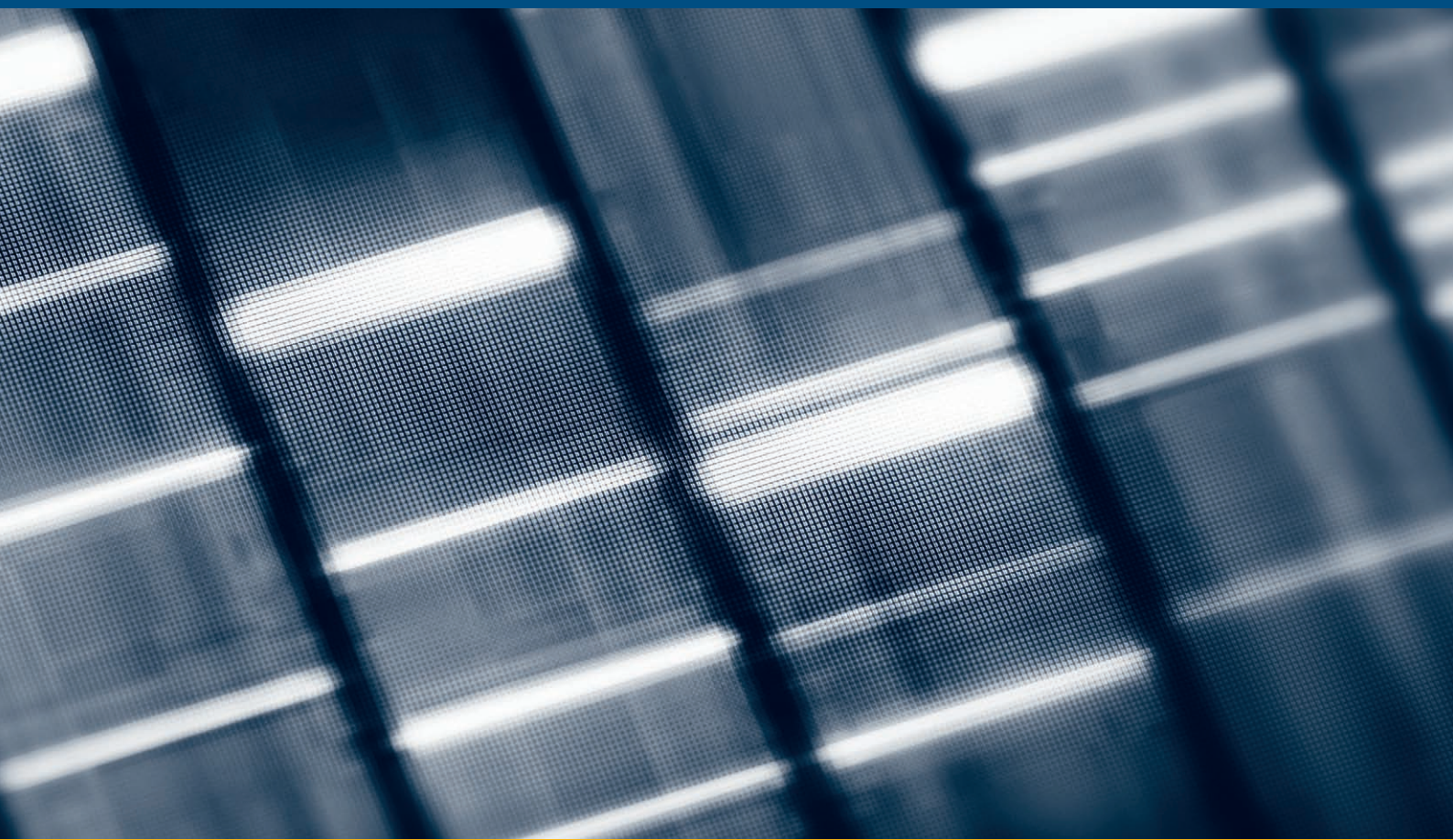
2017
Facts & Figures

The German Biotechnology Sector



BIOCOM AG

About the report

The report provides an overview to the current status of the German biotechnology sector. The figures and data presented are based on a biotechnology company survey which has been conducted by BIOCOM for the 11th time via the information platform *biotechnologie.de*. From 2005 until June 2015, the platform and the survey were financed by the German Federal Ministry of Education and Research, BIOCOM AG took over full responsibility for the platform and the report from July 2015.

As a leading information specialist for biotechnology and life sciences in Europe, BIOCOM has extensive knowledge and thirty years of experience, from basic research to the market. We are active in media, events and services. We offer a broad spectrum of services to our clients from industry and the public sector:

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Editorial Team
Sandra Wirsching, Simone Ding, Benjamin Röbig (Production)

Publisher
BIOCOM AG, Lützowstr. 33–36, 10785 Berlin, Germany
Tel. +49 (0)30 26 49 21-0, Fax +49 (0)30 26 49 21-11
info@biocom.de, www.biocom.de

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Sustainable growth

BIOCOM has been observing the German biotech sector for 30 years now, and in recent years the sector has shown a surprisingly constant upward trend. This was highlighted yet again in 2016, as German biotech companies had gained more money and had more staff on the payroll than ever before.

The good news is: This development isn't new, but the result of a constantly growing sector. It reflects a new strength for capitalising technologies and science and converting them into products and services. Obviously, over the last years, many German companies turned their know-how into turnover and staff. And this is in particular an observation made in small and middle sized companies, which makes the development an even more sustainable one.

Another interesting lesson learned from the last two years is that German biotech companies are increasingly attractive on an international level. This is not only true when it comes to financings, but also with regard to licensing deals with large pharmaceutical companies. One of the reason for that is the high competence in hot topics such as liquid biopsy, immuno-oncology, infectious diseases or cell therapies – biotech companies 'made in Germany' are particularly adept at providing suitable solutions or technologies in line with these trends. The 2016 figures strongly support the assumption, that the current growth is based on the success of many companies, in all subsectors and throughout the country.

