

Company founders: voices of experience

Laura DeFrancesco

Interviews with nine leading scientists who founded startup companies reveal some common themes and lessons.

The scientific credentials of a biotech company are among its most important assets. Scientific founders play a key role in raising the company's scientific profile and in securing venture capitalist funding, but what then? Founders can choose to take an active role in the management of their companies or pass this responsibility to others. Some are able to balance an active managerial role with an academic career, whereas others prefer to limit their involvement to overseeing the science through an advisory position. Here, we look at the choices made by eight scientists who founded one or more companies. What influenced their original decision to start a company? What were the challenges? We hear of their successes and disappointments, and the impact that starting a company had on their commercial and academic interests.

What drives a scientist to start a company? The answers were as varied as the personalities of the people interviewed. But some overriding themes emerged.

Finding a niche

Several of our founders saw something extraordinary in their fields, which they felt could be the basis of a company. Bruno Tocqué's work on splice variants, for example, led him to start ExonHit (Paris) (see **Box 1**). Alternative splicing is one way that eukaryotes generate diversity in protein species, but, when gone awry, it can also lead to catastrophic diseases. Back in 1997, there was no way to exploit splice variants in drug discovery or therapeutics. Although he was director of the Department of Gene Medicine at Rhône-Poulenc Rorer (now part of Aventis; Strasbourg, France) at the time, Tocqué and two of his colleagues decided to break away to start their own company. "Right from the

Box 1 Bruno Tocqué profile



Most recent position: founder and CEO of ExonHit Therapeutics

Location: Paris

Company focus: alternative splicing for therapeutics in cancer and neurodegenerative disease

Other positions held: director of the Department of Gene Medicine, Rhône-Poulenc Rorer (now Aventis; Strasbourg, France)

Words of wisdom: "When you start a company you need to have a clear idea of your objectives and which domain to exploit."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.

start, ...we knew that we ultimately wanted to build our own product portfolio and become a drug discovery company." They integrated drug discovery into their long-term plans and chose to focus on areas—cancer and neurodegenerative diseases—that played to the founders' strengths.

Similarly, Massachusetts Institute of Technology's (Cambridge, MA, USA) Phil Sharp, one of the founders of the RNAi company Alnylam, saw a large untapped potential in RNA interference, once it was demonstrated that it could be used to silence genes in humans (see **Box 2**). Sharp did not turn to Biogen (Cambridge, MA, USA), a company he

helped found in 1978, which has since grown into a 2,700-person, international company. Rather he felt a new company would be better able to develop and fine-tune the technology. "Mature companies are interested in product development and have an intense need to get products to market; they just don't have the time to dabble in new technologies. That's what happened with recombinant DNA—large pharmaceutical companies relied on small ones to carry out development."

And ACADIA Pharmaceutical's (San Diego, CA, USA) Mark Brann felt that starting his own company was the only way to bring new ideas forward (see **Box 3**). "I had the opportu-

Box 2 Phil Sharp profile

Most recent position: cofounder, member of the board of directors and chairman of the scientific board at Alnylam Pharmaceuticals, director of McGovern Institute (Cambridge, MA, USA), chairman of the scientific board at Biogen

Location: Cambridge, MA, USA

Company focus: RNAi therapeutics

Other positions held: cofounder, member of the board of directors at Biogen

Words of wisdom: "There is always a trade-off between doing new science and making a company grow and change. I really enjoyed those conflicts."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.



Laura DeFrancesco is Nature Biotechnology's Senior Editor for News & Features.

Box 3 Mark Brann profile



Most recent position: president and CSO of ACADIA Pharmaceuticals
Location: San Diego, CA, and Copenhagen, Denmark
Company focus: genetic technologies in drug discovery

Other positions held: CEO of Receptor Technologies, NIH investigator, tenured associate professor at University of Vermont, adjunct associate professor at the University of California, San Diego, USA

Words of wisdom: Working scientists should steer clear of running businesses: "There is a conflict of interest, which in my opinion doesn't work in the long term."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.

nity of working in large pharma but felt that an inherent conservatism in these large organizations would delay bringing the technology to the discovery process," he said. "I believed that starting my own company was the only viable option."

