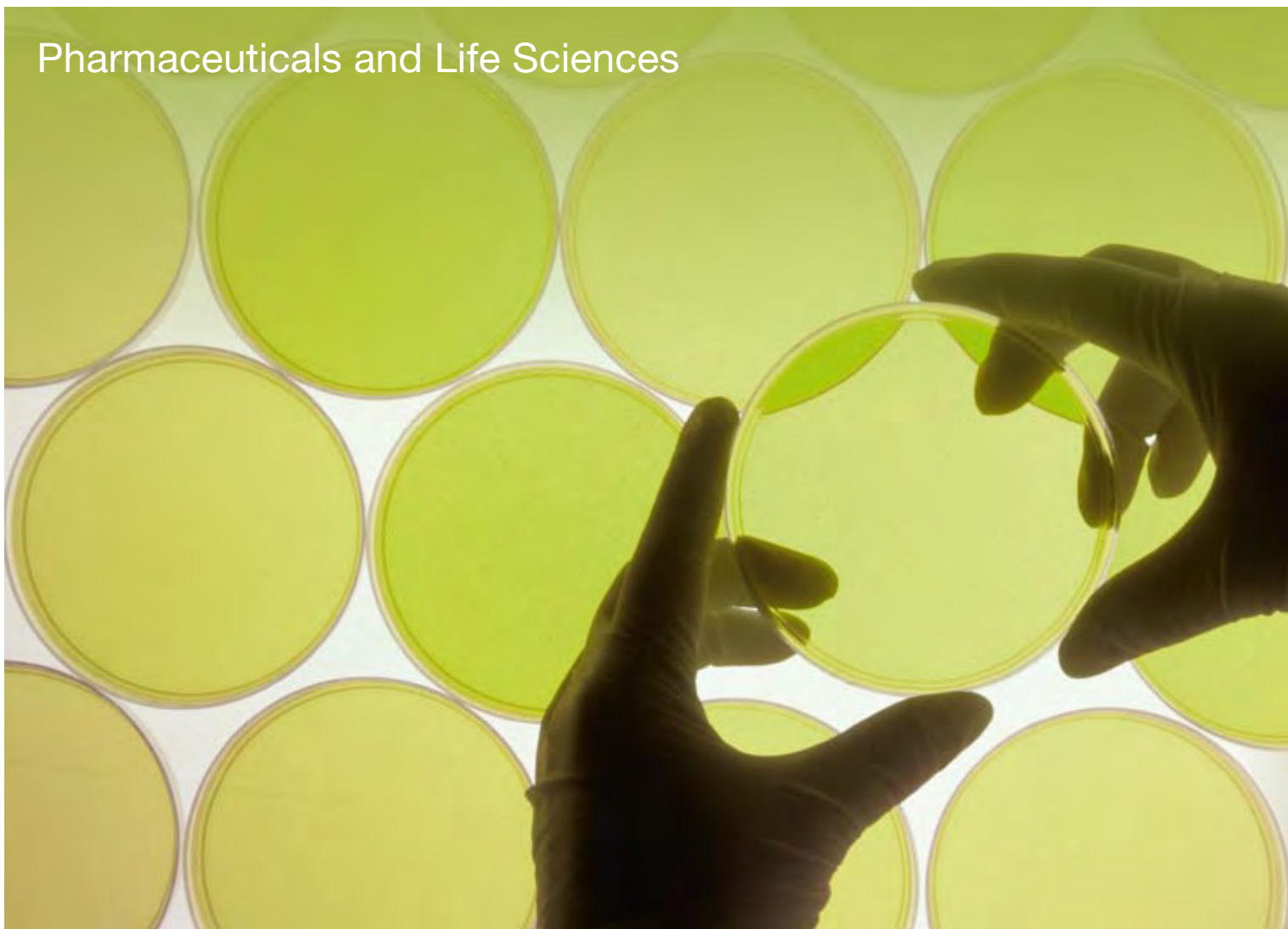


Pharmaceuticals and Life Sciences



# Drug Discovery and Biotechnology in Germany

# Drug Discovery and Biotechnology in Germany

## Preface of BIO Deutschland e.V.

Drug discovery nowadays is a highly innovative process by which new drugs are discovered and/or designed. It is expected that in the year 2010 at least 50 percent of all new approved drugs will come from the biopharmaceutical sector. The discovery and validation process is mostly carried out by new innovative and medium-sized companies. But despite advances in technology and greater understanding of biological systems, drug discovery is still a lengthy process. Specialised drug discovery companies need an ideal business climate, that is, political, economic and social conditions, to be able to cope with the entrepreneurial risks of drug development.

The Commission of Experts for Research and Innovation set up by the German Government has noted for the second year in a row that “Germany’s competitive position will be at risk in the medium and long term if research and innovation are not improved and the major obstacles caused by the taxation system are not removed.”<sup>1</sup>

Since their foundation, many biotech companies have invested their entire assets in innovative R&D. Expenditure on research is usually completely funded by equity capital. Expenditure on drug development is particularly high in biotechnology. It takes many years before companies make a profit. This is primarily due to the development periods of ten years or longer, which are typical of groundbreaking innovative drugs. In the current situation, investors are less willing and able to invest because of the need to account for the loss of the loss carry forward due to the investment. There is a fundamental discrimination against innovative drug discovery companies as compared with large, profitable pharmaceutical firms.

On behalf of the biotechnology industry, BIO Deutschland is working to have the increased discrimination against small and medium-sized drug discovery companies resulting from the 2008 Business Tax Reform Act overturned and replaced by innovation promotion that is fit for the future.

The Commission of Experts for Research and Innovation has made clear how important it is during the current worldwide economic crisis to improve conditions for research and innovation in a targeted way – especially and above all in the private sector. BIO Deutschland will continue to lobby for political activities to be rapidly undertaken so that innovative small and medium-sized companies are actively and sustainably strengthened and investments are made in one of the most future-oriented pillars of our economy.

Yours sincerely,



Dr Peter Heinrich  
Chairman of the Board of  
BIO Deutschland e.V.



Dr Viola Bronsema  
Managing Director of  
BIO Deutschland e.V.



Dr Peter Heinrich



Dr Viola Bronsema



Dr Kai Uwe Bindseil



Dr Jens A. Katzek

## Preface of the German BioRegions

The biotechnology landscape in Germany is particularly colourful. Start-up companies, so essential for the development of a new innovation sector, however, have quickly recognised that it is helpful for their own development to be in an environment which supports them.

Supply companies, scientific excellence, financial investors, and cluster management with its support network: all of these are factors relevant to the further development of German companies. The BioRegio competition in the mid-1990s was an important new initiative which finally led to BioRegions all over Germany, with approximately 200 start-up companies – a landscape which today is well established and attractive to investors.

A solid network represented by the German BioRegions supports the future development of the biotech industry in Germany. The BioRegions, with their close connections to the different actors at a regional level, have recently focused their common interests in a nationwide Council of German BioRegions within BIO Deutschland.

Biotechnology, however, was an international business right from the beginning and still is today. The Council of German BioRegions has developed the idea of bringing together all relevant information from the individual regions regarding drug discovery to create a bigger picture showing the strength and attractiveness of drug discovery expertise in Germany.

Although every region has its particular strength, Germany is like a jigsaw puzzle – every single piece is colourful, but the full picture emerges only when the pieces are viewed as a whole.

The study is intended as a contribution towards attracting further international investors. This will ensure that the industry continues to flourish and become ever more colourful over the coming years.

We would like to thank Dr Albrecht Läufer and Dr Ernst D. Jarasch from the Working Group as authors of the first part of the study, PricewaterhouseCoopers (PwC) for their great support and co-authorship, Dr Kathrin Adlkofer for compiling all the relevant information from the individual regions and the entire team for their efforts, all clearly demonstrating that Germany is an attractive place for cooperation!

Yours sincerely,

Dr Kai Uwe Bindseil  
Managing Director BioTOP and  
Chairman of the Council  
of German BioRegions

Dr Jens A. Katzek  
Managing Director BIO  
Mitteldeutschland and Project  
Coordinator of the Council  
of German BioRegions

## Preface of PricewaterhouseCoopers Germany

The pharmaceutical marketplace is changing significantly with huge challenges ahead for the industry and biotech as a whole. The major socio-economic trends expected to have most impact can be summarised as follows: increases in chronic disease due to the demographic shift; the health care payers' influence on how doctors prescribe with impending talks on pay for performance, and the growth of emerging markets and demand for innovative medicines. In addition, many governments are beginning to focus on prevention, which will create new opportunities in drug discovery.

Pharma's traditional strategy of placing all their bets on a few molecules, promoting them heavily and turning them into bestsellers worked well for many years. However, productivity in the lab is now plummeting, as attention switches from diseases that are relatively common and easy to treat to much more complex or rare diseases.

Moreover, the patents for many of the medicines launched by the industry in the glory days of the 1990s are due to expire over the next few years, leaving Big Pharma very vulnerable.

There is now a strong need to alter R&D business models to sustain future growth and performance. The changing R&D process will result in a much sharper increase in the number of biotech companies involved than in the last decade. The current need for funding through sources other than the capital markets is driving interest in biotech companies, helping to establish them as serious partners for Big Pharma in drug discovery and development.

Innovation is still strong in Germany's excellent research organisations and small to mid-size biotech companies, which will prove extremely valuable to the pharmaceutical industry. To get a clearer understanding of the great potential and opportunities offered by biotechnology-based drug discovery, we carried out an investigation of the German landscape of drug discovery and biotechnology together with the Council of German BioRegions. We would like to thank the authors and study coordinators for their excellent research and for bringing together all relevant data to demonstrate the attractiveness of Germany as a place to develop innovative drugs for our growing and ageing society with its changing needs.

We would also like to express our appreciation for the expert opinions we gained from a series of interviews with academics and managers from pharmaceutical and biotech companies, which we will share with you in this publication.

Yours sincerely,

Dr Volker Fitzner  
Partner, Chemicals and Pharma  
PricewaterhouseCoopers

Volker Booten  
Partner, Industry Leader  
Chemicals and Pharma  
PricewaterhouseCoopers



Dr Volker Fitzner



Volker Booten

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## Section A



Dr Ernst Dieter Jarasch



Dr Albrecht Läufer



Dr Claudia Ulbrich

## Executive summary and introduction

In recent years, Germany has become a significant source of innovative drugs developed through biotechnology. It is an important market for pharmaceuticals in general as well as for biopharmaceuticals. Germany has a strong, internationally recognised base of academic institutions and approximately 220 companies, large and small, working on new and effective compounds. Novel business models of cluster and network management between universities, the institutes of the four big governmental research associations (the Max Planck and the Fraunhofer Society as well as the Helmholtz and Leibniz Association) and small, medium, and large biopharmaceutical companies are set to become very efficient tools for the discovery and development of innovative compounds.

A total of 419 compounds are currently in Phase I–III clinical trials. The majority of these are being developed by small and medium-sized biotech companies presented in this study. At least 177 biopharmaceuticals, including biosimilars, have been registered to date. In 2007, biopharmaceuticals accounted for 15 percent of the German pharmaceutical market, with sales of 4 billion euros at wholesale level.

2008 was marked by major deals for Germany, such as the acquisition of Jerini by Shire Pharmaceuticals for 350 million euros, Morphosys' collaboration deals with Novartis valued at up to 1 billion euros, as well as the financing agreement of 65 million euros for GANYMED in the middle of worldwide financial turmoil in October 2008, and many other examples. All of these demonstrate that German drug discovery has matured and is truly working at international standards.

The fact that Harald zur Hausen was honoured with the Nobel Prize in 2008 for his work discovering the relationship between the human papilloma virus and cervical carcinoma – which has led to the first vaccines for cancer prevention on the global biopharmaceutical market – underlines the importance of German academic research for the development of successful and innovative methods of preventing or treating disease.

Bioprocess engineering has always been strong in Germany, but few are aware that the world's two largest biopharmaceutical manufacturing facilities are both based in this country – Roche Diagnostics in Penzberg and Boehringer Ingelheim in Biberach. A whole range of smaller companies provide services as custom manufacturers, process developers, custom research organisations for preclinical and clinical development, producers of laboratory supplies or of synthetic genes and new diagnostic techniques. This enables any start-up company to efficiently partner with service providers and to develop products in the shortest possible time at a reasonable price.

The German Federal Ministry of Education and Research (BMBF, Bundesministerium für Bildung und Forschung) has been playing a major role in fostering new research programmes and facilitating technology transfer, starting with the BioRegio competition in 1996. This was followed by BioProfile, BioChance, and the High-Tech Strategy of the Government which includes the High-Tech Founder Funds and the Pharma Initiative

along with the BioPharma competition. More than one billion euros have been spent through these dedicated federal programmes in the past ten years; the overall federal and state funding of biotechnology is far higher.

In a nutshell, the present study “Drug Discovery and Biotechnology in Germany” presents a business environment that is highly attractive for international partners, comprising creative academic research, innovative business models and clusters linking science and industry, intelligent government support, as well as innovative and dedicated medium and large pharmaceutical companies and, last but not least, an attractive pipeline of new drugs targeting major unmet medical needs.

This study adopts the unique approach of analysing the situation in drug discovery not only from the viewpoint of the industry but also from the viewpoint of small and medium enterprises and the academic world. It has been initiated jointly by PwC Germany and the Council of German BioRegions, an association of 30 life science clusters supporting emerging biotech companies and networking between industry and academia all over Germany.

All 30 BioRegions have been requested to supply short profiles of their “beacons” – companies or research institutions leading the way in the fields of drug discovery and biotechnology. Most BioRegions have responded. A total of 92 “beacons” have been reported by the BioRegions and are listed in Section B of this study. More than 30 interviews were conducted simultaneously with leaders from industry and academia. Many of their key messages have been quoted directly in the text. Based on material supplied by the BioRegions as well as on the results of the interviews and their own research, the authors of Section A provide a comprehensive picture of the current situation in Germany at the beginning of 2009 regarding drug discovery, biotechnology, research, and business.

We hope our readers will enjoy discovering new information and new potential partners while browsing through this study. For more information, PwC and the BioRegions will be happy to assist you.

Dr Ernst Dieter Jarasch  
CEO BioRegion Rhein-  
Neckar-Dreieck e.V.

Dr Albrecht Läufer  
CEO of Corvay GmbH  
and Head of “Life  
Science Initiative  
Niedersachsen  
– BioRegion”

Dr Claudia Ulbrich  
Senior Advisor  
Pharma/Life Science  
PricewaterhouseCoopers



“In order to turn excellent basic research in Germany into measurable economic benefit, we need a social paradigm shift towards a more efficient support of entrepreneurship. This involves, both in Germany and elsewhere, promoting and reinforcing such virtues as courage, perseverance, and pride in success.”

**Dr Bernhard Kirschbaum**  
Executive Vice President, R&D,  
Member of the Merck Serono  
Executive Board, Merck KGaA

## 1 Germany – more than 350 years of successful drug development

Germany is “the pharmacy of the world”. That was the case in the 1970s when Hoechst, Bayer, Behring, and Schering dominated the world’s pharmaceutical markets. With gene technology arriving in the United States much faster than in Europe, and European governments implementing cost reduction measures much earlier, the United States quickly rose to become the technological leader with the largest pharmaceutical market in the world.

How did Germany become the world’s pharmacy? And what can we learn from history so that we can at least catch up with the US? In short, it was a time of brilliant chemists, many of whom went into partnership with brilliant business people.

As early as 1668, Friedrich Jacob Merck acquired the “Engel Apotheke” (angel pharmacy) in Darmstadt, laying the foundations for what today are two major global players – Merck, Darmstadt, and Merck & Co. Since then Merck, Darmstadt, has been a big player in both chemical and pharmaceutical production. Whereas the other big manufacturer concentrated its strength on one sector (either chemical or pharma), Merck is successfully operating in both. Merck is thus the oldest pharmaceutical company in the world and still flourishing with the successful development and launch of Erbitux in the UK in 2004 and the takeover of Swiss Serono in 2006, strengthening the business’ pharma sector. The new division Merck Serono supports the Merck Group with its strong expertise and research activities not only in oncology and neurology but also in the fields of autoimmune, infectious, and many other diseases.

Industry leaders Hoechst, Bayer, Behring, Schering, Boehringer Ingelheim, and Boehringer Mannheim were founded much later than Merck.

Hoechst was set up in 1863 as Farbwerke Meister, Lucius & Brüning and focused initially on the production of dyestuffs based on aromatic coal and tar derivatives. Shortly before the turn of the century the company went public and enlarged its value chain from the production of inorganic acids to the development and manufacture of synthetic drugs. Notable milestones in the early days were: the development of potent analgesics in 1883, the launch of adrenaline production in 1904, and the introduction of the first non-addictive anaesthetic Novocain. Prior to World War I, the company had become global and exported 88 percent of its products across Europe. In 1923 the company gained the first licence for insulin production. After the two disastrous World Wars, the company was restructured and focused its activities primarily on the large-scale production of synthetics, but also continued operating in pharmaceuticals and dyes. By acquiring the majority interest in the French company Roussel-Uclaf the firm became the biggest pharmaceuticals manufacturer worldwide with the new name of Hoechst AG. In the 1990s, many restructuring measures took place, establishing core business areas: pharma, agriculture, and biotechnology. At the very turn of the millennium, Hoechst merged with the French pharma group Rhône-Poulenc to become Aventis, today Sanofi-Aventis, the biggest pharma player in Europe. At its site in Frankfurt, Sanofi-Aventis has the largest insulin production

facility worldwide using state-of-the-art equipment for biotech engineering processes. All in all, about 20 different compounds are being produced in their facilities based in Germany which are exported to 40 countries around the world.

In 1863, Friedrich Bayer and Johann Friedrich Wescott also founded the dyestuff company Friedrich Bayer et comp, which again marked the beginnings of a major chemical and pharmaceutical group, Bayer AG. As a salesman, Friedrich Bayer took care of the business side while Wescott provided the chemical input. The chemist Carl Duisberg joined the company in 1883 and proved a major force in Bayer’s rise to its status as a chemical giant. Gerhard Domagk, Nobel Prize winner in 1939, discovered the cell toxic activity of some dyes on microbial pathogens, thus paving the way for the use of sulphonamides as antibacterial drugs. Much earlier in 1897, Felix Hoffmann had achieved the breakthrough in synthesising acetylsalicylic acid, the compound in Aspirin, in a chemically pure and stable form. Despite the debilitating effect of the World Wars, Bayer managed subsequently to maintain its activities and went on to expand and strengthen its operations in pharmaceutical and pesticide research. Since then, brilliant scientists have contributed to the creation of excellent innovation power in Germany. In the late 1960s, Karl Heinz Büchel discovered an azole derivative, clotrimazole, which facilitated the treatment of many fungal infections. In 2006, Bayer acquired Schering, Berlin, itself a big pharmaceutical company with a 135-year old success story, today known as Bayer Schering Pharma with major activities in biopharmaceuticals (factor VIII, interferon-beta).

Schering can be traced back to 1851 when pharmacist Ernst Schering founded his pharmacy in Berlin. This evolved into the chemical company Chemische Fabrik E. Schering, and the industrial manufacturing of pharmaceuticals started in 1890 with piperazine, a drug aimed at combating signs of ageing and gout.

Boehringer is yet another chemical/pharmaceutical dynasty in Germany. As early as 1817, Christian Friedrich Boehringer established a pharmaceutical business as well as a chemical laboratory in Stuttgart, which became C. F. Boehringer in 1859 and was relocated to Mannheim in 1872.

In 1885, Albert Boehringer founded a chemical factory in Ingelheim on the banks of the Rhine river west of Frankfurt. This company was renamed C. H. Boehringer Sohn in 1892. During the 1960s, the two Boehringer companies were renamed Boehringer Mannheim and Boehringer Ingelheim. While Boehringer Mannheim was sold to Roche in 1998, Boehringer Ingelheim is the world’s largest, privately owned pharmaceutical company today with sales of 10.9 billion euros in 2007. Boehringer Mannheim’s former manufacturing site at Penzberg, south of Munich has been developed by Roche into the world’s largest biopharmaceutical manufacturing site, while Boehringer Ingelheim’s site at Biberach, formerly Schmidt & Thomae, is the world’s second largest biopharmaceutical manufacturing site. One of the most outstanding leaders within Boehringer was Rolf Krebs who pushed the early acquisition of a 10 percent stake in Genentech and campaigned for a united front to fight AIDS.

Rentschler developed in a similar way. Founded in post-war Germany to make vaccines for animals, Rentschler had at that time already begun



“There is still a great need for innovative drugs to improve treatment options for patients. Germany has developed high scientific standards and a maturing biotechnology industry, a good basis to provide a new generation of pharmaceuticals.”

**Dr Arndt Schottelius, MD PhD**  
Chief Development Officer,  
MorphoSys AG



“In Germany, a highly innovative approach to drug discovery is taken both academically and at the level of production, in order to develop more efficient medication to fight serious diseases with fewer side effects. However, to pursue this path efficiently with respect to international competition, we need much stronger networking among partners from academic research and industry. In Germany, this type of networking is currently being driven by various promising activities.”

Dr Peter Heinrich  
Chief Executive Officer,  
MediGene AG

to focus its activities on products engineered with biotechnology. The management decision in 1974 to produce interferon biotechnologically was a further step in this trendsetting direction. Today, Rentschler Biotechnology has a long history of successful operations in the field of biotechnological production of pharmaceuticals and chemicals.

The year 1884 marks the first successful technology transfer from academia to industry when Farbwerke Hoechst began commercially manufacturing a diphtheria serum which saved the lives of many children who would otherwise have died from this infectious disease. In 1890, Emil Adolf Behring together with Shibasaburo Kitasato discovered a serum therapy for diphtheria but it was only with the financial support of Hoechst that a commercial drug could be developed. Behring was honoured with the first Nobel Prize in Medicine in 1901 and acquired the name “von Behring”. In 1903, von Behring established the Behringwerke in Marburg together with pharmacist Carl Siebert, who was responsible for the commercial side of the enterprise. For nearly 100 years, the Behringwerke were a major producer of serum products and vaccines until 1996, when Chiron Behring was established as a joint venture, which was later fully taken over by Chiron and, in 2005, was acquired by Novartis to become Novartis Vaccines.

The last 20 years have been shaped by a few serial founders like Karsten Henco and Axel Ullrich and by the many governmental and private activities described in Chapters 3 to 5 of this study. Henco founded Qiagen in 1984 together with Metin Colpan and Jürgen Schumacher, and was co-founder of Evotec, Direvo Biotech, and a Swiss biotech company. Ullrich, the inventor of the first gene technology drug Humulin and of Herceptin founded several biotech companies, namely Sugen, Axxima, U3, and Kinaxo. Less prominent but also very successful is Herbert Stadler, founder of IBA, Biometra, Develogen, and Affectis amongst other companies.

## 2 The largest pharma market in Europe

This chapter provides an overview of the market environment in Germany for pharmaceuticals in terms of sales volumes, number of companies, structure of the industry, regulatory environment, and private and public funding. It also briefly describes the service industry supporting drug discovery.

### 2.1 Sales of pharmaceuticals

Germany is the third largest pharmaceutical market in the world and the largest market in Europe. In 2007, sales of 26.8 billion euros were generated at wholesale price level, an increase of 5.5 percent in comparison to 2006. About 4 billion euros of this were generated by biopharmaceuticals and approximately 1 billion euros by vaccines.

Most notable is the expansion of exports in the pharma sector. With export share increasing from 36 percent in 1995 to 57 percent in 2007, Germany is among the strongest exporters of pharmaceuticals in the world. The German Federal Statistics Office (Statistische Bundesamt) reports an additional growth of 11.2 percent in export rates in the first half of 2008 compared to the same period in 2007. Most of the pharmaceutical products were sold within the EU (69 percent, FSO), foremost in Belgium (26 percent), the Netherlands (10 percent), and France (5 percent). Outside of the EU, the major importers of pharmaceutical goods, “made in Germany”, were the United States (25 percent) and Switzerland (17 percent).

Pharmaceuticals worth 14.4 billion euros, i.e. an increase of 1.7 percent year-on-year, were imported to Germany within the first six months of 2008. Most of the imports originated from Ireland (29 percent), the United States (21 percent), and Switzerland (10 percent).

The share of biopharmaceuticals in the total pharmaceutical market has been continuously increasing over the last decade. In 2007, biopharmaceuticals accounted for 15 percent of the total volume of pharmaceuticals. Taking a look at specific therapeutic areas, the relative market shares are even more distinctive: in the field of immunology about half of the sales volume was generated with agents produced by genetic engineering. While the total pharmaceuticals market grew by only 5.5 percent in 2007, the biopharmaceutical market has seen growth of 28 percent since 2006.

The rise was driven especially by cancer drugs and anti-infective agents (drugs for prevention and treatment of infectious diseases) with a mean annual growth rate of 52 percent and 37 percent, respectively. Expanding need for anti-infective drugs has triggered immense growth in market share and boosted revenue to about 919 million euros, nearly a quarter of the total volume of biopharmaceuticals, driven by sales of vaccines for prevention of human papilloma virus (HPV) induced cervical cancer.



“Changes in the German health care sector are opening up new opportunities for the pharmaceutical industry going beyond the role of simply being a drug manufacturer.”

Dr Stefan Busch  
Vice President, Strategic Planning  
and Portfolio Management,  
Member of Management Board,  
AstraZeneca GmbH



“Innovations in biotechnology create competitive products for an international market and good perspectives for long-term employment.”

Dr Wolfgang Plischke  
Member of the Management Board,  
Bayer AG

In 2007, 40 new drugs were approved in Germany, ten of which were biopharmaceuticals. In total, over 180 biopharmaceutical drugs have been approved in Germany to date. The largest group comprises “other recombinant proteins”, such as insulin, erythropoietin (EPO), hormones, interferons, and coagulation factors, and consists of 108 substances for miscellaneous indications. Of the drugs that have been approved, 50 are genetically and biotechnologically engineered vaccines against various infections and 19 of the biopharmaceuticals are monoclonal antibodies.

Among the ten drugs approved in 2007 there is one vaccine against HPV, three antibodies for the treatment of colon cancer, macular degeneration and haemoglobinuria, and seven “other recombinant proteins”, e.g. for rheumatoid arthritis, a growth factor, one new EPO with prolonged action and two EPO biosimilars, as well as a compound against Hunter syndrome.

## 2.2 Industry structure

The market is dominated by big players, i.e. the three main German companies Boehringer Ingelheim, Bayer Schering, and Merck Serono, as well as the affiliates of all major international players, who are organised within the Association of Research Based Pharmaceutical Companies (VFA, Verband Forschender Arzneimittelunternehmen). The VFA operates a subsidiary, VFA Bio, which represents all large producers of biopharmaceuticals and some biotech.

**Boehringer Ingelheim**, with more than 40,000 employees and 11 billion euros of global sales, is focusing its R&D activities on respiratory diseases, metabolic and CNS disorders, and “Special Drug Devices”.

**Bayer Schering Pharma**, a worldwide leading specialty pharmaceutical company with 37,000 employees, focuses its research activities on four core areas: cardiology, oncology, women’s health care, and diagnostic imaging. In addition, the company has continued applied research and life cycle management activities for the indications haemophilia, multiple sclerosis, and dermatology.

In September 2006, **Merck** announced a bid to take over Serono, Europe’s largest biotech company. The new entity, Merck Serono, is now the third biggest biotech company worldwide. The focus of Merck Serono’s R&D lies in oncology using expertise from the fields of biotechnology, immunology, and molecular biology.

Another big player in Germany is **Abbott**, a branch of Abbott Laboratories, which has a long tradition of developing medicinal products. Its Ludwigshafen Centre of Excellence focuses on neuroscience discovery and serves as the headquarters of the European Clinical Development Centre.

The big pharmaceutical company **Roche** has several sites in Germany including its worldwide leading diagnostic divisions in Mannheim and Penzberg, focusing on the development of diagnostic methods for the life science industry.

Many big pharma companies are conducting R&D to discover and create new drugs. To this end, they set up their own R&D units or use the expertise of much younger and extremely dynamic players operating in the sophisticated biotechnology landscape in Germany.

In terms of the number of prescriptions, generics are dominating the market; in terms of revenue, innovator drugs have maintained their lead. Large generics companies like **Ratiopharm**, **Hexal** (via Sandoz, a part of the Novartis group since 2007), or **Stada** are not only strong in generics but have also managed to successfully register biosimilar drugs (erythropoietin, somatotropin). Europe and Germany have gained a leading edge internationally by revising regulations for biosimilar approvals, promising more business for CMOs and CROs. Generic producers are represented by the association of drug manufacturers BAH (Bund der Arzneimittelhersteller) and Pro Generika.

Another important group of companies comprises medium-sized pharmaceutical companies, organised within the BPI (Bund der Pharmazeutischen Industrie). Most of these companies only operate in Germany or in just a few European markets and tend to have a rather traditional portfolio. Some, such as Rentschler, have started to invest in biotech drug discovery.

Many biotech companies are represented by BIO Deutschland or DIB (Deutsche Industrievereinigung Biotechnologie). Only a few of these companies have managed to place products on the market so far, for example, **MediGene**.

All these associations provide valuable information about the industry on their websites for their members and can thus be good points of contact.

