How can AI be the key to unlocking new opportunities in the German biotech sector?

German Biotechnology Report 2024

The better the question.
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BIO DEUTSCHLAND

$40b annual incremental revenues

estimated to be generated by AI-enabled drug discovery for the pharma industry. Beyond drug discovery, AI has the potential to revolutionize the entire (bio)pharmaceutical value chain. More info on AI's game-changing role in (bio)pharma and how to harness its power starting **on page 7**.

€12.7b revenues

€1.1b total financing

€533m venture funding

€11.4b biobucks

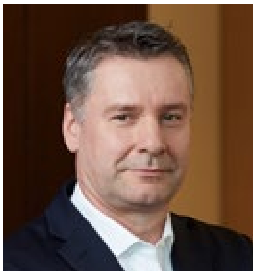
169 clinical candidates

Read more about the status quo of the German biotech industry and the year 2023 in review starting **on page 31.**

The enduring challenge of interpreting extensive scientific data sets

how AI-driven solutions are driving progress in drug discovery and development starting **on page 16.**

$1.2b patient recruitment costs on average and trials lasting six to seven years: AI offers valuable tools to address these challenges. More info on the power of AI in clinical trials – revolution through machine learning and deep learning analytics starting **on page 18.**



Klaus Ort
EY Europe West Life Sciences and Health Leader

Oliver Schacht, PhD
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Preface

Welcome to the 26th edition of our German Biotech Report, where we take a deep dive into the transformative potential of artificial intelligence (AI) within the biotech sector. Beyond its status as a buzzword, AI's profound influence on various industries demands a detailed examination of its role in biotechnology.

As the German biotech industry embraces AI, this year's report aims to explore the technology. We offer a nuanced analysis of the opportunities AI brings to the table, as well as the challenges it introduces. Our articles provide an in-depth look at AI's critical role across the biopharmaceutical value chain, with a special focus on generative AI in drug design and development, the enhancement of clinical trials through AI innovations, and the intricate ethical considerations that these advancements entail.

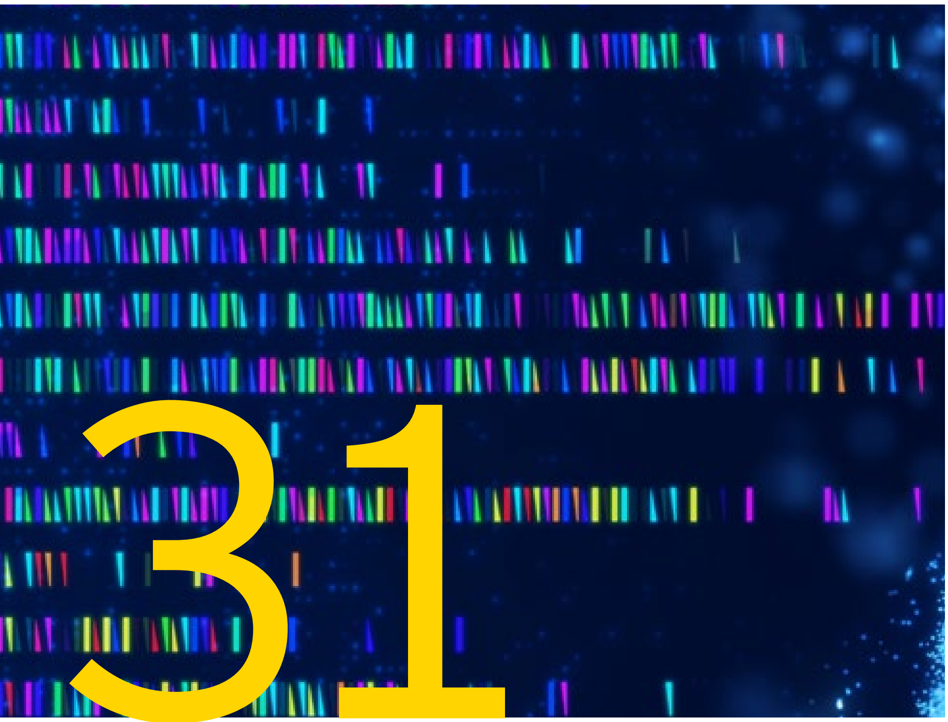
In line with our longstanding tradition, we also present a thorough analysis of the sector's performance over the past year, celebrating its achievements and addressing the hurdles that continue to shape the German biotech landscape.

This year marks the eighth anniversary of the collaboration between EY and BIO Deutschland, the German biotechnology industry association, in the joint effort of gathering and analyzing industry data, and it is with great pride that we co-produce this year's edition of the report. Our partnership has been crucial in data collection, insightful analysis, and enriching the report with the authentic voice of the industry.

We extend our gratitude to all those who contributed to the creation of this report, from the dedicated project team and contributing authors to the external industry experts who shared their valuable perspectives.

On behalf of all the contributors to the German Biotech Report 2024, we warmly invite you to join us on this informative journey. As you read the report, you will gain a deeper understanding of the current state and future prospects of the German biotech industry — a field poised to address some of the most pressing global challenges of our era by synergizing AI with human ingenuity.

Klaus Ort **Oliver Schacht**



German Biotechnology Report 2024

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AI adoption is not a sprint, it is a marathon. It is about understanding that every corner of the organization has a role to play, and that success lies not just in change, but in the ability to adapt, innovate and grow.

Holger Fehlbier
EY Strategy & Transactions, Europe West AI Leader

AI's game-changing role in (bio)pharma – and how to harness its power

A new era begins

Since man's new best friend ChatGPT entered the world stage in November 2022, it caught the attention of global executives and the public alike. According to OpenAI, ChatGPT acquired 1 million users just five days after its inception. Conversely, Instagram took 2.5 months to reach this many users.

ChatGPT, however, is only the most prominent protagonist of a broader artificial intelligence (AI) show cast. At the root of ChatGPT is a technology called Large Language Model (LLM), which is a subset of the diverse array of technologies that AI offers. Just as diverse as the number of AI technologies are their use cases across industries and their respective value chains – the most prominent application areas being content generation, process automation, problem solving and decision-making.

In this article, we will provide a concise overview of the AI universe – across various technologies and various (bio)pharmaceutical value chain steps, from drug discovery to clinical trials, and from supply chain to commercial. We believe exceptional business value (both top- and bottom-line) can be created if organizations can find a way to harness the transformative power of AI.

What is AI?

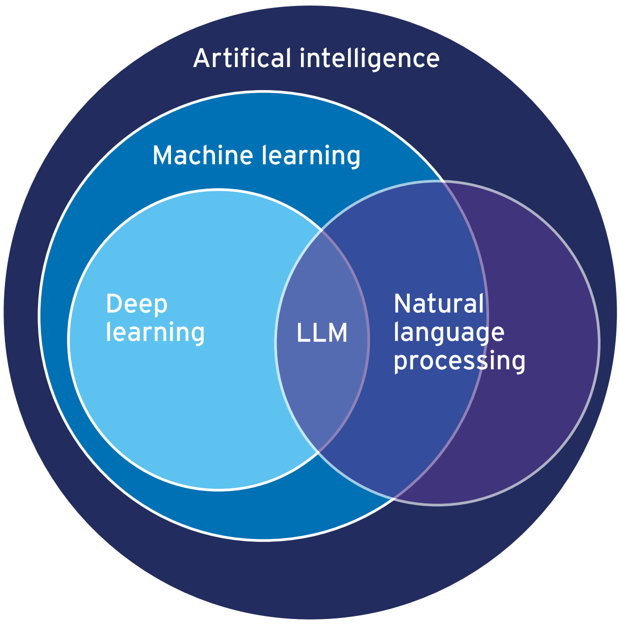
AI is not a new phenomenon. The term was coined in 1956 at the Dartmouth Conference. While humankind relies on genetics and experiences, AI models are shaped by algorithms and training data to perform tasks conventionally requiring human intelligence.

Initially, AI research focused on rule-based algorithms like the Logic Theorist (1956) and the General Problem Solver (1957). Basic machine learning (ML) then began to emerge, enabling machines to learn from data, acquire patterns, and improve their performance over time.

At the turn of the century, the term deep learning (DL) came into being. This is a subset of ML, using algorithms inspired by the structure and function of the brain to revolutionize data interpretation. DL is especially powerful for complex tasks like image and speech recognition. ML and DL set the stage for natural language processing (NLP), which enables computers to comprehend, interpret and generate human language. It includes a wide range of tasks like translation, sentiment analysis, and text summarization.

Large language models (LLMs) are a more recent (from the 2010s) advancement of NLP capabilities, primarily using DL techniques to process and respond to user inputs in a way that is contextually relevant and coherent. This is where ChatGPT sits – just the tip of the iceberg.

AI terminologies and their relationships



Finally, generative AI (GenAI) is a closely related but broader category, capable of crafting content across various domains. These can be text (like LLMs), but also extend to images, music, videos, and even molecular structures.

Why does it matter?

AI is here to stay. It has the power to sharply enhance human productivity, innovative capacity, as well as decision-making. Andrew Ng, a globally recognized leader in AI rightfully claims "AI will be the electricity of the 21st century."

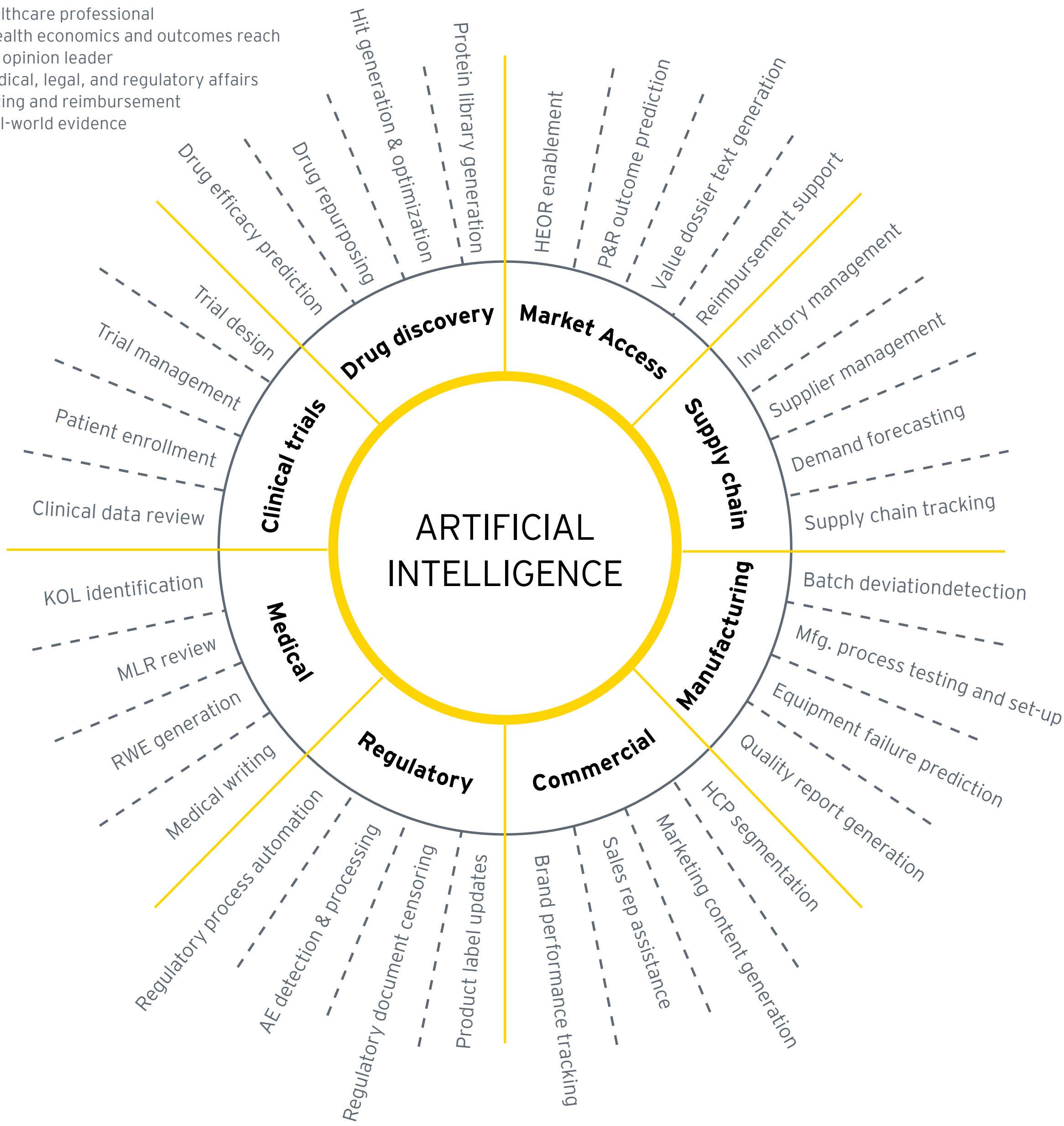
The (bio)pharma industry is predestined to be disrupted by AI, due to the vast amounts of data generated from diverse sources, including genomic data, clinical trials, patient records, and real-world data. Managing, analyzing and interpreting such data manually or with traditional methods is increasingly challenging and inefficient.

Take drug discovery as an example – which is the most advanced and impactful area of AI applications in (bio)pharma to date. AI can help in identifying and validating new targets (by analyzing vast biological and genetic datasets), screening drug candidates, enabling the design of novel compounds, as well as predicting the potential toxicity of compounds early in the drug discovery process.

Ten years ago, about 60 drug candidates were developed using AI. Today, the number has rocketed to 490 per year.

Selected AI use cases along the (bio)pharma value chain (non-exhaustive)

AE = adverse event
HCP = healthcare professional
HEOR = health economics and outcomes reach
KOL = key opinion leader
MLR = medical, legal, and regulatory affairs
P&R = pricing and reimbursement
RWE = real-world evidence



Prominent players in this field are US-based Insilico Medicine and UK-based Exscientia, setting historical precedents by advancing AI-generated molecules to clinical trials more than twice as fast than the average industry time of around five years. We estimate ~$40 billion annual incremental revenues to be generated by AI-enabled drug discovery, for the pharma industry. Beyond drug discovery, AI has the potential to revolutionize the entire (bio)pharma value chain. From our extensive AI use case library, we have chosen three examples in clinical trials, supply chain, and marketing to give a flavor of AI's transformative power.

Finding qualified participants for clinical trials has long been a challenge, especially for Phase 3 studies. This is where AI can help — not only to save time and cost, but to address ethical concerns of traditional trials. ML and GenAI can create patient "digital twins" — based on historical trial data — to simulate how a patient's health might progress over time (including how a patient might respond if they were not receiving the experimental treatment, i.e., in a control scenario). These predictive models can reduce the size of human control arms by 1/3 while maintaining statistical power.

In supply chain, one of the toughest nuts to crack is demand planning. Traditional forecasting approaches are often manual, backward-looking and "inside-out," influenced by sales history and demand planners' intuition. ML, in contrast, can analyze a much larger magnitude of influencing factors (such as historical sales, market trends, patient demographics, and disease prevalence) to identify trends that might not be evident to human analysts. ML algorithms can continuously monitor demand signals and make real-time adjustments to forecasts, which is crucial in responding to sudden market changes. A case study of an American multinational biopharma company demonstrates AI's impact on demand forecast accuracy: it was increased from 38% to 65% within eight months for the global portfolio.

In the old world, it could take a couple of weeks from a marketeer briefing an agency to getting an approved copy of marketing content back — too long, too costly. With the arrival of LLMs like ChatGPT, this task can be largely automated based on a pre-approved content library as well as marketeer input (such as target audience, core claims statements, and patient segment). In addition to texts, AI can also help to create or localize visuals for specific markets. The result can be >80% reduction in lead time (days vs. weeks), 2x click-through rates (due to better, more targeted content), and millions of euros saved on agency fees alone.

How to succeed in AI adoption?
AI is here to stay. It will transform every person's daily life and every single industry. While many (bio)pharma companies have embraced AI (either in-house or via partnerships) for the purpose of drug discovery, the breadth and depth of AI adoption vary significantly beyond the R&D space.

Leaders are continually screening a wide array of AI use cases throughout the (bio)pharmaceutical value chain, evaluating them based on impact, feasibility, and risk, and organizing prioritized use cases into actionable roadmaps. They make sure the chosen use cases are implemented at scale (across functions, countries and therapeutic areas), and that the organization is ready for the change (in terms of skills, processes, data platforms, and mindset, to name a few). They have also started to establish robust AI governance frameworks to manage risks associated with the use of AI, including setting standards, defining policies, integrating controls into various processes, and implementing teams with the right roles and responsibilities — to enable responsible AI by design.

In stark contrast, laggards find themselves in a situation where AI adoption is either non-existent, or significantly challenged. Their approach is often characterized by a lack of cohesion, with initiatives "mushrooming" across organizational silos without a unified strategy or clear objectives. This results in a failure to scale AI applications effectively, leading to inefficiencies and potential redundancies. A senior executive encapsulated this disjointed approach with a concerning observation: "I'm aware that my employees are experimenting with GenAI, but the specifics elude me. There's a real possibility they're creating overlapping applications in different corners of the company, or worse, inadvertently exposing sensitive data by sharing these with ChatGPT."

The two ends of the spectrum — as described above — highlight a pressing need for companies to establish a coherent AI strategy and a unified vision to harness the full potential of AI effectively and responsibly.

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Perfect match: biotech, big data and AI

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We have come a long way from using biotechnology merely to brew beer or to conserve our foods mostly by fermentation. The very fruitful co-development of analytic machines, computing power and molecular research in the last two decades has led to a massive amount of data stored in a host of different public or private databases around the globe. Additionally, health data is more and more often stored digitally and supplemented with data from health apps. According to the European Bioinformatics Institute (EMBL-EBI), the data it is storing is roughly doubling every year. The 2024 Nucleic Acids Research database issue and the online molecular biology database collection counted 1,959 operating databases, including genomics, protein sequences, human genes and diseases, plants, etc.

The biotech and pharmaceutical industries can now – theoretically at least – access an incredible amount of useful data and analyze it with ever better algorithms. With the help of artificial intelligence (AI), particularly machine learning (ML), large data sets can be analyzed to accelerate research and improve results. Living organisms generally exhibit a great deal of variability, and the interpretation of biological data is a challenge. This applies, for example, to the search for genetic causes of disease, the identification of target structures for the treatment of diseases and the search for the best drug candidates. Therefore, one of the sectors that benefits or seeks to benefit most from AI is medical biotechnology.

