

NEW METHODS IDENTIFY DRUGS FOR OBESITY AND DIABETES... AND OTHER DISEASES, TOO

Obesity and diabetes (types 1 and 2)—affect hundreds of millions of people worldwide. Identifying pharmaceutical agents that can prevent or cure these debilitating conditions will alleviate much human suffering and represents an exciting opportunity for emerging companies.

This opportunity has not been lost on two companies funded by BioAdvance. Using different methods, both Melior Discovery Inc., of Malvern, and Jenrin Discovery, LLC, of Philadelphia, have homed in on major metabolic disorders. Melior's lead compound is being developed to treat type 2 diabetes, while Jenrin is working on anti-obesity candidates.

Both companies are looking at compounds that have undergone clinical trials for other indications, and although the products demonstrated good safety profiles, they were, for one reason or another, dropped from the original pharmaceutical companies' lineup. Here, though, is where Melior and Jenrin diverge.

Melior, which in Latin means "most improved," is using a comprehensive battery of different animal models representative of multiple human diseases to identify potential new uses for

compounds. Melior President and CEO Andrew Reaume, PhD, MBA, refers to these compounds as "diamonds in the rough." The company is identifying compounds that have a good safety profile, are able to be administered orally and demonstrate other key characteristics of effective drugs. The original patents have generally expired; however, Melior is able to file new patents on the novel use identified by their "Indications Discovery" Platform.

The company, which was incorporated in January 2005, was up and running with a 5,000-sq. ft. vivarium and more than 30 animal models by June of last year. By August, Melior had already identified novel indications for two compounds and started to move these into development. The company also initiated several research collaborations with local and international pharmaceutical and biotechnology companies.

Melior's current lead compound was initially tested by another company in clinical trials as a potential treatment for another disease; however, Melior found that the compound had the ability to cause a decrease in blood glucose levels, but only when glucose levels were elevated. By comparison, other drugs that decrease blood glucose levels do this under all circumstances even when

blood sugar is depleted, causing a dangerous condition called hypoglycemia. In addition Melior's compound does not appear to cause gastrointestinal disturbances, which are also commonly associated with other classes of diabetes drugs.

Targeting obesity

Jenrin Discovery's lead molecules are targeting obesity. According to John McElroy, PhD, Jenrin's CEO, the company selects potential drugs by hunting through the preclinical and clinical literature. The specific goal was to identify drugs, again abandoned by a drug company, that produce weight loss as a side effect.

This side effect, McElroy explains, is an off-target effect, where the drug is binding to an unintentional receptor. By trying to find a common denominator for drugs with this secondary effect, McElroy was able to identify a common binding site,

which the company is currently calling the JDO binding site. The next step, says McElroy, was "to discover new drugs that would target the JDO binding site specifically and selectively." Once McElroy, who had previously been employed by Bristol Myers Squibb, identified this target, he used personal funds for a proof-of-concept study in animals. At present, Jenrin has one lead drug candidate that targets the JDO binding site, and has now identified a second obesity binding site.

Early money

Both companies came to BioAdvance as their first institutional investor. When Reaume, who was previously with Pfizer in New York, and with his founding partner, pharmacologist Michael Saporito, PhD, began looking for a vivarium facility to house their animal models, they found it—and initial financing—in Pennsylvania. "Philadelphia is a mecca of hard to find in vivo skill sets," explains Reaume - just the types of skills needed to staff up a facility geared to identifying new indications for small molecules. BioAdvance funding allowed the company to set up their research facility. Melior now employs 12 people in Malvern, and expects to be up to 20 employees in a year.

McElroy, on the advice of a friend, who told him that BioAdvance "helped

"The hardest money to ever get is seed money. It looks small in the scheme of things, but it is critical."