According to the BCG report Medical Biotechnology in Germany 2008, there are currently 371 companies in Germany specialising in medical biotechnology with revenues of about 5.0 billion euros in 2007. 97 of these companies are generating about 88 percent of the total turnover, by either developing biopharmaceuticals or already having products on the market. Sales have risen by 26 percent in comparison to the previous year. Apart from product sales (4 billion euros), smaller biotech companies are generating revenues through licence fees and milestone payments based on alliance agreements. Turnover from technology platforms and services experienced growth too, rising by 14 percent.

Almost 34,000 people were employed in the medical biotechnology sector in 2007. This corresponds to an increase of 4,000 employees or 14 percent year-on-year.

German biotech companies are attracting more and more potential buyers and cooperation partners. In April 2008 **GANYMED Pharmaceuticals**, a privately held cancer antibody firm, was able to close the third largest financing deal nationwide, with a total of 65 million euros in capital. Another big deal (150 million euros) was accomplished by Martinsried-based biotech company **U3**, founded by Axel Ullrich, founder of a number of companies. U3 was acquired by the Japanese pharma group Daiichi Sankyo adding some 27 skilled employees to Germany’s leading edge in research and development.



“Germany is a top location for biomedical research and outstanding young biotech companies. We need to support these adequately and actively engage in removing any obstacles in order to create equal opportunities with respect to US biotech companies.”

Dr Rainer Wessel  
Executive Speaker,  
GANYMED Pharmaceuticals AG



“Germany is a global leader in basic research and has a high potential for industrial success. This should be supported intensively.”

Prof Dr Jens Schneider-Mergener  
Former Chief Executive Officer,  
Jerini AG

Again in 2008, **Amaxa**, a globally active leader in transfection technologies, chose the same exit strategy and was acquired by Lonza, which will keep the German location and its employees while expanding its cell discovery business.

The takeover of the protein engineering company **Direvo Biotech** from Cologne by **Bayer HealthCare** for 210 million euros is another example of successful entrepreneurship in Germany.

The biggest deal in 2008 was announced in the summer months and finalised later in the year: **Shire** agreed to pay about 350 million euros to acquire Berlin-based **Jerini**, a biotech firm which had just received EU market authorisation a few months earlier for Icatibant, its innovative drug for the treatment of hereditary angioedema, a rare genetic disorder.

All these acquisitions were strategically conducted, adding and strengthening the portfolios of the buyers, namely, pharma companies, most of which had been involved in biopharmaceuticals prior to the takeovers.

A fruitful, strategic alliance has been established between **Trion Pharma** and **Fresenius Biotech**, which, based on Trion's research and development of Removab<sup>®</sup>, co-developed the drug for the treatment of malignant ascites throughout the advanced development stages up to European Market Authorisation, granted by the European Commission on 23 April 2009. Removab<sup>®</sup> is the first approved therapeutic bi-specific, tri-functional antibody, invented, developed, and produced in Germany.

## 2.3 Platform companies/service providers

Many German biotech companies have developed outstanding new technologies that demonstrate their innovative power.

The most prominent of these is **Morphosys**, Martinsried. Morphosys developed a technology for generating fully human antibodies based on the in-house library HuCAL (Human Combinatorial Antibody Library). The company's speciality consists of a new method for the large-scale in vitro production of highly specific human antibodies.

The company **Cellzome** with headquarters in Heidelberg uses a unique kinase fingerprinting platform to produce pathways of protein-protein and protein-small molecule interactions. These proteomic technologies provide a basis for the drug discovery process as well as a method of identifying drugs on the basis of kinase inhibitors.

Berlin-based **Noxxon Pharma** uses its innovative Spiegelmer<sup>®</sup> technology to develop new generation biopharmaceuticals based on specific oligonucleotides targeted against proteins similar to antibodies.

**metanomics Health** applies metabolite profiling to develop tools and solutions for drug discovery and development. metanomics Health develops and utilises the technology of metanomics, which is one of the largest and most innovative mass spectrometry-based metabolite profiling companies worldwide.

**GENEART** provides fast track oligonucleotide synthesis, sequencing and manipulation/engineering services as well as antibody production through genetic immunisation. GENEART is said to be the world market leader in gene synthesis.

Custom manufacturers (see also Chapter 5) all over Germany provide excellent service in process development and manufacturing of proteins and other products from bacterial, yeast, CHO, and other cell line systems. Examples are **Rentschler**, **Probiogen**, **Richter-Helm**, **Rhein Biotech**, **Vibalogics**, and **EUFETS**, a subsidiary of **Fresenius Biotech**.

CROs like **Covance** and **Parexel** have subsidiaries in Germany; medium-sized CROs, such as **Focus**, Neuss, together with smaller companies like **Aurigon**, Tutzing, round off the picture.

Last but not least, Germany is home to **Sartorius**, Göttingen, one of the largest providers of manufacturing equipment, as well as **Werum**, Lüneburg, the world market leader in process control software for biopharmaceutical manufacturing and a leading bioinformatics company **BIOBASE** in Wolfenbüttel.

In sum, the annual revenues generated by these service providers are estimated to exceed 1 billion euros.

## 2.4 Regulations

Regulations for market authorisation of drugs in the EU, North America, and in Japan are harmonised in accordance with the International Code of Harmonization (ICH).

Medicinal products intended to be marketed in Germany or other European Economic Area (EEA) states require official approval by either a national authority or authorisation from the European Commission.

In Germany, two agencies are responsible for granting permission to launch medicinal products for human use on the market: the **Paul-Ehrlich-Institut (PEI)**, Langen, and the **Federal Institute for Drugs and Medical Devices (BfArM)**, Berlin.

The **PEI** is a federal agency of the Federal Republic of Germany. It reports directly to the Federal Ministry of Health (BMG, Bundesministerium für Gesundheit) and is committed to the approval of clinical trials and the authorisation of medicinal products within the following groups: sera; vaccines; blood, tissue and bone marrow preparations; allergens; mABs; gene transfer medicinal products; somatic and xenogenic cell therapeutics and genetically modified blood components. The duties of PEI include the approval of clinical trials within the jurisdiction of PEI, participating in the approval of field trials (veterinary), processing applications and subsequent reapplications, testing medicinal products, monitoring, collecting and evaluating adverse reactions, taking measures to improve the acceptability of drugs as well as conducting inspections, consultations, and research. Above all, the PEI is responsible for the market authorisation of these medicinal products.



“Success through innovation must be visible. This provides Germany with a great opportunity to show that we can reach the top in the field of active ingredient development.”

Dr Frank Morich  
Chief Executive Officer, Noxxon AG



“Science and research need funding and planning security, not declarations of intent.”

Prof Dr Klaus D. Döhler  
Managing Director,  
Curatis Pharma GmbH

All other medicinal products are the responsibility of **BfArM**, which also operates under the auspices of the Federal Ministry of Health in Germany. As well as authorisation, it is accountable for general drug safety monitoring (pharmacovigilance) and drug safety improvement.

Apart from the national authorisation procedure, to license a drug in more than one EU country, applications must comply with the Decentralised Procedure (DCP) or the Mutual Recognition Procedure (MRP) if the compound has already been approved in one European country.

The Centralised Procedure results in EU-wide marketing authorisation. An approval for a medicinal product intended for use in all EEA countries (which may still mean that each country will add its own requests and stipulations) may be achieved by filing an application with the **European Medicines Agency (EMA)**, an equivalent to the Food and Drug Administration (FDA) in United States. The EMA employs a system of so-called rapporteur countries; when following the Centralised Procedure, the wise selection of the rapporteur country is key to the market success of a pharmaceutical product. Pricing and reimbursement levels, the country's position on innovative drugs, the experience of the country's regulatory agency, and many other aspects have to be taken into account. In many respects Germany serves as a good starting point for registering and launching a new drug in Europe.

## 2.5 Business models and private funding

Many biotech companies founded in the boom of the late 1990s shared the common vision of becoming fully integrated pharmaceutical companies like Amgen or Genentech. An IPO was seen as the obvious exit strategy for biotech investors. A few success stories have been recorded to date, chiefly **Qiagen**, **Medigene**, and **MorphoSys**. This vision ended abruptly with the stock market crisis of 2000/2001. The collapse in 2003 of the Neuer Markt, the Frankfurt Stock Exchange for innovative technology companies, marked the lowest point of this crisis in Germany. Between 2001 and 2004, not a single German biotech company went public, and thereafter only a few dared to opt for an IPO. These were not financial success stories. Since 2007, no IPOs have been recorded among German biotech companies.

In the years after 2001, major venture capital funds invested in advanced developments only, not in early high-risk projects and start-up companies. Biotechs that could not close the financial gap in their drug discovery and preclinical/early clinical development programmes had to change their business models and began to offer research and services on a contract basis in order to generate cash. For some companies with strong cutting-edge technology platforms, this shift opened up exciting new business opportunities when big pharmaceutical companies, faced with losing the patents for their best-selling drugs, sought collaboration with biotechs to fill their pipelines with innovative product developments. Outstanding examples are **MorphoSys** with its core technology HuCAL, **Evotec** with its fragment-based drug discovery and screening programmes, and **Cellzome** with its proteomic platform. However, these companies have continued to pursue their own drug development programmes in addition to their

alliances with, for example, Novartis, Boehringer Ingelheim, Pfizer, and Johnson and Johnson. In the end, successful drug development provides a far higher return on investment than even the most sophisticated contract research.

Serial founders form the backbone of the industry's success. In this respect, Karsten Henco, Jürgen Schuhmacher, Herbert Stadler, Axel Ullrich have already been mentioned above.

Until 2004, it was uncommon in Germany for private investors, apart from venture capital funds, to get involved in biotechnology. Since Dietmar Hopp, co-founder of the software company SAP, bought a majority stake in the cell therapy company **Cytonet** in 2004, he has invested more than 320 million euros in 15 biotech companies. His portfolio comprises drug developers such as **Apogenix**, **Curacyte**, **CureVac**, **GPC Biotech**, **Heidelberg Pharma**, **immatics**, and **SYGNIS**. More recently, the brothers Thomas and Andreas Strüngmann, who sold their generics company Hexal to Novartis, have invested considerably in biotechnology and bought stakes in **MediGene** and **Aicuris**, the former research department of Bayer AG in Wuppertal, as well as in younger, innovative drug discovery and development companies like **4SC**, **GANYMED**, **Glycotope**, **Nexigen**, and **Suppremol**.

As diagnostics will play an ever more important role in drug discovery, especially with regard to personalised medicine, it is important to mention **Mosaïques Diagnostics and Therapeutics** in Hanover, a company driven by inventor Harald Mischak and business mind Joachim Conrads, one of the very rare examples of a private investor who also acts as managing director.

These engagements provide proof of the positive opinions held by investors on the long-term perspectives of the German biotech industry. A current example is the strategic venture capital fund announced by Merck KGaA in March 2009. **Merck Serono Ventures** will invest in emerging biotech companies that are developing therapeutics in the areas of oncology, neurodegenerative and autoimmune diseases, and inflammation. Other examples of VC funds still active today are **TVM Capital**, **Life Science Partners**, **Atlas Venture**, **3i**, and **NGN Capital**, the latter being another example of long-term visionary, family investment as some members of the Boehringer Ingelheim family initiated this fund in 2005.

All these private investments have been complemented by a broad range of federal and state public funding programmes (see Chapters 3 and 4), which are particularly important, especially at the initial stages of an enterprise when up to 50 percent of research and development expenses can be covered by public funds.



“In the foreseeable future, classical biotech business models will have no access to capital markets. At the same time, strong alliances between research-oriented biotech and pharmaceutical companies with sufficient capital and good sales figures are becoming increasingly important.”

Dr Klaus Maleck  
Chief Financial Officer, Evotec AG



“Selective funding of universities and biotech companies to promote innovation and cooperation is both reasonable and necessary. This will foster a sustained development in Germany to become an attractive location for biotechnology innovation.”

Dr Ulrike Fiedler  
Managing Director,  
Scil Proteins GmbH

### 3 BioRegions playing a driving role

Germany has more biotechnology companies than any other European country. In 2007, there were approximately 495 small and medium-sized biotech companies, the largest segment of these (approximately 44 percent) is engaged in research and development in the medical/pharmaceutical sector. The vast majority of biotech companies (about 86 percent) have fewer than 50 employees, the small size reflecting the relative youth of most of these enterprises. More than 200 biotech companies operating today started their business in the years between 1997 and 2001 following the **BioRegio competition** organised by the German Federal Ministry of Research and Technology (BMBF).

In many ways the launch of the BioRegio competition in 1996 marked the beginning of an international visibility of Germany's biotech industry. BioRegio became a popular designation in other countries as well. There had been some biotech companies in Germany before, but these were scattered across the country and mainly active in technology development and distribution as well as contract research. Few were engaged in drug discovery and development or diagnostic research, the most notable exceptions being MediGene, Micromet, and MorphoSys in the Munich area.

While Germany had a strong reputation for its excellent academic research in molecular biology and medicine the transfer of scientific results into new enterprises lagged behind countries like the UK and particularly the United States, where a flourishing industry, driven by venture capital and focusing entirely on molecular and gene technology, had developed since the late 1970s and early 1980s. Big biotech clusters had formed particularly in the San Francisco Bay and Boston Area. In contrast, commercial biotechnology in Germany was concentrated in large pharmaceutical companies, such as Hoechst, Bayer, and BASF, which, however, had shifted most of their research and production facilities in molecular and gene technology to America.

The BioRegio competition initiated by Jürgen Rüttgers, at the time German Federal Minister of Education and Research, changed the perspectives of the German biotech industry dramatically. Launched in 1996, the competition was aimed at fostering the foundation of start-up enterprises, strengthening the growth of existing companies, and making venture capital available to ensure this growth. German regions were asked to develop concepts on how to approach these goals. Seventeen regions participated in the competition and the three best concepts were awarded 26 million euros each for commercially viable research projects over the five year period from 1997 to 2001. The winners were Munich, Heidelberg, and the Rhineland around Cologne, Düsseldorf, and Aachen. In addition, the smaller region of Jena received a special award.

The success of the BioRegio initiative cannot just be attributed the competition's prize money, much rather to other measures taken to foster an entrepreneurial life science industry: the very restrictive law that regulated gene technology was revised to facilitate work with methods and products involving gene technology. An “incentive to promote patenting and innovations” was initiated by the government to increase the number of patent applications and licensing agreements with academia, and technology transfer offices for research centres and universities

were set up. The programme “Business Investments Capital for New Technology-Based Firms” was launched, providing funds as co-investor for private equity funds.

BioRegio brought together all the players in the regions necessary for building a biotech industry: from academic institutions, big and small companies and industrial associations to local and regional politics and the finance sector. Activities were coordinated and promoted by BioRegio agencies established not only in the winning regions but in all regions which had participated in the competition and also in biotech areas which developed later. Under the umbrella of BIO Deutschland, the association of the German biotechnology industry, the German BioRegions Council, which serves as a platform to coordinate regional activities and international representation, presently comprises thirty members representing all biotech regions in Germany.

At the end of the BioRegio initiative in 2001, Germany had more than 500 biotech companies with a combined staff of over 16,000, mostly highly qualified employees. Thirteen biotech companies were listed on the stock markets. By way of comparison, the United Kingdom, the European country with the most mature biotechnology market at that time, had 46 public and about 380 private biotech companies with approximately 23,000 employees.

Besides the new biotech companies, the number of venture capital companies engaged in biotech also rose dramatically, from five in 1997 to more than 150 in 2001. The late 1990s were boom years and high profits could be gained by listing companies on the stock market. Stock price quotations for biotech companies often rose by several hundred percent following an IPO. When, however, the financial markets crashed at the end of 2001, stock prices for public biotech companies tumbled. Private companies dependent on venture funds felt the financial squeeze as investors, in the absence of public equity finance and exit opportunities, were focusing on late-stage products only. Companies had to cut back on staff and other costs, and had to reassess their business models in order to generate cash quickly rather than relying on revenues and profits in 10 or 15 years time. Between 2001 and 2004, the German biotech industry lost about a hundred companies – approximately 76 through insolvencies and the rest to mergers and acquisitions or removals.

When the industry recovered, the numbers of new biotech ventures grew more slowly and organically than in the enthusiastic years preceding 2000 when many non-viable companies had found investors. Start-up companies were often not financed by venture capital alone but by early cash generation through contract research or other services. By the year 2007, the number of biotech companies had reached 495, i.e. almost the peak level of summer 2001.

The biotech crisis of the years 2001 to 2004 would have hit the industry harder if the supporting networks of the BioRegions had not been in place. The inception of start-up companies and spin-offs from academia supported by the funding programmes of the federal and state governments (e.g. BioChance, GoBio) was facilitated by technology transfer offices and professional service companies, which also helped to acquire private investment. Laboratory space and other necessary



“There are good funding opportunities in basic research. To give innovative companies time to create real added value the gap between academic and industrial funding must be bridged, e.g. by funding clinical research.”

Prof Dr Hans-Ulrich Demuth  
Chief Executive Officer/Chief  
Scientific Officer, Probiobdrug AG

infrastructure were provided by technology parks and business incubators established within the framework of BioRegions. Training programmes were established to teach managerial skills to scientists interested in setting up their own business. Most importantly, the cooperation between science and industry, the centrepiece of the BioRegio concept, was greatly enhanced and intensified.

The outcome of the BioRegio competition is to some extent still reflected in the geographical distribution of biotech companies: Munich, Heidelberg, and Cologne are hotspots of innovative biotech companies in Germany today. In addition, Berlin has become a geographical focus for German biotechnology and clusters of biotech companies have also sprung up in most of the BioRegions established after 1996.

## 4 Academic research as an important basis for novel drugs

In 2008, an estimated total of 61.5 billion euros was invested into research and development in Germany. This corresponds to approximately 2.6 percent of the gross national product (GNP). By acknowledging the driving force of research in preparing for the “knowledge-driven society” of the future, as postulated by the European Commission in Lisbon in 2000, the German Government embraced the goal to increase spending on R&D to 3.0 percent of the GNP by the year 2010. This would mean an increase of 12 billion euros in two years.

Two thirds of all R&D in Germany are financed by companies and, naturally, most of these expenses are invested in applied projects with a clear market perspective within the industry. A significant amount (some 4 billion euros per year), however, is spent externally by companies on collaborative projects with academic institutions.

Most important biopharmaceutical innovations have originated from ideas and discoveries in universities and basic research centres. In fact, the biotech industry itself can – to a large extent – be considered a spin-off from academia – from its beginnings in the late 1970s at the University of California in San Francisco and Stanford up to the founding of German biotech companies originating from universities and the Max Planck and Helmholtz Institutes in the 1990s.

In the Federal Republic of Germany academic research is taking place and financed at different institutional levels. On one hand, by the 16 federal states (Bundesländer), all of which have their own ministries of research and education. On the other hand, research is centrally funded by the federal government (Federal Ministry of Education and Research, BMBF). However, the Federal Ministries of Health and of Economy are also involved in the fields of biomedicine and biopharmaceuticals.

As a result, the research landscape in Germany is highly differentiated and diversified: alongside the universities, including the medical schools and universities of applied science (Fachhochschulen) and directed and supported mainly by the federal states, there are four large research organisations which have established and run institutes with different approaches towards research and its social and economic impact:

- The **Max Planck Society for the Advancement of Science (MPG)** stands for basic research in new fields of science at the highest international level. The MPG is an independent non-profit association with an annual budget of about 1.4 billion euros, which is financed jointly in equal parts by the federal and state governments. The 80 Max Planck Institutes in Germany have approximately 13,000 staff members and 11,000 PhD students, postdoctoral researchers, and guest scientists, about one third of whom work in areas related to medical and pharmaceutical research.

- The **Helmholtz Association**, with 28,000 employees and an annual budget of approximately 2.5 billion euros, is Germany's largest scientific organisation, 90 percent are financed by the federal government and 10 percent by the states. The 15 centres of the Helmholtz Association provide particularly expensive equipment and infrastructure for national and international collaborations on a large scale. Their mission is "to perform cutting-edge research which contributes to solving the grand challenges of science, society, and industry". Four of these research centres are particularly important for drug discovery research. These are the German Cancer Research Centre, the Helmholtz Centre for Infection Research, the Helmholtz Centre Munich, and the Max Delbrück Centre for Molecular Medicine. In addition, some departments of Forschungszentrum Jülich and Forschungszentrum Karlsruhe also work on aspects of biopharmaceutical development.
- The **Fraunhofer Society** has more than 80 institutes and research units focusing on applied research with a direct impact on private and public enterprises as well as on society in general. Two thirds of its annual research budget totalling 1.5 billion euros is generated through contract research for the industry, the service sector, and public administration. Only one third of the budget is contributed by the German federal (90 percent) and state (10 percent) governments by way of institutional funding.
- The **Leibniz Association** combines a great diversity of institutes all over Germany, focusing on interdisciplinary research of strategic needs and social relevance at the junction between basic and applied science. The total annual budget of the 86 Leibniz Institutes (27 in the life sciences), which employ more than 14,000 people, is about 1 billion euros, covered in equal shares by the federal and state governments.

## 4.1 Universities

Germany has about 60 public universities conducting research in the life sciences. A useful indicator for ranking the research activities of universities is the amount of funding they are able to obtain from third-party sources. In 2005, such third-party funding for research in the life sciences amounted to about 1.8 billion euros, i.e. more than one third of the total finances from external sources. The majority of this (62 percent came from the German Science Foundation, DFG) was financed jointly by the federal government and the federal states. About 26 percent were provided by direct funding from the federal government and most of the rest by the European Commission as part of the 6th research framework programme, according to the German research ministry (Bundesbericht Forschung und Innovation 2008).

The universities of Berlin (including Charité, Germany's largest medical school, Free University and Humboldt University), Munich, and Heidelberg received the largest amount of external research funding in the life sciences sector followed by Freiburg, Würzburg, Tübingen, Hanover, Frankfurt/Main, Göttingen, and Cologne. Not surprisingly, these locations largely coincide with major BioRegions in Germany.

However, considering biotech spin-off companies from universities as one aspect of technology transfer from science to industry, the correlation with external funding is minimal. Apparently, innovative start-ups are mainly the result of the creativity and entrepreneurial spirit of individuals combined with efficient technology transfer facilities, the quality of which varies widely between universities. A number of companies presented in this study are spin-offs from smaller universities such as Bielefeld, Halle, Magdeburg, Münster, or Regensburg.

In 2005, the government launched the "Excellence Initiative" to strengthen cutting-edge research and competitiveness in order to make German science and research more visible in the international scientific community. A total of 1.9 billion euros of extra funding was provided for selected projects. In two rounds of the competition, the University and the Technical University of Munich, the Universities of Heidelberg, Freiburg, Göttingen, Constance, the Free University of Berlin, and the Technical Universities of Karlsruhe and Aachen were elected "Elite Universities". The Excellence Initiative also included funding for "Clusters of Excellence" concentrating research potential in specific fields. Some of these Clusters of Excellence have a focus on drug discovery and preclinical research, in particular:

- "From Regenerative Biology to Reconstructive Therapy" (Hanover Medical School);
- "Regenerative Therapies" (Technical University Dresden);
- "Cellular Stress Responses in Aging-Associated Diseases" (University of Cologne);
- "NeuroCure – Towards a Better Outcome of Neurological Disorders" (Charité, Berlin).

Many university hospitals and institutes have successful, long-standing collaborations with the pharmaceutical industry, most importantly in clinical trials. Supported by the Federal Ministry of Education and Research, a network of coordinating centres for clinical trials (KKS Network) has been established at 15 universities (Berlin, Cologne, Dresden, Düsseldorf, Essen, Freiburg, Halle, Hanover, Heidelberg, Leipzig, Mainz, Marburg, Munich, Münster, and Regensburg) providing a platform for transparent, patient-oriented development of new drugs and therapeutic principles. Some of these universities have special modules for paediatric trials as well. There are many institutes associated with but not part of the universities, e.g. the NMI-Natural and Medical Sciences Institute in Reutlingen which has pioneered developments in array technologies which are used in the pharmaceutical and biotech industries.



"To promote innovation, bridging the gap between academic research and industrial production is the key challenge, which can only be met by significant public funding. Measures such as BioPharma address this particular problem and will therefore positively impact Germany's role as a biotechnology hub."

Dr Jörn Erselius  
Managing Director,  
Max Planck Innovation, Munich

## 4.2 Max Planck Institutes

Max Planck Institutes enjoy an excellent reputation both internationally and within Germany. Engaging the best and brightest minds in science to conduct cutting-edge research at the interfaces of classic fields of knowledge, the Institutes claim no fewer than seventeen Nobel Prize Laureates among their ranks since 1954, and 54 scientists are amongst the most frequently cited in top international journals (ISI Ranking 2005). The Max Planck Society has become synonymous with outstanding research driven by the desire to seek answers to fundamental questions and to contribute to the benefit of human society, following the motto of its patron Max Planck (1919): "Insight must precede application". Science cannot thrive in an ivory tower. Groundbreaking ideas and inventions by Max Planck scientists have created new medical applications which are transferred to industrial products, especially to start-up companies by Max Planck Innovation, the technology transfer centre of MPG. Since 1996 about thirty biotech companies have evolved as spin-offs from Max Planck Institutes. In fact, renowned companies like Evotec, Develogen, MediGene, MorphoSys, Artemis (now TaconicArtemis), and SYGNIS (formerly Axaron) can trace some of their roots back to Max Planck researchers. Just like the US biotech company Sugent, bought by Pharmacia (now Pfizer), which developed a novel cancer drug, Sutent<sup>®</sup>, whose highly selective, multi-targeted specific mode of action was based on discoveries by Axel Ullrich and his team at the Max Planck Institute of Biochemistry.

Max Planck Society (MPG) has always been highly international. Its researchers come from virtually every country in the world and more than a quarter of its directors, who can independently determine the research areas of their departments, are from abroad. As part of a systematic internationalisation strategy to increase the presence of German science abroad, the Max Planck Institute Florida was founded in 2007 on the campus of the Florida Atlantic University in Palm Beach. The MPG also supports junior research groups and graduate student programmes in China together with the Chinese Academy of Sciences. Former guest scientists of Max Planck Institutes who have continued their research in their home countries with their own teams also receive financial support from MPG as partner groups.

More than thirty Max Planck Institutes are working in the biomedical sector; those engaged in fields directly related to medical and pharmaceutical research are listed below:

Name	Location
Max Planck Institute of Biochemistry	Martinsried
Max Planck Institute for Biophysical Chemistry	Göttingen
Max Planck Institute for Brain Research	Frankfurt/Main
Max Planck Institute of Colloids and Interfaces	Potsdam
Max Planck Institute for Developmental Biology	Tübingen
Max Planck Institute for Experimental Medicine	Göttingen
Max Planck Institute for Heart and Lung Research	Bad Nauheim
Max Planck Institute of Immunobiology	Freiburg
Max Planck Institute for Infection Biology	Berlin
Max Planck Institute for Medical Research	Heidelberg
Max Planck Institute of Molecular Biomedicine	Münster
Max Planck Institute of Molecular Cell Biology and Genetics	Dresden
Max Planck Institute for Molecular Genetics	Berlin
Max Planck Institute of Molecular Physiology	Dortmund
Max Planck Institute of Neurobiology	Martinsried
Max Planck Institute of Psychiatry	Munich

The Center of Advanced European Studies and Research (CAESAR) in Bonn is closely associated with Max Planck Society. Research projects at the centre focus on neurosciences aiming to be further developed into start-up companies.



Dr Ruth Herzog  
Head of Office of Technology  
Transfer/T010,  
German Cancer Research Centre  
(Deutsches Krebsforschungszentrum),  
Heidelberg

## 4.3 Research centres of the Helmholtz Association

### German Cancer Research Centre

The German Cancer Research Centre (Deutsches Krebsforschungszentrum, DKFZ) in Heidelberg is the largest biomedical research institution in Germany. As Ruth Herzog, Head of the DKFZ Technology Transfer, states:

“The purpose of the German Cancer Research Centre (DKFZ) is to conduct basic research and further develop the results for the benefit of cancer patients. To this end, the DKFZ forms strategic alliances: cooperating at the National Centre for Tumour Diseases with Heidelberg University Clinic as a partner to facilitate excellent and individualised therapy for cancer patients. The strategic partnership with Bayer Schering, in effect since January 2009, is intended to accelerate the development of new pharmaceuticals and to implement innovative ideas from DKFZ more rapidly. For new types of therapy concepts such as stem cell research for cancer therapy, the DKFZ is starting innovative ‘public-private partnerships’ and has found investors to start a non-profit limited company for translational stem cell research. The concept of the Heidelberg Institute for Stem Cell Research and Experimental Medicine (HI-STEM) is the core of the Rhine-Neckar BioRegion’s molecular and cell-based medicine cluster of excellence.”

Major advances developed at the DKFZ both in basic research and in new therapeutic approaches received special recognition when Harald zur Hausen was awarded the 2008 Nobel Prize in Medicine for his identification of human papilloma viruses (HPV) as tumour-causing agents. His research has led to the development of vaccines against HPV for the prevention of cervical carcinoma. These vaccines (Gardasil® from Merck & Co. and Cervarix® from GlaxoSmithKline) have been on the market since 2006 and 2007, respectively.

