Budding entrepreneurs at Harvard University's i-lab learn the skills needed to develop a new business.

HARVARD INNOVATION LABS/EVGENIA ELISEEVA

START-UPS

A sense of enterprise

Universities aid entrepreneurs by helping them to turn their research into companies. In return, universities can reap financial benefits.

BY NEIL SAVAGE

Michael Schrader knew he wanted to create a company, but he wasn't sure what it should do. After six years as a mechanical engineer in the automotive industry building plastic parts, in 2010 he began a master's degree in business administration at Harvard Business School in Boston, Massachusetts. In his quest for inspiration, he took a course in commercializing science at the Harvard Innovation Lab (i-lab).

The class heard presentations from researchers who among them had developed 17 different technologies that they thought had commercial value. One in particular caught Schrader's attention — a method devised by two engineers from Tufts University that uses a silk protein to stabilize vaccines. The vaccines could be formulated as powders and mixed with water when it was time to inject them, or embedded into a film that dissolves on the tongue like a breath-freshening strip. And, because they would not need to be refrigerated, they would be easier than conventional vaccines to distribute in places such as sub-Saharan Africa.

Along with other members of his class — an economics master's student, a former physics student earning a law degree and a postdoc in the chemistry department — Schrader spent the next few months looking into potential markets for the technology, making connections with business mentors and investors, and putting together a business plan. In 2012, the team founded Vaxess Technologies, which is attempting to bring vaccine formulations to market.

"We probably are a perfect model for how universities can forge together entrepreneurs and technologies to create companies," says Schrader, now chief executive of Vaxess. The technology has not yet entered clinical testing, but the company has raised more than US$5 million, hired 11 employees, and started filing patents of its own in addition to those it licensed from Tufts University.

Although universities often license technology developed in their research laboratories to existing companies that are looking for new products, they also move discoveries off the bench and into the real world by encouraging inventors to start businesses from scratch. They offer classes in entrepreneurship, introduce researchers to investors and business experts, and even launch their own venture-capital funds. The path is trickier for life-sciences spin-offs, which take more time and money to get off the ground, than for companies based on software or electronics. And Europe has not caught up with the United States in its ability to create businesses.

But universities are banking on entrepreneurs turning some of their research into products (see 'Start-up sampler).

HUBS OF INNOVATION

Universities tend to see commercialization as part of their remit to create and disseminate knowledge. "We exist on taxpayer money. We have an obligation to try to get our research out into society," says Regis Kelly, director of the California Institute for Quantitative Biosciences known as QB3. The institute is a collaboration between the Berkeley, Santa Cruz and San Francisco campuses of the University of California. It supports life-sciences research across the campuses and tries to bring that research to market by partnering with industry and promoting entrepreneurship.

Part of the mission of the University of Colorado Boulder's BioFrontiers Institute is to aid students and faculty members who want to start new companies, says Jana Watson-Capps, associate director of the institute. "It fits with what we want to do in providing an education for our students so that they can find jobs and be good at those jobs," she says.

A similar attitude is common in the United Kingdom. "We think it's important here in Oxford to see that the fruits of our research are actually developed to benefit society," says Linda Naylor, managing director of Isis Innovation, a company created by the University of Oxford to commercialize its research.

Harvard's i-lab, which was opened in late 2011 to help students in any of the university's schools to develop businesses, is a relatively new entry in a long line of such efforts at many academic institutions. Students learn about idea generation, business-plan development and marketing. Budding entrepreneurs can attend workshops on specific hurdles that they are likely to encounter, such as how to apply for a Small Business Innovation Research grant from the federal government. A group of 'experts in residence' provides students with business expertise and introduces them to potential investors. The i-lab holds competitions such as the President's Challenge, which awards ideas that address the world's big problems. Vaxess took the challenge's top prize of $70,000 in 2012, as well as winning $25,000 in Harvard's Business Plan Contest the same year.

Because the main thrust of the i-lab is education, the university never takes a stake in any of the companies created there, says managing director Jodi Goldstein. Any intellectual property developed in a Harvard research lab belongs to the university and must be licensed, but ideas generated in the i-lab belong to the students. Goldstein hopes that the i-lab can help a future Mark Zuckerberg or Bill Gates to pursue their billion-dollar idea while still completing their degree. "We have several pretty famous dropouts around here, and I don't think that's necessary anymore," she says.

