

# Rethinking ...

... thinking beyond, thinking more broadly

German biotechnology report 2013  
Executive summary

# Preface

Current economic forecasts in Germany are positive and provide more confidence again. This is mainly driven by a strong technology base ensuring the manufacturing of high value products with an excellent reputation in global markets. Nevertheless, there are concerns as well, e.g. about the increasing cost of energy or the growing ecological damage with its consequences for public health. This situation generates a need to **"Rethink"**:

- ▶ How can the transition to renewable energy sources be managed?
- ▶ How can the environment be better protected for future generations?
- ▶ How can technological innovations be leveraged best in order to sustain health care systems at affordable costs?

**"Rethinking"** is also the title of this year's German biotechnology report. In previous years we have thought about **"New rules"** for biotech companies in order to overcome the global financial crisis and about being **"On the right tracks"** to establish new business models. Along these lines, last year's title **"Tailor-made"** indicated that standardized models are no longer relevant but every single enterprise has to find its own way based on its individual strengths.

Why then **"Rethinking"** again?

This 14<sup>th</sup> edition of the German Ernst & Young biotechnology report attempts to widen again the perspective which had been narrowed down in previous years to more and more reflect individualized aspects - such as USPs, individual business plans or optimized financial strategies. It is about new opportunities in a changing environment with specific emphasis on applications in multiple industries.

During the last decade, biotechnology had been more and more deprived of its raison d'être and actual strength - generating and establishing new "bio-technologies" - and was essentially reduced to drug development; an extremely risky sector associated with high costs, long development cycles and fierce competition on the way to market. The consequences were inevitable: failures, failed financing strategies, bad reputation and vanishing trust in the capabilities of the whole biotech sector.

**"Rethinking"** therefore refers to reconsidering actual strengths as well as to analyzing and identifying fields with high demand for "bio-technologies". Fields in which, at the same time, biotech can secure a valuable share of associated value chains and benefit from attractive business models.

Rethinking within the therapeutic sector may mean to leverage new technology platforms for the generation of novel compound classes or to cover parts of pharmaceutical value chains. Rethinking may also mean **"thinking beyond"** and looking into new technology fields in the diagnostics sector around the topic of personalized medicine. Finally, rethinking also refers to **"thinking more broadly"** in terms of taking the new bioeconomy paradigm into account, in which "bio-technologies" will be leveraged much more widely in a variety of other industries that so far have been out of reach for biotech.

Our global biotechnology report **Beyond borders** - which is put together in close cooperation with the Ernst & Young Life Science Center Mannheim - also deals with the issue of extracting value from biotech capabilities. For the more mature and market-oriented US biotech sector it is primarily relevant to demonstrate the value of biotech developments to partners, regulators or reimbursement decision makers. "How to demonstrate value" is therefore the key theme of the report. This also includes the question of how far companies have come to address the domi-



Dr. Siegfried Bialojan

nating issues around demonstrating "patient benefit" and "health outcome" and whether there still is an "implementation gap".

Innovations in the medical device sector have traditionally originated closer to the patient and in cooperation with physicians. Now these innovations are starting to focus even more on the "patient outcome", with point-of-care applications, personalized diagnostics and many new IT solutions. The term "PI technologies" (Patient empowering and Information leveraging) has been coined to describe this movement. In our global medtech study **Pulse of the industry** these trends are addressed in detail.

Understanding the interaction of all disciplines in the life science industry will become a major key competency to support the building of a patient-oriented health system. Thinking and developing thought leadership along these lines, numerous discussions with all stakeholders, as well as sound knowledge of the facts all together establish a solid basis for the consulting expertise we offer to our clients.

I hope the study on hand will provide you with helpful food for thoughts and will be able to stimulate fruitful discussions. I would also be delighted to continue our dialogue on the topics raised in this report.

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**"Rethinking"**  
German biotechnology report 2013



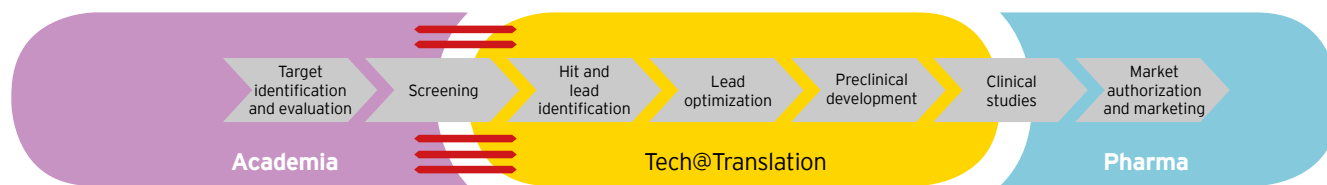
**"Beyond borders"**  
Biotechnology industry report 2013



**"Pulse of the industry"**  
Medical technology report 2012

# Overall perspective

## Tech@Translation: driving innovation efficiency



Source: Ernst & Young, 2013

### Rethinking - unique selling propositions in the therapy sector

For today's biotech companies - especially those in the medical space - it will be key to not just copy the pharma model but to define unique selling propositions which position them aside the dominating pharma players. The most important approach in this context is to put the focus on technology platforms. This also represents a return to the actual strengths and roots of "bio-technology" per se.

Technology platforms also provide an excellent basis for valuable and sustainable business models. Biotech companies with innovative platforms are attractive partners for big companies, which pay well even for non-exclusive partnerships and are less inclined to acquire the platform company.

A closer look at the nature of the platforms leads to a segmentation into distinct subtypes which display specific characteristics. In addition, each of these segments also provides best practice examples of companies representing the corresponding prototype.

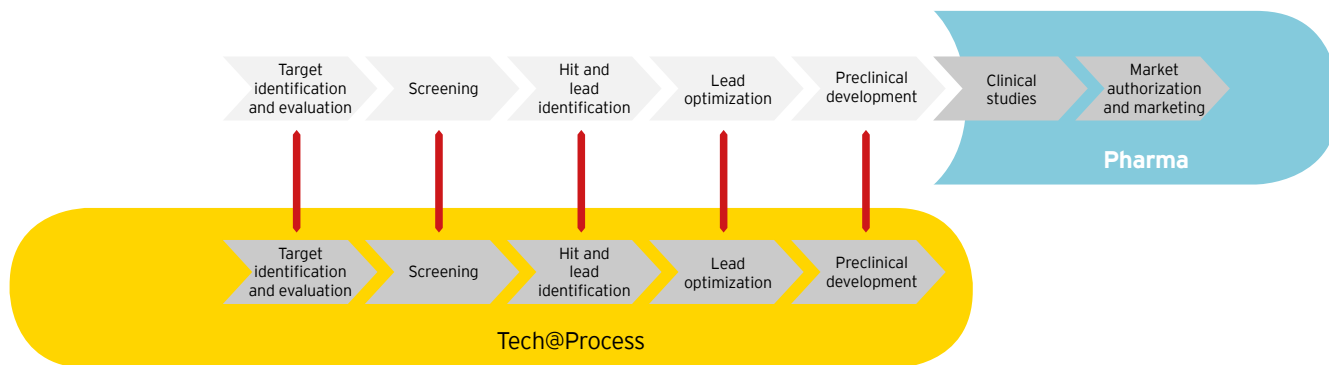
#### 1. USP "Tech@Translation": driving innovation efficiency

