# At ground level

Julian Bertschinger

**The hardest—and perhaps loneliest—period of being an entrepreneur might be just after your company is founded.**



I cofounded Covagen when I was 30 years old. Although my PhD and postdoc work had taught me to think in a focused manner and be product oriented, I was as green as they come concerning the nuts and bolts of launching a company. Picking it up as you go might not be the optimal way to learn, but I'm living proof that it can be done with the right team. Here's how we did it.

## Two men and a plan

The most important motivating factor, for me, was my education. I did my thesis in Dario Neri's lab at the Institute of Pharmaceutical Sciences at ETH Zurich. The research group there had just isolated an antibody fragment that binds to a tumor-associated marker, and proof-of-concept data showed that the fragment selectively targeted solid tumors in mice. Neri went on to cofound Philogen, based in Siena, Italy, and develop the antibody in collaboration with Bayer Schering in Berlin. Today, several derivatives of this antibody are in phase 2 trials.

Seeing this process firsthand showed me (and Dragan Grabulovski, my cofounder at Covagen, which is based in Zurich) that it was possible to move from the lab to the commercial side. This had our group thinking about products right away, which I believe is crucial when contemplating a biotech company. But the truth is that Covagen never would have been founded without the Venture business plan competition, organized every two years by McKinsey, in Zurich, and ETH Zurich. One of the winners of this competition was Glycart Biotechnology, also in Zurich, which took the prize in 1998 and eventually was acquired by Roche, in Basel, Switzerland, for CHF235 million (US$180 million) in 2005.

Grabulovski and I decided to take part in the Venture 2006 competition for two reasons: we were eager to learn how to write a business plan (we'd never written one) and we thought it would be interesting precisely because it was so different from the reports and scholarly articles we were used to writing.

The competition is divided into two phases. During the first, entrants submit a business idea outlined on a few pages, and the best ten ideas are awarded a prize. In the second, all participants receive free coaching from industry experts and venture capitalists, who then give advice to participants writing their first business plan. The ten best business plans are chosen by a jury and all receive the same prize amount of CHF2,500 (US$2,057).

We submitted our business idea, but I didn't actually expect us to be one of the winners; I was busy applying for postdoc positions abroad. Nevertheless, our idea was chosen out of about 100 applications to be awarded with a CHF2,500 prize. This surprised me—not because we doubted our entry, which was based on the Fynomer technology (**Fig 1**; **Box 1** and D. Grabulovski *et al. J. Biol. Chem.* **282**, 3196–3204 (2007)) but because we felt that it was too early to found a company on the available results: we had no *in vivo* data.

Looking back, the biggest effect of participating in Venture 2006 was that it let us begin to establish a business network—previously, we'd known only people within academia. At workshops during the second phase of the competition, we met Rudolf Gygax, a managing director of Novartis Venture Fund, who would be a key contact for us later on. He and Neri helped us to draft our first business plan.

The prize money was certainly useful, but the large amount of positive feedback we received was even more important. That boosted our confidence, and after winning, I thought for the first time that we really could found our own company.

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## Box 1 The technology behind Covagen

Covagen is built on Fynomer technology (**Fig. 1**), developed at the Institute of Pharmaceutical Sciences at ETH Zurich. Fynomers are a class of binding proteins derived from the Src homology 3 (SH3) domain of the human Fyn kinase (D. Grabulovski *et al. J. Biol. Chem.* **282**, 3196–3204 (2007)). The Fyn SH3 domain structure is made up of two anti-parallel β-sheets and two loops—n-src and RT—which are known to be involved in interactions with other ligand proteins.

