

SinuSys Finds Great Promise

in Kinder, Gentler Sinusitis Treatment

by
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Next-generation interventional ENT company SinuSys reported positive data at one year from its clinical trial of Vent-Os, a new device therapy for chronic sinusitis. With a kinder and gentler therapy option, the company believes it fulfills the need for an office-based (and patient-preferred) sinusitis treatment.

Companies that led the interventional revolution in the otolaryngology specialty, including Acclarent (now part of **Johnson & Johnson**), **Entellus Medical Inc.**, and **ENTrigue Surgical Inc.** (part of **Smith & Nephew PLC**), did a great service for patients suffering from chronic sinusitis. Not long ago, the only treatment option for unblocking the sinuses in recurrent sinusitis sufferers that had failed drug therapy was functional endoscopic sinus surgery (FESS), which was uncomfortable and disruptive to patients' lives. After a two hour FESS surgery, in which tissue is removed from inside the nose, some patients experience facial bruising and bleeding from the nose, which has to be packed with dressing, and many experience pain, discomfort, and a blocked nose for weeks after the procedure. Perhaps because of those drawbacks, only 540,000 patients underwent sinus surgery in the US in 2013, leaving a large chunk of the 29 million people who suffer from chronic sinusitis untreated.

Over the past several years, new companies offering interventions for the ENT (ear, nose and throat) specialty have revolutionized this space with minimally invasive balloon techniques for sinusitis that require no cutting or removal of bone and tissue. During these procedures, a balloon that's similar to the angioplasty balloon in cardiology is rapidly inflated in the patient's nose to unblock the sinuses. The patient goes home the same day. Sinus dilation (or sinuplasty) balloons have become an effective treatment for

suffering patients who have failed medical management. Otolaryngologist Peter J. Catalano, MD, VP, Surgical Services, Steward Health Care (affiliated with St. Elizabeth's Medical Center in Boston) says, "The options today are tremendously different than they have been in the past, and with that comes the opportunity to treat patients of all ages." These new types of interventions, which are effective and have minimal morbidity, return patients back to school or work the following day with minimal pain. "These are radical changes for patients and doctors," he says.

However, the first-generation interventional ENT companies haven't largely delivered on their promise of enabling office-based procedures, says otolaryngologist Jerome Hester, chief medical officer and a co-founder of **SinuSys Corp.** "Sinus dilation techniques using balloons have really had a tough time transitioning into the office space due to their complexity, even though that was one of their intended benefits." Sinus dilation balloons apply acute, abrupt pressure to open the blocked sinus ostia, and in practice, he says, it takes time and resources to manage the anxiety and discomfort of patients. "You need to be set up to do this. You can't fit it into a busy office day without dedicating assistants to it."

When Thomas Schreck, the CEO and a co-founder of SinuSys, approached Hester with the idea of using an osmotic drug-delivery technology to provide self-regulated, smooth, low-pressure dilation of the sinuses, Hester says he understood the advantages of the concept, "not only for the transition into the office setting but because gentler, lower pressures are physiologically beneficial to the patient," he says. Hester joined Schreck in founding SinuSys Corp. in 2010, with funding from family and friends. The company has raised \$15 million to date, with Emergent Medical Partners coming in for the most recent Series E round.

A Device with a Pharmaceutical Heritage

Whereas the first generation of companies offering new interventions for the ENT market modeled themselves after interventional cardiology, where angioplasty balloons and stents gave patients an alternative to open-heart surgery, SinuSys has taken its cue from the pharmaceutical industry. Prior to founding SinuSys, Tom Schreck co-founded and headed up two pharmaceutical companies. He was most recently the Chairman of AcclRx Pharmaceuticals, a specialty pharmaceutical company. In 1998, he helped spin out

DURECT Corp. around the *Duros* osmotic drug-delivery technology of Alza Corp.

Schreck said he considered the problem of sinus dilation in the office setting. "The primary issue is that too much pressure is being exerted by the physician performing sinuplasty, so it is more painful than it needs to be for the patient and it requires analgesia

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and sedation in the office. A lot of practices are not set up for that, nor do they want the cost and liability."

