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Selling a commodity can lead to failure, says Alex Lorestani, co-founder of biotechnology company Geltor.

## ENTREPRENEURSHIP

# On the rebound

*Entrepreneurs whose start-ups have flopped can learn from such failures to try again.*

BY AMBER DANCE

In mid-2018, entrepreneur Nathaniel Brooks Horwitz had a problem. He had co-founded a company, Nivien Therapeutics, to create a drug that would make chemotherapy work more effectively. He and his team had designed a small molecule to block a protein in the Hippo-YAP pathway that inhibits the efficacy of chemotherapy. In mice, it worked — but not well enough.

“We didn’t want to take a mediocre therapy into the clinic,” says Horwitz. He faced the devastating prospect of shuttering the

company and the hope it represented.

It’s a prospect that many start-up founders could end up facing sooner or later. At the rosy beginning, founders might hope to change the world with a new technology or medicine or rake in major financial rewards. The reality is different: many fledgling companies will close without achieving those goals, or will have to change their objectives to be more feasible or profitable. Although disappointing, a failure need not be the end of the road. Savvy and resilient co-founders learn from their mistakes, and many apply their entrepreneurial know-how again in the future.

Not all companies become blockbusters or go down in the flames of failure. Many plod along in a middle ground where they don’t earn vast profits, or they might be sold to another company, says William Bains, a biochemist and entrepreneur living near Cambridge, UK. A business might continue for years without increasing revenues or developing fresh products. “A lot of companies do that,” he says.

Because there’s no solid metric for failure versus success, and because company founders are understandably reluctant to tout their failures publicly, precise data on failure rates are hard to come by. When Bains analysed data ▶

► from the United Kingdom, he found that about one-quarter of start-up companies made it to ten years. Across the European Union, data from 2016 indicate that nearly 58% of businesses survive their first three years.

In the United States, just one-third of start-ups last a decade (see ‘Survival of the fittest’). CB Insights, a data-analysis firm based in New York City, reported in February 2019 that 70% of technology companies fail, usually within their first 20 months. In 2018, the firm noted, just 1% of 1,100 start-ups achieved the coveted status of ‘unicorn’ — a privately held start-up worth US\$1 billion or more.

“If you look at innovation, it’s fraught with failure,” says Daniel Batten, an entrepreneur, investor and entrepreneurship coach in Auckland, New Zealand. But, he adds, founders can give companies a better chance of success by learning important skills such as leadership and negotiation.

### FIFTH TIME’S THE CHARM

Bains knows failure well. He’s currently on his fifth company, Five Alarm Bio in Hauxton near Cambridge, UK, which aims to develop anti-ageing drugs. He doesn’t consider any of his previous ventures, in drug discovery and software, to be successes: one company, for example, dwindled when other managers and investors followed a different business plan from the one that he and his co-founders had envisioned. Another firm pursued a drug candidate that simply didn’t do what he hoped it would. A third folded as a result of bad timing: the anticancer candidate that the founders had identified seemed to hold promise, but Bains and his colleagues were seeking investments when the global economy tanked in 2008, and they couldn’t find anyone willing to take the risk.

Another company disintegrated, adds Bains, because he and another co-founder didn’t give it their all. Lesson learnt: “You can’t do entrepreneurship half-heartedly,” Bains says.

That’s just part of the knowledge that he picked up along the way. Working at the first company, he notes, gave him the equivalent of a hands-on business degree while he was

## WIND DOWN

### Why start-ups fail

The technology data-analysis company CB Insights in New York City reviews post-mortem reports by founders, investors and journalists. Here are the most common reasons that it cites for start-up failures:

- No market need
- Ran out of cash
- Not the right team
- Was out-competed
- Pricing or cost issues
- User-unfriendly product
- Product without a business model
- Ineffective marketing
- Customers were ignored
- Product was mistimed

earning a salary. Another key lesson was to find investors who would support his goals. Bains says that some investors simply want to build something that they can quickly sell off, whereas he is eager to do ‘cool science’ and to develop a useful medicine or product. He now avoids backers who seem only to be after a quick profit. With Five Alarm Bio, he and his co-founders have been honest about their differing goals, so that they can work together to achieve them all.

