global lifescience ventures

10 years' investing in the life sciences

Content

The German speaking market had no dedicated life science venture capital fund when Global Life Science Ventures (GLSV) was formed in October 1996, despite the concentration of world class, innovative research being conducted there. With the establishment of GLSV, the life science sector in those countries received more of the attention and funding opportunities it deserved, with GLSV taking a lead role with investments in such promising stars as Cytos (Switzerland) and Intercell (Austria), as well as Glycart (Switzerland), which was acquired by Roche last year at a most attractive valuation. GLSV remains a dedicated investor in these markets, with a host of recent new investments in German, Swiss and Austrian companies.

GSLV is far more than just a regional player: their extensive international experience in the life sciences industry has allowed them to play a significant role in the development of innovative companies across Europe and the United States. Several have become publicly listed, such as Exelixis, Sequenom and Coley – American companies with strong European ties – as well as Cyberkinetics and CombinatoRx. These companies have all benefited from the funds made available and importantly from the insights, know-how and extensive network of the GLSV investment team, led by founding partners Peter Reinisch, Hans Küpper and Hanns-Peter Wiese, joined by more recently appointed partners Holger Reithinger and Stephen McCormack and principal Kuno Jung.

It is with distinct pleasure that I congratulate GLSV on their notable 10th anniversary and wish them every continued success for the next decade of their impressive history!

Frederick Frank
Vice Chairman and Director,
Lehman Brothers

Member of the Expert Group, GLSV

This year GLSV is celebrating the 10th anniversary of its founding as a venture capital firm. Those familiar with our beginnings know the critical role played by the late Dr. Stefan Engelhorn in launching our first fund. Since then it has been an exciting period for us on the way to become an established and well recognized VC player. We have had the fortune to meet numerous, ambitious life science entrepreneurs and management teams, and have made many key investment decisions during this time, several of which have proven very successful. During this decade we have also witnessed many changes in the life science industry, which experienced the hype of the late 1990s followed by a decline in investor interest in the first years of the new century, before reaching new-found stability and momentum today.

The prospects for biotechnology, also in Europe, have seen a real turnaround. The sector has become recognised as a source not just of innovative ideas but of valuable new product candidates with great market potential, and small biotech companies have given new vitality to the pharmaceutical industry through various deals and M&A activities. While financing, especially of early-stage companies, remains difficult in Europe, there are new sources of investment becoming available, and the best projects do get funded. As we found in our most recent GLSV Biotech Investment Barometer, the current mood is one of increased optimism, and opportunities for successful investments are greater than ever.

On this occasion, we thought it would be fitting to collect our insights on the biotechnology industry, the how and why of investing in the life sciences, and our expectations for the future, through a selection of articles authored by the team members, most of them published earlier in various journals. We have also asked a few of our industry colleagues and collaborators as well as executives from some of our portfolio companies to offer their own impressions of the sector and of the role of GLSV in the development of their own businesses. We hope you enjoy this collection.

Dr. Hans A. Küpper
Dr. Stephen J. McCormack
Dr. Peter Reinisch

Dr. Holger Reithinger
Hanns-Peter Wiese
Dr. Kuno Jung
Rainer Hoegg

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Mid-1995: Dr. Stefan Engelhorn initiated GLS I as lead sponsor with the following vision:

Early-stage Life Science Venture Capital Fund (among the first in continental Europe). Investments world-wide, as Life Science industry is global and return to investors is dependent on the identification of globally dominant players and exits (IPO or trade sale). Own infrastructure in Europe only, in order to be close to portfolio as an early-stage lead investor. USA to be covered through own network and in close collaboration with leading local VCs. Seek for international investment syndicates.

February 1996: Dr. Peter Reinisch and Hanns-Peter Wiese started on the layout for the fund incl. its legal and tax structure.

Spring of 1996: Corange (family holding of the Engelhorns, one of the most successful Entrepreneurial families in Germany, that also founded Boehringer Mannheim, BASF, Mannheimer Versicherung, etc.), Vereinsbank and ING act as co-sponsors.

October 1996: the three sponsors committed EUR 12.5m each at the first closing.

November 1996: first and strategic investment in Oxford Bioscience Partners II to establish a cooperation with a leading US VC firm interested in co-investing in Europe.

April 1997: first investment in a biotech company: Exelixis, that went public three years later.

December 1997: final closing with additional commitments from institutional and family office investors bringing the total fund size to EUR 66m.

January 1999: Dr. Hans Küpper, senior R&D manager from Hoechst and Biogen, joined to complement a team with matching skills and experiences in industry (pharma, biotech) and VC.

September 2000: 18th and last new investment of GLS I.

May 2001: first closing of GLSV II including all limited partners of GLS I.

December 2001: first investment by GLSV II and opening of the office in Zug.

July 2002: final closing with additional institutional investors (further fund-in-funds and healthcare insurance, family offices) raising a total of EUR143m.

October 2004: Dr. Holger Reithinger, ex-Investment Director of 3i, joined the team.

January 2006: GLSV received the EVCJ Award for the "Venture Realisation of the Year 2005" in the category Life Science (Glycart).

Spring 2006: Dr. Kuno Jung and Dr. Stephen J. McCormack, two former CEOs of biotech companies in Switzerland and the US, joined the team.

September 2006: 17th investment by GLSV II.

November 2006: Dr. Stephen J. McCormack and Dr. Holger Reithinger are promoted to partner.

10 years of biotech investing in Europe

by the Global Life Science Ventures team

Europe's biotech sector has come a long way since our start in 1996. More than $28 billion has been invested in the European industry since, while the number of companies in existence has trebled from just under 600 to over 1800. More importantly, the composition of the European sector has changed dramatically, as it is now much more continental.

There is no doubt that 1996 was a landmark year for the European biotech industry. Before then, Europe's biotech sector was predominantly British, as the London Stock Exchange and its Alternative Investment Market were the only European markets available for biotech public listings. Moreover, most of the venture capital activity in the biotech sector was not only domiciled in the U.K. but tended to have a U.S. and to a lesser extent U.K. focus.

During 1996, however, continental stock exchanges – including Zurich, Frankfurt, Paris, and Copenhagen – opened their doors to biotech public offerings, although a number of the companies that floated in 1996 did so with a dual listing on NASDAQ, the U.S. high tech exchange.

Indeed, the emergence on the public markets of Genset SA, which floated on Paris and NASDAQ, Qiagen NV, on Frankfurt and NASDAQ, NeuroSearch A/S, on Copenhagen, and Innogenetics NV, on the pan-European EASDAQ exchange, had a profound catalytic effect on the continental biotech sector as they opened up exit opportunities for early stage financial backers as well as encouraging a new entrepreneurial spirit.

Genset, one of the pioneering genomics businesses, raised EUR 80 million in an IPO, on Paris' Nouveau Marche and NASDAQ, that yielded a four-fold plus return to its investors, and provided the company with a post-money valuation of EUR 285 million. Demand for NeuroSearch's IPO on Copenhagen was 17 times over-subscribed.

At the same time, the U.K. biotech sector was enjoying a substantial run on capital growth, driven mainly by what looked to be positive clinical development news coming out of British Biotech, which at the time was the U.K. and European industry's flagship company. Not only were companies able to raise money in over-subscribed IPOs, but it was also possible for them to return to the capital markets and raise additional money.

Nevertheless, by the end of 1996, while Europe's top four biotech companies – as measured by market cap – were British, there were four non-U.K. companies in the top ten.

Investors in the Belgian plant biotech company, PGS International, also received a valuation bump when the company was acquired by the German agrochemicals business AgrEvo for some EUR 584 million.

The emergence of IPO and trade sale exits were not the only triggers for increased interest in European biotech. The global news coverage of the creation of Dolly, a sheep cloned from a mature adult cell, confirmed the potential of Europe's science base, which at the time was still very much untapped commercially.

More importantly, the political landscape for European biotech was on the turn. Until the mid-1990s, much of continental Europe had a less than welcoming attitude to biotech. With unemployment in the European Union rising, and the realization that industries based on life science technologies could be crucial drivers of the European economy in the 21st century, politicians and governments became much more supportive of the sector.

Public programs

European Union initiatives over the past decade, such as the Framework Programs, the eventual implementation of the EU biotech patents directive, and the establishment of European orphan drug status, have underpinned the European biotech sector's development. On the downside, political resistance to GMO crops and products made from them has all but killed off European plant biotech efforts, despite having had a leadership position.

Probably the most significant event that took place ten years ago was Germany's creation of the BioRegio program, which was designed to identify the three most organized regions with the best plans to promote the transfer of biotech knowledge from the lab bench to the market. This program, which provided federal funding to support the development of entrepreneurial biotech companies, stimulated the creation of new venture funds and laid the foundations of Germany's leading position today in European biotech.

BioRegio is not without its critics. There is still an argument that the availability of soft money from government sources, that went some way to underwriting some of the investment risk, led to the establishment of companies that were unsustainable. Nevertheless, there is no getting away from the fact that it did have a profound catalytic effect on German biotech and even with its potential shortcomings the approach is still considered a role model for other ambitious state-sponsored initiatives.

Indeed, the growing political support for biotech from the mid-1990s onwards, coupled with easier access to capital, changed the face of European biotech and made it consequential in global terms. The rate of new company creations in Europe was outstripping the U.S. through to 2000, although in all other meaningful metrics – such as product launches, revenues, R&D spending, and employment – the gap between the European and U.S. biotech sectors was not closing. Nevertheless, by 1998, U.S. biotech companies realized that they would have to keep an eye on what is going on in Europe.

Consolidation

Consolidation and contraction within the European pharmaceutical industry, that started in earnest in the mid-1990s with the mergers of Ciba with Sandoz, to create Novartis, and Glaxo with Wellcome, has been an important trigger from new companies founded by experienced pharma executives with compound and technology legacies emerging from pharma.

> ***"In the last ten years GLSV has emerged as one of the top tier venture capital firms in Europe. GLSV's ability to identify exciting investment opportunities and to add value to portfolio companies has been demonstrated repeatedly. As a result GLSV is a sought after syndicate partner and lead investor for the best entrepreneurs and venture capital firms in their field."***
>
> Jonathan Fleming, Partner,
> Oxford Bioscience Partners

Other significant pharma mergers in the past decade have included Astra with Zeneca, Rhone-Poulenc Rorer with Hoechst to create Aventis, Sanofi with Synthelabo, GlaxoWellcome with SmithKline Beecham, to create GSK, and Aventis with Sanofi-Synthelabo, to form Sanofi-Aventis. Companies and management teams spinning out of European pharma companies have attracted considerable support from investors in recent years.

In the run up to the publication of the Human Genome, the technology platform business model that was popular in continental Europe was also a favorite among venture capitalists. Moreover, there were a group of technologies in which European companies were able to compete head-to-head, such as antibody and protein technology and vaccines.

Interestingly, there was a transatlantic disconnect between the valuations and ability to raise funds. At the turn of the century, Cambridge Antibody Technology and MorphoSys had much lower valuations on the European capital markets than their U.S. counterparts Medarex and Abgenix had on NASDAQ, even though the Europeans had achieved as many if not more significant commercial milestones.

European Biotech on the rise

It wasn't until 1999 that European companies actually managed to make real commercial headway by introducing innovative medicines into the marketplace. Chiroscience, subsequently acquired

by Celltech, which is now part of UCB Group, and SkyePharma were the first to reach the approval milestone. Chiroscience won FDA approval for Chirocaine, its long-lasting anesthetic based on a single isomer of bupivacaine, while SkyePharma got FDA approval for DepoCyt, an injectable sustained release formulation of cytrabine.

Since then a number of European companies have been successful in winning approval for molecules that they have developed. The most successful innovative molecule to emerge from an entrepreneurial European biotech firm is the anti-TNF monoclonal Humira that was developed by Cambridge Antibody Technology, now part of AstraZeneca, and marketed by Abbott. Approved as a treatment of rheumatoid arthritis, and being tested against a number of other inflammatory disorders, Humira was the European sector's first blockbuster.

The rising number of companies and the product development progress they were making did raise concerns that European investors might not have enough appetite to ensure that the sector would be able to grow sustainably.

By 2000, the number of European biotech companies had risen to 1570, was employing just over 61,000 people, was posting revenues of approximately EUR 8.7 billion and investing about EUR 5.0 billion in R&D. As in the U.S., 2000 was Europe's record year for financing. Europe's biotech sector raised more than EUR 6 billion in 2000, while the U.S. sector, which had an almost equivalent number of companies, raised five times that amount.

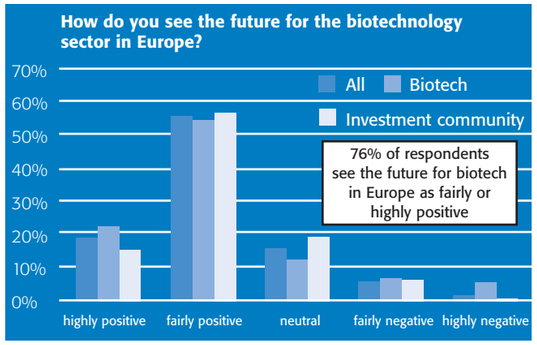
Increasing interest for VC

Biotech once again became a favorite sector among investors. Continental biotech companies saw their valuations rise almost 40% during the year, while the British contingent, which had been in the doldrums for a couple of years following some major blowouts at leading companies such as British Biotech, Cortecs and Scotia, rebounded strongly with a 92% leap in valuations.

Particularly strong were those companies – including proteomics firms such as Oxford Glycosciences or antibody companies such as Cambridge Antibody Technology and MorphoSys – that were expected to benefit most from the publication of the human genome. At the year end, Europe had ten companies with market capitalizations in excess of EUR 1 billion, and all but one of them were dual listed on both a European and a U.S. exchange.

In 2000, 39 European companies completed IPOs raising a total of almost EUR 3 billion, with a particularly strong contingent emerging from Germany, Scandinavia, and Switzerland led by LION Bioscience , MediGene, GenMab, and Actelion. More significantly, no one single market emerged as the European biotech exchange of choice. By the year end, Europe was home to 105 public biotech companies, with the London markets accounting for less than half the total (49) for the first time.

Europe's biotech companies were also able to raise EUR 1.2 billion, a record amount of money, from private equity and venture capital sources. Indeed, more money was put to work in 2000



than in the previous five years put together. More importantly, venture capitalists were more willing to invest larger and larger amounts as they sought to accelerate the development of their companies.

At the same time, venture capitalists with a focus on the life sciences were finding it easier to raise additional money for new funds.

First disappointment and consequences

Unfortunately, the biotech boom at the close of the decade was not sustainable. The bear market that was to grip the biotech market for the next few years was triggered first by the popping of the so-called genomics bubble, when after the publication of the human genome questions were asked about the financial sustainability of some of the business models employed, and then by the retreat from risky equities following the terrorist attacks on September 11, 2001.

Indeed, the ability of the European biotech industry to raise funds through IPOs fell dramatically between 2001 and 2003 when only nine modest transactions were completed. It was a similar story on the venture financing front, where the amounts put to work went into decline in 2002 and 2003, although they were still at higher levels than had been achieved pre-2000. Over both years, however, it was clear that venture capitalists were still willing to support with substantial sums those companies with robust business models. Indeed, many of the well financed companies did go on to complete IPOs in the following years.

The post-genomics financing drought triggered both a consolidation within the industry, essentially repeating what had earlier transpired in the U.S., and a slow down in new company formations. The exceptions were Switzerland and Austria, which started developing entrepreneurial biotech sectors after much of the rest of Europe. Concomitantly, there was an increase in pharma partnering within the European biotech industry, driven by the mutual needs of the partners to access cash (biotech) or innovative technologies and/or products (pharma).

There has also been an increase in the number of outright acquisitions of some of the leading European biotech companies by big pharma, including Serono, Celltech, Cambridge Antibody Technology and PowderJect Pharmaceuticals. There were also some notable pharma takeouts of private companies including Glycart Biotechnology and Domantis.

Upsurge and motivation

In 2004, the public markets re-opened and venture capitalist confidence in the sector returned, as exits such as IPOs and trade sales were once again possible. More than EUR 2 billion has been raised by European companies through IPOs, while the sector has raised approximately EUR 3.5 billion from venture capital and private equity sources.

In the past five years, Europe has established itself as being world class in a number of key sectors, such as biodefence with the likes of Acambis and Bavarian Nordic, immunology with Cytos, infectious diseases with companies such as Intercell and Nabriva Therapeutics, and also the next generation of protein technologies including Pieris, Ablynx, Domantis and Esbatech.

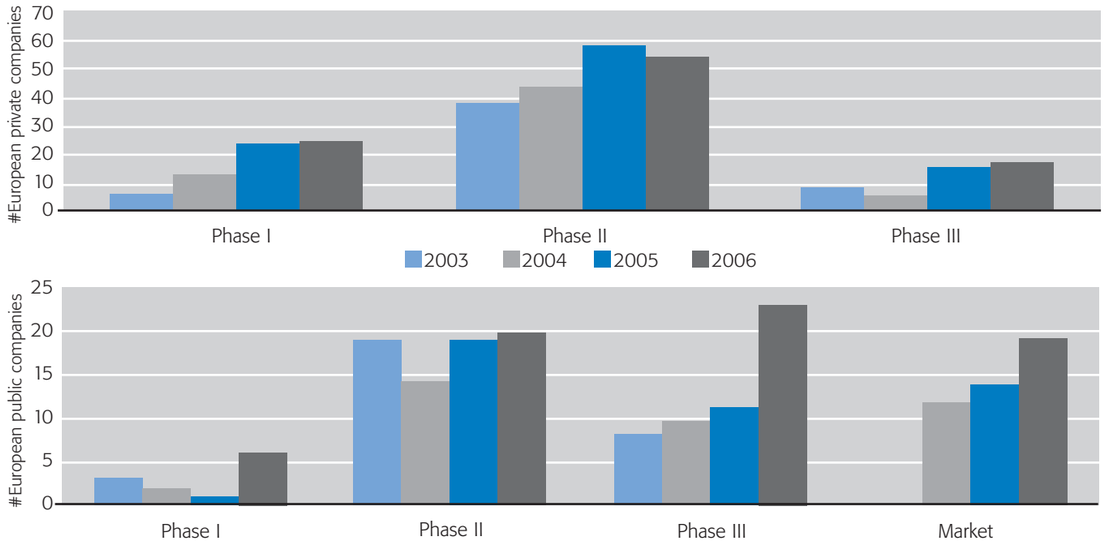
By the end of the 1990s, it was increasingly clear that ambitious European companies, and consequently their investors, would have to adopt global strategies because the industry was becoming borderless. Indeed, some of the most successful European companies have built substantial positions in the U.S. either by acquisition, as Shire Pharmaceuticals has done, or organically, as achieved by Qiagen.