The financial situation also mirrors a sustainable growth trend. On the one hand, we saw quite a number of double-digit VC rounds as well as some major multimillion euro pharma deals. On the other hand, several smaller rounds with local or regional investors took place. In addition, crowdfunding seems to establish itself as a further pillar in the financial sector to support the financing of start-ups or younger companies with a smaller capital need. Another positive trend of 2016: This year the number of new companies doubled compared to last year which might be a sign of a new founding wave in the German biotech sector.

This report will provide you with a solid database that coherently describes the sector. We hope you enjoy reading it.

Sandra Wirsching
Division Manager

BIOCOM AG
Lützowstr. 33–36
10785 Berlin
+49 (0) 30 26 49 21-63
s.wirsching@biocom.de

Outcome 2016

The biotech growth engine

Biotechnology in Germany is a growth engine. In 2016, all key figures such as employees, turnover and R&D expenditure were at an all-time high. Among the drivers are medical innovations, but also an upward trend of green chemistry.

In terms of key economic factors, 2016 was the best year for the German biotech sector ever. According to the company survey, which BIOCOM AG conducts annually via the information platform biotechnologie.de for more than ten years, the generated turnover of the German biotech sector for the third year exceeded €3bn (see key facts on p. 5). In 2016, total figures increased by 8% to €3.54bn compared to the year before.

Key figures with all-time high

Further upswing has been observed regarding spending on research and development (R&D). For the second time since 2010, the innovation budget cracked the one billion euro mark (+6.3%) and now stands at €1.1bn (2015: €1.04m). With a total of 20,280 (2015: 19,010), there were more employees than ever before working in biotech companies that are occupied wholly or predominantly with modern biotechnological methods. The total number of these companies rose to 615 (2015: 593). Thereby, the following figures and conclusions relate only to the 'dedicated' biotechnology companies, as defined by the OECD (see p. 12 for methods).

Stable financing situation

The financial investments showed stable conditions, but have not reached the record numbers of 2015. In 2016, around €505m were invested in German biotech companies. Compared to €550m in the year before, this is a decrease of 8.2%. A large proportion of the money (€216m) went into the private biotech sector, but the majority of the money (€258m) was invested into already listed public companies (+5%). In 2016, one German biotech IPO (€31.5m) took place.

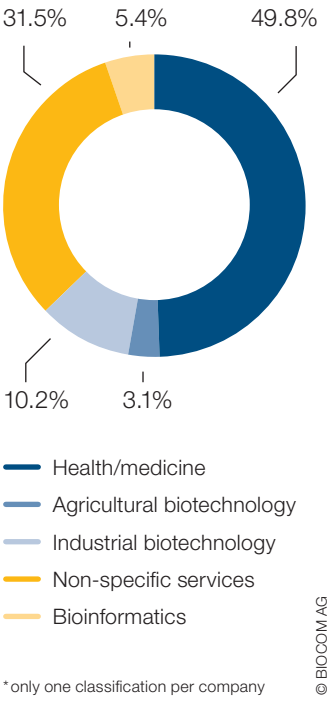
€3.54bn

Total turnover of the German dedicated biotech companies in 2016

Record employee numbers

There is sustained interest in biotechnological processes and services from big business. This is confirmed by a consistently high number of companies in which biotechnology represents only one aspect of business. In 2016, the category of 'other biotechnology-active companies' comprised a total of 137 companies (2015: 133). These included both pharmaceutical and chemical companies focused on innovative biotechnological processes as well as companies from the areas of environment, waste management, energy and agriculture. In 2016, a total of 22,000 people were employed in the biotechnology-oriented areas of such companies. Compared to the previous year (2015: 20,250), this represents a growth of

Fig. 1: Fields of activity in dedicated biotech companies*



*only one classification per company

8.6%. For the first time, total headcount in commercial biotechnology increased above the 40,000 mark to 42,280 (2015: 39,260) (+7,7%).

Strength in medical biotech

Observers of the German biotech sector will have noted a pretty unchanged picture of the sector when it comes to focal areas: the key task of most biotech companies is developing drugs or new diagnostic methods. 306 companies (49.8 %) belong to the field of 'red' biotechnology – a proportion that has remained steady for many years, but which showed an increase in turnover of 8.1% (€2.5bn), and an augmentation in R&D expenditure of 6.6% (€911m) in 2016.

High interest in immunotherapy

A large majority of the companies (158) are either in the preclinical stage of therapeutic research or developing technology platforms (see fig. 2). Here, 2016 demonstrated that German know-how is in greater demand than ever before. As it was already last year, in 2016 again German biotech companies hit the headlines with large investments involving foreign investors. This was true for the startup iOmx Therapeutics AG, based in Martinsried near Munich. The company is developing cancer therapeutics by targeting novel immune checkpoints. With its €40m Series A financing, co-led by US-based investor MPM Capital and French Sofinnova Partners, it was the largest German biotech VC round in 2016.

A strong tie to chinese research groups helped Jena-based Inflarx GmbH to close a €31m Series C financing in 2016, Staidson Hongkong Investment Company ltd. (STS) participated as new investor, further support

Key figures of the biotech sector in Germany

	2008	2009
Number of dedicated biotechnology companies	501	531
Number of other biotechnology-active companies	92	114
Number of employees in dedicated companies	14,450	14,950
Number of employees in the other biotechnology-active companies	15,520	16,650
Turnover of dedicated biotechnology companies	€2.19bn	€2.18bn
R&D expenditures of dedicated biotechnology companies	€1.06bn	€1.05bn

