RIVERVEST® News

WINTER 2010

Investing in Life Science Innovation

RiverVest co-leads $38.5 million Series B financing to advance breakthrough treatment for ear disorders

Otonomy, Inc. is on the verge of revolutionizing the way doctors treat hearing and balance disorders. “The ear is one of the last great frontiers of pharmaceutical science,” says Jay Lichter, Ph.D., co-founder of Otonomy.

“There are 30 million people who suffer from some form of hearing loss in the United States. And yet, prior to our company’s founding in 2008, there wasn’t a single company working to discover, develop or market drugs for treating hearing loss diseases.”

In January 2008, Dr. Lichter was stricken with a debilitating dizziness that led him to seek care from Jeffrey Harris, M.D., Ph.D., chief of the Division of Otolaryngology-Head & Neck Surgery at University of California, San Diego.

Dr. Harris diagnosed Dr. Lichter with Ménière’s disease, a disorder of the inner ear that affects balance and hearing. There is no known cause of the disease and no FDA-approved drug treatment to control its symptomatic episodes of vertigo, tinnitus (ringing in the ears), fluctuations in hearing or aural fullness. (See accompanying story).

Fortunately for the 615,000 Americans who suffer from Ménière’s disease, Dr. Lichter is an entrepreneur who specializes in therapeutic drug discovery and, because of his diagnosis, became highly motivated to dig deeper into the problem of treating ear disorders.

Dr. Lichter began exploring licensing opportunities to develop a sustained-release drug formulation proposed by Dr. Harris. “I checked the patent databases to see what was out there,” he says. “Nothing. This was wide-open territory, a very exciting white space.” By May 2008, the doctors had filed 25 patents and founded Otonomy.

“We’ve created an intellectual property estate that blocks anybody from injecting any drug with sustained release properties across the ear drum into the middle ear space to treat either middle or inner ear disorders,” says Dr. Lichter. “We’ve got the team, we’ve got the technology, we’ve got the money. We’re going to make Otonomy the Alcon of ear care.”

Jay Lichter, Ph.D.
Co-founder, Otonomy

The $38.5 million Series B investment will support Otonomy’s first two product candidates through pivotal clinical studies and move a third program into the company’s pipeline of locally delivered drugs to treat disorders of the ear.

Thermosensitive gel delivers sticking power for new ear therapies

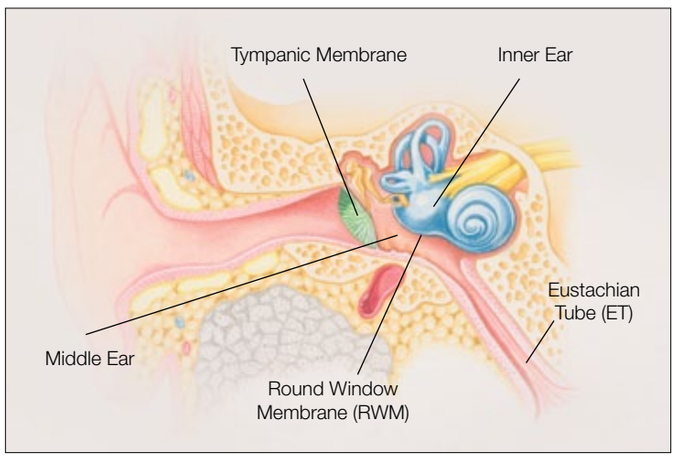
“The great challenge in treating ear disorders is reaching the cochlear (hearing) and vestibular (balance) organs that reside within the inner ear,” says RiverVest Venture Partner John McKearn, Ph.D., who began following Otonomy’s promising new ear therapy platform in 2008 and now sits on the company’s board of directors. “The inner ear is a privileged site. It is physically and chemically designed to reject foreign substances.”

“A physician would have to administer enormous amounts of oral or intravenous steroids to get equivalent exposure to the inner ear,” says Dr. McKearn. “Such a high dosage would put a patient at risk for systemic toxicity.”

In recent years, physicians have begun using intratympanic (IT) injections to deposit steroids directly into the middle ear via a small perforation in the tympanic membrane (eardrum). Once inside the middle ear, therapeutic drugs may be absorbed through a thin membrane called the round window—the gateway to the inner ear.

“The injections are effective,” says Paul R. Lambert, M.D., professor and chair of the Department of Otolaryngology-Head & Neck Surgery at the Medical University of South Carolina. “But they don’t last. The solution drains down the Eustachian tube as soon as the patient talks, swallows or sits up.” To address this problem, physicians administer multiple rounds of IT injections, each round requiring long periods of complete immobility.

“It’s impractical. Patients stop coming after two or three injections,” says Dr. Lambert. When contacted by Jeffrey Harris, M.D., Ph.D., about an extended release formulation he was developing, Dr. Lambert was enthusiastic about its potential.



Dr. Harris and his Otonomy business partner, Jay Lichter, Ph.D., who himself suffers from Ménière’s disease, proposed a single IT injection of a thermosensitive poloxamer combined with a steroid in a novel formulation they call OTO-104. “The poloxamer is liquid and thus easy to inject at room temperature,” says Dr. Lambert. “But as soon as it reaches body temperature, it gels.”

As a gel, the formulation adheres to the epithelial lining of the middle-ear space, where it can remain in place long enough to deliver the drug for a prolonged period of time to the inner-ear fluids.

“It’s an elegant solution with broad therapeutic application,” says Dr. McKearn.

OTO-104 is currently in a Phase 1b clinical trial to test safety and efficacy in treating patients with Ménière’s disease. A second formulation, OTO-201, is expected to enter clinical trials in 2011 for the treatment of middle ear infections (otitis media), a common childhood ailment.

