

AVID RADIOPHARMACEUTICALS AIMS TO HARNESS MOLECULAR IMAGING TO DIAGNOSE ALZHEIMER'S DISEASE

Alzheimer's disease afflicts about four-and-a-half million people in the United States, according to the Alzheimer's Association. About twice as many people suffer from mild cognitive impairment that may or may not progress to Alzheimer's. But currently, there's no reliable means to diagnose Alzheimer's in a living patient. According to neuropathologist Dan Skovronsky, M.D., Ph.D., the "gold standard" for diagnosing the disease is "looking at brains under a microscope" after autopsy.

Skovronsky, who is CEO and co-founder of Avid RP, Inc., notes that pathologists use dyes to stain abnormal tissue so it can be visualized under the microscope. While collaborating with Hank Kung, Ph.D., a radiochemist at the University of Pennsylvania, he and Kung realized that radioactively labeled tracers might be used in living patients to do the same thing. A tracer with specific avidity for the beta-amyloid plaques that characterize the brains of Alzheimer's patients could be visualized using standard medical imaging technology, such as positron-emission tomography (PET) and Single Photon Emission Computed Tomography (SPECT).

But developing Kung's molecular imaging agents into the basis for a company had to wait until Skovronsky finished his clinical training. "After three-and-a-half years, [Dan] decided that he would like to develop these compounds for human studies," says Kung. Thus, Avid—the name comes from the high avidity with which these agents must bind to the target tissue—was born.

Initial investment, proof of viability

The fledgling company—led by a scientist turned entrepreneur—needed to make a deal with the University of Pennsylvania for the rights to license the intellectual property. But it had to prove to Penn that it would find investors to finance the project and the people to develop the products. At the same time, it had to prove to potential investors that it would be viable.

Here's where BioAdvance made the difference. BioAdvance made the first investment commitment to Avid—of \$500,000. "The early vote of confidence from BioAdvance," Skovronsky notes, "is really what enabled us to convince the university to trust us to develop their intellectual

properties, and enabled us to convince investors to trust us with their money."

Avid, which has offices and labs in Philadelphia's Science Center, just downstairs from BioAdvance's offices, is already expanding into additional laboratories. It has two NIH grants and is partnering with pharmaceutical companies to develop its imaging compounds. The compounds can be used to monitor the efficacy of drugs that treat Alzheimer's patients, along with serving as diagnostics, making them especially valuable to pharmaceutical companies. And Avid is now looking beyond Alzheimer's disease to imaging diagnostics—again from Kung's lab—for cancer and depression.

In January, Avid announced an \$8.9 million first institutional financing from a group that includes Pfizer's Strategic Investments Group; Lilly Ventures; RK Ventures, LLC; and its first investor, BioAdvance.



Daniel Skovronsky, M.D., Ph.D.

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Dan Skovronsky,
President & CEO,
Avid
Radiopharmaceuticals

A MODEST MAN WHOSE WORK MAY SHINE NEW LIGHT ON DEBILITATING BRAIN DISEASES

Hank Kung, Ph.D., Avid's chief scientific advisor and source of its technology, is a modest man. Although he sees the field of radiology as changing, he doesn't put himself in the center of that change, although awards he's

amassing prove his research is, indeed, central to the emerging field of molecular imaging. The imaging agents from his laboratory at the University of Pennsylvania are important to a number of companies, including Avid

Radiopharmaceuticals. Kung talks about evolution in radiology: "Traditionally, radiologists are more anatomically specific." But, he explains, molecular imaging agents, such as those he developed that are licensed to

Avid are now becoming more specific—targeting individual diseases or disease processes. "The radiologists hope to open up the field of radiology to be more functionally specific," Kung explains.

BioAdvance Milestones

Funding early-stage life sciences firms from Philadelphia-region

\$10 million in seed investments made to 20 startup firms

9 additional academic and startup business projects funded

\$80 million in additional capital raised by portfolio companies including

- Acuity Pharmaceuticals \$16.5 million
- Protez Pharmaceuticals \$15 million
- Avid Radiopharmaceuticals \$8.4 million

Three exits through acquisition:

- Gelifex, purchased by Synthes, Inc.
- Alteris, purchased by Celldex, Inc.
- SansRosa purchased by CollaGenex, Inc.