There is a big need to better manage the translation of innovative ideas into commercial developments. In this role, biotech works as a transmission belt between academia and big pharma. Biotech has some key USPs to offer and can be well positioned in this field:

- ▶ A mindset for open innovation, including information sharing, knowledge and research tools
- ▶ Creativity and agility when dealing with complex biologic systems
- ▶ Know-how in early drug development
- ▶ A link to pharma players

Best practice examples are two recent alliances between Evotec in Hamburg and US elite universities Harvard and Yale. Evotec provided access to its drug discovery platform (including its compound libraries and screening capabilities) whereas academic scientists around Prof. Doug Melton at Harvard could test their research concepts. It is impressive that after only 18 months the collaboration with Harvard on novel regenerative diabetes treatments has resulted in a lucrative deal with Janssen Pharma/J&J.

**Tech@Process: covering sections of pharma value chain**



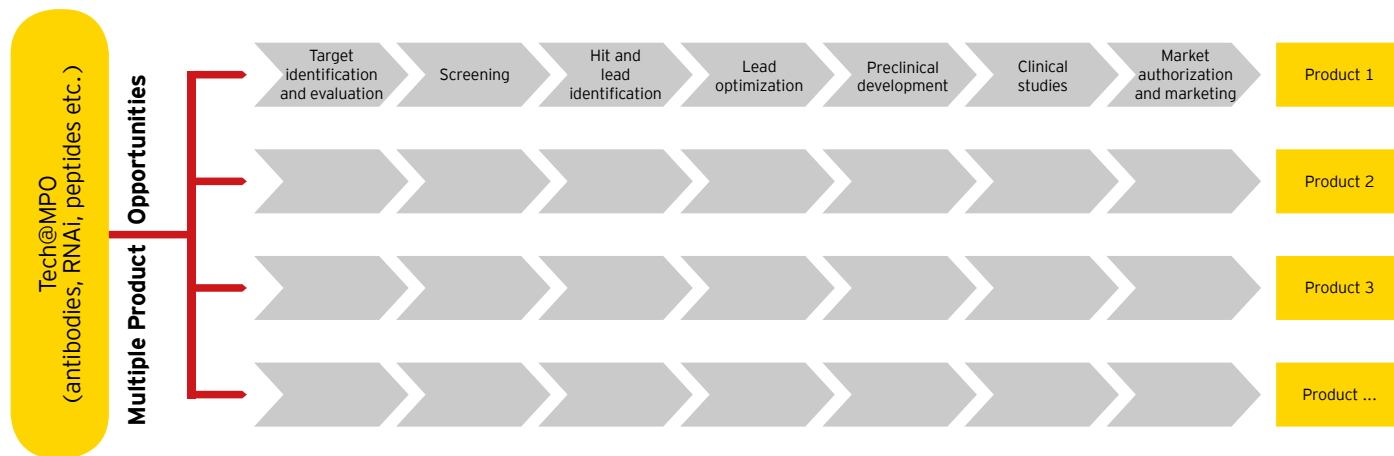
Source: Ernst & Young, 2013

**2. USP "Tech@Process": covering sections of pharma value chain**

Along with the ongoing trend towards outsourcing parts of the pharma value chain, technology platforms are established to cover significant sections and conduct the complete process externally. These platforms are often purchased initially as services with no obligation to share value. But with increasing scope of the platforms, the respective providers can ask for more lucrative risk-sharing deals.

Evotec again sets a prime example: Starting with its HTS screening platform, the company has added many further capabilities through acquisitions (e.g. OAI, Renovis, Summit / Zebrafish, RSIPL, DeveloGen, Kinaxo, Cell Culture Service) and thus created a complete drug discovery engine. Lucrative alliances with many international pharma players (Bayer, Boehringer Ingelheim, Cubist, Genentech, Roche etc.) have resulted from this. A similarly successful approach is for example pursued by the Belgian Galapagos and by the newly founded 4SC Discovery in Munich.

**Tech@MPO: generating compounds for multiple product opportunities**



Source: Ernst & Young, 2013

**3. USP “Tech@MPO”: generating compounds for multiple product opportunities**

The most advanced technology platforms are those that generate a sustainable stream of new products based on defined classes of compounds. In Germany, quite a few companies are offering this type of platform, e.g. in the fields of antibodies and derivatives, RNA/DNA, cell therapy, vaccines.

Representatives have succeeded in closing attractive deals with favorable conditions like MorphoSys (multiple deals, major one with Novartis), Pieris (Sanofi, Allergan, Daiichi Sankyo), CureVac (Sanofi Pasteur), NOXXON Pharma (Pfizer, Eli Lilly) in Germany or Ablynx (Nanobodies®), Symphogen (antibody mixtures), F-star (antibodies) and Santaris Pharma (cyclic RNA) on a European scale.

**4. USP “Tech@Disease”: knowledge platforms around diseases**

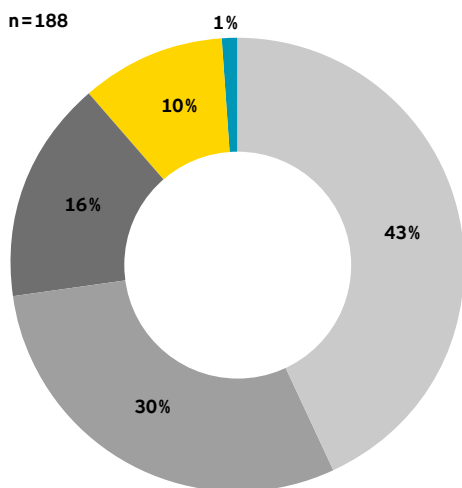
Platforms focusing on specific disease areas are not technology platforms in a narrow sense; however, they share common aspects. USPs are defined by specific knowledge of the “new biology” in a given therapeutic area.

