

START-UP



Windhover's Review of Emerging Medical Ventures

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Start-Ups Across Health Care

Biowave Corp.

Waves that relieve pain

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Norwalk, CT 06851
Phone: (203) 855-8610
Fax: (203) 286-2518
Web Site: www.biowave.com

Contact: Bradford E. Siff, Chairman,
President & CEO

Industry Segment: Neuromodulation
Devices

Business: Neuromodulation pain therapy

Founded: 2000

Founder: Bradford E. Siff

Employees: 4

Financing to Date: \$3.5 million

Investors: Meythaler Investment Partners
LC; JHK Investments LLC

Board of Directors: Ronald M. Burch, MD,
PhD (AlgoRx Pharmaceuticals Inc.);
Sunil J. Panchal, MD (H. Lee Moffitt
Cancer Center); L. Charles (Duke)
Meythaler (Fred Alger & Co.)

Medical Advisory Board: Sunil J. Panchal;
Stephen Hochschuler, MD (Texas Back
Institute); Ralph Rashbaum, MD (Texas
Back Institute); Brian Cole, MD (Rush
University Medical Center); Joseph V.
Pergolizzi, MD (Johns Hopkins University
School of Medicine); Ronald M. Burch;
Hugh C. Hemmings, Jr., MD, PhD (Weill
Medical College of Cornell University/
New York Presbyterian Hospital)

which has a similar device.

Biowave's founder, president, and CEO Bradford Siff believes his company's neuromodulation technology will not only compete against drugs and physical therapy, but it will also provide patients with a less risky and less costly alternative to implantable devices. The son of an inventor and entrepreneur, Siff is far from a garage shop tinkerer. With an MBA and a master's degree in engineering from Cornell University, he has raised more than \$3.5 million for Biowave, has overseen product design and development, and has designed protocols for and managed six clinical studies on the company's technology.

Siff and John Carter, PhD, an associate professor in engineering and medicine at Cornell and now Biowave's director of R&D, designed a device that mixes high frequency electronic waves and introduces them into the body through a disposable pad placed on the skin opposite the pain site. The signals pass through the body to a second smaller disposable pad at the treatment site. The nerve fiber membranes that lie between the opposing pads cause the electrical signals to mix, forming an electric field. This field contains a low-frequency component that is believed to interrupt the transmission of pain—a mechanism similar to that of local chemical anesthesia (lidocaine), except without any deleterious side effects, Siff says. The use of different-sized pads forces the low-frequency electric field to be focused on the pain site.

Biowave is developing two iterations of its technology, both of which comprise a portable instrument and a set of disposables. *Deepwave* is for use by physicians in clinics and hospitals; *Homewave* is a prescription device purchased by patients for follow-on

(Continued on next page)

Pain is the most frequent complaint that sends patients to the doctor.

For many, it can be relieved with simple treatments and a few aspirin. But for others, pain can be devastating. The **National Institutes of Health** estimates that 50 million lives are made unbearable by intractable, chronic pain. **Biowave Corp.** hopes to ease some of that suffering with non-invasive and minimally invasive neuromodulation technology designed to block pain at its source with a focused electrical field.

These days, when patients present to physicians with pain, the first step in treatment is usually physical therapy combined with prescription painkillers. If these drugs don't work, doctors resort to injection therapies such as facet block, epidural steroid, cortisone, and hyaluronic acid injections. Other

patients try to relieve their agony with TENS (transcutaneous electrical nerve stimulation)—devices that use electrical impulses to mask pain.

When all else fails, the last resort is often implantable neuromodulation devices such as spinal cord stimulators. These devices typically cost around \$25,000; an estimated 40,000 patients receive them annually. That adds up to a billion dollar market that analysts say is growing by 20% per year, making it a dealmaking focus for major medical device companies. Last October, **St. Jude Medical Inc.** paid more than \$1 billion to acquire **Advanced Neuromodulation Systems Inc.**, which has an implanted spinal cord stimulation device for chronic pain. In 2004, **Boston Scientific Corp.** paid more than \$700 million for **Advanced Bionics Corp.**,

therapy at home.

Deepwave is a minimally invasive (percutaneous) neuromodulation treatment intended as a replacement for the traditional first course of action—prescription drugs and physical therapy. In a hospital setting, treatments would begin within 24 hours of surgery and continue throughout the hospital stay.