Indeed the 2001-2003 financing drought had prompted a number of European companies, including IDM Pharma, Micromet, Cyclacel, and BioVex, to seek their fortunes as U.S. companies.

Europe's biotech landscape is now much more diverse, more continental and has in less than a decade created a number of highly sophisticated, very productive, sustainable businesses. These companies will provide the role models, experienced management and innovative healthcare solutions for future investments.

> ***"During many years of cooperation with GLSV as our investors as well as in the Boards of Artemis and Exelixis we have experienced our GLSV-colleagues as highly reliable and very professional partners."***
>
> Prof. Peter Stadler, CEO, Managing Director, Artemis Pharmaceuticals GmbH, Chairman of the "German Association of Biotechnology Industries" (DIB), Member of the Board of EuropaBio (the European Association for Bioindustries, Brussels)

European life science companies have expanded their pipelines



Biotechnology: 25 years in

by Dr. Hans A. Küpper, Partner, Global Life Science Ventures

The early days of the biotechnology industry

The biotechnology industry started some 25 years ago with the intention of exploiting the technology platforms of genetic engineering and gene transfer. The founding of the first companies, which included Amgen, Biogen, Cetus, Chiron and Genentech, marked the early stages in the development of the industry. Promises and expectations were high. Today, biotechnology has developed into a large research-intensive industry with over 4000 companies worldwide and parallel financing and venture capital funding to match.

The progress of science

Scientific landmarks in the early- to mid-1970s, which included the discovery of restriction enzymes, the first transfer of genetic material and the development of early DNA sequencing methods, have been complemented by the invention of PCR in 1983 and the completion of genome sequences for organisms as diverse as Drosophila, mouse, and, ultimately, humans.

In parallel, business successes have witnessed the public listing of Genentech, the first genetics company, in 1980, FDA approval of insulin in 1982, and the marketing of the first transgenic food — Calgene's Flavr Savr tomato. The considerable progress shows no sign of losing momentum. Some recent milestones include the cloning of Dolly by PPL Therapeutics, the sequencing of the human genome by Celera and the Human Genome Project, and the recent production of the first gene chip containing the full complement of human genes. [1]

Delivering real benefits

Gene transfer technology has already delivered significant benefits to the healthcare industry and patients. Safer recombinant products are reaching the marketplace and have replaced marketed biologicals previously isolated from cadavers (e.g. insulin, human growth hormone) and blood (e.g. Factor VIII). Proteins that were previously only available in minute quantities, such as interferons, erythropoietin, and growth factors, are now available through recombinant DNA technologies in large enough amounts for use as therapeutics.

Further developments are providing safer vaccines, new model organisms for studying the progress and treatment of disease (e.g. "humanized mice"), and novel genetically modified crops. Transgenic animals are being developed for the production of biologicals (Biopharming). The reengineering of metabolic pathways of microorganisms should provide novel antibiotics.

Evolution of the industry

The original fully integrated biotechnology company (FIBCO) business model, which was popular in the 1980s, is out of favour. From the 50 or so companies active in the mid-70–80s, the biotechnology industry has blossomed into over 4000 companies today.[2] This has entailed a transition from the "all rounders" of the early days to the more specialized platform companies of the late 1980s/early 1990s. Today, further diversification has led to platform- and indication-specific companies, in many cases supported by service companies.

Until 1975, the pharmaceutical industry was the "acceptor" of scientific discoveries and technologies arising from academia, which were used to develop and commercialize novel products for the marketplace. However, big pharma was not able to create the necessary innovative environment to accommodate the breakthrough technology of gene transfer and the rapidly progressing scientific developments of the late 1970s. Since the early days, the biotechnology industry has established itself as a major link between academia and pharma. The dependence of biotech on "Big Pharma", and vice versa, is today stronger than ever. In the future, it will continue to provide important new channels between the academic and pharmaceutical sectors of the life sciences.

The progress of the industry is reflected by recombinant biological products having established markets with multibillion dollar sales (e.g. erythropoietin, insulin, interferons, monoclonal antibodies, human growth factors). Interferon, which was the first anti-cancer drug from the biotechnology industry to be approved by regulatory authorities, achieved worldwide sales of around USD 3 billion in 2002.[3] Until today, more than 155 biotechnology drugs and vaccines have been approved by the FDA. Over 370 biotech drug products and vaccines are currently in clinical testing targeting more than 200 diseases.[4] In addition, more than one third of all pipeline products in active development worldwide are biopharmaceuticals and the global market for biopharmaceuticals is currently valued at USD 41 billion.[5]

Future trends

The establishment of the human genome nucleotide sequence can be compared with the foundation of the periodic table of elements in the 19th century. With the sequencing of the human genome complete, medicine is transforming itself into a "real" science. Understanding the human genome will eventually allow the molecular basis of diseases to be unravelled in a systematic way. If one were to look to the future, other technologies that may support major advances might include RNAi (RNA interference approaches), stem cells, organ modelling/regeneration, smarter vaccines, systems biological approaches for drug discovery, computer modelling for drug design, and rapid whole genome sequencing. In addition, pharmacogenomics is set to impact personalized drug treatments. In June 2003, Roche Diagnostics launched the first commercial pharmacogenomic microarray for clinical applications. Pharmacogenomics should improve drug efficacy, enable individualized drug treatments and reduce adverse drug reactions (ADRs). In 1998, it was estimated that over 2 million ADRs occurred annually leading to 100 000 fatalities per year.[6] The associated costs at the time were greater than the total costs of cardiovascular and diabetic care. New genes and their main functions appear to be discovered on an almost daily basis in areas as diverse as cancer, obesity, memory and longevity. It is still too early to predict where these breakthroughs will take the industry.

The issues and challenges

Despite the unquestionable progress that has been made, many of the key developments in biotechnology have taken longer than expected to reach the market. In part, this was due, at least initially, to an approach which was very much a 'molecule in search of a disease indication' (interferon, tumor necrosis factor, interleukin II).

Combinatorial chemistry and high throughput screening have not solved existing problems. The pressing issues facing the industry include constraints on healthcare costs, diminishing returns, and increasing competition through the rise of generics. The drug discovery and development process is becoming increasingly complex. The challenge is to integrate all the new approaches in a meaningful, productive manner. In this context, annual R&D spending has increased more than 12-fold since 1963 (Pharmaceutical Research and Manufacturers of America). However, the number of new chemical entity approvals has not followed suite.[7]

Some technologies have clearly not yet delivered on their potential due to larger than anticipated difficulties. For example, in 1993 the projected revenues for gene therapy products were estimated to reach around USD 3 billion by 2003.[8] However, most companies have since abandoned their gene therapy programs. Significant unmet medical needs remain to be addressed. Of about 30,000 known diseases, only one third can be treated effectively.[9]

What this means for investments

If the industry is to make further progress, investors need to identify and support the real needs of the healthcare industry. This means critically evaluating the potential of new companies and identifying those technology platforms that will save time and money on drug development, define novel pathways for the major indications, provide validated targets, and better predictive cell- and animal-based models to test for efficacy and toxicity. Not only must innovative companies benefit from the human genome sequence, they must also learn to make the transition to curative medicine and deliver more innovative products to the healthcare market.

Investors in the biotechnology community must be more selective. This involves finding and nurturing companies and projects with significant long-term potential and identifying those companies with a clear path to a positive cash flow. A responsibility also exists to achieve more realistic valuations. For example, on the 19th of May of this year, Genentech announced successful phase III results for Avastin, a novel angiogenesis inhibitor for cancer treatment. The share price increased by 44.7% to USD 54.85, which at the time corresponded to a market capitalization increase of USD 12.5 billion. Such changes are difficult to justify. Smaller companies are particularly prone to the damage unrealistic valuations may pose.

Conclusions

Few would dispute that biotechnology is an established business with many facets. However, indicators suggest that it is still immature. Consolidation will be necessary to ensure its future development. Biotechnology has and will continue to have a major impact on society. However, it has yet to reach its full potential. Companies must identify earlier and adapt more quickly to market needs and business models need to be more realistic in view of time and resource constraints. The cyclical financial market behavior does not reflect the overall real value of the industry. If investors are able to recognize and adapt to the changing needs of the industry, the life sciences should continue to be a productive target for venture capital.

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[Extract, first published in European Venture Capital & Private Equity Journal, December/January 2004, pages 2-4]

Biotechnology in Europe: turning the corner

by Dr. Peter H. Reinisch, Partner, Global Life Science Ventures

It is fair to say that today Europe lags significantly behind the US in almost all facets of the commercial development of biotechnology. A slow start was certainly a factor. However, the biotechnology industry regularly experiences cycles during its development and continental Europe recently experienced its first major downturn. Here we examine in detail where the industry in Europe stands today, the reasons for its latent development, and the measures that are being taken to make it competitive across the globe. The awareness, understanding and expectations of many of the younger biotechnology companies in Europe are now more realistic than ever before.

A global perspective

The US is the indisputable industry leader in the international biotechnology arena. It has the majority of the larger, publicly listed pharmaceutical and biotechnology companies as well as R&D centers. Biotechnology companies in the US have a very strong drug pipeline with around 300 product candidates in phase III clinical testing.[1]

For larger pharmaceutical companies, recent trends confirm that R&D is increasingly shifting to the US. The setting up of the Novartis Institutes for Biomedical Research, Novartis' global center for research, in Cambridge, Massachusetts, in May 2002, is but one example. In addition, US companies continue to make acquisitions giving them further critical, global mass.

In the pharmaceutical industry, the US remains the key market for the success of New Chemical Entities. Recent studies by IMS confirm that products first launched in the US achieve nearly twice the sales of drugs first launched outside this market.[2] In 2001, despite its traditional strengths in the pharmaceutical sector, only 12% of blockbuster sales (drugs with sales of over US$1bn) came from Europe. North America dominates growth across the biopharmaceutical sector.

The rise of Asia

Increasingly, Asia is gathering momentum as an engine of growth for the pharmaceutical and biotechnology sectors. It has demonstrated major expansion in science and technical innovation and is quickly building capabilities to bring novel chemical and biological entities to the market. Many argue that it is poised to shake both the US dominance in the biotechnology industry as well as Europe's long-standing tradition in scientific research. In the near-to mid-term, China, Japan, India, South Korea, Taiwan and Singapore are expected to be major players.

Consolidation in Europe

Despite having comparable numbers of companies, the US biotechnology industry employs more than twice the number of people as the industry does in Europe, has about twice the revenues, spends around three times as much on R&D, raises three to four times as much venture capital and has a significantly higher number of publicly listed companies.[1] However, this is only part of the picture.

After a slow start, the biotechnology industry in Europe quickly caught up in the 1990s. Since the widespread period of hype surrounding the life sciences in 2000, which coincided with the cracking of the human genome and the full swing of the dot.com boom, the biotechnology industry in Europe has been undergoing a period of healthy consolidation. The negative side of this process, insolvencies of companies, is very evident.

However, consolidation has been accompanied by positive developments that often go unrecognized. Namely, a solid infrastructure for the industry as a whole has been put in place, including access to experienced patent lawyers, improved capabilities for technology transfer from academic institutions to the private sector, more experienced managers, the creation of regional biotechnology clusters, as well as the services and expertise of experienced venture capital funds.

Where is the private equity?

Funding remains the major issue on the European landscape. In the region, a funding gap exists for early stage companies that may have viable technologies or drug candidates under development but which have no products in the clinic. In recent times, the level of investment in companies in Europe has fallen below the late 1990s level. In addition, the median time between financing rounds has been steadily increasing over the past three years. Seed and first round financing have been hit the hardest during the recent downturn.

In 2004, the number of European initial public offerings in the biotechnology sector did rebound somewhat. However, most of these companies are trading at prices significantly below their issue price. It is not clear if this rebound is sustainable or indeed whether it indicates an upturn. What is clear is that European companies have fewer exit opportunities. Merger and acquisition transactions are more or less stable and have not been compensating for a lack of exit opportunities on the stock markets. On the other hand, the recent acquisition of GlycArt by Roche is a visible example that suggests a new positive trend.

An opportunity for investors

Although financing is one of the clearcut limiting factors for Europe's biotechnology industry, it also represents a significant opportunity for investing into selective VCs. Investing at the low end of a cycle provides considerable return when higher valuations return to the market. Exciting investment opportunities exist for forward-thinking family offices and institutional investors. Today's market environment is an unprecedented opportunity for investors to support advanced, innovative biotechnologies at attractive valuations.

A roadmap already in place

The European Commission has been active in putting in place progressive recommendations to help Europe's industry address the challenges it faces. These efforts were started some years ago after a careful evaluation of the European biotechnology industry.[3] The recommendations were timely, the proposed strategy has now been adopted and the necessary measures for improvement are being put in place. In April 2005, for example, the European Commission put forward a proposal by which life science and other businesses stand to gain a larger portion of the proposed EUR 73bn EC research budget. Although not yet approved, measures like this have the potential to stimulate economic growth in Europe.

Four years ago, European leaders agreed to make the European Union one of the world's most dynamic and competitive markets by 2010. Increasing expenditure on R&D is a core component of the measures needed to reach this goal and to attain parity with the US, which currently devotes around 2.6% of its GDP to R&D.[5] Although the original goal of the European Union will not be met on time, these recommendations are likely to have large implications for the industry as a whole.

The birth of venture capital

In the US in the 1940s, two inspirational individuals succeeded in organising free market initiatives for start-up financing: Ralph E Flanders, president of the Federal Reserve Bank in Boston and later a US senator, and General Georges Doriot, a professor at Harvard Business School. Flanders' vision was to free fiduciary funds from the restrictions of the investment Act of 1940 allowing them to invest up to 5% of their assets in the equity of new enterprises. Doriot brought with him a vision founded on first-hand experience of innovation at academic institutions. Both were acutely aware that a great deal of the technology developed at the Massachusetts Institute of Technology (MIT) during World War II held great promise for commercial application.

In an environment free from government intervention, Flanders and Doriot succeeded in bringing together the academic community and publicly owned funds arising from the considerable wealth of larger institutions. By tapping into the pools of funds within these financial institutions they were certain that they could create a private and independent entity that could transform technological research into viable enterprises. This idea gave birth to the venture capital industry in the US.

The relevance to Europe

Despite Europe having a slow start in the biotechnology industry, many of the ingredients are in place today for it to develop into a key part of the global industry. However, in analogy to the history of professional venture capital in the US, two visions are relevant today for Europe. First, it is necessary to free fiduciary funds from the fear of investing in early stage biotechnology companies. This is the only way to create a long-lasting, sustainable biotechnology industry. Second, much technology development has taken place since the mid1990s both in the years of hype and the following downturn. As we progress further into the twentyfirst century it is worth pursuing these unprecedented opportunities for commercialisation.

It should be fuelled by fresh venture capital. The potential of this innovation is inextricably linked to the most fundamental of all human needs, namely health. The current shortage of short-to mid-term investment opportunities should be a "wake-up call" for financial investors who must seriously consider early stage opportunities in the interests of the long-term development of Europe's biotechnology industry. This has been the route to success for the biotechnology industry in the US.

The Flanders' message

On November 16, 1945, Ralph Flanders addressed the National Association of Security Dealers in Chicago:

"American business, American employment and the prosperity of the citizens of the country as a whole cannot be indefinitely assured under free enterprise unless there is a continuous birth of healthy infants in our business structure. We cannot depend safely for an indefinite time on the expansion of our old big industries alone. We need new strength, energy and ability from below. We need to marry some small part of our fiduciary resources to the new ideas which are seeking support."[6]

These messages are as pertinent to Europe today as they were to the US at the birth of the venture capital industry. There are reasons to be optimistic about Europe's potential. After a late start, Europe's biotechnology industry now has all the elements for success solidly in place. We just have to reach out and grasp the challenges.

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Optimism is back for European biotech

by Dr. Peter H. Reinisch, Partner, Global Life Science Ventures

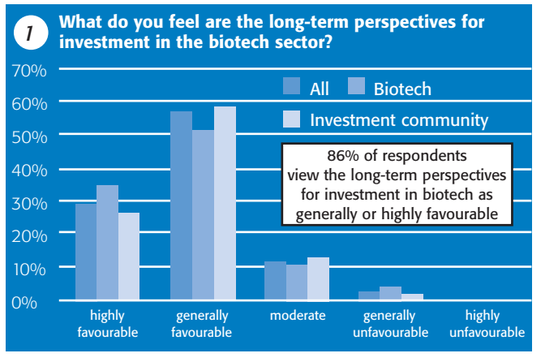
Survey of Biotech Executives and Investors Confirms Positive Views of Sector

As recently as a few years ago, the mood in the European biotech sector was rather gloomy, whether it was company CEOs scrambling for new funding to support the development of their pipeline, or investors unwilling to get burned again through highly risky investments. But things have changed. We are now witnessing a steady revival of the sector that is putting it on surer footing than ever before. Companies have learned from the mistakes of others, formulating solid business strategies aimed at driving marketable products through development, putting together more experienced management teams, and attracting renewed interest from investors and, increasingly, large pharma companies for early stage deals / transactions.

In order to obtain a more quantitative assessment of the current investment climate in the biotech sector and how it has been evolving, as well as elicit views about the future perspectives of the sector, Global Life Science Ventures recently carried out its GLSV Biotech Investment Barometer for the second consecutive year. 186 people responded to the survey sent out in September, including 54 biotech executives and 103 investors and analysts, with 88 % of respondents based in Europe. The Barometer results were presented at the 6th Annual Biotech in Europe Investment Forum, held in Zurich on 4–5 October 2006.