Medical biotech
Big data and AI can help the biotech and pharma industry reduce the high failure rate, significant costs and extensive times inherently tied to therapy developments. With the help of multimodal patient data such as genomic data, protein interaction or metabolomic data and AI, a list of biomarkers linked to a positive outcome can be identified and help to find an optimized list of druggable targets. Algorithms can be used to extract information of the activity of drugs against various targets and already marketed clinical assets can be used to find new targets to work on (drug repurposing). To improve clinical trials, synthetic control groups can be used to derisk early clinical trials and multiple biomarkers are used to form meaningful patient subgroups to inform trial recruitment. Real-world data (RWD) of patients, e.g., from medical records, health insurance benefits, genomic data, health apps or wearables, with AI can be turned into real-world evidence for the potential benefits of a medicinal product. In diagnostics, multiple data sources such as, image, "omics," histology, and clinical data can be used to create better predictive and prognostic models.

Structure prediction
Knowledge of the 3D structure of a protein is important to understand how a protein functions and interacts with other biomolecules. This kind of information is necessary to understand disease and to find suitable drug targets. However, calculating how proteins fold in three dimensions from the information given in the amino acid sequence has been a decades-old challenge for science. But the search for accurate protein structures has been truly revolutionized by AI in 2020. The Alphafold algorithm of the British company DeepMind, now part of Google's Alphabet, generates models of protein structures from their amino acid sequence in minutes and the results are more accurate than previously known. AlphaFold predictions are now freely available to the scientific community through the AlphaFold Protein Structure Database, in partnership with EMBL's European Bioinformatics Institute.

The database now holds over 200 million structures, including nearly all cataloged proteins known to science.

Industrial biotech
Besides the medical sector, the application of ML and AI is also gaining more and more momentum. Algorithms are, for instance, used to optimize microorganisms and enzymes for industrial biotechnology applications. AI models can suggest changes in protein sequences to improve the catalytic traits of an enzyme. The scale-up of laboratory size fermentation units to pilot and production scale is not straightforward or easy. Conditions for microorganisms in larger fermentation volumes vary from smaller entities when they float around. The differing conditions can negatively impact yield. Digital twins, mathematical models based on available data, e.g. form sensors, can simulate biomanufacturing processes. They can identify optimal process parameters to improve the productivity of fermentations and simulate and predict the microbial response.

Data integrity, quality and availability
The sheer amount of data alone is not a guarantee for meaningful analysis outcomes. The data must be of good quality, which often means manually curated, it must be in an interoperable format and finally, it must be available to the interested parties who work on improving the common good. All three prerequisites are not always met. The GRDP conform access and availability of research and health data in the European Union is still an issue slowly being tackled with the European Health Data Space (EHDS), the Data Act and according laws and directives in Germany. However, there is still a lot of room for improvement. The adoption of the electronic patient file in Germany for instance progresses extremely slowly. How much data the industry will have is also not entirely clear yet. Finally, recent polls show that the German public and medical personnel are mostly not ready to adopt digital data and data sharing.

Ethical questions of AI
There is no doubt that big data and AI are greatly advancing our understanding of life and are now indispensable for all kinds of biotech applications. Despite the great enthusiasm, there are also uncertainties regarding the use of AI, especially when it comes to patients. Issues that must be considered are, for instance, how to make sure that AI systems are transparent or how to ensure that they do not introduce or enhance biases. Especially in the case of diagnostics it is important to obtain reliable information when using the help of algorithms. Because who would be held responsible in the case of a misdiagnosis, your doctors or the AI? We therefore must make sure that AI systems are transparent and implement effective policies and regulations.

BIO Deutschland's engagement
High-quality data, computing power and AI are and will be the key drivers of biotechnological research in the future. For this reason, relevant members of BIO Deutschland joined forces in the Bio-IT, Big Data and E-Health working group back in 2014. The group's experts are committed to developing recommendations for tapping into the potential of health data with a special focus on the digitalization of health data, its availability for industrial research, interoperability and the dissolution of data silos. In a concerted manner the group supports and advances topics such as:

- Regulatory developments in the field of AI in medical research and health care
- AI-based business models in drug discovery and clinical development
- The use and analysis of biological data
- Data availability and data usage in health care (e.g., European Health Data Space (EHDS), Health Research Data Center at the Federal Institute for Drugs and Medical Devices (BfArM), activities within the project GAIA-X)
- The role of digital health applications and telemedicine and how this results in a relevance for research-based biotech companies

The use of and access to biological and health data is and will remain an important topic for the biotechnology sector and will be a decisive factor in its continued success. The BIO Deutschland working group Bio-IT, Big Data and E-Health will therefore continue its important work. Interested companies are cordially invited to get involved.

www.biodeutschland.org/de/bio-it-und-big-data.html

Generative AI in drug design and development

With the introduction of ChatGPT, generative AI (GenAI) has become a hot topic for many industries, including the biopharma industry. The immense potential of GenAI stems from its ability to generate new data based on underlying patterns learned from a provided training data set. In the era of big data of genomics and other molecular data, GenAI's capacity to detect patterns such as gene expression profiles, biomarkers, as well as functions and characteristics of molecules relevant to drug discovery, cannot be understated. Its implementation into AI-enabled workflows could lead to a significant reduction in the time required to advance a new molecule to preclinical candidate (PCC) stage by up to 40%, coupled with potential cost savings of up to 30%. Exploring a wide array of AI applications presents an opportunity to address the fundamental challenge of drug development, which typically spans years and requires substantial financial investment, from target identification to clinical trials costing billions of dollars.

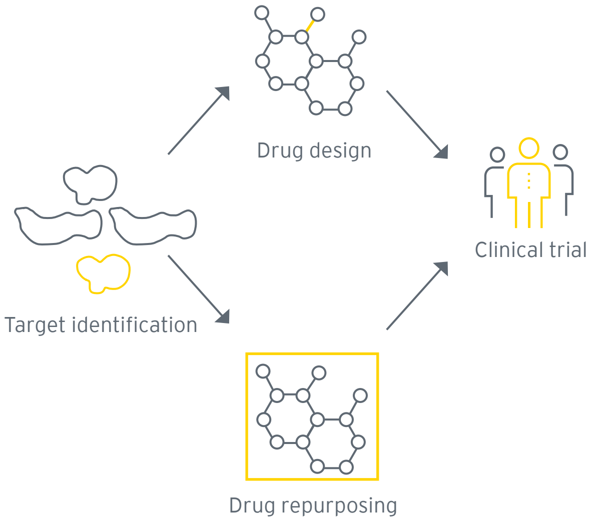
AI in novel target identification
In drug discovery, disease modeling and target identification represent critical initial stages, significantly impacting success rates throughout the development process. Traditionally, target identification has been a lengthy process, often spanning years to decades. However, AI is increasingly revolutionizing this process by leveraging its ability to analyze vast data sets and intricate biological networks, thereby playing an expanding role in modern drug target identification. Targeted drug therapy is particularly critical in cancer as traditional therapies often go along with severe side effects while targeted therapies tend to show higher efficiency, few side effects, and low drug resistance for patients. Existing targeted therapies face various limitations, including a limited number of druggable targets, inadequate coverage of the patient population, and challenges in addressing drug resistance. Consequently, the current focus of cancer research in targeted drug therapy revolves around using AI to identify novel therapeutic targets and assessing their potential druggability to overcome these drawbacks.

For instance, a collaboration between Bayer and the German AI company Aignostics, a spin-off from Berlin's Charité Universitätsmedizin, aims to advance precision oncology drug research by combining Aignostics' technology with Bayer's oncology expertise to create a new target identification platform. Utilizing AI-driven computational pathology algorithms and machine learning, the project seeks to find cancer targets with a "strong disease link" through AI models and accelerate the clinical development of targeted oncology drugs.

Drug design with optimal ADMET properties
Another significant challenge in drug discovery is to identify the most promising candidates among the vast number of synthesizable compounds in a reasonable time while maintaining optimal ADMET (absorption, distribution, metabolism, excretion, and toxicity) properties. The ADMET qualities are hard to predict and are the main reason for failure of drugs entering the clinical trial phase. AI-based generative models have emerged as a potent solution, capable of designing drug candidates with desired ADMET properties based on already existing biological and chemical knowledge.

One such example is a small molecular inhibitor INS018_055, developed by Insilico medicine's AI platform to treat idiopathic pulmonary fibrosis, a relatively rare but aggressive lung disease. Using conventional drug discovery approaches, Insilico estimated that the process would have required over $400 million and up to six years. However, leveraging GenAI, the company achieved the first phase of clinical trials in just two and a half years, at a significantly reduced cost. INS018_055 has now received the Orphan drug designation by FDA which is in Phase 2 clinical trial from early 2023.

AI application array in drug development



Here in Germany, Merck launched AIDDISON™, a pioneering software-as-a-service platform blending GenAI, machine learning, and drug design to accelerate drug development. Trained on 20+ years of validated data, it sifts through 60 billion compounds to identify those with optimal ADMET properties, offering synthesis suggestions. The platform also predicts whether it will be possible to make the compound through chemical synthesis.

AI for drug repurposing

Drug repurposing is a strategy for discovering new uses for existing or investigational drugs that are beyond the scope of the original medical indication. Repurposing of "old" drugs is increasingly becoming an attractive proposition as it promises lower overall development costs and shorter development timelines, especially if safety testing has already been completed for the original indication and the drug displays dose compatibility with the new indication. One of the classic examples of drug repurposing is the use of Remdesivir which was known for its potent in vitro activity against Ebolavirus and other RNA viruses as an approved antiviral treatment for COVID-19 which was shown to reduce recovery time of patients when administered early in the disease.

AI-assisted drug repurposing recently has made significant strides, particularly in accelerating the discovery process, reducing failure rates in clinical development, and testing phases, and avoiding safety testing in preclinical models and humans. A pioneering example comes from the global Pharmaceutical giant Sanofi, which has partnered with Germany-based clinical AI company Innoplexus to use its proprietary AI technology to find new opportunities for Sanofi's out-licensing portfolio by carefully expanding indications, prioritizing, and validating in the lab. As a vital part of this collaboration, Innoplexus will scan, analyze and enhance numerous out-licensing asset candidates across various therapeutic areas. Another important application example that leverages Innoplexus' technology focuses on the use of AI for the design of clinical studies. Please refer to page 18 for more details and a case study.

What's next?

Given the multitude of applications, the potential of GenAI in drug development is increasingly evident and is paving the way for personalized medicine. Its adoption not only leads to cost and time savings but also ensures operational efficiency, ensuring that new, urgently needed drugs reach patients in need and are tailored to their genetic makeup. In the following guest perspective, Prof. Michael Platten, founder and CEO of German biotech startup Tcelltech, will provide a detailed overview of the company's proprietary AI-based bioinformatics platform for personalized cancer treatments. As we continue to explore AI's capacity it becomes clearer that the outlined use cases are only the tip of the iceberg and that organizations can truly be excited about the transformational potential that AI holds for future advances.

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Harnessing AI and genetic engineering for personalized cancer treatments

Prof. Dr. Michael Platten
Founder and CEO, Tcelltech GmbH

Tcelltech is a spin-off from the German Cancer Research Center and Heidelberg University founded in 2022. Tcelltech is an early-stage biotechnology company using cutting-edge technologies in computational and molecular biology to engineer highly potent and specific personalized therapies based on T-cell receptor (TCR) targeting of solid tumors. By combining two proprietary platform technologies – explainable artificial intelligence (AI) to power TCR discovery, and innovative DNA vectors for genetic engineering – Tcelltech addresses key efficacy, safety and economic challenges that currently limit the full potential of TCR-T cell and soluble TCR therapeutics.

Technological approach
The AI-based bioinformatics platform *selecTCR* is a classifier that was developed by the founding team to retrieve tumor-killing TCRs from tumor-infiltrating T cells with high accuracy. Tumors are regularly infiltrated by T cells, but only a small fraction (less than 1%) are tumor reactive. SelecTCR applies explainable AI – using frameworks that allow understanding the predictions made by the model – to identify tumor-killing T cells based on their gene expression profile. To do so, T cells are extracted from the tumor after surgery and subjected to single cell sequencing. The resulting data is analyzed by selecTCR. Within less than two weeks from surgery, the TCRs from tumor-killing T cells are identified and can be used to generate personalized therapeutic TCR-T cells or soluble TCR therapeutics. This low turnaround time is possible as selecTCR – unlike other classifiers – does not require the a priori identification of the tumor antigen a TCR recognizes prior to classifying it's tumor-reactivity. The identification of tumor antigens remains a key bottleneck in creating a personalized tumor immunotherapy due to the myriad of ways such antigens can be generated. As it is antigen-agnostic, selecTCR for the first time provides a workflow that can be integrated into the manufacturing process of a personalized T cell product in a clinically meaningful timeframe. The Tcelltech team aims to further develop selecTCR to identify tumor-killing TCRs from the blood of cancer patients and to be used as a potential biomarker to predict response to currently approved immunotherapies such as immune checkpoint inhibitors.

With this technology at hand, Tcelltech seeks to develop *UNIPACT* – a universal personalized adoptive cell therapy product for solid cancers. UNIPACT consists of patient-autologous T cells that are genetically engineered to express patient-individual tumor-killing TCRs previously identified using selecTCR. Similar to chimeric antigen receptor (CAR)-transduced T cells, TCR-T cells are manufactured outside the body and then reinfused. This approach has several advantages over existing TCR-T cell technologies currently in development. Firstly, it can be applied to all patients, and by being a personalized approach it benefits from a much better safety profile than 'off the shelf' TCRs that may exhibit off-target toxicities.

In their R&D pipeline, Tcelltech will address the challenges associated with the personalized approach. The manufacturing and clinical implementation of individualized TCR-T cells requires a safe and cost-effective vector system to equip patient T cells with their tumor-killing TCRs. The currently approved lentiviral vectors used to engineer CAR T cells integrate randomly into the genome of T cells and have been shown to transform such CAR T cells into tumors in several instances. To circumvent the limitations of these viral vector systems, the Tcelltech founding team has developed non-integrating *nS/MAR vectors* as

the next generation of genetic modification vectors. These *nS/MAR vectors* are easy to manufacture and can be used for safe, efficient and persistent genetic engineering not only of T cells, but also stem cells – in part due to their ability to carry much larger therapeutic cargos. The main advantage of nS/MAR vectors over existing clinically approved vector systems is that nS/MAR vectors do not integrate into the genome to ensure persistent genetic modification of cells, which provides a safety feature to this technology.

By combining two powerful technologies – selecTCR and nS/MAR vectors – Tcelltech is in the unique position to manufacture a safe, specific and highly active TCR T cell product – UNIPACT – within six weeks from surgery, thus making this personalized cell therapy clinically feasible, even for patients with advanced cancer. In comparison to treatment with nonspecifically expanded tumor-infiltrating T lymphocytes (TILs), which have recently been approved for the treatment of melanoma, UNIPACT features enhanced tumor-specificity in that it only uses the relevant cancer-killing TCRs. Low production costs of DNA vectors and new technologies allowing for cell therapy manufacturing in an entirely closed system predict UNIPACT to be economically viable despite the personalized approach.

Opportunities

Tcelltech is currently seeking seed financing to develop a pre-IND briefing package for UNIPACT to be submitted to the regulatory authorities. At the same time, Tcelltech is open for academic and industry cooperations to employ the nS/MAR vector platforms for alternative use such as manufacturing of CAR T cells or NK cells.

www.tcelltech.eu

The enduring challenge of interpreting extensive scientific data sets: How can AI-driven solutions assist?

A common challenge for pharmaceutical and biotech companies when planning and executing on drug discovery and clinical development programs lies in effectively interpreting the extensive scientific information available to R&D and early commercial teams. This wealth of data, which includes literature, databases and experimental results, forms the cornerstone of efforts to improve our understanding of disease mechanisms of action, and optimize drug candidates for better efficacy and safety and eventually commercial returns. However, the task of meaningfully interpreting this vast array of qualitative and quantitative information presents a threefold challenge.

First, the sheer volume and complexity of data and information demand dedicated and specialized professionals, who should not only have a deep understanding of biological and chemical processes but need to be savvy data scientists as well. Moreover, given the amount of data, well-trained talent is needed for meticulous analysis, ensuring the generation of actionable insights (e.g., how can a target be made more druggable? How can the chemistry of a drug candidate be improved to limit side effects?). Additionally, advancements in computational tools and machine learning algorithms have enabled more efficient data processing and analysis, offering opportunities for enhanced insights and decision-making in drug discovery.

Second, given the rapidly evolving nature of scientific knowledge, it has become increasingly difficult for R&D and early commercial teams to stay up to date with the latest advancements, which is a critical aspect for driving innovation.The quantity and complexity of scientific information have gone from being a valuable resource to being perceived as a burden. As an example, the amount of information available for targets in lung cancer has increased by 50% in the last two four-year periods (i.e., ~4.5k publications between 2020 and 2023 vs. ~3.0k publications between 2016 and 2019).

Last, but not least, data fragmentation and data siloing pose a limitation for the use of AI-based tools. In fact, inadequate data sets (i.e., lack of consistency) can lead to unreliable output, hence limiting the full potential of AI-driven solutions for drug discovery and development. Hence, the need for solutions that enable data harmonization and data protection is, more than ever, on the rise.

These challenges present themselves at all stages of the drug discovery and development process as well as early commercial planning, from the identification of novel targets to the optimization of drug candidates and design of clinical programs that lead to differentiated launches with sizeable returns. While large pharmaceutical companies may have the resources to invest in addressing these challenges, smaller biotech firms, especially in their earlier stages, often face constraints on human and financial resources. Consequently, careful resource allocation has always been an imperative for biotech companies to navigate these obstacles and drive progress in drug discovery and development effectively, and ultimately avoid failure.

Despite these challenges, efficient resource allocation and the integration of advanced technologies such as AI hold promise for driving progress in drug discovery and development. In particular, large language models (LLMs) are being explored thanks to their potential for scientific synthesis and inference, augmenting conventional machine learning systems.

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Accelerating scientific insights by reinventing data-driven research

Richard Schlegel, PhD
Co-founder & Head of Commercial, Reliant AI, Inc.

Decision-making across early commercial and R&D in biotech and pharma depends on huge, ever-expanding, highly specialized data sets, requiring expertise to interpret, synthesize and derive actionable insights from.

Today, much of experts' effort is consumed by mental menial labor: identifying suitable data sources; scanning long documents to find the right facts; and organizing their findings. At Reliant AI, our mission is to massively accelerate the tedious, time-consuming analysis of highly complex scientific information: using cutting-edge machine learning, we can accelerate analysis 100x, enabling experts to focus their attention where it really counts.

Most generative artificial intelligence (GenAI) systems today fail in such complex technical areas – they are trained for a broad understanding of human language and search over data to provide the most likely answers rather than exhaustively return all relevant data. Our solution, Reliant Tabular, is different. It starts with a language data agent specifically trained for the life sciences. Using a broad set of publicly available biomedical R&D and commercially relevant data sources including scientific articles, publications, regulatory and health technology outcomes documents, we train our system to answer scientific and business-relevant questions about these datasets. The result is a model that understands what users in biotech and pharma are looking for, and the language this information is encoded in.