The outstanding example in Germany is AiCuris with its infectious diseases platform. Due to the higher risk profile associated with the development of individual drugs, this model relies more heavily on the backing of strong investors like the Strüngmann family office in the respective case. Again, deals with big partners are the major success factor (for example AiCuris with Merck & Co.).

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## Overview of German Tech@Companies active in the therapy sector

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- Development of therapeutics
- Tech@Process
- Tech@MPO
- Tech@Disease
- Tech@Translation

Source: Ernst & Young, 2013

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### German therapy sector associated with platforms

The sample of German biotech companies active in the therapeutic sector does indeed favor platforms as a major business positioning. Almost 60% of companies are split up into platforms around R&D processes (30%), MPOs (16%) and disease platforms (10%), whereas the remaining 43% still adhere to the more traditional model of developing individual drugs with all the known downsides.

### Success parameters

Alliances with big pharma partners have become common success parameters for all platform models. The list of pharma partners is one reference to demonstrate success; another one is the generation of one's own product pipeline.

**Thinking beyond - new growth market  
“diagnostics and PI technologies”**

Despite slowing growth in the overall diagnostics market, molecular diagnostics in particular remains an important growth driver, with global revenues of US\$52 billion and a projected CAGR of 7% for the years 2012 to 2017. This development is closely linked to the rise of personalized medicine and the increasing relevance of companion diagnostics.

The field is also very much dominated by new technologies. On the one hand, it is about generating and handling big data. On the other hand, more traditional segments such as point-of-care applications or home monitoring are based on sophisticated technologies. Since everything is centered more and more around individual patients and these patients own their data, a new paradigm has been defined with the term “PI technologies”, which reflects the two themes “Patient empowering” and “Information leveraging”.

With their technologies, biotech companies can thrive in this environment. Thus, they are able to define specific USPs and establish best practices in the diagnostics sector.

**1. USP “Tech@BigData”**

Quite a few German biotech companies are active in the big data field generating information through next-generation sequencing approaches (e.g. GATC Biotech, Alacris Theranostics, CeGaT). Major success factors are mostly customer-defined:

- Strong IP
- Optimized organization
- Shortest time-to-delivery
- Optimal quality
- Best price

In addition, there are further discriminators:

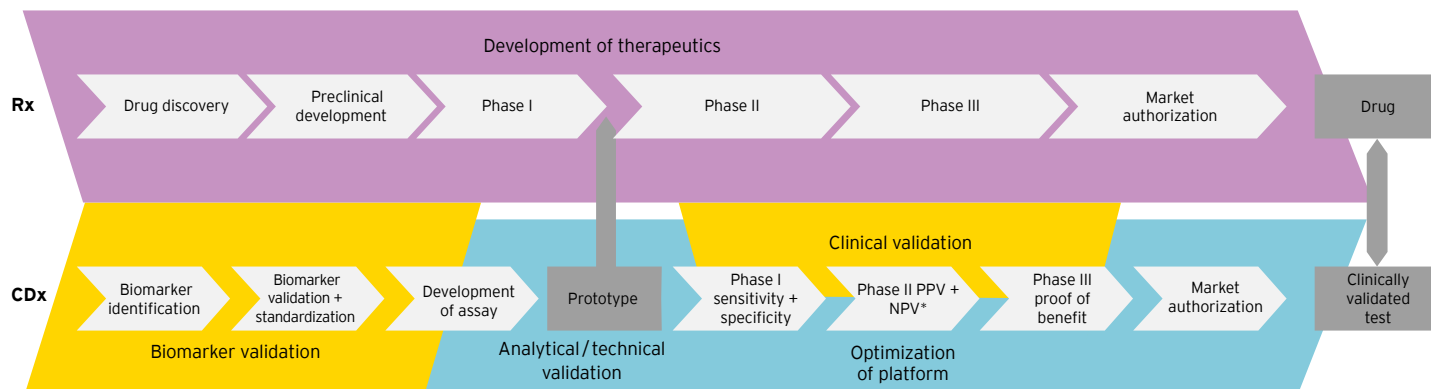
- Portfolio of technology platforms
- Scope of service offerings
- Potential to develop a service model into a product model (e.g. test kits)

The other field of big data activity is bio-informatics. In Germany, this is also a space heavily populated with companies that can be divided into three groups:

- Interpreters of big data generated by NGS approaches
- Integrators of big data from various sources (life science knowledge management)
- In silico research providers



## Rx-CDx-model: development of companion diagnostics



\* PPV = positive predictive value, NPV = negative predictive value

Source: Ernst & Young, 2013

### 2. USP "Tech@CompanionDiagnostics"

The development of personalized medicine approaches and companion diagnostics (patient stratification, disease monitoring etc.) is by far the most attractive perspective. This market is still small in absolute figures but has tremendous rates of growth and is expected to hit US\$40 billion in the US by 2015 (from US\$28 billion today). A good indicator is the number of ongoing drug development projects that are associated with biomarkers and companion diagnostics. Whereas in later stages only 30% of drugs are developed in parallel with respective biomarkers, already 50% of phase I and even 60% of preclinical developments go hand in hand with companion diagnostics.

Strong drivers are the payors aiming to reduce cost as well as regulatory agencies caring for patient safety. Most importantly, companies engaged in this field will have to achieve that the established value-based pricing of the drug part in these dual development tracks also becomes adapted to

the diagnostics component. This field is particularly interesting for biotech companies because, firstly, the development of companion diagnostics relies more on disease biology rather than the test specifics. Secondly, their validation and development phase mostly runs parallel to those of drug development - which is also more and more in a one-to-one partnership with pharma companies. Eventually, these biotechs will have the chance to either reach the market or partner with diagnostics companies for the test development and marketing part.

There are numerous German biotech companies associated with this sector providing best practice, most importantly by leveraging systems biology or sequencing approaches. Again, technological capabilities predominate, such as high-throughput sequencing and array technologies as well as biobanks and expertise in clinical validation of biomarkers. These fields also increasingly attract the attention of VC investors.

### 3. USP "Disease Detection"

The application of biotechnology to the detection of disease-causing agents based on an improved understanding of disease biology is the traditional segment of molecular diagnostics. PCR is still the technology of choice in many cases, alongside arrays and immunological tests. The competitive edge for players in this field is defined by:

- ▶ Time-to-delivery
- ▶ Reliability
- ▶ Test format (e.g. multiplex)
- ▶ Standardization
- ▶ Therapeutic value (better, faster, targeted therapy)

Again, this is a sector in which VC investors that have abandoned the therapeutics field can find attractive opportunities to place their bets. Nevertheless, the predominant business model still is a service offering.