Favourable Long-term Perspectives

We found that the future of investment in the sector was regarded very positively, with 86 % of respondents viewing the long-term perspectives for investment in biotech as highly or generally favourable – a massive endorsement of the biotechnology sector unchanged from a year ago (fig. 1). What has increased is the relative optimism compared to a year earlier: 55 % of respondents now have a brighter outlook than a year ago, when the corresponding figure was already 46 %. For Europe specifically, three quarters of respondents see the future as fairly or highly positive.



We see various reasons for the increasingly healthy outlook. The sector is approaching overall profitability as an increasing number of drugs issued from biotech reach the market, and investors also appear increasingly confident about achieving profitable exits. 74 % of our Barometer respondents expect the IPO window to remain open for more than six months in Europe (67% in the US), a sign of increased stability. As pharma companies scour the biotech sector for development programs of interest that they can use to fill their pipelines, mergers and acquisitions have become an interesting alternative to IPOs as a means of exit for investors. As later stage deals become rarer, pharma companies are looking even further back in the pipeline for deals of interest, thereby providing a welcome additional source of capital that can complement VC money.

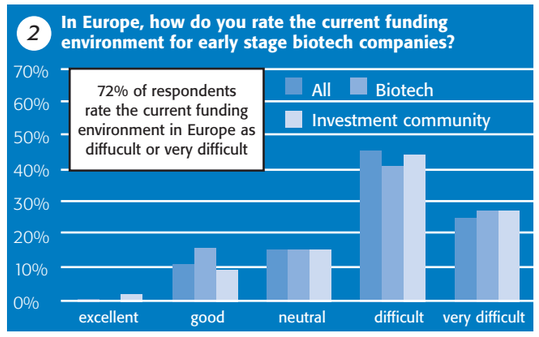
European Biotech Stocks Expected to Outperform

For European public companies, prospects also look promising. European biotech stocks in particular are regarded as undervalued by 64 % of respondents, compared to just 28 % for US stocks. Even among investors and analysts alone, who have the greatest stake in accurately assessing valuations, the difference was striking. In addition, 63 % of respondents expect overall biotech shares to outperform the stock market in the next year.

Difficult Early-stage Funding

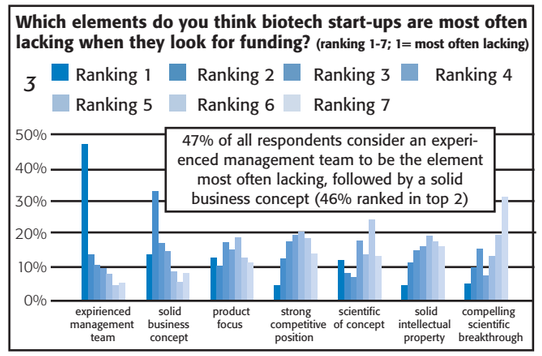
Situation One of the points for concern that emerged from our survey, though hardly an unexpected one, remains the difficult funding situation for young biotech companies in Europe. In fact, 72 % of respondents considered the current funding environment for early-stage biotech companies in Europe to be difficult or very difficult (fig. 2), a much higher figure than the 26 % who expressed the same view about the US, and two of five respondents ranked insufficient funding as the single greatest threat to the sector. In replies to the Barometer's one open question on possible measures to improve the financing and profitable growth of European biotech companies, respondents suggested a range of possible solutions, including tax incentives for early stage investments, increased government financing, rules to avoid dilution of founder shareholder value, greater access to pan-European capital, and support for scientific research and education.

The positive aspect of this situation is that, from an investor's point-of-view, the smaller amount of venture capital funding currently available in Europe means that the most promising biotech projects in development can be bought into at more attractive prices than is possible in the US. This is a message we are working to communicate.



Experienced Management: A Key Element

For start-ups looking for funding, the importance of recruiting experienced managers early on is outlined by the nearly half of respondents (and 55 % of investors and analysts) who rank this the element that is still most often lacking, followed by a solid business concept. (fig. 3)



The activity that most interests investors is, not surprisingly, therapeutic products, ranked first by 60 % of respondents. Vaccines and medtech were considered next most attractive by similar levels of respondents, followed by diagnostics, platform and bioinformatics companies, respectively.

A final note of interest: with much of the attention in the sector focused on Europe and the US, there is a tendency to forget about the major developments going on in Asia in centres such as Singapore and Australia, as well as in emerging markets. Biotech executives were clearly more aware of the Asian biotech scene than investors and analysts, with fully 69 % (vs 53 %) agreeing that developments in Asia were highly or fairly significant for the biotech sector.

In conclusion, as we have been saying with conviction for some time now, we believe that the European biotech sector now has all the elements in place to achieve sustainable success, and for discerning investors, the opportunities are now unprecedented. Increased investment will help build further confidence and ensure that Europe secures its rightful place as a center of biotech innovation.

[First published in BIOforum Europe 12/2006, pages 2-3]

The impact of biotechnology on modern health-care and drug development

by Dr. Peter H. Reinisch, Partner, Global Life Science Ventures

Health is the most fundamental of human needs, and the priority accorded to healthcare reflects the overriding importance of health to people's lives and general well-being. In this article we will argue that, in the 21st century, biotechnology is set to play a decisive role in the development of the healthcare sector, meeting unmet medical needs and bringing to market powerful, innovative new drugs.

Biotechnology has already yielded safer, affordable therapeutics, and the most successful drugs issued from biotechnology have already included several blockbusters with sales in excess of $1 billion (Eur 784 million). The sector is proving to be one of the most important drivers of the healthcare industry and a source of innovation for pharmaceutical companies. Extending well beyond the techniques of "gene cloning" or "gene transfer", biotechnology today encompasses breakthrough developments in many medical research areas, including pharmacogenomics, RNA interference applications, stem cell research and protein therapeutics.

There are huge unmet medical needs

The extent of currently unmet medical needs is apparent if one considers that of about 30,000 known diseases, only a third can be treated and most lack cures[1]. There are only limited or, in many cases, no effective treatments available for AIDS, Alzheimer's disease, multiple sclerosis, the many different forms of cancer and cardiovascular disease, as well as inherited diseases such as muscular dystrophy and cystic fibrosis. Where treatments exist they often have significant side effects, and many individuals do not benefit from treatment. Chronic, noncommunicable diseases (NCDs) alone now account for 59 percent of the 57 million annual deaths occurring worldwide. The burden of chronic diseases is set to have a major impact on healthcare systems and economies across the world, with an expected cost in 2007 of over $200 billion.

New infectious diseases also regularly arise, and AIDS and avian flu are just two major examples of the challenges these represent. Today, there are still no marketed vaccines for AIDS, malaria, and tuberculosis, the "big three" in the infectious disease panorama.

With the steady increase in lifespans in the developed world comes also an increase in degenerative diseases and morbidity, leading to rising healthcare costs and greater demands on increasingly fragile healthcare systems. There will therefore be a growing need for cost-effective new drugs and solutions to decrease the amount of time spent by patients in hospitals.

Modern science can make a difference

Although these challenges are considerable, history has repeatedly shown that research into the causes of diseases leads to more effective treatments. Insulin has saved many diabetics from an early death, and penicillin has saved countless lives. Vaccines have been developed against childhood diseases such as measles, mumps, diphtheria, tetanus and rubella, as well as the debilitating disease polio, and smallpox has been eradicated.

A more recent example is AIDS, which shows the tremendous progress medical science can make in transforming an invariably fatal disease into a manageable one. Biotechnology has had a major impact on several fronts in the fight against AIDS, including the following breakthroughs:

- Identification and sequencing of the HIV virus.
- Development of diagnostic tools to prevent infection through blood products and identify infected individuals.
- Introduction of reverse transcriptase and protease inhibitors, which have greatly reduced the annual number of deaths from AIDS in developed countries and allowed infected people to lead relatively normal lives.

Recombinant technology will also certainly be instrumental in developing a future vaccine against AIDS.

For other acute and chronic diseases, like the different forms of cancer, biotechnology offers equally strong hopes for new therapeutics that may turn them into manageable diseases like AIDS or, to use a classic example, diabetes.

A milestone in the progress of biotechnology was the completion of the Human Genome Project in 2003. Genomics is providing a new set of approaches and tools as well as considerable insight into a wide range of human diseases and conditions, the benefits of which will only become evident in the coming years. This progress represents a quantum leap in our ability to understand physiological processes and diseased states, and will help scientists to identify new potential drug targets.

The biotechnology industry can rejuvenate big pharma

The promise of biotechnology can be further understood by looking at the problems faced by the pharmaceutical industry, the traditional source of new medications. Until about ten years ago, the pharma industry had an enviable track record in terms of research productivity and commercial success: new medicines were discovered, developed and marketed at a rate that supported double-digit sales growth across the industry. But today, big pharma is struggling to transform basic scientific innovation into commercial products. Many of today's pharmaceuticals are not living up to expectations regarding innovation and direct benefits to the patient compared with their cost, and pharma's label as the "innovator industry" is being called into question[3]. The number of new active pharmaceutical substances reaching the market in 2004 was close to 20-year lows.

The cost of bringing a new medicine to the market, generally in the range of $0.8 billion to $1.7 billion, is one major barrier to the investment in innovative drugs. Although there have been more products entering the pipeline recently, fewer are advancing through development, with the biggest bottleneck at phase II clinical testing[4]. But another, more fundamental issue is big pharma's relative difficulty to quickly exploit the latest academic know-how and turn it into new treatments.

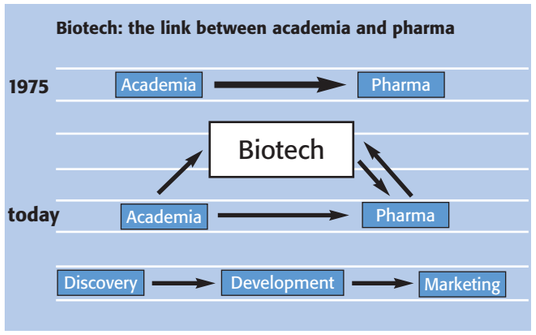
Innovation is not the pharma industry's only challenge. By 2008, patents on more than 58 products are expected to expire worldwide, putting potential revenues of about $50 billion at risk[5] while spurring growth in the generics market.

Finally, there is the issue of safety. Following several recent high-profile product withdrawals and questions about drug safety, the pharma industry has increasingly come under the spotlight of regulatory authorities and the public at large. The industry and the regulatory agencies will have to work harder to convince the general public that they can bring safe drugs to the market. Some observers predict a tightening of legislation to prevent similar events from happening in the future. The overall effect could be even slower times to market for drugs in development.

The biotechnology industry, with a flexibility and culture of innovation that have often been lacking in the pharmaceutical industry,

> ***"GLSV has repeatedly proven to be at the forefront of biotech innovation. By building on solid operational experience and providing constructive input, GLSV offers a sound platform helping us to create value. Knowledgeable, experienced, supportive, that is GLSV."***
>
> Evert Küppers, CEO, Pieris AG

and with an acute ability to tap into the latest discoveries on the academic front, harbours many of the newest life science technologies and is in a strong position to provide solutions to the issues mentioned above. These technologies are already driving growth in the biotechnology sector, with sales now growing at around 20 to 30 percent per year, compared to the pharma industry's single-digit growth. They also bode well for the sector's future. As biotechnology companies increasingly retain ownership of their developmental compounds and create more blockbuster drugs, they are poised to continue to grow faster than their pharmaceutical counterparts.



Biotechnology offers more specific medicines addressing multiple targets at different stages of a disease, tools to empower life science research and development, as well as routes to new biopharmaceuticals offering improved benefits to patients. It is also well positioned to help fill the compromised drug pipelines of many pharma companies, as can be seen by the numerous in-license agreements. The pharma-biotech partnering opportunities that have developed over the years, with an order of magnitude increase in partnerships since 1993, have been instrumental in shaping the healthcare sector, and are a healthy sign for both industries.

Healthcare challenges, bio-technology solutions

As mentioned at the outset, unmet medical needs are the main

driver of growth for the biotech and pharma industries. Biotechnology can provide better targeted biopharmaceuticals addressing different stages of a disease. Genomic and proteomic approaches offer new information on the mode of action of drugs that will lead to better, safer treatments. Biotechnology also allows the development of tools that can advance research and development in different therapeutic areas.

Recent examples of how biotechnology can provide solutions stem from the field of cancer therapy. In February 2004, two new drugs were approved by the U.S. Food and Drug Administration (FDA) for cancer treatment. Avastin, from Roche, is a monoclonal antibody (mAB) that attacks the blood vessels feeding a tumour, thereby preventing growth – an entirely new mode of action for a cancer drug. The benefits of this new targeted approach are reflected in the record speed with which Avastin was adopted by prescribers. Erbitux, a drug from Bristol-Myers Squibb/Merck KGaA/ImClone Systems used for the treatment of colorectal cancer, is a genetically engineered version of a mouse antibody that also contains human components. Erbitux targets a specific protein present in larger than usual amounts on the surface of rapidly proliferating cancer cells, thereby inhibiting their growth. These two recent success stories were preceded by products like Herceptin and Rituxan, MAbs which are widely used today for the treatment of breast cancer and lymphoma, respectively. MAbs are now one of the fastest growing product classes in the biopharmaceutical industry, with the European market alone set to grow at a compounded annual growth rate of 34.1 percent, reaching $11.4 billion (Eur 8.7 billion) by 2011[6].

Other innovations in biotechnology are leading to a substantial transformation of the healthcare sector by providing new tools that can lead to greater efficiencies and improved safety. An example is pharmacogenomics, a tool with great potential for physicians for assessing patients' genetically-linked risk factors for certain diseases. In time, genetic testing via rapid genome-wide sequencing methods will become routine, and drugs will increasingly be given in connection with patients' individual genetic profile. For example, for metastatic breast cancer, diagnostic tests can already identify whether individuals are overexpressing particular proteins linked to the disease. Pharmacogenomics will also have a large impact on drug development and on the way clinical trials are designed and executed by allowing the selection of the most appropriate target groups.

Toxicology issues can also now be addressed earlier in the drug development process, and new biotechnologies are now allowing for the identification and use of improved biomarkers for diagnostic purposes as well as the use of new "humanized" laboratory model systems[7].

Biotechnology: an industry with momentum

Over the past quarter of a century, more than 150 biotechnology drugs and vaccines have been introduced, and more than 370 are currently in clinical trials[8].

Biotechnology products accounted for 10 percent of the global pharmaceutical market in 2004, and seven biotechnology products were among the top 50 drugs worldwide in 2003, representing combined sales of $15.1 billion[9]. In 2003, licensed products from biotechnology companies amounted to more than $70 billion in revenues for the top 20 global pharmaceutical companies[10]. Twenty brands of biotechnology products, including Erythropoietin (EPO), several interferons, granulocyte-colony-stimulating factor and insulin, each had sales of over $1 billion in 2004[11].

There are now over 4,000 biotechnology companies worldwide, with some of the leading ones, such as Amgen and Genentech, rivalling their pharmaceutical peers in terms of market capitalisation (in the range of $50 to $80 billion). Amgen is now ranked among the top 20 global pharma companies in the world and is expected to break into the top 10 by 2008[10].

Blockbuster drugs

Despite claims that the blockbuster model is compromised, the number of drugs with sales of over $1 billion continues to increase annually, and other candidates are in the pipeline[12]. Biotechnology has already demonstrated its clear potential to generate blockbusters. Erythropoietin (EPO) is a good example. Initially introduced in 1989 as a niche drug for treating kidney disease-related anaemia, it has since found applications for the treatment of cancer and AIDS patients. This shows that the successful introduction of a therapeutic for one indication can open up new market opportunities with other indications. EPO is without doubt the top selling biotechnology therapeutic; in fact, in 2004, EPO (adding together the sales figures for all brands) was the best selling human medicine, with sales of over $11 billion[11].

As an ever-increasing percentage of marketed healthcare products are derived from biotechnology, success stories of this kind will become more widespread. Erbitux is predicted to achieve sales of over $1 billion by 2008[10], and Avastin's sales already exceeded this figure in 2005, with predictions that they could reach over $8 billion by 2010 as the range of indications for which the drug is prescribed grows.

Biotechnology-based products are potentially less vulnerable

As mentioned, two distinct but major threats that can affect pharmaceuticals at different times during their life cycle are safety issues and the eventual expiration of patents. Products issued from biotechnology appear to have key advantages in these respects. Traditionally, pharmaceuticals have often been discovered through the random screening of chemical libraries for a desired activity, followed by clinical testing for an acceptable safety profile. Side effects with a low incidence may not be discovered until a drug has been on the market. Products based on biotechnology, on the other hand, are often designed from the beginning with specificity for their desired targets – as is the case with MAb-based drugs. While unwanted side effects can never be ruled out, the tendency towards more specific drug-target interactions is clearly an advantage and offers the possibility of lower toxicity and greater acceptance[13].

Because they tend to be much more complex molecules than traditional drugs, biotech products are also more difficult and more expensive to copy and have approved by the regulatory authorities. This fact makes them potentially less vulnerable to competition from generics once their patents expire[14].

Investing in the healthcare era

The Russian economist Nikolai Kondratieff identified regular innovative cycles lasting 40 to 60 years that were based on technological and economic developments and appeared to drive world economies[15]. Following four cycles driven by heavy industry[16], the current Kondratieff cycle is based on the sweeping influence of information technology. The foundation of the sixth Kondratieff cycle will be healthcare, a motor of growth and employment in the 21st century, and biotechnology will be its primary driver.

To allow the healthcare era to reach its full potential and for biotechnology to play a decisive role in shaping the future, we must take every opportunity to invest in the best early-stage life science companies. In a recent article published in the European Venture Capital Journal[17], we have looked at how venture capital funding of early-stage companies has progressed in Europe and at its impact on the biotechnology industry. Investing in true innovation is a necessity if we are to create new jobs, develop new drugs and technologies for unmet medical needs, and benefit from the exciting developments taking place in the life science sector. This ultimately will lead to healthy capital gains for investors, for whom the current market environment represents an unprecedented opportunity.