With Reliant, a clinical researcher can have answers within minutes instead of hours. Answering a basic query such as "Which clinical trials include a specific subset of patients?" requires hours of reading detailed descriptions of a large number of clinical trials. Reliant AI is able to read through these trials, digest the information and extract the answer within minutes.

But a strong language model alone is not enough for real work applications. A trusted human scientist or analyst reports their findings along with cited sources and explanations of their reasoning – enabling colleagues to interrogate and verify the data. Proper analytical software should do the same. For every fact and insight it generates, Reliant Tabular maintains data lineage – providing a direct link between each statement and its underlying sources.

Finally, we've developed an application tailored specifically to the actual workflows of life sciences expert users – how they get data into and out of a research project. For many tasks, a lot of the work is simply finding relevant data sources to begin with – that is why Reliant Tabular is directly integrated with the most important databases for pharma. Tabular is being plugged into the largest trials databases, publication repositories, national HTA databases, subscription commercial platforms and more.

Human experts have rich contextual knowledge of problems and a capacity for judgment that AI should not try to replace. However, burdened with the volume and complexity of data, it has become increasingly difficult for scientists and analysts to juggle the workload of the critical aspects of problem solving with the laborious part – until now, they have been the only ones equipped to do both! In the next few years, we will see AI help to share this load. By cutting through the overload of information, AI can turbocharge our ability to execute the difference-making work in medicine.

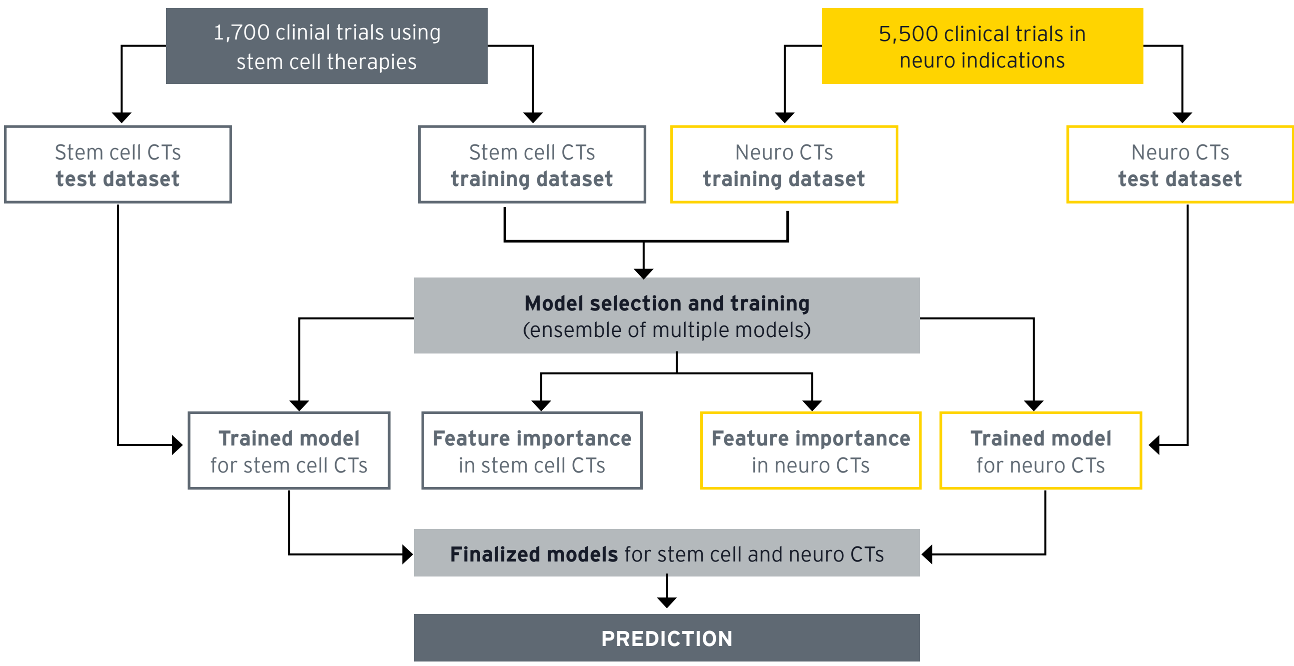
www.reliant.ai

Unleashing the power of AI in clinical trials: revolution through machine learning and deep learning analytics

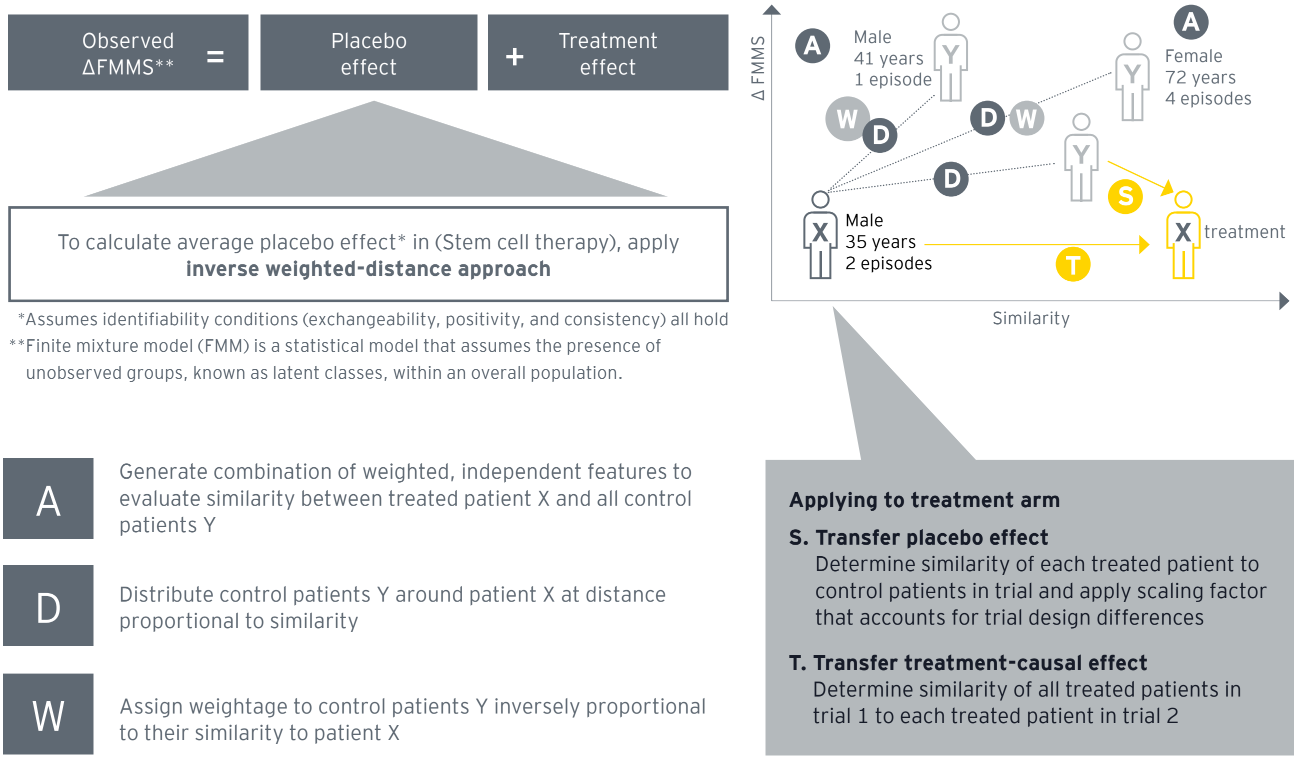
The evolution of artificial intelligence (AI) is steadily transforming the life sciences industry and holds significant potential for streamlining processes in the field of clinical trials that were once lengthy, tedious and costly. AI has quickly become essential in revolutionizing clinical trial methodologies, impacting protocols, patient selection, trial site identification, regulatory compliance, retention strategies, documentation management, and adverse event monitoring. Its integration aims to expedite trial timelines, improve operational efficiency, and enhance regulatory compliance, ultimately delivering cost-effective and patient-focused health care solutions. With patient recruitment costs averaging $1.2 billion and trials lasting six to seven years, AI offers valuable tools and insights to address these significant challenges.

Our partner Innoplexus, a clinical AI company, has AI technology that crawls through as many as 10 billion web pages a day to aggregate disparate public data from scientific publications, historical clinical trial designs as well as chemical and molecular databases. This technology builds and updates a giant knowledge graph of relationships between data, using natural language processing and algorithms trained on high-quality medically annotated training data. Using the

Training data set



Modeling scenarios across two clinical cohorts



features extracted from the data, the models simulate millions of scenarios to determine the probabilities for the outcome of ongoing clinical trials. Furthermore, the clinical trial prediction (CTP) model evaluates the most significant features responsible for the predicted outcome: whether it is a drug's biological and physiological mode of action or other parameters, such as trial design, investigators, sites, etc., which can be used to optimize the current and future trials.

Case study

Problem statement: Innoplexus' CTP model was applied to advise an Australian biotech to understand the factors driving the incongruent results of modified stem cell therapy for a neurological indication in three Phase 1/2 trials, which was expected to perform consistently across all three similarly designed trials.

Approach: Two AI models were developed to simulate biology-agnostic trial results and isolate optimal trial features for a successful clinical trial:

- Model 1 was trained specifically on past clinical trials with stem cell therapies.
- Model 2 was trained on neurological clinical trials, with greater weight on trials related to the indication of interest.

Machine-learning algorithms were deployed over clinical cohorts and natural history databases from the National Registry to identify patterns and relationships in vast patient-level data sets that would be easily overlooked manually. This approach enabled identification and removal of confounding effects by creating a "pseudo-population" in which treatment was assessed as an independent measured confounder.

Outcome: A decision/classification tree-based patient binning was provided based on characteristics that could be predictive of high response to treatment in Indication 1 (Trial 1) vs. Indication 2 (Trial 2). These findings were biologically validated using gene expression data from NCBI's GEO database, a public functional genomics data repository, for Indications 1 and 2. Differences in regulated genes associated with inflammation and immune response, such as expression of complement factor H in Indication 1, were found to be significantly associated with response to treatment. These biomarkers were nominated to be added to the pre-screening of patients at trial entry for both indications.

Client story: Global healthcare company
Sponsor of the project: Head of Global Development Unit for Immunology, Hepatology, and Dermatology and Head of Global Drug Development.

Problem statement: The client was looking to identify potential scenarios to optimize clinical trial patient stratification and create labels based on the genomic marker for clinical symptoms and biomarker data, using publicly available multi-omics data.

AI value-adds: In working with our partner Innoplexus, the client was able to leverage AI to pool and normalize all the publicly available patient-level multi-omics data for autoimmune and inflammatory indications. Within two months, high-confidence disease severity biomarkers across ankylosing spondylitis, psoriasis and psoriatic arthritis were delivered, from control, pre-treated and post-treatment cohorts of patients, generated via whole genome and transcriptomic analysis.

Outcome: The client was able to refine grouping using sub-indications and severity, based on expression biomarkers and select patient "endotypes," that shared clinical and/or molecular characteristics to define the trial cohort for their ongoing Phase 2 trial in psoriasis.

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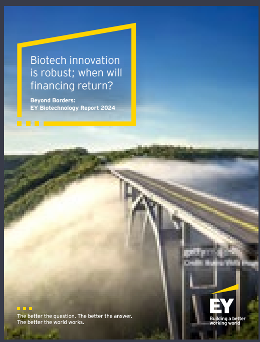
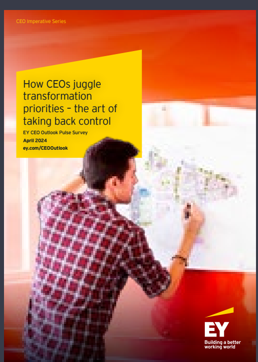


EY Beyond Borders Biotechnology Report 2024
Biotech innovation is robust; when will financing return?

EY Autoimmune Index 2024
How to assess new innovations in the continuously changing landscape of autoimmune diseases?

EY M&A Firepower Report 2024
Life sciences companies are returning to dealmaking amid cost and revenue pressures – how will they find the right deals to secure value?



EY CEO Outlook Pulse Survey 2024
How do CEOs navigate between immediate profits and future sustainability aspirations?

Council of German BioRegions as an enabler for merging AI and biotechnology

Dr. Jens Hellwage
Managing director, InfectoGnostic Research Campus Jena

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Large data sets, complex problems and interdisciplinary R&D approaches – biotechnology shows tremendous potential to benefit from artificial intelligence (AI). This technological convergence promises to have transformative effects on medicine, industry and everyday applications. As the central network of regional biotech clusters in Germany, AK-BioRegio – the Council of German BioRegions – plays a crucial role in merging both cutting-edge research areas.

Founded in 2004, AK-BioRegio promotes meta-networking of 25 bioregions by facilitating national and international partnerships and projects, sharing best practices and reducing innovation barriers. As reliable trend radars, the member regions are at the forefront for identifying AI-based solutions to biotechnological challenges and to foster the required ecosystem to facilitate implementation: Bioregions across Germany have already implemented AI-driven approaches into their R&D landscape.

Berlin Partner offers a wide portfolio of initiatives and startups excelling in AI-driven health care solutions. With its mix of scientific institutes, biotech, health tech and IT companies as well as medical institutions, the Berlin-Brandenburg metropolitan region is a hotspot for computational biology and medical informatics. As a prominent example, Ada Health has been pioneering AI-powered symptom-checking since 2011: Starting off originally as a clinical decision support tool for doctors, they later refocused on supporting patients who might be experiencing new health problems. Their app-based AI solution is assessing symptoms and medical urgency, to then, in turn, suggest possible causes that could initiate further examination by medical professionals. This simple and streamlined tool has garnered global acclaim and shows promising results – especially for rare diseases that might get overlooked. Other initiatives set standards for AI adoption in universal health care, like TEF-Health, a large-scale EU funded project led by the Charité – Universitätsmedizin Berlin that aims for standardizing certification and quality control to facilitate market access for trustworthy AI.

In Lower Saxony's BioRegioN, the Lower Saxony Research Center for Artificial Intelligence and Causal Methods in Medicine (CAIMed) has established a unique platform connecting scientists from the fields of computer science and medicine. The center focuses on linking research, clinical and patient care data, as well as using AI and causal methods. CAIMed strives for deeper understanding of the relationship between the cause and effect of diseases like cancer, cardiovascular diseases and infections, thus paving the way for better prevention, diagnosis and therapy. Well-known companies are also making use of AI as a key technology, such as Sartorius AG, which launched the Sartorius AI Lab (SAIL) together with the German Research Center for Artificial Intelligence (DFKI). The goal is to explore AI in platform solutions for the biopharmaceutical industry. At PharmaInformatic Boomgaarden, on the other hand, the use of AI both enables the targeted development of effective drugs and systems for bioavailability assessment that have the potential to replace animal testing in the future.

Thuringia's InfectoGnostics Research Campus Jena is drawing great benefits from cutting-edge AI-driven solutions to improve infection diagnostics and imaging. Notably, the AI startup "Nanozoo" is pioneering bio-informatics approaches to automate data-intensive biology from sample to report while leveraging AI algorithms to improve, for example, accuracy, efficiency and speed for outbreak tracing of infectious diseases.

Other approaches for AI application are pursued by the Leibniz Institute of Photonic Technologies (Leibniz-IPHT): The Leibniz researchers are harnessing AI to refine biophotonics techniques, that enable rapid bacteria detection and antibiotic resistance profiling. Also, collaborative endeavours with the University Hospital Jena have yielded breakthroughs in tumor border delineation through combining multimodal imaging techniques and machine learning, offering new avenues in precision medicine. InfectoGnostics is also one of the leading partners in the BMBF-funded consortium AVATAR for anonymization of personal health data through the creation of digital avatars in medicine and care. Additionally, Thuringia is funding initiatives like the Thuringian Centre for Learning Systems and Robotics (TZLR) that is enabling projects for application and transfer of AI methods into (health care) practice.

Represented by BioRN, the Rhine-Neckar bioregion has made significant strides in AI-assisted image analysis, especially for cancer diagnostics. For example, the DKFZ (German Center for Cancer Research) in Heidelberg has developed an AI assistance system that can diagnose black skin cancer more accurately on digital images than experienced dermatologists. The system can substantiate the diagnosis by naming and describing the relevant structural features of the skin change in technical language and drawing them into the images. With a focus on basic research and academia, the AI Health Innovation Cluster (AIH) is bringing together renowned research institutions in the Heidelberg-Mannheim region. To date, 52 research projects have been funded, tackling diverse medical domains ranging from cancer research to neuroscience and back surgery, fighting sepsis and long COVID-19, and understanding the health-economic impact of heatwaves. Heidelberg has also established itself as an important location both for start-ups and companies with AI technologies: Aleph Alpha is a major European competitor with its "Luminous" language model. Decision support companies such as Paretos, image synthesizers such as RabbitAI and training data optimizers such as Quality Match have also been able to convince investors and customers alike. In addition, established companies such as NEC Laboratories Europe (deeply involved in AI research, particularly in the field of biomedical applications) or business intelligence company SAS operate out of Heidelberg.

Saxony is experiencing rapid growth in AI research and startup creation. Since 2014, the Centre for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI) with locations in Dresden and Leipzig and the "Meiler-Lab" at Leipzig University, have been important drivers of this development. The aim of the Meiler Lab, which focuses on computer-aided drug research and methods for determining the structure of membrane proteins, is to improve the treatment of viral infections, cancer and neurodegenerative diseases. Biosaxony, the bio-region for Saxony, also founded the startup accelerator "MEDICAL FORGE" in 2022, which has already attracted companies such as Modality.AI, diafyt and Saventic. Modality.AI has developed an AI system for assessing neurological and psychiatric conditions, diafyt combines sensor technology and AI to improve the management of metabolic diseases such as diabetes. Another example is Saventic, which is working on AI-controlled diagnosis of rare (hidden) diseases. Other examples of biosaxony actively supporting AI-driven entrepreneurship and research are the Dresden-based companies Katana Labs (AI-supported software solutions for image-based cancer diagnostics) and Altavo (voice prosthetics using non-invasive radar sensor technology and AI for improvement).