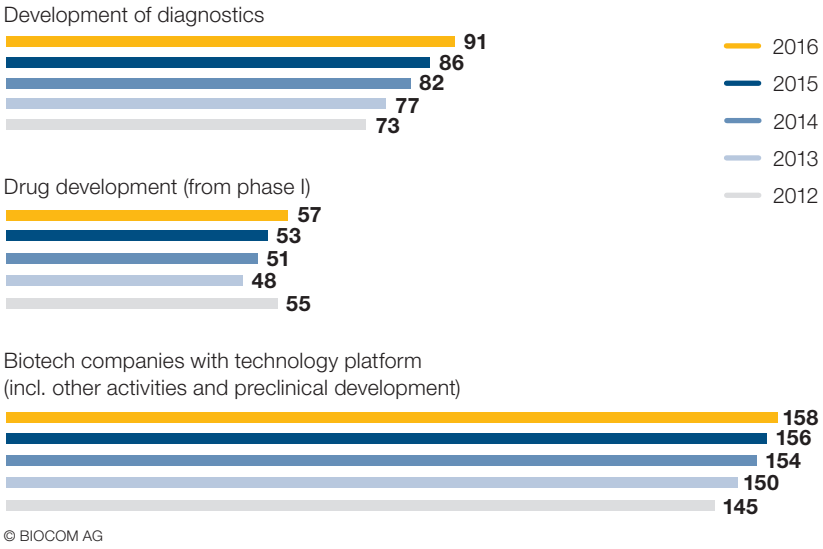
came from bm-t Beteiligungsmanagement Thüringen GmbH, KfW group and several other industrial and private investors.

Double-digit VC financings

In 2016, Tübingen-based CureVac AG succeeded to add further €26m to its record €100m financing round from 2015. The fresh cash came from the new investors Baden-Württembergische Versorgungsanstalt für Ärzte, Zahnärzte und Tierärzte (via the LBBW Asset Management Investmentgesellschaft mbH, Stuttgart), and the Landeskreditbank Baden-Württemberg. CureVac plans to utilise these funds to advance the development of its messenger RNA product portfolio.

Another double-digit VC round was completed by German-French company Allecra Therapeutics SAS. The antibiotics specialist

Fig. 2: Main areas of activity in dedicated biotech companies in the field of health/medicine (only one classification per company)



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2010	2011	2012	2013	2014	2015	2016
538	552	565	570	579	593	615
125	126	128	130	131	133	137
15,480	16,300	17,430	16,950	17,930	19,010	20,280
17,000	17,570	17,760	18,450	19,200	20,250	22,000
€2.37bn	€2.62bn	€2.90bn	€2.86bn	€3.03bn	€3.28bn	€3.54bn
€1.02bn	€0.98bn	€0.93bn	€0.90bn	€0.95bn	€1.04bn	€1.10bn

Fig. 3: Turnover and R&D expenditure of dedicated biotech companies

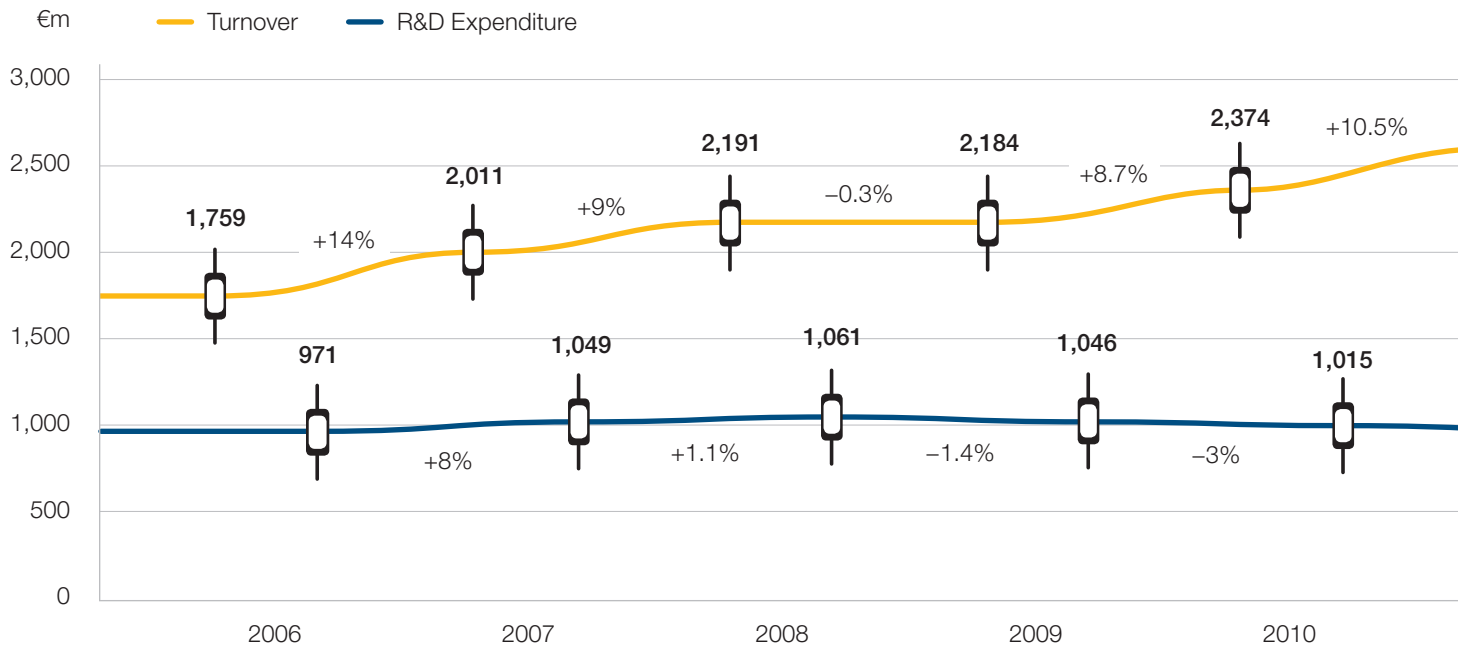
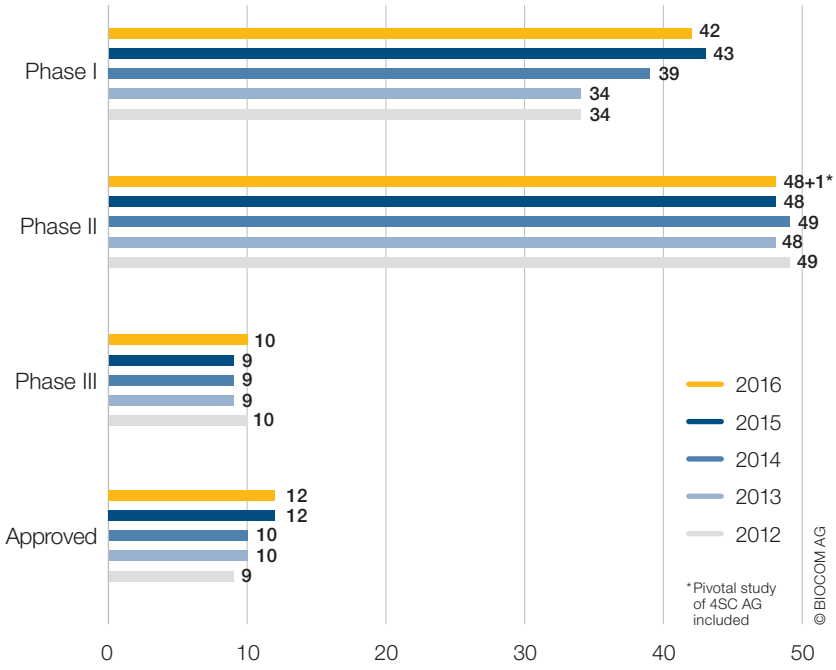


