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What Drug Developers Can Learn From Silicon Valley

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I think Silicon Valley's most valuable asset is a ruthless focus on experimenting with product-market fit. Silicon Valley software companies have the mentality of pushing out products, getting market feedback, and then going back to the drawing board if the market responds poorly. Imperfect products are a learning experience — an experiment — rather than a reason to close shop or fire people.

As a graduate student and postdoc at Stanford in the early 2000s, I often looked with envy at friends getting rich by selling their software companies for tens of millions of dollars a year after founding. Besides the obvious financial rewards of software startups, the speed of progress blew me away. Even in academia, students who worked in software would often finish their degrees two to three years before students who slaved away at the bench. How could biotechnology, and bench-science companies in particular, possibly iterate as quickly as the software industry?

YOU NEED A COMPELLING BUSINESS PLAN AND DATA

I founded GigaGen in 2011. In classic Silicon Valley style, I initially worked out of my garage and had no cash. All I had was a Ph.D. in genetics and a drive to find better ways to analyze immune repertoires.

While I continued to lead the company with a Silicon Valley mindset, I relied on life sciences growth vehicles to fuel my next steps. First, I raised seed financing from a local VC and won a few NIH grants. I hired smart scientists and engineers to solve the technical problems. I also filled an advisory board with smart academics from Stanford. We filed patent applications. After two years, we reduced the technology to practice and generated a compelling data set. Unfortunately, our business plan was not as compelling as our data. As a result, I went through the painful process of laying off staff.

Without staff to manage, I had little else to do but reach out to anyone and everyone who would talk to me. By necessity, I was like an Apple product manager showing the latest beta-release iPhone to dozens of opinion leaders. I met with several people a day, showing them my data and asking for advice on how to apply the new technology.

The results were startling. It became clear that it was extremely effective to hypothesize use cases — in this case, drugs — and then ask interviewees for their thoughts on those hypothetical use cases. If I only showed off the technology and told them how useful I thought it was, they would nod but would not provide any insight. I needed to do experiments. I needed to test hypothetical uses as systematically and rigorously as the experiments I was used to doing at the bench.

Eventually, I hit upon three specific use cases that got very specific people very excited. One application was in the field of plasma-derived antibody therapeutics. Plasma-derived antibody therapeutics, specifically intravenous immunoglobulin (IVIG), is a $10 billion industry that has seen little innovation in decades. I found strong interest to use my technology to make a recombinant IVIG alternative to plasma IVIG. Another application was the replacement of hybridoma-based screening of mouse repertoires for discovery of checkpoint inhibitor drugs. I found that many checkpoint inhibitor programs were struggling to tease good antibodies out of mice, since checkpoint inhibitor targets are often not highly immunogenic. Finally, I found a strong interest from the T-cell community. I heard that the T-cell community was eager for new technologies to help them develop cellular therapies. It was difficult to get the T-cell groups to verbalize their needs — they just wanted "more" and "better" data — but by showing them a hypothetical product

that my technology could generate, and constantly asking questions, I began to uncover their needs through a series of iterative "yes" and "no" responses from dozens of experts in the field.

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With these three product applications in hand, I applied for several NIH grants and won millions of dollars to finance the three product directions. Around the time that these grants started, NIH launched a new program called "I-Corps." This program is a commercialization accelerator based on a methodology called Lean Launchpad, which was developed by serial entrepreneur and Silicon Valley guru Steve Blank. NIH had recruited Steve Blank to adapt Lean Launchpad specifically for new biotechnology companies. In his program, teams — composed of key executives from the company — interview more than 100 potential customers, or experts, within 10 weeks. The idea is that after more than 100 interviews you should have refined your product to fit market need based on feedback or decided to drop the product entirely. The process is similar to what I had already been doing organically, but more organized and supported by mentors and peers.

The results were again startling. The Lean Launchpad process literally saved us tens of millions of dollars and several years by homing in on a product that customers actually wanted, versus what we thought they would want. Most importantly, we very specifically defined the "minimal viable product" for each research program. After hundreds of interviews, we were introduced to business development executives for Barcelona-based Grifols, one of the original and leading producers of plasma IVIG. We had already spoken to countless experts in plasma IVIG and had already progressed our laboratory data package through an NIH grant. Fortunately, the executives were impressed and described our company and technology to their bosses, which led to a $50 million financing and codevelopment deal in July 2017. Normally, a company might raise tens of millions of dollars to achieve such a milestone, but we only spent $225,000 of NIH money. Clearly, the Lean Launchpad process saved us millions of dollars and brought our impactful innovations to a Big Pharma that saw future commercial value.

A NEW FOCUS ON COMBO DRUGS

Our experience with recombinant IVIG was so powerful, we went through the NIH I-Corps process (i.e., an eight-week program providing funding, mentoring, and networking opportunities to help commercialize promising biomedical technology) a second time — for our immuno-oncology programs. Unlike recombinant IVIG, immuno-oncology is an extremely competitive and crowded field. Our challenge is to differentiate ourselves from this crowd. We found that most new companies in the immuno-oncology antibody field focus exclusively on a single target, whereas Big Pharmas have moved vigorously toward drug combinations against multiple targets. It became clear we needed to structure our drug discovery and development programs around combinations. Thus, we are currently using our T-cell expertise to test combinations of antibody drug candidates against 16 different targets.

Much has been written about innovation challenges at large pharmaceutical companies. Small biotechnology companies are in the business of innovation to help fill this gap. We specifically work with bigger companies to help them with their innovation challenges. Thus, surprisingly, in early stages, we are not just innovating for doctors and patients, but also for a third customer — the large partner company. To find what the partners are looking for, we can use methods such as the Lean Launchpad to determine product-market fit with precision. Though biotechnology may never be as fast and efficient as software, we can make innovation and development faster — through nothing more than a Silicon Valley way of thinking. L

GigaGen CEO DAVID JOHNSON, PH.D., MBA, is an inventor, entrepreneur, and expert in single-cell genomics with a track record of bringing new medical technologies to market.

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