In Bavaria, particularly at BioPark Regensburg, the Artificial Intelligence Regensburg (AIR) Initiative exemplifies cross-industry collaboration. Certified according to the European Cluster Excellence Initiative, the AIR Initiative aims to promote the integration of AI across industries and capitalizes on synergies within the region. One of the primary objectives of the AIR Initiative is the development of a robust platform for knowledge and technology transfer among local innovation clusters. Through this initiative, the regional community within the health care industry has witnessed enhanced networking opportunities, allowing for the pooling of activities, skills, and events. Notably, the project received funding from go-cluster (goAIR), enabling the piloting of a LoftOS-based platform as a white-label solution with approximately 50 participants in the AIR community. This collaborative endeavor has facilitated the exchange of expertise and fostered innovation, driving forward-thinking initiatives in health care and beyond.

Looking forward, the fusion of AI and biotechnology will continue to bear enormous potential not only in revolutionizing R&D, but also in enhancing diagnostics, improving the efficiency of healthcare delivery and opening new pathways for personalized medicine. With a strong focus on cross-industry collaboration and ecosystem building, the German bioregions will continue to play a central role in shaping the landscape of AI-driven biotechnological advancements.

www.infectognostics.de

Exploring funding opportunities for AI innovation in biotech

Germany's R&D incentives structure stands securely on dual foundations: non-repayable cash grants, provided through various programs via a competitive application process, and an R&D tax credit. The primary focus areas within the German funding landscape extend beyond the all-encompassing R&D tax credit, aiming toward sustainability, energy transformation and decarbonization. Funding opportunities are particularly high for first movers and, thus, innovative projects.

Interested parties looking for national funding specifically related to artificial intelligence (AI) within the biotech sector should not shy away from taking a closer look at potential funding opportunities for adjacent disciplines such as health care and digital research, as well as large funding programs on the EU level and analyze them with regard to a possible fit (even if the fit may not be apparent at first glance). It is advisable to keep a constant eye on the funding landscape as calls are often not only very topic-specific but also short-termed and there might not always be a suitable call open.

- **Health research**
  While the segment remains one of Germany's largest funding landscapes endowed with almost a billion euros annually and covering diverse topics from research to medical technology and digital technologies for health and care, AI is not a focus topic yet.

- **Digital research**
  National funding is strongly focused on research in the field of quantum computers, IT security and microelectronics, among others.

- **EU level**
  Interested parties may locate suitable calls within the expansive framework of the Horizon Europe program and Digital Europe. However, many of these calls come with very specific requirements (e.g., with regard to partnering or content) and require a good preparation to ensure successful applications.

- **National level**
  Regional funding programs as well as the German R&D tax credit, which allows for open-topic funding for research and development, programs. The R&D tax credit has a funding rate of 25% for eligible costs limited to a maximal funding of 1 million EUR per company group per year. Its appeal arises from the fact that it is possible to submit an application retrospectively (even for projects that have already been completed) and that an increase in the maximum funding may be expected shortly (currently in the political decision-making process). Companies interested in applying retroactively for the R&D tax credit for projects initiated in 2020 should expedite their applications, as the first deadlines will expire at the end of 2024. Companies should anticipate enough lead time to not only meet the two-stage application process (an application for a certificate must first be submitted before an application can be submitted to the tax office) but also possible delays (e.g., inquiries by the certifying authority in the application process).

Even if it may initially seem difficult to find the right funding, it's worth staying tuned. We encourage companies to approach the search for funding very proactively, define possible strategic funding topics early, and precisely examine the framework conditions and requirements of the selected call before starting an application.

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Are we ready for the AI revolution? Navigating ethics, innovation and trust in biotechnology

In the ever-accelerating realm of artificial intelligence (AI), the biotechnology sector faces new frontiers that demand careful navigation. The implications of AI in these areas are far-reaching, shaping the future of health care, drug discovery, patient outcomes, and ethics in profoundly significant ways. It is the dawn of a new era when AI governance and risk management with a focus on responsibility, ethical integrity, and compliance are quickly emerging as critical components to ensure responsible stewardship of these powerful technologies.

AI governance in biotechnology must rise to the challenge of balancing innovation with accountability. The development and implementation of AI systems carry a unique set of considerations in these fields, where decision-making can have direct consequences for human health and wellbeing. In such a context, establishing trust through responsible practices is paramount. Organizations must adopt approaches that prioritize ethical integrity, ensuring that AI systems' design, deployment and operation meet the highest standards of transparency, fairness and respect for human rights.

Crucial to this approach is risk management, which in the context of biotechnology goes beyond conventional business considerations to address the profound ethical and societal impact of AI. The rapid pace of AI development means that risks can evolve just as swiftly. A forward-thinking risk management strategy must include ongoing assessment and reevaluation to keep up with the changing landscape and to safeguard against new vulnerabilities.

While biotechnology companies are eager to harness the transformative power of AI, they must also prepare for a regulatory environment in flux. AI-related regulations are being drafted and debated around the globe, with a clear trend toward a risk-based approach to AI regulation. This implies that the complexity of compliance efforts ought to be proportional to the potential risks posed by the AI systems in use, with heightened scrutiny likely to be applied to high-risk applications. Companies would do well to engage with these developments proactively, establishing a culture of compliance that can adapt as regulations evolve.

Given the transformative potential of AI in biotechnology, it is incumbent upon organizations to embrace an overarching, cross-functional approach to governance. Such an approach must seamlessly intertwine ethical considerations into the fabric of organizational processes, fostering an enduring sense of trust among stakeholders while simultaneously navigating the intricacies of the developing regulatory framework.

We invite industry leaders and stakeholders from the biotechnology sector to join us in a commitment to responsible AI governance. Let us pave the way for innovation that is both transformative and trustworthy, ensuring that the advancements we make today will benefit society safely and ethically tomorrow.

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Redefining life sciences transactions: How will AI shape the future of deal-making?

Advances in technology are also expected to influence how transactions like acquisitions, carve-outs, licensing deals and further strategic partnerships and alliances will be executed in the future. As artificial intelligence (AI) and its applications advance, companies looking both to acquire/in-license or to sell/out-license assets can benefit from leveraging AI. It will allow them to, for example, accelerate the speed at which targets are identified, partnerships are assessed, and their potential is evaluated. AI has the potential to accelerate deal-making by allowing pharmaceutical and biotechnology companies as well as investors to identify opportunities and make decisions faster.

AI's strength in assisting during the transaction process is rooted in its ability to rapidly sift through and structure vast volumes of data such as scientific literature, patents, clinical trial registries, market intelligence data, financial information on potential assets or partners. This data not only lays the foundation for investment decisions but also contributes significantly to managing the complexity of transaction processes overall.

Examples of potential AI use cases

- **Asset and partner screening**
  Leveraging AI to analyze large volumes of data faster will enable life science companies to identify and analyze relevant assets and suitable partners more efficiently.

- **Due diligence**
  Through its capacity to analyze vast amounts of unstructured data, AI will speed up the data-driven assessments of potential assets and partners. AI-driven predictive models also have the potential to be leveraged to forecast market trends and dynamics, significantly speeding up market attractiveness assessments.

- **Financial modeling and valuation**
  AI can enable the automated collection, structuring and integration of financial data from various sources. Additional AI-empowered applications in this context include the creation of valuation models and the performance of predictive and scenario analyses, to provide decision-makers relevant insights and assessments of risks, facilitating informed decision-making and more effective negotiations.

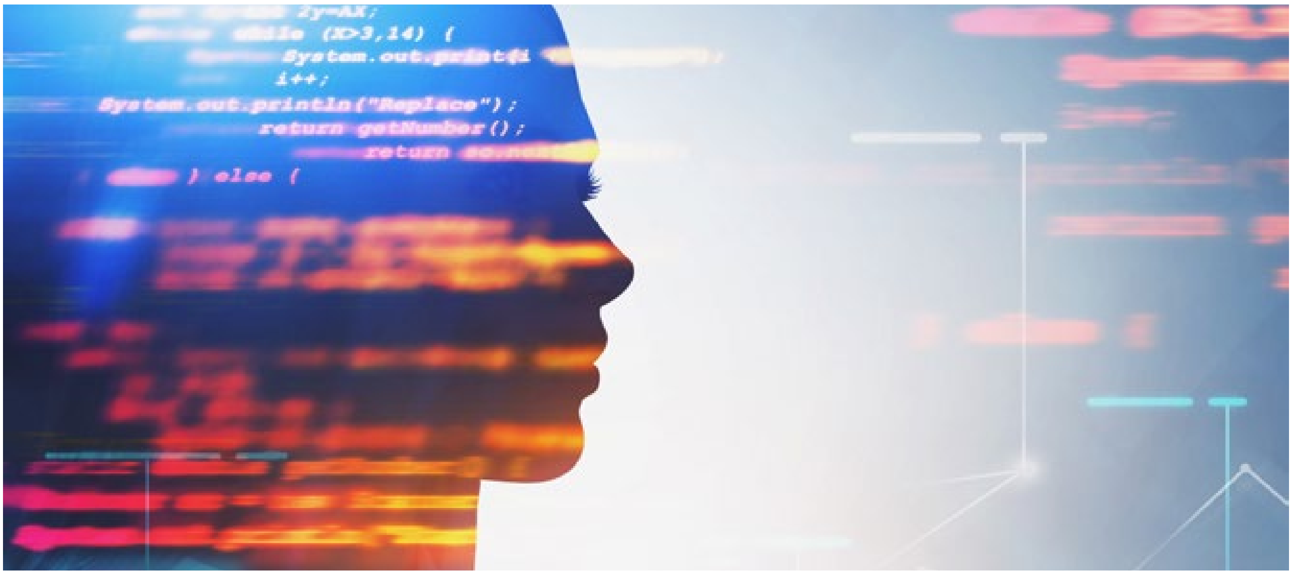
There is no doubt that AI has the potential to increase the speed of deal-making in the future. Nevertheless, for a successful application it should be utilized as part of a structured transaction process, executed by experts on the life sciences industry as well as on strategy and transactions, to maximize success.

Here are our top five key imperatives to guide dealmakers in crafting and executing an effective transaction strategy powered by AI:

1. Value leadership
Adopt a comprehensive strategy that integrates AI throughout the entire transactions cycle to maximize efficiency .

2. Talent cultivation and workflow innovation
Foster knowledge to develop teams with a strong understanding of AI capabilities and limitations. Redefine transactions workflows with AI, investing in training to seamlessly integrate technology with human expertise.

3. Secure Infrastructure
Create a robust technological framework capable of integrating AI tools, ensuring data compatibility and system scalability. Implement robust security and consistently review metrics to maintain a digital core that's both advanced and secure.



4. Ethical AI commitment
Establish ethical guidelines and compliance standards for AI utilization to maintain integrity throughout the transactions cycle.

5. Ongoing strategy evolution
Develop a flexible transactions strategy that can adapt with the evolving landscape of generative AI and beyond.

Artificial intelligence at EY

EY is developing several tools, skills, and capabilities to achieve more business efficiency through GenAI. This also allows to maximize deal-making efficiency for clients in the life sciences space and beyond.

For example, within the platform EYQ M&A Document Accelerator, EY has developed available products, including:

- **The EYQ Document Chat,** an AI-driven chatbot equipped with document intelligence, which efficiently extracts insights from various document formats and enriches them with real-time information sourced from the internet.

- **The EYQ Document Batch Analyzer,** a smart assistant for large-scale document analyses, providing quick and clear answers to pre-defined question sets.

In M&A operations, integrating AI technologies like the EYQ Document Chat and the EYQ Document Batch Analyzer yields many advantages.

The EYQ Document Chat supports users in summarizing documents, improving writing styles, drafting content for reports or presentations, or translating them to different languages. These functions are especially useful in M&A tasks such as proposing questions on financial trends, generating report-ready narratives, analyzing content, facilitating tasks like separation planning, and creating deliverables.

The EYQ Document Batch Analyzer offers an efficient alternative to traditional methods, providing transparent insights into extensive documents like contracts, supplier offers, and company/annual reports. This tool can be particularly advantageous for M&A activities, aiding in identifying pertinent M&A answers to questions from contracts, analyzing contract details like involved parties and clauses, and assisting in financial statement analyses.

The future will show how the journey will continue, allowing the further identification and evolvement of areas in which AI can be leveraged. EY is committed to continue developing AI solutions to support clients in their future endeavors, enabling more efficient business solutions, transactions, and transformations.

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Investor's insight into AI in biotech: faster analytics and lower costs drive grow

Dr. Hubert Birner
Managing Partner, TVM Capital Life Science

Artificial intelligence (AI) is increasingly used throughout the life science and biopharmaceutical industry today. Large amounts of high-quality data processing are required for everything from drug discovery to target identification and drug safety, as well as functional to structural genomics. AI technologies have become highly valuable to pharma product development.

A key prerequisite for AI to support advances in the biotechnology sector is the digital transformation of the workplace and the full integration of AI technologies into traditional research and development processes. While the integration of AI into European startups is emerging somewhat slower than in the US – this is partially driven by access to corporate funding and the earlier nature of AI-driven startups – there is not necessarily a difference in the makeup of AI companies from Germany vs. the US. Life science innovation is a global business and access to global data is required or at least beneficial to educate and develop AI.

However, AI alone is not a magic silver bullet and research progress is not solely dependent on AI. Innovative startups need people with core expertise in the areas where AI is used and it is vital to recognize that AI serves as an enabler rather than an independent value driver. For example, capability building by research scientists is critical, as they are the ones who can harness the power of AI effectively, by integrating it with their human expertise. For this reason, TVM Capital Life Science invests in companies where AI serves the core product development. ROI expectations remain the same as, but AI offers the advantage of accelerating growth and reducing time to significant data, all while decreasing costs.

Transforming medical biotechnology
AI has come a long way, but it still has limitations, primarily around context and data quality. It cannot interpret the context of data and is not (yet) capable of understanding the meaning behind data or of providing explanations beyond the raw data patterns. Poor data quality affects the performance, accuracy and reliability of AI models. These limitations cut across scientific disciplines and require developing foundational algorithmic approaches that can contribute to scientific understanding or acquire it autonomously, making them critical areas of focus for AI innovation.

However, the use of AI and machine learning in the following processes is exciting and can lead to significant growth opportunities:

Drug target identification
AI is used to generate data from various sources (genomics, metabolomics, proteomics, etc.) to help identify new targets for the treatment of disease.

Drug screening
AI can be widely used to analyze data on the potential activity of certain drugs and to select those that are more likely to be effective.

Image screening and interpretation
AI has an enormous potential to analyze medical images (radiographs, CT scans, MRI images) and to significantly improve reporting based on digital images.

Predictive modeling
AI can be used to analyze electronic health records, to make predictions about an individual's health and to predict the likelihood of developing certain diseases. One significantly growing area of interest is the diagnosis of cancer at an early stage. AI and machine learning can provide enormous benefits to doctors by assisting the analyses of routine health records, medical images and slides, biopsies and blood tests to improve risk stratification. Oncological diseases like breast cancer and cervical cancer have reasonable cure rates when detected early and treated accordingly. AI-based systems significantly help diagnose cancer more accurately and avoid case errors.

Success stories
Companies in the space of AI-driven biotechnology are increasing in number and generating higher levels of funding. The number of AI-driven companies in drug discovery and development increased from 62 in 2011 to 400 firms in early 2023.[1] The common industry view is that the application of AI in large molecule drug discovery is increasing rapidly – especially in predicting large-molecule functions and large molecule candidates. Established biopharma companies are also investing in building AI capabilities both internally and through acquisitions or partnering and continue to build up relevant infrastructure.

Among the many interesting AI companies, we would like to point out a few examples:

In drug discovery, UK-based Exscientia, founded in 2012, was one of the first companies to apply AI technology. It was the first company to automate drug design and the first to have an AI-designed molecule enter clinical trials. In 2021, the company closed an upsized IPO of $510.4 million on Nasdaq.

Genesis Therapeutics is likely one of the most visible US startups in AI-supported drug discovery at the moment. Founded in 2019, it uses a proprietary generative and predictive AI platform called GEMS (Genesis Exploration of Molecular Space), to accelerate and optimize small molecule drug discovery. Genesis closed a $200 million series B round in 2021 and closed a deal with Lilly for a potential total value of $670 million.

At TVM, we recently co-led a $16 million series A funding with Solas BioVentures for Vektor Medical, a pioneer in non-invasive, AI-based arrhythmia analysis technology. The funding will support commercialization of vMap, Vektor's AI-based arrhythmia analysis tool, created to improve cardiac ablation outcomes, optimize workflows and increase procedural efficiency. This technology is transforming how EPs approach ablation procedures.

Munich-based Smart Reporting, founded in 2014, is harnessing the value of medical data for better image screening and interpretation. It provides AI-assisted radiology and pathology reporting software for structured diagnostics and is used by more than 16,000 physicians in over 90 countries. In November 2023, it announced a broad collaboration with 3M Health Information to expand into international markets. Overall, data processing especially in the pathology field will also contribute to more efficient drug discovery in the future.

And last but not least, any review of the successful use of AI in biotech companies would be remiss without the mention of BioNTech, a true German AI pioneer. Its AI is designed to recognize individual tumor cell mutations and form the basis of cancer vaccines precisely targeted for this purpose. In October 2023, the company treated the first patient in a Phase 2 cancer vaccine trial.

The outlook
AI and machine learning will continue to drive innovation in biotechnology. As this process advances, we must remember these technologies offer not only advantages and promising benefits, but also bring up ethical risks and perils. An ethically mindful and balanced approach is essential.

One key aspect in the ethical use of AI in biotechnology is the traceability of input and output. It is essential for building trustworthy AI systems. AI can only be used responsibly and lead to widely acceptable data analyses if that transparency is provided.

From an investor perspective, "AI enhanced search engines" and "AI supported match making" are helping VCs today to get a comprehensive list of potential investment targets onto their radar screen more efficiently.

We use AI at TVM for due diligence, writing investment memos and database research. Just as we view these tools as sustentative to core product development in the companies we fund, we will never allow an AI platform to take over investment decisions. We will view AI as a very important supportive tool for our investment process.

We are open for cold pitches from startup companies: Please email them to info@tvm-capital.com.

1 Nature Reviews Drug Discovery, December 2023, 949-950.

> German biotech innovation is strong, although it lacks access to liquid capital markets. Whilst investors increasingly focus on companies in the later stages of development, young biotech companies must demonstrate solid fundamentals, a strong management team, and good science to succeed in securing financial resources.

Nicole Damani
EY Strategy & Transactions, EMEIA Life Sciences Leader

German biotech industry in numbers

In 2023, shaped by international and national conflicts, many of the previous year's macroeconomic challenges persisted or even intensified: faltering economy, accelerated inflation, high interest rates and consequently a reluctant investment sector. Despite its substantial capital needs and high-risk nature, the biotech sector remains a beacon of innovation, offering opportunities for significant returns and solutions to pressing worldwide issues.

