by Carole Bass

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Nanotechnology Now

The science of the very, very small could have a very big future.

On a quiet street in West Haven, an old factory building conceals what could be the future of medicine.

Up the stairs, past the stacks of pizza boxes made by the building's main occupant, you'll find the labs and offices of NanoViricides Inc. There, in a conference room outfitted like the rec room of a 1950s science geek—wood-paneled walls decorated with posters titled "Metabolic Pathways" and "The Molecular Pharmacopoeia"—the startup company's president and chairman, Anil Diwan, will tell you that he has developed a "game-changing technology" for virus-killing drugs.

Using nanotechnology—the science of the very, very small—Diwan makes drugs that seek out and destroy viruses the way antibiotics attack bacteria, he explains. Tests of his drugs for HIV, flu and severe pinkeye show that "there is nothing to match it anywhere in the world," he claims. "In nanomedicine, we are probably the leaders in antiviral medicines, not only in Connecticut but in the world."

Just one problem: These unmatched, game-changing drugs work in test tubes and lab animals, but have not yet been tested on people. How long until NanoViricides starts its clinical trials?

"If I had all the money in the world, 18 months," says the lean, bespectacled Diwan.

And with the money he has?

"We don't have any money," Diwan says, then breaks out into one of his frequent bursts of laughter at what he seems to see as his own brilliant absurdity.

In his pleated pants, running shoes and dress shirt with a pen in the chest pocket, Diwan looks every bit the biochemical engineering Ph.D. that he is. He's also a highly unconventional entrepreneur. Launched in 2005 with no institutional affiliation, Nano-

Inframat CEO David Reisner holds one of the Farmington firm's hip joints with ceramic nanocoating, expected to come onto the market in 2009.

Viricides is one of perhaps a dozen small Connecticut companies striving to carve a niche in the growing but still nascent field of nanotechnology.

Some, like NanoViricides, are working in nanomedicine. Others, like Inframat and its sister company U.S. Nanocorp, both based in Farmington, are developing nano-enabled materials for uses as diverse as fuel cells, Navy propellers and filters to clean up contaminated water. While government officials talk about creating an infrastructure to make Connecticut a nanotech leader, the scientist/entrepreneurs who run these companies are trying to forge their own paths.

NanoViricides is publicly traded. Inframat's financing relies heavily on military contracts and overseas partners. Neither has access to venture capital.

"I've been called a VC without the C," says Inframat co-founder and chief executive David Reisner. "We have a mix of technologies and applications, and we never know until the last minute what the front-runner's going to be. We knew it would take about five years to develop individual products. But nobody in the nanotechnology community realized how difficult it would be to get these great products into the marketplace. Acceptance is very slow."

The Ph.D.s who work in nanotech like to say that their technology is "very simple." To a layperson, the technical explanations are actually quite complicated, but basically nanotech is the science of creating and manipulating materials at the scale of molecules and atoms. (Nano, from the Greek for dwarf, literally means "one-billionth part of.") At that size, ordinary substances like carbon and common metals take on extraordinary properties, such as becoming water-soluble, conducting electricity and catalyzing chemical reactions. Those novel characteristics give nanomaterials their value.

The tiny materials are becoming big business. The U.S. government spends about $1.5 billion yearly on nanoresearch. The consumer market already boasts more than 600 nano-containing products worldwide, from stain-resistant fabrics to sunscreen that turns clear on your skin. New York-based Lux Research projects that by 2014, 15 percent of manufactured goods—a global market of $2.6 trillion—will incorporate nanotechnology.

With its research universities and educated population, Connecticut should be well-situated to grab a piece of that expanding pie, the state's Advisory Council on Nanotechnology figures. But, the council warned in 2006, "The need to act is urgent because the pace of technology advancement is fast, the competition is aggressive and we risk falling behind."

The state's nano strategy includes industry-university collaboration, small-business

grants and a college curriculum to train future nanoscientists. Most ambitious, the strategy calls for a Center for Nanoscale Sciences to be jointly housed at Yale and the University of Connecticut. But the state has yet to fund its share of the plan.

According to Mary Ann Hanley, Gov. Rell's policy adviser on workforce development, the governor included $10 million for the nanoscale science center in her budget proposal this year, but then snatched it away when overall budget projections took a turn for the worse.

"It was almost there," Hanley says of the funding. "We saw it and then it was gone. It was a tough one."

Hanley says her office will again ask for the $10 million in next year's budget request. The idea is to get a federal match, plus contributions from Yale and UConn, to reach the $25 million startup cost for the first five years.

Sam Brauer, a member of the advisory council who has also done consulting work for the state through his Stamford-based firm, Nanotech Plus, pegs Connecticut's total nano-derived market at "less than $100 million, and I wouldn't be surprised if it's less than $50 million.

"There are good, talented people who are doing good work on a shoestring," he says. "But you can't work on a shoestring forever."

As they wait for government or university help, startup companies are used to stretching their dollars, of course. They find low-rent digs. They scrounge used equipment. Sometimes, they even look for inspiration in a fish tank.

David Reisner rummages through his bag and pulls out a shiny, dark-gray sphere, about an inch-and-a-half in diameter, its flat bottom punctuated by a hole in the center. "That," he says, setting it on his trapezoidal conference table, "is a hip joint."