> ***"Working with Global Life Science Ventures has been a truly value added experience for Neurogesx. Having investors with industry experience located in Europe has opened many doors that otherwise would not have been available to us."***
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> Tony diTonno, CEO, Neurogesx

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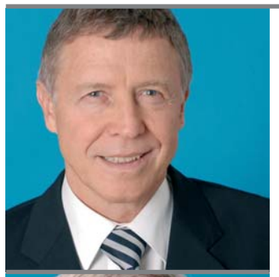


„Biotech-Unternehmen scheinen zunehmend der Antrieb für das Wachstum in der Biopharma-branche zu sein“

Dr. Hans A. Küpper und Hanns-Peter Wiese, Partner, Global Life Science Ventures

Mit dem Verkauf von GlycArt an Roche und dem IPO von Intercell konnte Global Life Science Ventures in einem schwierigen Marktumfeld erfolgreiche Exits vollziehen. Das GoingPublic Magazin sprach mit den GLSV-Managern Dr. Hans Küpper und Hanns-Peter Wiese über erfolgreiche Exitstrategien, die Zusammenarbeit von Biotech- und Pharmaindustrie und das Fundraising.

Dr. Küpper, Herr Wiese, wir gratulieren zum erfolgreichen Verkauf Ihres Portfoliounternehmens GlycArt. Wie kam es zu diesem überraschend frühen Trade Sale an Roche?

Dr. Küpper: Es war einfach die richtige Gelegenheit zum richtigen Zeitpunkt, aus der alle Beteiligten aus Biotechund Pharma Nutzen ziehen konnten. GlycArt wurde 2001 als Spin-off der ETH Zürich gegründet und entwickelt Methoden zur Steigerung der klinischen Wirksamkeit von therapeutischen monoklonalen Antikörpern. Die attraktive Bewertung hob die Bedeutung von GlycArt's einzigartiger Plattformtechnologie für Roche hervor. Roche und GlycArt hatten bereits seit über einem Jahr erfolgreich zusammengearbeitet und so ein gutes Arbeitsverhältnis aufgebaut.

Wiese: Andere Unternehmen hatten ebenfalls ihr Interesse an GlycArt zum Ausdruck gebracht, aber Roche ist ein ausgezeichneter strategischer Partner und hat die attraktivsten Bedingungen angeboten. Beide Unternehmen ziehen ganz klar Nutzen aus den bestehenden Synergien. GLSV war der Lead-Investor in der ersten Finanzierungsrunde (Serie A) des Unternehmens, hatte einen Sitz im Aufsichtsrat von GlycArt und spielte auch eine aktive Rolle dabei, den Trade Sale-Prozeß in Gang zu bringen.

Was ist an GlycArt so außergewöhnlich? Warum war Roche bereit, 235 Mio. CHF für den Erwerb von 100 % der GlycArt-Aktien zu bezahlen?

Dr. Küpper: Monoklonale Antikörper (mAbs) sind äußerst wertvolle Therapeutika für die Biotech-Branche und den gesamten Gesundheitssektor. Insbesondere Roche investiert viel in die nötige Infrastruktur zur Herstellung von mAbs im großen Maßstab, zum Beispiel in der neuen Anlage in Penzberg, Deutschland. mAbs sind ideale Kandidaten für die gezielte Krebstherapie in einem Bereich, in dem Roche bereits weltweit zur Führungsspitze zählt. Der Preis für GlycArt, ein junges Unternehmen mit einer präklinischen Pipeline anstatt vielversprechenden klinischen Arzneimittelkandidaten in der Spätphase, deutet ganz klar darauf hin, welch hohen Wert Roche der Technologie von GlycArt beimißt. Roche kann GlycArts Ansatz zur verbesserten Wirksamkeit von mAbs für jeden seiner Therapeutika-Schwerpunkte nützen. Der Ansatz könnte auch zu verbesserten Folgeversionen von bereits verkauften mAbs wie z.B. Herceptin und Rituxan führen. Durch die strategische Übernahme sollte möglicherweise die Konkurrenz ausgeschlossen werden.

Die Übernahme von GlycArt durch Roche ist das jüngste Beispiel für eine lohnende Zusammenarbeit von Biotechnologie und Pharmaindustrie. Steigt Ihrer Meinung nach das Interesse an Übernahmen in der Biotechnologie durch Pharmaunternehmen im allgemeinen?

Dr. Küpper: Die Pharmaindustrie hat schon immer mit der Biotech-Branche zusammengearbeitet gerade in Bereichen, die ihr helfen, ihre Pipelines zu füllen. Neu ist, daß die Biotech-Branche jetzt bereits eine echte Erfolgsgeschichte gewinnbringender Produkte vorweisen kann und das Wachstum der Biotechnologie dasjenige vieler Pharmaunternehmen bei weitem übertrifft. Biotech-Unternehmen werden zunehmend zum Motor für das Wachstum in der Pharmabranche. Die Biotechnologie kann die Bedingungen für Innovationen schaffen, die für die Forschung und Frühphasenentwicklung notwendig sind, während die großen Pharmaunternehmen über genügend finanzielle Mittel verfügen, um die klinische Entwicklung, Produktion und Vermarktung zu realisieren. Sowohl Pharmaindustrie als auch Biotech-Branche profitieren von dieser Situation.

Eines der letzten europäischen IPOs Ihrer Portfoliounternehmen wurde von Intercell durchgeführt. Welche Kriterien sprachen für ein IPO an der Wiener Börse? Und sind Sie mit der Wertentwicklung am Anschlußmarkt zufrieden?

Wiese: Es wurden mehrere europäische Börsenplätze, die für eine Notierung von Intercell in Frage kamen, in Betracht gezogen. Intercells Hauptsitz befindet sich jedoch in Wien, und letztendlich hat sich das Unternehmen für die Notierung am heimischen Markt entschieden. Der Aktienkurs von Intercell hat sich während der vergangenen Monate gut entwickelt und liegt heute bei 35 % über dem Emissionskurs (8. September).

Warum hat sich Intercell gegen ein IPO an der deutschen Börse entschieden?

Wiese: Diese Möglichkeit wurde ebenso wie ein IPO an der SWX Börse in Zürich oder an der Londoner Börse erwogen. In Deutschland spielte auch das Börsenumfeld eine Rolle, das nach wie vor nicht überzeugt. In Österreich ist die Firma jedoch sehr bekannt und kann dort als erster Biotech-Börsengang vom sog. „local hero“-Effekt profitieren, was letztlich die Wahl stark beeinflußt hat.

Was für Maßnahmen müßten Ihrer Meinung als Venture Capitalist nach ergriffen werden, um die deutsche Börse für Exits attraktiver zu machen?

Wiese: Meines Erachtens liegt der mangelnde Erfolg weniger in der Börse selbst als in der Einstellung der meisten Deutschen. Wenn man überhaupt den Börsen oder den Banken einen Vorwurf machen will, dann den, daß sie bei der Auswahl der Börsenkandidaten zuviel darauf aus waren, kurzfristig Fees zu verdienen, statt langfristig eine Börse aufzubauen mit soliden Wachstumswerten im Tech-Bereich. Vielleicht sollte man einmal darüber nachdenken, die Fees an die After Market-Performance zu knüpfen, was letztlich dem üblichen Lock-up der Altinvestoren entspräche und dafür sorgen könnte, daß auf mehr Qualität geachtet würde.

Mit Coley Pharmaceutical Group, Memory Pharmaceuticals und Cyberkinetics Neurotechnology Systems hatten Sie vor kurzem drei weitere Exits durch IPOs in den USA. Sind Sie mit der Wertentwicklung dieser Unternehmen am Anschlußmarkt zufrieden und haben Sie in der Zwischenzeit bereits Aktien verkauft?

Wiese: Zwei der Unternehmen werden momentan unter dem Ausgabekurs gehandelt, aber das gibt nicht den tatsächlichen Wert ihres Produktportfolios wieder. Intercell wird über dem Ausgabekurs gehandelt, und Coley war bei dem kürzlichen Börsengang um einiges überzeichnet. Es ist also zu früh, um über Zufriedenheit eine endgültige Aussage zu machen. Wir verfolgen die Strategie, erst dann Aktien zu verkaufen, wenn unserer Meinung nach bestimmte Werttreiber in der Bewertung realisiert wurden.

Einige Venture Capital-Unternehmen befinden sich gegenwärtig im Fundraising, und in letzter Zeit gab es auch einige Pressemitteilungen über Closings. Wie steht es denn um Ihre Pläne für das Fundraising?

Wiese: Wenn man die für Folgerunden reservierten Mittel einrechnet, haben wir über 60 % unseres zweiten Fonds investiert. Wir planen in naher Zukunft das Fundraising für unseren dritten Fonds, GLSV III, zu beginnen und sind zuversichtlich. Die Gesundheit ist ein grundlegendes Bedürfnis des Menschen, und privates Venture Capital ist nun einmal unentbehrlich für die Unterstützung von Early Stage-Unternehmen, die die eigentliche Innovationsquelle für die Pharmaindustrie bilden.

[First published in GoingPublic Biotechnology 2005, October 2005, pages 96-97]

The science of biotechnology investing

Dr. Peter H. Reinisch, Partner, Global Life Science Ventures

What limited the amount of funding available to continental European life science ventures before GLSV was established?

There wasn't a real awareness of the need for such a fund. In the US after WWII, professional venture capital was started in order to commercialise research done for military purposes. Consequently, the US is very advanced in this field while in Europe we were late in realising the need for venture capital. We were also slow to see the new opportunity for investment in biotechnology, despite Europe's long history in science and many significant breakthroughs.

What do you see as being the most compelling reasons for investing private equity in the healthcare sector?

Health is a universal priority, the most fundamental of human needs, and the healthcare sector is relatively sheltered from market forces. The huge number of unmet medical needs, including treatments for some of the most devastating and widespread diseases – just consider the impact of AIDS, cancer, Alzheimer's, SARS, etc. – will ensure a market for innovative new drugs and biotechnological approaches for many years to come. Biotechnology has become the driver of the pharmaceutical industry, and a new positive trend in the number of successful exits demonstrates the rewards to be gained from smart investments in the sector.

Does the Engelhorn family play an active role in the day-today running of GLSV ?

No, GLSV was designed to be a completely independent entity from the very beginning. The role of the family is currently one of investors only, as limited partners, with two branches of the family having invested in the second fund. However, their role in establishing GLSV and its first fund was essential, with Dr. Engelhorn, a doctor who spent several years at Harvard Medical School as a researcher, playing a key role in getting it started. For GLS I the Engelhorns were a cornerstone for the whole fund by being the lead sponsor and with their reputation as entrepreneurs, their industry insights and their success with Boehringer Mannheim – the largest and most profitable biotech company in Europe at that time. Life science businesses are investment intensive and often come with high risks attached, as seen with the current Vioxx controversy. On the other hand, the rewards for success can be great.

How does GLSV select its investments to mitigate risk?

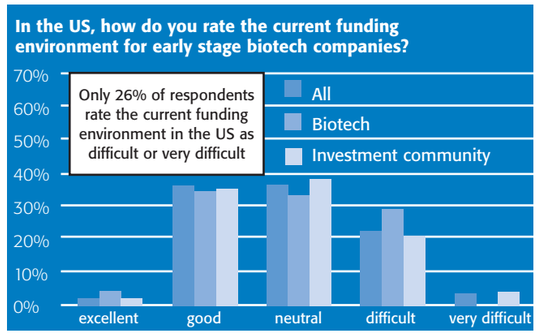
Of course there is a risk involved and sometimes risks only be come apparent at a very late stage – as with Vioxx. However, with a fund you have a portfolio and balance the risks across the portfolio. When ever you invest, you have to do so with professional insight and expand your knowledge base for each specific deal, as each one has to have the upside potential to recover risks in others. We do this by using our extensive professional network and using the right experts during due diligence who can give precise risk profiles. In addition, we normally take a seat on the board of our investments and are therefore able to help the management and understand risks as they emerge. Life science investments can also be controversial in terms of development techniques used such as animal testing.

What is GLSV 's view regarding animal testing?

You can't avoid animal testing completely because before testing on humans you must have animal data. Our companies try to do in vitro cell-based testing as much as possible, but it remains very important to have solid animal data to reduce the risks in clinical studies. The vast majority of the public accepts the necessity of animal testing for the development of effective medical treatments.

The biotechnology and healthcare sector has suffered lately in terms of valuation. Is this really a good time to invest in early stage companies?

This is exactly the time to invest as a venture capitalist. The industry did recently experience a downturn, but we now have clear indications of a new upswing. Presently we are in a period where biotech shares are undervalued, and this is a unique opportunity for investors. Life science investments do take longer than in other industries, but if you go in at this stage and intend to stay in, the chances of an upside are very strong.



What are the current trends in life science investments? Is it true to say that it is difficult for companies to achieve a successful exit at this point in time?

There are clear signs of a recovery, and the industry is ready for a healthy rebound. Of the 27 companies in which GLSV has invested, 11 companies – seven of which have European roots – have already gone public or found a new home via a trade sale. This year alone, GLSV has achieved 3 successful exits of companies in our portfolio. The purchase of Zurich-based GlycArt by Roche for 235 million Swiss francs in July was a highlight and a confirmation of the soundness of our investment strategy. In August, another of our portfolio companies, Coley Pharmaceutical Group, carried out the largest biotech IPO in nearly a year, while Intercell was a few months earlier the first ever biotech IPO on the Vienna Stock Exchange. We have several other candidates in our portfolio ready for an exit.

> ***"In 2004 I was approached by GLSV to lead an exciting new venture as CEO. I have to say, I was impressed by the quality of GLSV's due diligence, the resilience of the team to close this early-stage round in difficult times, their early pre-closing financial commitment rescuing the company, and their strategy to build reserves for financing the long-term growth of the company. Finally we closed a $10m Series A round together with Atlas Venture, and the lead product is now in phase IIa clinical trials."***
>
> Rainer Henning, PhD, CEO,
> Fibrex Medical

What does the future hold for your fund and what are your personal expectations for healthcare?

The number of unmet needs in the healthcare sector is huge. If one considers that there are about 30,000 identified diseases of which only a third can be treated, one quickly understands the great expectations from the biopharmaceutical industry. Biotechnology companies are a hotbed of innovation, and many have already proven their ability to deliver effective and commercially successful medications to the market as well as help fill the pipeline of the pharmaceutical industry with innovative new drugs. Our portfolio companies have a number of exciting products in clinical trials. Just a few examples include vaccines for Hepatitis C, Japanese encephalitis and several chronic diseases, and treatments for types 1 and 2 diabetes and cancer. The main limiting factor, especially in Europe, is funding. On the strength of our track record and by carefully selecting new companies to join our portfolio, GLSV will continue to attract both new and existing in vestors who recognise the opport unities for successful investment. We intend to raise a third fund in the near future.

[Extract, first published in Families in Business, Sep./Oct. 2005, pages 47-48]

Hans Küpper discusses science and venture capital

by Dr. Hans A. Küpper, Partner, Global Life Science Ventures

Can you tell us more about Global Life Science Ventures (GLSV) and what makes it unique in the venture capital industry?

At present, there are two main areas for high technology investments: one is information technology and the other is biotechnology. Today, if you want to be involved in high technology development, you have more or less to invest in either of these technologies. We at GLSV are an independent venture capital fund that is based on the very attractive investment opportunities offered by the life sciences. The sector encompasses many prominent technologies having a large impact on healthcare in general and consequently there is a big demand for products coming from the biotech industry. We have many pressing challenges such as chronic and degenerative diseases associated with older age, infectious diseases as well as noncommunicable diseases such as cancer, and increasing morbidity. What you clearly need is better diagnostics, approaches to prevent disease onset, and new therapeutics. GLSV supports early stage companies that often come from universities or other institutions and which offer innovative approaches in their area. The unique selling points of these companies should in some way allow them to eventually become dominant players in their markets worldwide. So far we have invested in 29 life science companies. Our investment focus is Europe. However, we also support companies in the USA. We do lead investments in Europe and consider co-investments through syndicates – with a strong local lead investor – in the USA. Some companies in our portfolio who have already gone public include Sequenom, Exelixis and Memory Pharmaceuticals in the USA, as well as Cytos Biotechnology in Switzerland. We have also made investments in a range of companies that are still private, like Coley Pharmaceuticals, CombinatoRx and Intercell.

Is there such a thing as a typical day for you, and if so could you describe it?

Every day is different and this clearly contrasts with some of the jobs I had before. The venture capital industry is actually a peoples industry and you have to have the right contacts, the right networks and the right access to information, therefore, most of the time you are involved in networking. Keeping up with the latest developments in science, either by going to meetings and conferences, through your network of experts, or publications and the Internet, is crucial. You have an intense travel schedule – sometimes you travel to attend board meetings of one of your companies. Then there are the many business proposals that you have to look through and reach opinions as to whether they are interesting propositions or not. If a project is potentially interesting, you will meet with representatives of the companies and discuss the proposition from the science side, or from the business, marketing or financial perspectives; this is all quite time consuming. Once you have invested in a company, it's almost like a marriage; for the following years, you are committed. Because you want them to be successful, you provide your network of contacts to the companies and you discuss upcoming issues and try to work things out. Most importantly, you must be able to understand from the technology side what they are doing, which makes it very important to keep up with the latest science.

How do you think biotech companies view venture capital companies?

One element biotech companies look for is to establish a long-term relationship. I think biotech companies are interested in smart money. By this I mean they also want access to the networks and experience of the venture capitalist. At GLSV, we believe that one of the ways we differentiate ourselves from other funds is through the people that work here. I have told you about my background but all members of our team have a high level of industry knowledge and complementary skills.

What was it like working for Biogen in the early days, and how did the company develop in the years you were there?

It was very exciting – like myself, most of the early employees came from academia and the biotech industry was still very academic in its approach at that stage. It was exciting because Biogen had very high scientific standards. Several high calibre scientists like Wally Gilbert and Philip Sharp, who both received the Nobel Prize, were directly involved in shaping the company as founders of Biogen. The fundamental technology platform of Biogen at that time was the gene transfer technology. We tried to look for applications for this technology, which were really broad. We were looking at every field – not only healthcare but also agriculture and industrial enzymes. One of the first undertakings I was involved in was the development of a foot-and-mouth vaccine. We were also looking at vaccines for other animal diseases as well as improving industrial microbes and plants through genetic engineering. However, the major undertakings at that time were interferon alpha, a hepatitis B vaccine, and then interferons beta and gamma, as well as other cytokines, which at that time were thought to be the most important biologicals. We were also trying to clone erythropoietin and the coagulation factor FVIII. Unlike at the university, we also had direct contact with patent law firms and we were travelling a lot to visit different companies in the USA, Japan, everywhere… It was a gold rush!