This article delves into the German biotech sector's key performance metrics, unveiling several warning signs:

- Industry metrics lagging behind international benchmarks
- Funding drought in early-stage venture-investment
- No IPOs for the second consecutive year

Yet, the German biotech sector continues to demonstrate its resilience and capacity for high-quality innovation, capturing the attention of investors and alliance partners alike:

- Strong growth in number of employees and R&D expenses
- Revenues and market capitalization pointing upward over the long term
- Clinical pipeline growing and maturing
- High-value venture capital rounds supported by international financing consortia
- Innovative companies at the forefront of cutting-edge biotechnology
- Incoming biobucks from alliances on a very high level
- Large-volume M&A deals in the first quarter of 2024

2023: a year of growth
According to most industry key figures, 2023 was a year of expansion for the German biotech sector.

Revenues were the exception, showing a sharp 51% decline to €12.7 billion, primarily due to reduced demand for COVID-19 vaccines. However, compared to the pre-pandemic year 2019, revenues for private and public companies have followed an upward trend, with an 138% increase and an average annual growth rate of 24% (see Databook for details).

While the number of companies inched forward by 3% to 996 (784 companies with headquarters in Germany and 212 German subsidiaries), the workforce grew by a strong 10%, surpassing the 60,000 mark. R&D expenditure climbed by 10% to €4.4 billion – a very positive sign for an industry fundamentally reliant on the strength of its own innovative capabilities.

German biotechnology at a glance

3%	10%	–51%	10%
996 companies	**61,705 employees**	**12.70 €b revenues**	**4.40 €b R&D expenses**

	Private companies			Public companies			Subsidiaries		
	2022	2023	in %	2022	2023	in %	2022	2023	in %
Key figures									
Number of companies	747	763	2	23	21	–9	197	212	8
Number of employees*	26,173	30,984	18	20,162	20,232	0	9,842	10,489	7
Financials (€m)									
Revenues	4,034	4,386	9	20,911	7,014	–66	1,207	1,297	7
R&D expenses	1,010	1,208	20	2,782	2,965	7	211	230	9

**for private companies and subsidiaries in Germany, for public companies worldwide. Source: EY analysis, BIO Deutschland and Capital IQ.*

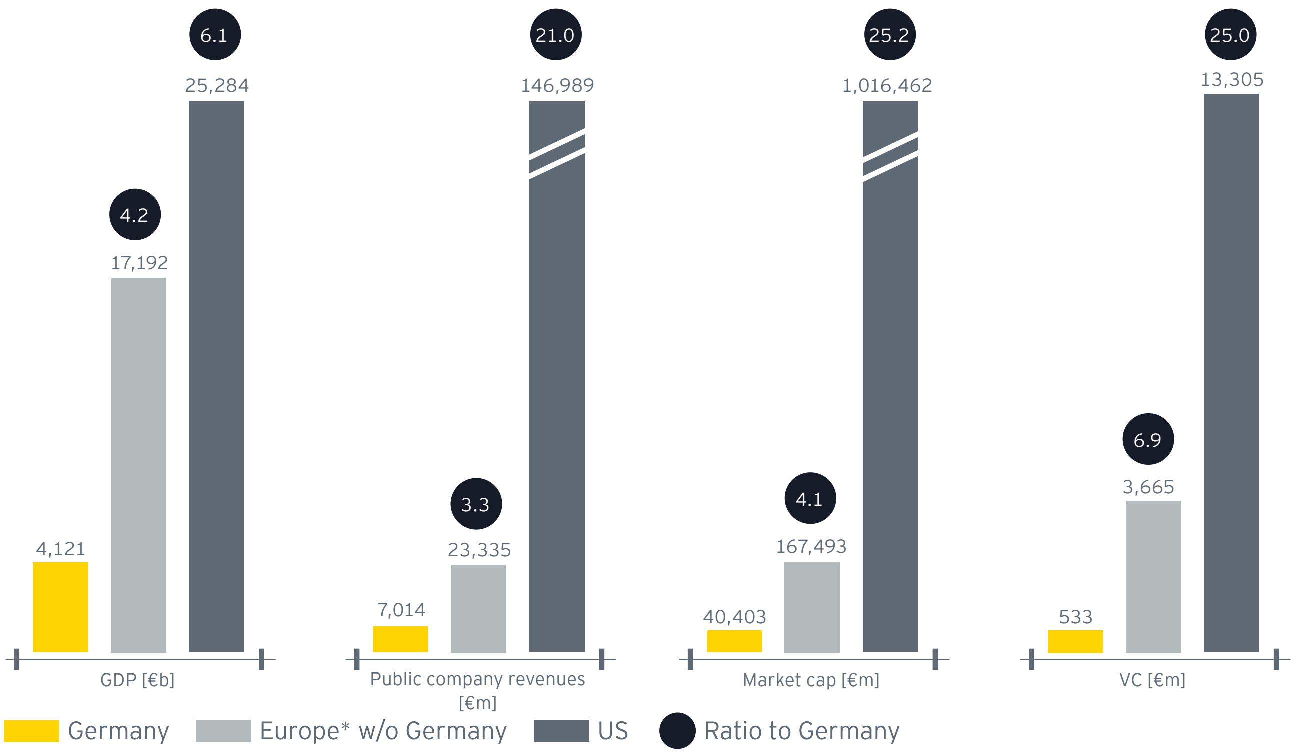
International standing of Germany's biotech industry
When comparing industry metrics of Germany, the rest of Europe and the US, and benchmarking them against the relative economic sizes of the entities, it becomes clear where Germany's biotech industry stands from an international perspective. Drawing on the GDP data for the year 2023, the combined economy of the other European countries is approximately four times the size of Germany's economy, and the US economy is nearly six times larger. A closer look at the biotech sector shows that the international ratios of selected industry metrics deviate from what would be expected based on the relative economic sizes, indicating how Germany's biotech sector is performing in the international comparison.

Within Europe, German public biotech companies perform well as the revenues by public biotech companies from the rest of Europe are only 3.3 times higher than those of their German counterparts, and the market capitalization of these companies is 4.1 times larger. However, VC funding of the private companies, a critical indicator of the health of the biotech innovation ecosystem, reveals a gap, reaching 6.9 times that of Germany – 1.6 times what would be expected based on the relative economic sizes.

In relation to the US, the leading player in biotechnology, the difference from the German biotech industry is blatant, revealing ratios in the double digits throughout all analyzed parameters. VC raised by US biotech firms is 25 times that of the German sector. Underscoring this disparity, VC rounds in Germany in 2023 were significantly smaller with an average of €23 million against €37 million in the US – a 1.6 times difference.

When looking at these ratios over time, it becomes evident that the German biotech sector is making progress in catching up to its bigger brother in the US, as the ratios were significantly higher in 2016 (e.g., market cap: 50x and VC: 49x). However, as the gaps currently remain more than three times what would be expected based on the relative economic sizes, this analysis underscores the need to implement actions to unlock the industry's full potential and boost Germany's competitive position. In the next section, Oliver Schacht, chairman of the German biotech association BIO Deutschland, will discuss the recommendations of various government advisory bodies on the advancement of German biotechnology.

International comparison of biotech sectors in Germany, Europe and the US, 2023



Source: EY analysis, Statista, Capital IQ and Dow Jones VentureSource. **EU-27, UK, Switzerland, Norway, Israel*

Dossiers are silver; action is gold

Oliver Schacht, PhD
President, BIO Deutschland e. V.

At first glance, biotechnology appears to be highly valued by the German government. The Federal Chancellor's "Future Council," bolstered by biotech expert Özlem Türeci, provides strategic insights to guide the administration. In 2023, this Future Council presented the Federal Government with the dossier "Lost in Translation – Approaches to Unleashing the Social and Economic Potential of Biotechnology." The document boasts an analysis of the strengths and weaknesses of German biotechnology and provides the government with detailed actionable recommendations for a strong German biotech location.

Although Olaf Scholz's predecessor, Angela Merkel, did not have her own Future Council, she did maintain an innovation dialog, resulting in a comprehensive document on the topic of the innovation potential of biotechnology in 2017. In the same year, the then-Federal Chancellery Minister Peter Altmaier logically concluded at the Research Summit: "I therefore ask myself whether, in addition to the Digital Agenda, which involves all ministries that have expertise in this area, we do not also need a Biotechnology Agenda that formulates and brings together the challenges in a similar form."

The Future Council is by far not the only advisory body of the German Government. Together with the Commission of Experts for Research and Innovation (with German acronym EFI) and the Forum #FutureStrategy, the Future Council forms the tip of the "advisory triangle" on research and innovation of the Federal Government. The EFI Commission also sees biotechnology as an important key technology. The panel of experts regularly makes recommendations relating to the biotechnology sector. For example, in 2024, the Commission recommended that the German Government should support the revision of the European genetic engineering legislation. A similar topic was already addressed in a 2021 report, where the commercial exploitation of research in the field of genome editing was named a priority. More generally, the EFI has been calling for an improvement of the framework conditions for biotechnology research for years. The Forum #FutureStrategy has replaced the High-Tech Forum of the previous governments and steers the implementation of the "future strategy research and innovation" (2023) that came with a big promise: "through the targeted promotion of biotechnology as a key technology, we will provide new impetus for sustainable value creation in Germany."

All relevant advisory bodies (and some others, such as the Dialogue Platform Industrial Bioeconomy of the Federal Ministry of Economics or the Economic Forum of the Social Democratic Party) have recognized the importance of biotechnology, formulated the strengths and weaknesses of Germany as a location for this key technology, and made recommendations for action. You could say that everything has been said. Yet, implementation leaves a lot to be desired. Many measures are timid and fragmented. Even relatively cost-neutral recommendations concerning regulation and bureaucracy are only implemented slowly or not at all. For instance, simplification of the radiation protection approval for clinical trials is currently being taken up in the federal Medical Research Act, but the recommendation is over a decade old and implementation still underway.

While on paper it has long been recognized that biotechnology is integral to Germany's future competitiveness and technological sovereignty in Europe, the full realization of this potential requires the swift implementation of expert-recommended actions. Now it's time to decisively put words into action.

www.biodeutschland.org

Financing trends in 2023
In 2023, the German biotech industry succeeded in raising around €1.1 billion, a 17% increase over the previous year. Putting aside the exceptional years 2020 and 2021, fueled by the pandemic's impact, and Qiagen's exceptional $500 million financing in 2018, this marks the second-highest overall financing in the industry's history, only surpassed by the biotech boom year 2000.

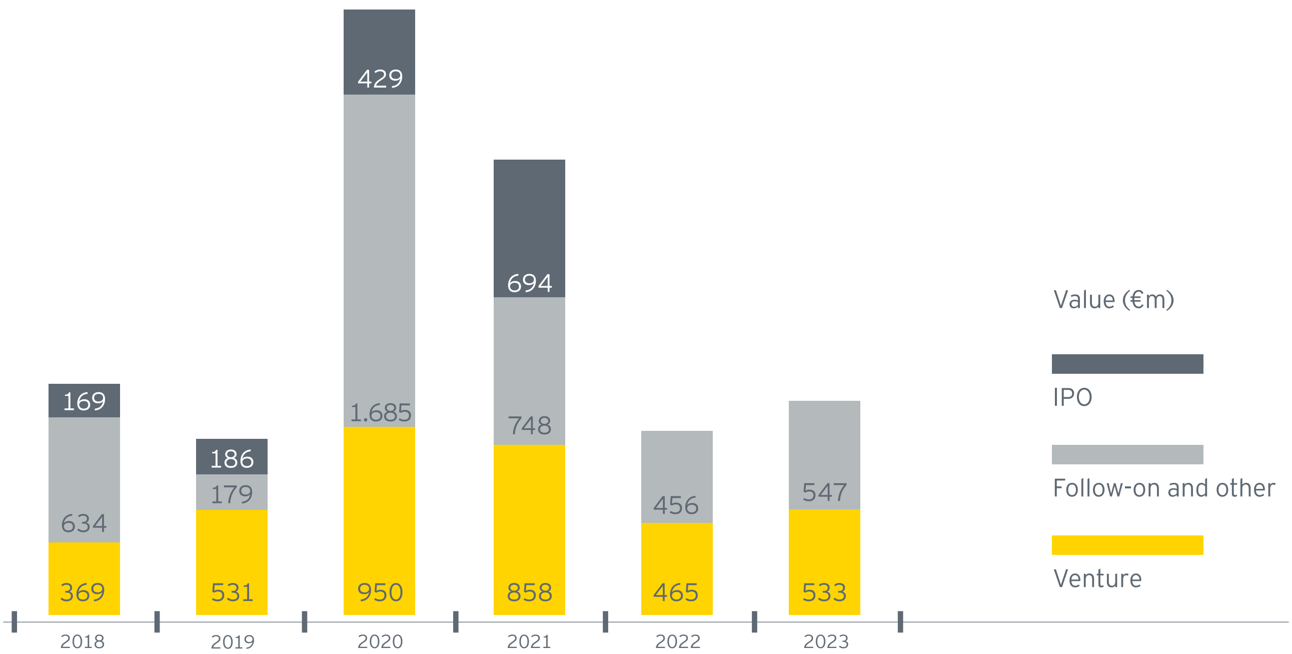
Venture capital on the rise
Venture funding was up 15% in 2023, and the €533 million raised surpassed pre-pandemic levels. Nearly half of this funding went to targeted radiopharmaceuticals specialist ITM, which raised €255 million, marking the biggest German biotech VC round of the year. Apart from that, other trending innovations like gene and cell therapy, novel foods, and AI-powered solutions have captured investor attention. Of the top 15 VC rounds, 87% saw participation from foreign investors and 53% from family offices and private investors.

Challenges in early-stage venture investment
Alarmingly, the analysis of early-stage venture funding in the German biotech sector indicates a significant financing gap as investors are acting risk averse and increasingly focus on companies in the later stages of development (see Databook for details). This implies an undercapitalization of young startups and poses a serious threat to the industry's sustainable growth.

IPOs — a missing link in the financing cycle
For the second consecutive year, the German biotech sector did not register any IPOs. This trend is a growing concern, as exits are an indispensable component of a functional financing cycle. The fact that the last 10 IPOs opted for NASDAQ and the most recent domestic stock market debut occurred back in 2016 underscores long-standing calls for the improvement of IPO conditions in Germany (e.g., strengthening the participation of new and existing investors as well as improving infrastructure and know-how). In the US, IPO investments in biotech showed some signs of recovery with a modest 16 IPOs collecting $2.6 billion, while Europe saw only two IPOs raising $338 million.

Insights into follow-on and other financings
Financings by listed German biotech companies registered a robust capital inflow of €547 million in 2023, a 20% increase over 2022. Putting aside the exceptional years 2018, 2020 and 2021, this marks the highest capital raised by public companies in the industry's history. The most successful financings were completed by CureVac (€234 million follow-on offering), MorphoSys (€103 million follow-on offering) and Formycon (€70 million PIPE).

Capital raised by German biotech companies



Source: EY analysis, BIO Deutschland, Capital IQ and Dow Jones VentureSource.

AaviGen: Strong investment backing paves way for cardiac gene therapy

Prof. Dr. Patrick Most
Co-founder and CEO, AaviGen GmbH

Prof. Dr. Marc Lerchenmüller
Co-founder and CFO, AaviGen GmbH

Founded in 2019, AaviGen GmbH is a pre-clinical stage biotechnology company specializing in the development of transformative gene therapies for genetic and acquired cardiovascular and cardiopulmonary diseases. Leveraging a proprietary portfolio of heart-specific recombinant Adeno-Associated Viruses (AAVs), AaviGen delivers therapeutic genes directly to the diseased heart cells via a single intravenous injection. The company aims to address the unmet needs of millions of patients worldwide, ultimately reshaping the clinical landscape of cardiovascular care.

AaviGen's mission is to advance precision medicine by providing safe and effective gene therapies for heart-related ailments. Combining cutting-edge technology and the interdisciplinary expertise of its founders, Dr. Martin Busch and Professors Hugo Katus, Marc Lerchenmüller, and Patrick Most – spanning clinical cardiology and pneumology, virology and genetic vector engineering, gene therapy medicinal product development, health economics and regulatory affairs – the company strives to improve patient outcomes and quality of life.

In fulfilling its mission, AaviGen can build on the vital support of key partners. The company's fundraising record includes a €5m Series A and a €17m Series B round, both contributed by DH-LT-Investments GmbH, owned and led by the Hopp family. Securing the Series B marked a milestone for advancing cardiovascular gene therapies, enabling AaviGen to distinguish itself from the competition by demonstrating that its next-generation Cardiac AAV Platform (next-CAP) overcomes obstacles in heart targeting and transduction. The company's new vector generation with unrivaled cardiac specificity attracts market interest for both its technology and lead product with international scientific and investor conferences, like the American Society of Gene and Cell Therapy meeting or the Bio Europe, serving as catalyzing events. Through committed fundraising, AaviGen gained insights into effectively communicating its technology's value, managing investor expectations, and forming partnerships. These lessons will also shape future fundraising efforts.

The company's prospects are further strengthened by its international advisory board and the backing of local institutions. Drawing on the international visibility and reputation of its founders in science and business communities, AaviGen assembled a team of experts advising the company on its R&D course as well as on regulatory affairs and corporate development. AaviGen also benefits from the backing of local stakeholders, including the Universities of Heidelberg and Mannheim and the state of Baden-Wuerttemberg, which provide accommodating structures for AaviGen to unfold its potential. In that spirit, AaviGen encourages the furthering of efforts by local stakeholders to advance translational science.

In all, AaviGen is well-positioned to advance its course. The secured financing will enable the development of its lead product toward clinical testing within the next three to four years. Further developing its proprietary platform technology, the company also evaluates the expansion of its portfolio of cardiac-specific AAV capsids to cover various heart conditions and enable personalized therapies. From a corporate development standpoint, the company will internationalize and continues to forge strategic partnerships with industry leaders to bring these innovative treatments to patients worldwide.

www.aavigen.com

Alliances trends in 2023
Continuing the high performance of 2022, German biotech companies signed collaboration and licensing deals worth up to €11.4 billion in 2023, the second-highest total potential value in the industry's history. While incoming biobucks saw a significant decrease compared with the peak year 2022 (minus 49%), the outgoing biobucks continued their upward trend (plus 190%).