In conclusion, biotech companies are increasingly involved in the development of diagnostics. And even though they still act the role of provider for big pharmaceutical and diagnostics companies, overall lower hurdles (risk, timelines, cost) provide better opportunities to build sustainable positions. This will become even more attractive when the "valuation" issue can be resolved.



**Thinking more broadly - bioeconomy and biologization of industries**

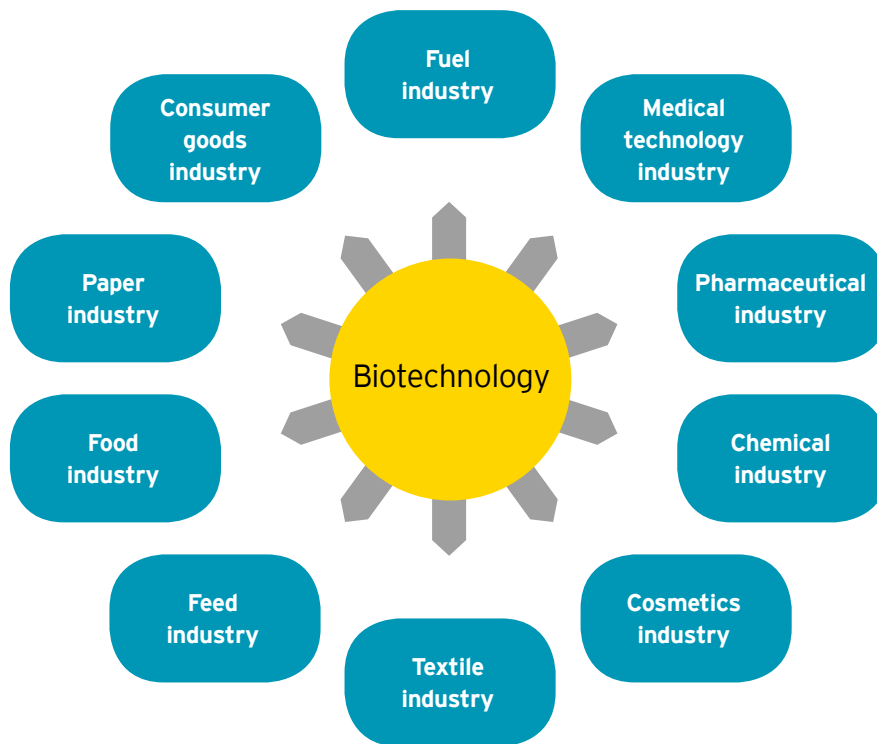
Even though biotechnology is mostly associated with medical applications, the scope of "bio-technologies" is much broader. Even in the public discussion, the term "biologization" has been introduced to indicate that "bio-technologies" can affect many different industries. Experts estimate that by 2030 one third of industrial production may come from biotech processes. Since these developments are expected to also gain commercial impact, the term "bio-economy" has become popular.

Major drivers are:

- Technical progress in biotechnology
- Simplification of complex chemical processes
- Cost advantages
- Energy savings
- Resource conservation (renewable energy vs. fossil fuels)
- Environmental protection (CO<sub>2</sub> emission)

Broadening the scope includes the identification of potential new target markets.

**Biologization of industries**



Source: Ernst & Young, 2013

**Biotechnology "reloaded"**

In this context, the definition of biotechnology must be reconsidered: As an ever so small segment of 400 companies (in Germany) it will never be able to demonstrate its true value. In light of the much wider scope and impact on so many industries the economic value of these industries should be taken into account to reflect the real value of biotechnology.

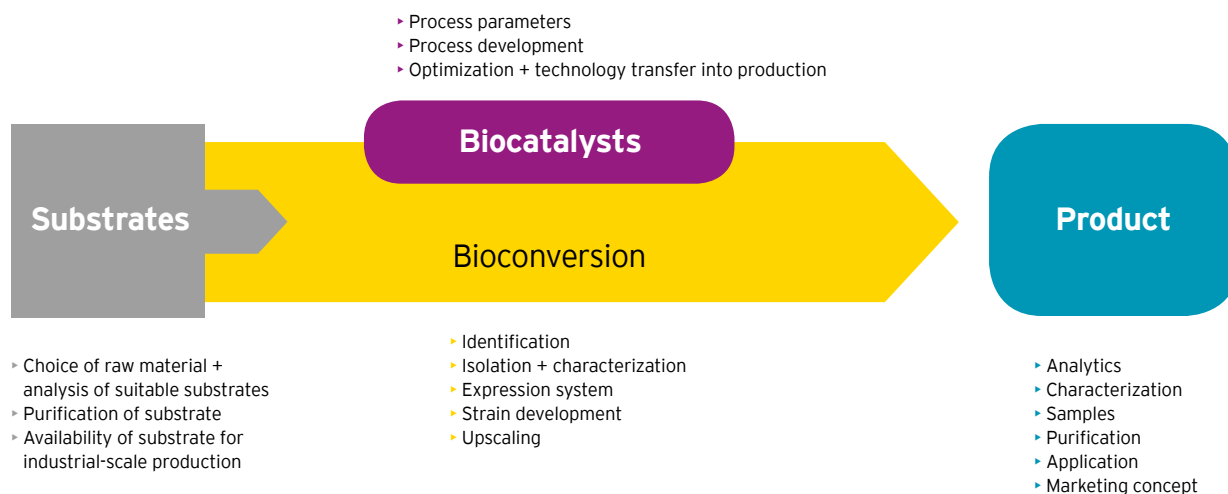
For pharma, this shift has happened: Nobody would doubt the impact of biotechnology on this sector. Nevertheless, the situation of biotech companies remains difficult as they still are at best in a technology provider role with limited participation in value generation. Will biotech companies be better off in these new industries? The answers are open. So far, these questions can only be addressed by observing best practice examples which might turn into role models for the sector as such.

**Industrialization of biotechnology**

Broadening the scope includes another aspect: The maturing biotechnology sector enters a new phase. While so far the biotech sector has been more like an experimental ground for innovative technologies and processes, it now moves ahead towards industrialization.

In the medical sector, this has been successfully demonstrated by best practice companies such as Evotec and MorphoSys. Industrial biotech companies are following: BRAIN, a leading German white biotech company, has entered a new phase aiming at industrialization of its former technical focus. The overall goal is to acquire market players in various industries in order to build complete value chains that are hooked to and fit BRAIN's technology base of industrial biotech solutions.