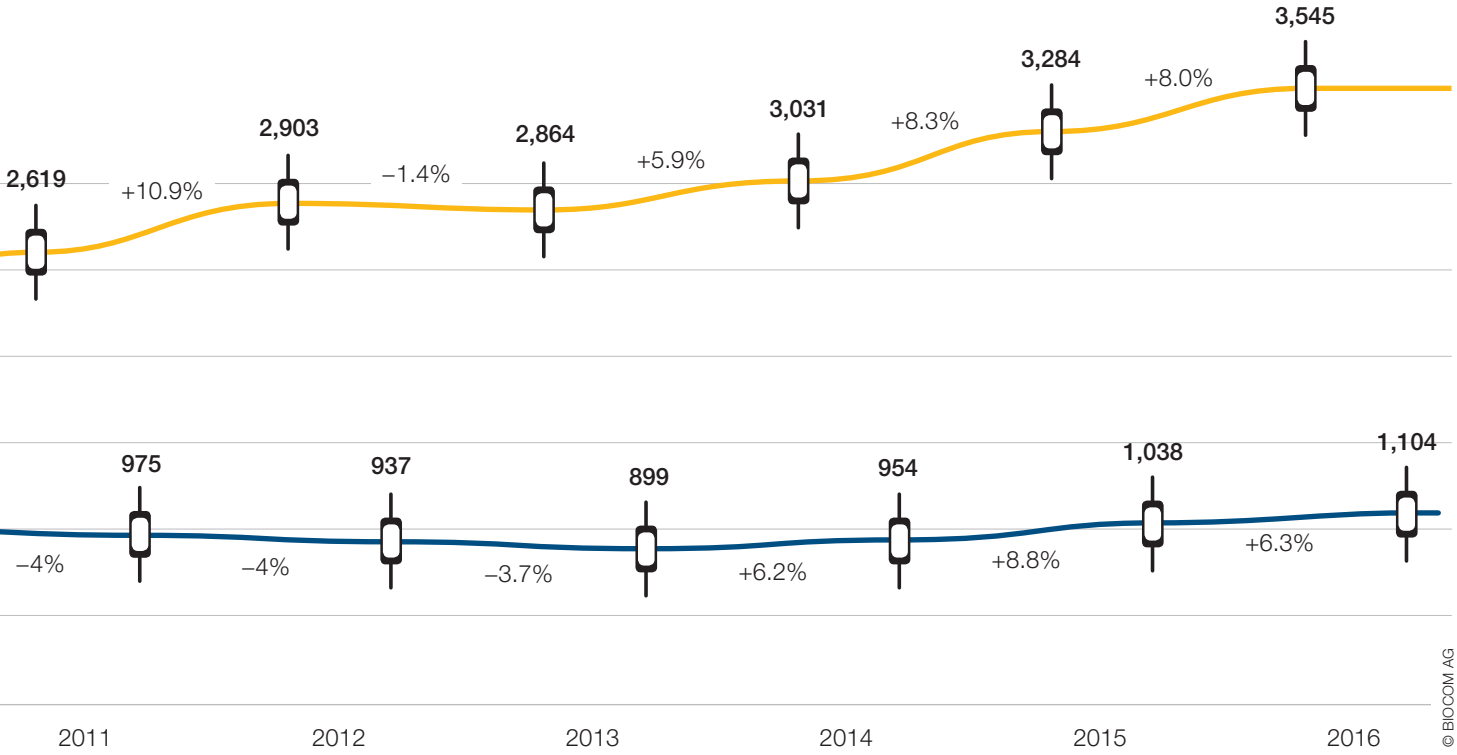
Fig. 4: Drug candidates of dedicated biotech companies



raised €22m in a Series B financing led by Forbion Capital partners and Sofinnova to further develop its novel treatments to combat multi drug-resistant Gram-negative bacterial infections. Some movements also took place in the preclinical area. Among others, the autoimmune specialists from Berlin Cures entered the group of drug developers with the start of a phase I clinical trial to treat heart insufficiency.

