European biotech hasn't hit the street

The growth of European science as a whole is directly linked to the success of European biotech. The failure to realize this fact is a grave mistake

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Some 40 years ago, Soviet President Nikita Krushchev made the bold prediction that within the following 10 years the socialist economy of the Soviet Union would out-compete the capitalist economy of the USA in terms of per capita income, economic welfare, growth and high technology. About three years ago, European statesmen met in Lisbon, Portugal, and agreed on an agenda to set high expectation levels for the next decade of European economic development: the B-Europe programme was launched with the aim of overtaking the USA in regard to key economic parameters, including the growth of biotech industries. History often repeats itself, so we should know that euphoric predictions by politicians should be treated with caution. We can already make the first sobering projections for the results of this programme: if nothing changes the European dream will fail, and in 2010 the biotechnology gap between the USA and the European Union (EU) will be even larger (BioCentury, 2003a). What does this mean for the biotechnology industry? How will this affect academic biomedical research in Europe? And what can be done?

Europe is no longer the continent where most of the headquarters of traditional pharma companies are located. Today, only three (Novartis, Basel, Switzerland; Aventis, Strasbourg, France; and GSK, Uxbridge, UK) of the top ten pharmaceutical companies that are globally active can still be considered to be European (BioCentury, 2003b). Even worse, those that are still active in Europe are relocating and shifting their strategic R&D investments to the USA. This process is not driven by a lack of good quality science in Europe, but rather by the fact that the USA is the world's largest consumer market, and it will be hard to reverse this trend. A prime

example of this phenomenon is Novartis' major investment in the San Diego and Boston areas. Boehringer Ingelheim's Chief Executive Officer, Rolf Krebs, straightforwardly described the situation as follows: "We have to go where we are making the most money, which is the US. We are under increased lobbying from US Congress and Senate members to return R&D money to the market place where we make our profits".

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But traditional pharma is not the only driving force for European biotech: there are also the biotech start-up companies themselves. Today, there are about 1,500 biotech companies in Europe, which at first sight is surprisingly more than the 1,200 in the USA (Ernst & Young, 2002). However, most European companies are too small for viability and are at a disadvantage in terms of accessing sufficient capital. For example, more than one-third of US biotech companies are publicly listed—in Europe this figure is less than 10%. Furthermore, compared with the USA, where 1.5% of the gross domestic product (GDP) is directed into equity investments, we have a qualified, but too small, biotech venture scene in Europe, in which only 0.38% of GDP is invested (European Private Equity & Venture Capital Association (EVCA)/PricewaterhouseCoopers, 2002). This dramatic difference will make the current squeeze on the companies even tougher in the next few years.

Europe equals the USA in having a vital and strong academic base in the fields of molecular biology and biomedical research. Europe has excellent academic institutions and universities, with top-class research groups of international repute. However, these often lack critical mass, or to put it another way, they lack adequate investment and strategic commitment compared with top US institutions. In general, academic research in Europe is on too small a scale and is not sufficiently clustered in centres of excellence. The quality and output per capita of academic and university research in many EC countries with adequate GDPs and wealth are below those of the USA (BioCentury, 2003a), with the exception of Sweden, Switzerland and the UK (EVCA/PricewaterhouseCoopers 2002). The mainly public universities of Europe often have cumbersome administrative structures that do not focus sufficiently on the most efficient use of capital in their institutions. Also, the European academic environment does not encourage spin-off R&D companies, nor is it geared towards promoting the commercial development of research.

Academic staff in Europe have not yet fully grasped that an underdeveloped biotech sector will have a negative impact on the associated sciences in European universities. There is a dangerous misconception among many European scientists that the fate of the biotech industry only concerns the personal well-being of biotech staff and professors who own stocks in companies. Due to the existing employment policy that safeguards lifetime positions for most academic staff, scientists in public academic institutions do not worry too much about the outside

world. But in reality, most European nations have to cut back spending and secure their public budgets, and only a visible and sustainable value-creation chain of a growing and successful biotech scene will, in the long run, convince politicians to spend sufficient money on academic research. Thus, academia and biotech are interdependent for several reasons, as set out below.

Research councils, universities and academic research institutions justify their expenditure on the basis that it is their remit to produce qualified people. However, without a biotech-driven job market that creates not only jobs in companies but also in patent, financial and business advisory offices, there are no future prospects for these diploma, graduate and postdoctoral trainees. European countries receive no return for their investment in advanced education if jobs are only available in the USA or, especially these days, in Asia. The grim and already existing reality is that we educate academics for other budding biotech markets. In this context, it should be noted that, at present, only a fraction of the graduates of biomedical schools in Europe find jobs that require their qualifications in the private sector. A European continent resigned to educating people for other regions is a situation that must be resisted to the utmost.