The DKFZ is also at the cutting edge worldwide in the field of tumour immunology. Research by Peter Krammer and his team focuses on cell proliferation and programmed cell death (apoptosis) to better understand the role of the immune system in cancer, AIDS, and autoimmune diseases. The findings are translated into new approaches for clinical application and have led to drug candidates to treat cancer and other indications targeting the signal pathways of apoptosis. The spin-off biotech company Apogenix is developing these innovative protein therapeutics.

### Helmholtz Centre for Infection Research

The key scientific objective at the Helmholtz Centre for Infection Research (HZI) in Braunschweig revolves around infectious diseases by studying fundamental principles such as the interaction between bacterial pathogens and their hosts on the one hand, and by developing strategies for the diagnosis, prevention, and treatment to combat dangerous infections on the other. The HZI with over 600 employees consists of five departments: (i) Cell and Immunobiology, (ii) Microbiology, (iii) Structural Biology, (iv) Molecular Biotechnology, and (v) Experimental Mouse Genetics. The major questions addressed in these departments are:

- What are the fundamental mechanisms of an infection and of the immune system’s reactions?
- What turns certain bacteria into pathogens?
- Why are some people particularly sensitive or particularly resistant to infections?
- How can we influence infection processes to prevent or cure diseases?

Answers to these questions will play a part in successfully combating infections caused by bacteria and viruses with new drugs and vaccines. For example, bacterial communities that are exceptionally well-suited to fight attacks by the immune system and antibiotics, often form aggregations of so-called biofilms which are responsible for severe illnesses. Disturbing the signalling cascade in the microbial communication, which leads to the formation of biofilms, opens up a novel route for the development of anti-infective therapeutics.

### Helmholtz Centre Munich – German Research Centre for Environmental Health

The Helmholtz Centre Munich (HZM) studies the complex interactions between environment and genetic predisposition. It is located in Neuherberg near Munich and employs a total of more than 1,500 staff members. Research at the HZM addresses questions such as how genes and the environment shape life, what factors contribute to our health and how we can develop strategies that prevent damage to both health and environment. With this approach, scientists at the HZM aim to identify health risks for humans and threats to ecosystems as early as possible in order to unravel the mechanisms that underlie the development of disease and to develop concepts leading to permanent prevention and cure. In pursuing these goals, a large epidemiological cohort study investigating the health status of 200,000 Germans over the period of the next twenty years has been initiated by the HZM.

Genetics play a key role in understanding the interaction between genome and environment as a starting point for all research at the HZM because the genome is partly responsible for how sensitively organisms respond to drugs or harmful influences. The Institute of Experimental Genetics (IEG) at the HZM studies, for example, the regulation of cell proliferation and differentiation by steroids and the role of peroxisomes in sterol and steroid metabolism as well as Zellweger syndrome (a hereditary peroxisomal disease) and various cancers. The Genome Analysis Centre at the institute provides a platform for the application of methods in genome, proteome, and metabolome research. The institute is also a partner of the European Mouse Mutant Archive (EMMA), the largest collection of relevant mouse mutant strains for basic biomedical research in the world. EMMA is a



“Especially in times of crisis, education and research become increasingly important. In the future, developing new active ingredients should be focused on disease prevention.”

**Prof Dr Walter Rosenthal**  
Scientific Director,  
Max Delbrück  
Centre for Molecular Medicine,  
MDC (Max-Delbrück-Centrum für  
Molekulare Medizin), Berlin

non-profit partnership of institutes all over Europe, supported by the European Commission, directed by Martin Hrabé de Angelis, also director of the IEG and Speaker of the National Genome Research Network (NGFN).

#### Max Delbrück Centre for Molecular Medicine (MDC)

The Max Delbrück Centre for Molecular Medicine (MDC), Berlin, combines molecular-biological basic research with clinical research in order to develop new diagnosis and treatment methods for serious diseases. Researchers at MDC cooperate closely with Robert Rössle Cancer Clinic, also on the Berlin campus, and Franz Volhard Cardiovascular Clinic at the Charité, the university medical school of both Humboldt University and Free University of Berlin. Since 2007, Charité and MDC have jointly operated the Experimental and Clinical Research Centre (ECRC), a translational institution to merge research and clinical application – “from bench to bedside”.

Research at MDC with its 740 staff members is centred around three large programmes, each combining basic science such as molecular genetics and cell biology of the diseases with clinical research:

- **Cardiovascular and Metabolic Diseases.** This includes heart disease, hypertension vascular disease, and kidney failure. In studying the causes of metabolic diseases the focus is on computational and molecular modelling, the role of miRNA, the function and dysfunction of ion transport, and systems biology of gene regulatory elements.
- **Cancer.** With a focus on signal transduction and growth control, structural genome research, and tumour immunology. The objectives are to utilise the knowledge gained from basic research at the molecular level for the development of improved diagnostics and new treatments of cancer.
- **Function and Dysfunction of the Nervous System.** By studying the molecular and cellular bases of the healthy and pathological nervous system, new approaches for treatment of CNS diseases are pursued.

Collaborations include projects with the Max Planck Institutes for Infection Biology and Molecular Genetics in Berlin as well as many other scientific institutions in Germany and abroad. The MDC also closely collaborates in pharmacological research with the Leibniz Institute for Molecular Pharmacology (FMP, see Chapters 4 to 5), which moved to the MDC-Campus in Berlin. The former director of the FMP, Walter Rosenthal, became Scientific Director of the MDC in 2009.

#### Research Centre Jülich

Two institutes of the Research Centre Jülich (Forschungszentrum Jülich, FZJ) have to be presented in the context of this study. The Institute of Neurosciences and Medicine (INM) is devoted to interdisciplinary research on signal processing in and between individual nerve cells, in neural circuits, and in the complex networks of the human brain. Ion channels, which are essential for the transmission of signals between cells, are examined using sensitive biophysical technologies. The Institute of Biotechnology (IBT) focuses on the development of biotechnological processes for manufacturing pharmaceutical and chemical products. Together with the Institutes of Molecular Enzyme Technology and Bioorganic Chemistry of the University of Düsseldorf, the IBT forms a biotechnology centre at the FZJ which has established new chemical and enzymatic processes for the synthesis of small molecules. Thanks to its former head Christian Wandrey from the University of Bonn, the IBT has

played an outstanding role in developing and improving fermentation technology and technical biocatalysis as a basis for biopharmaceutical manufacturing in Germany.

## 4.4 Research centres of the Leibniz Association

There are 27 Leibniz Institutes devoted to research in the life sciences. Those with relevance to drug discovery and biopharmaceuticals are listed in the table:

Name	Abbr.	Location	Major research areas
Bernhard Nocht Institute for Tropical Diseases	BNI	Hamburg	Leishmania, Malaria, filariasis, tropical viral diseases
German Diabetes Center	DDZ	Düsseldorf	Molecular, cellular and clinical diabetology
German Institute of Human Nutrition	DIfE	Bergholz-Rehbrücke (Potsdam)	Nutrigenomics: Relation between nutrition and health from molecular basis to clinical application
German Primate Center	DPZ	Göttingen	Biological and biomedical research with primates. Coordinator of the European Primate Network
Leibniz Institute for Molecular Pharmacology	FMP	Berlin	Signal transduction, amyloid formation, protein-protein interactions
Research Center Borstel for Medicine and Biosciences	FZB	Borstel	Pneumology (infection biology, allergology and chronic inflammatory diseases)
Hans Knöll Institute for Natural Product Research and Infection Biology	HKI	Jena	Pathogenic bacteria and fungi
Heinrich Pette Institute for Experimental Virology and Immunology	HPI	Hamburg	Virus-host interactions and cellular dysregulation by pathogenic viruses
Institute for Neurobiology	IFN	Magdeburg	Mechanisms of learning and memory
Leibniz Institute for Research on Arteriosclerosis	LIFA	Münster	Cytokines, chemokines and enzymes in atherosclerotic plaque formation

The Hans Knöll Institute (HKI), Jena, has developed a novel drug against tuberculosis which has recently been licensed to the US company Inverness and its subsidiary CLONDIAG in Jena, a spin-off of the HKI. The Leibniz Institute for Molecular Pharmacology (FMP), Berlin, focuses on the

development of new concepts for interfering pharmacologically with protein functions. At the Leibniz Institute for Neurobiology (IfN), Magdeburg, the composition and dynamics of synapses and the interaction of their proteins are a special research focus with the objective of finding new drug targets in neurons. Other aspects are the communication mechanisms at both the cellular and the circuit level in behaviour and learning processes.

## 4.5 Fraunhofer Institutes

Five institutes are especially significant for drug discovery and biopharmaceutical developments in Germany. These institutes have joined forces in the Alliance Life Science of the Fraunhofer Society to offer a broad range of methods and services:

The **Fraunhofer Institute for Biomedical Engineering (Fh-IBMT)**, with locations in Potsdam, St. Ingbert, and Lübeck, focuses on developments for molecular and cellular biotechnology and medicine, e.g. in the areas of microarray technology, cryotechnology, biocompatibility, extremophile research in particular at the interfaces between technical and biological microsystems.

The **Fraunhofer Institute for Immunology and Cell Therapy Fh-IZI**, in Leipzig. Core competencies are in cell-therapeutic (tissue engineering) methods of regenerating non-functioning tissue and organs. The institute also works closely with hospital institutions performing quality tests and clinical studies on their behalf.

The **Fraunhofer Institute for Interfacial Engineering and Biotechnology Fh-IGB**, in Stuttgart develops and optimises processes and products for medical and pharmaceutical businesses, for example. The institute has developed a three-dimensional skin model which has received accreditation for biological compatibility tests avoiding animal testing.

The **Fraunhofer Institute for Molecular Biology and Applied Ecology Fh-IME**, with two sites in Aachen and Schmallenberg. The Fh-IME in Aachen, focusing on molecular biology and biotechnology, has developed a monoclonal anti-HIV antibody (2G12) selected for production in tobacco plants which has passed preclinical testing and is about to enter Phase I clinical study. The development is part of an integrated project (Pharma-Planta) within the European 6th Framework Programme which is coordinated by Fh-IME.

The **Fraunhofer Institute for Toxicology and Experimental Medicine Fh-ITEM**, in Hanover. Research and services include preclinical studies on pharmaceuticals, toxico- and pharmacokinetic as well as pharmacogenetic studies, drug registration studies and clinical drug research and development for the indications of allergy, asthma and chronic obstructive pulmonary disease.

## 4.6 European Molecular Biology Laboratory – EMBL

EMBL is one of the top research institutions in the world and the flagship of European molecular biology. It is financed by public research funds from twenty member states including nearly all of Western Europe and Israel. EMBL, which has its main laboratory in Heidelberg, is designed to perform basic research in molecular, cellular, and developmental biology and to train scientists to the highest international standards, offer services to scientists in member states, and to develop new instruments and methods in the life sciences. It was at EMBL that Christiane Nüsslein-Volhard and Eric F. Wieschaus, now honoured with the Nobel Prize, made their discoveries of genes that control the development and body plans of flies and fish. EMBL also pioneered bioinformatics developing the first public DNA databases and coordinating a wide range of biological data from DNA and RNA sequences and genomes to microarray-based gene expression, protein sequences, and macromolecular structures. New mass spectrometry techniques combined with non-invasive purification of macromolecular complexes made EMBL one of the leading centres for proteomics, and was the technology behind the drug discovery activities of EMBL's spin-off company Cellzome.

## 4.7 Technology transfer

Technology transfer at the interface between academic research and industry has in the past reflected the diversity of the academic landscape. At universities in particular, technological transfer offices were often understaffed and underpaid yielding unsatisfactory results. This scene is changing rapidly, however, and professional and efficient technology transfer companies have been established.

The Max Planck Society has set up **Max Planck Innovation (MI)** as the central technology transfer centre for Max Planck Institutes all over Germany. MI organises the transfer of new ideas and inventions from Max Planck scientists to industrial products, providing professional support and issuing licences to innovative companies. It has been pivotal in the foundation of start-ups that are essentially spin-offs from Max Planck Institutes.

Most scientific results from Max Planck Institutes relevant to therapy are, however, still in the early stages of development and not yet of interest to the pharma industry or private investors. In order to develop these leads into marketable products, MI founded the **Lead Discovery Centre (LDC)** in 2008. The LDC, located in Dortmund close to the MPI for Molecular Physiology and the associated Chemical Genomic Centre, is a commercial research company integrating the areas of biology, medicinal chemistry, and pharmacology along with professional project management. It is active in the identification and characterisation of innovative leads and their preclinical development to drug candidates.

Drug discovery has historically been conducted within the pharmaceutical and biotech industries on account of the associated high risks and costs.



“Excellence in the field of basic research is a key to groundbreaking innovation. Thus, it makes no sense to support research activities solely for the purpose of practical implementation. Rather, we need to establish more effective tools to recognise promising basic research at an early stage as well as to safeguard and develop the results effectively. In these respects, I see a weakness in Germany while, at the same time, the main task for us and our partners is technology transfer.”

Dr Christian A. Stein  
Managing Director, Ascenion GmbH

Nowadays, multiple initiatives are being instigated in the area of academic drug discovery to create research driven drug discovery networks and to build links between academia and industry. The **European ScreeningPort** located in Hamburg, Germany, is a recent addition to the ranks of drug discovery service providers for the academic sector within Germany and Europe. The aim is to fill up industrial pipelines with the innovative science taking place in academic laboratories.

One success story for technology transfer by Max Planck Institutes has been Sutent®, a cancer drug which acts by blocking several molecular targets simultaneously. Its medical application was developed by the US biotech company Sugen. After the company was bought by Pharmacia (now Pfizer), Sutent® was developed into a marketable drug approved for the treatment of gastrointestinal stromal tumours and renal cell carcinoma by the FDA and the EMEA in 2006.

The technology transfer company **Ascenion** was set up by the Life Science Foundation formed by life science research centres of the Helmholtz Association together with some institutes of the Leibniz Association. Ascenion is the exclusive partner of twelve life science institutes of the Helmholtz and Leibniz Associations as well as of the Hanover Medical School. It also coordinates technology transfer from the German National Genome Research Network. Since its inception in 2001, Ascenion has negotiated close to 300 agreements between research and industry and has promoted and accompanied 18 spin-offs through their foundation and early growth. Ascenion holds equity in twelve of these companies and is responsible for the asset management and commercialisation of the intellectual property generated by all Helmholtz centres in the life science area, with the exception of the German Cancer Research Centre (DKFZ).

The greatest success of the **DKFZ Office of Technology Transfer** in the biopharmaceutical sector has been the licensing of the Human Papilloma Virus vaccine for the prevention of cervical carcinoma to Merck & Co. and GlaxoSmithKline. Together with EMBLEM, an affiliate and the commercial arm of the European Molecular Biology Laboratory (EMBL), the DKFZ is also responsible for technology transfer at the University of Heidelberg's Clinics & Medical Faculty.

**EMBLEM** (EMBL Enterprise Management Technology Transfer) was established in 1999 to identify, protect, and commercialise the intellectual property developed in the EMBL world, from EMBL alumni, and from third parties. EMBLEM facilitates and accelerates the transfer of innovative technology from basic research to industry by working closely with industrial partners to develop new diagnostics, drugs, therapies, and machinery and equipment. EMBLEM has also been involved in the foundation of spin-off companies from EMBL such as Cellzome in Heidelberg and Cenix Bioscience in Dresden.

The **ipal** (innovations, patents, licences) is financed jointly by the three universities and technical universities of applied science in Berlin as well as the Investitionsbank Berlin, the subsidy institution of the Federal Land of Berlin. It works as a patent usage agency exclusively for Charité University of Medicine, as well as Robert Koch Institute and Paul-Ehrlich-Institut, two central institutions for health protection and pharmacovigilance of the German government.

## 5 Indication areas, novel drug candidates, key players

### 5.1 Major therapeutic areas and development pipeline

In Germany, like in most Western countries, the major causes of disease and death are cardiovascular diseases and cancer, followed by diseases of the respiratory tract, metabolic and neurodegenerative disorders. The incidence of these illnesses correlates to a large extent with age. In view of our rapidly ageing population, their frequency will increase further unless effective treatments are made available. The average life expectancy of German females is presently 82 years and that of males 76 years. By 2050 it will be close to 90 years for both genders. Half of the children born in 2050 are expected to live up to one hundred years. The greatest challenges facing present-day medical research and industry are to find cures for major threats such as cardiovascular disease, all principal kinds of cancer, pulmonary, neurological, or endocrine disorders as well as other unmet medical needs including treatments for most rare diseases.

Both pharmaceutical industry and biotech companies have taken on these challenges. Major research and development activities focus on the indication areas of cardiac infarction, strokes, and thromboses, all principal kinds of cancer, COPD and asthma, diabetes and obesity, and Alzheimer's and Parkinson's disease. There is also a strong focus on the development of new drugs against HIV/AIDS and hepatitis C infections. However, other kinds of infectious diseases, such as malaria, the most important cause of death in developing countries, are only areas of intense research in academic institutions rather than in commercial enterprises.

Big pharmaceutical companies are active in most of these areas, although with different focal points. They usually concentrate their efforts on indications affecting large populations, aiming for blockbuster products. Biotech companies, on the other hand, often conduct research in niche indications, taking advantage of or aiming for Orphan Drug Designation for the treatment of rare diseases.

**Boehringer Ingelheim** has drugs on the market or in the pipeline in all major indication areas: respiratory and metabolic diseases, cardiovascular diseases, and diseases of the CNS as well as oncology and virology (HIV/AIDS), immunology and inflammation. Examples in advanced clinical studies are new developments for the treatment of type II diabetes (DPP-IV inhibitors and sodium-dependent glucose transport inhibitors), and an epidermal growth factor inhibitor against lung cancer and an inhibitor of tumour angiogenesis as well as a new therapy against COPD. The company has a strong focus on Parkinson's as well as major depressive disorder, strokes, and hypertension.

**Merck KGaA**, Darmstadt, which has intensified its biotechnological research and development after the acquisition of Serono, provides drugs as **Merck Serono** in the areas of cancer, multiple sclerosis, infertility, metabolic and cardiometabolic diseases as well as psoriasis. Research and development is mainly in the areas of neurology (Parkinson's, multiple sclerosis) and



“To generate growth, the big pharmaceutical companies no longer exclusively rely on the productivity of their own research pipelines. On one hand, this explains the latest wave of mergers. On the other hand, there is an increasing trend toward in-licensing product candidates and various types of cooperation with innovative biotech companies. Hence, the competitive advantage goes to those who are successful in finding new ways of cooperation between Big Pharma and biotechnology.”

Prof Dr Torsten Strohmeyer  
VP Medical & Regulatory Affairs,  
GlaxoSmithKline GmbH & Co. KG



“The UCB-WILEX alliance represents a new kind of flexible and innovative approach to biopharmaceutical product development.”

Prof Dr Olaf Wilhelm  
Chief Executive Officer, Willex AG

oncology, but the company is also interested in autoimmune diseases (systemic lupus erythematoses and rheumatoid arthritis) and inflammation. There are 28 projects undergoing clinical trials at present, for example studies to expand the application of Erbitux, the company's best-selling drug for the treatment of lung and gastric cancer. Also in advanced stages of clinical development are a vaccine (Stimuvax) for the treatment of non-small cell lung cancer (NSCPC), and a small-molecule integrin inhibitor for treatment of glioblastoma.

**Bayer Schering Pharma** presently has 20 projects in Phase III clinical trials, six of which are new medical entities (NME). There are 19 more NMEs in Phases I and II, mostly in the areas of COPD, acute cardiac infarction, pulmonary inflammation, stroke, thrombosis, and multiple sclerosis. In the oncology sector, Bayer has a small molecule multikinase inhibitor Sorafenib, which has orphan drug status for the treatment of advanced liver and kidney carcinomas, and clinical studies are on the way for the treatment of NSCPC and metastatic melanoma. Bayer is also developing a tracer methodology for the early diagnosis of Alzheimer's disease.

Cancer is by far the most important indication area for innovative drug development by German biotechnology companies. **MediGene**, which was the first German biotech company to place drugs on the market (Eligard, a hormone preparation for the treatment of prostate cancer, and polyphenon against genital warts) is developing a novel drug (EndoTAG) in Phase II for pancreatic cancer and Phase I for breast cancer. Also in Phase II are oncolytic viruses for the treatment of metastases of colon carcinoma. **Immatics** has product developments against colorectal carcinoma and renal cell carcinoma (both in Phase II) and **CureVac** against prostate cancer and NSCPC carcinoma. **Willex** is developing small molecule drugs for the treatment as well as early diagnosis of various types of cancer. The company is also pursuing the development of a therapeutic antibody in the indication renal cell carcinoma. Recently, the company has taken over the oncology portfolio of UCB for further development. **Antisense Pharma** has developed a DNA-based antisense drug candidate presently in Phase IIb against malignant brain tumours. Silence Therapeutics has developed novel proprietary siRNA, which has been chemically modified to result in a blunt-ended, chemically stabilised molecule, which contains only naturally-occurring RNA. The company has preclinical programs for pancreatic cancer, lung cancer, prostate cancer, and liver cancer. The medium-sized pharma company **biosyn** has developed compounds based on haemocyanins for use in bladder cancer and as carriers for therapeutic vaccines.

Recombinant antibodies have become an important substance class in the search for effective new drugs against cancer. **MorphoSys** is presently transforming from a platform company into a drug developer, and, on the basis of its HuCAL patent family, is building a strong therapeutic antibody pipeline, mainly through partnerships, but also increasingly on its own. The focus is on antibody-based drugs against cancer and other life-threatening diseases.

**TRION Pharma** has developed Removab®, a novel trifunctional antibody against malignant ascites, which is developed for the market by **Fresenius Biotech**. The Marketing Authorisation has been granted by the European

Commission in April, following the EMEA recommendation in February 2009. It has also developed an antibody against gastrointestinal cancer. **GANYMED Pharmaceuticals** has developed strict tumour-specific “ideal” antibodies (iMABs) for the treatment of solid tumours, one of which is about to enter clinical trial for metastatic gastro-esophageal carcinoma. **Micromet** has two antibodies in clinical trials against Acute Lymphoblastic Leukaemia, Non-Hodgkin's Lymphoma, and metastatic breast carcinoma. **Affimed Therapeutics** is developing novel antibody formats for the treatment of Non-Hodgkin's and Hodgkin's Lymphoma which are about to enter clinical studies. GlycoTope also develops second-generation glyco-optimised antibodies for the treatment of cancer.

**Apogenix** is developing protein therapeutics targeting modulators of the apoptosis pathway (programmed cell death). Currently the company focuses on the treatment of glioblastoma and on the immunological orphan indication “acute graft-versus-host disease”. The immunological company **Vakzine Projekt Management** is developing vaccines for the treatment of prostate cancer; it is also active in the indication areas of multiple sclerosis and infectious diseases, namely tuberculosis and human cytomegalovirus. Novel immunological therapeutics for the treatment of insect venom allergy and inflammation are being developed by **PLS-Design**.

Treatment of neurodegenerative diseases and neurological disorders are also important indications for drug development by the biotech industry. **SYGNIS Pharma**, a company formed in 2007 by fusion of Axaron and LION in 2007, has a drug candidate, AX200, which successfully completed Phase II studies for the treatment of stroke and has received Orphan Drug Designation for the treatment of amyotrophic lateral sclerosis and spinal cord injury. **PAION**, after its initial set-back for its drug Desmoteplase against acute ischemic stroke, is now entering another Phase III study for its drug in a restricted indication of stroke. **Axxonis Pharma** has identified new compounds which protect neurons against ageing and degeneration for the treatment of neurodegenerative diseases. **Affectis Pharmaceuticals**, a spin-off from the Max Planck Institute of Psychiatry, has developed a drug candidate against depression, targeting a newly discovered ion channel in the brain. Alzheimer's disease has been the major indication for research and development of small molecule drugs by **Merz Pharma**, a medium-sized pharma company and by **Probiodrug**, a company in Halle (Saale) which has in vivo data supporting a potentially causative new treatment of neurodegeneration in Alzheimer's. The treatment options available today can only temporarily slow down the progression of the disease.

**Schwarz Pharma**, which was bought by the Belgian biopharmaceutical company **UCB** in 2006, is dedicated to research and development of central nervous system disorders such as epilepsy, as well as multiple sclerosis, allergies, respiratory diseases, and inflammation. **Revotar** develops innovative drugs for inflammatory indications such as psoriasis, asthma, COPD, and acute lung injury. In January 2009, the company started a Phase II study to evaluate the safety and efficacy of Bimosiamose 5 percent Cream for the treatment of patients with chronic plaque-type psoriasis. **IDEA** has developed a non-steroidal, anti-inflammatory drug currently in the registration process.



“Real innovations are rare, but they are very important for Germany as a location for business. However, they must also make an impact on the market.”

Dr Dirk Pelster  
Chief Operating Officer,  
TRION Pharma GmbH



“In Germany, the drive toward innovation in active ingredient development is strong. Target-oriented thinking will further improve both practical implementation and medical benefits effectively.”

Dr Bernd Eisele  
Chief Executive Officer,  
Vakzine Projekt Management GmbH



“We are convinced to have promising clinical candidates at advanced stages of development in our pipeline, enabling us to contribute to the effective development of active ingredients in Germany.”

Dr Frank Striggow  
Chief Executive Officer,  
Keyneurotek Pharmaceuticals AG

**Jerini** has successfully registered a peptide drug against hereditary angioedema. The company was recently bought by **Shire**, also an important developer of treatments against metabolic diseases caused by genetic defects. **Cytonet**, a cell therapy company, has developed therapeutic liver cell preparations for treatment of genetically induced metabolic diseases of the liver as well as acute liver failure. This cell-based medication is now going through Phase III clinical trials. **Phenex Pharmaceuticals** focuses on the development of small molecules targeting nuclear receptors for the therapy of metabolic syndrome and type II diabetes. **Curatis Pharma** also develops small molecules for the treatment of metabolic diseases. Treatment of metabolic and endocrine disorders, particularly diabetes, is the focus of **Develogen**. The company develops small molecule anti-diabetic drug candidates as well as a novel somatostatin analoga to fight acromegaly and diabetic retinopathy.

## 5.2 Process development and manufacturing

In addition to the actual drug developers, many other market players along the value chain are significant in maintaining a sustainable drug discovery environment.

Excellent quality, reliability, and efficiency have always been the hallmarks of Germany as a production site thanks to its highly skilled workforce. Bioprocess engineering has been strong since the early days of brewing technology. The first biotech plant managers were brewers some 40 years ago. Bioprocess engineering was then established under Professors Fritz Wagner and Joachim Klein in Braunschweig at today's HZI, Helmholtz Centre for Infection Research, and Professors Hermann Sahm and Christian Wandrey in Jülich at the Nuclear Research Centre (Kernforschungsanlage Jülich). Scholars who studied under these pioneering master minds have gone on to become the heads of the world's largest plants.

Investors and customers of German partners are attracted by the high level of productivity and the focus on new technologies. In this field, Germany certainly plays in the top division. According to the German Association of Research-based Pharmaceutical Companies (VFA), a fermenter capacity totalling 640,000 litres is available in Germany, putting it in second place worldwide after the United States. The trade fair organiser Interphex presents annual awards to the “Facilities of the Year”. Last year, four out of five of these awards went to German companies, namely to Boehringer Ingelheim, Roche (Penzberg), and IDT Biologika (Dessau).

**Roche Diagnostics** in Penzberg received the award “Best Project Execution” for its new Herceptin® production site Biologics IV. At present, Roche has more than 4,500 employees in Penzberg and sees itself as one of the biggest biotech research and production sites in Europe. In fact, it is the biggest R&D and production site not only for pharmaceuticals but also for innovative, biotechnologically engineered compounds and for state-of-the-art diagnostic technologies within the huge Roche group. In the course of the TP expansion strategy, Roche is investing an additional 172 million euros into strengthening its activities in the development of therapeutic proteins by designing new cell lines, optimising established processes, and creating new ones, as well as supplying clinical developers with protein

derived APIs. In addition, Roche Diagnostics has invested about 1.5 billion euros over the last ten years in its site at Mannheim, expanding its research and production capacities and creating new jobs.

Another big player in Germany and globally is **Boehringer Ingelheim**. Founded almost 135 years ago, it is still exclusively family-owned. This fact, along with many others, accounts for the numerous acknowledgements it has received as one of the best employers in Germany and abroad. Boehringer employs almost 40,000 people worldwide, about 10,000 of whom work in Germany. The company currently has about 135 affiliated firms in and outside of Germany and its headquarters are based in the geographically attractive Ingelheim, situated on the left bank of the Rhine, near Frankfurt. Boehringer researches, develops, and manufactures pharmaceuticals as well as biopharmaceuticals, focussing on human and animal health. In fact, it is one of the world's largest suppliers of biopharmaceuticals to industrial customers. In the past ten years, Boehringer has made huge investments to expand its production and research facilities. The German sites in Dortmund, Biberach, and Ingelheim accounted for 44 percent of the investments made in 2007 (654 million euros in total). Boehringer invests a large part of its revenues in R&D activities (16 percent in 2007). In October 2007, Boehringer decided to continue its expansion strategy and invested a further 35 million euros in a new research centre for animal vaccines in the northern part of Germany (Hanover), which is set to become the fourth largest site in Germany.