## Bioconversion as a central platform



Source: Ernst & Young, aevotis GmbH, 2013

### Technology platforms for biologization of industries

In general, the industrial biotech technology platforms comprise of:

- ▶ Natural compound platforms (organisms, metagenomes)
- ▶ Bioconversion platforms (catalyst design via genetic engineering)
- ▶ Application innovations for biotech products (silk protein products)

Companies widely differ with respect to their objectives and prioritization. While some focus on biomass utilization and renewable energy sources (the front end), others are dedicated to novel enzyme functions and end products that meet market demands.

### Biotech - role as "Impact Factor" in many industries

Biotech - at least in Germany - is suffering from a bad reputation caused by failed models, development failures and immense capital destruction. This is solely based on the unilateral focus on the drug development track with maximal risk, maximal cost and a close link to the pharma industry which has a similarly bad reputation.

Can a shift in focus towards the bio-economy paradigm change the role and reputation of biotech? First, it would be necessary to realize the potential of biotech in the above described new areas in such a way that its impact is put in relation to the size and relevance of these industries. This can be achieved by bringing forward arguments that are more in line with modern lifestyle:

- ▶ Environmentally friendly processes
- ▶ Renewable energy sources (biomass instead of oil/gas)
- ▶ Energy-saving processes (fermentation instead of chemistry)
- ▶ Natural cosmetics with clinically proven effects
- ▶ Functional food/clothing

# Key financials of the German biotech sector

## Key metrics of the German biotech industry

	Private companies			Public companies			Total industry		
	2011	2012	11/12	2011	2012	11/12	2011	2012	11/12
<b>Key metrics</b>									
No. of companies	392	390	-1%	14	13	-7%	406	403	-1%
No. of employees	8,248	8,428	2%	1,684	1,589	-6%	9,932	10,017	1%
<b>Financial data (€ m)</b>									
Revenues	870	922	6%	215	206	-4%	1,085	1,128	4%
R&D expenditures	600	586	-2%	180	141	-22%	780	727	-7%
Loss	-308	-287	-7%	-111	-203	83%	-419	-490	17%

Source: Ernst & Young, 2013

### Number of companies remains constant

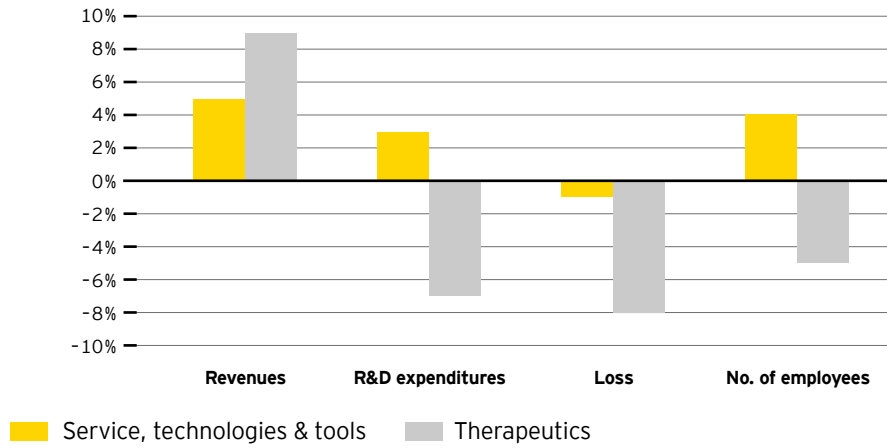
- -1%; one public company less (november AG insolvent)
- Four takeovers: Corimmun/J&J, Cellzome/GSK, SymbioTec/Lipoxen, Scil Technology/Nanohale

### Number of employees crosses the 10,000 mark

- However: significant number of cutbacks in public sector due to failures of clinical trials (e.g. Agennix, WILEX, PAION)
- Slight increase of employee numbers in private companies (+2%), mostly in service providers (+5%) and diagnostics companies (+8%); drug developers reduce employee numbers by 5%

## Dynamics of key metrics: private German companies

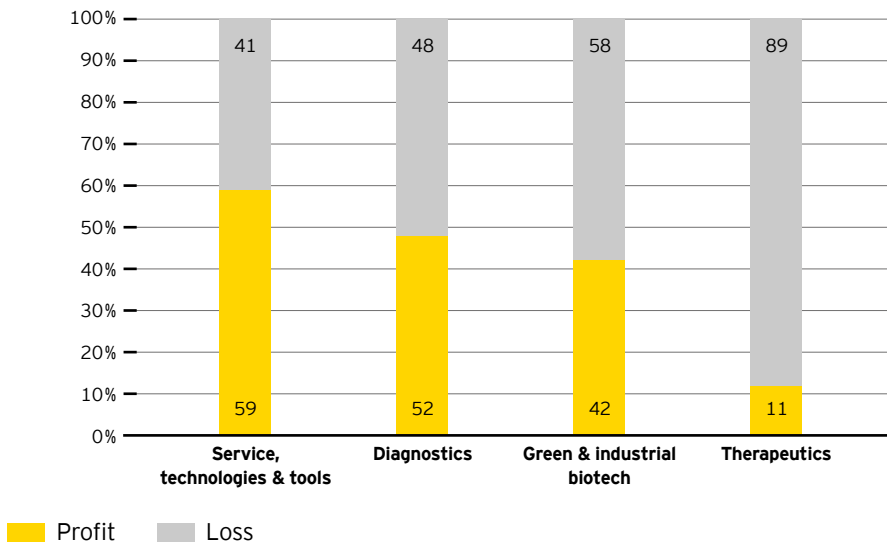
Rate of change 2011/2012



Source: Ernst & Young, 2013

## Profit and loss of private German companies by business area, 2012

Percentage of companies (n=208)



Source: Ernst & Young, 2013

### Revenues show positive trend

- Revenues of private companies rise (+6%) while those of public companies diminish slightly (-4%)
- Private companies: Increase of 5% for private service / tool companies; 9% for drug developers, which includes major upfront payment (€110m for AiCuris in Merck & Co. deal)
- Public companies: e.g. PAION (+725%, from €3m to €26.8m caused by sale of Desmoteplase to Lundbeck)

### R&D expenditures decreasing

- 7% overall decrease in R&D expenditures;
- Public companies -22% due to sale of products (PAION) or business units (MorphoSys)
- Decrease in R&D expenditures of private companies (-2%); primarily in those of drug developers (-7%) mainly due to company transactions; tool providers spent 3.5% more on R&D

### Loss figures show divergent trends

- Overall increase of 17%
- Private companies were able to decrease aggregate loss by 7% to €287m, mainly because some loss-making firms disappeared from the statistics via takeover or cessation of business
- Aggregate loss of public companies increased by 83% due to development failures (e.g. Agennix from €41m to €146m)