Ultimately, if we fail to promote a viable and vigorous biotech industry in Europe, academic institutions will face a cash shortfall due to a lack of partnering opportunities and of charities that support basic research (*Nature*, 2002). Without private investment into biotech there will be no overflow of money into academic institutions; furthermore, national and EU institutions will become hesitant to pour money into basic research if there is no prospect of an economic return through tax revenues and stimulation of the job market. Let us take a warning from the dot-com fiasco and remember how popular the internet industry was just a few years

ago, and how much this has now changed in the public and political perception.

A European biotech industry that fails to deliver or runs out of steam will also have a negative impact on our public and academic health-care institutions. Only an integrated relationship between health-care institutions, academia, traditional pharma and a vigorous biotech industry has the power to keep the European medical sector at a level at which it is not solely engaged in reproducing treatments developed elsewhere—that is, in the USA. If we do not achieve this, medical institutions in Europe will become second class.

The recent start-up boom in Europe, particularly in Germany, has led to the perception that mushrooming companies are synonymous with a blooming and sustainable biotech industry. This rosy picture becomes less convincing if, for example, one looks at the renowned *Tornado Insider* study (2002), which

analysed the distribution of the top 100 European high-tech companies (Table 1). This shows that on a per capita basis, countries with fewer than eight million inhabitants are leading the field, whereas Italy, France and Germany are far from having an established and balanced start-up industry. At best, these large countries are at the middle of a learning curve of how to build such industries.

Many European senior academics have become involved in new firms during the past ten years, and so the myth has been created that there is at last an entrepreneurial shift in Europe from academia to biotech. Close up, however, few academics have really left their tenured positions for a biotech company. Even worse, many professors in Europe keep their chairs and at the same time run companies that may collect public subsidies; sometimes, company research is carried out in university labs, employing university staff, without proper compensation to the university. We often find a 'half professor/half CEO' culture that might be beneficial to the individual, but almost never works for a company; nor does the university profit from it. Another myth is that European universities and academic institutions encourage R&D transfer to companies. The fact is that most European universities and public research organizations have not established patent and intellectual property (IP) capabilities that come close even to those of second-class universities in the USA. In many European countries, professors pay for the filing of patents out of their own pockets, and frequently neither the universities that have financed the underpinning research nor the key members of the contributing R&D team reap the rewards of an eventual return.

How can we turn this situation around? One step forward would be to encourage mobility between academia and industry. Different standards for terms of employment, patent policies and financial rewards make academia and industry less closely linked than we would like to think. European tenure systems provide just one example: under the umbrella of freedom of research and the progress of science, many countries still have ancient legal frameworks for academic careers. This creates large disincentives for senior academics to leave their position, even if there is an attractive option in the biotech industry. Why should

a professor quit his chair for the insecurity of the current biotech scene? This is understandable, but in order to spur entrepreneurial spirit in Europe, life-long employment in academia has to be abolished. In addition, income parameters and reward strategies in the private sector and academia need to become more compatible than they are now. Achievements in academic careers should be rewarded to the same extent as achievements in biotech industries; US universities, for instance, provide salary incentives to their staff: professors can receive an extra bonus in proportion to the number of research grants they have attracted to their institutions. Creative solutions for both sides are urgently needed. This is an age-old issue, but it is the source of too many inequalities that impede the exchange of scientists between academia and industry.

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We also need to expand the horizons of students of the life sciences. Traditional science-driven courses and lectures offer little discussion on topics such as how firms operate, what venture capital is and where it comes from, what career opportunities companies offer, or even how to apply for a job and write a CV. This is not surprising—even business schools underwent a long debate before they opened their gates to entrepreneurs and invited them to give lectures to students of economics or business administration. The academic tradition in Europe does not embrace such an exchange between industry and academia, and we have to start linking these two universes. Students and scientists have to see, touch and feel the excitement and challenges of the biotech industry. It is remarkable how Singapore has set a global standard in this regard during the past five years (Singapore Ministry of Education, 1998). We should start to restructure curricula with a view to preparing young students for industry. It is easy to do, and not too costly, but is likely to have a huge impact on the students' attitude towards biotech. Why not invite executives of companies as speakers to the innumerable academic colloquia, seminars and lecture series held