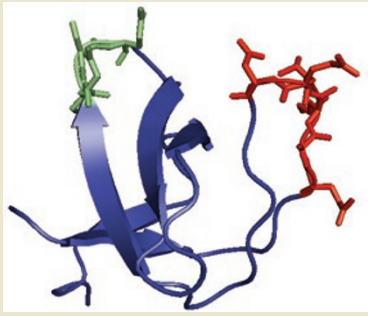

**Figure 1** Fyn Src homology 3 (SH3) domain structure. The RT-Src loop is shown in red, and the *n*-Src loop is shown in green. (Protein Data Bank entry 1M27)

Fynomers can be produced in bacteria at high yields and are approximately 20 times smaller than antibodies. Additionally, they have the advantage of being easily assembled in a modular manner to yield bispecific and/or multivalent proteins, which might allow new treatment modalities that are challenging or impossible to explore with traditional antibody formats.

## Box 2 Securing our funding

I was able to found Covagen with an initial investment (in several tranches) from the Novartis Venture Fund. The first tranche came after signing investment documents, and the following tranches were hinged on attaining research milestones.

It was crucial that Novartis Venture Fund was prepared to invest in us at a very early stage. Corporate venture funds are beneficial in this way: they are usually more likely to do early-stage investments than most private venture capitalists because corporate funds can afford longer times to exit. If you've hit upon an interesting idea in academia, you might look to corporate venture funds first.

In 2009, Covagen was able to attract three other investors: the corporate venture fund MP Healthcare Venture Management, of Boston; Ventech, of Paris; and Edmond de Rothschild Investment Partners, also of Paris. We also have received some funds via our research collaboration with Roche, which was secured in June 2009.

To move our interleukin-17A inhibitor into preclinical and clinical development, we are planning to raise additional money this year, so we are seeking one or two venture capitalists to join our existing investors.

### Founding Covagen

We stayed in contact with Gygax, and he invited us to present our project at the Novartis Venture Fund headquarters in Basel. The fund was interested in investing, and we sat down to negotiate our first term sheet. I had absolutely no idea what the difference was between a binding contract and term sheet, and this was my initiation. I learned what Series A shares are, how to calculate pre-money and post-money valuations, what drag-along and tag-along clauses are, why a high liquidation preference for investors is bad for holders of common shares and how anti-dilution protection for investors can hurt founders in a down round. I was moving into a whole new world.

It is very important to understand every word in term sheets and agreements. You should always know what you are signing. To do this, first make sure you find a lawyer who intimately knows relationships between venture capitalists and biotech startup companies, and then be persistent enough to ask your lawyer about every single expression or phrase you do not understand. (You can familiarize yourself somewhat with the terminology by using the internet, in particular http://www.investopedia.com/terms/v/venturecapital.asp, but also ask your lawyer directly.)

When we finally signed the term sheet, we found it just meant more paperwork. We still needed to establish a licensing agreement with ETH Zurich and negotiate the investment and shareholder's agreements. I admit that when I first read the investment document drafts, I thought the beginning definitions weren't very relevant. But after further reading and questioning our lawyer, I quickly realized that those definitions are actually one of the most important things in a contract.

Once all the details were ironed out (**Box 2**), we founded Covagen in December 2006 and signed the investment agreements with Novartis Venture Fund. The real work was about to start.

### The lonely lab

Grabulovski still had to finish his PhD thesis. This made me Covagen's only employee from December 2006 until May 2007, and Covagen was a startup in every sense of the word. My first task was to open a bank account so Novartis Venture Fund could transfer in its investment.

When that was done, I set up Covagen's homepage (be sure to check for domain name availability before you decide on a company name). A friend of a friend runs a company offering website design and e-mail hosting services, and he helped me create Covagen's website. Here's a tip: make sure that you can administer the website yourself so you will not have to pay a web designer for every small change or update. In addition, I opened a Covagen e-mail account, and here, too, I made sure I could independently set up additional e-mail accounts.

But there remained a very big need—work space. We had no laboratory. Unfortunately, ETH Zurich does not offer incubator space for spin-outs. Startup companies usually try to find space within the department they originated from, but in our case there was no room available. After asking around within ETH Zurich, Grabulovski learned of an empty laboratory not attached to any department, and we were able to make an arrangement to allow us to rent this space. In addition, our former institute enabled us to access some rather expensive instruments for an affordable fee.