Andrew Reaume, PhD
President and CEO
Melior Discovery

(continued)



Funding early-stage life sciences firms from the Philadelphia region

MILESTONES

\$10.5 million in seed investments made to 21 startup companies

9 additional academic and commercial projects funded

\$91.4 million in additional capital raised

Recent fundraisings

- Marillion Pharmaceuticals
\$1.5 million
- Melior Discovery
\$3.7 million

Companies in Pivotal Trials

- Yaupon Therapeutics

Cpanies in or through Phase II Trials

- Acuity (2)
- Alteris
- Eagle Vision
- Yaupon

Companies in or entering Phase I Trials

- Avid
- NuPathe
- Protez
- Therquest

Investments in areas such as:

- Addiction
- Alzheimer's Disease
- Antibiotics
- Cancer
- Cardiology
- Migraine
- Metabolic Diseases
- Ocular Diseases
- Pain
- Respiratory Disorders

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entrepreneurs start companies in the life sciences," presented to BioAdvance. Eight months later, BioAdvance invested \$500,000 in Jenrin.

Both firms are now at the stage of obtaining additional financing. Despite their initial emphases on drugs for metabolic diseases both are branching out to other disease areas. Melior is developing a drug for incontinence and inflammatory bowel disease indications. Reaume notes that Melior's business model is to develop a pipeline of drugs addressing

varied indications. These may be out-licensed to partners who will participate in later stage clinical development and commercialization. The company closed \$3.7 million in financing in July 2006.

Although Jenrin is advancing a second obesity target, the company is also exploring possible drugs for diabetes and for inflammatory diseases. Both firms see BioAdvance's seed funding as critical to their start. McElroy notes BioAdvance's \$500K served as a "massive multiplier," allowing the company

to file seven more patents, identify a lead drug candidate, and leverage this to obtain a second investment. Reaume adds, "The hardest money to ever get is seed money. It looks small in the scheme of things, but it is critical."

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FROM EARLY SCIENCE COMES AN INNOVATIVE COMPANY

When BioAdvance announced on May 17 that it invested \$500,000 in Midway Pharmaceuticals, Inc., a Spring House, PA, company focused on a unique method of preventing bacterial-mediated diseases of the gastrointestinal (GI) tract, the company's CEO Rifat Pamukcu, MD, saw what was presented to BioAdvance as a "science project" take one of its first steps to becoming "a real company."

Midway came out of research conducted by a group of scientists at the University of Chicago: John Alverdy, MD, Eugene Chang, MD, and Elaine Petrof, MD, who had been studying how bacterial pathogens manage to invade the gastrointestinal mucosa, and a unique means of inhibiting this entry. Chang introduced Pamukcu, a gastroenterologist by training who has led another biopharmaceutical company, and who studied under Chang, to the technology. Pamukcu saw a company in this technology—using a unique polymer that works like an artificial mucin to form a barrier, preventing bacterial entry into the cells of the GI tract.

With the University of Chicago assisting with travel expenses and patent filings, along with in-kind services from the scientists involved, the group began to form a company around this potential product.

The product has multiple indications for GI tract diseases, which make up a large market worldwide. Such indications include diseases that we do not usually think of as bacterially mediated, such as inflammatory bowel disease (Crohn's disease and ulcerative colitis) and systemic infections resulting from GI-tract damage from radiotherapy or chemotherapy in cancer patients, along with travelers' and other infectious diarrheas, (including early childhood diarrheas frequently fatal in less developed countries).

Why not Pennsylvania?

Although Midway originated in Chicago, Pamukcu, a seasoned business leader who moved his previous company Cell Pathways, Inc. from Denver to Pennsylvania years ago, and who still lives here, saw southeastern Pennsylvania as the logical place for a new biopharmaceutical firm.

He notes the presence of consultants in preclinical and clinical development, skilled employees, a "growing local VC and angel community," proximity to New York financial markets and Boston venture capital firms, affordable laboratory costs, and an affordable cost of living.

Furthermore, Pamukcu states, "You tend to go where the money is. Seed capital is incredibly difficult to find right now. That is where BioAdvance made the difference." He notes that BioAdvance has the experience to take a concept and make it into a company that will help to grow the biotech industry in southeastern Pennsylvania.

Midway's next step is to develop the polymer into a product that can lead to a pipeline. And, of course, the plan is to leverage BioAdvance's investment into the next investment. "I'm always looking for my next investment," says Pamukcu.

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