Table 1 | Distribution of the top 100 European biotech companies

Country	No. of high-tech companies ⁺	Population (millions)	Gross domestic expenditure on R&D in 2000 (% of GDP)*
Sweden	9	8.9	3.78
Finland	5	5.2	3.76
Switzerland	5	7.5	2.64
UK	32	59.7	1.86
Italy	3	58.1	1.04
France	10	59.1	2.13
Germany	12	81.9	2.52
Austria	1	8.1	1.86

⁺Europe's Elite, Tornado Insider, Summer 2002, 34, 34–65. *GERD (Gross Domestic Expenditure on R&D)—as a percentage of GDP. Eurostat-online, Free Data, General Statistics (<http://europa.eu.int/comm/eurostat>).

throughout the year in Europe at most academic institutions? This is good for the students, good for academia and good for the biotech industry.

It is easy to talk about spin-offs and start-up firms coming from university campuses, but it is tough to meet this goal if potential entrepreneurs do not know how to go about it. The somewhat cosmetic attempts to set up start-up consulting agencies 'generously' provided by governments or universities are not enough. Universities have to actively manage this, and need to seed organizations that support and serve academic entrepreneurs to get them on their feet. This is not only a question of money, but also a matter of attitude, management style, networks and know-how. There is no great magic to introducing these changes: it should be easy to copy the services and procedures of, say, the Massachusetts Institute of Technology (Cambridge, MA, USA) in the top institutions in Europe. Success might take longer than expected, but if this process is not managed properly success will never come (McKinsey & Company, 2001).

Protection of IP and its commercialization are still foreign and under-valued in most European state universities and research institutes, and these policies need to be changed. In many countries, protection of R&D results and their commercialization are up to the initiative of the inventors, who are usually high-ranking professors. Academic institutions should either have their own patent and licence offices or at least have access to such facilities. The decision of whether or not to file a patent on a scientific result must be based on well-defined processes, flanked by competent advisors who scout through departments, and not on individual professors.

An increasing patent portfolio at universities and other public research institutions will foster the commercialization of scientific results and pave the way for a spin-off culture. We should also change our way of thinking about the differences in investment and return models applied to spin-offs and academia. Why shouldn't universities take shares in the companies that originate from their lab benches? Why shouldn't they get royalties from patents that were filed or developed under their auspices? The Boyer–Cohen patent relating to gene cloning that was filed in the early 1970s kicked off the age of modern biotechnology and led to the foundation of pioneering biotech companies, but it also created substantial revenues for Stanford University (CA, USA) and the University of California, San Francisco.

In the USA, large agencies such as the National Institutes of Health do not restrict their grants to universities and academic bodies, nor do they limit their scope to basic research, provided that the quality of the application merits support. By contrast, most of the national research councils in Europe do not support private R&D projects and/or are extremely reluctant to finance projects that move from the laboratory into clinical trials—that is, towards a product. This distinction between public and private organizations is increasingly unjustified: the era of genome sequencing has shown that segregation between the two is not helpful. Everybody would agree that the public genome projects have been speeded-up by private institutions such as The Institute for Genomic Research (TIGR; Rockville, MD, USA) and Celera (Rockville, MD, USA): the complete sequence of the workhorse

of all molecular biologists, *Escherichia coli*, was only reported by the public consortium years after TIGR had delivered the complete genome sequence of at least a handful of organisms, although the project had been launched long before TIGR appeared on the stage.

At first glance, companies receiving R&D grants may be seen as competitors to academic institutions. One should, however, bear in mind that the inclusion of commercial grant recipients moves academia and biotech closer together. Companies will lobby governments to increase the funding volume of grant agencies—to the advantage of academia—and academics sitting on the steering committees of such funding organizations can, in turn, control the quality and direction of company research. The other advantage, as seen in the USA, is that academic institutions and companies can extend their repertoire of R&D topics to include applied projects, treatments against orphan diseases and clinical programmes. Such an expansion of R&D programmes will also strengthen the clinical research at European academic hospitals, seen by analysts as a weak part of European life science.