Based in the southern part of Germany is the cutting-edge manufacturer **Rentschler Biotechnology**. It was Rentschler who obtained the world's first approval for an interferon-derived drug. On the strength of its former success, Rentschler still offers a first-class full service for developing, producing, and approving (bio)pharmaceuticals in accordance with the strict GMP guidelines.

The same high manufacturing standards are adopted by many other manufacturers in Germany. Examples in the west include **Rhein Biotech (Dynavax Europe)** in Düsseldorf, **BIBITEC** (co-founded by Jürgen Schumacher) and **PlasmidFactory**, both in Bielefeld. Each of them produces active pharmaceutical ingredients derived either from cell lines or prokaryotes for use in clinical trials on humans. Rhein Biotech and BIBITEC have strong expertise in cell culture techniques for the expression of recombinant proteins and in purification, whereas PlasmidFactory focuses on the production of plasmid DNA for research and industry, for example, for vaccination or drug delivery. On top of that, Rhein Biotech combines process development with unique product development skills and became the first company worldwide to develop a generic hepatitis B vaccine from bench to market in 1999.

Northern Germany is home to **Richter Helm Biotec**, for example, which supplies (bio)pharmaceutical industries with products developed and manufactured to high standards. **Essex Animal Health** in Lower Saxony is a subsidiary of Essex Pharma in Munich and focuses on developing and producing veterinary vaccines.

**Riemser** began in 1992 as a spin-off from the Friedrich Löffler Institut, Riems/Greifswald, the oldest virus research institute in the world. Starting with the development and production of veterinary drugs, the company now focuses on human pharmaceuticals (Antiinfectiva, Dermatologica,

Oncologica) and has successfully developed into the most dynamic mid-sized pharmaceutical company in Germany (86 million euros turnover and 640 employees in 2008).

**Miltenyi Bioprocess**, the contract manufacturing division of Miltenyi Biotec based in Teterow near Rostock since 2002 with 165 employees, provides services for the production of biopharmaceuticals like recombinant proteins and monoclonal antibodies and the production of conjugates of biomolecules.

**Nycomed** has a manufacturing site for pharmaceuticals in Oranienburg near Berlin. Similarly, **Bavarian Nordic** has a GMP site for contract production in Berlin. Again in the eastern part of Germany, established pharmaceutical suppliers and new biotech companies conduct state-of-the-art contract development and manufacturing. **IDT Biologika**, one of the prize winners of the Interphex award, provides services throughout the whole development chain of an API for clinical testing or even commercialisation from formulation and large-scale production to packaging and quality assurance.

**GlaxoSmithKline Biologicals**, formerly Sächsisches Serumwerk (SSK), Dresden has been a specialist in the development and manufacture of flu vaccines for about 100 years. Each year, some 30 million vaccine doses leave GSK Biologicals' production line, accounting for 10 percent of flu vaccines worldwide. Moreover, GSK Biologicals was the first company to gain authorisation for pre-pandemic and pandemic H5N1 vaccine and, in the case of a bird flu pandemic, has the capacity for the large-scale production of a pandemic vaccine within a short period of time.

**SCIL Proteins**, a relatively small but highly dynamic company, offers a wide range of expression services for recombinant proteins using microbial systems. The proteins can be produced under GMP and non-GMP conditions, depending on the client's purposes. The company carries out pre-fermentation development, such as cell line design and up-scale process planning through process control and validation to refolding extracted proteins and analysing quality. **BIOMEVA** produces biopharmaceuticals in recombinant microbial systems under GMP conditions using up to 1,000 fermenters. The Heidelberg-based company's roots go back to the early 1980s.

A point worth noting is that all of these companies have proven excellence in process development and optimisation. One more institution deserves mentioning here, even though it is not commercial. The **Max Planck Institute for Dynamics of Complex Technical Systems**, Magdeburg (MPI Magdeburg), is hugely involved in the optimisation of chemical and biotechnological processes. Experts from different scientific disciplines network with the objective of improving the performance and efficiency of processes employed by chemical and biotech engineers. MPI Magdeburg interacts closely with different pharmaceutical and biotech companies to ensure the exchange of knowledge and know-how.

## 5.3 Preclinical and clinical development

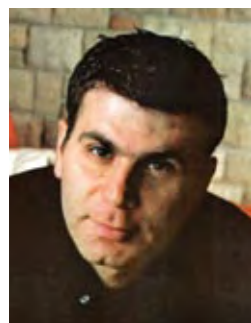
Prior to the market launch of a new compound drug, developers have to test their drug candidates in preclinical and clinical trials. Preclinical tests primarily require well-established *in vitro* and *in vivo* models. Many service providers work in this area in Germany.

The recently formed **Research Centre for Innovative Drugs and Therapy** at the University of Bonn combines drug discovery, optimisation, and approval of self-developed cell and animal models. It is also referred to as the PharmaCenter Bonn and is one of the "NeuroAlliance" consortium award-winning partners at the Pharma Competition initiated by the German Federal Ministry of Education and Research (BMBF). The broad scientific spectrum of PharmaCenter Bonn not only covers the investigation of new therapeutic approaches, but also pharmacological issues and the establishment of *in vitro* and *in vivo* disease models. PharmaCenter Bonn works closely with several pharmaceutical and biotech companies, as well as with academic institutions.

The **Fraunhofer Institute of Toxicology and Experimental Medicine** (Fraunhofer ITEM) is an institution of the Fraunhofer Society to promote applied research in the fields of life science, especially biomedicine, biotechnology, and toxicology. The Fraunhofer ITEM is based in Hanover and is active in four business areas: drug research, medical biotechnology and molecular medicine (1), clinical airway research (2), occupational and environmental toxicology and consumer protection (3), and testing and registering chemicals, biocides, and pesticides (4). In all these areas Fraunhofer ITEM offers its customers state-of-the-art testing technologies for chemicals, biocides, pesticides, and (bio)pharmaceuticals. For this purpose, primary and transgenic cell cultures, miscellaneous disease models (e.g. asthma and allergy), and many other techniques are available.

**Across Barriers**, based in Saarbrücken on the French border, develops and delivers testing technologies and services for the pharmaceutical, chemical, and cosmetics industries. The services provided by Across Barriers include permeability studies on the basis of established cell and tissue *in vitro* models, which are conducted for various indications at an early development stage. Thus, customers may benefit from valuable information on the real potential of the new agent, while avoiding long, expensive blind-alleys and cutting development costs.

After identifying a lead compound and testing *in vitro* efficacy, toxicity, and pharmacokinetic tests have to be carried out *in vivo*. To this end, tried and tested animal models for defined diseases are required. **Encepharm** in Göttingen, in the heart of Germany, offers well-established animal models for depression, multiple sclerosis, and Parkinson's. Through cooperation with individual research institutions, Encepharm has a wide range of techniques at its disposal.



“Germany has very strong basic research and manufacturing expertise. Looking into the future, we need to leverage these key sources and enhance our competitive advantage. The industry needs to embrace innovative computational modeling as a key element in making significant progress in R&D.”

Sion Balass  
Chief Executive Officer,  
Matrix Advanced Solutions Ltd.

## 5.4 Other services

To ensure the success of a drug development project, many other service providers are needed to complete the value chain, supporting customers with innovative methods and technologies.

Even at the initial stages of drug development, the search for promising compounds could be diversified by applying bioinformatics. Furthermore, simulation of in-cell processes, such as the side effects of a drug, can be conducted *in silico*. **BIOBASE** uses instruments developed in-house, such as pathways databases, protein libraries, and analysis tools supporting drug discovery.

**Insilico Biotechnology** in Stuttgart is successfully offering computational models of living cells for the optimisation of production processes.

**ElexoPharm** in Saarbrücken, performs lead discovery and optimisation on a contract research basis using a broad range of analytical and synthetic methods.

Synthesis of nucleic acids for research and drug development purposes is one of the essentials for companies operating in drug discovery, not only in Germany but also worldwide. Though relatively young, **GENEART**, Regensburg, has become the global leader in the manufacturing of synthetic genes. All forms of gene sequences can be created, optimised, manipulated, and manufactured to meet GMP standards.

**Newlab Bioquality**, founded by the Qiagen entrepreneur Jürgen Schumacher, offers comprehensive GLP/GMP compliant solutions for the quality control of biopharmaceuticals. The company was recently sold to the Charles River Group for 34 million euros. The **PlasmidFactory** is an innovative contract manufacturer of plasmid DNA, located in Bielefeld.

**Genix**, a ten-year old biotech company in eastern Germany, provides well-grounded, methodical solutions for the field of RNAi. A spin-off of the European Molecular Biology Laboratory, Heidelberg, and the Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Genix initially conducted research on and development of new targets for RNAi technology, following the decision to combine all acquired expertise to serve academic, pharmaceutical, and biotech partners in the development and testing of new therapeutic compounds. A whole range of human and rodent cell lines and optimised procedures are available, enabling Genix to conduct high throughput screenings and assay improvement within a short timeframe.

**Glycotope** offers an analogue tool for lead optimisation regarding the glycosylation patterns of a required protein. They offer their customers an elaborate set of tools comprising glyco-engineered cell lines for glyco-optimisation of biological compounds at the early development stage and right on up to GMP production.

Alongside the research activities in drug development, **CellGenix Technologie Transfer** offers GMP contract manufacturing services for cell and protein therapeutics on a large scale too. **PomBioTech** offers

custom-made recombinant, yeast-based expression systems. Additionally, the company is able to design and implement the whole fermentation process.

A number of young biotech companies in Rostock have developed validated, cell-based, pre-screening test systems for drug candidates, reducing the number of animal tests, for example **Cytocentrics**, **bionas**, **Neuroproof**.

## 5.5 Collaboration schemes and public funding

Developing new treatments from the research laboratory to the market place is a very expensive and time-consuming process, beyond the means of most biotech companies which are generally very small. In order to stimulate the transfer from science to industry and to support biotech companies in the early high-risk phases of product development, BMBF has restructured its funding policy in the area of innovative pharmaceuticals development under the title “**Pharmaceutical Initiative of Germany**” and has launched a number of funding initiatives. These funds provide financial support for research and development on new medicines in Germany.

The **GO-Bio** scheme supports high-risk projects with start-up potential in the early phases of the academic research laboratory. It offers support and encourages excellent young scientists to focus on the future commercialisation of their projects, to gain entrepreneurial expertise, and to build up a team for a start-up company. Under the **BioChancePlus** programme, the BMBF is supporting small and medium-sized biotech companies in order to broaden the scope in advanced technology and strengthen their position in the market. Funding is provided primarily to cooperative projects between partners supporting the integration of biotechnological research and pharmaceutical development.

At the heart of the Pharmaceutical Initiative is the **BioPharma Competition** launched in 2007 whose goal is to establish structural consortia of small and large companies and partners from science and clinical practice to join forces for the sake of effective drug development. A total of 100 million euros have been made available for the three winning teams.

The **Max Planck Drug Discovery & Development Center (DDC)** aims to accelerate the process from the early stages of therapeutic research carried out by Max Planck Institutes to market launch. Private investors and the pharmaceutical industry participate in this process by contributing towards a fund. At the centre of the consortium is the **Lead Discovery Center (LDC)** which closely collaborates with Max Planck Institutes all over Germany on the one hand and with the German pharmaceutical industry on the other, providing an effective infrastructure for the identification and characterisation of innovative leads and the preclinical development of drug candidates. Collaboration will be extended from the present partners to include other academic institutions outside of the Max Planck Society as well as biotech companies.

The **Neuroallianz** consortium has designed a strategic partnership model between public research institutions, the pharma industry (Schwarz



“Comprehensive alliances, significant takeovers, and successful clinical studies, particularly in the past 18 months, testify to the great potential for ‘drug discovery made in Germany’. Now, we have to follow up on this success and build ‘beacons’ of excellence to establish Germany as an acknowledged industry leader.”

Dr Thomas Höger  
Chief Executive Officer/Chief  
Financial Officer, Apogenix GmbH



“We are at the beginning of a positive development. Provided that conditions for research and development are further improved, we will be able to play an even more significant role in the future.”

Dr Daniel Vitt  
Chairman of the Management Board, Chief Science Officer, 4SC AG

Pharma/UCB group), biotech companies (Protagen, Priaxon, Life&Brain) and regulatory authorities along the entire added value chain. The twelve partners aim to facilitate the transfer of therapeutic and diagnostic approaches for the treatment of neurodegenerative diseases from the research stage to the market.

The consortium **New materials against neurological diseases (Neu<sup>2</sup>)** targets the transfer of therapeutic and diagnostic approaches for the treatment of multiple sclerosis patients from basic research to the market. The consortium consists of the University Medical School, Hamburg, the pharma company Merck, Darmstadt, the large biotech company Evotec and several start-ups from Hamburg and Kiel. The partnership is financed mainly from private sources through a fund. One partner in the multiple sclerosis consortium Neu<sup>2</sup> is the **European ScreeningPort**, a public-private partnership (University of Hamburg, Evotec) providing modern drug research capabilities such as automated molecular screening platforms, bioinformatics, and professional pharmaceutical experience for the academic community.

**ChemBioNet** is an interdisciplinary, open access, screening platform set up by biologists and chemists from two Helmholtz Centres (MDC and HZI), the Leibniz Institute FMP, and the University of Oslo, Norway in order to provide a link between scientists, required for high throughput process automation, data documentation and analysis in Europe to explore biological functions.

The European Commission has recently set up an **Innovative Medicines Initiative (IMI)** which also consists of public-private partnerships between academic research institutions, small biotech and large pharmaceutical companies. The structure of these European consortia has not yet been finalised. Whereas the principal concern of small biotech companies is to protect their IP, big pharmaceutical companies which provide 50 percent of the financing in order to attain the leadership in the consortium are more concerned with inflexible bureaucracy in the case of unforeseen developments.

Within the framework of the High-Tech Strategy of the German Government a **Top Cluster Competition** was launched in 2007. This competition was designed to strengthen the innovation power of the most efficient geographical clusters in Germany aiming to accelerate the process from scientific ideas and concepts to products, processes, and services in various areas of high technology. So far the only cluster in the life science sector to receive an award has been **BioRN – cell-based and molecular medicine in the metropolitan region Rhine-Neckar**, i.e. the Heidelberg BioRegion. Coordinated by a new cluster management company, biotech, pharmaceutical, and service companies joined forces with partners from academic institutions to develop promising drug discovery projects for industrial application. One of the core projects in the BioRN cluster has been the **Heidelberg Institute for Stem Cell Technology and Experimental Medicine (HI-STEM)**, a public-private partnership founded in 2008 between the DKFZ, the University Hospital Heidelberg, and the private Dietmar Hopp Foundation. HI-STEM, under its Scientific Director Professor Andreas Trumpp, aims to apply basic research on stem cells, particularly cancer stem cells, for developing effective drugs, for example against cancer cells that are resistant to existing medicines.

## 5.6 Success factors

The benchmark for German biotechnology is the United States. The two leading biotech clusters worldwide, namely around the San Francisco Bay and Boston Area, each have more biotech companies than all of Germany put together. Companies like Genentech (founded in 1976) and Amgen (founded in 1980) rival the largest international pharmaceutical companies in terms of market capitalisation, if not yet in revenues. German biotech companies, which for the most part started up twenty years or more later, are not yet in the same league. In view of this difference in size, the successes of the German biotech industry are better reflected by the changes that have taken place over the past years rather than by a direct comparison with the US.

Over the past five years, the number of biotechnological drugs and drug candidates in preclinical and clinical phases developed by German biotech companies (excluding big pharmaceutical companies) has almost doubled (to 354 in 2007). Significantly, the increase was strongest in late stage development (from 22 to 73 drug candidates in Phase II clinical trials and from 3 to 17 in Phase III). In 2002, there was just one biotech drug going through the registration process; in 2007, there were six. The first products have now entered the market. Including new product developments from the German pharmaceutical industry, there are more than 60 new drugs in Phase III clinical trials, many of which are derived from innovations attributed to biotech companies. These figures demonstrate a maturing development pipeline indicating that German biotech is leaving the stage of infancy behind.

Venture capital (VC) has been the driving force in biotechnology and has helped start-ups in this capital-intensive industry to grow rapidly. Germany is by far the largest destination of VC in Europe (more than 300 million euros in 2007 compared to approximately 140 million euros in the UK and in Switzerland). The average amount of VC grants has also been higher than in other European countries. Large international VC funds and private investors have targeted the German biotech market and invested strongly in companies with advanced pipelines.

Besides money, venture capital firms and private investors provide entrepreneurs with advice, contacts, and management skills. Running a biotech company successfully requires competence and expertise. In order to develop management and commercial skills, diverse programmes and initiatives have been set up at all organisational levels (municipal, state, federal government, and European Commission). These programmes aim to prepare excellent young scientists for an entrepreneurial and business career – starting with special training courses at universities and research institutions, coaching on how to prepare business plans and funding applications, through to specialised academic and MBA programmes designed to meet the specific needs of the industry.

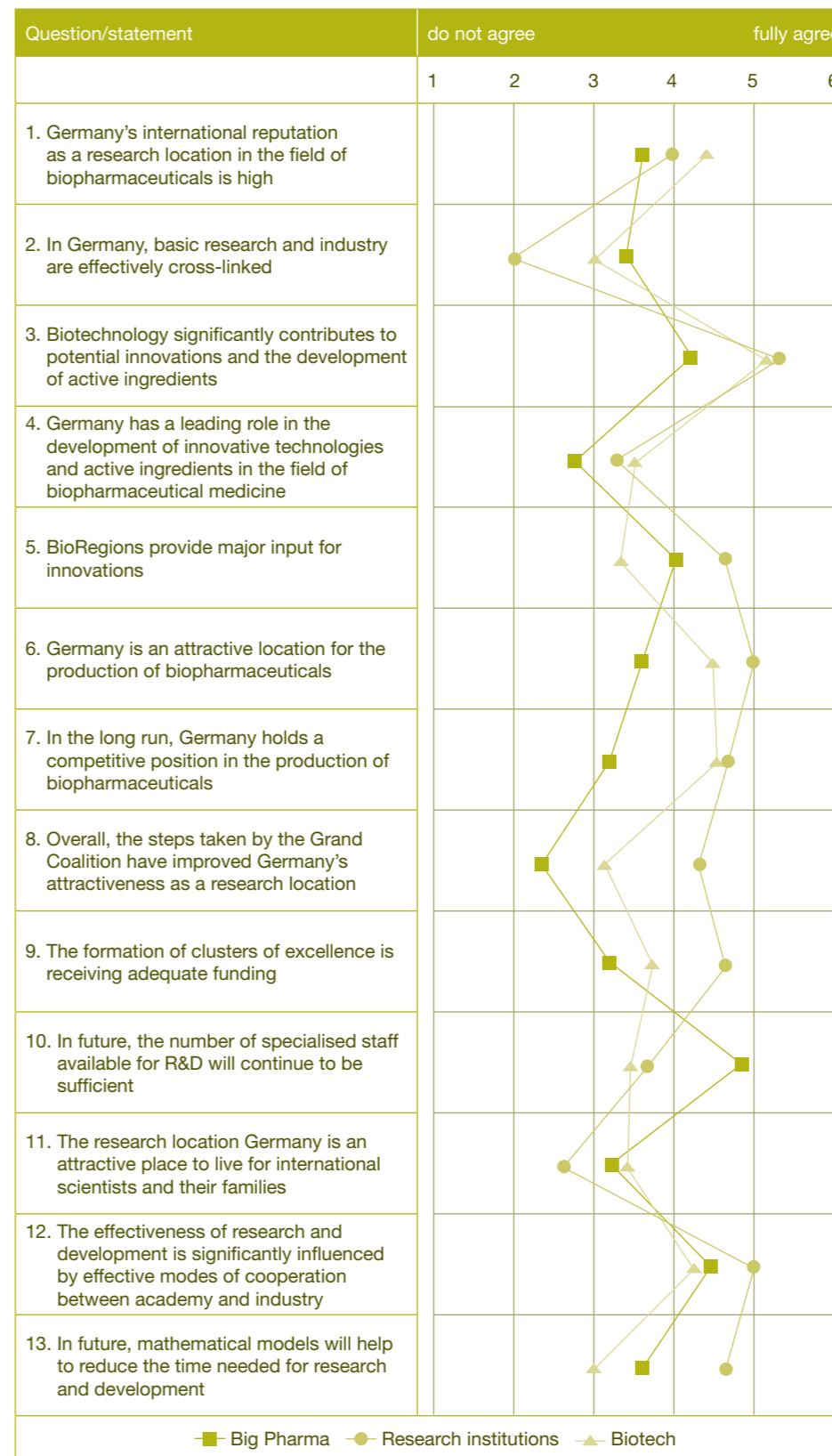
Entrepreneurship is contagious: when young scientists discuss business plans in a campus café, others will soon follow suit. This is one reason why entrepreneurship flourishes in clusters – because it becomes a way of life. Another main factor is that the infrastructure is already in place, which reduces the cost of starting up a business. Reliable infrastructure and networks are provided by incubators in modern technology and science

parks which have been created in all BioRegions throughout Germany. Indeed, a number of these parks and incubators (Heidelberg, Hanover, Berlin, Halle, Martinsried, and Weihenstephan) were founded before the BioRegio Competition of 1996 and played important roles in the formation of these clusters.

That German biotech has gained recognition and has become a respected international partner is perhaps best exemplified by the fact that BioEurope, the largest stand-alone partnering conference in the biotech-pharma world, has always taken place in German cities since 1998; the names of the conference cities read like a list of major BioRegions: Berlin, Munich, Stuttgart, Frankfurt, Cologne, Dresden, Düsseldorf, Hamburg, Mannheim/Heidelberg. In addition BIOTECHNICA, Europe's leading event for the biotech industry, takes place in Hanover and offers a platform, now annually, for innovation and knowledge transfer and networking.

Last but not least, the success of German biotechnology relies on the excellence of its scientific research. Universities and research centres have established exchange programmes and networks with academic institutions throughout the world. International conferences on topics at the cutting edge of research are attended by leading experts from other countries. Grants for graduate and post-graduate students are available at the best universities and research institutions. The most valuable prize in German research, the Leibniz Professorship (even higher prize money than the Nobel Prize), is awarded annually to a number of outstanding scientists from abroad who will pursue their research to the highest standards in Germany.

### 5.7 Quintessence of interviews conducted (chart)



Questionnaire evaluation

## 6 Vision

Biotechnology is not only an international business – it is also a fast developing business that is influenced by different factors and has a deep impact on one of our greatest interests – our health. Moderated by Dr Jens Katzek (CEO of BIO Mitteldeutschland), the following high-level panel of experts was asked to discuss the fundamental question of the future of drug discovery and biotechnology: Dr Viola Bronsema (Managing Director of BIO Deutschland e.V.), the authors of the first part of this study, Dr Ernst-Dieter Jarasch (Managing Director of BioRegion Rhein-Neckar-Dreieck e.V.), Dr Albrecht Läufer (CEO of Corvay GmbH) and Dr Claudia Ulbrich (Senior Advisor for Pharma/Life Science of PwC), and finally Dr Volker Fitzner (Partner Chemical and Pharma of PwC).

**Katzek: Ms Ulbrich, with a view to 2020, what will the future R&D model in the pharmaceutical industry look like?**

**Ulbrich:** The demand for medicines in general will grow strongly, since populations are growing older and healthier and people fall ill regardless of the economic environment. PwC estimates a doubling of the worldwide pharma market until 2020 to 1.3 trillion US dollars. In 2020, we will still see 50 percent of new drugs based on small molecules accompanied by novel compounds like cell therapy, RNA derived drugs, vaccines. The blockbuster sales model will co-lead the market with personalised medicines, a trend which strongly favours smaller innovative companies. New business models will be developed to serve the specific needs of personalised medicine.

**Läufer:** Especially human or humanised monoclonal antibodies will play a major role in the treatment of cancer and immunological disorders. In addition, vaccines, both preventive and therapeutic, will increasingly come from German biotech companies. The first vaccines for prevention of cervical cancer are already on the market. There is hope that metastases, chemotherapy-resistant cancer relapses, and currently untreatable metabolic (genetic) diseases can be treated with new biotechnological medicines and cell therapeutic approaches.

**Bronsema:** Innovations will still come from academic institutions. With further improvements in the transfer of technology to the industry, we can efficiently generate new innovations within the biotech sector, which is still dominated by small and medium enterprises. But strong SMEs will strengthen Europe as a whole and provide us with the appropriate position for the future.

**Katzek: Regarding the current unmet medical need, especially in the fields of cancer, neurodegenerative, cardiovascular, and infectious diseases, we expect to see a much stronger output of new drugs and vaccines. Which site-related factors in Germany are contributing to such a continuous pipeline?**

**Jarasch:** There are several factors coming together. Without any doubt, we have an excellent academic infrastructure, a good scientific and technical education system for highly qualified staff, and a large scientific and medical expertise accumulated at German universities, especially medical faculties as well as academic research institutes. Considering the various

academic associations that focus on four different areas, Max Planck on basic science and discovery, Helmholtz and Leibniz on applied science, and Fraunhofer on applied research and development in collaboration with industrial partners, we can be proud of our excellent basic and applied research. For the latter, the strong pipeline of over 300 existing and emerging biotech companies speaks for itself.

**Läufer:** Of course, not every Phase I project is going to make it to the market, but the establishment of different, highly interactive collaboration schemes, for example, the BioPharma competition or the Vakzine Projekt Management model will support the extension of collaborations between ‘Big Pharma’ and small biotech companies, e.g. Novartis-Cellzome, Boehringer-Ablynx, Boehringer-Morphosys, or Novartis-Morphosys.

**Katzek: Mr Fitzner, you mentioned once, that the ‘innovation deficit’ in Big Pharma has enormous strategic implications for the industry as a whole. What do you mean by this?**

**Fitzner:** Many pharmaceutical companies will need to decide what they want to concentrate on doing and to identify the core competencies they will require, a process which may involve exiting from some parts of research and development. But even those that regard research and development as a core element of their business will have to make fundamental alterations in the way they work. They may, for example, have to focus more heavily on speciality therapies, since most of the diseases for which there are currently no effective medications or cures are not amenable to mass-market treatments. In addition, the pharmaceutical companies need to reduce the time and costs involved in researching and developing such medicines to ensure that society can afford them.

**Katzek: So, you believe, that if the industry is to become more innovative, it has to change its R&D model to a closer collaboration with the biotech industry, academia, the regulators, governments, and health care providers?**

**Fitzner:** Essential for the future and for the evolving model between pharma and biotech is to get a comprehensive understanding of how the human body works at the molecular level and a much better grasp of the pathophysiology of disease (by which we mean the functional changes associated with, or arising from, disease or injury). A greater use of new technologies to ‘virtualise’ the research process and accelerate clinical development will assume a major role. This is a huge undertaking – and one that the industry cannot complete alone. It will require the support of biotech, academia, governments, technology vendors, health care providers, and regulators.

**Katzek: Ms Bronsema, does the current global financial crisis affect the pharmaceutical market as strongly as the consumer and automotive sectors?**

**Bronsema:** The pharmaceutical industry itself is actually not affected as strongly as the consumer and automotive sector by the credit crunch due to the consistent medical need for drugs in our society. Facing the expiration of patents with a significant loss of revenues within the next two to four years, the pharmaceutical industry is now striving to complete their pipelines with innovative drug candidates by acquiring biotech

companies. With the capital markets drained and the limited ability and/or willingness of Venture Capital to invest at this stage, biotechs are without any doubt seriously affected by the financial crisis, resulting in limited funding options with a focus on partnering with Big Pharma. Nonetheless, we believe that independent from the financial crisis both partners with their complementary needs are calling for new business models regarding R&D. Increasing costs of R&D and less market approvals are making the outsourcing of drug discovery or parts of the development to mature biotechs a necessity, as recently seen with UCB and Willex. Independency and flexibility of the biotech partner will be of utmost importance for successful collaborations.

**Katzek: Talking about the future of drug discovery without talking about the regulatory environment is like skiing without skis. So, what about the regulatory environment in Europe and Germany?**

**Jarasch:** We are confident that the regulatory environment will continue to improve with IP regulations as the basis for long-term investments into innovative drug development. Hopefully, a European patent system will emerge, and the fragmented regulation with one central EMEA agency and 27 national bylaws will also slowly converge into one proper European system in order to decrease the tremendous costs for translations.

**Ulbrich:** The industry has often argued that the regulatory process is an impediment to innovation. However, the leading agencies have clearly signalled that they are willing to consider new ways of developing and regulating medicines ('EMEA Road Map to 2010', in 2006 the FDA published its 'Critical Path Opportunities List'). We believe that we will see a fundamental change in the approval process by 2020, in the direction of a live licence.

The industry will have to work much more closely with the regulators than it has done in the past. Some companies have already recognised this. By 2020, we think that every company will have to operate in the same fashion and that working with the regulators will be built into the remuneration packages of development.

Patients must play their part, too; without access to medical data and volunteers for clinical studies, the industry will be unable either to make theoretical advances or to translate those advances into practice. Considering future pay for performance requirements the industry will have to adapt their clinical trial design to much more predictive planning with a selective patient population that can show efficacy of new drugs. Only this will allow drugs to be brought to the market much more quickly, generating revenues much earlier as a basis for further research activities in innovative medicine.

This will be our global challenge to serve the needs of a demographic shift in our society.

