

Entrepreneurship

Published online: 20 February 2007, doi:10.1038/bioent917

▼ Key ingredients for success in Europe

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Europe has a substantial big pharma presence and a continuing tradition of scientific excellence, but several factors still hinder the development of a vibrant biotech sector.

With numerous regions vying for the attention of life science firms, what key factors are required to encourage biotech venture creation? In the following article, serial entrepreneurs from the UK and Switzerland explore some of the key factors that affect startup creation outside of traditional biotech clusters. The article is an abridged transcript of a *Bioentrepreneur* roundtable discussion sponsored by Yorkshire Forward and the Sheffield Bioincubator; it was convened at the White Rose Forum, York, November 1, 2006. It has been edited to address the major themes of that discussion.

What critical factors are needed to foster successful biotech startups?

Tony Marchington. Right at the top of the list, I would put source of intellectual property (IP) and next to that I would put a source of people, and I mean the type of people who have done PhDs in university, who are then looking for work. People who have gotten a medical degree and who want to get into research or who have some sort of biochemistry degree.

Andrea Pfeifer. In cases where the IP and technology is in place, I think it's extremely important to have a few environmental factors. One is a good university. For example, at AC Immune, we are just across the street [from] the biggest university in Switzerland with excellent scientists. I think another one—and my company has struggled with this—is to have laboratory space where you don't have to invest substantially before you can actually be up and running experiments. There must be some sort of established biotech infrastructure that enables startups to rent space—and not too expensively.

The other aspect that helps is if you're in an international environment where you have easy access to airplanes and so on because it is easier to get investors in. AC Immune went through a big due diligence with a big pharma where we had to somehow fly these people in; it's easy if you're close to an airport. I think for us equally important was the tax environment we were in. I was able to negotiate several years' tax exemption for our company.

When I was doing a consultant job in Germany, I had the hardest time convincing scientists in German universities to actually think about IP and the importance of filing IP before publication. I had to convince them that they're extraordinary scientists but not maybe the best ones to start companies and actually run them. The experience I had was extremely difficult compared with my experience in America. It's one thing to get the scientists involved as founders of the company; but it's another to convince them that you need an experienced management to bring success. Unfortunately, there are not so many good managers for starting these very early phase companies and bringing them to success.



Tony Marchington established in 1989 Oxford Molecular and is a former member of the Department of Trade and Industry's (DTI's) Competitiveness Advisory Group in the UK.

Colin Garner. I think access to facilities is a very important factor in getting science companies to happen. My impression is, certainly in the UK, in the Oxbridge science parks and some of the London ones, there is laboratory accommodation available, albeit at a price. In York, where Xceleron is based, there is not a large amount of space. I know Sheffield has, of course, the Bioincubator. York has a bioincubator, as well, but that's pretty much full to capacity already. So, we're in a situation where we've pretty much filled up our own space.

One interesting aside to this is that we're trying to do the same thing in the United States, in Maryland. We need premises there, so we have made a direct comparison of what it costs in the United States and

what it costs in the United Kingdom. And I'd say it's about half the price in the United States compared with the United Kingdom for the same amount of space. And I imagine in Tennessee it's probably even cheaper than Maryland.

T.M. Isn't it interesting that none of us puts a requirement for a local VC [venture capital] environment? That's very, very interesting for me because I think the fundamentals of actually getting a business going, like we have, you do actually focus on those mentioned points, and you assume if you get those points right, the money will be forthcoming from somewhere. Having said that, it isn't half convenient to be able to pick the phone up in Oxford and Cambridge and London and be within a few minutes of a billion dollars of potential investment.

One of the things that I'm working on personally at the moment is to try and get a fund together of the right size that can actually do biotech investment properly. I think you've got to [have] £100 [\$195] million to be able to do biotech with any degree of seriousness. What these companies need, in my experience, more than anything else, they need an awful lot of early-stage mentoring. They need a lot of people who've done it before and even those who've got the scars down our backs several times as I have, have been there and done it. We all know we are still stepping into the unknown with every one of these companies.

How can a favorable biotech funding environment be encouraged?