As well as education and expertise, the i-lab provides a workspace for fledging companies. Meeting rooms, computer workstations and private storage space are available, as are a workshop for building prototypes and a pair of 3D printers. The i-lab is also planning to address one of the stumbling blocks that often trips up biology-based companies: finding a space to turn a discovery made in a university lab into a more marketable version. It is building a 1,400-square-metre wet lab with 36 research benches. When Vaxess reached that stage, it moved to LabCentral in Cambridge, Massachusetts. The provider of office and laboratory space takes care of regulatory requirements and provides administrative support and laboratory personnel so that new companies don't have to spend time and money setting up their own space. It opened in 2013 with a $5-million grant from the Massachusetts government (part of an initiative to bolster life-sciences business in the state) along with support from the Massachusetts Institute of Technology and the venture-capital arm of health-care giant Johnson & Johnson. Schrader considers this industry–government–academia web of support essential to his company's launch. "We have really taken advantage of this growing entrepreneurial ecosystem," he says.

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At QB3 in California, start-ups can rent lab space for as little as $85–100 per square metre per month. Unlike conventional landlords, who prefer to rent out an entire space, start-ups can rent a few hours in a fume cupboard or a shelf in a freezer, for example. "You only pay for what you actually use," Kelly says. Charging is important, mainly because it is a way of weaning its users off the university teat. "It gets people more used to being in the private sector," he says.

The need for lab space is just one reason why starting a life-sciences company can be much more challenging than, say, launching a business based on software. Any sort of pharmaceutical or medical device is subject to regulatory requirements, which leads to safety tests and clinical trials "If you're going to make a new drug you might need ten years and a billion dollars," says Watson-Capps.

These time and capital requirements make it much more difficult to drum up investment for a life-sciences start-up. Although investors might be willing to risk a couple of hundred thousand dollars on a promising software idea, most life-sciences companies need initial funding of a few million dollars. "Obviously, people don't want to throw away a million dollars, so they have to do a lot more due diligence," Kelly says. And because the time to realize a return on the investment can be so long, trading equity in the company in exchange for, say, legal services is not as popular as it is for other types of start-ups, he adds. These disparities are apparent in the investment statistics. Of the $77.3 billion in venture capital invested in the

LICENSING TECHNOLOGY

Innovation income

When it comes to commercializing research, universities often emphasize their desire to spread their discoveries, but they also reap financial rewards from licensing technology and investing in spin-off companies. Isis Innovation, for instance, took in £24.6 million (US$34.9 million) in revenue in 2015, of which it returned £13.6 million to its founder Oxford University, UK, more than double 2014's £6.7 million. The university also earned more than £30 million in cash and stocks from the 2014 sale of the games and technology company NaturalMotion (in which it had a stake of about 9%) to Zynga in San Francisco, California, for $527 million. NaturalMotion was co-founded in 2001 by Torstein Reil, then a PhD student in Oxford's zoology department studying neural systems. Reil used his research to create computer simulations that more accurately mimic how animals move, and turned them into a company that makes popular games such as Clumsy Ninja.

But licensing income tends to make up only a small part of a university's revenue stream. Harvard University in Cambridge, Massachusetts, which last year issued 50 licenses to patents it owns and saw 14 firms started on the basis of its technology, had licensing revenue of $16.1 million in 2015. But that is a fraction of Harvard's 2015 budget of nearly $4.5 billion, of which the university spent $876 million on research.

Jana Watson-Capps, associate director of the University of Colorado Boulder's BioFrontiers Institute, says that income from all licensing — not just from spin-off companies — is valuable to the university and goes back into funding research. However, she adds, licensing income is relatively small and comes so long after the initial investment that it's not a major consideration at the institute. A similar attitude prevails at Oxford. Although the university welcomes the licensing income, it's not the only motive for promoting spin-offs, says Linda Naylor, managing director of Isis Innovation. "The university is very clear it wants to create impact," she says. "They're not there to make any quick money." N.S.

START-UP SAMPLER

Universities seeking to commercialize research spin off scores of companies. These examples show the range of entrepreneurship spawned in the life sciences.