**Katzek: Do you, Ms Bronsema, as Managing Director of BIO Deutschland, a political lobby organisation, agree? What do you think the German biotech industry is aiming for?**

**Bronsema:** Every country has its own strengths but also its own challenges. A successful economy does not work just by continuously

supporting areas of strength but also by looking at potential weak points, for example, in the regulatory or economic environment. I am therefore glad that our Chancellor Ms Dr Angela Merkel said that she, together with our finance minister, will adapt the tax system according to the new needs.

If we improve the legal environment for innovative companies, this will of course give us a competitive advantage as well, which will make cooperation with us more attractive for international investors.

We may be reluctant to accept it, but we do have a reputation to lose: insulin, RNAi, angiogenesis blocker, cancer vaccination, intelligent toothpaste, ecological washing powder, the starch potato, or stem cell research – you name any one of these recent developments and I will name a German scientist or company who is a major player in this field. We are the world's leading location for the production of biopharmaceuticals second only to the US. And we are the strongest advocate for white biotech in Europe. Therefore, I think we have the potential to become the biotech engineers of the world.

## Section B

### 1 Selected company profiles by BioRegions

Directed by Dr Kathrin Adlkofer, 30 BioRegions have been asked to supply short profiles of their “beacon” companies and eminent research institutions in the fields of drug discovery and biotechnology. These are listed in the following Section B of this study.



**Dr Kathrin Adlkofer**  
Managing Director  
Norgenta North German Life  
Science Agency



## 4SC AG

**Founded**  
1997

**Employees**  
64

### Area of research and development

4SC is a drug discovery and development company that uses its cheminformatics-based technology platform to discover and develop new drugs to treat patients suffering from diseases with high medical needs. The company has been generating a risk-balanced and continuously advancing pipeline of projects using its own technology platform, 4SCan®, which transfers traditional high throughput screening from the laboratory to the computer screen. 4SC's therapeutic focus centres on cancer and inflammatory diseases since these indications combine significant market potential and high medical needs with reasonable development time and cost in the early clinical stages. 4SC has been listed in the Prime Standard segment (regulated market) of the Frankfurt Stock Exchange since 15 December 2005.

In addition, 4SC AG expanded its project portfolio considerably with the acquisition of eight drug projects from the Nycomed's oncology pipeline in July 2008. The drug candidates acquired exhibit distinctive synergies with the project pipeline developed by 4SC. Three drug substances derived from these projects have already been integrated into the company's advanced development pipeline. Other candidates may follow in future. So far there is one product in a Phase II trial and the others are in late Phase I.

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## Across Barriers GmbH

**Founded**  
1998

**Employees**  
37

### Area of research and development

Across Barriers GmbH provides its customers with services and consultancy in preclinical and pharmaceutical technological development in line with GLP and GMP. Starting with analytical and physicochemical characterisation and progressing to in vitro testing of active compound properties for the feasibility of bioavailability and bioequivalence in in vitro models (e.g., GI, skin, pulmonary, cervical, BBB), and also customer-oriented consultancy on drug formulation. We also perform BCS classification.

Furthermore, Across Barriers GmbH is involved in current European research projects such as MEDITRANS, dealing with targeted nanomedicine, Pulmonet and MEMTRANS. The general objective of Pulmonet is to elucidate basic molecular, cellular and tissue-related mechanisms involved in the generation of various acute and chronic pulmonary diseases. One of Memtrans' goals is to optimise and pre-validate in vitro-cultured cell models to predict oral absorption and pharmacokinetics of efflux systems substrates.

### Indication

CNS, pulmonal, gastrointestinal, dermal, unguinal, cervical, buccal

### Stage of research and development

Across Barriers GmbH is working as a service provider in the preclinical field. Research activities are also performed in the preclinical field.

### Collaboration

Yes, documented by mutual research publications with PARI Pharma Aerosol Research Institute GmbH, Hexal Gentech ForschungsGmbH, Hexal AG, Chemische Fabrik Kreussler & Co. GmbH, Beiersdorf AG, BASF Aktiengesellschaft, Experimental Toxicology & Ecology and Cognis Deutschland GmbH & Co. KG, among others.

MEDITRANS collaborates with N.V. Organon, Bayer Schering Pharma and Merck Serono Istituto di Ricerche Biomediche "Antoine Marxer", among others.



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## Affimed Therapeutics AG

**Founded**  
2000

**Employees**  
26

### Funding

Affimed has raised a total of around 43 million euros from grants and venture capital fundraisings. The most recent fundraising was completed in February 2008 and raised a total of 30 million euros from a consortium of top-tier European and US life science investors.

### Area of research and development

Affimed is a private biopharmaceutical company specialising in the discovery and development of next-generation antibodies. With a powerful research engine based on three distinct human antibody libraries and proprietary antibody formats, Affimed is developing a broad portfolio of antibodies to target cancer and other life-threatening diseases with unmet medical demand. The high diversity of the company's three completely different antibody libraries allows Affimed to identify antibodies against even the most difficult of targets.

Affimed has developed an array of antibody formats, including proprietary TandAbs and Flexibodies, unique tetravalent antibodies providing broad therapeutic applications, for example, for the recruitment of cytotoxic immune cells to generate a number of highly potent reagents for the main indications of cancer. Further features comprise bispecific inhibition of signalling pathways or antagonising multiple antigens or epitopes with a single molecule.

Affimed's TandAbs have demonstrated superior potency and efficacy compared to conventional monoclonal antibodies in in vivo and in vitro preclinical studies.

Affimed's product pipeline includes candidates with a high market potential in the indications of oncology, autoimmune diseases and thrombosis. Affimed's lead programs are TandAbs for the treatment of Non-Hodgkin's (AFM11/AFM12) and Hodgkin's Lymphoma (AFM13), which is entering into clinical study in 2009. Both programmes will be developed until clinical proof-of-concept. Additional preclinical programs include AFM 20, a TandAb targeting a broad spectrum of solid tumours, AFM15 for autoimmune diseases and AFM14 for thrombosis. Furthermore, Affimed has discovery programmes in leukaemia, myeloma, lymphomas and solid tumours, as well as non-cancer indications such as autoimmune diseases.

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## AiCuris GmbH & Co.KG

**Founded**  
2006

**Employees**  
48

### Area of research and development

AiCuris is a pharmaceutical company focused exclusively on the discovery, research and development of innovative, resistance-breaking antiviral and antibacterial agents for the treatment of severe and potentially life-threatening infectious diseases. AiCuris has core research and development expertise in pharmacology, microbiology, virology, pharmacokinetics, medicinal chemistry and clinical trials.

### Indication

Anti-infectives  
Infectious diseases: human cytomegalovirus (HCMV), the hepatitis B virus (HBV), the hepatitis C virus (HCV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), nosocomial bacterial infections caused by resistant Gram+ or Gram- pathogens.

### Stage of research and development

One compound is in Phase II clinical trials and an additional five have reached Phase I. One more candidate compound is expected to enter clinical trials in the second half of 2009. Overall, nine development compounds are actively pursued, including two immune modulators.

### Collaboration

4SC, Arevi Pharma, Lindopharm, Bayer Schering Pharma, as well as other contract research organisations



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## Antisense Pharma GmbH

**Founded**  
1998

**Employees**  
55

### Area of research and development

Business Strategies

Antisense Pharma focuses its innovative strength on therapies targeting cancer. The company identifies and develops DNA-based antisense drugs, which specifically knock down key cancer proteins. With scientific excellence and an experienced management team, Antisense Pharma has grown from pioneer to leader in the development of anti-cancer drugs targeting transforming growth factor beta. Applying the selective antisense technology to targets responsible for the malignant transformation and progression of cancer is a unique approach to combating cancer.

### Products and technologies

With the unique combination of drug discovery technology and expertise in the development of antisense pharmaceuticals providing the groundwork, the company's proprietary product portfolio can cover the R&D pipeline from discovery to late-stage clinical development. The pipeline comprises innovative drug candidates for indications with high unmet medical need. AP 12009, a TGF-beta2 inhibitor, is in an advanced stage of clinical development for aggressive tumours like malignant brain tumours, colorectal carcinoma, pancreatic carcinoma and malignant melanoma.

### Indication

Cancer

### Stage of research and development

Phase III for AT 12009

### Collaboration

The company holds a solid international portfolio of patents and patent applications claiming antisense oligonucleotides and target proteins. Antisense Pharma is involved in international collaborations with corporations as well as academic institutions. It is interested in strategic partnerships with pharmaceutical companies to co-develop and commercialise innovative therapeutics.

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## AplaGen GmbH

### Founded

AplaGen is a biopharmaceutical company, located in the suburban areas of Aachen (Germany), founded in 2001 by a team of scientists from Aachen University of Technology and local entrepreneurs.

### Employees

Currently, AplaGen employs 20 individuals, mostly with natural science qualifications and PhD degrees, with activities in the following fields:

- Drug design, molecular modelling
- Synthesis and analysis of peptides
- Cell biology and biochemistry
- Biopolymer chemistry and biopolymer analysis; aggregation analysis

For the four above-mentioned R&D specialties, AplaGen provides own lab space and facilities.

### Area of research and development

AplaGen is a biopharmaceutical company with broad expertise in peptide design, synthesis and analysis. AplaGen has successfully created a portfolio of own products with patent protection for the development in major indications and markets, including the anaemia market (Erythropoiesis-stimulating agent [ESA] market) and the thrombocytopenia market. In parallel to developing its own pipeline products, the company engages in "Innovation Partnerships", collaborations with pharmaceutical and biotech companies, which aim at significant long-term value generation by unique strategic profiling of the drug(s) under investigation. The platform technologies include both HES conjugation and peptide development capabilities. AplaGen's Innovation Partnership provides new solutions for product differentiation and for enabling superior pharmacological profiles and life-cycle management opportunities. The Innovation Partnership seeks co-development alliances with leading pharmaceutical and biotechnological companies.

### Indication

Haematology, oncology

### Stage of research and development

With its pipeline products Hemomer and Thrombomer, AplaGen is in the preclinical stage, Hemomer being more advanced than Thrombomer.

### Collaboration

- Cooperation with Bayer Health Care and Animal Health for peptide modification
- Cooperation with a major European pharma company as exclusive provider of HES-conjugation solutions for their whole protein pipeline



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## Apogenix GmbH

**Founded**  
2005

**Employees**  
26

### Area of research and development

Apogenix is a biopharmaceutical company developing innovative protein therapeutics which exert their therapeutic effect by targeted modulation of signal pathways. The first focus lies on the CD95 system, which primarily regulates apoptosis and the invasive growth of cancer cells. The second focus lies on the IL-4 system that plays an essential role in the development of apoptosis resistance in cancer cells. These different approaches enable the company to pursue a variety of larger indications such as HIV infection or cancer as well as orphan indications, such as acute graft-versus-host disease (aGVHD).

The company is currently concentrating on two projects – APG101 and IL-4 blocker – which, respectively, are in clinical Phase I and advanced preclinical development. The therapeutic potential of Apogenix's protein therapeutics has been demonstrated in a variety of animal models e.g. for acute graft-versus-host disease (aGVHD) and cancer (glioblastoma).

Apogenix was founded as a spin-off of the German Cancer Research Center (DKFZ) and is located in Heidelberg, Germany. Since its inception in autumn 2005, the company has raised 15 million euros in the first financing round and 28 million euros in the second financing round in April 2008 and has been awarded 3 million euros in public grants.

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## Bayer Schering Pharma AG

**Founded**  
1871

**Employees**  
More than 37.000

### Funding

### Area of research and development

Bayer Schering Pharma is a worldwide leading specialty pharmaceutical company focusing its research activities on four core areas: cardiology, oncology, women's health care and diagnostic imaging. In addition, we have continued applied research and lifecycle management activities in the indications of haemophilia, multiple sclerosis and dermatology.

### Indication

Therapeutic indication

Four business units with the following indications:

- Women's health care: oral and non-oral contraception, menopause management, gynaecological therapy
- Specialty medicine: multiple sclerosis (MS), haemophilia A, cancer therapies to combat solid tumours and hematologic malignancies
- Diagnostic imaging: contrast media for classic X-ray procedures and computer tomography (CT), for magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA), clinical research of innovative approaches in the field of molecular imaging
- General medicine: hypertension, coronary heart disease and diabetes, antibiotics to fight respiratory, urinary and surgical infections, testosterone deficiency, erectile dysfunction, venous thromboembolism

### Stage of research and development

Phase I: 9 projects

Phase II: 22 projects

Phase III: 20 projects

(Status: January 2009)

### Collaboration

Yes

External alliances are a key component of Bayer Schering Pharma's strategy for maintaining a competitive portfolio of products and technologies. Successful partnerships allow us to combine expertise in research, development, production and marketing; adding greater value to BSP, our partners and customers. Bayer Schering Pharma co-operates with numerous institutes or companies in all phases of the drug development value chain.



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## BCRT (Berlin-Brandenburg Center for Regenerative Therapies)

**Founded**  
2006

**Employees**  
more than 100

### Area of research and development

The BCRT set out to translate innovative scientific findings into regenerative therapies.

Our therapeutic strategies focus on the stimulation of the endogenous tissue regeneration capabilities of the human body.

For the benefit of our patients, the centre pools the excellence of internationally recognised researchers and clinicians in Berlin-Brandenburg to advance new therapies for battling diseases such as heart attacks, strokes and lymphoma or to accelerate bone healing. The centre will integrate molecular as well as cell-based approaches with new biomaterial developments into regenerative therapies.

The centre is funded by Europe's largest university hospital, the Charité, and Germany's largest research organization, the Helmholtz association. This partnership reflects our firm commitment to bring clinics and research together. In addition, the BCRT is substantially funded by the German Federal Ministry of Education and Research and supported by more than fifteen recognised institutional partners.

### Indication

- Therapeutic indication
- Immune system, cardio-vascular system, nervous system and musculoskeletal system

### Stage of research and development

Different products in preclinical phases

### Collaboration

Yes, e.g. Bayer Schering Pharma AG

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## BIBITEC GmbH

### Founded

2001 as a spin-off from the Institute of Cell Culture Technology, University of Bielefeld

**Employees**  
9

### Area of research and development

BIBITEC Gesellschaft für Prozessentwicklung mbH is located at the University of Bielefeld, Germany, and specialises in the production of proteins derived from mammalian cells.

BIBITEC was founded as a spin-off from the Institute of Cell Culture Technology, University of Bielefeld, in 2001 by Dr J. Lehmann, Dr D. Lütkemeyer, Dr H. M. Schulte and Dr J. Schumacher.

Today, BIBITEC employs 9 persons.

A five-year erythropoietin (EPO) project was recently completed. This project involved the process development as well as the GMP-compliant production of EPO for use in Phase III clinical trials. The entire production and purification process was successfully transferred to a third party for large-scale production and market supply.

### Our core competences include:

- mammalian cell culture techniques,
- upstream and downstream process development,
- GMP-compliant production of protein APIs for use in clinical tests (Phases I-III), process optimisation,
- validation studies and
- GMP consulting.

Furthermore, we offer monoclonal antibodies for diagnostics, growth factors for cell culture and oligosaccharide reference standards for R&D.

### Collaboration

BIBITEC gained long-lasting collaboration with NewLab BioQuality GmbH and Nordmark Arzneimittel GmbH & Co. KG.



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## BIOBASE GmbH

**Founded**  
1997

**Employees**  
130

**Funding**  
Procured investments

### Area of research and development

BIOBASE is a content and solutions provider for the life science industry. The company's products and services help to identify potential drug targets or biomarkers and increase understanding of potential side effects of drug candidates. All work is done in silico (on computer) and is therefore both faster and less expensive than the traditional approach of animal testing or lab experiments. BIOBASE provides content via standard databases and corresponding analysis tools (software), as well as custom solutions, including knowledge process outsourcing/custom curation and biomarker services. These products and services are mainly applied to the interpretation of high throughput data sets from micro array expression, the analysis of gene regulation, the development of systems biology disease models, drug safety/risk screening, the identification of disease-related mutations for personalised medicine, and to the prediction of targets for the optimisation of plant resilience and yield.

**Indication**  
Platform technologies

**Stage of research and development**  
Ongoing. BIOBASE is an active member of a number of national and European research consortia.

**Collaboration**  
Eighteen out of the twenty largest pharmaceutical companies are customers of BIOBASE. Many of them are not only buyers of BIOBASE products, but actively cooperate in a variety of customised curation and data analysis projects.

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## Biofrontera AG

**Founded**  
1997

**Employees**  
28

### Area of research and development

Biofrontera is a specialty pharma company in late-stage development focused on therapeutic products for dermatological diseases. The company has its headquarters in Leverkusen, Germany, and a staff of 28 employees. Biofrontera was founded in 1997 by Prof Lübbert, who is currently the CEO of Biofrontera.

The company has a well diversified, late-stage pipeline with a combined peak sales potential in excess of 1 billion euros.

Biofrontera aims for rapid growth by concentrating on the following corporate strategies:

- Focusing on the rapidly growing dermatology market
- Vertically integrating distribution channels in Europe
- Adopting a 'risk-optimised' drug development strategy that includes topical versions of approved products and/or improved formulations of the existing drugs through superior efficacy or better side-effect profiles
- Sustaining growth through acquisition of a broad portfolio of products

Since October 2006, the Biofrontera shares are listed on several German Stock Exchanges.

**Indication**  
Dermatology

### Stage of research and development

Reliéva crème (market introduction in H2/09 as a cosmeceutical product line) for psoriasis, atopic dermatitis and itching  
BF-200 ALA (Phase III) for actinic keratosis  
BF-derm 1 (Phase II) for chronic, antihistamine-refractory urticaria  
BF-37 (Phase II) for psoriasis  
BF-1 (Phase I) for migraine prophylaxis

**Collaboration**  
Collaboration with Grünenthal Pharma AG on the production and marketing of Biofrontera's products BF-200 ALA and Reliéva



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## Bionorica AG

**Founded**  
1933

**Employees**  
409

### Area of research and development

#### Business strategies

Bionorica AG is one of the most successful manufacturers of phytotherapeutics in Germany. The product range focuses on diseases of the respiratory tract, gynaecological disorders and medications for the treatment of pain. The know-how of Bionorica in phytotherapy has grown over 75 years and the company develops rational herbal medicinal drugs under similar standards as chemically synthesised drugs.

More than 30 patents have resulted from the continuous development and exchange of ideas, as well as the successful cooperation with about 70 scientific institutions in Germany and abroad. One of the subsidiaries, Bionorica Ethics GmbH (formerly Delta 9 Pharma GmbH), develops new active substances and medicines in the field of pain relief.

Bionorica is Marketing Authorisation Holder in more than 50 countries all over the world. Marketing and sales in foreign countries are carried out by subsidiaries or contractual partners.

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## BioPlanta GmbH

**Founded**  
1992

**Employees**  
12

### Area of research and development

BioPlanta is one of the leading companies in applying bioengineered approaches for discovery, development and commercialisation of fine chemicals and pharmaceutical compounds using its proprietary bioreactor technology. This technology – the BioPlant System – is particularly suitable for manipulating plant metabolism to generate active compounds with higher value than field plants. The system is adaptable to the special requirements of different plant species and culture types, such as shoots, roots and micro-tubers. The control and variation of cultivation conditions enables customised content and spectra of the specific compounds. This innovative platform technology was installed to manufacture plant derived chemical compounds for pharmaceutical-, flavour- and food-related industries. It allows an efficient screening of new active compounds, the design of innovative drugs and the production of high-quality drugs following the European GMP guidelines.

### Indication

The main focus of our research is on plant active substances for the treatment of cancer, lipometabolic disorders and inflammations.

### Stage of research and development

The current status of our work in the area of drug discovery and development is preclinical research.

### Collaboration

Yes, BioPlanta currently cooperates with pharmaceutical companies.

### Further information

At the moment there are two products in the preclinical research stage.



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## biosyn Arzneimittel GmbH

**Founded**  
1984

**Employees**  
approximately 80

### Area of research and development

biosyn Arzneimittel GmbH was founded 1984 and is one of the original biotechnology companies. As a research oriented company biosyn focuses on oncology and intensive care medicine.

biosyn Arzneimittel GmbH has specialised primarily in the fields of oncology and intensive care medicine. biosyn currently offers around 30 drugs approved in 15 countries.

biosyn's development strategy is based on biologic molecules and trace elements that have proven efficacy with few side effects. Hemocanin based products like IMMUCOTHEL® or VACMUNE® are used in bladder cancer or as carriers for therapeutic vaccines. Selenium compounds like Sodiumselenite (selenase®) are used by sepsis patients to reduce mortality.

A double-blind, prospective study (SIC) demonstrated that a high dose of sodium selenite reduces the mortality rate of sepsis patients. The mortality rate among patients who were administered the drug was 42 percent as opposed to 57 percent in the control group. A high dose of selenium leads to a significant reduction (14.3 percent) in the mortality rate even in cases of severe sepsis, such as septic shock.

### Further information

biosyn Vertriebs AG in Balzers, Liechtenstein, and the biosyn Corporation in Carlsbad, California, USA, are subsidiaries of biosyn. biosyn also has a scientific office in Austria.

### Certificates/GMP-Standards

biosyn's laboratories in Fellbach are GMP-certified.

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(Managing Director)

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## BIOTECTID GmbH

**Founded**  
1999

**Employees**  
17

### Area of research and development

The company undertakes research in the field of immunology and develops biopharmaceuticals for molecular imaging with the aim of making visible chronic sources of inflammation by means of imaging procedures and localising them objectively. Its own laboratories were initially set up in Leipzig. Biotectid, which has now moved to the Leipzig BioCity, has its own certified GMP facility, as well as laboratories with highly modern equipment. The company is integrated into a powerful network of renowned partners from the fields of research and development, science and business, and has built up a fast-growing patent portfolio. In 2008, Biotectid successfully performed the first clinical trial with its lead-product EP1645, a fragment of a monoclonal antibody which binds selectively to the CD4 molecule on the surface of specific inflammatory cells.

### Indication

Inflammatory autoimmune disorders, rheumatoid arthritis, vulnerable (high risk) arteriosclerosis plaques

### Stage of research and development

Rheumatoid arthritis: first clinical trial (phase I/II) successfully completed.  
Arteriosclerosis plaques: preclinic completed, 1st ex vivo clinical trial finished

### Collaboration

Yes

### Further information

Biotectid has a unique coupling platform under development as a fundamental basis for further imaging products.



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## Biotie Therapies GmbH, Subsidiary of Biotie Therapies Corp.

**Founded**  
2002

**Employees**  
Approximately 75

**Funding**  
Biotie Therapies Corp, Turku is a public company, listed in Helsinki on NASDAQ OMX Helsinki Ltd

**Area of research and development**  
Biotie is a drug discovery and development company focused on the central nervous system and inflammatory diseases. It has a broad range of innovative small molecule and biological drug candidates at different stages of clinical and pre-clinical development. Biotie's products address diseases with high unmet medical need and significant market potential, including addiction and psychotic disorders, rheumatoid arthritis, psoriasis and chronic obstructive pulmonary disease (COPD). The most advanced product, nalmefene for alcohol dependence, is currently in phase III clinical development by licensing partner H. Lundbeck A/S.

The commercial value of the pipeline has been demonstrated through existing alliances with top-tier global pharmaceutical companies such as Lundbeck, Roche and Wyeth.

**Indication**  
CNS, inflammation

**Stage of research and development**  
Discovery to clinical phase III

**Collaboration**  
Lundbeck, Roche, Wyeth, Seikagaku, Somaxon

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## Boehringer Ingelheim Pharma GmbH & Co KG

**Founded**  
1885

**Employees**  
39,800 employees worldwide (2007), 9,952 employees in Germany (2007)

**Area of research and development**  
Innovative new medicine for human and animal health

**Indication**  
Respiratory diseases, cardiovascular diseases, central nervous system (CNS) diseases, oncology, virology, metabolic diseases, immunology and inflammation

**Stage of research and development**  
Several NBEs (New Biological Entities) in development (number and indication areas not disclosed)

**Collaboration**  
Yes, e.g. biopharma manufacturing collaborations with Amgen, Bayer, Genzyme, GSK, Merck Serono and Wyeth



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## CellGenix Technologie Transfer GmbH

### Founded

1994 as a spinoff of the University Medical Center Freiburg

### Employees

Approximately 45

### Area of research and development

CellGenix Technologie Transfer GmbH is an innovative biopharmaceutical company headquartered in Freiburg, Germany. CellGenix develops, manufactures and markets cell and protein therapeutics for cancer and orthopaedic patients, as well as high-quality reagents for therapeutic ex vivo cell processing.

CellGenix's research focuses on the development of GMP-grade ex vivo cell processing tools like cytokines, serum-free media and closed kit systems. A patient-specific idiotype vaccine (IdioVax®) against Non-Hodgkin's B-cell lymphoma has been tested in Phase II clinical trials and developed in collaboration with Freiburg's University Medical Center.

Together with its distribution partners, CellGenix markets a variety of products and services for clinical cell therapy applications: cord blood cell processing and banking; autologous chondrocyte transplantation; as well as GMP-grade cytokines, serum-free media and kit systems for ex vivo cell processing. Additionally, they offer specialised GMP contract manufacturing services.

### Indication

GMP-grade ex vivo cell processing tools like cytokines, serum-free media and closed kit systems for cell therapy in oncology, immunology, stem cell therapy and tissue engineering.

### Stage of research and development

IdioVax® is in Phase II clinical trials. It has been granted the orphan drug status by the EMEA. Several GMP manufactured growth factors as well as serum-free media for adult stem cells will be launched throughout 2009.

### Collaboration

The company owns Metreon Bioproducts GmbH, which was founded in 1996 and which is specialised in cell processing. CellGenix also owns shares in American Fluoroseal Cooperation (Afc) in Gaithersburg, Maryland (USA), and in CellPrep S.A. in Buenos Aires, Argentina.

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## Cellzome AG

### Employees

90

### Area of research and development

Cellzome is a privately owned drug discovery company which is identifying a new generation of kinase-targeted drugs to treat inflammatory diseases. Its pipeline of small-molecule therapeutics is driven by Kinobeads™, a proprietary technology for the screening and profiling of kinases in relevant cells and tissues.

Cellzome is applying its distinctive Kinobeads™ technology to the discovery and development of innovative, selective, kinase inhibitors targeting key inflammatory mediators in immune receptor signalling and chemotaxis, including PI3Kγ and Zap-70.

Cellzome's business strategy is to generate shareholder value by:

- Developing a pipeline of small molecule pharmaceuticals, initially for inflammatory diseases
- Collaborating with leading pharma companies in return for research payments, milestone payments and royalties on sales.

The management team has strong scientific and commercial credentials, and is backed by some of the biotech industry's most experienced investors. Cellzome is intent on developing both organically and through merger or acquisition, whilst maintaining its values of transparency, commitment and mutual respect.

Cellzome's holding company is headquartered in the United States and employs about 90 people at its two operating subsidiaries in Cambridge, UK, and Heidelberg, Germany.



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## Celonic GmbH

**Founded**  
1998

**Employees**  
Germany: 17  
Worldwide: more than 50

**Funding**  
Company is profitable

### Area of research and development

Starting at cell-line development, Celonic is able to guide its customers up to the production of Active Pharmaceutical Ingredients (API) according to GMP. Celonic is readily equipped to produce biopharmaceuticals to market demands.

As a spin-off from the Research Center Jülich, the initial idea to found a company was based on the invention of a fluidised bed bioreactor that allows an unsurpassed biomass/volume ratio. Consequently following the business model of organic growth, Celonic has become a reliable partner offering a one-stop-shop for mammalian cell culture technology.

In order to be ready for preclinical and clinical analytics, Celonic was certified for GLP in 2007. Ten years after the foundation of the small Juelich based start-up, Celonic's success factors are the focus on one exclusive recombination system and its timing. The company's technologies are marketed at a moment when all experts foresee a bottleneck in capacity for the production of protein biopharmaceuticals.

### Stage of research and development

Celonic offers cutting-edge technologies to produce protein biopharmaceuticals that are regulation compliant in an extremely short time frame.

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## Cenix BioScience GmbH

**Founded**  
1999

**Employees**  
30

### Area of research and development

Cenix BioScience is a contract research organisation focused on the discovery and pre-clinical development of innovative therapeutics, specialising in advanced applications of RNA interference (RNAi) gene-silencing technology, combined with high-content in vitro and in vivo phenotyping analysis.

### Indication

All applicable disease areas, e.g. cancer, immunology, CNS, infectious diseases

### Stage of research and development

Cenix has worked with and/or is currently working with numerous national and international Pharma and Biotech companies (e.g. Bayer Schering, Merck, Boehringer Ingelheim, Altana, Astra Zeneca, Johnson & Johnson, Alnylam, Regulus, Siena Biotech)

### Collaboration

Yes



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## CEVEC Pharmaceuticals GmbH

**Founded**  
2001

**Employees**  
13

### Funding

CEVEC Pharmaceuticals is financed by private investors, Sparkasse KölnBonn and the KfW public bank.