Growing relevance of diagnostics

A growing part of the biotech sector (91 firms) is dedicated to the development of diagnostics, which reflects the increasing demand for early disease detection, e.g. in the field of infection diseases, and the relevance of accompanying diagnostics for therapeutic treatments, e.g. for a personalised medicine in the field of cancerous diseases. This growth is underlined by a large



increase of turnover (€1.79bn, +9,3%) and R&D expenditure (€280m, +15,9%), showing the importance of these companies for the German biotech sector. Some financings such as the €4.25m secured by Regensburg-based Lophius Biosciences GmbH or the €25m debt financing by listed Curetis N.V. are reflecting this positive trend.

Drug developers with full pipeline

A total of 57 German biotech companies are fully dedicated to drugs and have one or more candidates in clinical development (see fig. 4). Last year, a total of 101 biologically active compounds were in one of the three phases (2015: 100). The establishment of a robust clinical pipeline is partly due to the high overall interest in immuno-oncology and cell therapies. In addition, many German companies succeeded in developing their technology platforms to

Drug candidates in clinical phase III

	Product	Indication
AiCuris	Letermovir	Infectious disease
Ascendis	ACP-001	Growth hormone deficiency
DermaTools Biotech	Dermapro®	Wound healing
Formycon	FYB201	Macular degeneration
immatics biotechnologies	IMA901	Renal cell carcinoma
Lipid Therapeutics	LT-02	Ulcerative colitis
Mologen	MGN1703	Metastatic colorectal cancer
Oncoscience	Theraloc	Pontine glioma
Paion	Remimazolam	Anaesthesia
Vasopharm	VAS-203	Traumatic brain injury

Fig. 5: Main areas of activity in dedicated, industrial biotech companies (multiple classification was possible)

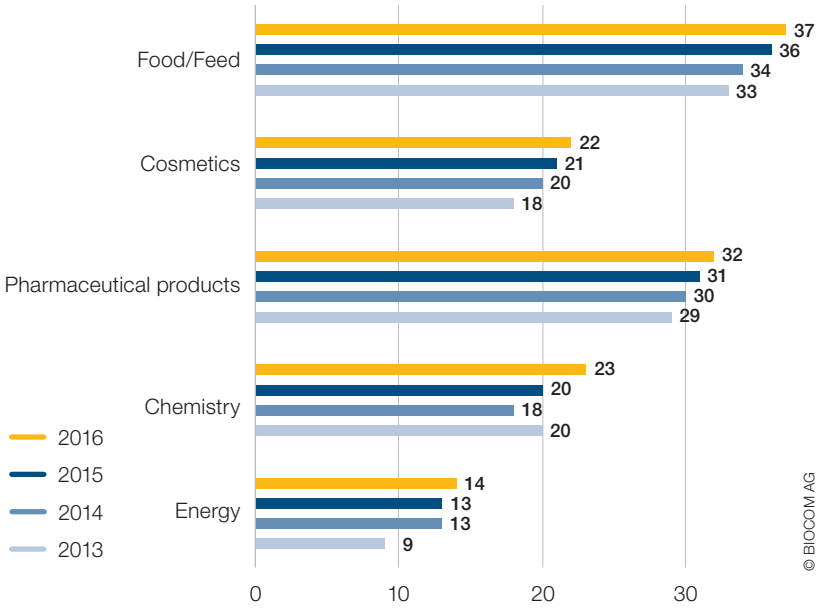
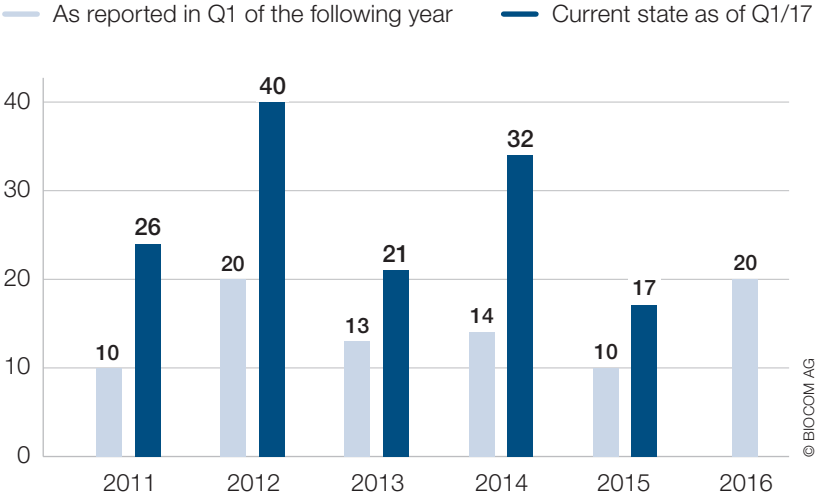


Fig. 6: Number of annual new biotech start-ups over the time



advanced stages which are now resulting in clinical projects. In 2016, a total of 42 active substances were recorded in phase I (2015: 43). The majority of clinical candidates of German companies were in phase II in 2016, amounting to a total of 49 active substances (2015: 48). Here, there was little change in the number of trials, however some movement took place. Among others, listed company Pieris, which is advancing novel biotherapeutics through its proprietary Anticalin technology platform, completed a new phase II trial with its anemia drug candidate PRS080. Another new Phase II trial was started by Munich-based Multimmune GmbH that focuses on new cancer therapeutics. 4SC AG started a pivotal clinical trial to evaluate the epigenetic cancer drug resminostat for maintenance treatment of patients suffering from advanced-stage cutaneous T-cell lymphoma (CTCL). Total numbers of phase III candidates raised to 10 this year. Most of the trials are still ongoing ones from last year. Only Vasopharm GmbH from Würzburg started a new phase III trial with its VAS203 drug candidate to treat acute brain injury. To conduct this trial the company secured a €20m financing co-led by existing investors Entrepreneurs Fund, Heidelberg Capital Private Equity and new investor, UK based Fort Rock Capital.