# Financing the German biotech sector

## Financing in Germany: fluctuation rather than an upward trend

- ▶ Venture capital financing doubled from €87m to €207m; private company financing still 35% below pre-crisis levels (2006/07)
- ▶ Increase solely due to two major financing rounds from family offices (CureVac / Dietmar Hopp, BRAIN/Putsch family)
- ▶ Remaining venture capital decreased further to only €25m
- ▶ Public financing doubled from €44m to €80m
- ▶ No IPOs since 2006

## New names on the family office list

- ▶ Putsch family (RECARO) invests €60m in BRAIN (together with MIG Fonds) to industrialize white biotech platforms
- ▶ MEY Capital Matrix (car supplier Webasto group) invests in GNA Biosolutions and conoGenetics

## Crowdfunding also in biotech?

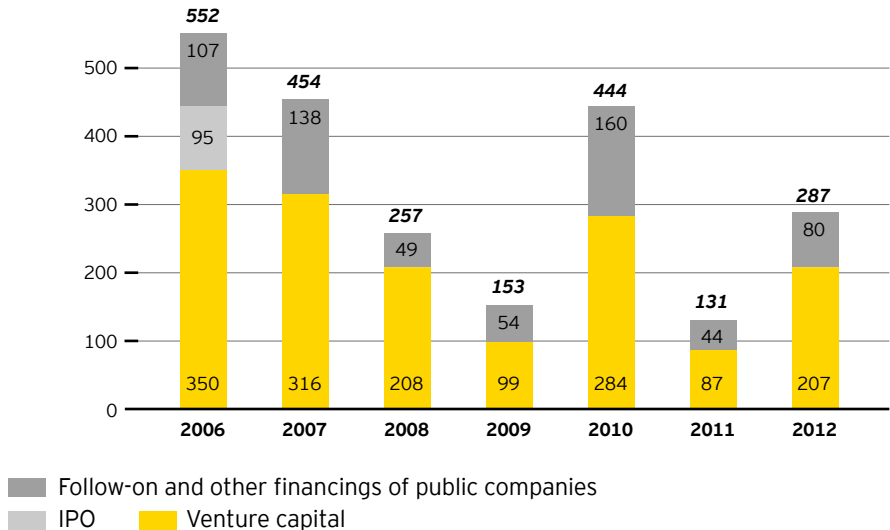
- ▶ Mentality favors donations rather than high-risk return-driven investments
- ▶ More funds for private investors (e.g. MIG Fonds - 13 funds, €60m each, share units from €3,000-5,000; AMD Therapy fund - planned volume €60m; share units €3,000; 10-year time line; therapy focus only, investors in cooperative organization; MEY Capital Matrix - bonds for private investors)
- ▶ Web-based crowdfunding platforms collecting money for biotech projects are emerging (poliwogg.com, cureLauncher.com, sciencestarter.de)

## Business angels more visible in company financings

- ▶ Overall smaller financing rounds provide better ground for BAs to play a role
- ▶ Better organization and cooperation of BAs enable bigger stacks in rounds
- ▶ Support from EIF BA program further strengthens BA role
- ▶ Some best practice examples for BA-driven rounds in NRW: AyoxxA Biosystems, Algix Pharmaceuticals, AudioCure Pharma

## Capital raised by German biotech companies

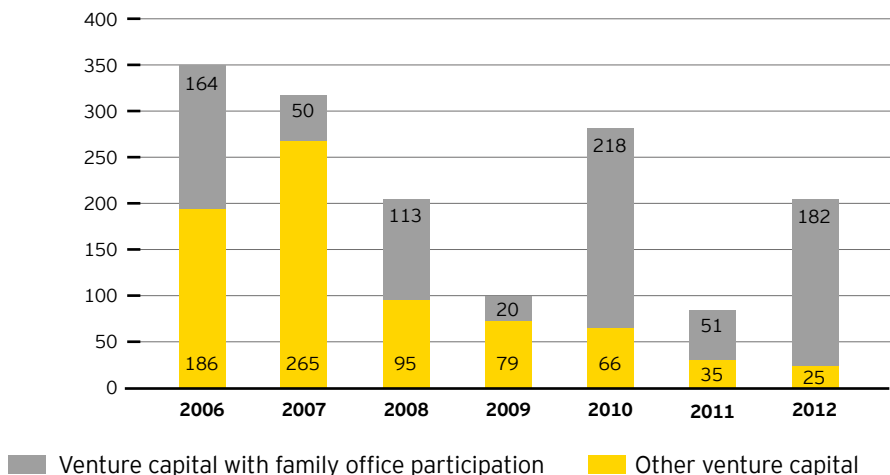
Sum (€m)



Source: Ernst & Young, 2013

## Venture capital and family office participation in Germany

Sum (€m)



Source: Ernst & Young, 2013

## Traditional VC as an exception?

- ▶ Only one typical VC round for Affimed with €15m for bispecific antibody program from European and US investors (LSP Life Sciences Partners, BioMedPartners, OrbiMed) in addition to a family office

(Aeris Capital) and a strategic (Novo Nordisk) investor

- ▶ Only few German VC investors left in investment mode: Wellington Partners, CREATHOR VENTURE, Peppermint VenturePartners; most investments into diagnostics, medtech, technology companies