### Area of research and development

CEVEC has developed the innovative human cell-based CAP® (CEVEC's Amniocyte Production) Technology for production of biopharmaceuticals, such as recombinant proteins, antibodies and viral vectors. The highly efficient and proprietary CAP® Cell Line is derived from human amniocytes, is of non-tumour origin, and provides competitive expression levels and authentic human post-translational modification (glycosylation, carboxylation, etc.). It is comprehensively documented. The CAP® Technology is especially designed with complex, demanding biologics in mind, where authentic human post-translational modifications can be crucial for performance and safety.

CEVEC's newest cell generation is CAP-T™ for rapid transient expression of recombinant proteins. With CAP-T™, customers can proceed from gene to milligram and gram amounts of protein within only two weeks. Fast process times and high yields make it an ideal tool for screening, assay development, drug discovery, and pre-clinical drug development. CEVEC offers services in the field of CAP-based cell line development.

### Indication

Platform technology for the production of biologics in all indications

### Stage of research and development

CEVEC has several internal product-development projects in early stages.

### Collaboration

CEVEC has ongoing collaborations with several large pharmaceutical and biotech companies and contract manufacturing organisations.

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## Coley Pharmaceutical GmbH

**Founded**  
1997; acquired by Pfizer in 2008

**Employees**  
42

### Area of research and development

Founded in 1997, Coley Pharmaceutical GmbH in Düsseldorf, Germany, focuses on nucleic acid-related technologies such as oligonucleotide chemistry, analytics, delivery and immunology, and was the latest addition to Pfizer's Biotherapeutics and Bioinnovation Center (BBC) in 2008.

Together with Pfizer's Research Technology Center (RTC) in Cambridge, MA, USA, Coley today focuses on unlocking the full potential of RNAi therapeutics. Headquartered at the RTC, Pfizer's RNAi centres – located both in Düsseldorf and Cambridge – bring together a large set of disciplines as diverse as bioinformatics, genetics, or immunology, along with the core skills in siRNA cell biology and oligonucleotide chemistry. Applying these capabilities across different sites, the RNAi centres combine the best of both worlds – small innovative scientific groups, with the backing of a large pharma.

### Indication

Cancer

### Stage of research and development

Preclinical

### Collaboration

Coley Pharmaceutical GmbH is a 100% subsidiary of Pfizer Inc.



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## Conaris Research Institute AG

**Founded**  
1999

**Employees**  
4

### Area of research and development:

CONARIS is engaged in the preclinical and early clinical development of innovative drugs with special expertise in inflammatory indications. CONARIS' mission is to add value to innovative compounds and drug candidates by filling the gap between their discovery and characterization on one side and their early clinical development on the other. New assets are acquired by collaborations with academic research institutions, other biotech or pharma companies.

The aim is to develop new drug candidates right up to their proof of concept in humans and to add significant value to these compounds. The late clinical development and marketing will then be performed by out-licensing these projects to pharma partners.

CONARIS has established a substantial in-house technology platform and a network of associated partners to fulfil all requirements for fast and efficient preclinical development of new drug candidates, such as lead optimisation, physical and chemical characterisation, lab scale production, GMP development, proof of concept studies in various disease models and toxicity studies.

### Indication

Inflammatory diseases, autoimmune diseases, infection

### Stage of research and development

CR5/18 out-licensed since December 2008 (preclinical status)  
CR7/01 R&D

### Collaboration

Ferring Pharmaceuticals

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## Curatis Pharma GmbH

**Founded**  
1999

**Employees**  
5

### Funding

Development of acetyl-GLP-1-(7-34) amide is financed through licence fees from Haemopressin® and Cortirel®

### Area of research and development

Developed to market: Haemopressin® (terlipressin) und Cortirel® (human corticorelin [hCRH])  
In development: Acetyl-GLP-1-(7-34) amide

### Indication

Haemopressin®: Portal hypertension, bleeding oesophageal varices, hepatorenal syndrome  
Cortirel®: Diagnosis of pituitary corticotropic function  
Acetyl-GLP-1-(7-34) amide: Metabolic diseases

### Stage of research and development

Haemopressin® has obtained marketing approval in various European and Asian countries and has been out-licensed to International Speciality Pharmaceuticals (IS Pharma plc) in Chester, United Kingdom, which is marketing it in cooperation with national distributors in the UK. Cortirel® has obtained marketing approval in Germany. Acetyl-GLP-1-(7-34) amide is in pilot phase preclinical development.

### Collaboration

- Metagon Biopharma KG, Hanover, Germany
- International Speciality Pharmaceuticals (IS Pharma plc), Chester, United Kingdom
- Orphan Therapeutics, LLC, Lebanon, New Jersey, USA
- Torrent Pharmaceuticals Limited, Ahmedabad, Gujarat, India

### Further information

Terlipressin has obtained marketing approval as Haemopressin® and is marketed in various European and Asian countries for the treatment of bleeding oesophageal varices and hepatorenal syndrome. Human corticorelin (hCRH) has obtained marketing approval in Germany as Cortirel® for the diagnosis of pituitary corticotropic function. Acetyl-GLP-1-(7-34) amide is in pilot phase pre-clinical development for metabolic diseases.



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## CureVac GmbH

**Founded**  
2000

**Employees**  
59

### Funding

In 2003 CureVac closed a 2.6-million euro series A financing round with Leonardo Venture as lead investor, to facilitate the establishment of a GMP production unit. Since 2006, CureVac has raised an additional 35 million euros in a second venture round, enabling the company to advance the research, development and production of mRNA-based therapeutics. Lead investor in this series is the dievini Hopp BioTech holding GmbH&Co. KG which is a venture capital firm owned by the Hopp family.

### Area of research and development

CureVac is a biopharmaceutical company pioneering the direct therapeutic application of messenger RNA (mRNA), the biomolecule that physically transfers genetic information from the nucleus to the cellular protein production machinery. By making mRNA available for therapeutic purposes, CureVac seeks to introduce an innovative class of drugs into today's medicine. Building on a unique body of knowledge in RNA research, design and cGMP production, the company has established a range of proprietary technologies. These include: RNActive® for the design of modified and formulated mRNA targeting a broad range of therapeutic applications, RNAdjuvant® for the use of RNA as an immune stimulant, PUREmessenger® for the GMP-production of long-chain mRNA up to 15,000 nt. Based on these technologies, the company is building a growing pipeline of innovative product candidates. CureVac clinically develops RNActive®-derived vaccines for the treatment of prostate cancer and non-small cell lung cancer (NSCLC).

### Indication

Immunology, main focus to date: cancer

### Stage of research and development

- Clinical Phase I study for the treatment of prostate cancer in Europe
- FDA approval for a Phase I/IIa study to treat prostate cancer patients in USA
- Planned clinical Phase I for the treatment of non-small cell lung cancer
- Research work on adjuvants and messenger mRNA based therapeutics in general

### Collaboration

Yes (undisclosed)

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## Cytonet GmbH & Co. KG

**Founded**  
2000

### Area of research and development

The Cytonet Group, founded in 2000 as a spin-off of Roche Diagnostics GmbH, is now the largest cell-therapeutic company in Germany. In 2007, Cytonet won the German Industry Innovation Prize in the category 'Start-Up Companies'.

The Group's objective is the development, manufacture and marketing of cell-therapeutic products which, using specially processed human cells, enable a permanent or transient curative alternative to orthotopic transplantation. In cooperation with leading university hospitals, Cytonet combines the necessary competencies for this objective to develop and launch innovative cell-therapeutic products. Cytonet has its focus on liver cell therapy in urea cycle defects in newborn babies and children. Multicentre clinical studies have already started.

Furthermore, the company supplies blood stem cell and bone marrow preparations for haematopoietic reconstitution in haematological and/or oncological settings, and as an investigational medicinal product for the treatment of myocardial infarctions. Apart from adult stem cells, Cytonet uses erythropoietin for the targeted induction and maturation of stem cells for the formation of blood vessels and organ structures as part of an "in vivo stem cell therapy". The company aims to apply the technology for liver diseases in the future.

Headquarters are in Weinheim, near Heidelberg, Germany, and production and development sites are located in Hanover and Heidelberg. In 2008, Cytonet took over the production facilities of its American cooperating partner VESTA Therapeutics, Inc. The company will now have its own site in the highly significant US biotechnology market.



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## ElexoPharm GmbH

**Founded**  
2005

### Employees

6 (Senior Scientists, Chemists/Pharmacists, Technical Assistants)

### Area of research and development

ElexoPharm is focused on the discovery and optimisation of new drugs. In order to obtain highly active and selective compounds with a convenient pharmacokinetic profile we are able to identify and to optimise the first biologically active hit compounds faster and more efficiently than others due to our long experience in rational drug design. This ensures a quick development of new lead compounds. Our team responsible for synthetic and analytical chemistry consists of highly qualified organic chemists with broad expertise in modern synthetic methods and the latest purification and analytical techniques. We can perform retro-synthetic analysis and synthesis of small molecules, natural products and peptides. Thanks to the access to a broad range of spectroscopy and spectrometry techniques, we succeed in elucidating the structure of unknown substances efficiently and quickly. Our own research projects focus on cardiovascular and oestrogen-dependent diseases.

### Indication

Oestrogen-dependent diseases, cardiovascular diseases

### Stage of research and development

Preclinical phase

### Collaboration

ElexoPharm has existing collaborations with pharmaceutical companies, i.e. Bayer HealthCare, Pharmacelsus.

### Pipeline

ElexoPharm has developed nonsteroidal 17beta-hydroxy steroid dehydrogenase inhibitors for the treatment of breast cancer showing IC50 values in the low nanomolar range. The compounds are in advanced preclinical stage. ElexoPharm has developed selective CYP11B2 inhibitors as lead compounds for the therapy of congestive heart failure, myocardial fibrosis and hyperaldosteronism and regard this novel therapeutic strategy as superior to the existing ones. The compounds are in advanced preclinical stage.

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## Encepharm GmbH

**Founded**  
2004

### Employees

6

### Area of research and development:

Encepharm was founded in September 2004 as a spin-off from the German Primate Center (DPZ). On a fee-for-service basis, Encepharm offers tailored research services and preclinical studies in the field of depression and neurodegenerative disorders. Encepharm's team has extensive expertise in the relevant disciplines and exclusive access to specific animal models for the investigation of depression, Parkinson's disease and multiple sclerosis. Through cooperation agreements with the DPZ, the University of Göttingen and local Max Planck Institutes, Encepharm is able to offer the full range of services including sophisticated techniques such as magnetic resonance imaging. In this way Encepharm is ideally positioned to meet the strong and increasing demand of the pharma and biotech industry for research services that produce meaningful results in the field of CNS disorders and support the selection of innovative therapeutic targets and drug candidates, as well as their preclinical development.

### Indication

CNS

### Collaboration

Yes



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## Essex Animal Health

**Founded**  
1967

**Employees**  
120

**Area of research and development**  
Manufacturing site for veterinary vaccines

**Indication**  
Vaccines

**Area of research and development**  
No research & development work on site

**Collaboration**  
Site belongs to Schering-Plough

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## European ScreeningPort GmbH

**Founded**  
2007

**Area of research and development**  
European ScreeningPort (ESP) is a public-private partnership which offers fee-for-service small-molecule screening to academic institutions.

The goal is to transform this exciting new science taking place in Europe's academic laboratories into chemical tools and high-quality assets of explicit value to potential major partners in the pharmaceutical industry and, ultimately, to patients.

**Drug discovery services for the European biomedical research community include:**

- experience in pharmaceutical industry R&D covering multiple target classes and therapeutic areas,
- access to high quality compound libraries and state-of-the art high-throughput screening facilities and
- direct access to pharmaceutical-scale medicinal chemistry and bioinformatics infrastructure and processes.



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## Evotec AG

**Founded**  
1993

**Employees**  
386

### Area of research and development

Evotec is a leader in the discovery and development of innovative small molecule drugs. The company has established a powerful platform that is applicable to targets across all therapeutic areas and has specific expertise in the area of central nervous system (CNS) related diseases where it is currently building a pipeline of drug candidates for partnering. Through research collaborations and proprietary projects, Evotec is providing the highest quality research results to its partners in the pharmaceutical and biotechnology industries.

Evotec's proprietary projects specialise in finding new treatments for diseases of the Central Nervous System (CNS). The focus of research is on major CNS related conditions, including sleep disorders, Alzheimer's disease, pain management and smoking cessation – fast growing therapeutic areas with large unmet medical needs. Evotec has a diverse product pipeline with candidates at various stages of development.

**Indication**  
CNS

**Collaboration**  
Boehringer Ingelheim  
Roche

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## Experimental and Clinical Research Center (ECRC)

**Founded**  
2007

### Employees

About 300 ECRC-associated researchers and support staff

### Area of research and development

The Experimental and Clinical Research Center (ECRC) was jointly established by the Max Delbrück Center for Molecular Medicine and the medical faculty of the Charité.

One major objective of the ECRC is to expand and strengthen interdisciplinary activities between basic and clinical researchers and shorten the route between discovery and clinical applications.

The general mission of the ECRC is to use molecular approaches in order to improve the diagnosis and treatment of the most prevalent human diseases, namely cardiovascular and metabolic diseases, cancer and neurological disorders. A focus will be on the development of non-invasive imaging technologies. Our long-term goals entail the generation and use of tailored, small molecular weight compounds, antibodies, vaccines, or modified cells in therapy (including preclinical, as well as Phase I and Phase II clinical trials).

### Indication

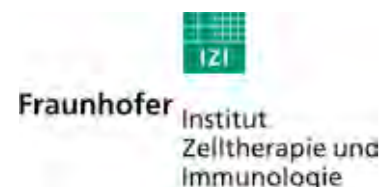
Therapeutic indication  
Cardiovascular diseases, metabolic diseases, cancer, leukaemia/lymphoma, CNS (stroke, multiple sclerosis, epilepsy)

### Collaboration

MDC/ECRC is currently cooperating with Siemens Medical Solutions and Bruker Biospin on the development and application of ultrahigh-field MR in biomedical imaging.



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## Fraunhofer Institute for Cell Therapy and Immunology

**Founded**  
April 2005

**Employees**  
140

**Funding**  
Funds raised through the Federal Republic of Germany, the Free State of Saxony and contract research.

**Area of research and development**  
Its objective being to find solutions to specific problems where medicine, life sciences and engineering overlap, for partners active in medicine-related industries and businesses. The Institute's core competencies can be found in regenerative medicine, or more precisely in cell-therapeutic methods of regenerating non-functioning tissue and organs through to biological substitution with tissue cultivated in vitro (tissue engineering). The Institute works especially closely with hospital institutions, performing quality tests and clinical studies on their behalf. Additionally it also provides assistance in obtaining manufacturing licences and certifications.

**Indication**  
Oncology, immunology and immune mediated diseases, inflammatory diseases, transplantation, infectious diseases, haematology, cardiology, neurology

**Stage of research and development**  
Applied research

**Collaboration**  
Yes, the institute is cooperating with multiple pharmaceutical companies.

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## Fraunhofer Institute for Molecular Biology and Applied Ecology (Fh-IME)

Fraunhofer Institute for Molecular Biology and Applied Ecology (Fh-IME) has sites in Aachen and Schmallenberg. The Aachen site focuses on molecular biology and biotechnology, and was responsible for the production of the anti-HIV antibody. The Schmallenberg site focuses on environmental chemistry, ecotoxicology and ecology. Fh-IME is a constituent entity of the Fraunhofer-Gesellschaft (FhG).

**Founded**  
The Aachen site was recently established in 2006. The Schmallenberg site was established in 1959 and will celebrate its 50th anniversary this year.

**Employees**  
192 (both sites)

**Funding**  
Funding was received as part of the EU's Sixth Framework Programme (FP6).

**Area of research and development**  
Fh-IME is coordinating and actively participating in Pharma-Planta, an EU Sixth Framework integrated project that started in February 2004. The primary project goal is to develop an innovative production pipeline for plant-derived pharmaceutical proteins (PDPs) in compliance with all appropriate regulations. Initially, eight target molecules representing four key indication areas were chosen, of which three anti-HIV antibodies (Abs) were selected for fast-track production. After evaluation of these Abs in several plant production systems the monoclonal anti-HIV antibody 2G12 was selected for production in tobacco plants. Fh-IME successfully carried out pilot-scale production and downstream processing of 2G12 and established a novel cGMP-compliant production process allowing linear up-scaling and production of sufficient antibody quantities. Clinical grade 2G12 has passed pre-clinical testing and Phase I clinical studies are planned for later this year. Further clinical studies will follow, so that 2G12 can ultimately be used as first plant derived antibody product for the prevention of HIV infections in HIV-endemic regions.

**Indication**  
HIV/AIDS, infectious diseases

**Stage of research and development**  
The plant-based monoclonal 2G12 antibody successfully passed preclinical testing in December 2008 and Phase I clinical studies are planned for the 2nd quarter of 2009.

**Collaboration**  
Yes. Fh-IME currently has more than 20 research collaborations with national and global pharmaceutical companies. Due to reasons of confidentiality their names cannot be disclosed.



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## Fraunhofer Institute of Toxicology and Experimental Medicine (ITEM)

**Founded**  
1981

**Employees**  
267

**Funding**  
Two thirds research revenue, one third is contributed by the German federal and state governments in the form of institutional funding.

### Area of research and development

- Investigations into issues of preventive medicine
- Research into novel diagnostic techniques and innovative therapeutic concepts
- Investigations for drug registration purposes
- Investigations into the toxicology and chemical safety of engineered nanoparticles and their therapeutic use
- Development of new ex vivo and in vivo techniques
- Toxicological and pharmacological investigations
- Clinical studies for the indication of airway diseases (Phases I-II)
- Genomics, proteomics and metabolomics
- Chemical risk assessment
- Studies on the effects and mechanisms of the action of airborne substances (fibres, particles, gases)
- Bioavailability studies
- Aerosol measurement and characterisation, as well as the creation of aerosols
- Registration and notification of chemicals and biocides
- Bio-analytical investigations (metabolites, protein and DNA adducts, biomonitoring)
- GLP, GCP, GMP quality assurance systems
- API manufacturing process development (USD, DSP)
- GMP and non-GMP manufacturing of APIs

**Indication**  
Lung diseases, cancer

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## Geneart AG

**Founded**  
1999

**Employees**  
190

### Area of research and development

GENEART with headquarters in the BioPark Regensburg has developed into the world's leading manufacturer of synthetic genes since entering the market in the year 2000. Today, GENEART AG is one of the foremost global specialists in the area of synthetic biology.

The company contributes the key technologies necessary to develop and produce new therapeutics and vaccines. Furthermore, GENEART customers rely on the company to improve enzymes, such as the ones used as additives in detergents, and to construct genetically altered bacteria, which produce complex biopolymers or degrade polymers like plastic or petroleum.

In its R&D program, GENEART AG collaborates with several well-known international universities and research institutes. Among these are the Universities of Regensburg, Oxford and Helsinki as well as NIH, Harvard, Yale, the EuroVacc Foundation and the International AIDS Vaccine Initiative. The EU, the German Federal Ministry of Education and Research (BMBF) and the Bavarian Research Foundation (Bayerische Forschungstiftung) support several GENEART research projects. The GENEART AG has also granted research-related

**Indication**  
Vaccination

**Stage of research and development**  
Phase II HIV vaccine



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## GlaxoSmithKline Biologicals

### Founded

The Dresden site was founded as Saechsisches Serumwerk and Institute of Bacteriotherapy in 1911. About 80 years later the British pharmaceutical company SmithKline Beecham acquired the company. In 2000, when SmithKline Beecham merged with Glaxo Wellcome, the site became a part of the new global corporation GlaxoSmithKline.

### Employees

More than 600 employees

### Area of research and development

GSK Biologicals Dresden has specialised in the development and manufacturing of flu vaccines for many years. The core product – seasonal flu vaccine – has been produced, egg-based, in Dresden since 1975. Presently, GSK Biologicals is developing a novel seasonal flu vaccine for elderly people targeting greater vaccine efficacy. The company also holds the world's first registrations for a pre-pandemic and pandemic H5N1 influenza vaccine, approved by the European authorities since May 2008. In case of a flu pandemic the Dresden GSK site is prepared to produce pandemic vaccine. GSK is involved in the research and development of a cell-culture-based influenza vaccine in North America. Because of its experience in influenza vaccines the Dresden site is a key candidate for the establishment of future large-scale production.

### Indication

Vaccines

### Stage of research and development

The clinical trial for the new seasonal flu vaccine is currently ongoing. Market entry of this new vaccine shall be in 2011/2012.

### Collaboration

GlaxoSmithKline Biologicals, Dresden, is closely integrated within the worldwide GSK-Biologicals network, and thus any cross-cooperation is done via GSK Biologicals, Belgium.

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untemehmen/dresden.html

## Glycotope GmbH

### Founded

2001

### Employees

Approximately 55 in Berlin and 45 in Heidelberg

### Funding

More than 50 million euros

### Area of research and development

GLYCOTOPE GmbH, a worldwide leading Biotech Company in the field of glycomics, has developed new technologies for lead optimisation of antibodies and other biopharmaceuticals. The glycooptimisation technology is based on a toolbox of innovative glycoengineered human cell lines (GlycoExpress™) which are perfectly suited to the production of glycooptimised products with a new patent protection.

GLYCOTOPE currently develops two unique proprietary and two second-generation antibodies – all of which are glycooptimised and conducive to cancer therapy – as well as one glycooptimised second-generation protein hormone. The first clinical trial will begin in 2009.

GLYCOTOPE operates in two locations: Berlin and Heidelberg (cGMP facility with four suites, max. 2 x 300 L mammalian cell fermentations and a track record of over 25 years).

Finally, as a one-stop service shop, GLYCOTOPE offers the development of biopharmaceuticals from early preclinical stage to the production under cGMP, adding value through humanisation and glycooptimisation technologies.

### Indication

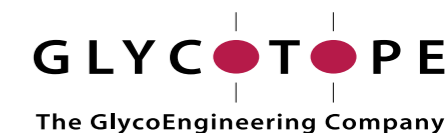
Therapeutic indication: cancer, immunology, infertility

### Stage of research and development

Five therapeutic products are currently in preclinical development. The first clinical phase I trial (therapeutic antibody) will begin in 2009.

### Collaboration

Yes, with around 15 companies overall from Biotech and Pharma



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## Heidelberg Pharma AG

### Area of research and development

#### Preclinical services

Heidelberg Pharma AG is a drug development company that focuses on cancer. The company has also provided services for the preclinical development of anti-cancer and anti-inflammatory drugs since 2008. Heidelberg Pharma is situated near Heidelberg in Ladenburg, Germany.

Heidelberg Pharma AG offers services in the field of lead optimisation and preclinical drug profiling. During this phase, the company's expertise in bioanalytical analysis and in vitro and in vivo pharmacology capabilities go hand in hand to assure optimal results in form of creative solutions, accurate reporting and qualified data, referenced against clinical standards.

#### Discovery and development

Despite more and more specific antibodies having been developed successfully for the treatment of cancer, there still is a need to increase their anti-tumour efficacy. The discovery of a highly potent yet targeted therapy may be achieved by coupling a highly potent toxin to an antibody with high affinity and specificity for a tumour cell associated target. Heidelberg Pharma is currently exploring a number of linker and toxin technologies to build an optimal antibody-toxin candidate.

HDP 15.0022 is an enhanced prodrug of clofarabine. This new patent-protected chemical entity was derived from the nucleoside clofarabine using the company's proprietary EPD Technology. Preclinically, HDP 15.0022 is significantly more effective than clofarabine and lacks its severe myelosuppression. Heidelberg Pharma expects EPD-clofarabine to provide a new potent anti-cancer drug to be taken orally once a day.

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## Helmholtz Centre for Infection Research/ Twincore/TRAIN

### Founded

1965

2006 renamed from Society for Biotechnological Research to Helmholtz Centre for Infection Research

### Employees

Around 600

### Area of research and development

At the Helmholtz Centre for Infection Research (HZI) we are studying pathogens that are medically relevant or can be used as models for researching infection mechanisms. Among the scientific questions we explore are: What turns bacteria into pathogens? Why are some people highly sensitive and others resistant to infections? How can we intervene in the infection process? Understanding these mechanisms will contribute to combating infectious diseases with new drugs and vaccines.

The HZI works closely with the Hanover Medical School (MHH): Both run the Centre for Experimental and Clinical Infection Research (Twincore), which combines the basic research of the HZI with the clinical research and experience of the MHH. The HZI is also a partner of the interdisciplinary biomedical group Translationsallianz in Niedersachsen (TRAIN). The main goal of both collaborations is to benefit the patient by shortening the path from basic research to new applied diagnostics, vaccines and therapeutics.



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## IDT Biologika GmbH

**Founded**  
1921

**Employees**  
650

### Area of research and development

IDT Biologika operates one of Europe's premiere integrated pharmaceutical and biological development and manufacturing facilities with the expertise and quality control necessary to supply world markets. IDT Biologika is known for the development and production of biological products. On the veterinary market IDT has secured an excellent position with its comprehensive range of vaccines and pharmaceuticals. With future human vaccines in mind, IDT Biologika provides development and manufacturing capacities for Phase I to III clinical trials as well as for commercial supply. Our new production facility features two manufacturing lines that allow segregated operations for the preparation of cells, virus propagation and purification using highly efficient technical systems. One of the most noteworthy challenges is safeguarding all operations in a multipurpose structure – preventing cross-contamination and expensive lead time between manufacturing campaigns. Within the last years IDT Biologika has also become a strategic partner for sterile liquids. Our fully-integrated services range from formulation development and clinical manufacturing through large-scale production, packaging and quality control.

### Indication

Prevention of infectious diseases, therapeutic vaccines for chronic diseases including cancer

### Stage of research and development

IDT Biologika develops technologies and manufactures vaccines and pharmaceuticals for Phase I to III clinical trials for third parties.

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## immatics biotechnologies GmbH

**Founded**  
2000

**Employees**  
65

### Funding

54 million euros

### Area of research and development

immatics is dedicated to the development of innovative cancer immunotherapeutics. Its proprietary technology for the identification of tumour-associated peptides (TUMAPs) enables the development of innovative anti-cancer vaccines for multiple cancer indications. immatics is currently developing two multi-TUMAP products in clinical Phase II studies – IMA901 for the treatment of renal cell carcinoma (RCC) and IMA910 for the treatment of colorectal carcinoma (CRC).

With its unique proprietary XPRESIDENT™ discovery platform, immatics is constantly identifying very large numbers of naturally-presented TUMAPs directly from primary tumour tissue and has identified more than 50,000 TUMAP sequences.

immatics identifies TUMAPs that occur as natural ligands of HLA class I and II receptors. These can activate cytotoxic T cells and T helper cells, which have the ability to eradicate cancer cells once they have been effectively.

### Indication

immatics is a biopharmaceutical company dedicated to the development of innovative cancer immunotherapeutics.

### Stage of research and development

- IMA901 (renal cell carcinoma) – clinical Phase II
- IMA910 (colorectal carcinoma) – clinical Phase II
- Further product candidates are currently in pre-clinical development.



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## IMTM GmbH

**Founded**  
1996

**Employees**  
40

### Area of research and development

IMTM is dedicated to the development of new therapeutic options for inflammatory diseases and fulfils unmet needs through preclinical services for special immune toxicology including large animal facilities.

IMTM has developed a new therapeutic concept, PETIR™ Drug Design (peptidase targeted immunoregulation), which represents an effective approach to inhibiting chronic inflammation. This unique PETIR™ technology promises a breakthrough in the treatment of a large number of inflammatory and autoimmune diseases.

PETIR™ drugs act on central pathological inflammatory processes including the activation of natural T regulatory cells (Treg) and the direct suppression of activated inflammatory T cells, as well as other concomitant cells through one combined mode of action.

The targeted diseases include autoimmune diseases like multiple sclerosis or inflammatory bowel diseases, allergies like bronchial asthma, dermal diseases like acne or psoriasis, as well as transplant rejection and atherosclerosis.

### Indication

Autoimmunity, chronic inflammation

### Stage of research and development

IP10.C8 – First-in-Class topical PETIR™ drug:

Phase II psoriasis,  
Phase II acne

IP10.C9 – First-in-Class oral PETIR™ drug:

Phase I inflammatory bowel diseases (Crohn's disease and ulcerative colitis)

### Collaboration

Yes

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## ImVisioN GmbH

**Founded**  
2005

**Employees**  
4

### Funding

ImVisioN has raised in excess of 8 million euros to date.

### Area of research and development

ImVisioN is a clinical stage immunotherapy company developing innovative treatments to cure allergies. Safe, fast acting, efficient and convenient curative immunotherapy can transform the current standards of allergy treatment and address a large patient population. Lead products target patients suffering from allergies against cat dander, birch pollen or house dust mites.

ImVisioN's innovative allergen immunotherapy combines intralymphatic immunotherapy (ILIT) with Modular-Antigen-Transportation (MAT) proteins. ILIT involves the injection of immunotherapeutics directly into the lymph node. Lymph nodes contain high amounts of antigen presenting cells (APCs) together with their corresponding immune cells, which are necessary for a curative immune response. MAT proteins are tailor-made recombinant allergens for ILIT that are rapidly taken up by APCs and improve the introduction of the allergen to the immune system. ILIT with MAT molecules is expected to be safer and more efficacious in inducing the desired immune response than conventional allergens.

