

Siegfried Bialojan, PhD

is the Industry Leader in Health Sciences at Ernst & Young AG, responsible for the coordination of the company's business relations with pharmaceutical, biotech and medical devices companies in Germany. He heads a team of scientists which conducts regular industry surveys to establish thought leadership and to benefit client projects.

Dr Bialojan's background is in biology and medicine, and his post-doctoral research was carried out at the German Cancer Research Institute, Heidelberg. He has been with the company since 2001.

Julia Schüler, PhD

is a senior industry specialist in Health Sciences at Ernst & Young AG. She is the project leader for the company's German biotech reports. Her background is in biology with a PhD in business administration, and she is a Certified Biotechnology Analyst. She has been a manager at Ernst & Young since February 2001.

Keywords: *biotechnology, Germany, key industry data, business models, products, deals, financing*

Siegfried Bialojan, PhD
Ernst & Young AG,
Wirtschaftsprüfungsgesellschaft,
Theodor-Heuss-Anlage 2,
68 165 Mannheim,
Germany

Tel: +49 (621) 4208 11405
Fax: +49 (621) 4208 42102
E-mail:
Siegfried.Bialojan@de.ey.com

Commercial biotechnology in Germany: An overview

Siegfried Bialojan and Julia Schüler

Date received (in revised form): 30th June, 2003

Abstract

The title of Ernst & Young's 2003 Biotechnology Report, 'At the Crossroad', describes the present situation of the German biotechnology industry. This paper discusses and analyses the major findings of the Report. Major drivers in the current development include external factors such as the general economic downturn, the closed capital markets and the resulting consequences with respect to the financing situation. In addition, the pharmaceutical industry – the major client for the emerging biotechnology companies – erects higher hurdles by refocusing on later stage products with blockbuster potential. These factors are mostly identical in all regions of the globe. However, they hit the biotechnology industry in Germany relatively harder as it is still relatively young and therefore more vulnerable.

In fact, the maturation process of the German biotechnology industry has been abruptly stopped. Unfortunately, this takes place at a time when the dynamic development during the past five years has not yet created a substantial number of stable and mature companies. Critical mass has become a major issue.

INTRODUCTION

The current status of the German biotechnology industry is characterised by:

- a trend towards slightly decreasing key industry data (ie number of companies/employees, revenues, R&D expenditures, losses), and
- the shrinking volume of venture capital (VC) finance;

but also on the positive side by:

- a slower increase in net losses based on cost-saving programmes and higher cost sensibility, and
- an increasing number of products in Phase I of clinical development, thus proving the solid science base and the ability to transfer science into products.

Owing to difficulties in the context of the unfavourable financing situation and the fact that considerable revenue streams

are still missing, consolidation of the industry is mandatory. The industry is facing an acid test, which – in the years to come – will separate the successful from the unsuccessful companies, particularly affecting firms that are essentially eligible for financing and those with business models that will not receive financing. Such a consolidation has been expected in the industry for some time and was predicted to occur via mergers and acquisitions. However, since, arguably, the majority of the current German companies lack the critical mass for sustainability, consolidation will inevitably also result in an increase in insolvencies and liquidations.

The same facts are applicable to small biotechnology companies in other countries, even in the USA and the UK. The respective consequences in these industries might not be as visible as in Germany because a greater fraction of companies there has reached critical mass and greater sustainability, thus leading the news flow and providing a more positive perspective for the industry as a whole.

Nevertheless, there are no doubts that

the industry in Germany will continue to exist and will grow from a stronger basis after this consolidation. The growth potential of the biotechnology industry and the respective market certainly exist and the role of biotechnology as an innovation motor is well accepted.

AN ANNUAL COMPARISON OF GERMAN CORE BIOTECHNOLOGY COMPANIES AND EMPLOYEES

The number of core biotechnology companies focusing predominantly on the commercialisation of modern biotechnology has reduced for the first time since the strong growth of the German biotechnology industry that started only 6–7 years ago in the mid-1990s.