## Venture capital financings of German biotech companies, 2012

Company	Volume (€m)	Announcement	Round	Investors
CureVac	80.0	September	4	dievini Hopp BioTech holding
BRAIN	60.0	November	2	MIG Fonds, MP Beteiligungs-GmbH, undisclosed investors
AiCuris	25.0	January	3	Dom Capital, FCP Biotech Holding, Santo Holding, private investor
Affimed Therapeutics	15.5	October	5	Aeris Capital, BioMedPartners, LSP Life Sciences Partners, Novo Nordisk, OrbiMed Advisors
Phenex Pharmaceuticals	5.0	October	4	CD-Venture, CREATHOR VENTURE, EVP Capital, KfW, LBBW, Swiss Life, private investors
Proteros biostructures	5.0	August	2	BayBG, institutional investors
Algiax Pharmaceuticals	4.3	May	1	HTGF, KfW, private investors
CEVEC Pharmaceuticals	2.8	October	4	Peppermint VenturePartners, CREATHOR VENTURE, Midas Group, NRW.BANK
AyoxxA Biosystems	2.6 *	September	1	Wellington Partners, HTGF, NRW.BANK, Rainer Christine, Gregor Siebenkotten
Rodos BioTarget	2.0	November	1	HTGF, Invest-Impuls, KfW, private investors
conoGenetix biosciences	1.5	April	1	MEY Capital Matrix, Bio <sup>M</sup>
t-cell Europe	1.5	May	Seed	Constantin Bastian Leander Venture Capital, HTGF, ILB
Cysal	1.0	November	Seed	eCAPITAL entrepreneurial Partners, HTGF
JeNaCell	0.7	October	Seed	HTGF, STIFT
AMP Therapeutics	n/a	January	1	Boehringer Ingelheim Venture Fund, Novartis Venture Fund
AptaIT	n/a	March	1	BioNTech, Prefound
AudioCure Pharma	n/a	May	Seed	Jürgen Schumacher, HTGF
Axiogenesis	n/a	June	n/a	V+ Management
cube-biotech	n/a	December	1	CREATHOR VENTURE Management, undisclosed business angels
Enzymicals	n/a	June	n/a	BRAIN, Braun Beteiligungs GmbH
Epivios	n/a	July	Seed	HTGF, Life Science Inkubator, TTHU, private investor
Eternigen	n/a	September	Seed	IBB Beteiligungsgesellschaft mbH, private investors
GeneQuine Biotherapeutics	n/a	November	Seed	HTGF, Innovationsstarter Hamburg
GNA Biosolutions	n/a	December	1	MEY Capital Matrix
MYR	n/a	March	2	Maxwell Biotech Venture Fund
OakLabs	n/a	February	Seed	HTGF
oncgnostics	n/a	March	Seed	HTGF, STIFT
Revotar Biopharmaceuticals	n/a	February	6	bmp Beteiligungsmanagement, existing and undisclosed investors
Transimmune	n/a	June	1	QureInvest

\* 2<sup>nd</sup> tranche in January 2013 brings total financing to € 3m

Source: Ernst & Young, 2013

## Follow-on financings of German public biotech companies, 2012

Company	Volume (€ m)	Date	Type
MOLOGEN	22.0	June-19	PIPE
WILEX	16.1	August-3	PIPE
4SC	12.6	June-13	PIPE
Biofrontera	11.5	March-2	PIPE
WILEX	9.9	January-9	PIPE
co.don	3.9	August-20	PIPE
MOLOGEN	2.7	March-27	PIPE
Biofrontera	1.4	February-3	PIPE

Source: Ernst & Young, 2013

### Regionalization of VC activities

- ▶ Associated with federal state governments or regional banks
  - 66% of rounds include local investors
  - Examples: Investitionsbank Berlin, bmp Beteiligungsmanagement (Brandenburg), eCAPITAL (Münster), Bio<sup>M</sup> Venture Capital (Munich), BayBG Bayerische Beteiligungsgesellschaft (Munich)

### Commitment of corporate venture funds in Germany

- ▶ Novartis Venture Fund and Boehringer Ingelheim Venture Fund invest in AMP Therapeutics
- ▶ Typical CVC investment (early platform, early participation in innovation without big commitment, high-potential therapy areas, too early for regular pharma alliance)

### No IPOs in Germany since 2006

- ▶ Capital market still not showing interest in biotech sector
- ▶ Similar situation in Europe with only one bona fide IPO (Adocia; specialty pharma-like; €27m); total of €31m raised in 2012

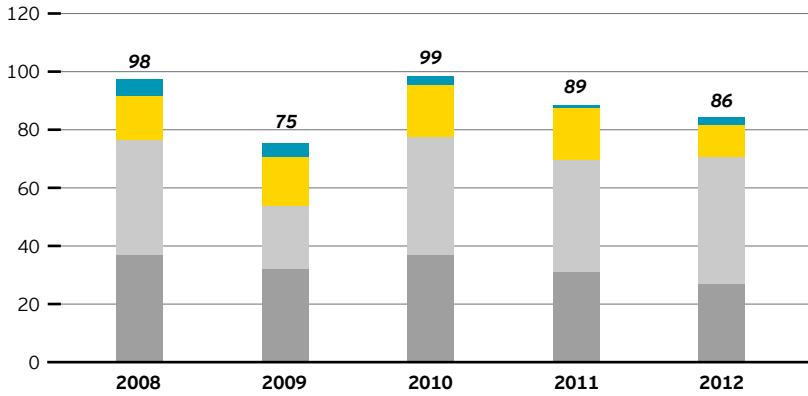
### Follow-on financing in Germany increased, but still small

- ▶ Only €80m raised, primarily PIPEs to existing investors
- ▶ Rounds associated with good clinical results: e.g. MOLOGEN/€25m, WILEX/€25m (in expectation of phase III data from Rencarex<sup>®</sup> study which unfortunately failed later in 2012), 4SC/€13m (for clinical studies) Biofrontera / €13m (good newsflow on distribution agreements with Allergan and Desitin Arzneimittel)

# Transactions by German biotech companies

## Alliances of German biotech companies

No. of transactions

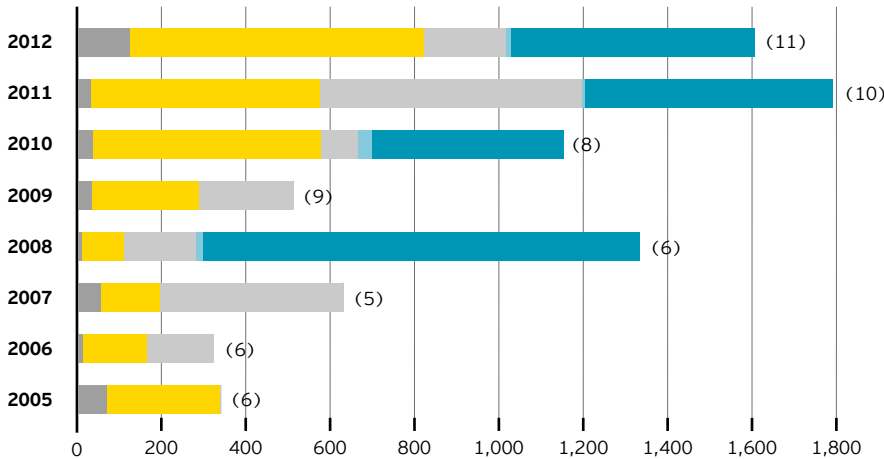


Product/Asset acquisition Service Licensing Cooperation

Source: Ernst & Young, 2013

## Payments to German biotech companies resulting from alliances

Sum (€m), No. of transactions (in brackets)



Upfront payments Milestone payments  
Others and not fully disclosed payments  
Upfront payments (mega deals) Milestone payments (mega deals)

