

This isn't a 'biotech bubble,' it's 'Philadelphia's moment' to become a center for gene therapy, says Penn-based CEO

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*Steven Nichtberger's Cabaletta Bio office. The former Merck executive ran biotech pioneer Tengion until its clinical trials failed, and now heads Cabaletta Bio, one of a string of University City biotech companies that has gone public.
Image via Joseph N. DiStefano, The Philadelphia Inquirer*

Smart, small biotech companies -- dozens in the U.S. over the last two years, including several in the Philadelphia area -- have gone public before they've made a profit, a sale, or even a product.

Is too much money chasing too few winners? Will this end like the dot.com blowup of 2001?

"This is not a bubble," insists Steven Nichtberger, serial start-up CEO. "It's Philadelphia's moment."

He *would* say that: Nichtberger is boss at one of those newly public, pre-profitable University City companies, Cabaletta Bio, with Penn doctors Aimee Payne and Michael Milone. The firm was backed by biotech investors from Boston, New York and California, before its initial public stock offering last fall.

But consider where he's been: He previously headed Tengion Inc., which had 100 employees and a state-of-the-art East Norriton factory. It was worth more than \$400 million at its peak during another biotech build-up 10 years ago, only to fade, with many peers, when its technology failed to produce cures.

Times have changed, Nichtberger said in his Cira Center office, a seven-block walk from Penn's medical school: "The science at Tengion was very new. There were no contract-manufacturing organizations in those days. We had to take a lot of risk and build out our own manufacturing up front. But the science did not bear out. It went sideways."

But "that was yesterday's biotech ecosystem. Science has advanced in Philadelphia, in gene therapy and cell therapy, unleashing what is a much more modular, predictable path for product development."

When Nichtberger graduated from Penn in 1983, he went to work for Merck. Corporate drug development followed a slow, risky, chemical course: "You would ask, 'What are the sequences in a living being that lead to a disease?' And you'd find the rate-limiting step, say, in the creation of cholesterol in the body. And ultimately discovered, for example, statins, and a billion-dollar platform."

And then it was back to the drawing board. Discoveries weren't cumulative; the next insight might take years to prove. Or disprove. "Chemical projects are very difficult to predict, whether you have efficacy, and safety."

Nichtberger says the government-backed Human Genome Project, which substantially completed the mapping of human genes in the early 2000s, marked not just new access for medical science, but the basis for a "compression" of cure technology.

Instead of finding insights and trying to prove them over many years, "we can now treat many diseases and conditions as genetic engineering problems" whose treatments can be tested and proven rapidly, by medical standards. "It's huge, it's exciting, and it's compelling, medically."

These processes, he says, are place-based: "Gene and cell therapies are not widgets you can make in Kansas and ship around the country. Manufacturing is central to success in gene and cell therapy, and Philadelphia is where the people who [developed] the manufacturing are. Here is where the future economy is coming together. Philadelphia is not going to lose this one." Real-estate developers are rushing to finance clean-room labs and offices to house "the talent we are all competing for."

Just at Penn, doctors who pioneered the use of genetic data include James Wilson, whose labs developed adeno-associated vectors -- "like trucks," Nichtberger says, that deliver altered genes to patients; Jean Bennett and a team who partnered with CHOP to develop the first FDA-approved corrective gene injections to fix a genetic eye disease; Carl June, a leader in the group that signaled human T-cells to attack potentially cancerous B-cells, the basis for another groundbreaking treatment, Novartis' Kymriah, and more recently the founder of Tmunity Therapeutics, which occupies Tengion's old site in East Norriton.

It is an expansive community, with branches at CHOP, Jefferson and other medical centers. "And that is why money has been flowing here from everywhere on Earth, from Boston and California and China, into Philadelphia." Not just to those other biotech centers, Boston and San Francisco.

Is there really room for the billions that investors are pumping into cell and gene therapy developers? "Some investments will succeed. Some will fail. The money will advance to the very best. The money is flowing to biotech because the timeline has been compressed, the returns are increased, and there is evidence to substantiate that."

Nichtberger has made the most of his Penn ties. After Tengion and before Cabaletta, he was recruited to teach a class. Since 2012 he has presented the Life Sciences and Management program, where he showcases discoveries of University City gene therapy leaders, and draws blue-chip venture capitalists and pharma bosses.

In 2011 Nichtberger presented T-cell data from June's lab to his inaugural class. The next year Bennett showed a grainy video of a student struggling through a maze before her blindness treatment, and then rushing through it, blind no longer.

Partners at Bain Capital and Deerfield Management Co. were among the visitors to the class that second year. By 2015, Deerfield and Bain were among the early investors in Bennett's company, Spark, which Roche bought for \$4.3 billion in December. "They stood to make hundreds of millions, because they had an advance view of what's coming," said Nichtberger.

"So now I can do any project I want to do. Because this ecosystem is centered right here at Penn."

Even good science can bring in dumb money, I remind him. The biotech community "has way too much money available, for way too many investments," he says. "Many are going to fall by the wayside."

The Penn-trained scientists at Nichtberger's company, Cabaletta Bio, are developing T-cells that don't kill human B-cells indiscriminately but target destructive ones. In 2018 he raised \$38 million from three out-of-town firms, then \$50 million three months later, before going public in October. He has raised enough money to run the 25-employee company for the next couple of years as it ramps up clinical trials.

"Our intention is to build an important company, building important treatments for diseases, that we manufacture, using cell therapy, in Philadelphia."



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