With a total of 360 companies, there is a slight decrease compared with the previous year's total of 365. Following the already depressed growth rate in 2001 of 10 per cent, the development is now negative. This can be considered as the beginning of the expected consolidation wave. For the first time, the number of companies going out of business (31) outnumbered the new formations. Only 25 new firms were established.

Besides the stagnation in the number of companies, there is also a reduction in the number of employees. The decrease in the number of employees over the 360 surveyed enterprises amounted to 7 per cent when comparing 2001 with 2002. The total employment figure decreased from 14,408 to 13,400. Thus, in the past year the German core biotechnology industry contracted by roughly 1,000 employees. This decrease clearly stands in contrast to the two previous years, in which the maturing industry could still realise employee growth rates of over 30 per cent, based on successful financing rounds.

For the first time, the number of employees per company has also been reduced, after continuous growth over the past few years. In 2002, 37 persons on

average were employed per biotechnology company. Upon closer examination, it becomes evident that more than three-quarters of all enterprises employ fewer than 30 people. Fortunately, the number of companies with more than 100 employees has slightly increased. This is a very important observation, as these companies – as seen with the US examples such as Amgen, Genentech and Chiron – are essential as country leaders of the industry, demonstrating its potential and providing positive news flow.

The conclusion from the existing dichotomy in employee distribution in Germany is obvious: weak companies seem to become weaker and strong companies with already achieved critical mass are in a good position to move forward on their growth curve.

FINANCIAL DATA OF THE GERMAN CORE BIOTECHNOLOGY COMPANIES IN AN ANNUAL COMPARISON Revenues

After the high revenue growth rates of the German core biotechnology companies over the past few years, the industry did not remain exempt from the impact of generally poor market conditions. With a negative growth rate of –3 per cent, the revenues of the industry decreased for the first time to €1,014m. This figure is well comparable to the situation in Europe (–2 per cent); the more advanced and mature biotechnology industry in the USA increased revenues by 13.5 per cent, based primarily on stronger product sales.

The revenue figure in Germany was affected by the net contraction in companies; the newly established firms could not offset this decline. Revenue streams are also stagnating among the publicly traded enterprises, which still represent only a small portion of the total number of German biotechnology companies, but nevertheless contribute nearly half of the total revenues. Nearly 60

Dynamic growth of the German biotech industry has been interrupted

Stagnating and slightly reduced key metrics

Only 12 public companies contribute to 50 per cent of the industry's revenue

Strong efforts to reduce burn rates; stretching of financial proceeds

per cent of public companies had to deal with a reduction in sales in the past year. In contrast, a few companies excelled with strong revenue increases; eg GPC Biotech announced a strong gross revenue increase of over 50 per cent. Among seven of 12 quoted enterprises, revenues range from €15–70m, whereas the maximum revenue amounts to about €300m.

Besides the already more established public companies, the German biotechnology industry is still characterised by very young and research-focused firms. Many of these enterprises still do not have significant revenues. The average revenues for private companies are €1.4m per company. However, this average does not accurately represent reality, as half of these companies still do not have any revenues.

Biotech industry in Germany is still very young

The economic strength of the German core biotechnology industry is still not comparable with that of established industries, particularly illustrated by the typical US biotechnology company Amgen, which generates four times as much revenue as the entire German industry combined. However, it should be kept in mind that Amgen was founded in 1980 and that it has generated revenue only since 1989 (nine years after inception), primarily through its blockbuster Epogen and other products. If average development times (9–12 years) for therapeutics are considered, it becomes obvious that German companies cannot be prominent yet on the market and revenue side.

Losses

In 2002, the German core biotechnology industry reported losses before taxes of €661m. Thus, the loss in absolute terms continued to increase compared with the previous year. However, the rate of increase (20 per cent) has decreased significantly compared with previous years. This was unexpected, since the early stage industries in particular are typically loss-making based on investments in their growth and building up of capabilities along the value chain. These figures

demonstrate that the German biotechnology companies in the current difficult economic environment are trying hard to reduce their burn rates. Based on these measures, these companies manage to stretch available financial proceeds over a longer period. By contrast, biotechnology industries in other European countries and the USA still have more than doubled their loss figures as they are continuing to invest heavily into further growth and product development. This also demonstrates that the biotechnology industry overall is still far from reaching break-even. Experts expect this to happen no earlier than 2007–2010.