But not all the issues are purely scientific. Domantis (Cambridge, MA, USA) founder Greg Winter, for example, saw founding a company as a way of expanding his group out from the confines of academia (see Box 4). He felt that his work at the UK's Medical Research Council (MRC; Cambridge, UK) on producing fully human antibodies offered a great commercial opportunity. Yet to develop the idea, he needed more people than he had room for at MRC's campus. As there was no prospect of enlarging his group, he decided to set up a company instead. It may not be the best reason for creating a startup company, he admits, but "I needed more hands at the bench, as there were huge technical challenges."

First steps and missteps

The first time out of the blocks can be tough. For example, when Brann attempted to commercialize his genetic research at the US National Institutes of Health (NIH; Bethesda, MD, USA), his inexperience with business and the restrictions placed on him by the NIH made this first outing difficult. Equally challenging was keeping investors happy. Although he was able to raise capital, balancing investor expectations with realistic timelines

for technology development was a constant battle. "The research had long-term goals and a fast return for investors was not possible." This sent Brann back to academia and several years later, after building working relationships with companies while at the University of Vermont (Burlington, VT, USA), he was ready to give it another go. Learning from his experience, he started small and let the company grow gradually, establishing commercial contracts to keep the company afloat.

Though reluctant to move into the commercial arena, Affitech (Oslo, Norway) founder Ole Jørgen Marvik was inspired to start a company based on phage display technology in 1997 (see Box 5). This was at a time when seed money was relatively easy to come by. But as a platform company, they had trouble convincing investors that they should focus on therapeutics. "We were a technology looking for a problem," he says. Bowing to pressure, they focused on diagnostics, a particular strength of Norway's drug industry. But in the end, it proved to be the wrong decision, and they eventually found investors who would support their efforts to build an antibody therapeutic pipeline. "This was a valuable lesson; it is better to be bold and follow the long-term strategy, even when it represents a greater challenge," says Marvik.

Starting a company from his post at the University of Dundee, UK, Cyclacel founder David Lane ran into all kinds of problems until the university's technology transfer office hooked him up with a creative venture capitalist, Chris Evans (Merlin Ventures, London), who was able to find the right terms to keep all the parties happy—the university as well as the charity sponsor of Lane's research (see Box 6). Lane says, "We started from absolutely nothing and there wasn't much guidance on what you should do. At that time, there was no incubator environment." Even after these initial problems, it wasn't smooth sailing. With the high level of uncertainty in a startup, retaining staff who are key for R&D can be a challenge. In the

Box 4 Greg Winter profile



Most recent position: cofounder, director and chairman of the scientific advisory board, Domantis, head of the Division of Protein and Nucleic Acid Chemistry at the

Medical Research Council (Cambridge, UK)

Location: Cambridge, UK

Company focus: therapeutic applications of antibody domains

Other positions held: cofounder and director of Cambridge Antibody Technology, Scotgen

Words of wisdom: "You are either an entrepreneur or not, and no amount of training will turn you into one."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.

early days, Cyclacel took in a scientist interested in broadening the company's research portfolio to include gene therapy, only to have him leave for another company. This left the company with researchers and intellectual property it couldn't exploit. "At that stage, if it had been anyone but Chris funding us, we might have been in considerable trouble. I realize now, that this sort of situation is very common. You have to be able to adapt to change," he says.

Perhaps the greatest challenge for a fledgling company is getting through tough economic times, such as the past few years. Preparing for lean times is critical, as Vernalis (Winnersh, UK) founder Colin Dourish points out (see Box 7). "The key thing I have learned over the past six-to-seven years is the importance of having enough cash in the bank...I have learned that it is a good strategy to raise money, even when it is not needed, so that there is always a sufficient cash cushion

Box 5 Ole Jørgen Marvik profile



Most recent position: founder and member of the board of Affitech

Location: Oslo, Norway

Company focus: human antibody therapeutics

Other positions held: CEO of Affitech, cofounder and chairman of the Norwegian Bioindustry Association, board member of EuropaBio

Words of wisdom: "The most important task for a technology platform company is to convert its capabilities into products that can sustain the business over time."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.