Biotech companies must grow, consolidate or die: small is not beautiful. There are still too many firms of less than a crucial size, often based on a single technology, with insufficient funding to sustain them through difficult phases and without the resources to support growth. As yet, the often-predicted consolidation wave in the biotech sector has not occurred in Europe. The nature of the European biotech scene is characterized more by slowing down than by creative and aggressive forward-looking strategies. 'Let's wait and see, and apply for the next public grant,' is a more common approach in the current biotech scene than one would expect from such a dynamic industry. We are very good at writing research grants and involving institutions from different nations, as is often required by EU funding rules, but when it comes to merging firms across borders we encounter many, mostly irrational, roadblocks. 'I'd rather remain CEO of a company that fades away than merge with a partner to form a unit that is fit for survival,' is a pattern often seen in current biotech industries. If we truly want to compete with the USA in the next decade we have to

get to grips with consolidation and 'a new game' perspective in the biotech scene (BioCentury, 2003c; *Biotechnology Investor's Forum*, 2002).

Money has an important role in innovation and R&D, but all too often it is poorly managed. Most rectors, deans and department heads of European universities are distinguished scientists who have usually been promoted to these positions without any management training, or competence to conduct large operations and manage budgets. Furthermore, they are often surrounded by bureaucrats and non-progressive administrators, who govern public universities according to century-old rules. This is a bad and frequently devastating cocktail that leads to the paralysis of R&D in public academic institutions. By taking the control processes and standards of the best companies in the field as a model, financial management in academia could be greatly improved. This should be of importance to every university manager, and also to all European politicians who are eager to improve the situation of our universities.

Indeed, money is a sensitive issue in Europe. The general perception is that academia does not talk about money at all, while biotech only talks about money. Academics often think that people in industry earn much more than they are worth, and biotech people often think people in academia earn more money than they deserve. It is rarely stated openly, but the money issue is more crucial than one would think when it comes to constructive co-operation between academia and industry. For example, there is no question that if a professor is a consultant

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to a biotech firm he is reimbursed, but if the CEO of a company gives strategic advice to a university he is expected to do it for a handshake. Accepting venture capital is often perceived by the academic world as selling one's soul to the devil. In addition, certain academics declare venture capitalists to be stupid, and boast about scientists who sold investors stories that they themselves did not believe. Reported cases of fraud on the stock market are often perceived by academia as proof that the world of money is untrustworthy. Academics should be reminded that one has to stick to ethical standards, whether one submits a publication to a journal, a grant proposal to the research council or a business plan to an investor.

The EU is still at a very early stage of developing the service industry around its biotech scene. There are plenty of companies—probably even too many—but we do not see enough qualified service providers, and we definitely have a gap in getting the legal frameworks up to the speed of the current markets. Qualified patent lawyers, public relations agencies, lobbyists and legal consultants who combine their disciplines with basic know-how are still few. To give an example, the setting-up, legal counselling and implementation of stock option plans is anything but trivial and needs qualified advice that is still hard to find in many EU countries.

Finally, success is the best motivation. The rise of a handful of strong, mid-cap pharma companies in the USA, such as Genentech (San Francisco, CA, USA), Amgen (Thousand Oaks, CA, USA) and Biogen (Cambridge, MA, USA), which were spun off from academia as biotech companies about two decades ago, has set a positive precedent to repeat this pattern. It is, however, unlikely that these legendary breakthrough stories will be repeated in Europe. The European stories will be different, but in the end as impressive as the ones in the USA. To establish the European biotech industry on a sound footing we need visible and profitable products to provide a role model. But we need role models in both academia and industry—in

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1. Encourage mobility between academia and industry
2. Expand the horizons of life science students to biotech industries
3. Improve management of spin-off processes
4. Change intellectual property policies
5. Include biotech and applied projects in public funding agencies
6. Grow, consolidate, cross-border or die
7. Control cost-management in academic institutions
8. Stop the hypocrisy towards money
9. Establish a professional biotech service environment
10. Create positive role models through successful biotech companies

order to make this happen many institutions will have to dramatically restructure, focus and simply speed along with the global pace of biotech.

The EU is absolutely right in setting high goals and standards in its B-Europe programme. This is the growing sector and industry of the coming decades. For this very reason, we must not ignore the warning signs that urge us to act now if we are to meet the goals set for 2010. In the closely interlinked worlds of academia, biotech companies, venture capital investors and traditional pharma industry we all sink or swim together. Getting closer to each other can create only win-win situations. The biotech bubble has burst, and new games have to be played. Critical mass, speed, time-to-market, realistic planning and well-managed cost/return ratios should be the top keywords on the agenda for the 'next generation' biotech enterprises. Equally, academia cannot sit back and relax. It also has to put in place new opportunities to create a sustainable research environment that can have a creative and fair relationship with the private sector.

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