### Indication

Allergies

### Stage of research and development

Lead product in Phase I/II clinical studies

### Further information

Cat-MAT (IVN201) immunotherapy to treat cat dander allergies in Phase I/II  
Birch-MAT immunotherapy to treat birch pollen allergies in preclinical  
Mite-MAT immunotherapy to treat house dust mite allergies in research



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## InterMed Discovery GmbH

**Founded**  
2006

**Employees**  
30

### Area of research and development

InterMed Discovery is an emerging world-class Natural Product lead-discovery company, driving innovation through the generation of novel product candidates for the life science, food and cosmetics industries. Using one of the most powerful validated Natural Product discovery engines, InterMed Discovery generates proprietary product pipelines of early stage pharmaceuticals and functional ingredients and also supports partners in research and lead generation.

Whether you are interested in the possibilities NP research offers, the technical background of our work or the products, services or consultancy we supply – we welcome you and are glad to answer your questions.

### Indication

Cancer, anti-infective, anti-fungal

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## JADO Technologies GmbH

**Founded**  
2001

**Employees**  
14

### Funding

11 million euros venture capital  
over 3 million euros in grants

### Area of research and development

JADO Technologies is the world's leading developer of cell membrane pharmaceuticals using its proprietary Raft Intervention Technology to enable development of small molecule drugs with innovative modes of action in allergy and infectious diseases. As awareness of lipid membrane drugs and their advantages over current therapeutics increases, JADO is already leading the way with a rich portfolio of products.

Raft Intervention Technology: rafts are specific membrane domains on which many physiological processes are dependent. Each raft is a highly specific process target offering an innovative mode of action for drugs with high potency, selectivity and safety.

### Indication

Allergic diseases (e.g., asthma, antihistamine-resistant urticaria, atopic dermatitis), infectious diseases (e.g., influenza, HIV, tuberculosis), Alzheimer's disease

### Stage of research and development

Product 1: clinical phase IIa  
Product 2: preclinical proof of concept



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## KeyNeurotek Pharmaceuticals AG

**Founded**  
2000

**Employees**  
27

### Area of research and development

KeyNeurotek Pharmaceuticals, a privately held biotechnology company, is focused on the development and marketing of innovative drugs against autoimmune diseases and degenerative disorders of the central nervous system (CNS). The company has unique functional, tissue-based high-throughput screening platforms for compatible ex vivo and in vivo studies (TELOMICS). Based on this, KeyNeurotek Pharmaceuticals pursues a number of drug candidates in various pre-clinical and clinical stages. The most advanced compound, KN38-7271, a CB1/CB2 cannabinoid receptor agonist, is currently in Phase IIa with 97 comatose patients with traumatic brain injury and has been granted the orphan drug designation by the EMEA. Study results are expected in H2/2009. At present, there is no targeted therapy for these patients. The company's second clinical lead candidate is KN203, a  $\mu$ -opioid receptor agonist with superior effects on bladder muscle regulation. KN203 is in Phase IIa/proof-of-concept investigation with patients with urge urinary incontinence/overactive bladder.

### Indication

CNS, autoimmune diseases, urology

### Stage of research and development

Two lead projects in Phase IIa/proof-of-concept studies

### Collaboration

Bayer  
Grünenthal  
Others

### Further information

KN38-7271, traumatic brain injury (TBI), Phase IIa  
KN203, urinary incontinence/overactive bladder, Phase IIa

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## Lead Discovery Center GmbH

**Founded**  
2008

**Employees**  
30–40

### Area of research and development

The Lead Discovery Center GmbH (LDC) was jointly developed by Max Planck Innovation and the Max Planck Society as an innovative approach to advance findings from excellent basic research into the development of new medicines.

With a world-class team of drug discovery experts and seasoned managers, the LDC offers the full scope of drug discovery services – from target to lead – according to the highest industry standards. As an independent enterprise with an entrepreneurial outlook, we collaborate with research institutions, universities and industry. Our aim is to transform promising and early-stage projects into pharmaceutical leads that reach initial proof-of-concept in animals and that meet the increasing need for novel therapeutic agents.

In selecting projects for drug discovery partnerships, the LDC places first priority on the quality of the research, its medical and commercial potential, and innovativeness. Overall, the LDC aims to establish a risk-diversified, well-staged pipeline of highly-differentiated projects that address new targets or pathological processes, have novel modes of action or build on new chemical scaffolds.

### Indication

The indications are not constricted and include cancer, neurodegenerative diseases, metabolic syndrome, infectious diseases and other conditions with high unmet clinical needs.

### Stage of research and development

Several projects in different stages, predominantly in the screening phase

### Collaboration

Several collaborations, details not disclosed



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## Leibniz Institute for Neurobiology (IfN)

**Founded**  
1992

**Employees**  
180

### Area of research and development

The IfN is a centre for learning and memory research investigating learning-induced plasticity in animals and humans at all organizational levels of brain function.

- The Neurochemistry Dept. studies the composition and dynamics of synapses, important drug targets in neurons. Molecular models for the interaction of proteins in the synapse are developed.
- In the Neurophysiology Dept. associative mechanisms in communicating neurons are investigated at the circuit and cellular levels with respect to animal behaviour, motivation or ageing.
- The Auditory Learning and Speech Dept. focuses on the processing of complex auditory patterns and how the brain understands spoken language. New findings about the plastic properties of the cortex are used to develop innovative neural prostheses.
- The Behavioural Neurology Dept. is dedicated to understanding the influence of evaluation and motivation on human behaviour. Patients with dysfunctions in evaluation and motivation systems are treated with deep brain stimulation.

### Indication

Dementia

### Stage of research and development

Basic and applied research of learning-induced plasticity

### Collaboration

Cellartis AB, Göteborg, Sweden  
Xigen SA, Lausanne, Switzerland  
Biotest s.r.o. Konarovice, Czech Republic  
Dr Willmar Schwabe Arzneimittel, Karlsruhe  
Probiodrug AG, Halle (Saale)  
FAN gGmbH, Magdeburg

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## Leibniz-Institut für Molekulare Pharmakologie (FMP)

**Founded**  
1992

**Employees**  
251 (160 research scientists)

**Funding**  
5.8 million euros

### Area of research and development

FMP research focuses on the structure, function and interaction of proteins. In interdisciplinary approaches new concepts of pharmacological interference are being developed. This places the institute's research activity at the forefront of drug development. The unique combination of technology platforms at the FMP – including a state-of-the-art NMR-facility, an open screening platform, and a mass spectrometry lab – provides an ideal environment for research projects in this field. The institute manages the central compound collection of the German Initiative for Chemical Biology, ChemBioNet and coordinates the Network for Drug Discovery & Development Berlin-Brandenburg, NetDDD. Together with the HZI (Braunschweig), it is the founding and coordinating institution of EU-OPENSREEN, the European Infrastructure of Open Screening Platforms (ESFRI-Roadmap 2008). It is a member of the Leibniz-Association and is legally represented by the Forschungsverbund Berlin e.V.

### Collaboration

Yes, with companies operating nationally and internationally



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## Matrix Advanced Solutions Germany GmbH

**Founded**  
2004

**Employees**  
14

### Area of research and development

Matrix employs a proprietary drug discovery process that generates high-quality drug candidates and solutions across the drug development value chain. The process radically improves the economics of drug discovery and will ensure that Matrix becomes a leading provider of validated drug candidates. Matrix can revolutionise the pharmaceutical industry's approach to drug discovery and development by approaching the challenge from a different perspective. Rather than using sequential screening techniques that attempt to simplify the analyses in the early stages of drug discovery, Matrix uses its proprietary technology, CADDIS®, to mimic the complexity of the human body and simultaneously evaluate drug candidates based on a large number of variables. The fundamental difference between CADDIS® and traditional drug discovery is its multi-parameter research approach – CADDIS® searches for candidates that best fit all the necessary criteria from the outset of a project and as a result finds the optimal candidates to succeed in clinical trials. The platform has been validated through the development of three drug discovery projects: a thrombin inhibitor, an antibiotic and a fungicide. Matrix intends to develop a robust portfolio of 8 drugs within 3 years. They will be developed in partnership with leading academic institutes, biotech and pharmaceutical companies.

### Indication

- Thrombin inhibition
- Cancer
- RNA viruses

### Stage of research and development

Our thrombin inhibitor is currently in an advanced preclinical phase and is showing exceptional efficacy, low toxicity and high selectivity, as well as bio-availability.

### Collaboration

- Licensing and partnership agreement with BiolineRx ([www.biolinerx.com](http://www.biolinerx.com)) for the clinical development and commercialisation of our thrombin inhibitor
- Joint sales and marketing agreement with ethica Clinical Research Inc. ([www.ethicaclinical.ca](http://www.ethicaclinical.ca))
- Two EU sponsored projects with over 15 academic and commercial institutions to establish early diagnostics for Prion neurodegenerative diseases

### Further information

Pipeline of the compounds in our region (sorted by status and if possible statements with respect to their indication areas)

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## Max Planck Institute for Dynamics of Complex Technical Systems Magdeburg (MPI Magdeburg)

**Founded**  
1996

**Employees**  
216 (as of 31 July 2008)

### Area of research and development:

The Max Planck Institute Magdeburg is dedicated to the engineering sciences and bridges the gap between basic research and industrial applications. The main research activities are focused on the analysis and synthesis, the design and control of processes in chemical and bioengineering. Scientists from different disciplines such as engineering, chemistry, biology, mathematics and computer sciences add their specific knowledge to the research work, thereby developing new methods and tools for designing modern, efficient processes for both current and future industrial applications.

### Examples of research

The research group Bioprocess Engineering focuses on establishing highly developed cell culture technologies and sophisticated product recovery steps aiming to achieve the full potential of biotechnological production methods.

The Systems Biology group develops and uses new mathematical models to describe cellular processes such as signal transduction and regulation. This knowledge has great impact on the development of novel therapeutics by computer simulation (in silico) studies. A main topic of the research group Physical and Chemical Foundations of Process Engineering is the design of processes capable of isolating and purifying fine chemicals. A particularly difficult task in this area is the separation of chiral compounds which are essential in pharmaceutical industry.

### Indication

Cell culture technologies, signal transduction, cell metabolism, in silico studies, separation of chiral compounds

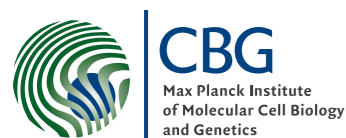
### Collaboration

The research group Bioprocess Process Engineering is collaborating with the following pharmaceutical companies:

- Bavarian Nordic
- EMC microcollections GmbH, Tübingen
- Biologika GmbH, Dessau-Roßlau
- Merckle Biotec GmbH, Ulm
- ProBioGen AG, Berlin
- Sartorius AG, Göttingen
- The Max Planck Institute Magdeburg also maintains relations with Bayer Schering Pharma AG and Astra Zeneca GmbH.



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## Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG)

### Founded

MPI-CBG was founded in 1998. Since February 2001, scientists from over 40 nations have been working under one roof.

### Employees

The Institute has a core staff of about 400 scientists, who form a network of 25 research groups

### Area of research and development

The Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG) is one of 78 institutes of the Max Planck Society, an independent, non-profit organization in Germany. At the MPI-CBG researchers study different topics at the intersection between cell biology and developmental biology: For example, they study how the growth of cells is controlled and why this control process fails to function properly in cancer cells.

### Indication

Once science has an understanding of how cellular control systems work, currently incurable illnesses such as cancer or Alzheimer's disease may be diagnosed earlier and prospectively more effective treatments can be developed.

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## medac GmbH

### Founded

1970

### Employees

580

### Funding

100% private company

### Area of research and development

medac is a pharmaceutical company that has specialised in the treatment of malignant diseases. Many years of experience have made the company one of the leading manufacturers of oncology products in Germany and in international markets. medac also offers new and well-proven therapeutic options in the fields of urology, autoimmune diseases and fibrinolysis. Moreover, medac is one of the few companies also engaged in the field of diagnostics. Besides special diagnostics to detect infectious diseases, medac combines therapeutic and diagnostic tools to establish the highest efficacy in treatment procedures.

### Indication

Oncology, haematology, autoimmune diseases, diagnosis of infectious diseases, cancer diagnostic

### Stage of research and development

Phase II: 1 product  
Phase III: 2 products

### Collaboration

Yes, various European companies



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## MediGene AG

**Founded**  
1994

**Employees**  
130

### Area of research and development

MediGene AG is a publicly quoted (Frankfurt: Prime Standard: MDG) biotechnology company located in Martinsried/Munich, Germany, with subsidiaries in Oxford, UK, and San Diego, USA. MediGene concentrates on researching, developing and commercialising new drugs in two therapeutic areas: cancer and autoimmune diseases. MediGene is the first German biotech company to bring drugs onto the market. At the moment, our drugs are distributed by partner companies. Medium-term, we intend to start our own marketing activities. MediGene has several drug candidates in clinical development, some of which providing substantial sales potential. In addition, we possess innovative platform technologies, which enable the search for other therapeutic substances. Licensed products complement our proprietary drug portfolio.

### Indication

MediGene's drug portfolio on the market: Eligard® (prostate cancer); Veregen®/Polyphenon® (genital warts)

### Stage of research and development

EndoTAGTM-1 (Phase II finalized for pancreatic cancer; Phase II started for breast cancer; Phase-I for various other solid tumour indications)  
RhuDex® (Phase II started for rheumatoid arthritis)  
Oncolytic viruses (HSV) (Phase II started for colon tumour metastases)

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## Micromet AG

**Founded**  
1993

**Employees**  
100

### Area of research and development

Micromet AG, located in Munich and Bethesda (USA), puts novel concepts in immunotherapy to work. Using proprietary technologies, the company is building a strong pipeline of innovative drug candidates for the treatment of cancer, inflammation and autoimmune disease. Two candidates are currently in clinical trials. The company has established a powerful drug development platform, BiTE™ (bi-specific T-cell engagers), a unique drug format that leverages the outstanding cytotoxic potential of T cells to precisely eliminate pathogenic cells. In addition, Micromet is exploiting the potential of SCAs (single-chain antibodies) for the development of novel drug candidates. The company has attracted both top-tier life science investors and corporate partners such as MedImmune/AstraZeneca, Inc., Enzon Pharmaceuticals Inc., Bayer Schering and Merck Serono.

### Indication and stage of research and development

Micromet's drug portfolio and indications:

- Blinatumomab (MT103/MEDI-538) Phase II: acute lymphoblastic leukaemia
- Blinatumomab (MT103/MEDI-538) Phase I: non-Hodgkin's lymphoma
- Adecatumumab (MT201) Phase II/I: metastatic breast cancer

### Collaboration

In May 2006, Micromet AG merged with CancerVax Corporation (formerly NASDAQ: CNVX) to form Micromet, Inc. (NASDAQ: MITI).

### Further information

Latest finance news from 2008: Micromet closed a 40-million US dollar private equity placement and Micromet expanded their committed equity financing facility to 75 million US dollars.



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## MOLOGEN AG

### MOLOGEN AG

**Founded**  
1998

**Employees**  
44

#### Area of research and development

MOLOGEN AG is a German biotechnology company located in Berlin, specialising in the development of innovative DNA-based therapeutics and vaccines against diseases with a high medical demand.

The proprietary platform technologies MIDGE® (Minimalistic Immunogenically Defined Gene Expression) and dSLIM® (double Stem Loop Immunomodulator) build the foundation for the company's business activities.

MOLOGEN AG focuses on cancer treatment and combating infectious diseases in humans and domestic animals.

Founded in 1998, MOLOGEN AG was one of the first German biotechnology companies to go public. Shares are listed on the General Standard segment of the Frankfurt Stock Exchange (ISIN DE 0006637200).

#### Indication

Cancer, infectious diseases, immunology, gene therapy, vaccines

#### Stage of research and development

- Cancer therapy with dSLIM® (MGN1703): clinical phase Ib/IIa
- Cell-based gene therapy against cancer (MGN1601), orphan drug status: preclinical
- DNA vaccine against human leishmaniasis (MGN1331), funded by EU: preclinical
- DNA vaccine against FeLV (MGN1225): preclinical

#### Collaboration

Vetsuisse Faculty, University of Zurich, Switzerland  
Max Planck Institute for Infection Biology, Berlin  
University of Veterinary Medicine, Hanover  
Infectious Disease Research Institute (IDRI), Seattle, USA

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## MorphoSys AG

**Founded**  
1992

**Employees**  
350

#### Area of research and development

MorphoSys AG (listed on the Frankfurt Stock Exchange: MOR) is one of the world's leading biotechnology companies focusing on fully human antibodies. MorphoSys is developing the next generation of antibodies with its proprietary technologies, not only for research and diagnostics purposes, but also as highly effective and precise therapeutics. HuCAL® (Human Combinatorial Antibody Library) is a very powerful technology for the rapid and automated production of specific antibodies. The most distinctive feature of the library is its unique capability to optimise fully human antibodies to predefined specifications, allowing MorphoSys researchers and their partners to "Engineer the Medicines of Tomorrow". MorphoSys's goal is to establish HuCAL® as the technology of choice for antibody generation in all market sectors. Sectors of indication are cancer, immunology and CNS, for example.

MorphoSys is a profitable high-growth company, building a strong therapeutic antibody pipeline with more than 50 projects in development – mainly with its 13 partnerships, but also increasingly on its own. Notably, the cooperation with Novartis will account for 40 million euros per year until 2018. With total operating revenues of 62 million euros in 2007 – an organic increase of 17 percent over 2006 – MorphoSys will profit from the successful drug development of its partners through milestone and future royalty payments for marketed HuCAL-based drugs.



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## Nexigen GmbH

**Founded**  
2007

**Employees**  
10

### Area of research and development

Nexigen GmbH develops new drugs with fewer unwanted side effects and innovative modes of action. Nexigen's proprietary drugs target disease mechanisms, which common technology is unable to address. Nexigen's technology is able to close the gap between small molecule drugs and therapeutic antibodies.

Nexigen developed a technology which allows the discovery and optimisation of peptide-derived drugs to target intracellular proteins. Its technology platform is broadly applicable to various indications.

The company's own drug discovery pipeline focuses on anti-viral and cancer indications.

### Indication

Anti-infectives (HIV, HCV), cancer

### Stage of research and development

Drug discovery

### Collaboration

Yes, with a top-10 pharma company

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## Novosom AG

**Founded**  
1999

**Employees**  
20

### Area of research and development

By enabling the development and commercialisation of innovative oligonucleotide therapeutics, Novosom AG is a biopharmaceutical company that is working towards clinic therapies. The company has taken a major step towards functional oligonucleotide therapeutics with the discovery of the Smarticles technology: The adaptation of the therapeutic principle to the cell's interior. As such, Smarticles is establishing itself as an enabling technology for oligonucleotide systemic therapies. Novosom and its partners develop unique oligonucleotide therapeutics for inflammation, autoimmune, oncology and liver diseases. Oligonucleotide therapies comprise antisense, decoy and RNAi drugs that inhibit the production of targeted proteins with absolute specificity. They are the next major product generating engine of the pharmaceutical industry and are able to work around a number of unsolved issues which other therapeutics face.

### Indication

Inflammation, autoimmune, oncology

### Stage of research and development

Smarticles have received IND (Phase I clearance) from the FDA for a DNAi candidate in oncology (collaboration with ProNAi Therapeutics).

Novosom is developing an anti-CD40 product candidate based on an exclusive licence from Isis Pharmaceuticals for the use of CD40 antisense inhibitors. CD40 is a well established target for both inflammatory and autoimmune diseases, for indications such as Crohn's disease, organ transplant or rheumatoid arthritis.

### Collaboration

Yes. Multiple undisclosed collaborations with international pharmaceutical and biotech companies. Public collaborations include Boehringer-Ingelheim, Isis Pharmaceuticals and ProNAi Therapeutics.

Novosom is participating as a consortium member in two research projects funded by the European Community. Research focuses are oncology (FP6 Apotherapy project) and atherosclerosis (FP7 AtheroRemo project), both funded by the European Community. Additional activities include academic collaborations with several universities and other research institutions.



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## NOXXON Pharma AG

**Founded**  
1997

**Employees**  
41

### Funding

NOXXON raised 37 million euros in a Series C financing round in May 2007

### Area of research and development

NOXXON Pharma AG is a privately owned biopharmaceutical company focusing on the development of innovative therapeutics based on its unique proprietary Spiegelmer® Technology. Spiegelmers are highly specific oligonucleotide therapeutics, designed to deactivate their target protein through a direct molecular interaction, working on a similar concept to monoclonal antibodies. They are non-toxic and non-immunogenic. Furthermore, they are produced entirely by well established chemical processes.

NOXXON's lead products are NOX-A12 – an SDF-1 antagonist for stem cell mobilization and neovascular disorders – and NOX-E36 – an MCP-1 antagonist for the treatment of lupus nephritis.

### Indication

Oncology, immunology, ophthalmology

### Stage of research and development

NOXXON's lead programmes will enter clinical development in 2009

### Collaboration

NOXXON cooperates with pharmaceutical companies in the discovery and development of novel therapeutics. Among its partners are:

- Pfizer Inc. – licensing and drug discovery partnership. Multiple targets.
- Hoffmann-La Roche – licensing and drug discovery partnership. Multiple targets in inflammation.
- Eli Lilly and Co. – licensing and discovery collaboration in migraine.

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## Partec GmbH

**Founded**  
2000

**Employees**  
75

### Area of research and development

Since 2002, Partec is active in the development of dedicated diagnostic solutions for HIV/AIDS, tuberculosis and malaria, which are especially adapted to the requirements and infrastructural situation of developing and emerging countries. The key technologies used by Partec for the instrumentation are fluorescence-based flow cytometry and fluorescence-based microscopy. Partec introduced the first mobile/portable and battery – or solar panel – operated device classes in flow cytometry and fluorescence microscopy.

Furthermore, Partec develops uniquely affordable and easy-to-use reagent kits which are partially designed based on lyophilized monoclonal antibodies – fluorochrome combinations. These “dry” kits are a breakthrough for treatment programmes because the use of this new class of reagents offers for the first time in HIV monitoring, AIDS patient follow-up diagnostics and malaria testing to eliminate any needs for cooling chain and cool storage as is required for conventional kits.

### Indication

Immune status diagnostics

### Stage of research and development

CyFlow® and CyScope®, including reagent kits, have already been successfully introduced to the market.

### Collaboration

Yes



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## PharmaCenter University of Bonn

**Founded**  
2008

### Area of research and development

The Research Center for Innovative Drugs and Therapies at the University of Bonn brings together the expertise of research groups including pharmacology, medicinal chemistry, cell biology and clinical sciences. The common interests of the members of the PharmaCenter Bonn converge in drug development and pharmacotherapy.

### The major scientific aims are:

- Pharmacological modulation of signalling pathways focussing on membrane proteins, GPCRs, kinases and phosphatases
- Development of new therapeutic concepts – focus on chemicals (“small molecules”), e.g. allosteric modulators, dimer-specific ligands
- Investigation and development of experimental therapeutic approaches – focus on biologicals, such as stem cell, RNA and nano-technology-based therapies
- Establishment of in vitro models (viral vector platform) – clinically relevant animal models of human diseases (knockout and transgenic mice, lentiviral transgenesis)
- Pharmaceutical approaches to overcome drug resistance (focus on antibiotics and chemotherapy)

### Collaboration

Schwarz Pharma/UCB, Protagon, Priaxon, Life&Brain GmbH

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## Phenex Pharmaceuticals AG

**Founded**  
2002

**Employees**  
18

### Area of research and development

Phenex Pharmaceuticals is a privately financed biotechnology company focusing on innovative drug candidates that act on nuclear receptors (NR); a well-accepted pharmacological drug target class.

Its lead project, FXR, focuses on the development of an innovative, small-molecule-based approach to oral antidiabetic and lipid lowering treatments. Phenex's proprietary FXR agonist Px-101 demonstrates potent triglyceride and cholesterol lowering capabilities in conjunction with an improvement in insulin sensitivity. This project is in preclinical development and a first Phase I clinical trial is scheduled for late 2010.

At the same time, Phenex is developing a different type of FXR agonist for innovative therapeutic approaches in hepatologic indications with unmet medical needs, such as liver regeneration, non-alcoholic steatohepatitis and liver fibrosis.

Phenex is offering its resources and capabilities in the field of NR to customers within the pharmaceutical industry, through everything from contract services to integrated research collaborations. More than 50 international companies in Europe, Japan and North America are customers of Phenex.

In October 2008, Phenex raised 8.2 million euros from a syndicate of institutional and private investors. Phenex is investing these proceeds into its proprietary drug discovery programmes targeting FXR and LXR, two key nuclear receptors involved in different disease physiologies. The company's value driver is its FXR project, which aims to develop a breakthrough therapy for metabolic syndrome and type 2 diabetes. Phenex is drawing together leading experts from the fields of nuclear receptor biology, medicinal chemistry, metabolic diseases, gastroenterology and hepatology to develop these innovative therapeutic concepts.



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## Pieris AG

**Founded**  
2001

**Employees**  
35

### Area of research and development

Pieris AG is a biopharmaceutical company engaged in the discovery and development of Anticalins<sup>®</sup> for the diagnosis and treatment of life-threatening human disorders. Exploiting extensive know-how in protein engineering as part of a broad intellectual property portfolio, the company applies a balanced risk business model to the development of its Anticalin<sup>®</sup> candidates. Recognising the enormous market potential of protein-based drugs, Pieris is committed to becoming an integrated drug discovery and development company.

Anticalins<sup>®</sup> are derived from lipocalins, a family of low molecular weight proteins that are naturally and abundantly expressed in human tissues and body fluids. While the overall structure of hypervariable loops supported by a conserved  $\beta$ -sheet framework is reminiscent of immunoglobulins, lipocalins differ considerably from antibodies in terms of size, being composed of a single polypeptide chain of 160–180 amino acids which is marginally larger than a single immunoglobulin domain.

In terms of therapeutic focus for its proprietary pipeline, Pieris is currently engaged in Anticalin<sup>®</sup> programs with broad potential application in oncology. Partnered therapeutics programmes span a range of potential therapeutic areas.

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## PLANTON GmbH

**Founded**  
2001

**Employees**  
15

### Area of research and development

PLANTON focuses on the development of antimicrobial peptides as a therapeutic alternative for presently available antibiotics. The ongoing development of resistant microbes overcoming antibiotics that are present on the market is an increasing medical problem making the development of new innovative antibiotic drugs necessary.

To target this yet unmet need, PLANTON has combined its comprehensive knowledge of antimicrobial peptides and its proprietary technology to work on recombinant protein production to advance the development of a new class of antibiotics.

All peptides developed by PLANTON are human bio-molecules with a broad antibiotic efficacy and a special mechanism avoiding resistance of human pathogens. The molecules in development are protected by appropriate intellectual property rights.

Currently preclinical development is ongoing and first clinical trials are planned in the near future.

### Indication

Anti-infective treatment

### Stage of research and development

Preclinical status



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## PlasmidFactory GmbH & Co. KG

**Founded**  
2000

**Employees**  
16

### Area of research and development

PlasmidFactory is a contract manufacturer for plasmid DNA from research scale up to industrial scale for R&D, DNA vaccination, gene therapy, virus production, drug delivery and tumour therapy. Besides the service production of plasmid DNA, the company offers a gene synthesis and optimisation service, In Stock plasmids for reporter gene vectors, mock transfections, pDG vectors for AAV virus production and pEPI vectors with S/MAR. PlasmidFactory's R&D and all services are carried out in Germany. With two BMBF grants and European research collaborations (FP6), the company is the leading force in gene vector development.

PlasmidFactory has developed capillary gel electrophoresis (CGE) for quantitative analysis of plasmid DNA topologies. CGE is a useful tool for plasmid quality control, storage and stability assessment. At present, a highly efficient minicircle DNA system is being developed to obtain non-viral vectors without antibiotic resistance elements, other selection markers or bacterial (CpG-containing) sequences.

### Indication

Various sectors that are in the focus of gene therapy or DNA vaccination: cancer, infectious diseases (e.g. hepatitis), diseases caused by genetic defects (e.g. haemophilia, cystic fibrosis)

### Stage of research and development

Plasmid DNA for R&D, pre-clinical and clinical studies

### Collaboration

Yes, details not disclosed

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## PLS-Design GmbH

**Founded**  
2004

**Employees**  
12

### Funding

Privately financed

### Area of research and development

Diagnostics:

- Innovative diagnostics for Insect venom allergy tests based on patent-protected recombinant allergens.
- Allergen-specific chimeric IgE for allergy test standardization.
- High-affinity IgE quantification tool for monitoring anti-IgE therapies.
- Chimeric IgY-technology to reduce false signals in clinical relevant assays.

Therapeutics:

- Novel therapeutics for insect venom allergy using recombinant allergens.
- Anti-inflammatory drug based on enzymatic depletion on Complement.

Drug development:

- Patent-protected proprietary selection system for PNA-aptamers.

### Indication

Immunology, inflammation, drug development

### Stage of research and development

- Clinical Phase I with partner:  
CompDepletin/Hc3-1496 (Anti-inflammatory drug).
- Preclinical, licensing opportunity:  
Allergy therapeutics.
- R&D, licensing opportunity:  
Allergy standardization, Chimeric IgY-technology, PNA-Aptamers.
- Product development with partner :  
Allergy diagnostics, IgE-AviQuant (Monitoring of anti-IgE therapies).