Thanks to a nanoceramic coating made at Inframat's pilot plant in Willington, this replacement hip joint will last 25 years, Reisner says, compared to the 10-to-15-year life span of current implants.

Using nanoscale materials, ceramic coatings can be made extraordinarily hard or soft, dense or porous. Reisner says Inframat is working with an orthopedics manufacturer on federal Food and Drug Administration approval for the hip replacement, and hopes to have a product on the market in 2009.

The idea grew from work the company has done for the Navy, making a wear-resistant coating for minesweeper propeller shafts.

"Traditional ceramics don't have the toughness to withstand that kind of abuse," Reisner says. A nanocoating, he explains, is both tougher and more flexible: "You can hit it with a hammer and it won't break." The Navy has been using this coating for about eight years, he says, with no sign of the scoring that usually mars propeller shafts.

According to Reisner, the Navy will save $34 million in maintenance over the lifetime of each ship—yet, "ironically, Inframat never saw a nickel" in royalties or sales because the Navy funded the research and development but then chose other companies to do the actual coating work.

That's life at a high-tech, low-budget startup. Still, Reisner boasts that Inframat and U.S. Nanocorp have garnered $23 million in research-and-development contracts, largely from the military. (Inframat makes coatings and has developed a system for plasma spraying—a sort of high-temperature paint gun, only for coatings instead of paint—in which it replaces the traditional powdered raw material with a liquid. U.S. Nanocorp focuses on energy, particularly batteries and fuel cells.)

Getting other people to pay for your research is part of the shoestring game. At the Civil War-era former thread mill that functions as the company's pilot plant, Reisner proudly shows off another part: a 16-foot-high industrial spray dryer, which looks like a stainless-steel funnel on stilts, used to dry nanoceramic mixtures.

"This cost $250,000 in 1998," Reisner says. "I got it from the Navy for a dollar" after persuading the military—which bought the dryer for Inframat's contract work—that taking the monstrous machine apart and moving it would cost almost as much as it was worth.

Then there's the fish tank. Using nanofibrous magnesium oxide, Inframat makes a "birds'-nest" material whose very high surface area makes it great at soaking up water contaminants. Water filtration is a big market. In the U.S., old lead-lined pipes are corroding, leaking the toxic metal into the drinking-water supply. In India and elsewhere, groundwater contains naturally high levels of arsenic.

But there's a problem: Because of its huge surface area, the Inframat product takes up a lot of space. How do you compact it without losing its adsorption? The answer: Grow the nanomaterial in a porous foam that's normally used for cleaning fish tanks. An Air Force contract financed part of that research.

Despite Inframat's frugality, the 12-year-old company is not yet making money. Chairman and co-founder James Hsiao estimates annual revenues at "a few million" and projects profitability "shortly."

Inframat is "probably the biggest purely nanotechnology company" in Connecticut, says Brauer, the Stamford-based consultant. Yet "if NanoViricides hits, they will dwarf Inframat instantly."

Brauer calls the drug developer "an intriguing gamble"—intriguing enough that he has bought some NanoViricides stock himself. The company's market capitalization is about $150 million, Diwan says, thanks in part to "a few Wall Street folks who had come to believe in me as either a crazy guy or a brilliant guy."

Diwan co-founded NanoViricides with CEO Eugene Seymour, a Los Angeles physician who specializes in HIV. At their first business meeting, Diwan relates in his stream of crazy guy/brilliant guy stories, "I was three hours late. I had not prepared a proper presentation, so I just took out a napkin and scribbled on it: 'This is what I'm making. Does it work?' 'Yeah, maybe it works.'"

How it works is unusual. Most nanotherapies rely on the minuscule particles to penetrate disease cells and destroy them from within—the world's smallest Trojan horses, attacking cells much larger than themselves.

NanoViricides' technology, by contrast, swarms a virus from the outside. First it "tricks the virus into thinking it's a cell," Diwan explains. "Once it's on the virus, it spreads like an oil slick. We are able to slime it completely," causing the virus to dissolve.

"You know that viruses dismantle when you throw soap at them," Diwan says. "We are making the world's most expensive soap."

In animal tests, Diwan asserts, his flu drug works eight to 10 times as well as the widely prescribed Tamiflu. "Nobody believes it. But we have demonstrated that it works."

Unlike academic researchers, NanoViricides never publishes its animal studies, which are performed under contract by a Boston-area company. Asked why not, Diwan smiles: "Our god is FDA," which accepts private as well as published data, he responds. "Our god is not scientific researchers. We don't want to appease the wrong gods." He adds, "We are really scared about competition. Once the script is written down, anybody can do it."

Diwan and his handful of employees write their scripts in a 1,500-square-foot chemistry lab, just down the pizza-box-filled hallway from their office. Here it's easy to see how the company has managed to spend only $6 million in two-and-a-half years. The lab benches are old desks, covered with plastic and hiked up to proper height on 4-by-6 timbers. Leading me to another makeshift bench, Diwan points to a black-painted cardboard box: "This is my darkroom."

"My chemistries," he says, "are very simple. I can do them in the kitchen." NanoViricides shareholders—and infectious-disease patients—can hope he cooks up a recipe for success.