

## An Unlikely Hot Spot

By Lisa M. Jarvis

Nearly six years after Pfizer closed down its site in Kalamazoo, the life sciences industry there is growing steadily

BY THE END OF JANUARY, nearly 90 inches of snow had blanketed Kalamazoo, Mich. Downtown buildings were frosted with icicles, and awnings sagged under the weight of the snow. Snowplows with nowhere to turn created mountainous mazes in parking lots and transformed the center of neighborhood cul-de-sacs into mini-North Poles.

Taking in the landscape, a visitor would surely scoff at the notion that Kalamazoo is a "hot spot." But under the snow and ice, a cluster of life sciences businesses is germinating. By talking up local financial backing, readily available facilities, a deep pool of scientific talent, and affordable housing and education, Kalamazoo is attempting to make itself into a biotech hub. Given the early success of life sciences service companies and the city's growing number of drug discovery and medical device firms, the proposition isn't as crazy as it sounds.

To an outsider, particularly someone from a coastal biotech center, Kalamazoo probably seems like an unlikely competitor. But southwest Michigan has a strong foundation in the life sciences: Upjohn Pharmaceutical opened its doors in Kalamazoo more than a century ago, the medical device firm Stryker has been in the area for 60 years, and the contract research firm MPI Research has been around for more than a decade.

The life sciences scene in Kalamazoo—particularly chemistry-driven drug discovery—took a major hit when Pfizer closed down the old Upjohn site in 2003. Leaving about 1,000 scientists and related staffers without jobs, the move had the potential to create a devastating vacuum for intellectual capital. To stem a mass exodus of scientific expertise, the city and state provided seed funding for potential entrepreneurs to start businesses.

The first companies were primarily service providers that emerged from the closure of the Pfizer site. Having covered those businesses in their nascent days (Nov. 3, 2003, page 17), C&EN returned recently to explore whether local officials and entrepreneurs succeeded in nurturing seedlings planted far from the biotech industry's usual fields on the East and West Coasts.

Kalamazoo, it turns out, has done pretty well for itself. The service companies started almost six years ago have largely graduated from the "incubator" stage to being fully operational and, in many cases, profitable. As Ron Kitchens, chief executive officer of the local economic development group SouthWest Michigan First (SWMF), likes to say, "We're one of five places in the country where you can take a drug from discovery to tableting."

And importantly, local officials are cultivating a second wave of entrepreneurs—biotech firms attracted to Kalamazoo because of ready capital, a strong scientific workforce, and the infrastructure and services needed to start or expand a business.

It made sense for the first group of companies to be service oriented, Kitchens says. Although the former Pfizer scientists had discovered and developed many drugs, the intellectual property stayed with Pfizer. "There were great scientists who couldn't take any of their IP with them," Kitchens says. "But they had relationships with former suppliers that allowed them to build service organizations."

There were also new facilities primed for service companies. Anticipating upheaval in the drug industry, SWMF began planning an incubator space for entrepreneurs as early as 1998. The Southwest Michigan Innovation Center, a 58,000-sq-ft facility with lab and office space for rent, conveniently opened its doors just two months after Pfizer closed in 2003.

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Financially, it was also a safer bet to invest in contract research organizations (CROs) and other service companies. "It is much less costly to invest in a CRO, and once they are started they are self-sufficient," Kitchens notes. A drug company, on the other hand, needs years and potentially hundreds of millions of dollars to get a product to patients.

SEVERAL FIRMS have been particularly successful. Kalexsyn, a chemistry-driven CRO, has built its own \$5.5 million facility in Kalamazoo. It is starting to augment its staff, once dominated by older, ex-Pfizer scientists, with younger chemists who can benefit from the mentoring of their more experienced peers. Proteos, a CRO focused on peptides, has grown from seven ex-Pfizer scientists to a staff of 17. It has become the anchor company at the Innovation Center, taking up over 10,000 sq ft of lab space.

