CARDIONOMIC:
TARGETING THE ROOT OF ACUTE HEART FAILURE

A neuromodulation device inserted in the pulmonary artery has the potential to increase heart contractility without the negative effects of inotropic drugs.

by
MARY STUART

Forest Lake MINNESOTA

CONTACT
Steve Goedeke
President & CEO

sgoedeke@cardionomicinc.com

WHO'S BEHIND IT
New Enterprise Associates, the Cleveland Clinic, and Greatbatch Inc.

YEAR FOUNDED
2011

UNMET CLINICAL NEED
Acute Decompensated Heart Failure still has high rates of hospitalization, morbidity, and mortality

SOLUTION
A neuromodulation platform that increases heart contractility

FUNDING TO DATE
$2.35 million

INVESTORS
NEA, Greatbatch Inc., and the Cleveland Clinic

BOARD OF DIRECTORS
Ali Behbahani, MD (NEA); Jon Heavey, MD (Cleveland Clinic Innovations); Karen Shanahan (Cleveland Clinic); Dan Kaiser, PhD (Greatbatch Inc.); Steve Goedeke

MEDICAL ADVISORY BOARD
William T. Abraham, MD (Ohio State University), Michael Bristow, MD, PhD (University of Colorado Cardiovascular Institute); Michael Felker, MD (Duke University); Gary Francis, MD (University of Minnesota Medical School); Brian Olshansky, MD (Professor Emeritus, University of Iowa Carver College of Medicine)

For more than one million patients hospitalized with acute decompensated heart failure (ADHF) the prognosis is bleak. Only one in three patients hospitalized with heart failure survives for five years or more. These patients experience rapid weight gain due to fluid buildup in the lungs and throughout the body, which makes it difficult for them to breathe and sleep. Once hospitalized, it's likely they'll soon return to the hospital with the same symptoms. Half of them return within six months and 24% within the first month. Because US hospitals are now financially penalized for excess 30-day readmissions in heart failure patients who are on Medicare, developing technologies to keep these patients out of the hospital has become a top priority.

> *"A new approach is needed, one that targets the primary cause of worsening heart failure, namely, decreased cardiac contractility."*
>
> *–William Abraham*

According to heart failure expert William T. Abraham, MD, "In more than three decades, we have seen little improvement in the outcomes of ADHF patients." Abraham, Professor of Internal Medicine and Chief of the Division of Cardiovascular Medicine at Ohio State University College of Medicine, has participated in more than 100 multicenter clinical drug and device trials focused on heart failure and cardiac transplantation. "This is one area of cardiology in which we have made little progress," he says. "A new approach is needed, one that targets the primary cause of worsening heart failure, namely, decreased cardiac contractility."

That's the goal of start-up **Cardionomic Inc.**, where Abraham serves as chief medical officer. Cardionomic is developing a neuromodulation therapy designed to increase heart contractility and "rebalance hemodynamics and restore renal function, thereby treating both the root cause and the symptoms" of acute heart failure," says Abraham.

Cardionomic was founded around technology licensed from the Cleveland Clinic to Denali Medical II, an incubator backed by the venture capital firm New Enterprise Associates (NEA). The company's core patents have issued, and funding of $2.35 million has been provided by NEA, the Cleveland Clinic, and **Greatbatch Inc.**, a manufacturer of products for cardiac rhythm management and neuromodulation. Steven Goedeke, the president & CEO of Denali II and a long-time veteran of Medtronic Inc., leads Cardionomic.

Goedeke explains that patients with ADHF currently have three medical therapy options, all with limitations. Intravenous diuretics relieve the symptoms of fluid overload but are associated with worsening renal function and worse outcomes. Vasodilators also provide symptomatic relief. They improve cardiac output by dilating blood vessels but can cause dangerous drops in blood pressure. Finally, a class of drugs known as inotropes does get at the root cause of ADHF by increasing contractility. However, these drugs can cause vasoconstriction or vasodilation and are known to stimulate tachycardia

and atrial fibrillation. As a result, inotropes are associated with high rates of in-hospital mortality.

Cardionomic believes it has found a way to increase contractility with a device therapy that avoids the harmful systemic effects of inotropes. Goedeke explains that the company is developing an acute neuromodulation therapy that stimulates, from within the pulmonary artery, nerve branches associated with the autonomic nervous system. The concept is to deliver the acute therapy for a few days while a patient is in the hospital, and by doing so, "calm the neurohormonal storm that leads to ADHF, and improve end-organ perfusion and thus patient outcomes."

The Cardionomic therapy aims to selectively stimulate nerve branches that head into the ventricle where they are specifically responsible for contractility. "We have a local, nonsystemic, controllable ability to drive contractility without the negatives associated with inotropes," says Goedeke.

The company is first developing an acute therapy for patients who present at the hospital with ADHF while also building the foundation for a chronic implantable device.

The first embodiment of the company's platform will be a catheter that goes into the pulmonary artery via jugular access, in the manner of the Swan Ganz catheter used for blood pressure monitoring, and a pulse generator located on the outside of the patient's body, where it is controlled by a clinician. Once inside the artery, the device will deploy electrodes to stimulate the nerve branches that signal heart cells to contract.

Many clinical specialists are familiar with delivering Swan Ganz catheters, Goedeke says. "We wanted to match the skill sets of the providers in the care pathway." According to Abraham, "This will be a technology that will ultimately be able to be used by virtually any cardiologist who has the basic skills for right heart catheterization: interventional cardiologists, electrophysiologists, heart failure specialists, or general cardiologists." Notes Goedeke, "We are designing this product so that it is deliverable by a range of physicians in a range of settings, including the ED [emergency department] in rural Minnesota at 2 o'clock Sunday morning." That will take some time and evidence generation, he acknowledges, but that's the goal.

"Initial human studies demonstrated that the therapy did not cause arrhythmias in the treated subjects and that it can improve contractility in heart failure patients even when they are on beta blockers."

– Steven Goedeke

At this stage of development, however, Goedeke notes that the ideal pairing is a cardiologist or heart failure doctor with an electrophysiologist who is comfortable with navigation and fluoroscopy so investigators can confirm what is happening. The company has tested its therapy in 18 human subjects, the majority of them in Europe. "We have extensive human and preclinical data that shows that we can selectively improve contractility without driving heart rate."

Ultimately, Cardionomic expects its therapy to be offered as a chronic implantable device for ambulatory patients who have responded well to the acute therapy. The device would activate upon sensing the onset of ADHF and apply the therapy to "avoid fluid overload, the neurohormonal response, and hospitalizations," according to Goedeke. He admits that's many years away but believes that such a device would have a significant positive impact on patient outcomes over the long term.

The company is now raising a $6 million round to develop a custom product (proof of concept was obtained with off-the-shelf components) and take it to the clinic to demonstrate additional therapeutic efficacy. Goedeke notes that at this point, several major risks have been taken off the table. Initial human studies demonstrated that the therapy did not cause arrhythmias in the treated subjects (an unknown when the company first started) and that it can improve contractility in heart failure patients even when they are on beta blockers. In effect, "We have critical evidence of safety and efficacy," says Goedeke.

Cardionomic's value proposition is its potential to improve outcomes and lower the cost of care by avoiding hospitalizations, shortening the length of stay, and avoiding worsening heart failure. "Worsening heart failure has a high prevalence, so it is a win for all stakeholders," says Goedeke. Abraham adds, "If it works and is safe, it will do very well in the marketplace. At the present time, there are few if any evidence-based therapies for acute decompensated heart failure. If Cardionomic can demonstrate that [its device] improves in-hospital and post-discharge outcomes, it could become a standard of care for these patients."