

TARIS Biomedical Inc.

(A#2009900200)

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Issue: *Start-Up* Sep. 2009
Section: Start-Ups Across Health Care (Medium Length Article)
Article Type: Emerging Company Profile
Industry Segment: Pharmaceuticals/Pharmaceutical Technologies/Drug Delivery
Therapeutic Categories: Gynecological, Urological; Gynecological, Urological/Bladder Disease
Companies: Bioniche Life Sciences Inc.; Johnson & Johnson; Johnson & Johnson/Ortho-McNeil Pharmaceutical Inc.; Massachusetts Institute of Technology
Summary: "Treat diseases locally" is a mantra espoused by a growing number of companies but few as yet have actually mustered the means to do so. TARIS Biomedical believes it has what it takes to become a pioneer of minimally invasive drug delivery devices. Its first product offering will be a pretzel-shaped device the size of a paper clip that will release medication inside the bladder, initially as a treatment for interstitial cystitis.

Further Analysis:	Title	Magazine	Issue	Article ID
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	Women's Health: Breaking the Incontinence Barrier	<i>Medtech Insight</i>	Oct. 2008	<u>2008400076</u>

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TARIS Biomedical Inc.

Treating bladder disorders from the inside

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Web Site: www.TARISbiomedical.com

Contact: Christine Bunt, COO

Industry Segment: Drug-Device Convergence

Business: Delivering drugs through osmotic pressure

Founded: April 2008

Founders: Christine Bunt; Michael Cima, PhD; Robert S. Langer, ScD

Employees: 9

Financing to Date: \$15 million

Investors: Flybridge Capital Partners; Polaris Venture Partners; Flagship Ventures

Board of Directors: Dennis Ausiello, MD (Massachusetts General Hospital); Kevin J. Bitterman, PhD (Polaris Venture Partners); Christine Bunt; Michael J. Cima (Massachusetts Institute of Technology); Michael A. Greeley (Flybridge Capital Partners); Ed Kania (Flagship Ventures); Robert S. Langer (Massachusetts Institute of Technology); Ernest Mario, PhD (PPD Inc.)

Scientific Advisors: Michael J. Cima; Joseph Grocela, MD (Massachusetts General Hospital); Robert S. Langer; Robert Mayer, MD (University of Rochester); Robert M. Moldwin, MD (Arthur Smith Institute for Urology and Long Island Jewish Medical Center); J. Curtis Nickel, MD (Queens University); Kenneth Peter, MD (William Beaumont Hospital); Shahin Tabatabaie, MD (Massachusetts General Hospital)

"Treat diseases locally" is a mantra espoused by a growing number of companies but few as yet have actually mustered the means to do so. **TARIS Biomedical Inc.** believes it has what it takes to become a pioneer of minimally invasive drug delivery devices. Its first product offering will be a pretzel-shaped device the size of a paper clip that will release medication inside the bladder, initially as a treatment for interstitial cystitis (IC).

Why focus a technology with the potential to be a broad platform first on bladder disorders? COO Christine Bunt says the degree of unmet need among millions of patients suffering from IC and other bladder conditions provides compelling reason to start there. She makes a good case and that's hardly surprising; doing so is her professional specialty. Prior to co-founding TARIS, Bunt was VP of marketing and commercial development at CombinatoRx Inc. and before that led commercialization of rofecoxib (*Vioxx*), rizatriptan (*Maxalt*), and cardiovascular hospital products at Merck & Co Inc.

Bunt explains that in the US, about four million people are suffering with IC at any given time. It's a flaring condition, similar in that way to rheumatoid arthritis and Crohn's disease. With IC, chronic inflammation in the bladder tends to flare three times a year, causing people to experience severe pain and very frequent voiding. Far worse than an ordinary urinary tract infection, Bunt explains that job loss is not uncommon among people with IC, and the suicide rate of this patient population is five to seven times the national average.

Just two treatments have been approved for IC, and Bunt says neither of them works very well. An oral pentosan polysulfate sodium product (*Elmiron*) marketed by **Johnson & Johnson's Ortho McNeil-Janssen Pharmaceuticals Inc.** showed in clinical trials a response rate of 35% at best, she says. There is a long onset of efficacy for that medication, "as much as six to nine months, if it works at all," she notes. The second approved drug, dimethyl sulfoxide or DMSO (*RIMSO-50*), is a liquid "instillation" product delivered by catheter directly into the bladder, to bathe the inflamed organ's lining with medication. Catheterized patients retain the solution for 30 minutes, and the bath may be performed frequently depending on the severity of the disease.