Box 6 David Lane profile



Most recent position: CSO of Cyclacel, professor of molecular oncology, University of Dundee, UK

Location: Dundee, UK

Company focus: small molecule drugs for cancer and other diseases

Other positions held: cofounder and director of Cambridge Antibody

Words of wisdom: "You have to be able to adapt to change."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.

for when the market is uncertain," he advises. ExonHit's Tocqué agrees. He suggests that companies take advantage of every financing opportunity. "You are going to have to work miracles with very little money," he says.

People, people, people

Almost all would agree on the importance of getting the right people, based not just on their expertise, but on their attitude as well. Starting at the top, having good management in place can keep a company together during hard times, as Dourish found out. "Ideas can go awry and projects may fail, but if you have a strong management team, it is possible to adapt," he says.

Bringing people together from various backgrounds can also enrich the experience and expand the possibilities. In fact, in Marvik's Affitech, two other companies were spawned from the talent that had collected around his company. "Early on, one of the most inspiring lessons we learned was the value of bringing people together with different backgrounds and skills," he says. And it's not just people in your company. Marvik stresses the importance of outside collaborators. "If I were to give advice about setting up a company, I would emphasize the importance of collaboration and finding the right people."

And Vidar Hansson, founder and CEO of photodynamic therapy firm Photocure (Oslo, Norway), finds that the intellectual capital of a company rests not just in the number of patents a company has acquired, but in the minds of the people who work there (see Box 8). Hansson feels the key to getting the most from his employees is to get them invested in the company. He says recruiting people with the right attitude and then rewarding them through stock options and other incentives, makes them each feel a responsibility for the company. "We always try and get hold of the best people and they need to be competent, engaged, imaginative and excited by what they are doing."

Learning by doing

The lessons learned the first time a scientist

starts a company and enters the business world are often the hardest. But some take these early experiences and put them to good use later in starting new companies. And of course, timing is everything.

Adrian Hill, cofounder of therapeutic vaccine company Oxxon (Oxford, UK), felt that time was working against him (see Box 9). It took several years to work out the details among the three other cofounders, investors and the Wellcome Trust, which as funder of the research had an interest in the company. Although he was quite impatient, feeling the hot breath of competitors, the other parties involved had no such incentive to move quickly. In the end, though, he felt it was for the best. "In retrospect, the time delay wasn't all bad as it gave time for our technology to gain acceptance. It also made it easier in terms of managing my academic workload," he says.

Dourish, who with four fellow Wyeth researchers, formed their own company when Wyeth closed down its research operations in the UK, formulated a two-part plan. One part was to establish a preclinical contract research business to bring in revenue, and the other part of the business was drug discovery. But before long, a conflict developed between the needs of the contract business and the drug discovery and development needs. And so they integrated the contract business into the drug discovery operation.

In the early days, nobody had any experience with companies. As Sharp points out, when he was starting Biogen back in the 1980s, there was no 'biotech.' "The words 'biology' and 'technology' had not yet been amalgamated." They had to find people prepared to take risks, develop the technology and have the mind-set to make it work. But fast forward 20 years to when Alnylam was on the drawing board, and there were people available who had been in the business for 20 years, with experience in turning technology into products. And these days, pharmaceutical companies have a different attitude toward biotech. "There is also a great deal of interest from large pharma companies who see start-ups as an essential part of the future."

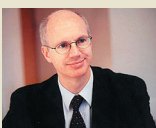
The great juggling act

Some of our interviewees split their time between business and science; others have chosen to stick with one or the other. What do they say about their choices?