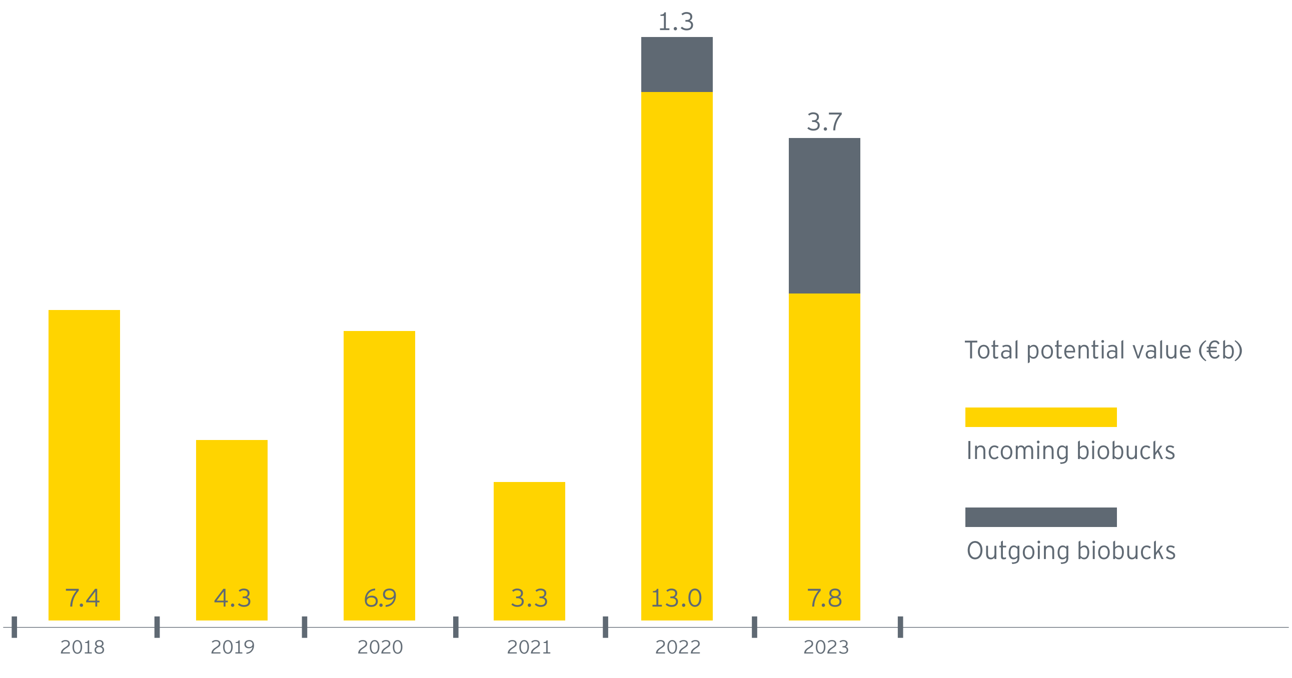
Tracing the track of outgoing biobucks
The sole driver behind these increasing investment activities was commercial leader BioNTech, in-licensing four clinical-stage assets to strengthen its oncology portfolio. BioNTech gained access to two antibody-drug conjugates, a bispecific antibody and a checkpoint antibody candidate.

Incoming biobucks – a significant revenue stream
Despite the slump of the revenue-generating deals, the total potential incoming biobucks recorded for the year 2023 is still the second highest after the record year 2022. As usual, this category is dominated by deals with large (bio)pharma partners searching to fill their innovation gap, as numerous key products face the loss of patent protection. The top six deals are providing the partners with the highly sought-after access to potential first-in-class assets.

The top alliance of the year was signed by Evotec and Bristol Myers Squibb (BMS), extending and expanding their strategic neurodegeneration partnership and leveraging several of Evotec's AI-powered precision medicine platforms. With up to €3.7 billion, this was also the biggest potential-value alliance in the European biotech sector. Other major German biotech alliances emphasize the appetite for new therapeutic modalities like bispecific T cell engagers (Immatics and Moderna; up to €1.7 billion) and antibody-drug candidates (Tubulis and BMS; up to €945 million). The inspiring success story of young Tubulis reaching this remarkable agree-ment will be described in the next section by Dominik Schumacher.

Deal structures at a glance
A closer look at the up-front payments reveals that most deals have a high portion of non-guaranteed payments, signaling the leverage large (bio)pharma companies have in creating alliance deal structures (see Databook for details). However, partnership goes beyond the provision of financial resources, creating significant added value for biotech companies seeking to increase their footprint in the industry and sharpening their profiles. Biotech companies benefit in many ways; for example, through access to networks as well as to valuable resources and expertise in areas like regulatory compliance, intellectual property protection and product scalability.

Alliance deals by German biotech companies



Source: EY analysis and Biomedtracker.

Tubulis: Pushing the boundaries of ADC development

Dr. Dominik Schumacher
Co-founder and CEO, Tubulis GmbH

Tubulis is developing a pipeline of uniquely matched antibody-drug candidates (ADCs), each with an indication-tailored design to develop novel ADCs with superior properties. The company was founded in 2019 as a university spin-out by Dr. Jonas Helma-Smets, Dr. Ingo Lehrke and myself, together with our scientific co-founders, Prof. Christian Hackenberger from the Leibniz Research Institute in Berlin, and Prof. Heinrich Leonhardt from Ludwig Maximilians University in Munich. Our unique approach in the field and the overall momentum through data and approvals have allowed us to establish the company as an up-and-coming leader with strong support from high-tier international investors and a team of 52 highly motivated experts. In March, we were able to further strengthen our financial position with the closing of an upsized and oversubscribed €128 million Series B2 financing round, led by EQT Life Sciences and Nextech Invest. With Nextech Invest, Frazier Life Sciences and Deep Track Capital we managed to add three experienced US-based funds to our investor syndicate.

We have built a unique suite of platform technologies that address the key bottlenecks of the ADC space, stability and payload-driven toxicity. To unlock the true value of ADCs, we tailor each ADC to its respective indication and optimize its design by combining a wide range of target molecules, innovative payloads and conjugation technologies. This approach enables us to maximize the tumor engagement. Additionally, our capabilities extend beyond traditional payload classes and expand antibody conjugation options through novel chemical groups that build stable ADCs with the right drug-to-antibody ratio. Over the years, we have built a strong team and are advancing our pipeline, with the first program entering the clinic in 2024. Our two lead candidates, TUB-040 and TUB-030, are both strong therapeutic candidates for the treatment of solid tumors with encouraging preclinical proof-of-concept data. Our overall goal is to expand the therapeutic potential of ADCs and make an impact on the treatment of solid tumors, allowing us to achieve prolonged responses with less toxicity.

In 2023, we signed an important strategic licensing deal with Bristol Myers Squibb (BMS) to develop differentiated ADCs together. The new partnership allows us to combine BMS' deep oncology and clinical development expertise with our innovative and unique approach to ADC design. Having the leading player in oncology by our side is also a great validation for the company we've built. Through this collaboration, we aim to explore the capabilities of our technologies to generate truly differentiated drug candidates across a broader range of solid tumor indications to help patients.

When entering into discussions with BMS, we initially faced the very common challenge of balancing the need for transparency and collaboration with a big pharma partner while also protecting our proprietary technology and know-how. However, after initial discussions, we quickly learned that despite being a larger organization, BMS shared the same core values and spirit as the Tubulis team. Thus, we were able to overcome potential differences in the organizational setup and decision-making processes by establishing open communication channels on various levels – not just among the negotiating BD teams but also in the R&D department. This approach proved to be a key component in the successful initiation of our collaboration after the deal was announced in April of last year, enabling us to kick off our efforts successfully.

We are very excited about the progress we've made in 2023, and with the closing of our Series B2 financing round as well as our next-generation ADCs advancing toward clinical evaluation in 2024, this year has been off to a great start towards becoming the next ADC success story.

www.tubulis.com

M&A market in 2023
After the near disappearance of the M&A market in 2022, the overall numbers suggest that the market rebounded in 2023, with the total potential value accelerating by 189%. However, the detailed analysis paints a more nuanced picture. While investment activities by German biotech companies fueled the recovery, surging by 508%, sell-side transactions by German biotech companies continued their downward trend, plummeting even further by 63%.

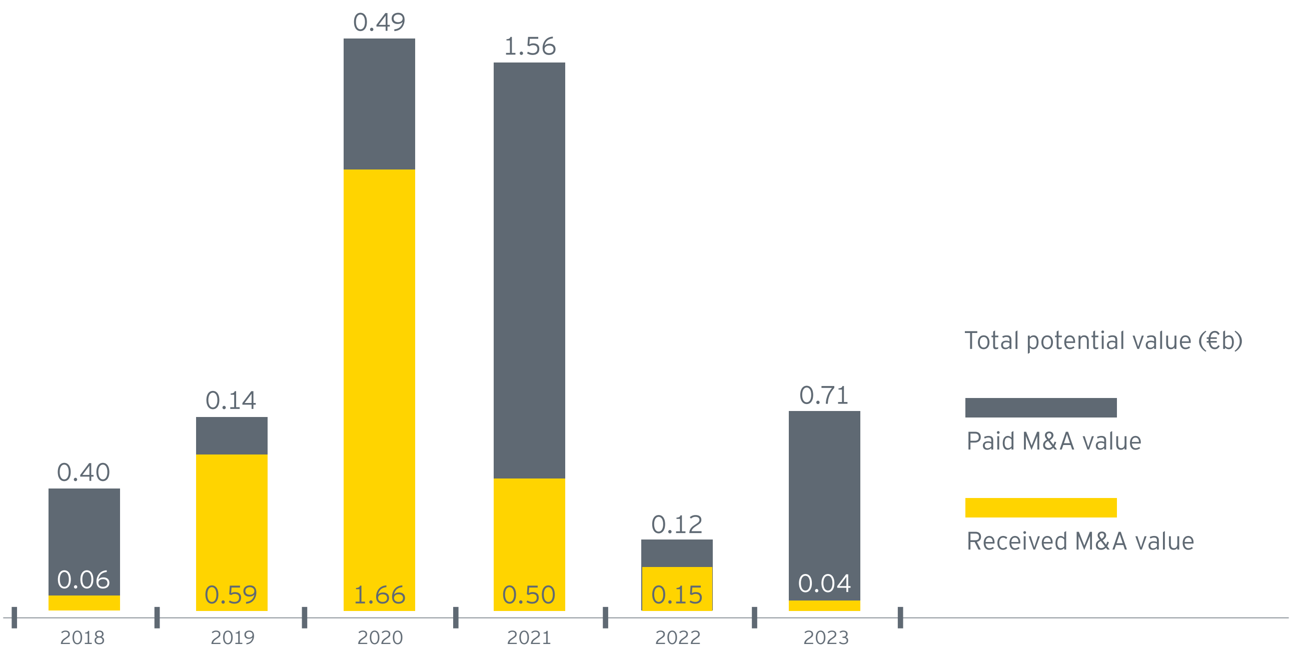
The decline in received M&A value
This resulted in the lowest received M&A value on record, comprising only two acquisitions with low- to mid-double-digit values of the two German biotech companies Synimmune and Epigenomics.

This is in stark contrast to the findings of the international EY M&A Firepower and Beyond Borders reports, which both find big pharma embrace big dealmaking once again in 2023, for numerous key products facing the loss of patent protection. Fortunately, there are signs that also the German M&A market might be reviving. In February 2024, MorphoSys signed an agreement with Novartis to be acquired for €2.7 billion with shareholders benefiting from a 94% premium – the largest M&A transaction in the German biotech industry's history.

Shortly after, in March 2024, privately held Cardior Pharmaceuticals from Hannover agreed to be acquired by Novo Nordisk for €1 billion – the most valuable M&A exit of a private German biotech company since 2020. These success stories obviously set an end to the muted M&A market and underscore the innovation power and international attractiveness of the German biotech industry.

The upsurge in paid M&A value
On the flip side, the year 2023 marked a high point for outgoing M&A transactions, with German biotech companies looking for inorganic growth through acquisitions. The paid M&A value nearly reached its peak, topped only by the remarkable figures from 2021 – a record year shaped by MorphoSys' €1.4 billion deal to secure Constellation Pharmaceuticals. This underscores the proactivity of the maturing German biotech scene in investing and expanding through strategic acquisitions, with the most significant moves taken by BioNTech (acquisition of InstaDeep for €500 million), Qiagen (acquisition of Verogen for €139 million) and Ariceum Therapeutics (acquisition of Theragnostics for €40 million).

Mergers and acquisitions by German biotech companies

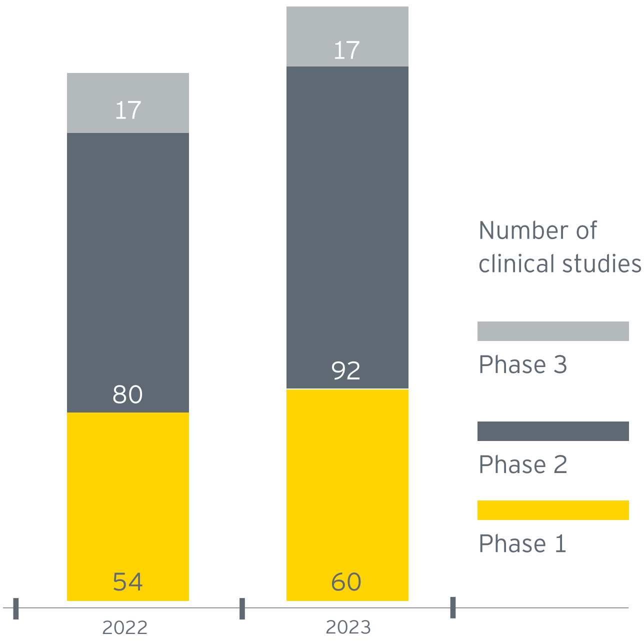


Sources: EY analysis and Capital IQ.

Growing and maturing clinical pipeline
Despite global challenges and the difficulty of securing investments, German biotech drug developers have expanded their therapeutic pipelines, illustrating the sector's resilience and dedication to driving innovation and addressing patients' unmet needs. With an increase of 12% over last year, there were 169 assets across all clinical phases. While the number of assets in Phase 3 remains unchanged compared with 2022, the number of Phase 1 and 2 clinical studies grew by six and 12 assets, respectively. With an increase of 15%, Phase 2 clinical studies exhibited the highest growth rate, indicating robust advancements and resulting in an overall maturing pipeline profile. Looking back at the 10-year period from 2012 to 2022 with an average annual growth rate of a mere 2% (128 clinical studies in 2012), the current figures are a strong testament to the dynamic and inventive spirit prevalent within Germany's biotech industry.

Beside established players expanding their clinical activities, the early-stage pipeline is boosted by new entrants iOmx Therapeutics (drug candidates against novel immune-oncology targets), Thermosome (thermosensitive liposomes for targeted tumor therapy, e.g., for soft tissue sarcoma), and tiakis Biotech (anti-inflammatories, e.g., for respiratory diseases).

Clinical studies by German biotech companies



Sources: EY analysis and Biomedtracker.

Huge diversity of modalities and indications
The well-stocked clinical pipeline encompasses innovative therapies from all kinds of drug classes, ranging from monoclonal antibodies and small molecules to mRNA and other nucleic acids, peptides, proteins, and cell-based therapies.

The focus lies on the field of oncology, with 94 ongoing clinical studies (56% of all clinical studies) and the highest diversity of drug modalities, including new breakthrough therapies in the fight against cancer like antibody-drug conjugates, bispecific antibodies, targeted radiopharmaceuticals, checkpoint modulators, mRNA vaccines and cell-based therapies.

Infectious diseases are the second most tackled disease area, represented by 23 clinical trials; notably, less than half of these trials are reminiscent of the COVID-19 pandemic, such as vaccines and antivirals.

Additional considerable endeavors tackle autoimmune, neurological and cardio-vascular diseases (see Databook for details).

AI and biotechnology — technological convergence for the future of innovation

A key technological trend opening new possibilities for the future of the biotech industry involves the deployment of innovative AI solutions, such as machine learning (ML) and generative AI (GenAI). Technological advancements facilitating the proliferation of data-generating capabilities have given rise to vast opportunities for AI-powered biotechnology, generating insights from the constantly growing amount of data available. Whether confronted with extensive quantities of data, commonly referred to as big data, or complex, multifaceted data frequently termed "wide data", AI stands as an indispensable tool in overcoming the interpretation bottleneck, recognizing underlying patterns and making sense of biological information in entirely new ways. The market for AI tools specifically tailored for life sciences applications is experiencing substantial growth and attracting tech giants like Google, Microsoft and NVIDIA. In this milieu, the first generation of AI-powered biotech companies has emerged, leveraging the technological convergence of biotechnology and AI as a pivotal part of their business model.

Besides well-known AI adopters like BioNTech, Centogene, QIAGEN and Evotec, Germany's biotech scene is giving rise to numerous innovative AI-powered biotech startups. These companies target a broad spectrum of application domains, including generative and predictive models for the discovery or optimization of

Selected German biotech startups leveraging artificial intelligence

Company	City	AI-powered biotechnology
Aignostics	Berlin	ML for digital pathology to support pharmaceutical research, clinical trials and biomarker development
aimed analytics	Bonn	Modular system using ML to support drug discovery and biomarker development
Alacris Theranostics	Berlin	Digital twin to model the tumor response to specific therapies or therapy combinations
biotx.ai	Potsdam	Causal inference modeling for drug discovery, drug repurposing and prediction of clinical trial outcomes
BioVariance	Tirschenreuth	Individualized data structures using ML for clinical diagnosis and personalized medicine solutions
cAHRmeleon Bioscience	Heidelberg	Multi-omics platform using NLP for patient stratification and prediction of therapeutic responses in oncology
Cambrium	Berlin	GenAI for the creation of protein and bio-based materials that meet given performance specifications
Cortex Discovery	Munich, Regensburg	DL for drug discovery and prediction of physiological function and target activity in all therapeutic fields
CrystalsFirst	Marburg, Hamburg	ML for drug discovery and structural biology across protein families and modalities
DNTOX	Düsseldorf	ML for chemical screening with a focus on neurotoxicological hazard assessment
Epsilico	Berlin, Göttingen	GenAI for the creation of protein therapeutics for hard-to-drug targets in oncology, autoimmune and respiratory diseases
Exazyme	Berlin	Protein design app using ML for the development and optimization of biocatalysts or antibodies
Genome Biologics	Frankfurt am Main	ML and disease modeling for drug discovery in cardiovascular and cardiometabolic diseases
GOENOMICS	Göttingen	ML for genome annotation services

DL = deep learning, GenAI = generative AI, ML = machine learning, NLP = natural language processing molecules, causal inference models for the simulation of clinical trials, or the creation of superior diagnostics and personalized medicines. Their products and services harbor great potential to lead the next phase of bioscience innovation, as their data-driven algorithms in combination with biotechnological ingenuity may outperform existing solutions in terms of accuracy, speed and cost efficiency. They are also appealing acquisition targets, as companies worldwide seek to incorporate AI-powered biotech solutions into their portfolios. This is exemplified by BioCopy's recent takeover of Frankfurt am Main based Perspix Biotech, known for its machine learning and robotics technology for drug discovery across various biological drug modalities in oncology.