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$46 Million preferred stock financing puts IDEV on clear path to profitability

IDEV Technologies, Inc. (IDEV) recently completed a $46 million preferred stock financing led by a strategic global healthcare company and joined by new investor Piper Jaffray and previous investors RiverVest Venture Partners, PTV Sciences, Bay City Capital and Heron Capital.

In August 2006, RiverVest led a $19 million Series B round of financing to support IDEV's development of the SUPERA® self-expanding nitinol stent.

"We saw great promise in SUPERA's patented interwoven design, which offers improved flexibility, radial strength, and kink and crush resistance compared to other marketed stents," says Jay Schmelter, managing director of RiverVest and member of IDEV's board of directors.

Since then, SUPERA has moved rapidly through a series of milestones and is currently CE marked for biliary and peripheral vascular use in Europe and 510(k) cleared for biliary use in the U.S. The company's next-generation delivery system, VERITAS™, was recently launched in Europe and is on track for introduction in the U.S. by year's end.

"This is an exciting time," says Christopher M. Owens, president and CEO of IDEV. "In addition to completing the financing and successfully launching VERITAS in Europe, we've seen significant progress in our key initiatives."

Key initiatives include completing the ongoing, multi-center SUPERB IDE clinical trial, which seeks to demonstrate SUPERA's safety and efficacy in treating subjects with obstructive superficial femoral artery (SFA) disease. Data from this study will be submitted for FDA approval to allow vascular labeling in the U.S.

In addition to funding the SUPERB study through completion, proceeds from the latest series of financing will be used to initiate clinical trials in support of other peripheral indications, develop new interventional products, and increase sales and marketing initiatives to support continued revenue growth.

"We anticipate this financing will drive IDEV to cash flow positive and advance its strategy to address the unmet clinical needs of the nearly 120 million patients who suffer from peripheral artery disease," says Schmelter.

MILESTONES

- **Centerre Healthcare Corporation** is currently constructing its fifth inpatient rehabilitation hospital, which is expected to open in early 2011, in partnership with Harris Methodist Hospital Fort Worth.
- **CGI Pharmaceuticals, Inc.** was acquired by Gilead Sciences, Inc. (Nasdaq: GILD) on July 8, 2010, for up to $120 million in cash, with the majority as an upfront payment and the remaining as a milestone payment based on successful completion of a Phase 2 clinical trial.
- **MacroGenics, Inc.** entered into separate collaboration agreements with Boehringer Ingelheim and Pfizer Inc. in October 2010 that will provide more than $75 million in non-dilutive capital over the next three years with the potential for additional large success milestones.
- **Mpex Pharmaceuticals, Inc.** presented positive Phase 2b results of its cystic fibrosis clinical trial at the annual meeting of the American Thoracic Society in May 2010.
- **Tryton Medical, Inc.** raised approximately $20 million through an outside-led Series D Preferred financing in September 2010 that is expected to finance the company to cash flow positive operations.

Excaliard's anti-scarring drug produces safe, visible results

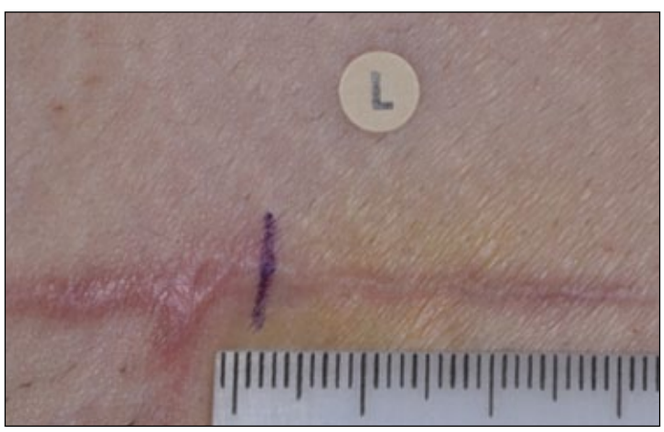
Only three years after RiverVest co-founded Excaliard Pharmaceuticals, the company's lead drug candidate, EXC 001, is nearing completion of three Phase 2 clinical trials. The new chemical entity is showing significant promise in reducing the severity of skin scarring following a surgical procedure.

EXC 001 is a second-generation antisense medicine that works at the molecular level to intercept and break down the gene products that cause fibrosis. "It is an exciting and novel approach that represents the first time an antisense medicine has been used for this significant, unmet clinical need," says Nicholas Dean, Ph.D., co-founder and chief scientific officer of Excaliard.

In a randomized, double-blind multicenter study conducted in the U.S., EXC 001 or placebo was administered intradermally adjacent to the surgical incision in patients who were undergoing elective abdominoplasty surgery, or "tummy tuck." Data reported at 12 weeks post-surgery demonstrated statistically significant improvement (see photo).

In addition, EXC 001 was well-tolerated with no clinically important adverse effects. The 24-week post-surgery data will be released in December 2010.

Excaliard has focused its initial clinical programs on skin scarring in cosmetic surgical procedures. More than 1.5 million cosmetic surgeries and 5 million reconstructive procedures were reported in the U.S. in 2009. An additional 35 million non-cosmetic surgeries are performed annually, creating significant treatment opportunities. Conservative market projections suggest a potential of more than $1 billion in annual sales in the U.S. alone.



Photograph of scar from an abdominoplasty procedure. To the right of the blue line, the incision was treated with EXC 001. To the left, the incision was untreated.

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