Certain scientists say that to do good science, you have to step away from the business side of the company. Brann, who serves as CSO at ACADIA, gave up the role of CEO early on, as he felt that the fiscal responsibilities of being CEO got in the way of doing good science. "There is a conflict of interest, which in my opinion doesn't work in the long term," he says.

Cyclacel's Lane wanted to keep his hat in the academic ring. He says that companies need someone at the helm who will be there all the time and can talk to investors. So, in 1996, when Cyclacel was formed, they made the decision right away to hire a CEO. "Many biotechs make this decision when they have been going for two or three years, and that can be harder. If you can make the decision early, it is probably better." Lane feels that being removed from management has the added advantage of giving him an objective view of

Box 7 Colin Dourish profile



Most recent position: senior vice president, research, and CSO of Vernalis, professor of psychopharmacology at the University of Durham, visiting professor of neuroscience and psychological medicine at Imperial College of Science, Technology and Medicine, and a William Pitt Fellow of Pembroke College, Cambridge, UK

Location: Winnersh, UK

Company focus: structure-based drug discovery

Other positions held: CEO of Cerebrus (acquired by Vernalis in 1999), director of neuropharmacology at Wyeth

Words of wisdom: "The key thing I have learned over the past six-to-seven years is the importance of having enough cash in the bank."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.

Box 8 Vidar Hansson profile

Most recent position: Founder, CEO Photocure, professor of biochemistry at University of Oslo

Location: Oslo, Norway

Company focus: photodynamic therapy for oncology and dermatology

Other positions held: chairman of the board of Laurus (2000)

Words of wisdom: "We had a very strong ambition—and that is very important to any new company."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.

the company science. "At the end of the day, in a company like ours, there is a lot going on and what you have to do is make sure that the science is right."

But not everyone can choose between science and business, especially in a small company. Dourish, who kept the title of CEO at Vernalis for only nine months, is still involved, nonetheless, with corporate and commercial activities. "I think that is common in small organizations; people wear a lot of different hats," he says.

For Sharp, though, the decision has been an easy one. "My first interest has always been as a faculty member of MIT," he says. So with Biogen and Alnylam, two companies he helped to found, he has restricted his involvement to providing scientific advice at the board level.

So what does it take?

Wanting it, some would say. More important than the trappings of a company is the will to succeed. In the early days of PhotoCure, Hansson remembers only one thing mattered—the idea that they were going to make it as a global pharmaceutical company. "We had no telephones, no computers or any other essential equipment, but we did have a very strong ambition—and that is very important to any new company," he says.

And preparation can be key, though finding the right people to give advice and even finding the time to seek it out can be tough, according to Lane. "Bioentrepreneurs need better mentors," says Lane. "It would have been great if someone had explained to me exactly how share options work, how capital gains works. When you are busy, it's quite a hurdle to find these things out for yourself."

For Oxon's Hill, keeping your founders on board is important, but the demarcation between academia and commercial interests has to be crystal clear. "In a situation like ours where there is an interdependence between commercial and academic interests, it is important to define clearly what each party is doing," he said.

And then there are the intangibles. As Winter sees it, some people just have it. "I have the feeling that you are either an entrepreneur or not, and no amount of training will turn you into one."

Note: This article is based on research carried out in 2003 by De Facto Communications, London. A pdf document of transcripts of the original interviews is available as supplementary information on the Nature Biotechnology website.

This story was reprinted with some modification from the Building a Business section of the Bioentrepreneur web portal (<http://www.nature.com/bioent>), 22 March 2004, doi:10.1038/bioent796.

Box 9 Adrian Hill profile

Most recent position: chairman of the scientific advisory board of Oxon, and Wellcome Trust Principal Research Fellow in the Nuffield Department of Clinical Medicine, and professor of human genetics at the University of Oxford

Location: Oxford, UK

Company focus: pharamcines (therapeutic vaccines)

Words of wisdom: "The demarcation between academic and commercial has to be crystal clear unless people are prepared to leave the university and join the company. Managing the industry-academic relationship is very important."

Note: A transcript of the original interview is available as supplementary information on the Nature Biotechnology website.