medicine. He did a fellowship in interventional cardiology at the University of California, San Francisco and is currently board certified in interventional cardiology. He spent more than 14 years in clinical practice and served as the Chief of Cardiology at the Michigan Heart and Vascular Institute in Ann Arbor, MI prior to launching his entrepreneurial career.