Do you ever miss anything about being in R&D or being in the lab?

No, although it's an interesting question. A researcher wants to be creative, which is something very human, and for the most part as a scientist you think that you can only be creative by designing an experiment and then looking at the result, interpreting it, maybe doing more experiments and – ultimately – by discovering something. But during a long career, you realise that you can also be creative by building up teams, hiring the right people, putting them together, strategically guiding what they're doing, which eventually leads to results and success. As a venture capitalist, you can be creative by building companies, providing networks, making the right contacts and setting the right strategic directions. You should be able to discuss science in detail but also be in a position to take a much broader view and look at the bigger picture. At the end of the day, I have to say I'm not really missing anything because you can be extremely creative as a venture capitalist, and you have to be creative otherwise you have a problem!

> ***"GLSV has been an excellent VC to work with. They bring both expertise and an extensive European network of contacts, and they are active and supportive in using their network to help build the company. The partners of GLSV are a pleasure to work with, a team that you feel that you are truly partnered with in trying to build an important enterprise."***
>
> Alexis Borisy, CEO, Combinatorx

Over the many years that you have been involved in science, you must have seen considerable advances in the biotech industry. What advances have surprised you the most?

There are always new surprises, and I hope the best ones are still to come! But some of the important discoveries were the early breakthroughs of restriction enzymes and the transfer of genetic material in the 1970s; these were groundbreaking changes. The early DNA sequencing methods developed in the 1970s also come to mind, as well as monoclonal antibodies, hybridomas, PCR and, eventually, the completion of total genome sequences, first of drosophila and mouse but then also of humans. I think these were watershed discoveries with huge implications. The implications were so tremendous that recommendations and laws had to be introduced to regulate their use.

What do you think are the major challenges facing the biotech industry today, and are they similar challenges to those faced, say, 25 years ago?

The landscape in the industry is always changing, as is the demand from patients, medical professionals and customers, which include among others the pharma companies. Some of the first companies founded included Amgen, Biogen, Chiron and Genentech. At that time – about 25 years ago – there were about 20–30 companies. Now you have about 5000, which is quite a difference! The companies specialized, expanded and diversified… 25 years ago there were many more pharma companies, which disappeared due to mergers and acquisitions. The picture today is an enormous increase in the number of biotech companies, but a parallel decrease in the number of big pharma companies, which results in a tough competitive landscape! What also needs to be borne in mind is that many biotech companies today can only demonstrate marginal improvements to already existing technologies in specific areas – with a marginal competitive edge. For example, take vectors for gene therapy; perhaps 20 companies or so have worked on this approach and each has used a different vector, which makes it very difficult to differentiate the best company or approach from the rest. This is something I think has really changed. In the beginning we had groundbreaking technologies, but now there are perhaps not enough companies with truly outstanding approaches or novel technologies. For the biotechnology industry, we will probably see consolidation as we have experienced in the pharma industry. Some companies will merge, others will be acquired and some will disappear.

What are the current biggest trends in pharma and biotech investments; where is the smart money going?

A clear trend in past years has been to invest in later stage companies, with more advanced technologies or products, in part because the industry had experienced too many unfulfilled promises about technologies and products that were supposed to accelerate drug discovery and development! Obviously the biotech industry has to react to these trends. One consequence is that companies will not only have to provide a technology platform, but will also have to develop this technology into Phase I and II products. Investors are always looking to reduce risk and one approach is to invest in later stage products. I personally believe that there are excellent technologies around. At the same time, I have 400–500 business plans per year, and 20 of these might be compelling. Eventually, you might invest in no more than 3–5 companies a year. In earlier years, you had fewer business plans but the strengths of the companies were more immediately apparent. You have to be very, very selective as an investor.

What do you think are the emerging trends?

Some of the recent trends – which look extremely promising – are RNAi technologies (RNA interference approaches), perhaps more at the R&D stage initially, but in time there should also be advances in therapeutic applications. Stem cells clearly have considerable potential. You might also think about organ remodelling, which includes, for example, growing pancreatic beta and islet cells for diabetics, or even parts of a liver. The more we understand about the immune system, the better is our approach to developing more promising vaccines. Another important trend includes personalized medicine. The more information we know about the genetic background and its influence on disease, the better we can define the pathways involved in disease. This should allow us not only to slow disease processes but also, in time, to prevent the onset of disease in the first place. There will be a clear move towards preventive medicine. You can only do this if you know what certain modifications or changes in the genome really mean. Other trends concern therapeutics for the CNS, which is an extremely complex organ. We are now starting to understand certain pathways, and companies like Memory Pharmaceuticals in the USA are working to improve cognitive function in diseased and even non-diseased states; developing an effective treatment for Alzheimer's disease remains one of the major challenges for the future.

How do you think the elucidation of the human genome sequence has affected the biotech industry?

In my opinion, the elucidation of the genome sequence can be compared with the establishment of the periodic table of elements in the 19th century because we now have a real basis for understanding disease at the molecular level. We can now start to unravel and understand different diseases in a systematic way. It gives us a real basis for the development of diagnostics, defining new pathways and identifying new drug targets. The benefits also relate to personalized medicine and predisposition to disease and ultimately to prevention of disease onset. If you think about it, medicine to date has been largely trial-and-error. You went to the doctor and he or she said: 'Okay, you probably have this or that disease, why don't you try this medicine and come back in a week?' If it worked, the doctor said 'Okay, carry on taking it', if it didn't work, 'Oh, try something else!' Therefore, one can compare today's standard of medicine with the field of chemistry before the periodic table of elements was established, an event which transformed alchemy into the science of chemistry we know today.

How do you think recent progress in areas such as pharmacogenomics, systems biology, immunotherapies and the like have impacted the biotech industry?

The progress in these areas has had a huge impact. We have several companies in our portfolio who work in these fields. For example, take immunotherapies and a company like Cytos Biotechnology, which was founded in 1995. The initial technologies that support the patient's own immune system to fight disease originated from the work of Dr. Renner and others at the Swiss Federal Institute of Technology in Zurich. We were the first venture capital company to invest in Cytos. They have since had a successful public listing and have been able to develop a broad pipeline of immunodrugs offering new treatment options across several disease areas. They have also secured two big agreements with Novartis and are quite successful. Another company is Agendia in The Netherlands who has developed an interesting prognostic test based on gene expression profiles in breast cancer. What the company and its collaborators demonstrated is that a certain expression profile in cancer can predict whether this cancer will metastasize in a short time or not. That provides the doctor with additional help to initiate the right therapy. I think these are extremely important areas of endeavor and some of them are still in an early development phase. Many big pharmaceutical companies are already prepared to implement pharmacogenomics. The FDA is starting to request the genetic background of patients involved in clinical trials. This will change the whole pharma industry because you will have drugs associated with genetic tests. Big pharma is not ready for this yet but this will eventually be the only way to take advantage of personalized medicine. Pharmacogenomics offers the possibility of selecting drug treatments that maximize therapeutic effects and minimize or even eliminate drug side effects. In time this will be the optimal approach for the individual patient in a population.

Increasingly, biotechnology companies are becoming bigger than pharmaceutical companies. How do you think this will affect their relationship in the future?

I think there are still only a few companies, such as Amgen, Genentech and Biogen, that can compete with the big pharma companies – most are still in some way largely dependent. The reality is that it takes more than 15 years to really be in that position – most biotech companies are much younger. What is particularly interesting is that until 1975 – before most of the first biotech companies had been established – there was a strong relationship between pharma companies and universities. The pharma industry was traditionally the acceptor of scientific discoveries, and developed these discoveries into products. However, with the advent of gene discovery and gene transfer technologies in the 1970s, big pharma was not flexible enough at the outset to create a sufficiently innovative environment for these new technologies. This is where biotech came in, as an acceptor and incubator for these novel technologies. Biotech develops technologies and products up to a certain stage and passes them on primarily to the pharma industry. This is a very central role in the link between science in academia and the pharma industry. I think with large biotech companies you also have a 'grey zone'; some might forward integrate and become fully independent; however, in general, the Genentech's and Amgen's mainly focus on biologicals, and big pharma has focused on small molecules so far. Biotech therefore has an established role and there is a strong dependence on big pharma, and vice versa.

If you personally were investing in an area of biotech or drug discovery, what would it be?

As a VC company, we're always looking for the one technology to invest in! As an investor, you try to have a very balanced portfolio. You look for balance in terms of maturity – that is, some early stage companies and some at a later stage. It is important not to put all your eggs in one basket, which means you should not exclusively focus on CNS or cancer or cardiovascular. The most important thing is that you believe in the company as well as in its technology or products, which must be developed, and which might take 5–10 years before they reach the market. This needs strong intellectual property protection and you have to have the right team driving it. The management team, the intellectual property protection, and the potential market are key. If you look at a company, you also need to look at the exit possibilities, which means looking for the preferred route for returning value to investors. Interesting areas are CNS research, like Alzheimer's, cancer and new approaches in immunology. However, it is difficult to classify by therapeutic area because each project has to be considered on its individual merit.

[Extract, first published in Drug Discovery Today Vol. 9, Nov. 2004, pages 909-912]

> ***"GLSV has developed into one of the most stable and valuable pillars of the Life Science VC scene in Europe. Their high quality is best demonstrated through the fact that they sucessfully maneouvred through the heavy storms of the past five years."***
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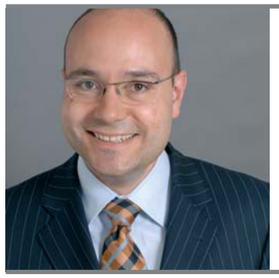
> Prof. Horst Domdey, CEO, Bio-M AG



Early-late companies: The new sweet spot for European biotech venture capitalists?

by Dr. Holger Reithinger, Partner, Global Life Science Ventures

In the complex and ever-shifting landscape of the biotechnology industry, the challenge for venture capitalists to target companies that promise attractive returns on investment is as great as ever. The traditional model, based on more than 20 years of VC experience in the US, is straightforward: invest early, obtain a major share of the company, obtain external validation of the concept through a partnership with a leading pharma company, build up a steep valuation curve, and exit by IPO. But with the large majority of biotech companies still unprofitable, a temperamental IPO market, cash-hungry clinical trials and a history of many money-losing investments, VCs have become wary of throwing money at concepts which are interesting from a scientific point of view but unproven. The current trend is for VCs to focus on late stage biotech companies where the risk is greatly reduced.[1] This trend is visible in recent successful fundraisings by funds focusing on rather later stages, such as BB Biotech, whose founding team surprisingly came from traditional early stage VCs.

And yet, investing at the end of the value creation chain is, in a sense, contradictory to the VC philosophy of assuming a significant but calculated risk in the anticipation of achieving high potential returns. An additional consequence of reduced interest in early stage companies is that fewer late stage companies are emerging. With large pools of venture capital chasing relatively few remaining late stage opportunities, these financing rounds have also become increasingly expensive, and at the same time often uninteresting as a result of companies' tendency to in-license late stage products with a questionable product profile or unknown history. The question then is: how can VCs realise the returns expected of them while keeping the risks under control?

Global Life Science Ventures (GLSV) sees the solution in targeting relatively young companies at a specific stage in their development and assuming a highly active role in the value creation process. The strategy is to enter at a point where a maximum impact can be effected while keeping cash burn to a minimum, and where it can be ascertained in a relatively short period of time whether the investment is delivering the expected results. This means being able clearly to formulate important risk reducing, technical milestones, with the money tranched against achievement of those results. About a year before a lead product is scheduled to enter phase I trials, a biotech company is still considered too early for many investors, but it is precisely at this point where there is a great potential for impact and a maximum upside.

Using the investment for company building, increasing the headcount and growing the internal structure might not always be the optimal use of resources, as it can lead to a sharp increase in the cash burn rate without adding significant value. In fact, as has been argued by Hal Broderson in his discussion of virtual biotechs[2], outsourcing to a network of contracted experts can take a company to critical decision-making points at a far lower cost than with the fully integrated model. The capital should best be used to invest in projects that create maximum value, and which can be evaluated within 12 months for their validity.

Another important aspect is the VCs' influence on the strategy of the company. In GLSV's model, the investors, together with the CEO, formulate a very focused strategy leading to a well-managed project rather than an operational business. For this model to be successful it ideally needs a specific type of CEO, typically not the general manager type of personality but rather a narrowly focused project leader with strong execution-oriented leadership, who can live and act in a virtual organization.

This approach does not in itself remove the inherent risk that a preclinical drug candidate will fail to meet clinical expectations. However, in addition to understanding the underlying science and complexity of the platform or technology, VCs can make a difference by providing an optimal strategy and financing scheme for the validation of such novel concepts. Due to the early stage of the investment, this approach also provides the possibility to capture a 25% to 30% share of the company at a particularly advantageous point in the value-creation curve, and direct the use of limited invested capital in an optimally efficient manner. In favorable cases, the result can be a rapid transition from an early stage to late stage company, with attractive exit opportunities. As was observed by Arthur Klausner[3] with respect to exiting via an IPO, it is often about providing public stock buyers, "with the types of companies/products that they desire while investing the smallest amount of money for the least amount of time." Two recent investments carried out by GLSV are examples of the investment model described above.

The first case is Vienna-based Fibrex Medical. The company was founded on the basis of a new mode of action in the inflammation process and the identification of a first compound, but was still considered much too early for nearly all investors. The lack of an experienced management team was another reason for many investors not to initiate any serious due diligence on the basic science. However, GLSV recognized early on the potential of the lead product candidate, for which most results had been generated at the University of Vienna. With a due diligence package, GLSV attracted an industry experienced CEO for this early venture and closed a significant financing round of US$10m together with Atlas Ventures and two smaller funds in early 2005.

The investment strategy at the time was to fund the final preclinical development programme and subsequent clinical phase I and IIa trials for the lead product candidate in reperfusion injury, an indication for which all previous product candidates had failed. In addition, non-dilutive funding was used to generate enough data in a second indication. The size of the company was kept at a ceiling of about seven people to keep the operational burn rate very low and maintain flexibility in the use of the funds. Within a time frame of less than one year, Fibrex transformed itself from an early stage venture to a later stage clinical product company, and not surprisingly it became attractive to the majority of funds looking for first clinical data. However, the existing investors are prepared to fund the company further until proof-of-concept in humans, which is an important factor in the game. With a second indication following closely behind and a potential third on the horizon, with an underlying technology based on a new mode of action, and with strong entrepreneurial management and a flexible structure, Fibrex has changed completely within just 12 months after financing.

The early-late concept is also illustrated in the financing of Neuraxo Biopharmaceuticals, a pre-clinical company that received more than EUR12m in September 2005, in a financing round led by GLSV and Biomed Invest. Neuraxo's area of expertise is nerve regeneration, an area of huge interest, and its first challenge is to test a new concept and compound in acute spinal cord injury (SCI), another indication where every past attempt has so far failed for various reasons. Based on excellent pre-clinical and proof-of-concept data, Neuraxo's lead candidate will be in the clinic less than nine months after financing, with the possibility of showing preliminary results to investors within a 15month time frame. Although the compound targets the niche indication acute SCI, GLSV sees the prospects as very encouraging, with the compound's orphan drug status providing further protection and the huge chronic SCI market on the horizon. Again, the company is led by an experienced management team not afraid to work for a small organization in a project management-like role. It cannot be excluded that they will need to look for a new job in a short time frame if the novel concept of nerve regeneration does not prove itself in humans. However, if it does work out as hoped, they will participate integrally in the sharp increase in value of the company.

These examples illustrate some of the ideas GLSV has had in order to cope with the early stage dilemma of the last years. Of course, an experienced VC cannot build a portfolio solely with companies like Fibrex and Neuraxo. Both companies will have to face the same cold wind of clinical development as any other biotech company, and later stage investors are looking for more balanced pipelines and more strongly financed companies. Even with the business model GLSV is pursuing, the firm continues to look for diversity. These companies are nonetheless a key strategic element in GLSV's portfolio.

GLSV's recent trade sale of the preclinical company GlycArt to Roche confirmed that there is an attractive market for small, early stage ventures, as long as the underlying IP position is solid and the concept promises a future competitive advantage. In fact, big pharma is showing increased interest in identifying promising drug candidates relatively early on in their development, as late stage deals become rarer. Without predicting a new trend in the industry, some international pharma companies have already directly approached VCs with the idea of obtaining access to their early stage portfolio companies. Maybe we will return to where the industry started: the novel concepts created in universities will be pursued commercially in small biotech companies financed by VCs, and the more regulated part of the development and later marketing will be done by pharma, as proposed decades ago by Jürgen Drews.[4] Eric Schmid, senior analyst at Cowen & Co, recently expressed the view that smaller companies with late stage products will be able to command a higher price to be acquired[5]. By translating early ventures very quickly and creatively into later stage branding, GLSV is building attractive assets for further VC investments or possible acquisitions, as well as IPOs.

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After the hype: The horizons for biotech

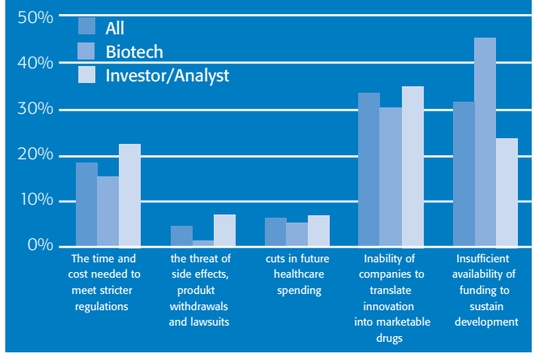
by Hanns-Peter Wiese, Partner, Global Life Science Ventures

Hanns-Peter Wiese at Global Life Science Ventures scans the future in his examination of likely funding scenarios

Early 2005, 'Critical I' released a report on the European biotech industry, which concluded that the financing gap was the industry's biggest barrier, forcing many companies to close down after three to five years. With European companies far more dependent on venture capital than their US counterparts, which have greater alternative sources of funding, the concern has been that small European biotech companies are not receiving the support needed in order to remain viable. A year later, this financing gap is still very much present, and no one reasonably expects it to just disappear. Yet, there are cautious signs of optimism.