Services as a solid business model

Apart from the health sector, the second largest pillar of the German biotech scene is comprised of companies (186) that are not active in a specific field. This includes all companies providing services exclusively or primarily for other biotech firms,

or which function as suppliers. In 2016, all these companies together had a turnover of €740.8m (+7.4%) and an R&D budget of €113.5m (+4.6%), demonstrating that the service business model has proven to be a guarantee for continuous growth within the German biotech sector since 2011 when turnover was €556m.

More turnover in bioeconomy

There are 63 companies developing industrial applications in various other sectors (see fig. 5), which highlights the relevance of biotech processes throughout the industry as a whole. This is also reflected by a rise of 9.5% in industrial biotechnology turnover. The takeover of Berlin-Based Organobalance by Danish Novozymes also demonstrates the dynamic in this field. The application of biotechnology in the plant breeding and agricultural sector has decreased over the years, but since 2015 the situation is slightly improving. In 2016, the 19 companies generated a plus of 2.8% in turnover (€33.2m).

New start-up peak

With a total of 20 start-ups already known today the founding dynamics in 2016 doubled compared to 2015, now reaching levels last seen in 2012. As shown in figure 6 on the left, there is an increase of total start-up numbers during the course of the year and, from experience, a further plus can be expected for 2016. Most of the newcomers known today are active in the health biotech area (14), four in the non-specific services field and two in bioinformatics. Four insolvencies and six liquidations were reported in 2016.

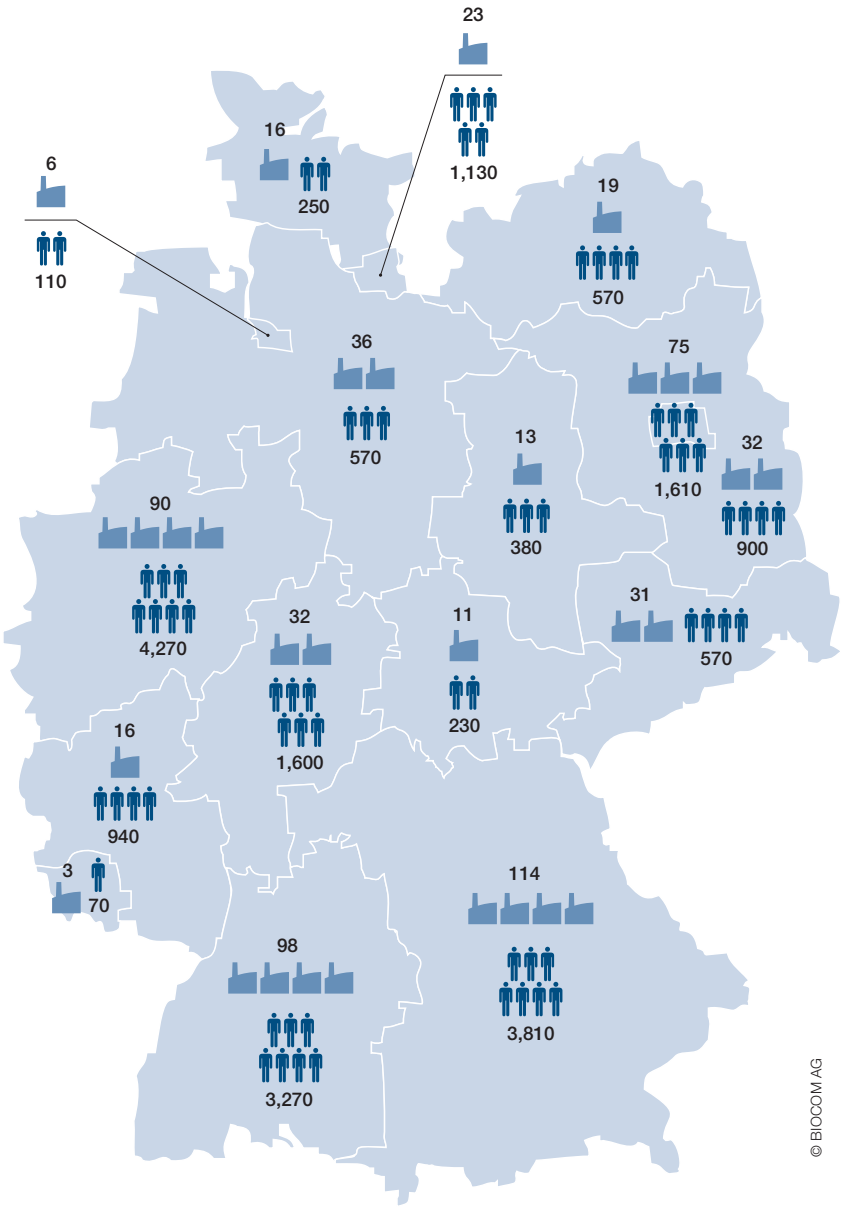
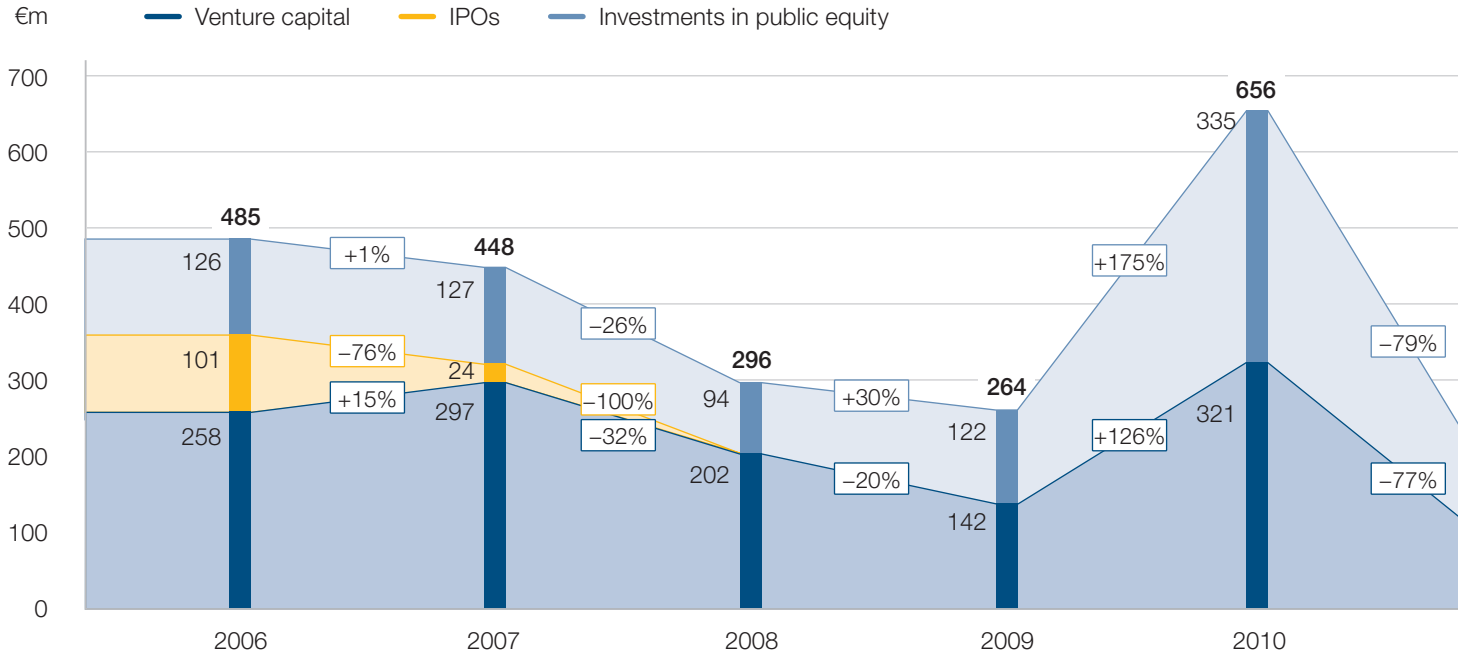