Schreck also believed that abrupt balloon dilation wasn't the best thing for patients in terms of physiology. "Biological structures – cell structures, privileged membranes, very sensitive cilia – would prefer to be gently expanded and remodeled."

Coming from the pharma side, he says he looked at things differently. "Usually the FDA would ask for dose ranging studies. They would want to know the maximum tolerated dose, but they would also want a dose-ranging study to see the minimum effective dose." In the case of the new balloon dilation treatments, the therapeutic agent in question was pressure. "If one found the minimum effective dose of pressure, could we cause a shift where patients would feel more comfortable?" While the balloons delivering 180 psi of pressure are effective in treating sinusitis, "We're saying 'less is more.' We've been waiting for a simpler, kinder, gentler intraoffice procedure."

Schreck drew on his experience with the *Duros* osmotic drug delivery technology to develop a novel solution. The *Vent-Os Sinus Dilation System*, the first product from SinuSys, is essentially an osmotic stent. It's a capsule that swells in the presence of mucosal and other fluids in the nose. Delivered into the sinus cavity by a cannula system that looks very much like the olive-tip suction device with which ENTs are already familiar, the implant is positioned at the max-

CHRONIC SINUSITIS (CS) STATISTICS

1 Chronic sinusitis affects 12% of the US population or 29 million people, making it more prevalent than heart disease and asthma

2 CS resulted in 12.6 million physician office and 1.2 million out-patient department visits in 2005 (according to the CDC)

3 CS was responsible for \$8.6 billion in direct health care costs in 2007

4 In the US, approximately 4 million patients with CS are managed by 10,000 Otolaryngologists*

*Leerink Research Report, *Intersect ENT*, August, 18, 2014

Sources: Intersect ENT Prospectus, July 2014

illary ostia. The patient is relocated to the waiting room or a spot where he or she can sit quietly in a chair for about an hour, during which time the implant gradually swells to a fixed 5-mm diameter. In the intervening time, the doctor and the nurse are free to attend to other patients and office duties. After expansion, the capsule is removed and the patient is free to return to activities of daily life immediately. "The Vent-Os device was designed to be a one-handed, no-nurse, low-impact, low-cost, high-reward solution for the physician and the patient," according to Schreck. He also notes that the procedure requires a very limited anesthetic protocol, which involves placing pledgets soaked with anesthetic in the nose for 5-10 minutes before the procedure commences. "To date, these procedures have been limited to no analgesics or sedation, and 99% of our cases have been done in the office," he says.

Otolaryngologist Catalano, a clinical investigator for the *Vent-Os* clinical study, notes that gentle and gradual dilation has other benefits. It is known, from balloon angioplasty in cardiovascular applications, that abrupt dilation can overstretch the tissues and cause unintentional damage to a vessel, as well as initiate the release of histamine and other inflammatory agents. While the effects of sinuplasty on tissue haven't yet been characterized, Catalano says, "We have learned that there are two benefits from low-pressure dilation. There is very little trauma to the tissue that is being dilated, there is no tearing or bleeding, and there is enough time for the tissue to stretch, as opposed to a quick stretch." The second benefit, he says, is that there is much less recoil with slow dilation. "When you acutely and abruptly dilate a space [with a balloon], you get some recoil of the sidewalls and you lose 20-25% of the original dilation diameter. With *Vent-Os*, you probably only get about 5-6% recoil," he says.

The osmotic drug-delivery platform that forms the basis of *Vent-Os* has a long his-

tory. Schreck says, "The intersection of the porosity of the membrane and osmotic agents are exceptionally well characterized and well understood since the beginnings of Alza. We really know how these rate-controlled membranes work." They can also be reliably manufactured at a very low cost, Schreck says, an important feature of a cost-effective product.

Clinical Validation

Vent-Os gained a CE mark in September 2012 and 510(k) clearance in the US in December 2013. In September 2014, at the annual meeting of the American Academy of Otolaryngology in Orlando, FL, Catalano presented one-year results of a clinical study on the *Vent-Os Sinus Dilation System* involving 34 sinusitis patients treated at five sites. At one year, 93% of sinuses were visibly clear and functional in the 27 patients available for evaluation. The remaining 7% were excluded because the ostia simply could not be observed upon examination, notes Hester. As compared to patency results from balloon dilation technologies, *Vent-Os* was as effective if not more so, says Catalano.