At the Sachs Bloomberg conference in Zurich last October (2005), GLSV released the results of its Biotech Investment Barometer – a survey conducted among analysts, investors and biotech executives in Europe. 45% of biotech respondents mentioned insufficient funding as the greatest threat to the industry (see Figure 1). At the same time, close to half of respondents were more optimistic about the sector than a year earlier (see Figure 2). As Tilman Dumrese of Bank Sal. Oppenheim says, there is a very positive trend in the industry, reflected not just in the successes of giants like Genentech from the US, but also in smaller European listed companies like Intercell or Cytos, and the resulting favorable sentiment should make it easier to raise money in the future. This is supported by BioCentury's Bernstein Report on BioBusiness from 2nd January: a comparison between the US and Europe in the number of biotech IPOs in 2005, the amount raised and their aftermarket performance surprisingly showed Europe to be ahead on all counts. Mr Dumrese's view is also echoed by Geraldine O'Keefe of Fortis Bank, who notes that more generalist investors are taking an interest in the sector, recognising that value is added at each step along the way, as a company matures and products move through the pipeline.

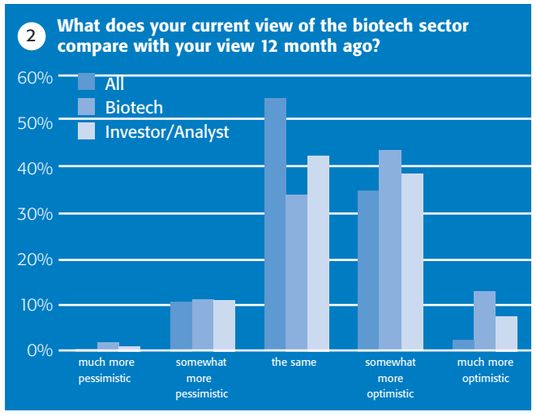
1 **What do you consider to be the greatest threat to the biotechnoloy sector?**



What is nonetheless clear is that the hype of a few years ago is long gone, and investors in biotech are much more conscious and calculating of risks than they used to be. European investors are even more risk averse than their US counterparts; for example, Denise Pollard-Knight of Nomura Phase4 Ventures favours biotech companies within 12 months from the clinic. The result has been a shift towards financing of later stage companies with products more likely to generate revenue in the foreseeable future, while companies based mainly on a technological platform will find funding very difficult. As one biotech executive also pointed out in GLSV's survey: "The investment required to ensure that a company reaches maturity is increasing. I therefore predict that fewer companies will get funded, but those that do will have access to greater funds."

Today, the onus is very much on the biotech company to prove its worth to potential investors. In a sector that has still not attained overall profitability, exciting scientific concepts are not enough to lure hardened investors. While an innovative technological platform remains a key ingredient, serious product candidates addressing large unmet medical needs or defined niche indications, as well as a competent management team – ideally with big pharma experience in clinical and business development, regulatory affairs and marketing – are elements that investors are expecting to see before they decide to part with their cash. The situation

2 **What does your current view of the biotech sector compare with your view 12 month ago?**



is frustrating for fledgling companies struggling to stay alive long enough to crank out product candidates, but it does at least ensure that the limited amount of capital available is used to support the drug candidates most likely to reach the market.

In this respect, a biotech company's success in raising capital, whether at inception or through various follow-on rounds of finance up to the IPO level, is more about the story they have to tell than any other factor. As Sam Fazeli of Piper Jaffray puts it, trying to evaluate whether an IPO window is currently open or shut is in some ways meaningless: you only find out whether it is open by trying, and the result is very much dependent on the company's specific situation.

This is not to say that timing is simply irrelevant for a promising company looking for new sources of funding. Depending on the phase of their funds, VCs may be focused on managing their current portfolio and have to wait to realize returns on previous investments before being able to make new ones. There is also no doubt that, hard objectivity notwithstanding, a particularly successful exit or product launch tends to make investors more positive about the sector as a whole, while a failed IPO, even for reasons linked more to the biotech company concerned than to external factors, can send a chill throughout the industry. But the wide swings of the pendulum seen in the past are likely to be more subdued in the future as the industry matures and attains a certain stability.

The increased interest of big pharma in establishing partnerships with and acquiring biotech companies in order to fill their pipelines is also providing an attractive alternative to IPOs, allowing companies to finance their development, while providing VCs with returns on investments that help fuel further investment cycles. A much-cited, award-winning example is of course last year's purchase of GlycArt by Roche for CHF235 million. The reverse situation, in which big pharma companies spin off entities that do not fit into their core portfolio, can also lead to the creation of viable new biotech companies with solid management expertise and a product pipeline. Examples include BioXell, a Milan-based company spun off from Roche to exploit a library of vitamin D analogues, and Nabriva, recently spun off from Sandoz, Vienna, to develop a new generation of antibiotics.

Local market conditions can also play a role in the availability of funding. For example, Geraldine O'Keeffe believes that funding has become tougher in the UK than elsewhere in Europe, perhaps because investors there have learned from experience to become more risk averse. In France, the shortage of VC investment in biotech companies became even more dramatic in the past year. On the other hand, there are definite glimmers of light on the European landscape. According to an article in Germany's Süddeutsche Zeitung on 2nd March, citing a report in Transcript magazine, VC investment in German biotech companies climbed 38% from 2004 to 2005, reaching a level of EUR 345 million that matched the boom years 2000/2001.

Given the trend amongst VCs to focus more on later-stage companies, what are the implications for ambitious start-ups high on innovation but without any products in the clinic? Will Europe's biotech pipeline eventually run dry? The picture is not as dire as that. First of all, as suggested by Ernst & Young's William Powlett Smith in a recent issue of the European Venture Capital Journal, universities are likely to hold onto their intellectual property and bring their new technologies further along in development before spinning off private companies. Increased collaborations between universities and biotech and pharma companies will also help more established companies with products in the clinic and on the market feed their pipeline with new, innovative technologies. And there is an increased awareness at European and national levels of the need for increased public funding to help launch innovative biotech companies. Switzerland affords an excellent paradigm for the role to be played by public funding in bringing start-ups to the point where they can attract VC interest, mentions Tilman Dumrese. In fact, publicly sponsored incubators throughout Europe are providing a breath of life for fresh start-ups. A good example is Geneva-based Eclosion, an incubator for new life science companies that combines state-funded infrastructure and management support with private sector investment. Furthermore, there remains a definite interest in seed funding by VCs, several of which have replenished their coffers by raising new funds recently. However, according to Sam Fazeli, for reasons of timing and availability of new funds for investment, it may simply be another two to three years before momentum in VC seed investments picks up.

A continuous stream of innovative new technologies in the life sciences is essential for the future of the European biotech industry and the development of new therapies for diseases. If innovation is not encouraged, life sciences in Europe will wither, while they flourish in the up-and-coming Asian markets. At the same time, from an investor's perspective, the biotech industry is subject to the same rules as any other industry; namely, investments have to be based on an acceptable risk profile that will lead on average to healthy returns. As previously noted, the European biotechnology industry is now in good shape, with the elements for success in place. Still relatively sheltered from the issues of patent expirations and generic copies that are posing difficulties for big pharma, the industry as a whole is expected to become profitable in the not-too-distant future. If European governments further facilitate the access of startups to seed funding, while allowing Europe to function more like a single capital market, innovative entrepreneurs should be able to raise the capital they need to successfully bring new drugs from the laboratory to the market, and the European biotech industry will thrive.

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Developments in the tax environment of private equity funds in the last decade – the German view

by Sonya Pauls, Partner, and Christian Schatz, Associate, SJ Berwin LLP, Munich

The developments in the German private equity fund market over the last decade have been significant. The increased role of German funds in the international PE market place is reflected in amounts raised by German private fund houses in 1996 (approx. EUR318 million) compared to the amounts raised only in the first three quarters of 2006 (approx. EUR1,025 billion, source: Bundesverband Deutscher Kapitalanlagegesellschaften e.V.).

It is therefore fair to say that Germany nowadays has to be considered an important player in the international private equity scene. However, Germany has not always been an easy country for German private equity funds or for German investors in non-German private equity funds. Several changes, in particular, in the administrative practice, caused significant uncertainties for fund managers and investors alike.

The following overview on these developments from a German tax perspective will focus on two aspects of the German tax environment, the environment for German private equity funds on the one hand and the environment for German investors investing in non-German private equity funds on the other.

The tax neutral fund

The main aim of all tax related structuring of private equity funds is to establish a fully tax neutral entity. First and foremost, the fund should be a fully tax transparent entity in order to avoid any tax leakage at the level of the fund itself. In addition, distributions should not be subject to taxation in the relevant jurisdiction (e.g. by a withholding taxation).

Why is the tax neutrality key?

A tax neutral fund structure principally provides for a fair risk allocation with regard to taxes. The fund does not need to consider the consequences of taxes caused at fund level with respect to its investors, e.g. potential double taxation issues in relation to income generated by the fund or any tax credit entitlements on withholding taxes that may apply to particular investors.

In addition, the investor can assess its tax exposure on the basis of its home jurisdiction and generally does not need to consider further jurisdictions when looking into tax consequences of an investment. A tax neutral fund structure should also not influence the investor's overall tax position, e.g. should not taint other income of the investor and should not adversely affect the tax status of the investor.

Most popular structure: Limited Partnership

The universally most commonly employed vehicle for private equity funds is the limited partnership. Most jurisdictions regard limited partnerships as being tax transparent and do not charge taxes on distributions of such funds.

Some jurisdictions offer special private equity vehicles, such as France with the fonds communs de placement à risqué – FCPR. These special type vehicles are generally employed where limited partnerships are treated as non-transparent. Consequently, special type vehicles such as the FCPR are generally also structured as fully tax neutral for both domestic and foreign investors.

German limited partnerships as fund vehicles – Ups and downs in the last decade

German funds are generally structured as limited partnerships (Kommanditgesellschaft). When structuring a German fund, tax transparency of the fund has been and remains the crucial issue.

Germany imposes trade tax on limited partnerships having a trade and business in Germany. This trade tax is structured as a municipal tax. The rates may therefore vary between the individual municipalities and can amount to up to 20%. Although Germany introduced tax exemptions in the last ten years which reduced the effective trade tax burden on capital gains and dividends significantly, fund managers as well as investors generally consider the achievement of a non-trading status for their relevant fund essential.

The late nineties & early 2000

Even until the late nineties, no official criteria on the qualification of private equity funds existed in Germany. This astonishing lack of statutory guidance led to the rise of many non-German fund structures.

However, several funds – especially those based in Munich – gradually succeeded in achieving binding tax rulings which helped them not only to understand what the applicable criteria were, but a ruling also protected their tax status as non-trading funds. It turned out that the Munich tax authorities had the most pragmatic approach to private equity fund structures in Germany as they had intensively considered private equity funds and their structures, whereas for many other tax authorities private equity remained a 'strange animal'.

With this administrative practice Munich built up a high international reputation as a private equity fund location. Non-German investors were able to invest in Munich based funds on the basis of a binding tax ruling. The number of German funds structured as German limited partnerships increased significantly during these years. A good example for this development is the second Global Life Science Ventures fund generation which also offered a German limited partnership vehicle to investors protected by such a tax ruling.

Soon thereafter, a general discussion on the tax treatment of private equity funds started in Germany mid2001. This discussion had a dramatic effect on the structuring of German private equity funds. As the criteria for non-trading were in discussion and no further tax rulings were issued, the confidence in Germany as a fund location collapsed. Until the end of the discussion at the end of 2003 only a very low number of funds were raised in Germany. At that time a number of fund managers decided to resort to offshore funds based e.g. in Jersey and Guernsey or even to relocate management.

The last years

Since the end of 2003 the situation has improved. On 16 December 2003 the German tax authorities issued a guidance letter on the tax treatment of private equity funds. This guidance letter, accompanied by further statements, summarizes the view of the German tax authorities on the 'trading/non-trading' criteria (e.g. holding period, leverage).

This guidance letter may generally be regarded as a positive development although some of the criteria are not in line with market practice and a number of open issues remain. This positive development is supported by an increasing number of tax authorities who are willing to issue tax rulings on private equity funds again.

Although the main concern relating to German funds has been alleviated to some degree, there are certainly still good and valid reasons to go abroad with private equity funds – especially for international fund teams.

Things may even become better in the next few years. The grand coalition forming the current German government has announced the introduction of private equity legislation which shall come into force in 2008. This legislation is intended to set a tax framework for private equity funds that should be attractive for all market participants, fund houses as well as investors.

German nationals investing in non-German Private Equity Funds: From the Foreign Investment Tax Act to the Investment Tax Act FIFA?

How is the football association related to private equity funds? This was a question a number of funds raised when German investors stated FIFA issues (German Foreign Investment Fund Act) in connection with their proposed investment into international funds. This German legislation introduced in the Seventies was regarded as a significant restriction on German investors for quite a long time.

The late nineties

In the late nineties, some uncertainty still existed whether FIFA was applicable in relation to non-German private equity funds. The law itself stated only general definitions on what a foreign fund is but did not provide for a clear scope of applicability with respect to non-German private equity funds. Moreover, the German tax authorities did not provide sufficient guidance in this regard for some time. The market reacted by structuring German parallel funds for German investors.

Early 2000

With the beginning of the new millenium a new age for German investors into non-German private equity funds may be said to have begun. The German financial supervisory authorities started to issue non-binding guidance letters stating the criterion of entrepreneurial influence (e.g. majority shareholdings, board seats) as the way out of FIFA. Provided a fund can sufficiently prove its entrepreneurial influence on portfolio companies under these guidance letters, FIFA is not any longer an issue for German investors under these guidance letters. According to our experience, the German tax authorities also follow this view.

Recent years

In 2003, FIFA was replaced by a new investment legislation that was comprised of the Investment Act (Investmentgesetz) and the Investment Tax Act (Investmentsteuergesetz). During the legislation process it was clearly stated that private equity funds shall not fall under this new investment legislation, although there was no explicit exemption incorporated in this legislation. The German tax and financial supervisory authorities clarified the situation by issuing guidance letters in 2005 according to which the new investment legislation would not be applied in relation to typical private equity funds structured as foreign limited partnerships. German investors should therefore no longer be advised to request German parallel vehicles and should be able to invest directly in foreign private equity funds.

Further development

It is expected that the private equity legislation which is anticipated to come into force in 2008 will further improve the situation and provide the much needed legal certainty in the structuring and taxation of private equity funds. Private equity will hopefully, at last, be recognized as a valuable asset class by the German legislator, as already recognised in other jurisdictions. Such a development would certainly further facilitate the growth of the German private equity scene and would also have a positive effect on Germany as a whole.

It's people business

by Jean Deléage, Ph.D., Founding Partner & Director of Alta Partners, San Francisco

Dr. Deléage began his venture capital career in 1971 in Paris, France, with Sofinnova and started its very successful American subsidiary, Sofinnova Inc. in 1976 in San Francisco. He co-founded Alta Partners in 1996. He was an early investor in many of the leading companies in the field today, including Genentech, Chiron, and Cephalon.

Alta Partners is a San Francisco based venture capital firm, specializing in life sciences. Over the past decade, Alta Partners has raised seven funds, and currently manages nearly $2 billion in capital. From early on in its history, Alta Partners developed a co-investment model by finding like-minded fund managers around the world. As international investors in a truly international industry we depend on competent syndicate partners across the world. Easy to wish for but not so easy to find. NonUS investors usually have problems in understanding the FDA and the drug approval process in the US. Global Life Science Ventures is one of the few exceptions. The principals have outstanding international experience, both scientific and industry, that gives them the insight required to understand an investment thesis.

The selection of the right syndicate partners has become more crucial over time as the complexity of the technology has grown and the requirements of the regulators increased. This has resulted in the companies requiring more support, both financial and managerial. Portfolio companies that take their products into clinical trials need more money over a longer time and are therefore more dependent than ever on the financial markets to support them. Even as public companies, there is an increasing tendency for them to go back to their original VC investors, who understand them well, for continued support and financing. As a result, VC investors may work alongside private and public equity investors to take a more active role in financing public biotech companies.

For the syndicate partners this will mean that the working relationship with other co-investors may well last longer than originally anticipated, requiring more investment of both money and time into their joint portfolio companies.

While everybody would like to be the lead Investor in a deal, over the long term and as more money is invested in an individual investment, the relationship between the different investors may need to change from being rather competitive towards working together to ensure success driven by team work. This process will require the syndicate partners to work together as equals with high levels of confidence between the individuals involved, as well as having a similar mind set and complementary analytical skills.

Finally, the more input required from the investors and the necessity to delay an exit from the investment in order to ensure success, the more important it is to get on well with all the other syndicate partners all of the time. Struggling or failing investments may result in considerable stress at a board level within the company itself, which may be reflected within the board meetings of the various co-investors. If you have many VCs on the board of a company, each representing different opinions and objectives, you may end up with many discussions and few decisions. It is therefore essential to have that people-to-people chemistry and trust in each other's abilities to ensure that egos do not prevail where a calm and measured response is required, allowing a sensible and rapid decision making process to take place.

All of these parameters are fulfilled in our ongoing relationship with GLSV.

Recognizing long-term potential

by Dr. Wolfgang A. Renner, Chief Executive Officer, Cytos Biotechnology

Dr. Renner has headed Cytos Biotechnology since he co-founded the company in 1995, and has been Chief Executive Officer since the company's incorporation. Dr. Renner has received many distinctions for his work, including the first prize of the "Swiss Economic Award" 1999, the "Entrepreneur of the Year 2000 Award", the third prize of the "European BioTechnica Award of Excellence in Biotech Business" 2004, and the "Swiss Equity Award" 2006. He obtained his PhD in 1995 from the Swiss Federal Institute of Technology (ETH) in Zurich.

When I co-founded Cytos in 1995, I was finishing my PhD at the ETH in Zurich and saw the opportunity to capitalize on a technology developed as part of my thesis. Based on this technology we developed "generic" versions of the first biotech products that reached the market in the early 1980s. This project was funded by a third party, which allowed us to start our business and hire the first employees. It was clear, however, that this project would finance the company only two or three years, so we had to come up with new ideas that could form the basis for long-term growth.

We embarked on the development of two technology platforms. The first one was given the name DELphi™. It enables the identification of new drug targets and candidates using a viral expression screening and production system. At the time, genomics was a field receiving a tremendous amount of attention, in large part due to the ongoing human genome sequencing projects. There was a real need to develop tools to make sense of all the new information emerging and use it to develop therapeutics against newly-identified disease targets.