Each treatment consumes a single-use set of disposable patches, a larger feed pad and a smaller pain site pad called a Percutaneous Electrode Array (PEA). The patented PEA provides a direct conductive pathway for current through the outermost layers of skin. PEAs are comprised of 1,000 microneedles, 3/4 of a millimeter in length, in a 2.5-inch diameter patch. PEAs feel like sandpaper to the touch, are comfortable, and cause no irritation, says Siff.

PEAs are applied to the patient by a nurse or physician assistant. The patient carries the 8 × 5 × 2-inch, 3-pound device to the waiting room where he or she can control the intensity and read a magazine during the 30-minute treatment.

Siff reports that clinical studies of *Deepwave* have shown that following a 20 to 30 minute treatment, patients experience an immediate up to 80% average reduction in pain and a significant increase in range of motion and mobility. "The benefits last for up to 24 hours, without the side effects that are common to drugs, surgery, and implanted devices," he says.

Biowave's *Homewave* is a non-invasive neuromodulation system prescribed for home use by physicians for their patients to maintain their comfort level following successful *Deepwave* therapy in clinics or hospitals. The battery-operated *Homewave* device is about half the size of the *Deepwave* device, and it utilizes proprietary reusable pads. *Homewave* therapy comprises one 20-minute treatment per day for as long as needed.

Together, Siff and Carter now share five patents covering the Biowave technology. Several additional patents

are pending, and others on new technology will be filed shortly. "We are building a strong patent fence around our technology," he says.

Siff anticipates that Biowave's technology will compete against all treatments for pain—drugs, physical therapy, injection therapies, implantable devices, surgery, and TENS—the only other electronic pain treatment that has received marketing clearance by the FDA.

TENS might seem to be Biowave's most direct competition. Companies such as **Encore Medical Corp.**, which



"The bottom line is that Biowave not only has better efficacy immediately post-treatment over TENS, but it has a significant benefit over a 24 hour period making it the only practical once-per-day treatment."

— Brad Siff.

owns **Empi Inc.** and acquired **Complex Technologies Inc.** last November, and **RS Medical Corp.** are the major players in this \$500 million, primarily home-use US market. Yet Siff thinks that Biowave can demonstrate an advantage here because its technology generates an electrical field in deep body tissue, not just across the surface of the skin, like TENS.

He reports that results from clinical trials bear that out. An interim analysis of one double-blinded randomized crossover study at **Weill Medical College at Cornell University** comparing Biowave with TENS found that the Biowave treatment provided an 83% percent reduction in pain after one hour and the improvement was still 73% 24

hours later. By comparison, TENS showed a 63% reduction in pain after an hour and only 30% after 24 hours. The bottom line, says Siff, is that Biowave not only has better efficacy immediately post-treatment over TENS, but it has a significant benefit over a 24-hour period making it the only practical once-per-day treatment.

Biowave inked a licensing deal with an undisclosed Japanese medical device firm in June 2005. That firm ran several successful clinical trials, obtained regulatory approval for the device, and launched in Japan at the end of October 2005. Siff says the Biowave device captured 5% of the Japanese market for chronic pain relief in the first two months.

In the US, Biowave received marketing clearance for its *Deepwave* device using non-invasive pads from the FDA in December 2005. The company is in the process of filing a 510(k) application for its minimally invasive PEAs for use with its *Deepwave* device in doctor's offices, clinics, and hospital settings, as well as another 510(k) application for its home prescription *Homewave* device that utilizes non-invasive pads. The company expects to receive marketing clearance from the FDA on both of these applications by the middle of 2006.

Siff anticipates launching in the US market in the third quarter of 2006. He is in the midst of negotiating strategic partnership deals for distribution initially in orthopedic/sports medicine, pain clinic, and post-operative markets. Distribution partners will also cover follow-up *Homewave* sales to the physician-referred patients from these markets.

On the reimbursement front, Biowave is applying for its own CMS codes, but in the meantime, Siff says that physicians can use existing miscellaneous neuro or orthopedic codes.

The company's initial markets in the US, for joint pain, back pain, and for post-operative use in clinics and hospitals alone are about \$2 billion in size. The physician-referred home prescription US market has a potential

of about \$1 billion, Siff says.