But after that first crop of companies, local officials realized they would need to look outside Kalamazoo's borders to continue to build the city's life sciences business. Many scientists left the area after Pfizer shut down, and most of those who remained were gainfully employed. In order to keep up the momentum, Kalamazoo would need to scavenge the nation for entrepreneurs willing to bring their businesses to Michigan.

In 2006, SWMF established a life sciences venture capital fund with two goals: to spur economic development and to sustain the science base in Kalamazoo. The fund was pumped with \$50 million to help companies get their start, but the money had strings attached. Any company that got investment had to be willing to relocate some of its operations to Kalamazoo.

For many, the requirement to pick up and move from a more cosmopolitan locale to a sleepier, snowier town is a tough sell. In the early days of the fund, it was often a deal breaker. "Some companies just can't do it," says Patrick G. Morand, the SWMF Life Science Fund managing director. "I've learned to get into that part of the conversation within the first 10 minutes of a meeting."

But Morand is not apologetic about the requirement. A basic tenet of the fund is to develop life sciences in the area, and most of the entrepreneurs living and working in Kalamazoo argue there is value in this scientific-minded, results-driven community. The fund is run on capital from the private sector, so despite its location-driven mandate, it is not dependent on state or federal money—often slow to arrive and currently hard to come by.

Focused on early-stage investing, the fund looks for several criteria in a potential partner. Entrepreneurs obviously need clear access to IP, a handle on the market size for their product, and a good management team, Morand says. More abstractly, the entrepreneurs should have "an appreciation of other people's money," he notes. So far, 10 companies have matched those criteria, and Morand expects to fund another four or five this year.

An early addition to the fund's portfolio is Metabolic Solutions Development, a diabetes drug discovery firm that can trace its roots to the Upjohn site. Cofounders Rolf Kletzien and Jerry Colca had both worked at Upjohn and survived as it changed hands, first to Pharmacia and then Pfizer. Both scientists moved to Pfizer's St. Louis site when research ended in Kalamazoo, but

they still had a lot of ideas about a promising diabetes target they worked on in their Upjohn days.

As they began to put together plans for a company, they were drawn to Kalamazoo not just by their history but by the financing options and the wide range of local service companies. Before receiving funds from SWMF, Colca and Kletzien had put up their own money to hire **Ash Stevens**, a Detroit-based contract manufacturer, to make the active pharmaceutical ingredient for their lead drug candidate. Since setting up in Kalamazoo, Metabolic Solutions has been able to use local service providers for 95% of the work needed to open an Investigational New Drug Application for its lead diabetes drug.

"People think of San Diego or Boston when they think of biotech," says Colca, Metabolic Solutions' president and chief scientific officer. "But none of those areas have the concentration of pharmaceutical development services that we have here."

OTHERS HAVE also been drawn by the combination of funding, lab space, and local service providers. Executives at Emiliem, a tiny biotech that takes a systems biology approach to designing cancer-fighting molecules, first heard about the resources available in Kalamazoo when a Kalexsyn manager visited their California offices. Emiliem was already collaborating with Van Andel Institute, a cancer research center in Grand Rapids, about an hour's drive away. It had decided to shift its chemistry services to Kalexsyn and was working with Invitrogen, in Madison, Wis., for screening. "All of a sudden, it made sense to come here and set up an office," Emiliem President and CEO Dale Johnson says.

For others, the decision to come to Kalamazoo came down to sheer economics. James Duncan, CEO of Monteris Medical, a medical device firm founded in Winnipeg, Manitoba, is developing a minimally invasive laser that heats and destroys brain tumors with the help of magnetic resonance imaging (MRI) and thermal data. Duncan says he had always planned to establish commercial operations in a U.S. city.

Chicago and Minneapolis were on the short list because of their proximity to Manitoba, but as executives were raising capital, they learned about the SWMF fund. Cash and facilities were available, not to mention a legion of workers experienced in making both drugs and devices. "We have an enormous need for very skilled regulatory and clinical people," Duncan notes. Suddenly, Kalamazoo was a contender.