Fig. 7: Dedicated biotech companies and their employees, distributed according to federal states

Fig. 8: Sources of financing for dedicated biotech companies



Top 3 financing rounds of private companies in 2016

	Capital raised
iOmx Therapeutics AG	€40.0m
InflaRx GmbH	€31.0m
CureVac AG	€26.5m

Top 3 financing rounds of listed companies in 2016

	Capital raised
Morphosys AG	€115.4m
Probiodrug AG	€14.9m
Pieris AG/Biofrontera AG	€14.8m

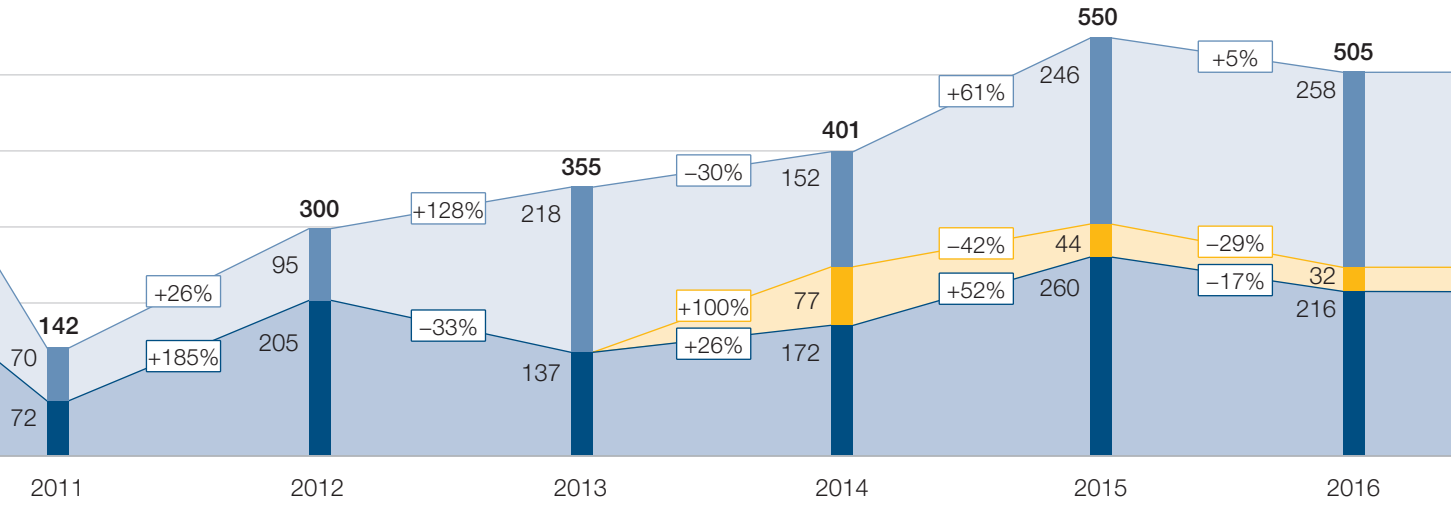
Dynamic employment market

In terms of jobs, the German biotech sector is a dynamic employment market. In 2016, the 615 dedicated companies reported a total increase of more than 1,270 employees. As already observed in 2015, most of the increase this year was generated by middle-sized companies.

Positive financial environment

The financial situation also mirrors a sustainable positive trend over the last years: in 2016, around €505m was invested in German biotech companies, which did not reach the record levels of 2015 (€550m), but still is a high amount of money compared to previous years. The majority of the money was spent in public companies (€258m, +5%). With bioeconomy pioneer BRAIN AG, the first biotech IPO since 2007 took place at the German stock exchange in Frankfurt.

Total numbers of listed German biotech companies increased to 21. Among them are five firms that are listed on a foreign stock exchange. In 2016, Berlin-based



Noxxon Pharma choose that way, too, and went public on Euronext in Paris.