The Interstitial Cystitis Association web site explains that DMSO is the only approved instillation product for IC, and because of its ability to penetrate the lining of the bladder is often combined with other medicines including analgesics, heparin, bicarbonate, and steroids. Marketed by **Bioniche Pharma USA LLC**, DMSO instillations can cause patients to have a strong garlic odor on their breath or skin for 24 hours after each treatment, and some individuals experience flu-like symptoms. Because of these side effects, Bunt says the product is "hardly used."

At present, Bunt says most urologists prefer to treat IC patients experiencing disease "flares" who can no longer manage their condition with oral medications—typically a mix of NSAIDs and mood elevators such as amitriptyline HCl (*Elavil*)—with instillations of the topical anesthetic lidocaine. The typical regimen is three times a week, in some patients daily, for a total duration of six to 12 weeks. "It's still horribly inconvenient, but has been shown to be effective in several controlled trials," she says, adding that the National Institutes of Health and the Food & Drug Administration recognize that 90% of instillation treatments given to IC patients are performed off-label.

Given the good results already established for lidocaine instillations, TARIS Biomedical has decided its first product will be a lidocaine-releasing device. Like other companies gearing products to a specialized medical market, Bunt says TARIS has worked closely with urologists to understand how this subset of physicians currently work with patients, and what *their* needs are, in addition to understanding the needs of patients.

The device TARIS is developing seems likely to fit in well with the existing approach to caring for IC patients. Individuals with advanced disorders have frequent cystoscopies scheduled to monitor progression of the disease, which can become so severe that the pain becomes neuropathic and exceedingly difficult to relieve. In the worst cases, the bladder becomes fibrotic from chronic inflammation and is ultimately removed, sometimes leaving patients with "phantom" pain even after the organ is gone.

Because advanced IC patients are regularly catheterized for disease monitoring anyway, Bunt reckons it will be simple enough for urologists to insert and remove her company's device during scheduled visits. The device has the potential to provide sustained delivery of lidocaine for weeks or months, she says—clearly a huge improvement over thrice-weekly instillations during disease flare-ups.

Bunt explains that the TARIS device is deliberately simple. "We studied carefully what went wrong with other [implantable medical] devices," she says, explaining that hindsight showed some were too big or too heavy while others had too many moving parts, or impaired an organ's function by being anchored in it.

The device TARIS is developing works through osmotic pressure. Much as the sustained-release drug-delivery specialist Alza (long since acquired by Johnson & Johnson) enhanced many pharmaceutical

companies' drugs by encasing medication in a coating with just a tiny hole drilled in it, the TARIS device is a silicon tube with a laser-drilled hole. [W#200110056] A salt formulation of lidocaine will fill the tube and steadily fizz or pump out through the hole when immersed in the liquid inside the bladder. That's the beauty of osmotic pressure: the denser concentration of salt naturally wants to move into the less-dense fluid and steadily pushes out. "We can easily control the release rate by changing the surface area," she notes.

Designing the device so it wouldn't be voided out from the bladder was an intriguing technical challenge, Bunt says: "The bladder is an amazing organ; so much pressure is created." About 10 prototypes were tested in laboratories at the **Massachusetts Institute of Technology** before the problem was solved with a wire that runs the length of the tube. Bunt explains that the wire can be straightened out and pushed through a catheter, but then shape memory makes the device fold up again into a pretzel that floats in the urine and cannot be pushed out through the urethra. Credit for the device design goes to a PhD student, working in the MIT laboratories of Michael Cima and Robert Langer, who has since been hired by TARIS.

The company anticipates beginning clinical trials this autumn, and Bunt believes that making its device removable—implanted by cystoscopy and removed that way—will makes it good not only for IC but also for additional indications such as bladder cancer and possibly over-active bladder. "We're very interested in bladder cancer," Bunt declares, noting that here as in IC, intravesical therapy or instillation is the standard of care after surgical removal of the tumor. Again as in IC, bladder cancer patients are scheduled for frequent cystoscopies to monitor their progress, which presently finds recurrence in some 70% of patients who've had tumors removed. "There is a tremendous opportunity for us to step in and provide sustained-release medication," Bunt asserts.

Although Bunt says TARIS intends to "be in the bladder for a long time," she says the vision of the company extends well beyond this organ. "We want to be seen as a pioneer in the combination of drugs and devices," she announces. This first pretzel-shaped device could go into other organs where shape retention would be beneficial, she muses, and the start-up already has intellectual property covering manufacture of a bioresorbable drug delivery device. Bunt declines to discuss specifics of where beyond the bladder TARIS might seek to deploy a drug delivery device, but it's not hard to imagine such an item delivering, say, hormones or medications inside ovaries, testes, or lungs.

With its trio of esteemed co-founders including MIT's Michael Cima and Robert Langer, a stellar board of directors and venture capitalists who have already invested \$15 million in the year-and-a-half-old company, TARIS has excellent odds of making a major impact with minimally invasive devices for drug delivery. [W#200930279]--Deborah Erickson