### MANAGING EXPECTATIONS

Horwitz gave Nivien Therapeutics his all. In 2016, while studying molecular and cellular biology at Harvard University in Cambridge, Massachusetts, he heard about the work of Harvard faculty member Marc Kirschner on inactivating the Hippo–YAP pathway in models of pancreatic cancer. Horwitz, Kirschner and Nikita Shah, a student in regenerative biology at Harvard, raised money to found the company. Horwitz, at just one semester shy of completing his bachelor’s degree, took leave from university to work full time on the fledgling business, based in San Francisco, California.

He hoped that blocking the Hippo–YAP pathway in humans would help to shrink tumours and to prolong survival. But he also knew that Nivien’s approach was a long shot. Kirschner’s work followed decades of research that had failed to put much of a dent in pancreatic cancer’s dismal overall 5-year survival rate of around 10%. And successes in animal studies, such as Kirschner’s, rarely yield products that work in people, and even then only after several years of hard work. Horwitz was careful to ensure that Nivien’s investors understood the reality of the situation.

Patients reading about the company’s plans didn’t always pay attention to that note of caution, however. One motivation that pushed

Horwitz to work 90-hour weeks, without taking any holiday, was the letters that he received from people with cancer and their loved ones who were eager to hear about clinical trials. For Horwitz, the worst part of shutting down the company was realizing that it would dash people’s hopes. The administration associated with dismantling the company was the easy part.

When a start-up goes down, investors get back any leftover money, notes Iain Thomas, who is head of life sciences at Cambridge Enterprise, a subsidiary of the University of Cambridge, UK, that helps faculty members to license their inventions or start spin-offs. In some cases, it might be possible to sell off some of the company’s assets.

Nivien’s investors, having been briefed on the risks of drug development, took the failure in their stride. Horwitz was also able to help Nivien’s employees find new jobs quickly, because he had established a large network in the biotechnology and pharmaceutical world.

And he has no regrets: “We did it for the right reasons, gave it a proper shot and shut down when it became clear it wouldn’t work,” he says. “I wouldn’t change anything fundamental about that formula.”

Horwitz returned to Harvard to finish his undergraduate degree at the end of 2018. On top of that degree, he picked up a variety of skills from his time at Nivien, including how to build a team, file patents and raise money; how to discover potentially useful molecules; and how to design preclinical studies. He’ll apply that entrepreneurial know-how in the job he is starting in June at a biotechnology venture-capital firm in Boston, Massachusetts.

### PROBLEMS TOO BIG

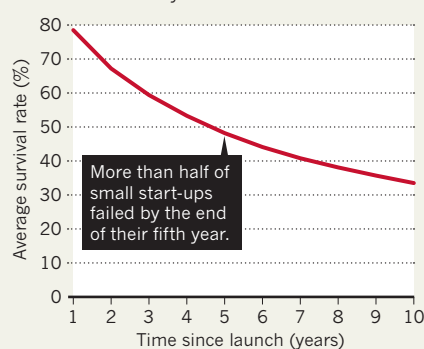
Hidde-Jan Lemstra, an entrepreneur in Utrecht in the Netherlands, has also tasted start-up defeat. While living in Cambridge, UK, in 2013, he went for a beer with his friend David Leal-Ayala, a PhD student at the University of Cambridge who was developing methods to remove laser toner from printer paper. After this ‘unprinting’ process was applied, the paper would be available to print on again and again. It sounded like a good idea to Lemstra, who proposed that they turn it into a business.

The pair then co-founded Reduse with another local entrepreneur, and set about turning Leal-Ayala’s technology into a product. “It worked great in the lab, under perfect circumstances and with a ridiculously expensive laser at a ridiculously slow speed,” says Lemstra. The group solved the speed issue, but simply couldn’t find a laser cheap enough to make unprinting financially feasible.

Lemstra concluded that the problem was too big to be solved by a start-up — but others in the company didn’t agree. Leal-Ayala was among those who wanted to carry on. Those in Lemstra’s camp were ready to give up while there was still some money left to return to the investors. “This created no animosity

### SURVIVAL OF THE FITTEST

One-third of US small businesses (with fewer than 500 employees) that launched in 2003 remained afloat ten years later.





between us at all,” says Lemstra, “but it did create healthy discussions.”

As chief executive, he made the call to wind down Reduse in 2016. He recalls feeling a mixture of not just disappointment, but also relief that he could move on from the problem. As with the backers of Nivien, the start-up’s investors were understanding.