R&D expenditures

In 2002, R&D expenditures from German core biotech companies have decreased, dropping significantly by 11 per cent to €1,090m. The pressure for many companies to cut costs did not exempt expenditures in R&D. For the further progress of the industry, this could be counter-productive, as only further investments into innovations will assist in the goal of creating marketable or licensable products. It is hoped that this is just a temporary phenomenon and only a symptom of the current poor economic situation. The more mature industry in the USA has continued to increase its R&D expenditures by 30.8 per cent; Europe combined has added 6 per cent over the 2001 figure.

The role of public core biotechnology companies

Concerning the key data of the German core biotechnology industry, the publicly quoted companies hold a special position. In 2002, these firms together represented only 3 per cent of all German core biotechnology companies. However, they held 30 per cent of all employees and generated half the entire revenues, as well as 42 per cent of the total loss. Their R&D expenditures represented 20 per cent of the R&D investment made by the German biotechnology industry as a whole. This fact shows that not all

German public biotechnology companies invest most of their cash into R&D. While this phenomenon (high R&D expenditures) is typical for research-intensive companies in the pharmaceutical and biotechnology sector, it is less pronounced at companies such as MWG Biotech and Qiagen, which are strongly focused on marketing and sales. At the other extreme, MediGene's R&D expenditures, for example, amount to nine times its revenues.

FINANCING AND CAPITAL MARKETS

In 2002, the European stock markets remained low. In total, only a total of €134m could be raised from public markets. Slight movements were observed in the USA, with a total of US\$456m (+119 per cent compared with 2001) and US\$6.08bn (+14 per cent) raised through initial public offering (IPO) and other public offerings, respectively. It is primarily because of these activities that in the USA, the total amount of equity money for the biotechnology industry increased by 10 per cent in 2002. Analysts are more optimistic now that some more IPO deals might be seen in 2003 among a select group of outstanding candidates. Whether these positive signals will also affect the markets in Europe is still questionable; the lack of a common European stock exchange, as well as the less mature industry, might delay any upturn of the public markets in Europe.

Europe remains heavily dependent on VC as the only source of private equity money. In Germany, without any deal at the stock market, the total amount of invested VC – about €200m – is slightly greater than the level in the year 1999. However, the maximum single amount raised is 40 per cent lower than the amounts raised in the highest financing rounds over the past two years. Altogether, compared with 2001, capital invested into the German biotechnology industry has dropped by more than 50 per cent. In contrast to 2000, the worldwide 'boom year' in equity financing, the

German biotechnology industry has had access to less than a sixth of the equity raised at that time. This sharp drop in VC invested in Germany is in contrast to the situation in Europe as a whole and the USA, where the VC remained stable at a relatively high level. Europe raised a total of €1,155bn (–16 per cent compared with 2001); in the USA, VC financings added up to US\$2.164bn (–10 per cent).

The reasons for this phenomenon in Germany are threefold. First, the VC community in Germany is also still immature and is itself facing a major consolidation. There are too many small VC investors with insufficient industry expertise that have invested in the previous boom years with the perspective of making big money fast. Many of them are not positioned to cope with the actual downturn; they do not have the financial power to finance companies through their development until they reach break even; most of them are at present more engaged in portfolio management and portfolio consolidation rather than in considering new investments.

Secondly, there is a clear trend in the VC community towards later stage investments, which usually are more transparent with respect to their risk profiles and their market returns. This is a general feature, also seen in the USA and other European countries, where a 'funding gap' affects largely younger companies in their early stage of technology and product development. It also explains the situation in the German biotechnology industry, which – as a logical consequence of its young age – still has a very early stage pipeline of development projects (see below). In ongoing financing rounds, companies find it extremely difficult to identify a VC partner willing to take over the lead, to assemble a reasonable consortium and perform due diligence and valuation tasks.

Finally, there are also issues in the ramifications (mainly taxation) in Germany that create higher hurdles for investors in Germany.