Interest of pharma and crowd

A closer look into the financings of the private firms, which secured a total of €216m in 2016, reveals that despite overall lower levels (-17%) than in 2015, a lot of double-digit rounds were raised. Foreign investors participated in eight of the 21 private financing rounds, demonstrating that German companies are able to attract high levels of interest. In addition, two crowdfunding campaigns for biotech companies took place in 2016. Some major multimillion euros licensing deals, such as BioNTech with Genentech (€278m), or Medigene with Bluebird Bio (€917m), or Proteros with MSD (€157m), further support the theory that German firms are quite attractive from an international point of view. The growing attractiveness of German technology platforms was also highlighted by several mergers and acquisitions. Nine out of 15 buyers came from abroad, the others were takeovers by German companies or German-German consolidation activities.

Mergers & acquisitions in 2016

Buyer	Goal
Bioagilvtix Labs, LLC	IPM Biotech GmbH
Wuxi Apptec	Crelux GmbH
Promethera	CYTONET GmbH & Co. KG
BioNTech AG	4SC Discovery GmbH
Texcell	vivo Science GmbH
SYGNIS AG	Expedeon Holdings Ltd
Siemens Healthcare GmbH	NEO New Oncology GmbH
Myriad Genetics, Inc.	Sividon Diagnostics GmbH
Analytik Jena	Moldiax GmbH
QIAGEN	Exiqon A/S
Alvotech	Baliopharm GmbH
AGC Asahi Glass	BIOMEVA GmbH
Novozymes	ORGANOBALANCE GmbH
Evotec AG	Cyprotex plc
Astellas, Inc.	GANYMED Pharmaceuticals GmbH
Sartorius Stedim Biotech GmbH	Cellca GmbH

Methodology

Since 2006 BIOCOM AG has been providing an overview of the German biotech sector for the information platform biotechnologie.de, based on the OECD definition of biotechnology as it was first described and globally standardised in 2004 (www.oecd.org). From 2005 until June 2015, the platform and the survey were financed by the German Federal Ministry of Education and Research, BIOCOM AG took over full responsibility for the platform and the report from July 2015.

For the purposes of this survey, BIOCOM AG has compiled a questionnaire compliant with the OECD standards as used in the previous surveys. Between January and March 2017, a total of 784 companies were contacted and asked to complete the survey. When deciding on selection of the company, the OECD definition was used alongside an adjustment in line with the company database at BIOCOM AG. 506 of the companies answered either by questionnaire or by telephone, corresponding to a verification rate of 64.5%.

In accordance with the OECD guidelines, when selecting companies to participate, extreme care was taken to include all enterprises which are resident in Germany and which are active in biotechnology. As a result, companies that are majority-owned from outside Germany but have a company office with R&D activities in Germany were also considered. When surveying the employee figures, number of companies and fields of activity, the survey included only the German locations of a company. If an enterprise had more than one location in Germany, only cumulated figures and data for the company as a whole were considered.

With regard to the clinical pipeline of the dedicated biotech companies, special care was taken in this survey to represent the core development activities in this survey – especially in the early clinical development when a wide range of drug candidates are tested in different indications and formulations. For this reason, the report does not include all R&D projects, but focuses on the number of active compounds the company has in phase I and II tests.

With regard to counting newly founded companies, care was taken to compare the data of the current period under review with the data of the period under review of the previous year. This strategy has to be used to obtain a coherent picture because a steady number of new firms emerge continuously throughout the year. Due to the time-consuming founding procedures, the majority of start-ups are only officially registered as new companies a year or more after their initial founding.

The deadline for completion of the survey was 31.12.2016, for counting the start-ups 31.3.2017. Participating companies can be viewed in the biotechnology database at biotechnologie.de. All data published herein is based on the results of the survey. The database also offers an overview of biotechnological research in Germany. Every scientific institute or establishment can be searched for within the database according to a variety of criteria.

Definition areas of activity

Health/Medicine	Development of therapeutics and/or diagnostics for the field of human medicine, drug delivery, human tissue replacement
Animal health	As above, for veterinary application
Agricultural biotechnology	Genetically modified plants, animals or micro-organisms, as well as non-genetically modified plants grown using biotechnological procedures, for use in agriculture or forestry
Industrial biotechnology	Biotechnological products and processes for the handling of waste or sewage, for chemical synthesis, for the extraction of raw materials and energy etc.
Non-specific services	Equipment or reagents based on biotechnological principles, for research or provision of services in this field ('ancillary industry')

Further relevant terms

Biotechnology product	... is defined as a commodity or service, the development of which requires the use of one or more biotechnology techniques based on the list and single definitions above. It includes knowledge products (technical know-how) generated from biotechnology R&D.
Biotechnology process	... is defined as a production or other (e.g. environmental) process using one or more biotechnology techniques or products.
Biotechnology research and experimental development (R&D)	... are defined as R&D into biotechnology techniques, biotechnology products or biotechnology processes, in accordance with both the biotechnology definitions presented above and the Frascati Manual for the measurement of R&D (OECD, 2002).
Biotechnology employment	... is defined as the employment involved in the generation of biotechnology products as defined above. For ease of collection, it is suggested that employment be measured in terms of staff numbers rather than hours worked. However, where countries prefer, they can collect this information in terms of full-time equivalents, consistent with an R&D survey approach (as outlined in the Frascati Manual).

Survey based on the framework for biotechnology statistics

OECD
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

OECD Definitions

Biotechnology …
… is defined as the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.

A dedicated biotechnology firm …
… is defined as a biotechnology active firm whose predominant activity involves the application of biotechnology techniques to produce goods or services and/or the performance of biotechnology R&D.

An other biotechnologically active firm …
… is defined as a biotechnologically active firm that applies biotechnology techniques for the purpose of implementing new or significantly improved products or processes (per the Oslo Manual (OECD, 1997) for the measurement of innovation). It excludes end users which innovate simply by using biotechnology products as intermediate inputs (for instance, detergent manufacturers which change their formulation to include enzymes produced by other firms via biotechnology techniques).

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