It was this technology that was of great interest to the venture capital community. The Novartis Venture Fund was the first investor in our company. Soon thereafter, Global Life Science Ventures stepped in and led the first investment round, which brought in CHF 11 million. Although we were far from having any products on the market, they saw the potential of our technology and expressed confidence in the management team that we had built up.

Peter Reinisch became a board member as part of the financing round led by GLSV. While GLSV's financial support was obviously of great importance, Dr. Reinisch also provided significant guidance at the board level as we faced key decisions during the company's development. What was crucial to us was GLSV's understanding of the business and the need for patience, focusing on a long-term, 10-year horizon, and ensuring that the board members and the executive team cooperated over all these years.

Interestingly, the technology on which our company was originally based and which attracted investors such as GLSV is not the same as the one at the heart of our extensive pipeline today. Our broadly applicable Immunodrugs™ platform, also developed in-house, has since sprouted a large number of distinct development programs targeting very different diseases and conditions. The vaccine technology underlying the platform permits the generation of a strong immune response against a wide variety of antigens, even against those which would not normally elicit a response. These include both foreign molecules and molecules produced by the body and involved in disease processes. The Immunodrug™ product candidates in our portfolio include potential treatments for nicotine addiction, allergies, inflammation, hypertension, obesity, Alzheimer's, cancer, and several other conditions.

Even a few years ago, vaccines were on few people's investment priority lists. Nonetheless, our investors recognized the very real potential of the Immunodrug™ platform to spawn a whole pipeline of products, and they supported the decision to shift our resources towards its development. The wisdom of this strategy has become increasingly apparent with our successful IPO in 2002 and a steady rise in our stock price in the past two years.

The biotechnology business requires patient and supportive investors with a long-term commitment. But as we have shown, value generation occurs along the way, and patience is often rewarded.

Interview with Dr. Werner Lanthaler Chief Financial Officer, Intercell AG

Previously, Dr. Lanthaler was Head of Marketing and Communications of the Federation of Austrian Industry and, prior to that, a senior management consultant at McKinsey & Company International. His academic accomplishments include a doctorate from the Vienna University of Economics and Business Administration and postgraduate degrees from Harvard University. He has considerable experience working in the labor and capital markets of the United States, South America and Europe. Dr. Werner Lanthaler is also the author and co-author of a wide range of books and articles. At Intercell, his responsibilities include work in the departments of Finance, Administration, Human Resources, Investor Relations, and Marketing & Sales.

What was the starting position of Intercell at the time of the financing round prior to the Initial Public Offering (IPO)?

We were looking for new external investors who were ready to shoulder the risk of investing in an early-stage bio-technical enterprise. We were looking for investors who shared our belief in a medium-term strategy for developing into the most innovative producer of vaccinates.

What strategy did Intercell follow in that financing round?

We wanted to bring sufficient capital into the company so that we would not come under pressure. We wanted to be able to finance – after the private round – in the "Public Window", without being forced to do so.

The capital from the financing round was to be sufficient for positioning our antigens and adjuvants in a strategically optimal way.

What were the greatest challenges in that financing round?

The greatest challenges were to define the capital requirement for the planned growth step correctly. At the same time we wanted to create a suitable investor structure. Quite often, it is not easy to bring founders, initial shareholders and new investors together.

What target groups (European, international or others) were the main focus?

Our outlook was never regionally directed to countries or continents. Financing bio-technology will only work globally. It is important to bring the right investors on board and not just the ones, who only live close by.

Were investment banks and fund raisers involved in the preparations?

No, a financing round is an important growth step, not only financially but also culturally, which should be realized mainly inside the enterprise. Such a way of preparing and disciplining is important for the company, only thus will it be able to appropriately expand its structure and way of thinking.

At the time of the financing round, was an Exit or IPO already envisaged for 2005, if not, with what Exit perspective were investors approached?

No, an Exit 2005 was not promised. The perspective, though, was always existent for the investors – but without a time horizon.

What was the time schedule at the time of the financing round?

10 months.

When did participation by GLSV become feasible?

About 6 months before closing.

Chart development Intercell since IPO in EUR

What points of contact with GLSV were there, prior to the financing round?

GLSV is among the qualified investors in the field of vaccinates and supports mainly early-stage enterprises and spin-offs. Intercell at that time fitted well into their portfolio.

What were your own reasons, which lead to a participation of GLSV?

We have always been in command of a good and well balanced risk profile. Our vaccinate against Japanese encephalitis – with its clear development strategy and its advanced development status – represented a "near-term, low risk" product with a foreseeable time horizon. Our hepatitis C vaccinate provides the "upside potential" in our pipeline, that extra element of imagination, which an investor looks for.

What are the most substantial strengths which you identified in GLSV?

GLSV performed an excellent Due Diligence, from which everybody profited.

Which phases of the negotiations do you remember as the most critical?

We recall the negotiations concerning the first term sheet as a critical item.

And what were the dominant questions?

As is normal for bio-technological enterprises – valuation.

How were those bottlenecks overcome?

We always aimed for a structured dialogue with the VCs and thereby found solutions. Towards the end of the negotiations GLSV proved to be a good mediator between the different interests.

How did you enjoy the closing? How and where did you celebrate?

Among friends at a super celebration in Burgenland (Austria), with good claret and plenty of joyful anticipation of Intercell's growth.

How did co-operation with GLSV develop after closing?

Co-operation with GLSV after closing was also without any problems, constructive and very good on the whole.

Beyond financial aspects, what contribution can VC provide in co-operating with an enterprise?

Contacts, contacts, contacts, good questions and – last but not least – examples of how to learn from others.

Apart from GLSV, what particularly positive/negative experience did you gain from co-operation with VCs?

Interaction between US-VC-culture and EU-VC-culture was definitely very formative for Intercell. It is not enough to be the best in Europe. A bio-technological enterprise must be built with the aim of being a "global player."

What tips would you give to private enterprises on how to deal with the VC industry?

Never get nervous when everything takes longer than you would like it.

What changes do you think are urgently necessary in the VC industry?

More large funds in Europe, able to accompany an enterprise for a long time

Smart money

by Robert L. Bratzler, Ph.D., President and Chief Executive Officer, Coley Pharmaceutical Group

Dr. Bratzler has been President, Chief Executive Officer and a director of Coley Pharmaceutical Group since June 1998. Dr. Bratzler received his B.S. degree from the University of Michigan and his Ph.D. in chemical engineering from the Massachusetts Institute of Technology.

Coley Pharmaceutical Group is a biopharmaceutical company focused on discovering and developing a novel class of drugs, known as TLR Therapeutics™, for treating cancers, infectious diseases and respiratory disorders. Coley's proprietary TLR Therapeutics act by stimulating or modifying a specific class of targets, called Toll-like receptors (TLRs). Coley's clinical candidates target one such Toll-like Receptor, TLR-9, which is found in and on important immune system cells which, in turn, direct the immune system to fight disease. The Company currently has four drug candidates in clinical trials, including the lead product candidate, PF-3512676 (formerly known as ProMune) for cancers, which was licensed to Pfizer Inc. and is currently in Phase III clinical trials.

Coley was founded in 1997. It is an international company with head office operations in Wellesley, Massachusetts, USA, and research and development laboratories in Langenfeld, Germany and Ottawa, Canada. Coley began trading on NASDAQ in August 2005. The initial public offering of 6,900,000 shares was placed at $16.00 per share. Concurrent with the initial public offering, Coley also placed 625,000 shares with Pfizer at the initial public offering price. As a result, Coley raised a total of $110 million at the IPO. Until the IPO, the Company had raised $145 million in venture capital in a series of fundings in 1999, 2000, 2003 and 2004 in addition to $100 million revenue in license fees and milestones from collaborative partners. Global Life Sciences Ventures joined our shareholder register in the 2000 investment round and has remained a loyal supporter ever since participating in each subsequent round.

2000 was a boom year for Biotech investment with the NASDAQ Biotech Index reaching its all-time high of 1600 in early 2000. However the pressure on the sector increased during the year and the Index closed at 1300 towards the end of the year. Against this market, Coley was able to complete a private financing round of $60 million in November 2000. The new money raised for the company came from the existing supportive investors and included additional high quality investors such as Global Life Science Ventures, DWS, DVG, Commerzbank Private Equity, Robertson Stephens' Bayview 2000.

At that time, both new and existing investors had shown tremendous enthusiasm for Coley's rapid development over the past year. Since the last financing in 1999, Coley had expanded its management team, initiated four additional human clinical trials, demonstrated its products to be well tolerated, and had obtained promising immunologic data supporting CpG's ability to stimulate strong immune responses.

Successfully raising $60 million at still favorable conditions shortly before the global downturn obviously put Coley in a healthy position and allowed it to continue and expand internal research and development programs for both the proprietary and partnered products. Unlike many of its peers, Coley could avoid restrictions to its advanced development programs and continued the business and clinical development plan agreed with its investors.

Without the continuing support of leading investors such as Global Life Science Ventures, Coley might have had to scale down its operations and might accordingly have missed the key milestones that the investment community and its collaborative partners were anticipating.

In 2003, however, the timing for the company was not so good and the existing investors had to accept a round of finance at a lower valuation. Despite the ongoing progress and the fact that the company had met major milestones Coley was facing the most difficult financing round in its history, as biotech was entirely out of favor and most VC Biotech portfolios were underwater. At this point in time, it was still hard to imagine that markets would allow us to become a public listed company in 2005, following our last private round in September 2004.

Being supported by the investment community in difficult times has put the company in a strong position to hit major milestones. As a result, the company has been able to report positive results from the Phase II clinical studies for ProMune (now PF-3512676), and we were ready to move to pivotal Phase III trials in first line non-small cell lung cancer, and enter multiple collaborations with leading pharmaceutical and biotech companies, including Sanofi-Aventis, Chiron and many others.

Looking back at our funding history, Coley was very fortunate to have met with so much professional support and understanding from the existing investors and shareholders. Smart money – from smart investors who understand what is required and are prepared to back their understanding.

Witnessing the dawn of biotechnology – an attractive investment potential

by Dr. Stephen J. McCormack, Partner, and Dr. Kuno Jung, Principal, Global Life Science Ventures

The demand for new therapeutics, diagnostics and medical devices to fight diseases is as great as it has ever been. Despite the significant advances that have been made, it has been estimated that of the 30,000 diseases known today, still only a third can be treated effectively. Innovative, proprietary products that meet such needs, combined with the implementation of personalized medicine, will allow for attractive margins in spite of cost containment pressures. The biotechnology industry will benefit strongly from this steady demand and play a crucial role in contributing to improvements in healthcare. In the following, the major market drivers for the biotechnology industry are explored.

Ever-increasing pull from a growing and aging population

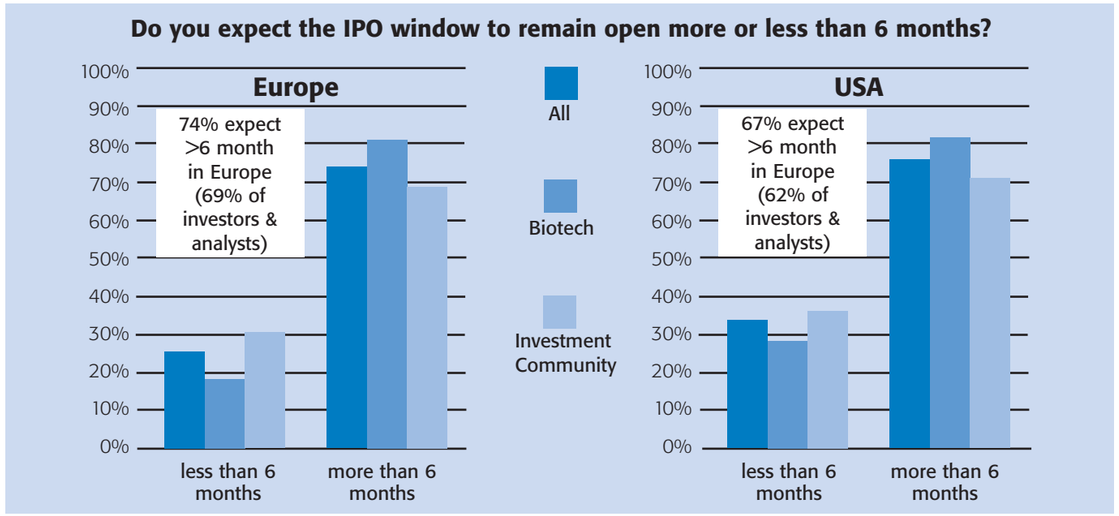
Growing and aging populations are significant drivers for the increase in demand for new and effective treatments. Worldwide, the number of people over the age of 60 is projected to double in the next 20 years. According to the UN, life expectancy in the developed countries has reached 68 years for males and 71 years for females as treatment options steadily improve. With this increasing longevity comes added pressure on the health authorities to reimburse diagnostics and therapeutics for age-related diseases. Examples include macular degeneration, expected to affect 1 in 3 adults over the age of 60, and neurodegenerative diseases such as Parkinson's and Alzheimer's, which are known to occur most frequently in the elderly.

Other important diseases affecting aging populations, including disorders of the central nervous system, autoimmune diseases, allergies, cardiovascular, kidney and liver disorders, and infectious diseases, are still without effective treatments for the the majority of sufferers. In addition, diseases of the elderly are often multi-faceted – it has been reported that half of the population over 65 suffers from at least three chronic diseases concurrently (i.e. multimorbidity).

Emergence of new diseases – and the need for new treatments

Infectious diseases are another major health concern, and the threat posed is amplified by the potential of infectious agents that were previously confined to specific regions to spread through international travel. Newly identified infectious diseases such as HIV, BSE, SARS and avian flu continue to emerge and can spread globally at an alarming rate. The need for new, effective vaccines is paramount.

While so far the main focus of vaccines was on the prevention of infectious diseases, progress is being made in novel approaches to prevent or treat certain types of cancer or diseases like Alzheimer's. For example, the Hepatitis B vaccine is being introduced to prevent HBV infection and the corresponding liver cancer, and the recent approval of a vaccine to protect against HPV



has the potential to save many thousands of women from dying of cervical cancer. Several vaccines for Alzheimer's disease are already in clinical trials.

With a better understanding of the molecular mechanisms of diseases and advances in individual genetic testing, it is also becoming possible both to identify individual medical risks and to provide personalized treatments. Currently marketed drugs are only fully effective in a certain percentage of patients; many other patients suffer from side effects. In the US alone it is estimated that the annual cost of drug-related morbidity and mortality exceeds $100 billion.

Medicine will, in the future, not only work towards better therapies to treat symptoms, but increasingly focus on means to prevent or delay the onset of disease. Along with vaccination, new prophylactic measures will be the mark of a more effective health care system.

The pharmaceutical industry requires novel proprietary products to replenish its pipelines. A number of key patents covering products with current combined revenues of more than $30 billion will expire in the next two years. This highlights a problem that is a major concern for multinational pharmaceutical companies. Companies facing patent expiries relating to more than 20% of their current revenues include Wyeth, GlaxoSmithKline, Merck & Co., Pfizer and Roche. As internal research programms have been unable to replenish the diminishing number of patented blockbusters in the product portfolio, business development strategies are increasingly aimed at identifying acquisitions to replenish pipelines. The share of biotechnology products approved in the USA increased from around 20% in 1999 to about 50% in 2004, and the percentage continues to increase. The strategy increasingly pursued by big pharma is to enter into collaborative R&D alliances and, in selected cases, to acquire small biotech companies with products mostly in advanced stages but increasingly also in earlier stages, of development.

Overall maturation of the biotech industry

The last 30 years has seen the creation of a biotech industry comprising more than 4,000 companies worldwide, including a number of highly profitable public companies mainly listed on the NASDAQ, such as Amgen, Genentech and Biogen Idec. In Europe as well, there are an increasing number of successful companies with products on the market listed on various stock exchanges such as Actelion (SWX), Qiagen and Medigene (TecDAX), Bavarian Nordic (CSE) and Acambis (LSE), and companies such as UCB, which have emerged as a result of an aggressive acquisition strategy and are listed on more than one exchange.

Following the global market downturn in 2001 and 2002, there was an industry-wide restructuring imposed by the market and investor opinion which favored later-stage products and resulted in a leaner and much more focused industry with a more mature business approach. Many companies have sharpened their strategy and focused their development programms on fewer and more targeted products, with the aim of getting them into clinical trials in the shortest time possible. The focus is now clearly on commercialization of products and product pipelines, rather than advancing the knowledge base and intellectual property positions. As a consequence, attractive opportunities exist for investing in the development of novel proprietary products and technologies which have already had considerable R&D resources applied to them in research labs since the late 1990s. Although their commerzialisation has suffered from delays, a substantial number of these product programmes are expected to move through the clinical stage and enter the market in the coming years.

There has also been a move towards increased consolidation within the sector as pharmaceutical players acquire biotech and biopharma companies to improve their competitive position and broaden their pipelines and portfolios. Examples from the past year include Merck's purchase of Serono, AstraZeneca's takeover of Cambridge Antibody, and UCB's recently approved offer for Schwarz Pharma.

Attractive investment potential in Europe

Europe's biotech industry continues to lag behind the United States in terms of maturity and commercialization, although the quantity and quality of life science research in Europe are comparable to that of the United States, as measured for example by the number of scientific publications and citations. As more funding from governments and private sources is devoted to biotechnology across Europe, the gap between Europe and the US may diminish.

An increasing number of serial entrepreneurs are starting to appear in the life science industry across Europe. Also, as more companies combine, there are an increasing number of managers from the pharmaceutical industry pursuing careers in smaller, private companies in which they can acquire a shareholding. The successes of this increasing band of senior managers will encourage others to join emerging companies, bringing much needed commercial acumen.

Across Europe there are many renowned research centers of excellence requiring support to identify and transfer clinical know-how and product development from the academic to the commercial arena. This creates opportunities that have not been pursued actively until now. Links between academia, industry and the financial community are beginning to be viewed with less suspicion following the growing success of such organizations across Europe. The result is a steady improvement in the cooperation needed to create successful businesses out of academic excellence. In addition, universities and other publicly-funded institutions are showing an increased awareness of their public duty to stimulate the commercialization of their research. As a result, they are actively seeking ways to encourage the creation of start-ups aimed at developing the technologies invented in their laboratories, and to support the resulting product candidates.