Once Biowave has established credibility in its initial target markets, it can then move into broader professional and consumer segments. The professional segment includes the 320,000 physicians and health care providers in the US whose focus is on alleviating pain in private practice, clinics, and hospitals. Their specialties range from orthopedics, neurology, and sports medicine to general and alternative medicine.

For now, Siff's immediate goal is establishing the credibility of Biowave technology through publishing clinical data in peer-reviewed medical journals. So far, the company's first dosage study, completed at Weill Medical College of Cornell University, was published as an abstract in *Anesthesia and Analgesia* in March 2003. This and the follow-on double-blinded randomized crossover study at Cornell will be analyzed together and submitted for publication early in Q2 of 2006. The company has also started a post-operative pilot study treating total knee replacement (TKR) patients at the **Hospital for Special Surgery** in New York City. This will lead to a controlled study on TKR patients, the results of which are expected to be submitted for publication within one year.

With all the enormous numbers that get bandied about in the discussion of pain it would seem easy for "good greed" to set in. But there are no exaggerated projections from Biowave. Siff has set more modest—and probably, realistic goals—for his company. What's ahead in the next decade? "I think we will have achieved sales well in excess of \$200 million, and Biowave will have proven itself," predicts Siff. He ultimately envisions the sale of Biowave to a large strategic partner with major distribution channels in orthopedic and sports medicine or pain management markets. But keep an eye out for Brad Siff. This competitive CEO is certain to be making waves somewhere else.—**Alan Hall**

MediWound Ltd.

Rapid, selective debridement of burned tissue

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Yavne, Israel
Phone: +972-8-9324010
Fax: +972-8-9324011
Web Site: www.mediwound.co.il

Contact: Marian Gorecki, PhD, CEO
Industry Segment: Wound Healing

Business: Enzymatic debridement of eschar in second- and third-degree burns

Founded: 2001

Founder: Lior Rosenberg, MD, CMO

Employees: 18

Financing to Date: \$14 million

Investors: Clal Biotechnology Industries Ltd.

The first step in treating serious burns is to remove the burned layer of skin, or eschar; this facilitates assessment of the extent of the injury, prevention of infection caused by necrotic tissue and preparation of the wound bed for healing or for skin grafts. Surgical excision is the current standard of care. It is an expensive, painful procedure performed under general anesthesia, and it is rife with complications that include excessive bleeding and scarring. It is also imprecise—surgical debridement frequently removes healthy tissue along with the eschar.

Israeli start-up **MediWound Ltd.** is developing a minimally invasive enzymatic alternative to surgical debridement. Its *Debrase Gel Dressing (DGD)* is derived from bromelain, a mixture of proteolytic enzymes extracted from pineapple plants. Bromelain is highly selective for necrotic tissue: when topically applied to the injured site, it quickly digests and removes the eschar, leaving a clean wound bed. This makes it easier for physicians to diagnose the extent of the burn, and to more easily distinguish partial-thickness burns that can heal without surgery from full-thickness burns that require excision of necrotic tissue and grafting. Because it preserves more healthy tissue than does surgical debridement, MediWound believes that treatment with *DGD* may reduce the overall need for skin grafts in deep

burns, and thus reduce hospital stays.

The company's technology was invented in the 1950s by a US physician, Gerald K.V. Klein, MD. Klein originally developed bromelain formulations for non-medical applications, including meat tenderizing. He later discovered bromelain's debriding activity. Working with fellow physician John C. Houck, MD, Klein went on to refine a method for extracting and purifying bromelain to boost its ability to digest necrotic skin tissue.

MediWound's founder and chief medical officer Lior Rosenberg, who is also head of the plastic surgery department at **Ben-Gurion University**, was intrigued by Klein and Houck's research. He licensed the technology from Klein's estate and, under a compassionate use protocol, began to use it on second- and third-degree burn victims at **Soroka Medical Center**. Rosenberg and his colleagues treated more than 250 patients between 1985 and 2000, and they published their findings in 2004 in *Burns: Journal of the International Society for Burn Injuries*. They found that, in most cases, one or two four-hour applications of the *Debrase* dressing completely removed the eschar. Patients experienced minimal side effects and blood loss.

Rosenberg established MediWound in 2001 to commercialize the technology. The company has an experienced

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