Consolidating the VC community with strong preference for late stage investments

VC still the only source of capital

Significant drop in VC investments

VC firms were the primary suppliers of equity; financial holding companies, business angels and investment banks have also participated as investors. The primary source of their capital is derived mostly from institutional investors, followed by public and/or state sources and private investors. However, the proportion of these additional investor groups is small compared with the VC share. It would certainly be desirable for the capital sources to be extended to alternative investors and strategic partners to reduce the sole dependence on VC companies. Again, taxation issues need to be addressed to attract a broader range of different investor categories (eg elevation of significant participation limit; capital gains tax).

This overall critical situation at the financing front – often described as a financing crisis – has significantly decreased the survival index regarding remaining cash reserves of the biotechnology companies worldwide. In the USA, 33 per cent (up from 17 per cent in 2001) have less than one year of cash; similarly, in Europe this figure has increased from 12 per cent in 2001 to 20 per cent in 2002. The consequence will be that many more companies will have to go through financing rounds this year; given the general situation at the VC side, many of them will not succeed.

At present, the preferred exit by investors is the trade sale, ie the sale of equity shares to another enterprise. The preference of an IPO has again clearly decreased compared with the past year. In 2001 there was still a glimmer of hope that the situation might improve. However, another year with sharply falling stock prices, from which German biotechnology stocks were not exempt, destroyed this hope. Therefore, other exit options were strongly favoured.

BUSINESS AND COMMERCIALISATION STRATEGIES

Product focus is still predominant in the current business models. This is true for biotechnology companies all over the

world. In the past few years, this business focus has been strongly pushed by investors and their prospect of generating higher revenues. Since product development, particularly in the area of therapeutic compounds, is a lengthy process and bears significant risks, more and more shifts in business focus are visible, where companies – without necessarily losing their product focus – leverage their technology platforms also by collaborating with partners and service deals with the aim of supporting the business with a short-term revenue stream. This leads to a reduction in dependence from VC investors and at the same time to a more stable enterprise able to better sustain critical situations. Companies in the USA seem to have adhered much earlier to this model of generating early revenues to stabilise the business.

After the hype in 2000 and 2001, where well-formulated promised success in the future was sometimes sufficient for a successful financing round, nowadays there is a clear refocusing on fundamentals, including an existing revenue stream early on. Following many experts' opinion, the key to success should lie in creating sustainable businesses rather than adhering too strictly to a defined business model.

TECHNOLOGIES AND PRODUCTS

Besides established platform technologies, such as genomics and proteomics technologies, as well as bioinformatics, a variety of further technologies have evolved, including the use of stem cells, new RNA technologies, nanobiotechnology, system biology and computer-assisted approaches. The business sectors in which modern biotechnology companies are most active, continue to be the development of therapeutic products, followed by molecular diagnostics.

The number of active compounds in the development pipeline of German core biotechnology companies slightly

Survival index increased: more than 20 per cent of Biotech companies in Europe have less than one year of cash

Refocusing on fundamentals is reflected in business models

decreased (177) compared with the previous year (183). On the one hand, this is due to the acquisition of companies by foreign corporations (eg Rhein Biotech by Berna Biotech, Switzerland). On the other hand, a set of products and/or projects was given up, or its development was delayed owing to financial bottlenecks.

Product pipeline is still at an early stage

Overall, the product pipeline in Germany is still at an early stage. Considering the young age of the German biotechnology industry (6–7 years) and the statistical benchmarks of normal drug development timelines (10–12 years), this is the picture to be expected. Of course, the industries in the USA and UK are much more advanced because of their longer existence. With 255 products in Phase III (public companies only), the USA is far ahead, followed by the UK with 23 drugs in Phase III out of a total development portfolio of 194 products (public companies only). In this comparison, Germany has to catch up: only 15 products are currently being pursued in the development pipeline of the public companies.

It is an optimistic sign in Germany to see many projects in advanced research status and entering the development programme, thus giving hope for continued maturation of the product pipeline. In particular, in 2002 the number of active substances in Phase I clinical development increased by 25 per cent, although the total number of active substances in the clinical development stage has not changed. Similarly to the situation in 2002, there are currently 60 products in clinical development, ie between the developmental Phase I up to the approval phase. However, the first product derived from R&D efforts of a German biotechnology company to reach the market is still awaited.