Source: Ernst & Young, 2013

### Number of alliances stagnating

- ▶ Quantity (86) slightly lower than average of the last four years
- ▶ Relative share of license agreements increasing over last four years from 39% to 51% in 2012 (44 deals)
- ▶ Relative share of cooperations decreasing from 38% to 33% and of service agreements from 19% to 13% (presumably because of a high number of unpublished deals)

### Payments from alliances remain on high level

- ▶ Total of € 1.6 b (€ 1 b without mega deals)
- ▶ Significant increase (€ 29 m to € 122 m) in aggregate upfront payments (mainly due to a single deal between AiCuris and Merck & Co., € 110 m upfront)

### Technology platforms prevail

- ▶ Top 6 German alliances all involve Tech@Company partners although all including assets in early-stage development based on the platform (Evotec/Janssen: Tech@Translation, Evotec/Bayer: Tech@Process, AiCuris/Merck & Co.: Tech@Disease, Phenex/Janssen: Tech@Process)
- ▶ Four Evotec deals in top list cover the complete pharma value chain from research (J&J/Harvard - diabetes) to early drug discovery (Bayer - endometriosis) to clinical development (Janssen - depression) to marketing (Zhejiang CONBA Pharmaceutical - inflammation)
- ▶ AiCuris/Merck & Co. deal with third-highest European upfront payment (€ 110 m); exploiting negotiation power based on good story to demonstrate value, strong investor backing (family office Strüngmann) and contingency strategy to conduct phase III study alone



**Diagnostics alliances with Curetis in the lead**

- ▶ Curetis as best practice company with six deals in 2012
- ▶ Collaboration partner Cemptra - scope of application
- ▶ Collaboration partners Horst Scholz and Heraeus Medical - parts for manufacturing
- ▶ Distribution partners Mediphos (NL), BioLine (RU), Advanced Technology Company (MENA) - distribution agreements in various regions

**Industrial biotech - supplier of big chemistry in broad scope alliances**

- ▶ evocatal/LANXESS - renewable resources for rubber production
- ▶ BRAIN/Evonik - functional modification of surfaces by microbial absorption
- ▶ c-LEcta/Sartorius Stedim - distribution agreement for Serratia Nuclease
- ▶ c-LEcta/Aquapharm - biocatalysts from marine organisms

**European alliances dominated even more by platform deals**

- ▶ Top deals all by Tech@Companies
- ▶ Dominance of Tech@MPO platforms (Molecular Partners - DARPin<sup>®</sup>; Genmab - MABs; Ablynx - Nanobodies<sup>®</sup>; Symphogen - MABs)
- ▶ Followed by Tech@Process (Evotec/Bayer, Galapagos/Abbott)

**Volume of upfront payments correlates with platform type**

- ▶ Upfront share of total deal volume clearly ranking from Tech@Process (4%) to Tech@MPO (10%) to Tech@Disease (21%)

**M&A transactions - little relevance in Germany**

- ▶ Only few deals overall (8)
- ▶ Trade sales:
  - Cellzome acquired by GSK after long collaboration that leveraged Cellzome's proteomics platform
  - Corimmun acquired by J&J; deal was focused on one lead asset only; remaining portfolio has been transferred to a new enterprise (advanceCOR)
  - Scil Technology acquired by Nanohale
- ▶ Minority stake acquisitions based on strategic considerations:
  - B. Braun Melsungen/CeGaT
  - CytoTools/DermaTools
- ▶ Partial acquisition: MorphoSys sold its research antibody unit to Bio-Rad
- ▶ Restructuring: Sygnis (failure in stroke program) acquired Spanish diagnostics company X-Pol
- ▶ Management buyout: Sovicell

The low number of M&A transactions in Germany can be interpreted as a consequence of a shift in business models in favor of more and more service models that has been observed over the last few years.



# Product development by German biotech companies

## Pipeline with weak late-stage part

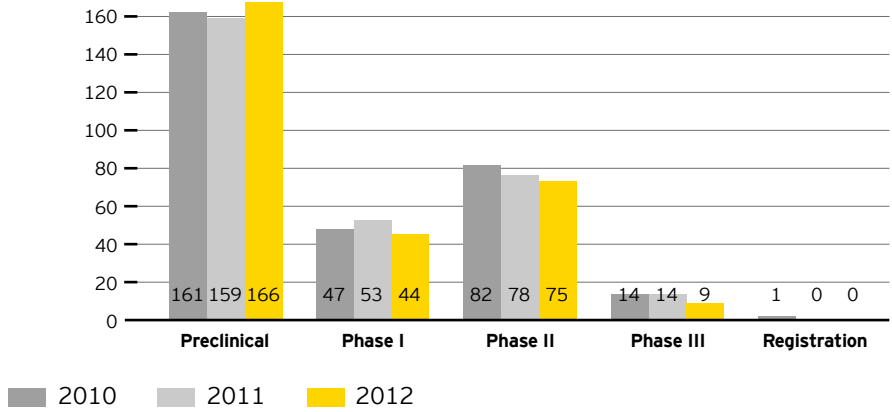
- ▶ Overall pipeline and distribution pattern of development phases remain constant over recent years
- ▶ Closer look reveals decrease in number of compounds from 304 (2011) to 294 (2012)
- ▶ Significant gaps in phase III (-36%) and no drugs in registration process in 2012
- ▶ Dynamics of intra-pipeline movements also with a bias towards early phases
- ▶ Failures in phase III shed light on development capabilities
  - WILEX/Rencarex®
  - Agennix/Talactoferrin
  - Antisense Pharma (stopped study due to recruiting issues)

## Late-stage gap connected to business model shift towards partnering?

- ▶ Development compounds eliminated from statistics if sold to partner with no remaining activities at originator
- ▶ Out-licensing or asset deals are preferred to co-development due to financial limitations

## Therapeutic pipeline by phase, Germany

No. of compounds in studies



Source: Ernst & Young, 2013

## Product innovation in phase II

- ▶ Novel drug mechanisms being tested for the first time in humans, e.g. RNA spiegelmers (NOXXON Pharma); catalytic DNAzymes (sterna biologicals), post-translationally modulated therapeutic proteins (Glycotope)
- ▶ Novel targets from basic research, e.g. Notch2 receptor, stromal cell-derived factor-1, zinc finger transcription factor
- ▶ New disease indications with so far insufficient treatment options, e.g. pancreatic cancer, solid tumors, myelomas

## Biologicals major product class

- ▶ 70% biological vs. 30% small molecule drugs
- ▶ Biologicals: 21% MABs, 19% recombinant proteins, 11% RNA/DNA compounds, 6% peptides, 8% cell therapies

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„Rethinking“  
German biotechnology report 2013

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