The deal with SWMF was closed last April, prior to the current credit crunch, but money was clearly the driving force. The entire executive team will move from Winnipeg to Kalamazoo. For many, lifestyle changes will come along with the move, Duncan concedes. "While there is an argument for why it makes sense, such as the low cost of living, Kalamazoo is still not Chicago," he says.

Yet Duncan says he hasn't had a hard time convincing employees of the rationale behind the move. "Everybody who works for us and those being recruited believe we are saving lives," he says. "If moving to Kalamazoo makes us more successful faster, then everybody is for it."

HEADING INTO 2009, the SWMF fund is starting to get more queries from companies like Monteris that are driven by economics. Although the financing crunch is hammering biotech firms around the country, it could actually be a boon for Kalamazoo. Many companies wouldn't bother talking to the venture fund in its early days; the hurdle of moving to Kalamazoo from balmy San Diego or bustling Boston was too high.

Today, with so many companies struggling to put together the capital to survive, Kalamazoo suddenly isn't looking so bad. "Companies that six months ago wouldn't talk to us are calling us up," Kitchens says. "The volume of e-mail is daunting. Our opportunities have grown exponentially." So much, in fact, that SWMF recently made a staff member "entrepreneur-in-residence," with the task of dealing with all the requests.

The successes in Kalamazoo tie into what appears to be wider acceptance of the Midwest as a real choice for life sciences investment, according to the Cleveland-based business development firm BioEnterprise. "The venture investment numbers show that investors have started to recognize the Midwest as a hotbed of biomedical company development, and that is leading to companies themselves becoming much more willing to consider a Midwest location for their base of operations," BioEnterprise CEO Baiju R. Shah says.

The perception has gone from "negative or neutral," to a recognition that many midwestern cities have skill sets that are worth a second look, Shah says. He notes that Minneapolis has a hub of cardiovascular companies, Michigan is strong in medical devices, and Wisconsin and Ohio have medical imaging expertise.

"That helps small companies realize that not only will both regional and national investors be willing to invest in them, but there's a talent base that you can draw upon for growing your company," Shah adds.

Some in Kalamazoo attribute the city's success to a special brand of midwestern fortitude. After all, they point out, by the time Pfizer shut its doors, the community had already survived exoduses of guitar-maker Gibson, Checker Cab, and General Motors. Local entrepreneurs and investors note that while the rest of the country waits for a bailout, their community is laying the foundation for a sustainable future.

Whether the life sciences cluster can fulfill its promise remains to be seen. One test of SWMF's model—and of the potential of Kalamazoo's discovery-based companies—will be whether firms are successful at attracting funding from national venture capital firms.

Executives at NanoMed Pharmaceuticals, which is using nanoparticle technology to develop improved versions of existing drugs, believe some of the bigger venture capitalists are starting to come around. CEO Stephen Benoit notes that NanoMed was able to meet with four top venture capital firms during the annual JPMorgan HealthCare Conference, held in San Francisco in January. Facilitated by SWMF's Morand, the meetings represented for Benoit a major step forward for his company, as well as the region.

According to Benoit, a successful life sciences center is one where investors can buy and sell companies in a short period of time. For NanoMed and some of the other companies in the SWMF fund, being able to raise a next round of funding "that is sizable and has a lead investor from a large regional or national top-tier firm" will be a crucial litmus, he says.

"We're not exactly a day trip for the big venture capital firms," Benoit notes. Most investors won't bother making the effort unless they can see many companies in one day, he adds.

Kitchens, ever the Kalamazoo champion, is confident the region will continue to flourish. After all, when he and his colleagues started the innovation center and later established the fund, the

naysayers were plentiful. "They told us it wouldn't work, but we've proved them wrong," Kitchens says.