T.M. It's very easy for us to criticize the investment climate and say that there isn't enough early-stage money for biotech companies, there isn't enough government support—this, that and the other—but actually the primary suspect is ourselves. We have to get into a discipline where we can present our companies in a way that becomes commercially attractive for the money markets, otherwise we're not going to raise money. Now having said all that, I fundamentally believe that there's still not anywhere near enough private money available for startup biotech companies. And secondly, I don't think that governments should get involved in this area at all. I think governments make a mess of anything they touch that's even vaguely commercial. What they should do is make the funds available and put them safely into the hands of people who know what they're doing. I think governments have a role to play in encouraging people and money into biotech and it certainly needs to support [it]. But I think there are smarter ways of doing it than are currently employed.

A.P. When it comes to government initiatives, one of my suggestions as consultant was to actually put these funds together, make something big and let market criteria decide who gets the support. Often many small initiatives of £10 [\$13] million and whatever lead to absolutely nothing, because it's not enough money in the first place and too many second-class companies are supported, which have no chance of making it in the market.

C.G. I think one of the things that one must recognize is that generally it takes twice as long as you expect it's going to take to develop a biotech product, and it takes twice as much money as you think it's going to take. In other words, investors need to recognize that they will have to put their hands into their pockets several times to make a success of the company. It's not just a simple "You need one round and that's it." You need several rounds of finance, so you have to have that available.

For successful start-ups there needs to be a critical mass of local VCs, business angels and support organizations, such as patent, accountancy



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Colin Garner is founder of CBAMS Ltd., which became Xceleron Ltd. Garner also was research director and founder of Biocode Ltd.

and legal firms that know the biotech space. Most of all, there needs to be a willingness by universities to support entrepreneurs as much as possible, rather than see entrepreneurship as a distraction from academic studies and undergraduate teaching.

We obtained our startup funds at Xceleron in perhaps a rather original manner. We didn't get money from venture capitalists or business angels. We actually got money out of the pharmaceutical industry. And we did this by pitching an approach of potential application for drug development, which might be able to accelerate drug development. We asked several pharma companies if they would be interested in putting in some money up front to buy what at that time was a rather expensive piece of equipment, costing in the region of about \$5 million. So we raised from GlaxoSmithKline [Brentford, UK], Johnson & Johnson [New Brunswick, New Jersey, USA], Novartis [Basel] and Pfizer [New York] something in the region of £1.5 [\$2.9] million. The University of York put some money in, so in the end we got about £2.5 [\$4.9] million, and the attraction was that there was no equity stake by those companies in our company. It was for services to be provided as we moved forward.

But I also want to mention the role of government. I agree entirely that government shouldn't actually get into funding companies and trying to manage companies, but I think certainly the tax environment in the UK is ... reasonably favorable for ... entrepreneurs in terms of when they realize a value on their asset, which is their company, [and] I think there are some very favorable tax advantages for small and medium enterprises. Interestingly, when we eventually did raise money through City of London, that money came from venture capital trusts, which are another tax-efficient vehicle for individuals to invest in risky enterprises that perhaps spread the risk across a variety of firms and again they get good tax breaks both on their investment and any capital gain they make out of that. So I think that is where government actually can help, by making the tax environment better.

What are the strengths of different regions in terms of biotech venture creation?

C.G. From our perspective, we are about to build a facility over in the United States, even though we're a UK-based business. We are doing this simply because this is where the largest market is for what we do. And it's quite interesting, we can talk about being international, but in fact the United States on the whole is not that international. It's very much US-centric. But being US-centric you can still do very well thank you, from a pharma or biotech point of view.

T.M. I have a slightly different take, I was involved in the Foresight Exercise [*Nature* **393**, 8–9, 1998] towards the end of the 1990s, and the aim of Foresight was to look across the major vertical sectors of industry in the UK as a sort of competitive exercise and decide which sectors should the UK be in, because we can't be in every sector. Competition will increase in world trade over the next 20 or 30 years, and the idea was to choose which sectors we should be in and be world class at. And I have to say when you look, there's one area where Europe is still undisputedly world class, and possibly the world's best, and it's in pharmaceutical (not biotech) research. More pharmaceutical-related innovations and more Nobel Prize winners come out of Europe; more fundamental ideas come out of Europe. So perhaps European biotechs could focus on that core expertise.

A.P. Gaining an international perspective is for me absolutely essential, and I think I would recommend [that] everybody in Europe—I actually did this for my PhD students—to get some experience in the United States for two or three years. I think it is so important to see the world from a different angle, and unless you have actually seen the world I don't think you can run a successful biotech, because at some point you will have to go into partnering. What's more, you need the skills and knowledge to survive. When you go to America at a young age it sort of hones your survival skills; you have to create your own career again and it's not easy.