And unprinting might still have a future. Lemstra made a lot of contacts in the printer industry while working at the start-up. When he was shutting down Reduse, he sent around a one-page list of the company’s assets — including a patent, designs and a prototype — that were for sale. “We ended up in a nice little bidding war,” he says. The buyer, who declined to be named, could yet make unprinting a reality.

Through Reduse, Lemstra learnt something about himself: even though he trained in business, he enjoys working with technology. He’s now a consultant to scientists with commercial ideas at Delft University of Technology in the Netherlands.

### PLANNING AND PIVOTING

As Reduse’s story shows, even a promising product might not work out for one reason or another. “There’s no secret blueprint to predicting what sort of ideas will work or not,” says Batten.

But it’s worth considering which types of idea don’t tend to work, says Alex Lorestani, co-founder of Geltor, a company in San Leandro, California, that makes designer, lab-grown collagen as an ingredient for consumer products such as cosmetics.

In 2012, while planning their business as graduate students at Princeton University in New Jersey, Lorestani and Geltor’s other co-founder, Nick Ouzounov, analysed biotechnology companies that had failed. Those companies, he says, often tackled a commodity — a product for which several vendors were already competing to offer the lowest price. Collagen, at that time, was available only from animal sources, but the duo predicted that their lab-made, animal-free version would be a high-value ingredient for manufacturers thanks to its unique origins.

Since becoming an entrepreneur, Lorestani has noticed other reasons for failure. Some companies don’t have a good strategy for getting a product to market quickly, he says. Others don’t own the intellectual property they need.

Start-up founders should also realize that they might have to amend their goals and plans — or ‘pivot’, in entrepreneurial lingo. Teams often modify their initial idea into something more feasible or marketable, says Justin Hodgkiss, a chemist at Victoria University of Wellington in New Zealand. He’s also the co-director of the MacDiarmid Institute in New Zealand, which has supported and trained several faculty members to found start-ups.

For example, Shalen Kumar, a native of Fiji who now lives in Wellington, hoped to help dairy farmers, particularly in low-income areas.



Shalen Kumar, co-founder of Auramer Bio, changed his company’s product focus to boost revenues.

The problem: fertility among domesticated cattle is declining. Buffalos could be an alternative because they make more-nutritious milk than do dairy cows. Kumar says that they can also survive in more-extreme environments. The challenge, however, is that it’s hard to tell whether a female buffalo is in heat, complicating breeding efforts.

In 2007, as an undergraduate student at Victoria University, Kumar had the idea to make an inexpensive, temperature-stable buffalo fertility test using aptamers — bits of nucleic acid that bind to specific target molecules. After attracting a couple of collaborators — including Hodgkiss, a founding inventor — and earning his PhD, Kumar co-founded Auramer Bio in 2015.

But a fledgling business needs income. Helping dairy farmers wasn’t going to do that quickly, says Kumar, and the science for the buffalo test wasn’t quite ready. So, for now, Auramer is developing tests for illicit drugs and human fertility — which the company expects to provide ready capital.

But Kumar isn’t giving up on the buffalos. If trials for the human-fertility test go well, he’ll move on to the buffalo version.

### LESSONS FROM FAILURE

It’s important to avoid taking a start-up’s demise personally, says Thomas. “Most spin-outs do fail,” he says. “Failure of an opportunity does not equate to failure of you, the individual.” In fact, Thomas says, the scientists he has worked with who didn’t succeed often walked away

feeling that they had a positive experience.

Start-ups can fail for all kinds of reasons (see ‘Why start-ups fail’). Some companies, such as Reduse, falter when they take something that performs well in the lab and then try to scale it up to work in the real world. Others don’t settle on the right business model. But many failures could be avoided with the right training, says Batten.

Hodgkiss agrees. “The vast majority of start-up failure is not due to failure of the business model,” he says. “It’s failure that’s people-related: leadership, communication, influence.” Founders have a greater chance of success when they seek training in all aspects of the start-up world, including those soft skills.

If a start-up folds, learning from your mistakes requires an honest, even brutal, self-assessment, Batten says. It’s easy to blame the market, the company’s board or others, but some of those errors might be the founder’s fault.

But a few mistakes are no barrier to trying again by starting another company. Batten, for one, says he’d be willing to invest in an entrepreneur with a failure or two in their history — so long as the person genuinely learnt from their experience and plans to avoid making the same mistakes this time around.

A failure, then, isn’t necessarily the end. It might provide the lessons and inspiration for the next big thing. ■

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