Investments in areas such as:

- Addiction
- Alzheimer's Disease
- Antibiotics
- Cancer
- Cardiology
- Chronic Pain
- Diabetes
- Diagnostics
- Devices
- Migraine
- Ocular Diseases
- Obesity
- Respiratory Disorders

PROTEZ PHARMACEUTICALS: SEASONED PHARMACEUTICAL EXECUTIVES FIND AN ANTIBIOTIC NICHE

Nosocomial infections—life-threatening infections that are picked up in a hospital—affect one in 20 people treated in the hospital. The annual death rate from these infections in the U.S. approaches 90,000. Such infections, along with those caused by antibiotic-resistant bacteria, increase our need for new, broad-spectrum antibiotics.

This is where small, young pharmaceutical companies, such as Malvern, PA's Protez Pharmaceuticals, Inc., can find their niche. Christopher Cashman, Protez' CEO, notes that some of the major pharmaceutical companies: Hoffman LaRoche, sanofi-aventis, and now, most recently, Sandoz, have spun off their antibiotic units to form smaller companies: Basilea, Novoxel, and Nabriva GmbH, respectively. Cashman notes, "...from a big pharma standpoint, there's a shift away from the research and early development of antibiotics, which creates a strong market opportunity for emerging, highly specialized companies like Protez."

Protez plans to take advantage of that opportunity. Founded by a group that includes Klaus Esser, Ph.D. and Dr. Luigi Xerri—two scientists from GlaxoSmithKline units specializing in anti-infectives and antimicrobials respectively—Protez is focusing on broad-spectrum antibiotics for in-hospital use and technologies that can extend the applications of currently existing antimicrobials.

The company was founded in December 2003 and purchased a small, Chicago-based company that had early stage, unique technology. It then identified a broad-spectrum antibiotic that was in preclinical trials with Dainippon Sumitomo. Protez licensed the compound, PZ-601, in May 2005. This is a broad-spectrum antibiotic in the carbapenem family that covers multi-drug-resistant Gram-positive bacteria and Gram-negative bacteria. The company is developing the drug with funding from a \$15 million Series B financing in August 2005, supported by BioAdvance Ventures, Birchmere Ventures, L Capital Partners, S.R. One and BTG. Protez expects to begin Phase I human clinical trials of

PZ-601 by the third quarter of this year.

Protez is also working on compounds that potentiate numerous existing bacteriostatic antibiotics (antibiotics that just slow bacterial growth), to create a cidal, or killing, effect and prolong the efficacy of these agents. Another of Protez's technologies will target bacterial biofilms, which may cause persistent infections, such as ear and urinary tract infections. These are particularly difficult to control with current drugs.

Cashman says the company is looking at a large market: for an intravenously dosed, broad-spectrum, in-hospital antibiotic, such as PZ-601 alone: about \$4 billion annually in the U.S. and Europe.

BioAdvance's input has been important to Protez's success. They came in just after BTG made its first investment in 2003: "The funding we've received demonstrates how a company can tap into the strengthened capital continuum in Pennsylvania," notes Cashman.

A MODEST MAN WHOSE WORK MAY SHINE NEW LIGHT ON DEBILITATING BRAIN DISEASES (CONTINUED)

Kung notes that the technology for imaging Alzheimer's disease has come a long way from its start 30 or 40 years ago, when investigators first showed that radiolabelled dyes could be used to stain post-mortem brain sections of Alzheimer's disease. Until now, definitive diagnosis of Alzheimer's was done under the microscope after the patient had suffered and died. But with the technology Kung and his colleagues have developed, agents can be used in SPECT and PET scanning to confirm the diagnosis of Alzheimer's disease in a living patient.

Kung and his laboratory specialize in developing radiopharmaceutical compounds for diagnosing neurodegenerative and other diseases. They developed a technetium-99m-labelled compound (TRODAT-1) that is used to visualize the dopamine transporters in the brain to aid in diagnosing Parkinson's disease. This molecule is used in Europe and is being developed by GE Amersham.

In February, Kung will receive the Monte Jade Mid-Atlantic Lifetime Achievement in Science & Technology Award for his work in

drug design, radiochemistry, receptor pharmacology, and translational research in imaging. In June 2004, Kung was honored for his work in developing radiopharmaceuticals with the Aebersold Award, given by the Society of Nuclear Medicine. But true to his modest mien, he declared, "I am dedicating this award to my wife, Dr. Mei-Ping Kung, who is the real scientist in the family. She is the best-kept secret of my lab."