The laboratory was empty, except for benches and desks, and somewhat dusty. On my second day, I brought rags from home and started cleaning. This wasn't really what I envisioned a biotech CEO doing, but the truth is, I was excited—I was starting a company from the very bottom! There was no network connection for my computer, no printer, no phone, no fax. However, after making a few calls with my mobile phone, the university's staff set up all the necessary connections within a few days. This is a benefit of staying within academia: when starting your company, all issues related to infrastructure need only minimal time and management resources.

After all that work, I thoroughly appreciated making the first company phone call and sending the first message from my Covagen e-mail account!

With communications behind me, I was left with the science. It's only when you start from scratch that you realize how many different instruments and tools, disposable plastic tubes, glassware, kits, antibodies and chemicals are needed for research, and I had none of it. I also realized how comfortable my life in the academic lab had been, where many instruments were available and I didn't have to think about budgeting. That was not the case at Covagen, where I became very cost sensitive. Comparison shopping takes time, and it was four months before the last instruments and reagents arrived. This neatly coincided with Grabulovski earning his PhD in May 2007, and he joined Covagen as CSO. I finally had company.

### Building a biotech

Established as Covagen, we now had several target proteins in mind to validate the technology, but we did not have a clear plan on which targets we wanted to focus on for the development of our first Fynomer-based clinical candidate. Choosing a good first target was the most important decision we needed to make because once we made the call, we'd invest most of our resources in that direction. We investigated many different targets to find one that was economically promising and in an area in which Covagen had freedom to operate. We decided to go for inhibition of the cytokine interleukin-17A, which is an attractive emerging target for diseases such as rheumatoid arthritis, psoriasis and uveitis.

In early summer 2007, we hired another person to help speed up our research. We had spent less money than we expected in the first half of 2007, so we had sufficient financial resources to hire. We felt that our first employee should be someone we already knew and someone we could trust to be dependable

and competent. As several investors had warned us, not getting along with co-workers is a big reason why many small companies fail. Personal frictions tend to increase even more if a company hits hard times.

We asked Simon Brack, an antibody engineering specialist we knew from our time in Neri's group, to join Covagen. Brack was returning to Switzerland from Oxford, where he'd worked as a postdoc. In October 2007, he became Covagen's third employee and was a great hire.

Even in a company as small as Covagen was then, there were a million administrative things to do, and they occupied a large amount of my time—I was finding it hard to do the necessary work on the bench to develop our technology, not to mention that creating documents and presentations for potential investors takes a lot of time. So at the very least, it felt good to know that if I had to leave the lab, I had four hands working while I was gone. Now, we are up to seven employees.

Advancing our technology is the most important task we have at Covagen, just as it was when we started. For this reason, all employees at Covagen are PhD scientists. We are a young and enthusiastic team; none of us is older than 33. This can be a problem at times: when talking to investors, I realize that we sometimes lack credibility. Quite often, investors do not believe our claims, and mainly that's because they do not believe I have enough experience. In some ways, they are right—I am a scientist still learning the business side of things. But we have been taught a lot about the varying aspects of drug development through working with Neri, and I believe a young group like us can learn fast if given the right advice.

Currently, we're getting that advice from Ray Hill, who was executive director for licensing in Europe at Merck & Co. and now is a visiting professor in neuroscience and mental health at Imperial College London. Hill sits on our board of directors. We've also established an excellent scientific advisory board, which will be of great help and value when bringing our first drug candidate to preclinical development and broadening our research activities.

## Conclusions

Even as our company grows, things continue to change quickly and will for the foreseeable future. The larger we get, the more important (and time consuming) communicating with employees, investors, our board of directors and our scientific advisory board becomes. My tasks are always shifting as we adapt, improve and complement our skills. But this fluid environment is partially what makes startup companies attractive workplaces.

Now, our company doesn't feel so young anymore. This year, we plan to bring our first drug candidate to good manufacturing practice production and preclinical development. That, of course, will require additional money, and we plan to close a financing round this year. Raising a sizable round is another challenge for me, and it means I'm no longer on the bench. My job is raising money now. In that regard, I've graduated to the role of a typical biotech CEO.

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