### Collaboration

Siemens Healthcare Diagnostics, USA  
InCode Biopharmaceuticals, USA  
GenWay Inc, USA



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## PomBioTech GmbH

**Founded**  
2006

**Employees**  
15

### Area of research and development

PomBioTech offers custom made fission yeast strains that are specifically tailored to meet your need. When dealing with proteins that are difficult to express functionally in other microbes, fission yeast has in many instances turned out to be a suited model system in our hands. At comparatively low cost the PomBioTech researchers will make a proof-of-concept study to check whether your protein of interest can be functionally produced by recombinant *S. pombe*. Later on, our fission yeast specific fermentation facilities may be used for production; alternatively, the tailor-made strains may be utilized by the customer himself. Currently, we have a variety of recombinant fission yeast strains at our disposal that express a set of different human cytochromes P450 and that can be directly used for the generation of P450 metabolite.

### Indication

Phase 1 and Phase 2 metabolism, CRO

### Stage of research and development

Different Cytochrome P450 expressing fission yeast strains are available

### Collaboration

Yes, e.g. Solvay Inc.

### Further information

We at PomBioTech have a variety of recombinant fission yeast strains at our disposal that express a set of different human cytochrome P450s. These include both liver P450s (like CYP3A4 or CYP2D6) that metabolize a large variety of xenobiotica and steroidogenic P450s (such as CYP11B1 or CYP11B2) that catalyse very specific steroid hydroxylation reactions. Using these P450 expressing strains, we are able to offer custom production of P450 metabolites up to technical scale. The list of human P450s that we have successfully expressed in fission yeast is constantly growing. For more information please visit our homepage: [www.pombiotech.com](http://www.pombiotech.com)

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## Probiodrug AG

**Founded**  
1997

**Employees**  
75

### Status of research and development

Probiodrug's core competence is the elucidation of the structure, biochemistry, biology and pathophysiology of regulatory peptides and enzymes modifying the activity of specific proteins and pathways.

Based on this expertise, the company is developing inhibitors and ligands targeting key enzymes such as proteases and kinases. The most promising compounds are then developed by Probiodrug as drug candidates for the treatment of major diseases such as Alzheimer's disease or chronic inflammatory disorders.

The company aims to bring these compounds through preclinical and clinical development up to proof-of-concept trials to provide a strong basis for selectively out-licensing its drugs to the pharmaceutical industry or entering into co-development partnerships.

### Indication

CNS, immunology



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## ProBioGen AG

**Founded**  
1994

**Employees**  
65

### Area of research and development

Contract cell line development, process development and manufacturing of mammalian cell-based drug candidates for Tox testing, Phase I and Phase II trials.

Proprietary cutting-edge platform technologies for vaccine manufacturing and immunogenicity testing successfully introduced into the market place last year.

### Stage of research and development

AGE1.cr – a new duck-cell line platform for flexible vaccine manufacturing fully established. First license deals closed in 2008.

ALN – artificial human lymph node technology used for preclinical contract evaluation of customers' new drug candidates.

### Collaboration

Yes

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## Proteo Biotech AG

**Founded**  
2000

**Employees**  
6

### Area of research and development

The Proteo Biotech AG is located in Kiel, Germany and researches, develops and markets nature identical compounds for biological and medical research as well as for use as pharmaceuticals. The main focus is on anti-inflammatory drugs, in particular on the Company's lead product, the human elastase inhibitor Elafin. Elafin is a highly potent down regulator of tissue destruction in the course of inflammatory diseases, especially those affecting blood vessels, lungs or muscles. For the clinical development of Elafin and the development of other product candidates, Proteo has established a network of world- renowned research institutes, physicians and hospitals all over Europe and the USA. Proteo intends to out-license selected indications and to establish international strategic alliances in order to open up new fields of application for marketing.

### Indication

Inflammatory diseases, reperfusion injury, transplantation, PAH

### Stage of research and development

Elafin:

- Phase I (i.v.), completed 2006
- Orphan Drug Status (EU) for the treatment of pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension
- Phase II, Kiel (i.v.) started 11/2008
- Phase II, Cairo (i.v.) granted

### Collaboration

Minapharm Pharmaceuticals SAE, Cairo, Egypt  
Artes Biotechnology GmbH, Andernach  
HBT Hycult Biotechnology, Netherlands  
Eurogentec S.A., Belgium  
CRS GmbH, Kiel  
University of Alberta, Canada  
University of Stanford, USA  
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## Rentschler Biotechnologie GmbH

**Founded**  
1974

**Employees**  
450

### Area of research and development

Rentschler Biotechnologie GmbH, Laupheim, Germany, is an international full-service contract manufacturer with more than 30 years of experience in the development, production and approval of biopharmaceuticals in compliance with international GMP standards. Furthermore, Rentschler provides regulatory advice and fill-and-finish services. As a pioneer in the development and production of biopharmaceuticals, Rentschler was the first company in the world to gain market authorisation for an interferon-containing drug. At present, Rentschler Biotechnologie has nine self-contained GMP suites with volumes of 30, 250, 500 and 2,500 litres, allowing the production of material for clinical trials and for market supply.

### GMP-certified services

- Cell Line and Process Development
- Production of Active Pharmaceutical Ingredients (API)
- Fill and Finish
- Analytics and Quality Control
- Regulatory Affairs
- Quality Assurance
- Corporate Project Management

### Indication

Contract manufacturing of therapeutic agents used in treating cancer, immunology, multiple sclerosis, viral diseases, anaemia, neutropenia, haemophilia, strokes, heart attacks, etc.

### Stage of research and development

Contract manufacturing of Preclinical Material/Phase I/II Material, Phase III/ commercial

### Collaboration

Preferred partnership agreement with Boehringer Ingelheim for a seamless project transfer to large-scale manufacturing of up to 15,000 L.

Cooperation agreement with CELLCA GmbH aimed at the development, application and marketing of a high-level expression system for mammalian cells.

- Scil Technology, Coriolis PharmaService: Formulation development
- Richter-Helm Biologics: Production of E.coli
- Various contract laboratories

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## REVOTAR Biopharmaceuticals AG

**Founded**  
2000

**Employees**  
25 in Hennigsdorf/Berlin

### Funding

Revotar raised 9 million euros in 2007/2008 and further commitments of another 3 million euros based on certain conditions to be met.

### Area of research and development

Revotar develops innovative drugs for inflammatory indications such as psoriasis, asthma, chronic obstructive pulmonary disease (COPD) and acute lung injury (ALI). Its lead candidate Bimosiamose, a pan-selectin antagonist, has already passed several clinical phase I and phase IIa trials in asthma, COPD and psoriasis with a good safety and efficacy profile in nearly 200 patients and volunteers. Revotar has built up a fully integrated drug discovery and development engine encompassing medicinal chemistry, analytics, molecular biology, pharmacology, ADMET, QA/QC, in vitro models and assays as well as cheminformatics in inflammation on the one hand and preclinical/clinical development and CMC on the other hand. In summer 2006, Revotar announced a Start-Up Development Agreement with a US pharma company for the further development of Bimosiamose in one major disease area.

### Indication

Revotar develops innovative drugs for inflammatory indications such as psoriasis, chronic obstructive pulmonary disease (COPD), asthma and acute lung injury (ALI).

### Stage of research and development

In January 2009, Revotar announced the start of a Phase II study to evaluate the safety and efficacy of Bimosiamose 5 percent Cream for the treatment of patients with chronic plaque-type psoriasis. The cream is a new topical formulation of the pan-selectin antagonist Bimosiamose. The Phase II study is designed as a randomized, double-blind, placebo-controlled multi-centre study comprising 105 male patients aged 18 years or older, or postmenopausal or sterile female patients. Revotar will initiate further phase IIa studies in the respiratory area during 2009/2010. Furthermore, Revotar has one repositioning project of an already marketed drug in preclinical development and further preclinical backup compounds in inflammatory diseases.

### Collaboration

Revotar maintains scientific collaborations such as with the Charité and various other international institutes and universities



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## Rhein Biotech GmbH (Dynavax Europe)

**Founded**  
1985

**Employees**  
61

### Area of research and development

Twenty-four years of excellence have made Rhein Biotech GmbH an expert in the development of biopharmaceutical products. Rhein Biotech offers innovative, custom-tailored solutions for strain development, analytical development, process development and GMP manufacturing. GLP conform testing of cell banks, proteins and clinical samples (cellular and humoral immune responses) complement the technical portfolio. Rhein Biotech's proprietary technologies are used worldwide by affiliates and renowned licensees for commercialisation of hepatitis B vaccines, combination vaccines, human insulin, human IFN -2a and hirudin. More than 500 million doses of 3-dose hepatitis B vaccines based on Rhein Biotech technology have been sold by licensees in more than 90 countries. Currently, Rhein Biotech is actively researching and developing vaccine and immuno therapeutics with particular focus on the hepatitis virus.

### Indication

- Vaccines, anti-infectives, immunology
- Contract development and contract manufacturing

### Stage of research and development

- Manufacturing of hepatitis B virus antigens for vaccines and diagnostics
- Final bulk hepatitis B vaccine
- Two-dose hepatitis B vaccine with a fast onset of immuno protection (Phase III)
- Therapeutic hepatitis B vaccine (Phase I)

**Collaboration**  
Yes

## Richter Helm BioTec GmbH

**Founded**  
1997

**Employees**  
110

### Funding

Privately owned

### Area of research and development

Richter-Helm BioTec is a dynamic and expanding biotechnology company located in Hamburg, Germany. The company was founded in 1997 as Stratmann Biotech and was acquired in 2007 by a joint-venture of Gedeon Richter Plc., Hungary, and Helm AG, Germany. The company operates a development facility and two cGMP manufacturing facilities for microbial production.

Richter-Helm offers highly specialised contract development and manufacturing services for the pharmaceutical and biotechnological industries. Additionally, Richter-Helm is seeking interesting biopharmaceutical development projects for its own pipeline and for co-development with partners.

### Richter Helm offers:

- contract development and manufacturing of recombinant proteins, plasmid DNA (industrial scale) and microbial vaccines according to cGMP,
- full development up to the finished product and
- global in- and out-licensing of biopharmaceutical projects.

### Stage of research and development

RHT-001, preclinical development  
RHT-002, preclinical development

### Collaboration

Active Biotech Research, TU Dresden, Therapeomics, Biogenerix, Nycomed, Sanofi-Aventis, Kuros, Athera, ImVisioN, Ludwig Institute for Cancer Research



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## RIEMSER Arzneimittel AG

**Founded**  
1990

**Employees**  
640

### Area of research and development

- RIEMSER is a mid-sized speciality pharmaceutical company that markets primarily branded speciality or niche products, mainly for the area of Human Rx Specialities.
- Business model: Currently, the 'Human Rx Specialities' segment focuses primarily on therapeutic products for dermatology, anti-infectives and dental. The company is expanding its oncology business. The company is also active in 'other specialities' in the area of OTC (mainly dermatology) and animal health.
- Riemser Arzneimittel AG incorporates pharmaceutical manufacturing facilities and business units, such as the Sanavita Pharmaceuticals GmbH in Werne, Fatol Arzneimittel in Schiffweiler, the well-established Leipziger Arzneimittel Werk, Rösch Medizintechnik in Berlin, Dr Herbrand KG in Gengenbach and facilities in Münster and Kleinostheim.

### Stage of research and development

RIEMSER AG owns more than 400 drug registrations in Germany as well as abroad.

Furthermore, RIEMSER has more than 200 trademarks and 70 patents and patent applications, supporting the development of new products.

In detail, these are: over 400 human medicine drug registrations in its home markets, over 200 trademarks and 70 patents, and over 30 animal health drug licences in both Germany and abroad.

RIEMSER AG completed, or is in the process of the completion of: over 40 clinical re-registrations and 36 post-marketing studies (phase IV).

### Collaboration

With commitment and in close co-operation with universities, academies, clinics and research institutes of international renown in Germany and Europe, the company carries out research on medical drugs for humans and animals.

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## Roche Diagnostics GmbH

**Founded**  
1998

**Employees**  
4,500

### Area of research and development

Roche Diagnostics GmbH is part of Roche, Basel, Switzerland. Roche is one of the world's leading research-focused health care groups for pharmaceuticals and diagnostics, and supplies products and services for the detection, prevention, diagnosis and treatment of disease. Roche is a world leader in vitro diagnostics, the leading supplier of medicines for cancer and transplantation, and a market leader in virology. At Penzberg, Roche operates one of the largest biotechnology facilities in Europe. Diagnostics research develops innovative reagents and test systems for the life science market, as well as for diagnosis, patient stratification and therapy monitoring. Pharmaceutical research involves the research, development and production of therapeutic human proteins and focuses on new protein projects.

Since 1998 the Roche Group has invested 1.5 billion euros in research and new biotechnology plants in Penzberg, creating over 2,000 new jobs, so that there are now more than 4,500 employees. Penzberg plays a key role in the internationally active Roche Group as a "centre of excellence for therapeutic proteins".

The company originated after the acquisition of Boehringer Mannheim/ Penzberg by Roche, Basel, in 1998.



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## Scil Proteins GmbH

**Founded**  
1999

**Employees**  
87 (Scil Proteins GmbH & Scil Proteins Production GmbH)

### Area of research and development

Scil Proteins is a privately owned company active in the discovery, development and manufacturing of biopharmaceuticals.

Scil Proteins Production – the contract manufacturing business unit of Scil Proteins – commands outstanding expertise in recombinant protein production in microbial expression systems. Based on stable and robust processes, the company provides non-GMP material for research and development, as well as GMP material for clinical trials and the market. A special field of expertise is the in vitro folding of proteins, a central step in the reactivation of biologically inactive proteins, such as inclusion bodies.

Scil Proteins Pharma – the company has established and validated a proprietary drug discovery platform called Affilin® technology. Affilin® molecules are small and robust natural human serum proteins engineered to gain high specificity and selectivity against a given disease related target. As biopharmaceutical drugs, Affilin® molecules combine the advantages of small and large molecules offering treatment opportunities in niche as well as large indications with high unmet medical needs.

### Indication

Therapeutic proteins

### Stage of research and development

Discovery

### Further information

Affilin® technology: platform technology with applications in several therapeutic indications, chromatography and diagnostics

### Lead candidate status

preclinical

## Scil Technology GmbH

**Founded**  
2003

**Employees**  
45

### Area of research and development

Scil Technology develops unique biomaterials that integrate bone or cartilage growth factors and synthetic scaffolds or implants. Applying its proprietary technology, the company combines the very best of prosthetic and bone augmentation technologies with pioneering regenerative medicine. What sets Scil Technology further apart is its proprietary protein coating technology that allows for a highly stable and homogeneous bonding of growth factors to scaffolds or implants. Scil Technology is using this expertise to develop applications for dentistry and orthopaedics.

Scil Technology has a pipeline of six therapeutic candidates targeting at either dental or orthopaedic indications. Each of these candidates combines a synthetic implant or biomaterial with one of the three bone or cartilage growth factors, rhGDF-5, rhBMP variant or rhCD-RAP, and incorporates Scil Technology's proprietary protein coating technology to ensure homogeneity and stability of the growth factor on the biomaterial.

Scil Technology collaborates with Pfizer in developing an innovative cartilage growth factor and with Medtronic in dental bone regeneration therapies, exploring a product that has just successfully finalised a Phase II trial.



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## SILENCE Therapeutics AG

### Founded

The company was established in 1998 as a spin-off from Ribozyme Pharmaceuticals Inc. Colorado, USA and financed by MPM Capital.

### Employees

38 in Berlin

### Funding

Approximately 30 million euros from venture capital (Apax, MPM Capital, Novartis Venture Fund) until 2005 and approximately 20 million pounds sterling from institutional investors (Fidelity, Insight, Artemis, Oak, Garthmore and other funds) through its holding company Silence Therapeutics plc listed on the Alternative Investment Market (AIM) of the London Stock Exchange after the reverse merger in 2005.

### Area of research and development

SILENCE Therapeutics AG is the leading RNAi therapeutics company in Europe. The Company has developed innovative, proprietary short-interfering RNA ("siRNA") molecules called "AtuRNAi" and a proprietary systemic delivery system for siRNA called "AtuPLEX".

SILENCE's Freedom to Operate is based on strong patents issued in the USA, Europe and other territories. As of February 2009, SILENCE is one of two biotech companies worldwide which own issued patents in the field of siRNA therapeutics.

### Indication

Cancer (in-house) and a broad range of other therapeutic areas with SILENCE's partners.

### Stage of research and development

Out of seven clinical siRNA programs worldwide, as of February 2009, there are 3 clinical programs (one in phase II, and two in phase I) with SILENCE's AtuRNAi molecules developed by SILENCE's partners Pfizer and Quark which confirms SILENCE's leadership in the field of siRNA therapeutics. SILENCE lead internal program Atu027 will enter in Q2/2009 a phase I clinical study with patients with GI, lung and other cancers.

### Collaboration

The company has established validating partnerships with AstraZeneca (15 million US dollars upfront/equity, 400 million US dollars milestone payments), Pfizer (95 million US dollars milestone payments) and Quark and academic collaborations with the Charité and various other universities in Europe and North America.

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## SYGNIS Pharma AG

### Area of research and development

SYGNIS Pharma AG, headquartered in Heidelberg, is a specialty biopharmaceutical company listed on the Prime Standard of the German stock exchange (Frankfurt: LIO; ISIN DE0005043509; Prime Standard). The company is focused on the research, development and marketing of innovative therapies to treat disorders of the central nervous system. These include strokes, amyotrophic lateral sclerosis (ALS) and neurological disorders resulting from injuries to the brain or spinal cord. All these disorders are characterised by the fact that, as the disease progresses, nerve cells are damaged and die. In this respect, SYGNIS takes a dual therapeutic approach that aims to effect both acute treatment and regeneration of the nervous system.

SYGNIS's product pipeline currently consists of three compounds, AX200, AX2001 and SY300, which are in clinical and preclinical development. AX200, the company's most advanced drug candidate, successfully completed Phase IIa of clinical development for the blockbuster indication acute ischemic stroke. The enrolment for a multinational Phase II efficacy study is planned to commence in spring 2009. Alongside its development in SYGNIS's lead indication of acute stroke, AX200 received the orphan drug designation for ALS and spinal cord injury from the European Commission in 2008.

In November 2007, SYGNIS agreed on a long-term manufacturing agreement with the Indian pharmaceutical company Dr Reddy's that secures the supply of AX200 until 2020, thus providing a solid basis for the future marketing of the drug.

In June 2008, SYGNIS acquired Amnestix Inc. of San Francisco, CA, a US pioneer in discovering disease mechanisms affecting the central nervous system, which also has an important business relationship with the world-renowned Translational Genomics Research Institute (TGen). Through the addition of Amnestix's drug discovery capabilities to SYGNIS's development expertise the company has created a discovery engine that will fuel SYGNIS's pipeline in the future with innovative projects for neurodegenerative diseases.



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## The Medicines Company (Leipzig) GmbH

### Founded

As IBFB in 1997 – fusion with The Medicines Company, Inc., Parsippany, USA, in November 2008

### Employees

20 in Leipzig; approx. 475 worldwide

### Area of research and development

The Medicines Company is focused on advancing the treatment of critical care patients through the delivery of innovative, cost-effective medicines to the worldwide hospital marketplace. The Company markets Angiomax® (bivalirudin) in the United States and other countries for use on patients undergoing coronary angioplasty, and Cleviprex® (clevidipine butyrate) injectable emulsion in the United States for the reduction of blood pressure when oral therapy is unfeasible or undesirable. The Company also has an investigational antiplatelet agent, cangrelor, in late-stage development and a serine protease inhibitor, CU-2010, in early-stage development.

### Indication

Cardiovascular indications in acute care settings

### Stage of research and development

The research unit in Leipzig aims to identify, discover and develop novel drug candidates for cardiovascular indications in acute care settings.

## Trion Pharma GmbH

### Founded

1998

### Employees

More than 100

### Area of research and development

TRION Pharma is developing a new class of trifunctional antibodies (triomab®) for highly effective cancer treatments. Two state-of-the-art production plants allow for cost-effective, large-scale manufacturing according to international GMP standards. The efficacy of the triomab® antibodies in terms of tumour elimination and induction of a polyclonal humoral and cellular anti-tumour immunity has been proven in animal models and in clinical trials. Together with their cooperation partner, Fresenius Biotech, catumaxomab, ertumaxomab and lymphomun/FBTA05 are being developed in clinical programmes featuring several clinical trials. The trifunctional antibodies are produced at TRION's site in Munich, Germany, and are based on a proprietary platform technology. Market entry for the first antibody, catumaxomab, is expected in late spring 2009.

First drug recommended for approval

In mid-February 2009 the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion, recommending approval of Removab® (catumaxomab) for the intraperitoneal treatment of malignant ascites. TRION's development partner, Fresenius Biotech, is prepared to launch Removab® upon final approval.



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## University of Applied Sciences, Bonn-Rhein-Sieg

### Employees

4 academics

### Funding

Wellcome Trust, application for funding submitted

### Area of research and development

My research is focused on the development of small molecules against molecular targets in the malaria parasite *P. falciparum* and related human pathogens. In particular we are interested in target evaluation of two genes involved in the biosynthesis of the novel amino acid hypusine in eukaryotic initiation factor 5A (eIF-5A). The modification of the initiation factor eIF-5A is responsible for the proliferation of the parasite. We recently discovered a drug with a dualistic mechanism, i.e., inhibition of hypusine biosynthesis and TNF decrease for the treatment of cerebral malaria. The drug has been used to treat Morbus Crohn. In the meantime, we have collected data which prove a suitable indication for different parasitic diseases. The elucidation of the drug's mode of action was awarded with the Innovation Award of the German BioRegions.

### Indication

Morbus Crohn, HIV, Malaria

### Stage of research and development

Clinical Phase II for Morbus Crohn, clinical study planned for malaria

### Collaboration

Collaboration with PharmaCenter at the University of Bonn. An industrial collaboration is desired.

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## Vakzine Projekt Management GmbH

### Founded

2002

### Employess

8

### Area of research and development

Vakzine Projekt Management GmbH (VPM) is a vaccine and biopharmaceutical development company with high potential for value creation. It acquires promising vaccine candidates from academia, develops them with a consortium of partners and commercialises the results. VPM develops its products by applying industrial standards (GxP) up to proof of concept. We have four promising projects in our pipeline: an improved, more soluble  $\beta$ -interferon and three vaccines, of which one is a therapeutic vaccine against prostate cancer. The other vaccines target human cytomegalovirus (HCMV) and tuberculosis. VPM holds exclusive rights to all four products.

### Indication

Multiple sclerosis, prostate cancer, tuberculosis, HCMV infection

### Stage of research and development:

A Phase I/II clinical study for prostate cancer with an allergenic vaccine has been successful completed. An improved manufacturing process is to be developed.

A GMP process including proprietary cell line is in place for Soluferon®, a 2nd generation interferon- $\beta$  with increased bioavailability. Preclinical studies are ongoing.

VPM1002 is a recombinant BCG vaccine for the prevention of tuberculosis, which is able to induce a CD8 T cell response and is crucial for immunity to *M. tuberculosis*, the causative agent of tuberculosis. An innovative GMP process, encompassing submerged fermentation, is in place. Preclinical PoC is completed and Pharm/Tox studies have been finalised. The vaccine is currently being tested in a Phase I open label, randomised, controlled, dose-escalation study to evaluate its safety and immunogenicity.

An innovative vaccine for HCMV is in the preclinical phase. It consists of dense bodies that contain all of the major antigens of HCMV, but lack the viral genome.

### Collaboration

Max Planck Institute of Infection Biology in Berlin, Fraunhofer Gesellschaft, ProBioGen AG, Viabalogics GmbH, EUFETS GmbH, LTP GmbH, Aurigon GmbH, TBVI, and NewLab GmbH.



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## vasopharm GmbH

**Founded**  
1998

**Employees**  
8

### Area of research and development

vasopharm is a pharmaceutical company dedicated to the discovery and development of innovative therapeutics for the treatment of cerebrovascular and cardiovascular diseases and their consequences. The company is focused on the development of therapeutics, which permits steering the bioavailability of biological NO, and covering the entire NO/ cGMP signal cascade and its functional counterpart NOX. vasopharm's drug candidate VAS203 represents a completely new class of NOS modulators targeting cerebral vessels and cerebral tissue, thus preventing life-threatening rises in intracranial pressure after a traumatic brain injury.

**Indication**  
CNS, Cardiovascular

**Stage of research and development**  
VAS203 in clinical Phase IIa in the indication traumatic brain injury

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## WDT Wirtschaftsgenossenschaft Deutscher Tierärzte e.G.

**Founded**  
1904

**Employees**  
30

### Area of research and development

Immune sera  
Vaccines  
Tuberculin

**Indication**  
Immunology

**Stage of research and development**  
Several products in different phases of development

**Collaboration**  
Yes, with several globally acting pharmaceutical companies



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## Wilex AG

**Founded**  
1997

**Employees**  
64

### Area of research and development

WILEX is a biopharmaceutical company based in Munich. The company was founded in 1997, has 64 employees and is listed on the regulated market of the Frankfurt Stock Exchange (Prime Standard).

WILEX's mission is to develop drugs and diagnostic agents with low side-effect profiles for the targeted treatment of different types of cancer, as well as for early detection of tumours. The product candidates are based on antibodies and small molecules. The substances RENCAREX® and REDECTANE® are currently undergoing a Phase III registration trial. The substance MESUPRON® is currently in a Phase II programme for two indications.

Rencarex is a chimeric monoclonal antibody in the indication renal cell cancer (RCC) and other solid tumours.

Redectane is a labelled antibody for specific diagnosis of malignant kidney tumours.

Mesupron is a small molecule targeting the urokinase plasminogen activator (uPA) system of solid tumours.

### Collaboration

In January 2009, WILEX and UCB Pharma S.A. agreed to enter a strategic partnership. WILEX acquired UCB's preclinical oncology portfolio of five programmes (small molecules and antibodies).

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## 2 Interview partners

Institution	Name
4SC AG, Munich	Dr Daniel Vitt Chairman of the Management Board, Chief Scientific Officer
Apogenix GmbH, Heidelberg	Dr Thomas Höger Chief Executive Officer/Chief Financial Officer
AstraZeneca GmbH, Wedel	Dr Stefan Busch Vice President Strategic Planning and Portfolio Management Member of Managing Board
Ascenion GmbH, Munich	Dr Christian A. Stein Managing Director
Bayer AG, Leverkusen	Dr Wolfgang Plischke Member of Management Board
Bionamics GmbH, Kiel	Dr Timm Jessen Managing Director
BioRN Cluster Management GmbH, Heidelberg	Dr Christian Tidona Managing Director
Boehringer Ingelheim GmbH, Ingelheim	Dr Manfred Reiffen CDept R&D Coordination  Dr Stefan Walke CDept R&D Coordination
Curatis Pharma GmbH, Hanover	Prof Dr Klaus D. Döhler Managing Director
Ganymed Pharmaceuticals AG, Mainz	Dr Rainer Wessel Executive Speaker, Chief Business Officer
Deutsches Krebsforschungszentrum (German Cancer Research Centre), Heidelberg	Dr Ruth Herzog Director Staff Unit Technology Transfer/T010
Evotec AG, Hamburg	Dr Klaus Maleck Chief Financial Officer
GlaxoSmithKline GmbH & Co. KG, Munich	Prof Dr Torsten Strohmeyer VP Medical & Regulatory Affairs
IMTM GmbH, Magdeburg	Dr Michael Träger Chief Executive Officer
	Prof Dr Jens Schneider-Mergener Former Chief Executive Officer, Jerini AG, Berlin
Keyneurotek Pharmaceuticals AG, Halle	Dr Frank Striggow Chief Executive Officer
Matrix Advanced Solutions Ltd., Göttingen	Sion Balass Chief Executive Officer
Max-Delbrück-Centrum für Molekulare Medizin (Max Delbrück Centre for Molecular Medicine, MDC), Berlin	Prof Dr Walter Rosenthal Scientific Director
Max Planck Innovation, Munich	Dr Jörn Erselius Managing Director

Institution	Name
MediGene AG, Munich	Dr Peter Heinrich Chief Executive Officer
Merck KGaA, Darmstadt	Dr Bernhard Kirschbaum Executive Vice President, R&D Member of the Merck Serono Executive Board  Dr Ulrich Betz Department Head Strategic Innovation and Research Portfolio Management of Merck Serono  Dr Christoph Hüls Vice President Operational Excellence R&D of Merck Serono
MorphoSys AG, Munich	Dr Arndt Schottelius, MD PhD Chief Development Officer  Dr Claudia Gutjahr-Löser Head of Corporate Communications & IR
Novosom AG, Halle	Sebastian Kehres Finance Director
Noxxon AG, Berlin	Dr Frank Morich Chief Executive Officer
Probiodrug AG, Halle	Prof Dr Hans-Ulrich Demuth Chief Executive Officer/Chief Scientific Officer
Scil Proteins GmbH, Halle	Dr Ulrike Fiedler Managing Director
TRION Pharma GmbH, Munich	Dr Dirk Pelster Chief Operating Officer
Vakzine Projekt Management GmbH, Hanover	Dr Bernd Eisele Chief Executive Officer
Wilex AG, Munich	Prof Dr Olaf Wilhelm Chief Executive Officer

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