In order to capitalize on the transformative power of AI, the German biotech industry must navigate the challenge of adapting to the rapid technological evolution while managing associated risks. Staying at the forefront of global competition necessitates a strategic emphasis on adopting AI technologies, attracting and nurturing skilled professionals, establishing responsible AI governance frameworks, and cultivating partnerships centered around innovation. By doing so, the industry can accelerate its momentum in driving forward scientific breakthroughs and tangible success.

Company	City	AI-powered biotechnology
iniuva	Hamburg	Virtual platform for small molecule drug discovery with a focus on protein misfolding in rare genetic disceases
IntegraSkin	Tübingen	Cognitive computing for clinical diagnosis and personalized medicine solutions in chronic inflammatory skin conditions
Katana Labs	Dresden	ML for digital pathology and spatial biology to support biomarker development and patient stratification in oncology
Labdao	Berlin	Open source ML tools for computational life science research
Mindpeak	Hamburg	ML for digital pathology, biomarker development and patient stratification
molab.ai	Munich	GenAI for the creation of therapeutic molecules and prediction of potency, selectivity and pharmacokinetic properties
myotwin	Göttingen	Digital twin of the human heart muscle for drug discovery and prediction of therapy responses
Noselab	Munich	ML for clinical diagnosis and patient stratification in neurodegenerative diseases
Nostos Genomics	Berlin	Variant interpretation platform using ML for the clinical diagnosis of genetic diseases
Pheiron	Berlin	Causal inference modeling for drug discovery, drug repurposing and prediction of clinical trial outcomes
Prosperodes	Braunschweig	DL for biomarker-based subtyping of neurodegenerative diseases
Silica Corpora	Berlin	GenAI for the creation of antibodies against given targets or epitopes
Tcelltech	Mannheim	ML for the identification of patient-derived T cell receptors to be used in cancer cell therapy
TRI Thinking Research Instruments	Hamburg	DL for automated microscopy and analysis of in-vitro cell cultures and assays

Source: EY analysis

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New modalities in personalized medicine once more opened up remarkable opportunities for new disease treatments through the power of biotechnology. To enable these technologies to reach the market, we have to invest now in the future of the German biotech industry.

Julia Schaft
Spokesperson, Council of German BioRegions

German biotech startups, 2023

Company	City	Federal state	Segment
AbTherix	Tübingen	Baden-Wuerttemberg	Therapeutics
Affluence Technologies	Aachen	North Rhine-Westphalia	Therapeutics
Avocet Bio	Göttingen	Lower Saxony	Therapeutics
CanChip	Potsdam	Brandenburg	Service
CARTemis Therapeutics	Berlin	Berlin	Therapeutics
Curnova microRNA Technology	Wiesbaden	Hesse	Therapeutics
Katana Labs	Dresden	Saxony	Service
Lambda Biologics	Leipzig	Saxony	Service
Leopard Biosciences	Gauting	Bavaria	Diagnostics
Mallia Therapeutics	Erlangen	Bavaria	Therapeutics
MEDEA Biopharma	Ludwigshafen am Rhein	Rhineland-Palatinate	Therapeutics
miproCure	Göttingen	Lower Saxony	Therapeutics
Mucosatec	Schiffweiler	Saarland	Therapeutics
myotwin	Göttingen	Lower Saxony	Service
navitapharm	Berlin	Berlin	Therapeutics
OncInnovat KmS	Darmstadt	Hesse	Service
Phaeosynt	Hannover	Lower Saxony	Diagnostics
REVIER Therapeutics	Heidelberg	Baden-Wuerttemberg	Therapeutics
SequantrixTM	Aachen	North Rhine-Westphalia	Therapeutics
Silica Corpora	Berlin	Berlin	Service
SMIN Therapeutics	Marburg	Hesse	Therapeutics
TimeTeller	Hamburg	Hamburg	Diagnostics
Trypto Therapeutics	Berlin	Berlin	Therapeutics
TWYCE	Tübingen	Baden-Wuerttemberg	Therapeutics

Source: EY analysis and BIO Deutschland.

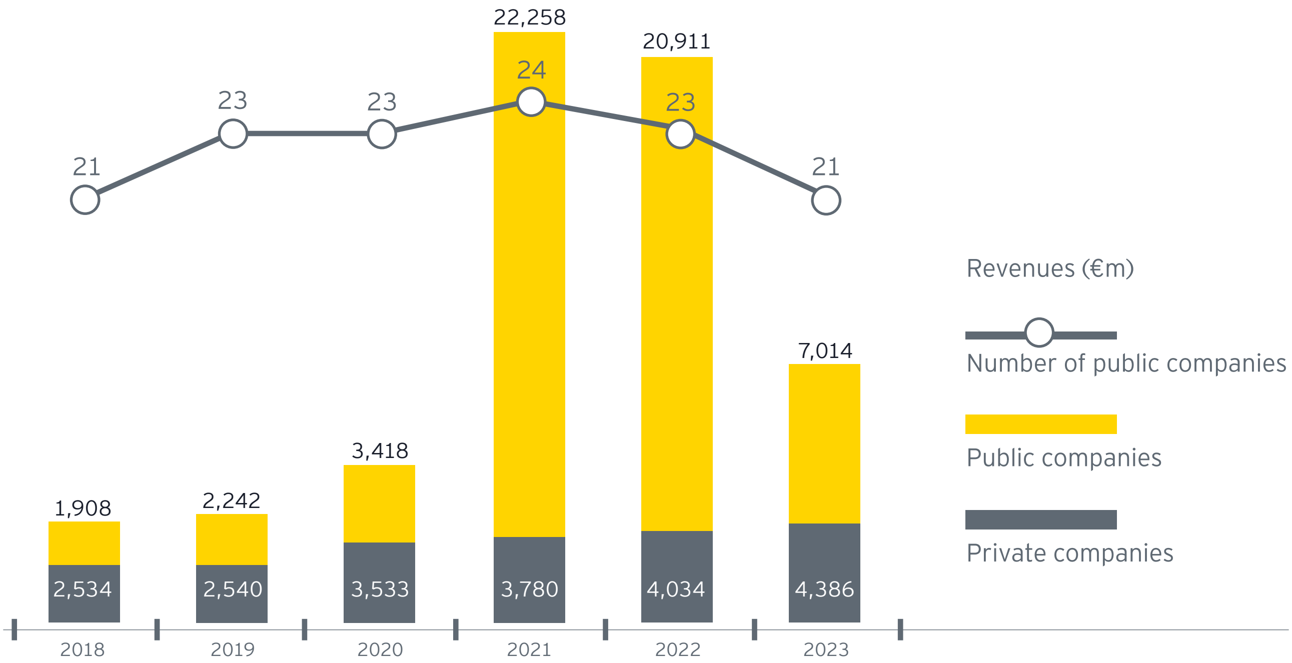
- The startup dynamic in the German biotech sector has been stagnating for years. The annual figures fluctuate between 20 and 30 newly founded companies, and 2023 was no exception. In total, 24 startups dared to take the step of bringing scientific results to application.

- The vast majority of 15 companies are active in the field of therapeutics. The range of lead molecules investigated is broad, as is the range of indications, such as fibrosis, hair loss, osteoarthritis and cancer. Three companies are leveraging AI-powered biotech solutions based on machine learning, generative AI and digital twin technology.

- Unlike in 2022, most startups did not come from the south of Germany, but from Berlin and Lower Saxony, followed by Hesse and Baden-Wuerttemberg.

- There are many reasons for the weak startup momentum in Germany. In 2023, the situation was exacerbated by the fact that startups had great difficulty obtaining seed money from venture capital investors. The German Federal Ministry of Education and Research's funding program "Gründungsoffensive Biotechnologie", or GO-Bio for short, which is particularly attractive for biotechnology startups, has been suspended since 2018 and was only relaunched in May 2024.

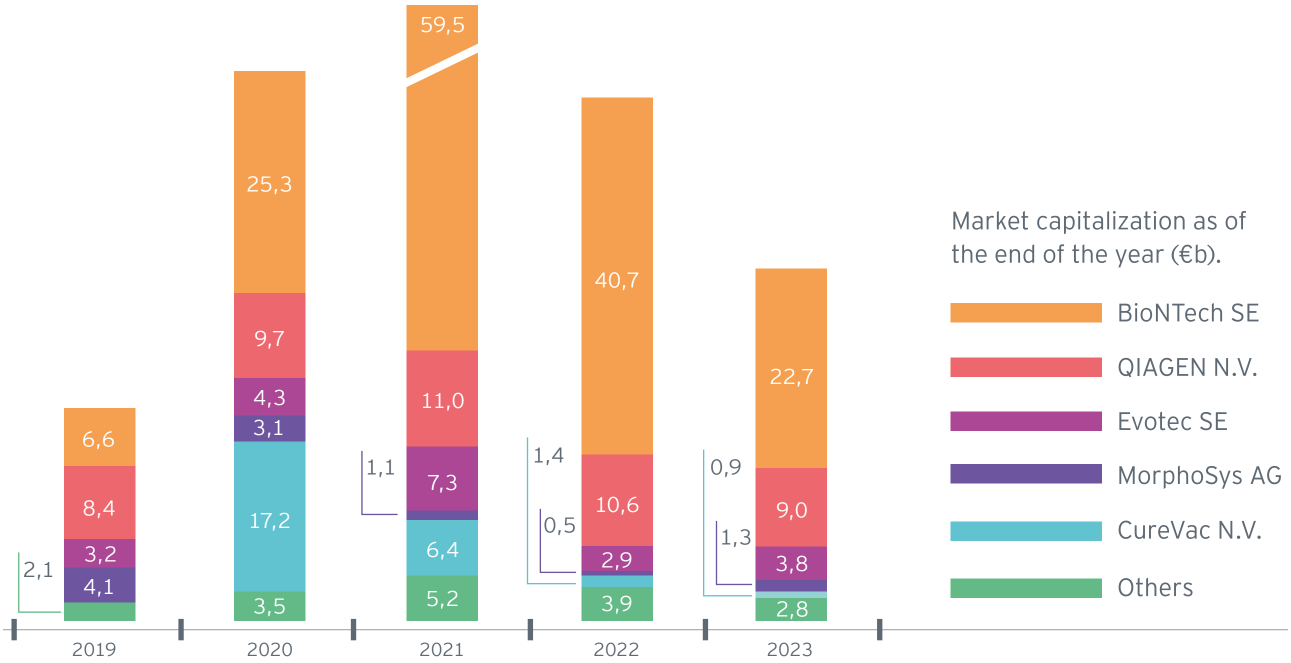
German biotech private and public company revenues



Sources: EY analysis, BIO Deutschland and Capital IQ.

- The total revenue of German biotech public and private companies declined sharply from €24.95 billion to €11.40 billion in 2023. This decline was driven by public companies with a -66% decline in stark contrast to the strong performance and a 9% increase seen in private companies.
- The revenue stream of public biotech firms was again dominated by Germany's largest biotech company, BioNTech, which alone contributed to 54% of the total revenues within this group. BioNTech's revenue, primarily including commercial COVID-19 vaccine sales, decreased by €13.49 billion compared to the previous year due to reduced demand.
- Revenues for the remaining public German biotech companies decreased by 10%, as 10 more companies also reported declining revenue figures. On a brighter note, there were also 10 companies that defied the downward trend and saw an increase in their revenues.
- There was no German biotech IPO in 2023 and consequently no addition to the count of public biotech companies. With the asset buyout of Epigenomics and the insolvency of PAION, the number of public biotech companies fell from 23 to 21.
- Despite recent challenges, the industry has shown remarkable resilience when compared to the pre-pandemic year 2019. Over this four-year period, public and private biotech companies achieved substantial growth of 213% and 73% and average annual growth rates of 33% and 15%, respectively. These figures indicate that the sector's fundamental strengths are intact and that it is well-positioned to navigate through the current economic turbulences.

German biotech market capitalization



Sources: EY analysis and Capital IQ.

- In 2023, the aggregated market capitalization of the 21 listed German biotech firms continued its declining trajectory, plummeting by 33% to reach €40.3 billion. However, when compared with the pre-pandemic year 2019, the total market capitalization registered a 66% increase. Except for MorphoSys, all series displayed long-term growth spanning over this five-year period.

- The primary driver behind the current downward trend was Germany's sole large-cap biotech firm, BioNTech. While BioNTech sill accounts for 56% of the total German market capitalization, its market value diminished by 44% compared with the prior year. This significant drop was driven by reduced revenues due to low demand for COVID-19 vaccines, a concurrent downward revision of revenue forecasts, and share buybacks. Since its IPO in 2019, the immunotherapy powerhouse has been a success story, signifying a remarkable 244% growth trajectory.

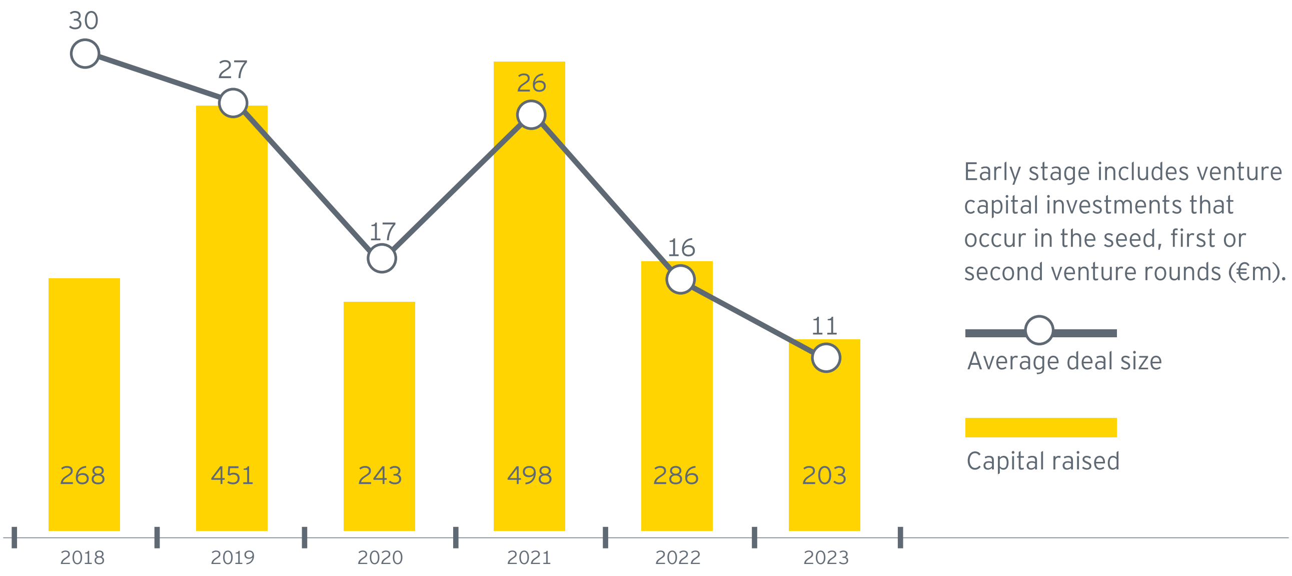
- Mid-cap categorized QIAGEN and Evotec encountered contrasting trends in 2023. QIAGEN underwent a 16% decrease in value, while Evotec successfully overturned its slump with a modest 31% stock price recovery. Over the five-year period both commercial leaders experienced growth by +7% and +17%, respectively.

- MorphoSys successfully gained 143% in 2023 largely attributed to the positive results from the Phase 3 study of pelabresib, an investigational selective small-molecule therapy against myelofibrosis. Over the last five years, MorphoSys had faced a 68% contraction but ultimately entered into an agreement to be acquired by Novartis for €2.7 billion in February 2024, far surpassing the €1.3 billion recorded for the year-end 2023.

- CureVac initially rode a wave of success during the early COVID-19 pandemic phases when the company went public in 2020, but continued its downward trend in 2023, plummeting by 41%.

- The remaining companies of small- and micro-cap size collectively registered a 34% increase when compared to the pre-pandemic year 2019. During the year 2023, they suffered a 28% decay in market value, but some firms recorded growth in their valuations grounded on positive clinical results and promising new alliances.

German early-stage venture investment



Source: EY analysis, BIO Deutschland, Capital IQ and Dow Jones VentureSource.

- Despite the growth and high level in venture spending overall, the slump in financing for young startups further intensified in 2023. Early-stage companies only secured €203 million, a mere 38% of total venture capital investment and a significant drop from previous years.
- Eighteen early-stage investment rounds were recorded, indicating sustained activity in seeking funds and investments. However, average deal size shrank to €11 million, significantly lower than the €23 million average observed over the preceding five years.
- Additionally, it must be noted that 35% of the early-stage total went to the €72 million investment in Complement Therapeutics, a Munich-based preclinical stage company developing innovative AAV gene therapies. Another 11% went to Berlin-based Ariceum Therapeutics, a developer of much-sought-after radiopharmaceutical products for hard-to-treat cancers.
- The distribution of early-stage venture capital depicts a scenario wherein a small share of startups secures a substantial portion of the available capital. The implication is that the multitude of early-stage firms may be undercapitalized and struggling for funding.

German biotech venture capital rounds, 2023

Company	Gross raised €m	Month	Round	Investors
ITM Isotope Technologies Munich	255.0	June	6	Temasek, BlackRock, QIA, Nextech, ATHOS, Carbyne
Complement Therapeutics	72.0	April	1	Gimv, Forbion, BioGeneration Ventures, Panakès Partners, Cambridge Innovation Capital, Hadean Ventures, Seroba Life Sciences
BrainRepair	50.0	February	n/a	unknown London based group
AMSilk	25.0	April	3	ATHOS, Novo Holdings, Cargill, MIG Capital
Ariceum Therapeutics	22.8	April	1	Andera Partners, Earlybird Venture Capital, Pureos Bioventures, EQT Life Sciences
Aavigen	17.0	July	2	DH-LT Investments
Bluu Seafood	16.0	June	1	Sparkfood, LBBW VC, SeaX Ventures, Manta Ray Ventures, Norrsken VC, Delivery Hero Ventures, Innovationsstarter Fonds Hamburg, Dr. Oetker
mbiomics	13.0	March	1	MIG Capital, HTGF, Bayern Kapital, private investors
Seamless Therapeutics	11.8	March	Seed	Wellington Partners, Forbion
Bind X	10.0	August	2	HG Ventures, K&K 1, Greeneering Invest, Saxovent
Anavo Therapeutics	8.5	May	1	M Ventures, INKEF, Taiho Ventures, Bioqube Ventures, MRL Ventures Fund
Cambrium	8.0	October	Seed	Essential Capital, SNR, Valor Equity Partners, HOF Capital
Tolerogenixx	7.0	July	1	DB Speciality, Kalodion Fond I, CventureS, Nisus, HTGF, Dr. Dr. Dorow, Dr. Dr. Fakler, Biotech Mountains
Transimmune	4.7	September	2	Bill & Melinda Gates Foundation
Labdao	3.3	May	1	Inflection, Village Global, North Island Ventures, Seed Club Ventures, ID Theory, Road Capital, Curve Labs, gmjp.lol, Molecule, Gnosis DAO, The LAO, Orange DAO, Beaker DAO, Spaceship DAO, Balaji Srinivasan
AATec Medical	2.7	July	Seed	private investors, family offices
Exazyme	2.0	May	Seed	AIX Ventures, Atlantic Labs
MicroHarvest	1.5	May	2	Simon Capital
DNTOX	1.4	June	Seed	HTGF, private investors (Barbara Korte-Sturm, Nikolaus Sturm), Bool Capital, AQAL Capital
Smartbax	1.2	May	Seed	Boehringer Ingelheim Venture Fonds, HTGF
Phialogics	0.6	April	1	HTGF

Source: EY analysis, BIO Deutschland, company press releases, Capital IQ and Dow Jones VentureSource.