Strong increase in Phase I clinical development

Ongoing public sponsoring programmes

However, many molecular diagnostics, as well as tissue-engineering products developed by German biotechnology companies, are already well established in the market. The ‘green’ segment of

biotechnology, which involves applications in agriculture and the food industry, is still weakly represented. In Germany, the core biotechnology companies in this field are primarily focused on the development of technologies for the production of therapeutically active substances in both transgenic plants and plant cells (‘molecular pharming’). With this approach, these companies are able to evade the ongoing discussion in Germany about genetically modified plants and food. At the same time, they focus more on promising applications with higher margins expected to come from serving the pharma industry. Small biotechnology start-ups of the ‘green’ biotechnology segment still rarely pursue projects to modify food characteristics in terms of input/output traits. In Germany, these projects are largely in the focus of big companies in the agricultural industry.

New initiatives in the federal state of Sachsen-Anhalt are heading towards establishing a green biotechnology industry in Germany with significant state money committed to build up infrastructure and to attract new company formations. Changes in regulations at the EU level and convincing the public with respect to risk issues around genetically modified organisms remain obstacles that need to be overcome before a new segment of green biotechnology, including the necessary commitment of the VC side, can be successfully established.

Enterprises dealing with the ‘grey’ segment of biotechnology, ie applications in industry and environmental protection, account for the smallest number of companies.

BIOTECHNOLOGY LOCATIONS IN GERMANY

The very successful jump-start of the German biotechnology industry, driven by the government initiative of the BioRegio competition, led to the formation of four major biotechnology hubs in Germany – Munich/Martinsried,

**Improved ramifications
planned by Government**

Berlin, Rhein–Neckar–Dreieck (Heidelberg) and Rheinland (Cologne). Follow-up government sponsoring initiatives are ongoing. The BioFuture, BioChance programmes especially encourage young scientists and entrepreneurs, whereas BioProfile points at the formation of commercial focuses around specific themes (eg Bioinformatics). After the initial programme of roughly €0.5bn, the current government initiative (Rahmenprogramm Biotechnologie 2001–2005) comprises a total of around €1bn that are being committed by the government scheduled to further foster biotechnology industry build-up (including the German Genome project). Clearly, this funding was absolutely essential to get the industry started. Major aspects include the provision of infrastructure (biotechnology parks, incubators, technology transfer, consulting, etc) but also financial commitments to help in starting up companies and to attract VC investors. Therefore, the government initiatives did fulfil their purposes.

However, criticism has also been expressed regarding too many company foundations based on insufficient business cases and inexperienced management. This might have caused the tremendous growth rates in previous years, making Germany top with respect to the number of companies in Europe and third in the world (after the USA and Canada).

In the current difficult economic situation affecting the young biotechnology industry, additional support is definitely needed. There is a continuing discussion on further state funding programmes – aimed at

supporting companies that have been propagated in the BioRegio and other funding programmes – to survive the present financing crisis. A major issue, however, is a stringent due diligence to prevent burning money in companies lacking sustainable business concepts. In this context, many experts are very reluctant to agree to this kind of state intervention and instead speak in favour of the market as the corrective instrument.

However, much more emphasis is given to improving ramifications through various tax benefit programmes. Very positive signs come from a new government initiative (High Tech Master Plan) that plans new measures to help companies (eg loss carry-on taxation) and also reattract investors and make Germany a place for new investments for foreign investors as well (eg elevation of significant participation limits, capital gains taxation).

In addition, there is still a significant commitment of the federal states to boost biotechnology industry settlement in most of the federal states. Given the low founding rate for new companies in these difficult times, this might seem somewhat questionable. However, most of these initiatives pursue distinct approaches to combine specific strengths of their regional science institutions and existing industry setting with corresponding dedicated profiles of the new centres to be established. In this context, new companies should be better prepared to become sustainable.

Finally, the question remains whether formation of a unified association for the German biotechnology industry could be an additional factor to push forward the right political decisions.