In addition to these emerging companies, there are an increasing number of well-positioned and well-funded spin-offs from European pharma companies with products in late pre-clinical or advanced clinical trials, or even on the market. These include Speedel (Novartis), Actelion (Roche), Basilea (Roche), Nitec Pharma (Merck Darmstadt), Elbion (Degussa), Lifecycle Pharma (Lundbeck) and Nabriva (Sandoz).

The time is now ripe to benefit from the learning curve

In order for the European biotech industry to become more competitive worldwide, the focus on commercialization of products and technologies is essential. Given the significant push from industry and the pull for new products and technologies, there is an unrecognized opportunity for investors in the life sciences arena. Adequate funding in well-managed companies can accelerate product development and yield superior returns for investors.

The life sciences have evolved dramatically with the increased understanding of the molecular basis of diseases and the ability to manipulate genetic material. This has made it possible to invent, develop and introduce to the market a new class of therapeutics: recombinant biologicals. Some of these products are already generating billions of dollars in sales. This has created a significant push and opportunity for the further commercialization of these new products and technologies.

Successful products of the future will result from technologies that can quickly identify and personalize therapeutics based upon target specificity, with minimal side effects. The deciphering of the human genome is already contributing increasingly to the identification of suitable molecular targets and corresponding drug products.

A wealth of opportunities

Looking beyond biologicals and pharmaceuticals, there will be further innovations in the development and commercialization of medical devices and the adoption of convergent technologies. We will see other biotechnology applications thrive outside of the medical field with the emergence of the so-called "green" and "white" biotechnologies and the invention and application of new bio-materials. To exploit these many opportunities will require funding from sophisticated investors, well positioned to screen for and select superior investment proposals, and who are able to recognize the potential of a proposal before it becomes common knowledge.

In 2005, Europe had more biotech IPOs than the US, raised more funds and showed better post-IPO performance

2005 Biotech IPO Performance

	Number of IPOs	Raised ($million)	Post-IPO ($million)	12/30 Mcap ($million)	Change
US	17	$793.8	$4,452.4	$4,019.9	-10%
Europe	22	$891.4	$4,625.7	$4,019.9	14%

Source: BioCentury, The Bernstein Report on BioBusiness (2nd. January 2006)

Dr. Hans A. Küpper, Dipl.-Chem., Partner

Dr. Küpper has a total of 36 years' experience in biotechnology and venture capital, with 19 years in the life science industry, where he has been involved in activities from research and R&D management to technology assessment and acquisition. In February 1999, Dr. Küpper joined us as a Managing Director of GLS I's advisory company, based in Munich, Germany. Since that time he has been advising GLS I and managing GLSV II in all aspects of investments. Dr. Küpper is a board member, or attendee, with a number of portfolio companies, one of which is now listed on the Vienna Stock Exchange and one at NASDAQ.

He received his PhD from the University of Heidelberg in 1974 and spent two years as a postdoctoral fellow at MIT in Boston with Nobel Laureate Prof. Khorana. After another four years at Heidelberg University he joined Biogen in Geneva, one of the pioneering biotech companies, in 1980. There he held various R&D and management positions with increasing responsibilities and was Assistant Research Director from 1982 to 1985. In 1985, he joined Behringwerke AG to build up and head their Molecular Biology department.

Later he became head of R&D and a member of the board of their Immunology/Oncology business unit. His major research focus was on gene regulation and vaccines. Since 1991 he has been increasingly involved in deal negotiations and various aspects of company restructuring, such as acquisitions, joint ventures and spin-offs. He headed the spin-offs of their vaccine unit (now Novartis Behring) and diagnostics business (now Dade Behring).

Dr. Küpper, born in 1944, is author of 50 scientific publications and 13 patent applications. He has served as a consultant for the pharmaceutical industry and the European Commission.

Dr. Peter H. Reinisch, Dipl.-Ing., Partner

Dr. Reinisch has over 14 years' experience in the life science industry that included senior management positions in the Corange group (Boehringer Mannheim and DePuy) for 11 years. He was responsible for the strategic coordination and business development of the diagnostics business worldwide. From 1994 to 1996 he advised Boehringer Mannheim and Corange, including from 1995 on the setting up of GLS I. He has acted as a board member, or attendee, with a number of portfolio companies, five of which are already public – four by IPO, one by reverse takeover. In addition, another company recently exited through a trade sale. He has been advising GLS I and GLSV II since the beginning in 1996 and is Managing Director of the advisory company based in Zug/Switzerland. Prior to Corange/Boehringer Mannheim, Dr. Reinisch held positions of increasing responsibility with Brown Boveri, the Institute for Automation, the Denner Group and McKinsey and Co., where he concentrated on high technology industries. He became CEO of Pfister, one of his clients.

Dr. Reinisch, born in 1940, first studied mechanical engineering, then graduated summa cum laude with a doctorate in Business Administration ("Betriebswissenschaften") from the Technical University of Vienna.

Hanns-Peter Wiese, Dipl.-Kfm., Partner

Mr. Wiese has 17 years' experience in private equity and venture capital, which he gained investing in Europe and the United States. His exposure to early stage investing in the life sciences extends back to 1996 when he advised HypoVereinsbank as co-sponsor on the setting-up of GLS I. Since then he has been a Managing Director of the office in Munich, Germany, advising GLS I and managing GLSV II in all aspects of investments. Mr. Wiese's responsibilities include the partnerships' financial, legal and administrative issues, which comprise the monitoring of all portfolio companies.

From 1993, he was a Director of Corporate Finance with HypoVereinsbank in Munich and Director of their associated venture capital fund, managed by Euro Synergies S.A. in Paris. Aside from its turnaround, accomplished in a new small team, he arranged equity financings for mature businesses as well as MBOs/MBIs of mid-sized companies across various industries throughout Europe. Apart from sharing general management functions, he held sole responsibility for the German-speaking countries. Several of the investments completed were listed on European stock exchanges.

Before that, in 1989 Mr. Wiese entered into venture capital, which in Germany in the late 80s was still in its infancy. He was an Investment Controller with 3i Investors in Industry plc, initially in the UK, then Investment Manager in their Frankfurt office. There he worked on a number of leveraged transactions, providing growth & development finance as well as MBO/MBI solutions to the typical German Mittelstand.

Mr. Wiese, born in 1959, has a master's degree in Business Administration (Dipl. Kfm.) from the University of Hamburg.

Dr. Holger N. Reithinger, Dipl.-Biol., Partner

Dr. Reithinger has over eleven years' experience in the life science industry including nine years in venture capital in the biotech and medical device sector. He joined GLSV in October 2004 as Principal. He came from 3i, where he was a Director at their German healthcare practice and a member of their European Sector Investment Committee. He started his venture capital career as an Investment Manager at Technologieholding VC GmbH in 1997, which at the time was a leading German venture capital firm for early-stage technology investments. Technologieholding was acquired by 3i in February 2000. Dr. Reithinger has served on the boards of several early-stage life science companies including Epigenomics AG (IPO 2004), MBT AG (assets sold to Medigene AG), 4SC AG (IPO 2005) and others. Before becoming a venture capitalist, he worked in industry as a product development manager at Biometra/Whatman Plc, where he was responsible for the identification, development and marketing of new molecular biology products.

Dr. Reithinger, born in 1966, holds a PhD in Biochemistry, which he obtained studying protein design in the department of Prof. Hartmut Michel (Nobel Laureate 1988) at the University of Frankfurt/Max-Planck-Institute of Biophysics. As an undergraduate, he studied Molecular Biology/Microbial Biology and Biochemistry at the universities of Heidelberg and Munich.

Dr. Stephen J. McCormack, Partner

Dr. McCormack has more than 20 years' experience in the life science industry and academia. He came to GLSV in May 2006 from NeuroSystec Corporation, a California-based biotech company focusing on the use of implantable devices to deliver novel drug compounds for the treatment of neurological disorders. He

co-founded NeuroSystec in 2003 and acquired the technology platforms from a European pharma and a US biotechnology company. He served as President and CEO and left the company well positioned for a strategic acquisition in the coming year. Previously, Dr. McCormack co-founded AlleCure Corporation in 2000 to develop therapeutic vaccines and small molecules to treat allergies, asthma and inflammatory diseases. As their President and CEO, he attracted top talent for the company's management team, pulled together a highly-regarded international scientific advisory board, and brought a vaccine through phase II trials in numerous countries. AlleCure was merged with two sister companies to form MannKind Corp. and was taken public on NASDAQ in 2004. Before founding AlleCure, he held various senior positions in industry and academia in the areas of management, business development and research.

Dr. McCormack, born in 1964, received his Ph.D. in Biomolecular Science and Engineering from the University of California, Santa Barbara, and attended the Advanced Management Program of Harvard Business School.

Dr. Kuno Jung, MSc, Principal

Dr. Jung brings with him ten years' experience in the life science and venture capital industry. He joined GLSV in April 2006 from Timaq medical imaging Inc., a globally-active clinical imaging contract research organization from Switzerland, which he served as CEO from its inception in 2003. There he was able to enter into service contracts with leading pharmaceutical companies and was awarded the Swiss CTI start-up prize in 2004. Prior to this he co-founded Aravis Ventures in 2001, a life science-specific venture capital fund, where he served as investment manager specializing in early-stage biotech investments located primarily in Europe. Since 1999 he has advised a number of biotech companies on strategic alignment and business development, and has also served as project manager at LUNAMed AG, a Zurich-based cancer therapy research company.

Dr. Jung, born in 1969, holds a PhD in Natural Sciences, which he obtained in 1999 from the Swiss Federal Institute of Technology (ETH) Zürich. He obtained an MSc in food science from the ETH Zürich in 1996.

Rainer J. Hoegg, MBA, Dipl.-Biol., Associate

Mr. Hoegg has four years' experience in the biotech industry and finance. With degrees both in science and business administration, his background includes hands-on experience as an assistant to the CEO of a former biotech start-up. Building on a professional relationship with GLSV since 2003, he joined the team in 2004 as Group Controller. His responsibilities currently include the monitoring of the performance of portfolio companies, the preparation of quarterly and annual reports to investors, as well as internal controlling and administration. He is also involved in the management of public shareholdings and provides analyst support to the investment team.

Born in 1973, Mr. Hoegg obtained an MSc in Biology from the University of Constance in 2000. Aiming for a career at the intersection of biotechnology and finance, he subsequently studied business administration with a focus on finance and accounting at the Technical University of Munich and at Virginia Polytechnic Institute and State University. His MBA thesis covered the valuation of biotechnology ventures and included the analysis and valuation of an established private biotech company from the Munich area.

global lifescience ventures

Agendia B. V.

is a phamacogenomics and diagnostics company that uses microarray-based gene expression profiling to predict disease progression or treatment outcome in various cancer indications. Their lead product is a prognostic breast cancer test differentiating primary tumour patients who are at risk to develop metastasis. ***www.agendia.com***

Coley Pharmaceutical Group, Inc.

discovers and develops novel drugs based on CpG oligonucleotides (CpG oligos or CpG molecules). These drug candidates activate the innate and adaptive immune systems to fight diseases, including cancer, infectious diseases, asthma and allergy. ***www.coleypharma.com***

CombinatoRx, Inc.

is a biopharmaceutical company that has created a unique drug development platform to produce breakthrough therapeutics for a wide range of large markets. The company uses a proprietary process called combination high throughput screening (cHTS) to discover new combinations of molecules with novel synergies and biological activities. ***www.combinatorx.com***

Cyberkinetics Neurotechnology Systems, Inc.

is active in the emerging field of neurotechnology. Founded in 2001, the company is developing innovative devices for the treatment of nervous system dysfunction by combining recent advances in neuroscience, computer science and engineering. Cyberkinetics' proprietary neurotechnology platform includes implantable devices that have the potential to control movement or communication via other external devices. ***www.cyberkineticssinc.com***

Cytos Biotechnology AG

is engaged in the discovery and development of a new class of biopharmaceutical products called Immunodrugs™. To stabilize, prevent or reverse the disease process, Immunodrugs™ instruct the patient's immune system to produce the desired antibodies or cytotoxic T cells to eliminate or block a disease-associated protein. ***www.cytos.com***

DeveloGen AG

is a drug discovery company developing novel therapies for metabolic disorders based on extensive model organisms and stem cell expertise. The company currently has two technology platforms focusing on metabolic phenotypic screens and harnessing key developmental control genes involved in stem cell differentiation and tissue regeneration.
www.develogen.com

Fibrex Medical Inc.

aims to become a leader in the development and commercialization of pharmaceuticals targeting fundamental mechanisms of inflammation-based tissue injury. FIBREX Medical has identified several synthetic peptides with novel mechanisms of action as lead compounds. ***www.fibrexmedical.com***

Healthgate Data, Inc

EBM Solutions was a B2B e-healthcare information company co-founded by five important US medical schools. In October 2003 it was aquired by HealthGate, a health content provider also offering customer specific solutions whithin an existing clinical information system. ***www.healtgate.com***

IMI Intellgent Medical Implants AG

is developing a Learning Retinal Implant System, the first product of its technology platform in neurostimulation. The company´s technology aims to provide patients with hereditary degenerative retinal diseases such as Retinitis Pigmentosa or Age-Related Macular Degeneration with useful visual functionality.

www.intmedimplants.com

Intercell AG

is a biotechnology company focused on the development of vaccines against infectious diseases and cancer. Founded in 1998, the company is developing novel therapeutic and preventative vaccines against infectious diseases including Japanese Encephalitis, hepatitis C and tuberculosis, and against certain types of cancer. ***www.intercell.com***

MediGene AG

is a publicly-quoted (Frankfurt: Prime Standard) German-American biotechnology company located in Martinsried, Germany and San Diego, USA. The company has the most mature drug development pipeline in the German biotech industry. MediGene's core competence lies in research and development of novel approaches for the treatment of various tumor diseases. ***www.medigene.com***

Memory Pharmaceuticals Corp.

is a neuropharmaceutical drug development company active in the field of learning and memory disorders. The company discovers and develops memory-enhancing drugs known as cognition enhancers. ***www.memorypharma.com***

Nabriva Therapeutics GmbH

a specialist antibiotic research and development company, was launched beginning 2006 as a spin-off from Sandoz GmbH. Nabriva is based in Vienna, Austria, and focuses on the development of small molecule antibiotics for use in community and hospital infections. ***www.nabriva.com***

Neuraxo Biopharmaceuticals GmbH

a biopharmaceutical company located in Duesseldorf, Germany, focuses on the treatment of nervous system injuries. Neuraxo`s key proprietary technology, the Regeneration Promoting Treatment, is the first and only existing therapy allowing the regeneration of injured nerves following their natural nerve tract, thus enabling the recovery of sensory and motor function.
www.neuraxo.com

NeurogesX Inc.

is a privately held specialty pharmaceutical company located in the San Francisco Bay Area. Their initial focus is to develop novel treatments to better relieve neuropathic pain and improve quality of life using advanced neuroscience insights and innovative delivery technologies. ***www.neurogesx.com***

Nitec Pharma AG

focuses on the development of anti-inflammatory drugs with an improved benefit-risk profile for patients suffering from chronic inflammatory diseases. The company also intends to in-license new and innovative products in the field of inflammation and pain.
www.nitecpharma.com

Pieris AG

is a biopharmaceutical company engaged in the discovery and development of Anticalins® for the diagnosis and treatment of life-threatening human disorders. Recognizing the enormous market potential of protein-based drugs, Pieris is committed to becoming an integrated drug discovery and development company.
www.pieris-ag.de

Santaris Pharma A/S

is a clinical-stage biopharmaceutical company developing next generation RNA-silencing drugs for the treatment of cancer and metabolic diseases. The company, which was created in May 2003 through the merger of Cureon A/S and Pantheco A/S, owns the exclusive worldwide rights to the use of locked-nucleic acids (LNA) in pharmaceuticals. ***www.santaris.com***

7TM Pharma A/S

is dedicated to the discovery and development of medicines acting through 7TM receptors (seven transmembrane segment receptors, GPCR), a vast class of targets for today's pharmaceutical industry. With its proprietary know-how on these receptors it aims to generate new compounds with non-obvious structures and a tailored profile. 7TM Pharma acquired Carex in May 2006. ***www.7tm.com***

Former investments which are fully exited: post IPO or through M&

Artemis Pharmaceuticals GmbH

is a leading genetics and functional genomics company that uses the vertebrate genetic model organisms zebrafish and mouse to identify and functionally validate novel genes in vivo. These genes can be used as novel screening targets, or as the basis for secreted proteins in clinically and commercially relevant diseases. In 2001, Artemis merged with Exelixis.
www.artemis-pharmaceuticals.de

Exelixis Pharmaceuticals Inc.

is engaged in the identification and development of small molecule drugs for a range of diseases. Through several unique model systems, the company discovers and validates high-quality novel targets for several major human diseases and is a leader in the discovery of potential new drug therapies for cancer and other proliferative diseases. ***www.exelixis.com***

GLYCART Biotechnology AG

uses its proprietary GlycoMAb™ glycosylation engineering technology to boost the natural mechanism of action of therapeutic antibodies for target cell ablation. The company develops its own GlycoMAb™–based portfolio of therapeutic antibodies targeting cancer and autoimmune diseases. The company was aquired by Roche in 2005. ***www.glycart.com***

Sequenom, Inc.

is a leading genetics company organized into two distinct business units: SEQUENOM Genetic Systems and SEQUENOM Pharmaceuticals. Sequenom Pharmaceuticals focuses on disease gene discovery, target identification, functional validation and ultimately, diagnostic and therapeutic product development.
www.sequenom.com

Global Life Science Ventures GmbH
Von-der-Tann-Str. 3
D-80539 München
Germany
Phone +49 (0)89 - 288 151-0
Fax +49 (0)89 - 288 151-30
Email: mailbox@glsv-vc.com

Global Life Science Ventures AG
Postplatz 1
CH-6301 Zug
Switzerland
Phone +41 (0)41 727 19 40
Fax +41 (0)41 727 19 45
Email: mailbox@glsv-vc.com

www.glsv-vc.com