

BioAdvance NEWS

Advancing the Business of Life Sciences

YAUPON THERAPEUTICS COMBINES THE EFFICIENCY OF A START-UP WITH A BIG-COMPANY PIPELINE PHILOSOPHY

Bringing a new drug into the clinic is a significant milestone for any young pharmaceutical company, but to have multiple candidates in the clinic is unusual. Yaupon Therapeutics Inc., founded in 2002, has two drugs in clinical trials (with one in a pivotal study), another entering phase II, and two more entering human studies this year.

The company was formed in 2002 by two researchers at the University of Kentucky and pharmaceutical executive Robert Alonso, Yaupon's CEO. "Our focus," says Alonso, "is to identify potential drugs from underserved academic centers"—research institutions that are highly innovative, but lack the substantial technology transfer offices prevalent at many larger institutions.

The company was originally founded on the therapeutic lobeline, developed from the plant *lobelia inflata*, known as Indian tobacco. Although lobeline has a long history of use dating back to Native Americans, Yaupon has seized upon a therapeutic area that until now has had no products—relapse prevention for methamphetamine addicts. Alonso points out that methamphetamine—known as crystal meth on the street—"is one of the most devastating drugs of addiction." The NIH estimates there are approximately one million users of meth in the US alone, and abuse is growing globally at such an alarming rate that many call it "the world's most dangerous drug."

Yaupon is studying lobeline in relapse prevention with an aim to help meth addicts re-enter the community after detoxification. It is known that dopamine is released in anticipation of and in response to amphetamines. When a meth addict returns to his/her social environment the brain will recognize the "old" environmental queues. This then causes the release of dopamine in anticipation of receiving meth, thus causing craving. The relapse prevention study will test the compound's ability to avert this anticipatory dopamine release and thus ease entry back into a social environment. Lobeline does this by metabolizing excess dopamine produced by the brain. The end goal is that the "detoxified" addict will have less craving and less chance for relapse when taking regular doses of lobeline.

Right now, lobeline is in a Phase 2A efficacy study at University of California (UC), San Francisco. Researchers at UC, Los Angeles, will lead a relapse prevention study in 2007, which will be the first of its kind in methamphetamine addiction.

When Opportunity Knocks
Although the company was founded based on lobeline, its business model allowed it to capitalize on a product ripe for advancing into late stage clinical studies. In June of 2004, company executives heard of an old cytotoxic agent that could be used topically for dermatological diseases. After developing a novel formulation, filing patents, and

working with the FDA, in 2006 Yaupon began enrolling for its pivotal study in cutaneous T-cell lymphoma (CTCL). This cancer is a type of non-Hodgkin's lymphoma affecting an estimated 20,000 patients in the US and 60,000 worldwide.

The pivotal clinical trial is being led by Fox Chase Cancer Center and includes the University of Pennsylvania, Duke University, Stanford University, M. D. Anderson Cancer Center, Harvard University and New York University. Alonso expects the clinical trial to be completed by mid-2008. Because the compound – Clearazide™ – has been fast-tracked by the FDA, Yaupon can begin filing parts of its paperwork with the agency right now. "The last thing to get filed is the clinical study report," notes Alonso. Once that is submitted, FDA review should be completed within six months and Alonso hopes the topical agent will be on the market by 2009.

Yaupon has two more candidates close to an IND: an orally administered smoking cessation agent (nornicotine — derived from the tobacco plant), and YT-1006 (a N-methyl-D aspartate [NMDA] antagonist that treats neuropathic pain). When YT-1006 is administered with morphine, it will decrease the amount of morphine required to block pain, prevent morphine tolerance from developing, while having a safer profile than other NMDA antagonists. Alonso is hoping to begin clinical trials in 2007.

A Big Company Philosophy

There are other companies that are developing drugs licensed from university sources, but what makes Yaupon unique is that it has moved its compounds into clinical trials without the types of major financial investments most other companies have required. Much of Yaupon's funding comes from National Institutes of Health grants—grants totaling \$15 million to date. And the company has raised \$6 million from investors such as BioAdvance, Ben Franklin Technology Partners of Southeastern Pennsylvania, TDH Capital Corporation, Osage Ventures, and Pennsylvania angels.

Alonso notes that Yaupon has a big company philosophy with a small company strategy, a result of the management team's experience in both large and small pharmaceutical companies. He also proudly notes that without its original investors, the company would not be where it is today. "My view is that BioAdvance is our most important investor because they brought a significant amount of visibility and credibility to our research efforts. With our investors behind us, Yaupon and its pipeline are clearly moving forward."