"I think the data that we presented at Orlando provided nice closure to the questions about our device. Its simplicity and patient tolerability are self-evident. Its clinical success is far enough out that it compares favorably to any other technique. We are happy to provide the patients with an option they didn't have before," says Hester.

These patients include, according to Schreck, 10-20% of the 29 million sinusitis sufferers in the US who have failed medical management and who aren't indicated for surgery. Many patients will continue to need sinus surgery, because they have polyps or complicated forms of sinus disease, but *Vent-Os* will ideally serve not only patients with chronic sinusitis, but the very large group of patients with recurrent sinus infections. "Between bouts of sinusitis,

their sinuses clear,” Catalano points out. “They’re good for a month, then they’re sick again.” A lot of children fall into this category, he says, for whom *Vent-Os* provides a new treatment option.

A Physician- and Patient-Preferred Product

The company has now kicked off its commercial phase and faces some of the education challenges of a market that’s still at a relatively early stage, particularly with regard to the referring primary care physicians, although the first-generation companies have already done a lot of leg work here. “The non-sinus docs, the internal medicine physicians and pediatricians, aren’t all aware of the availability of interventions in the nose that are usually an hour or less in duration and can be done with combinations of local and topical anesthesia,” says Catalano.

Schreck says the commercial strategy will build from an installed base of early adopters and the company has identified 20 to 30 of them. “Fortunately, we have doctors like Drs. Hester and Catalano who have achieved 90% procedural success. In their first or second procedure they are adept at the deployment of the device. As we had thought, it is a relatively straightforward and easy procedure and technique to learn and they have become successful with it.”

Once the company has established its installed base, it will embark on a sales and marketing strategy to funnel patients with unmet medical needs into office-based ENTs who have not yet treated chronic sinusitis “and are encouraged by our technology to do so,” says Schreck.

In early September, the company hired Robert Hoxie, most recently a veteran of ENT company **Gyrus ACMI**, where he was president and CEO, to lead the commercial effort. “The strategy is to duplicate what Bob did at Innerdyne and Gyrus ENT, which was to create a hybrid model between a direct sales force and agents, which worked really successfully.” Schreck notes that Hoxie personally knows many of the company’s early adopters. “That will help with creating the installed base, and working on creating a very high-quality procedural success platform that can now evolve and emanate nationally.”

Ultimately Schreck believes adoption will be driven by consumer demand. “Patients want to

end their suffering and they don’t want to undergo surgery.” Hester says that patients who are being treated recurrently with antibiotics and steroids will gravitate towards “a lunchtime procedure that can maintain the opening in the sinus for at least one year, reducing their risk of treatment and improving their quality of life.”

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As it unrolls its first product, the company is already at work on a next-generation, drug-eluting version of its sinus treatment, a natural extension of a platform that began in drug delivery. The success of **Intersect ENT Inc.**, developer of a bioabsorbable drug-eluting implant, has highlighted the opportunity in this product area. Intersect, which raised \$51.2 million from its initial public offering in July 2014, has treated more than 25,000 patients to date with its *Propel* implant, as an adjunct to the sinus surgery procedures that open the sinuses.

The markets that SinuSys is targeting are huge, Schreck says. “We have a total addressable market somewhere in the \$3-6 billion range if you take the 10-20% of sinusitis patients in the US and multiply that by \$995, the cost of our bilateral maxillary kit.” That’s just the home market. The problem is as big abroad. “We recently had a firm contact seventeen key-opinion-leaders in India, and we learned that of 140 million patients suffering from sinusitis, 100 million have the maxillary sinus implicated only. That is a direct market for our device.” Cost and simplicity will drive opportunities in emerging markets, says Schreck.

Schreck is optimistic that everything is in place for the success the company’s products. “We have great technology, great innovation, great procedural success, and the ability to manufacture reliably and redundantly and at low cost. That’s what makes a business.” 