Company	University	Technology	Founded	Financial milestone
OxSyBio	University of Oxford, UK	3D printing of tissues for research and clinical applications	2014	£1 million (US$1.42 million) funding, April 2014
Semma Therapeutics	Harvard University, Cambridge, Massachusetts	Creation of insulin-producing cells from stem cells to treat people with diabetes	2015	$44 million funding, March 2015
Click Nucleic Acids	University of Colorado, Boulder	DNA analogues for applications such as therapeutics and biosensing	2015	Seeking funding
Zephyrus Biosciences	University of California, Berkeley	Tools to allow single-cell sequencing using western blot protein analysis	2013	$1.86 million funding, August 2014
Clyde Biosciences	University of Glasgow, UK	Combination of stem cells and optical detection technology to test drugs for cardiotoxicity	2012	£2 million funding, April 2015
Ex Scientia	University of Dundee, UK	Small-molecule drugs that bind to a combination of targets	2012	Pharmaceutical contracts worth $6 million

United States in 2015, software companies took in $31.2 billion — 40% of the total. Pharmaceuticals and biotechnology received a mere 12%.

PLAYING CATCH UP

Europe lags behind the United States in producing start-ups of any kind, but the situation is improving. "We're certainly seeing a lot more spin-outs than we were a few years ago," says Naylor. "There is more money around that is willing to go into the early stage."

She attributes that growth, in part, to the UK government's creation of the Seed Enterprise Investment Scheme in 2012, which provides tax breaks to investors in start-up companies. "The UK has been one of the leaders in providing tax incentives for investors in start-ups of all types," says Karen Wilson, who studies entrepreneurship and innovation at Bruegel, an economic think tank in Brussels. Other countries across Europe, as well as Australia, have created their own tax incentives for investors modelled on the British scheme, although Wilson says that they're often controversial, derided as tax breaks for the wealthy. In the United States, tax incentives vary by state. The biggest legal change in the United States to promote spin-offs came in 1980, Wilson says, with the passage of the Bayh–Dole act, which allowed researchers to profit from inventions created with federal funding.

US and UK Universities have even been creating their own venture funds in recent years to invest in their spin-offs. The University of Cambridge, UK, created Cambridge Innovation Capital in 2013 with an initial fund of £50 million ($71 million). In 2014, the University of California began a $250-million fund. In May 2015, Isis launched Oxford Sciences Innovation to raise an initial £300 million from investors. And, in January, University College London opened the £50 million UCL Technology Fund, and the University of Bristol, UK, started its own enterprise fund (see 'Innovation income').

Entrepreneurial ecosystems in which inventors can find facilities, investors and business experts to help them to launch their companies are important for creating successful spin-offs, and they've been growing around many European universities, Wilson says. "There are an increasing number of these entrepreneurial hubs that are emerging across Europe, which are spawning these innovative high-growth firms," she says.

In the United Kingdom, Cambridge is popular for life-sciences start-ups, and in Munich, Germany, the focus is mobile technology. In Switzerland, start-ups are clustered around the University of Zurich and the Swiss Federal Institute of Technology in Lausanne, where they focus on computing and technology. In Finland, Espoo is a hub: in 2010, three institutions combined to form Aalto University, which has strengths in communications, energy and design. Linked by a bridge across the Øresund strait, Copenhagen and Malmo in Sweden, make up another life-sciences centre. In the past year, however, the influx of refugees from the Middle East has led to a tightening of border security and made crossing the bridge more difficult for everyone.

The clampdown on migration within Europe, says Wilson, is making it harder for fledging companies to grow and spread. Expansion of their markets has always been challenging for start-ups in Europe, she says, where pushing into another country means dealing with differences not only in language and culture but also in taxes and other regulations. Many European companies get to a point at which, when they need to grow into a bigger market, they move to the United States, either of their own accord or at the insistence of their investors. "If you have a successful start-up in Italy it's much easier to go scale it in the US than it is to try to scale it across Europe," Wilson says.

But many life-sciences companies won't grow on their own, particularly if their innovation is a drug — their endgame is often to be acquired by a large pharmaceutical company once they have advanced their therapy to a promising stage.

Although life-sciences companies demand more resources than other types of start-up, they have one characteristic that can make them uniquely appealing to investors — the potential for curing a disease or improving human health. As Kelly points out, "Almost any rich person has a sick relative." If investors are going to risk their money, knowing that many of the companies they invest in will fail, they may prefer investments that have a potential for making a difference, he says. "If they're going to lose money on a business, they might as well lose it on something that could have some benefit to society." ■

PATRICK HO/VAXESS

Vaxess Technologies are using silk proteins (L), which are extracted from cocoons (R), to stabilize vaccines.

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