- ITM, known for its targeted radiopharmaceuticals against hard-to-treat cancers, received an impressive €255 million from existing and new investors, marking the largest funding round of 2023 and the third largest on record, after Curevac's €200 million in 2020 and BioNTech's €290 million in 2019.

- Besides next-generation radiopharmaceuticals represented by ITM and Ariceum Therapeutics, freshly funded German biotech companies encompass the most trending areas within modern biotechnology like gene and cell therapy (Complement Therapeutics, Aavigen, BrainRepair, Seamless Therapeutics, Transimmune), smart biotech materials (AMSilk, Cambrium), novel foods (Bluu Seafood, MicroHarvest), microbiome-based therapeutics (mbiomics), and artificial intelligence-powered solutions (Labdao, Exazyme and DNTOX).

Top German biobucks alliances, 2023

Company	Company country	Partner	Partner country	Status	Potential value €m	Up-front €m
Evotec	Germany	Bristol Myers Squibb	US	Research	3,696.9	46.2
Immatics	Germany	Moderna	US	Research	1,682.1	110.9
DualityBio	China	BioNTech	Germany	Phase 2	1,543.5	157.1
MediLink Therapeutics	China	BioNTech	Germany	Phase 1	988.9	64.7
Biotheus	China	BioNTech	Germany	Phase 2	975.1	50.8
Tubulis	Germany	Bristol Myers Squibb	US	Research	945.3	21.0
Evotec	Germany	Sandoz	Germany	Research	591.5	
3B Pharmaceuticals	Germany	Novartis	Switzer-land	Phase 2	429.8	37.0
Evotec	Germany	Janssen Biotech (J&J)	US	Research	323.5	
OncoC4	US	BioNTech	Germany	Phase 2	184.8	184.8
BioNTech	Germany	CEPI	Norway	Phase 2	83.2	
Evotec	Germany	Bill & Melinda Gates Foundation	US	Research	2.3	2.3

Source: EY analysis, company press releases and Biomedtracker.

- Nearly half of 2023's total potential deal value went to experienced dealmaker Evotec, which inked four deals with disclosed terms, collectively worth up to an impressive €4.6 billion.

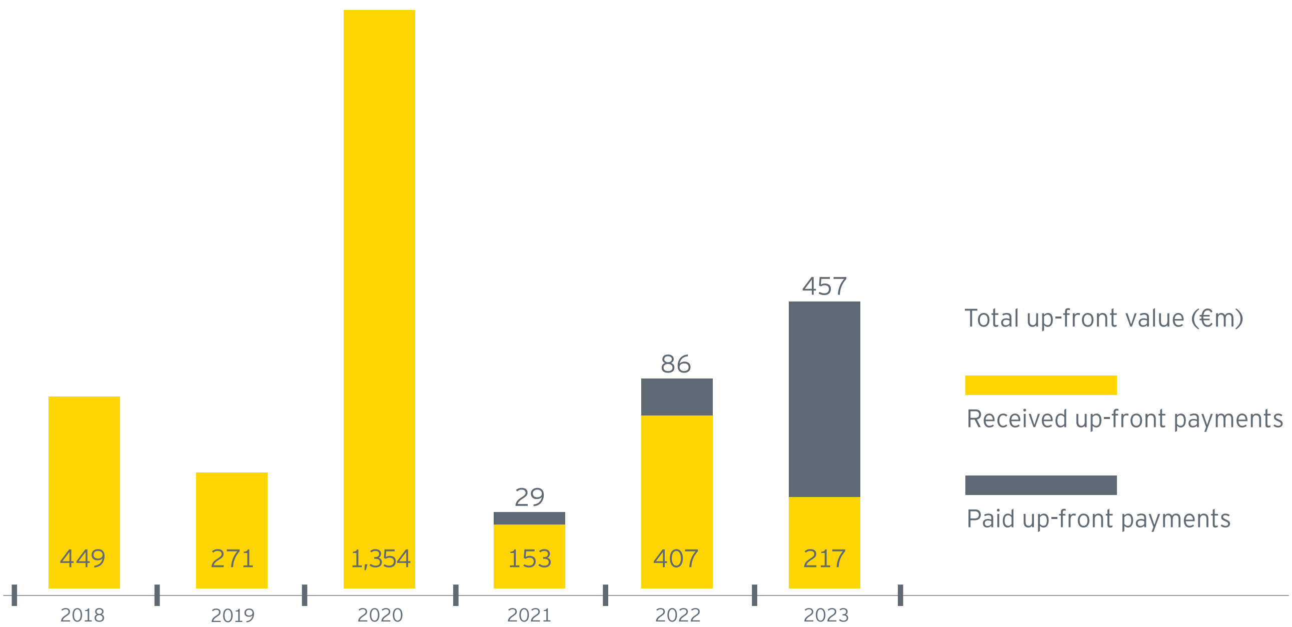
- The extension and expansion of the highly productive strategic neurodegeneration partnership between Evotec and Bristol Myers Squibb, originally signed in 2016, resembles the biggest alliance of the year 2023.

- The second most significant deal was signed by cancer immunotherapy pioneer Immatics and new partner Moderna in a strategic multi-platform collaboration combining mRNA and T-cell receptor technologies to develop novel therapies for cancer patients with high unmet medical need.

- The most active German biotech company on the buy side was BioNTech, in-licensing four clinical-stage assets to strengthen its oncology portfolio: two antibody-drug conjugates, a bispecific antibody and a checkpoint antibody, collectively worth up to €3.7 billion.

- Oncology stood out as the key therapeutic focus, with eight of the top 12 alliance deals rooted in this area. These include all in-licensing deals by BioNTech and the partnership between Immatics and Moderna. Besides bispecific antibodies and T-cell receptor therapeutics represented by Immatics, German biotech firms provided access to groundbreaking approaches in the fight against cancer like antibody-drug conjugates (Tubulis), targeted radiopharmaceuticals (3B Pharmaceuticals) and targeted immune-based therapies (Evotec).

German strategic alliances based on up-front payments



Source: EY analysis and Biomedtracker.

- In 2023, total up-front payments reached their second-highest value in the six-year period, with the peak seen in 2020, when MorphoSys out-licensed tafasitamab, a first-in-class Phase 3 antibody, which was approved by the FDA later in 2020, in a megadeal with Incyte that garnered a tremendous up-front payment of $900m.
- Despite the impressive figure, this upward trend was solely driven by the paid up-front payments, which skyrocketed by 432% compared with the previous year.
- For the first time, the industry saw most of the total up-front value in paid out payments, accounting for 68%. While at first sight this seems to indicate a transition toward an investment-heavy phase, it must be noted that the sole driver behind this trend was commercial leader BioNTech investing in its four in-licensing deals.
- In contrast, received up-front payments dropped by 47% compared with 2022 and reached the second-lowest value in the analyzed period. This development illustrates the leverage large (bio)pharma companies have in creating alliance deal structures, especially in the early developmental product stages.

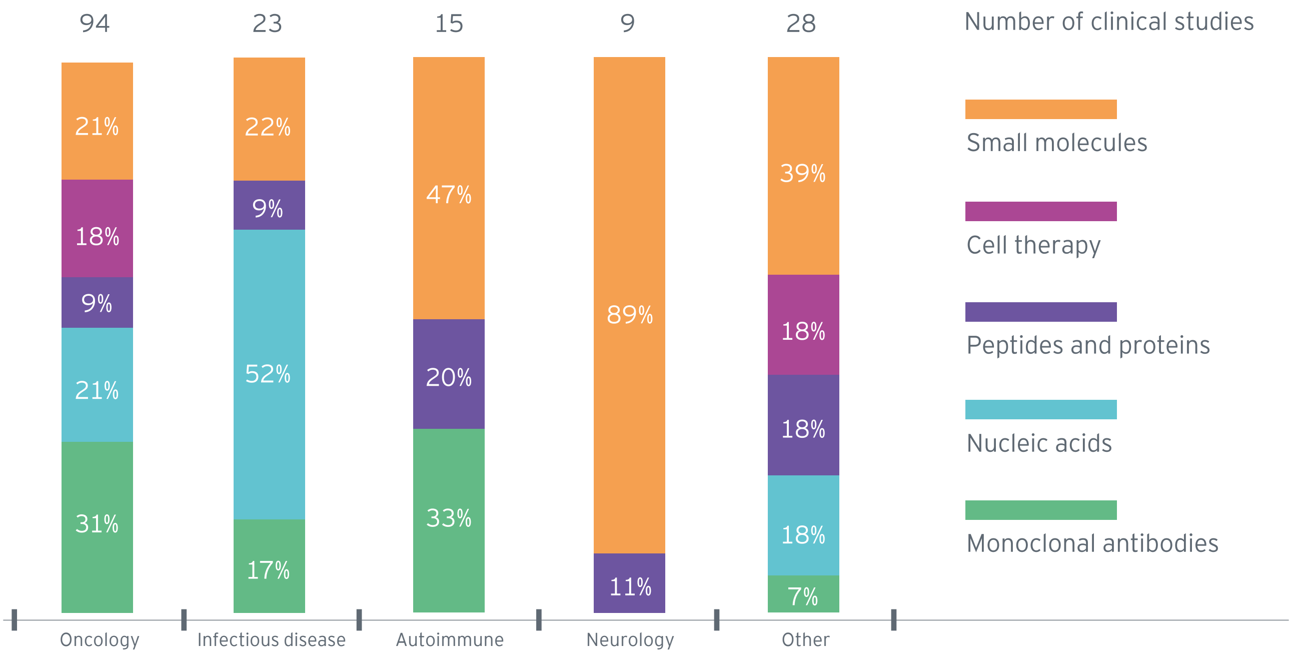
Top German biotech mergers and acquisitions, 2023

Target	Target country	Acquirer	Acquirer country	Potential value €m
InstaDeep	United Kingdom	BioNTech	Germany	500.0
Verogen	United States	Qiagen	Germany	138.6
Theragnostics	United Kingdom	Ariceum Therapeutics	Germany	40.7
Synimmune	Germany	VERAXA Biotech	Germany	32.7
Epigenomics	Germany	New Day Diagnostics	United States	11.1

Sources: EY analysis, company press releases and Capital IQ.

- In the top four M&A deals of 2023, German biotech companies acted as acquirers, looking for inorganic growth to expand their pipeline or technology platforms.
- Accounting for more than 60% of the total potential M&A value recorded in 2023, BioNTech made the most significant German M&A move with the acquisition of UK-based InstaDeep, a leading global technology company in the field of artificial intelligence and machine learning. The acquisition follows a track record of increasing collaboration between the two companies and marks a significant strategic investment aiming to strengthen BioNTech's position in the field of AI-powered drug discovery and development.
- Qiagen's purchase of US-based Verogen was the second most significant deal, strengthening the globally renowned molecular insights provider's leadership in Human ID/forensics with next-generation sequencing tools and technologies.
- Ariceum Therapeutics enhanced its portfolio with the purchase of UK-based Theragnostics, reaping an array of targeted radionuclide therapeutics and diagnostics, and a stronger footing in the US.
- In a domestic deal, VERAXA Biotech acquired Synimmune adding a clinical-stage Fc-enhanced cancer antibody to its proprietary pipeline of novel and differentiated oncology programs.
- Among deals with disclosed values, only one featured a German biotech M&A target being acquired by a foreign entity: US-based New Day Diagnostics acquired all assets of Epigenomics including Epi proColon and Epi proColon "Next-Gen" blood-based screening tests for the detection of early-stage colorectal cancer in a deal valued up to €11.1 million.

German clinical pipeline by therapeutic area and drug class, 2023



Source: EY analysis and Biomedtracker.

- The clinical pipeline of German biotech companies shows a diverse spread of research across different therapeutic areas and drug classes. The majority of assets in clinical studies are biologicals and new modalities like monoclonal antibodies, mRNA and other nucleic acids, peptides, proteins and cell-based therapies. Individual disease areas like neurology and autoimmune diseases are predominantly tackled with small molecules.

- With 94 clinical trials, oncology is the most active therapy area, accounting for more than 50% of all clinical studies. Next to smaller players, BioNTech is asserting its position as the leading innovator in Germany, developing holistic cancer treatments based on multiple platforms, spanning from monospecific antibodies to mRNA and cell-based therapies. Currently, BioNTech is developing more than 20 assets, targeting solid tumors, some of which have very high unmet need.

- The advanced pipelines of MorphoSys and Cardior Pharmaceuticals were pivotal for significant M&A deals in the beginning of 2024. By acquiring all outstanding shares of MorphoSys for €2.7 billion, Novartis aims to acquire the worldwide exclusive rights for the development and marketing of oncology assets Pelabresib and Tulmimetostat, currently in Phase 3 and Phase 2 clinical trials, respectively. In the second mega-deal, Novo Nordisk has agreed to acquire Cardior, a leading developer of RNA-based therapeutics against cardiovascular diseases, for up to €1 billion. Their lead compound, CDR132L, currently in Phase 2, targets non-coding RNA levels in heart cells, potentially reversing negative signaling effects and restoring normal function.

- An innovative example in the field of neurology is Priavoid, who is developing a group of molecules with anti-prionic effect, targeting potentially harmful prion-like oligomers which may be the underlying cause of Alzheimer's and other neurodegenerative diseases. Most notably, PRI-002 is currently being tested in a placebo-controlled Phase 2 study in 270 patients across initially six European countries.

Selected German biotech companies focusing on novel foods

Company	City	Federal state	Business focus
Bluu Bio	Berlin	Berlin	Cell-based fish and seafood products cultivated from fish cells
CellTec Systems	Lübeck	Schleswig-Holstein	Supplier for industrial cell technology and cultivated meat applications
Cultimate Foods	Berlin	Berlin	Cell-based fat for the production of alternative meat from porcine and bovine cells
Esencia Foods	Berlin	Berlin	Cultivated mushroom mycelium for animal-free seafood
Formo Bio	Berlin	Berlin	Precision fermentation for animal-free cheese
Infinite Roots	Hamburg	Hamburg	Cultivated mushroom mycelium to be used in alternative meat products
Innocent Meat	Papendorf	Mecklenburg-Vorpommern	Cell-based meat cultivated from porcine cells as well as animal-free differentiation media
Lovely Day Foods	Berlin	Berlin	Precision fermentation for proteins and flavors to be used in food and beverage products
Microharvest	Hamburg	Hamburg	Precision fermentation for single cell protein to be used in food, pet food and feed
MyriaMeat	Munich	Bavaria	Cell-based meat cultivated from bovine, porcine and cervine cells
Planet A Foods	Planegg	Bavaria	Precision fermentation for sustainable cocoa-free chocolate and palm-oil-free vegan butter
The Cultivated B	Heidelberg	Baden-Wuerttemberg	Cell-based biomass cultivated from mammalian and avian cells as well as cell lines, media and bioreactors for cultivated meat

Source: EY analysis and BIO Deutschland.

- Several innovative biotech companies from Germany are paving the way for sustainable biotech alternatives to conventional food. Their products range from alternative meat and seafood products produced through cellular agriculture to animal proteins such as whey and casein recreated through precision fermentation. Furthermore, they are working on other sustainable offerings like cocoa-alternative and palm-oil-free vegan butter.

- Biotechnologically produced alternatives to animal-derived proteins and other foods have the potential to contribute significantly to feeding a growing world population and to improve the sustainability of their production, e.g., by saving water and arable land, reducing greenhouse gas emissions, protecting forests and natural animal populations, securing biodiversity and preventing animal suffering.

- The approval of food derived from cell culture or precision fermentation is — as other novel foods like newly discovered fruits — strictly regulated in Germany. First approvals have been seen in the US, Singapore and Israel where the regulatory process is more transparent and faster than in the European Union where the regulation on novel foods governs the market access. In the EU, companies often must cope with lack of information and transparency or inadequate advice for market approval.

- Multiple cultivated meat market forecasts released in 2022 (Euromonitor, Barclays, GovGrant) predict double-digit shares of the global meat market by 2040 ranging between 10% and 35% of total meat sales.

- In a representative survey by the Good Food Institute, about 60% of Germans of all ages expressed openness to consuming cultivated meat, with acceptance soaring to over 80% among Generation Z, typically born between 1997 and 2012.

DATA EXHIBIT INDEX

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DEFINING BIOTECH COMPANIES

In the German biotech report, unless otherwise noted, EY and BIO Deutschland jointly analyze companies whose primary business focus is the commercialization of modern biotechnology. These companies are involved in the development or production of therapeutics, diagnostics, specialty chemicals, and novel foods as well as transgenic microorganisms, plants, and animals.

This definition encompasses a broad range of technologies and services within these areas such as recombinant DNA, cDNA, RNA, biochips, antibodies, proteins, tissue engineering, biological assays, cell cultures, cell therapy, gene therapy, drug delivery, molecular diagnostics, bioinformatics, and modern plant biotechnology.

However, it does not include companies that leverage classical biotechnological methods such as those used in traditional food production, along with solely analytical techniques, microscopic diagnostics, diagnostic devices, common immunology technologies, biotech product distributors, and traditional pharmaceutical as well as agro-industry companies.

Publicly traded German biotech companies analyzed for 2023:

- 4SC AG
- Affimed N.V.
- atai Life Sciences N.V.
- Biofrontera AG
- BioNTech SE
- BRAIN Biotech AG
- CENTOGENE N.V.
- CureVac N.V.
- Evotec SE
- Formycon AG
- Heidelberg Pharma AG
- Immatics N.V.
- Immunic, Inc.
- InflaRx N.V.
- Mainz Biomed N.V.
- Medigene AG
- MorphoSys AG
- TME Pharma N.V.
- Pieris Pharmaceuticals, Inc.
- QIAGEN N.V.
- Vivoryon Therapeutics N.V.

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