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INFRA SCAN MAKES BRAIN IMAGING PORTABLE

Funding early-stage life sciences firms in the Philadelphia region

Milestones

\$11 million in seed investments made to **21 startup companies**
And 9 additional academic and commercial projects

\$110 million in additional capital raised

Recent fundraisings

NuPathe Inc.
\$15 million
Yaupon Therapeutics
\$4 million

Companies in Phase III Trials

Yaupon Therapeutics

Companies in or through Phase II Trials

Acuity Pharmaceuticals
Alteris
Avid Radiopharmaceuticals
Eagle Vision
Infrascan

Companies in or entering Phase I Trials

Marillion
Melior
Protez Pharmaceuticals
TheraQuest
Yaupon

Investments in areas such as:

Addiction	Infectious Disease
Alzheimer's Disease	Metabolic Diseases
CNS Diseases	Ocular Diseases
Cancer	Respiratory Disorders
Cardiology	

BioAdvance Contact

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Getting into the clinic early is a goal of medical device companies, but InfraScan's handheld brain injury diagnostic device, the Infrascanner™, was in clinical trials long before there was a company to develop and market it.

The University of Pennsylvania's Britton Chance, now professor emeritus in the department of biochemistry & biophysics, developed the technology in collaboration with a leading neurosurgeon from Baylor College of Medicine, Claudia Robertson. Using near infrared (NIR) technology, the Infrascanner can detect the differential absorption of NIR between brain tissue that is not infused with hemoglobin, and injured brain tissue where blood (hemoglobin) is present or hematomas between the meninges. Initial clinical trials to determine the device's usefulness in rapidly and noninvasively identifying the presence of brain hematomas were carried out by Dr. Robertson and her colleagues. Their study ultimately found that this device could accurately and sensitively detect hematomas in and around the brain.

An Entrepreneur's Itch

But this story would have gone nowhere had it not been for the interest of entrepreneur and medical optics specialist, Baruch Ben Dor. Ben Dor, coming out of a startup company where he was CEO, itched to begin a company of his own. "Since my background is in medical optics, I contacted one of the gurus in the field, Dr. Chance, whom I knew [and] who had a lot of intellectual property," Ben Dor relates. After spending months working in Chance's laboratory, learning about his technologies, Ben Dor selected the NIR brain scanner because he saw this as the "most mature" in terms of its ability to get to market. "The proof of concept is done, and it is really ready for commercialization," recalls Ben Dor about this early phase of his search.

Now Ben Dor's hard work began. He wrote a business plan and tried to raise money. "I failed," he notes, but, like a good entrepreneur, he "listened to the feedback I got...."

He succeeded after following advice. People told him to improve the business plan and increase the size of his team.

To develop the technology further, he teamed up with Banu Onaral, director of the School of Biomedical Engineering, Science & Health Systems, and her colleagues at Drexel University. Onaral's specialty is biomedical signal processing and imaging. The new team was able to apply for and receive a Phase I SBIR grant from the U.S. Navy to help develop the device.

Building the Business

Now, with a prototype device in hand, Ben Dor worked on developing the business. He joined with two students at the Wharton School at Penn to enter Wharton's business plan competition. Things began to happen quickly then, explains Ben Dor: "In April 2004 we won the Wharton business plan competition." InfraScan incorporated in July 2004 and that summer, they received a pilot investment of \$50,000 from BioAdvance, which allowed the company to do some due diligence on their plan. In Jan. 2005, BioAdvance awarded InfraScan another \$450,000.

The company now has received \$1 million in grants from the Navy, an additional \$100,000 in grants from a U.S. Army SBIR, and \$500,000 from the Ben Franklin Technology Partners, aside from BioAdvance's investment.

Pilot clinical work began at the Hospital of the University of Pennsylvania last year, and researchers at Penn and Baylor are now enrolling patients in clinical trials for FDA approval. At present, 100 patients are enrolled at these sites, and the goal is to add two additional centers and enroll a total of 400 patients.

A New Way to Diagnose Brain Bleeding

What makes the Infrascanner so unique is that right now, there is no easy way to confirm the presence of brain hematomas in head trauma patients. The Infrascanner could be used in the ambulance or emergency room to rapidly detect brain hematomas



The Infrascanner®, a handheld device for brain imaging.

that need immediate surgery, can be used on head trauma patients in the ICU as a more accurate means of monitoring bleeding into the brain than physical exam techniques in use now or the cumbersome means of taking a CT scan once a day, and can have an immediate application in the battlefield to determine the extent of brain bleeding with head trauma. The latter use is of such great concern to the military that the Navy plans to put the Infrascanner through field testing in early 2007, to expedite adoption on the battlefield.

Ben Dor is optimistic that the company will have FDA clearance to market the Infrascanner in the U.S. in the second half of 2007. But even without FDA approval, the company is able to sell its product to physicians and hospitals in India, where other scanning methods are not readily available.

And the market is obvious: by conservative estimate, there are 1.5 million traumatic brain injuries in the U.S. each year, resulting in over 500,000 hospitalizations. And in the types of military excursions we now have, with soldiers suffering from traumatic brain injury even from being near, not necessarily in, a site of explosion, traumatic brain injury levels are relatively high. So the market for the Infrascanner is clearly there: and BioAdvance saw the possibilities and made the first investment.

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