One other aspect of this is that at AC Immune, from the very beginning, we were interested in having an international group of investors. One problem we encountered when talking with US biotech investors, however, was their colloquialism. This was very frustrating as they all liked the company but they basically wanted us to move to the US. This was something that I didn't want to do. Without actually having an office, a lab or whatever, I wonder whether it's possible for a non-US biotech startup to get US investment. On the other hand, the pharmaceutical community in the US has totally changed. When we were looking for a partner for our first Alzheimer product, six US companies independently contacted us. We had never talked to any of them, we were still small, we were never going to any of these big meetings; they contacted us out of the blue to see if we were interested in a partnering deal with the US. So the US pharmaceutical community has become extremely active because they think that there is a lot of technology, a lot of experts in Europe, which they haven't tackled yet.

How do we enrich the pool of experienced managers and entrepreneurs in biotech?

T.M. It's much easier to go into a market with good management and a large market and a good route to market with a lousy product than the other way round. And as scientists, we tend to put our emphasis on our products and services when in actual fact in business terms it's usually the other way round. And there are tons and tons of examples out there of very successful companies with lousy products. And we all use one

everyday and it's called Microsoft [Seattle, Washington, USA].

If you look at the typical biotech company that comes through your door, the management is largely untested. They are usually scientists. The market is usually itself in infancy. You look at the routes to market, they're sometimes well defined but very often management has no idea how they're actually going to turn their idea into a profit. There's no competition to go on, and the product itself, although it's scientifically at proof-of-concept stage, has a long way to go commercially.

Apart from university graduates, I actually think one of the most massive untapped sources of management available to the biotech industry is middle management in large companies. From my experience at ICI [now AstraZeneca; London], I came across tons of people there who were going into work each day, but really itching to do something different. Sometimes these individuals encounter glass ceilings and they either stay and get frustrated—and we all know that individual in the pharmaceutical company—or they decide to go in a completely alternative direction mid-career. And I think if one were thinking about it creatively, one could go to J.P. Garnier of GlaxoSmithKline and the other guys at the top of the industry and say, "Look, why don't you have a career advancement program within your companies, identifying guys 35, 40 years old, who are talented and energetic? Tell them that they're not going to get the next rung up for five years' time, so let's go place you in a startup company. We'll help you get the money, you go and run it for five years. You can then have the option of coming back to us. You will be a much better manager for having done that, and you'll have spun out a small company in the meantime."

A.P. I like the idea, but in reality it doesn't happen, at least not enough because first of all the management of big companies don't want their people thinking outside the company. And second, very few collaborators would like to leave the nice environment, safety, salaries, and comfort of a big company.

C.G. If you go to most biotech companies, many of the management staff came from big pharma. And the reason is that they got bored. They'll come to a biotech company if they have £30 [\$58] million to £50 [\$97] million in the bank. They won't come if there's £250,000 [\$487, 500]! That's the big difference. If there's cash in the bank, you offer them stock options, you have to pay them more than they would usually get within their existing pharma company because they're taking the risk, but the upside should be much greater.

T.M. My feeling is that the US can be a source of one very important commodity in this equation and that's the entrepreneurs. I think [Europe] has got the IP and if we put the money into this there are people that we know that could be head-hunting entrepreneurs in the US to come back to Europe and bring that business savvy to our IP and investment. I think that's quite an interesting opportunity to pursue.

But I take a very simple view of it and that is are you an entrepreneur or are you not an entrepreneur? It's a French word; it means somebody who starts something new. It's a self-fulfilling definition. You either do it or you don't. So spot[ting] the entrepreneur is like saying, well, which is the apple in that barrel of oranges, and by definition if you go to a VC firm and it's full of people who have never actually owned and run their own company, there isn't an entrepreneur. And when I go to a VC [firm] and sit down in a meeting I say, "Right, just so we get some common ground here, what's your own background?" And they go round it and I tell them, "Very importantly, has anyone here apart from myself actually set up and run their own business?" They answer, "Well no, I came close once...." My response is, "Okay then, so I'm the only entrepreneur in the room." That's the bottom line of it, and the phrase is way, way overused and applied to all sorts of people as an accolade they don't deserve.

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