

NEUROSTIMULATION DEVICES

Apnex Medical Inc. *Implant opens airways in OSA*

Apnex Medical Inc. is developing a device as tiny as a pack of gum that could become an enormous game changer in the bid to better treat obstructive sleep apnea, or OSA.

As many as 18 million people in the US alone suffer from OSA, according to the American Association for Respiratory Care, and the World Health Organization believes as many as 100 million people globally endure the condition.

Apnex wants to become a viable player in the market and is testing its device, known as the *Hypoglossal Nerve Stimulation (HGNS)* system, in both US- and Australia-based clinical trials. Company president and CEO Robert Atkinson sees the HGNS system as offering a novel alternative to the most common apnea treatment – continuous positive airway pressure, or CPAP, machines. The often-noisy CPAP option delivers compressed air to a patient through a mask covering part of the face while the patient sleeps, keeping the airway open. Atkinson says many patients have trouble staying with the machines, and ultimately eschew further treatment. And that is where Atkinson sees his marketing sweet spot.

“What we are targeting is not people who have a CPAP machine and are happy, but people who have tried and cannot comply,” Atkinson says. Reaching those people is important, he says, because a large percentage of OSA patients either avoid further treatment or remain undiagnosed. The condition can lead to an increased likelihood of heart attack, stroke, hypertension, motor vehicle accidents and death.

Apnex Medical is the second company to spin out of the medical device incubator Prospex Medical Inc., which Atkinson, Michael Berman and Chad Kugler founded in 2005. The St. Paul, MN-based company’s HGNS product is based on a fundamental concept invented more than 20 years ago, whose patent has since expired. **Medtronic Inc.** developed a similar device and sponsored a clinical trial about a decade ago, but dropped the project not long after. Another start-up – MN-based **Inspire Medical Systems Inc.**, spun out of Medtronic Inc. in 2007 – is pursuing development of its own version.

Investor interest has been solid, with the company raising \$30 million in venture capital over two rounds, including a \$14 million funding round from existing investors in December 2009. Atkinson says he sees the funding as a major validation of how far Apnex has already come.

“It is a recognition from our investors ... that we’ve built quite a bit of value over the last two years,” he says.

The technology is similar to a pacemaker in both size and concept. But instead of the heart, the device stimulates the musculature of the upper airway at the base of the tongue – the genioglossus – via the hypoglossal nerve. In obstructive sleep apnea, the muscle doesn’t always activate sufficiently, which can lead to a collapsed airway. The HGNS device is implanted just below the collarbone, with one wire lead connecting to the hypoglossal nerve. Another wire lead runs down along the rib cage.

Rather than wait for an airway obstruction to occur, the device is designed

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Business: Implantable device for treating sleep apnea
Founded: 2006
Founders: Michael Berman; Robert Atkinson; Chad Kugler
Employees: 25
Financing to Date: \$30 million
Investors: Domain Associates; New Enterprise Associates (NEA); Polaris Venture Partners; Michael Berman
Board of Directors: Michael Berman (Chairman); Brian Chee (Polaris); John Nehra (NEA); Nimesh Shah (Domain)
Consultants: Alan Schwartz, MD (Johns Hopkins University School of Medicine); Philip Smith, MD (Johns Hopkins); Atul Malhotra, MD (Brigham and Women’s Hospital, Harvard Medical School)

to prevent an obstruction from happening in the first place. The company explains the HGNS system as working with the body’s natural physiology and being fully automatic. An ear, nose and throat physician can implant the device in a simple surgical procedure, either in the operating room or on an out-patient basis. Once implanted, the device is programmed to suit the particular patient’s needs. It automatically turns on when a patient is asleep, and shuts off during waking hours. Patients can stop, start, pause or delay the device’s operation themselves.

Although the device concept is relatively straightforward, the 25-employee start-up company is not without competition.

To prevent sleep apnea, **Alaxo GMBH**, a German start-up launched in Novem-

ber 2008, uses a stent that a patient can insert into his or her nose and throat every night, and take out in the morning. That private company, based in Germany, is also betting on success because of a strong demand for alternatives to the CPAP system.

Restore Medical Inc., founded in 1999 in St. Paul, MN, developed its *Pillar* system for mild to moderate OSA. It involves three inserts that are implanted in the soft palate, using a minimally invasive delivery tool. Medtronic, its far larger Minneapolis neighbor, was interested enough in the technology that it bought the young medical device company in July 2008 for \$29 million.

And there are at least two companies developing products with concepts that seem similar to Apnex's, at least on the surface. Atkinson frames Inspire, based in Maple Grove, MN, as Apnex's "main competitor." Inspire's device includes an implantable pulse generator, a pulmonary pressure sensor and a connecting wire to the hypoglossal nerve. The technology, according to the company's web site, stimulates the hypoglossal nerve at low levels to keep the airway open. A programming device turns the electronic stimulation on when the patient goes to bed and off upon awaking.

Apnex and Inspire both operate on the basic principal of closed loop stimulation of the hypoglossal nerve, Atkinson says. He added that Apnex operates uniquely, however, with an approach that is both "proprietary and different."

The two products also use different implant sites. Inspire's sensor goes

into the rib cage, but Apnex's sensor is implanted under the skin, which Atkinson says is less invasive and presents a smaller risk of causing a collapsed lung (pneumothorax).

Another company, **ImThera Medical Inc.**, is a San Diego, CA-based start-up whose device would also stimulate the hypoglossal nerve and other crucial tongue muscles vital to breathing during sleep. The company announced on September 23, 2009 that it had completed development of its own device, though it is not for sale yet in the US. Human clinical trials for the device have begun in Belgium, according to the company, with initial results expected during the 2010 first quarter.

Getting the Apnex HGNS system to market is at least a few years away. Though the company is pre-revenue and working on a "very lean" budget, the product is involved in a safety and efficacy trial, with a completion expected by the middle of 2010. Apnex hopes the US Food and Drug Administration will approve a larger pivotal trial soon, with full commercial PMA approval hoped for in 2014.

The cost to install the HGNS would likely be similar to other neurostimulators such as **Cyberonics Inc.**'s VNS system, Atkinson says – \$5,000 for implantation and \$20,000 for the device itself. Atkinson says the clinical risk-benefit equation and the economics behind the proposed device will "clearly support reimbursement coverage."

"It is important to remember that all of the health risks and co-morbidities

associated with OSA, like hypertension, diabetes and heart disease, are an economic burden," Atkinson says. "We think our therapy will reduce the risk of these conditions."

Apnex will market its HGNS product initially as a second-line therapy to failed CPAP, targeting those who have been diagnosed with OSA and who have tried, but quit, the CPAP therapy. Longer term, the company hopes to position HGNS as a first-line therapy, targeting patients newly diagnosed with OSA. In the interim, Apnex hopes for European CE approval in 2011. The company has six pending patent applications, two of which are designed for other therapies. Long term, Atkinson is considering a number of options to grow its product development, such as possible corporate partnerships within the next 18 months.

"We have had quite a bit of interest," he says.

Apnex also faces a long-term choice of remaining independent or being acquired. Independence is feasible, especially if Apnex progresses enough to generate revenue and break even. But Apnex is also willing to entertain being acquired by larger players. Even companies that make CPAP machines are potential acquirers, he says, because they are lucrative operations that can help broaden Apnex's customer reach.

"We are open to both," Atkinson says. "And we want to keep both options open as long as possible."

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– MARK HOLLMER