

# 2021

**Value through  
Innovation**

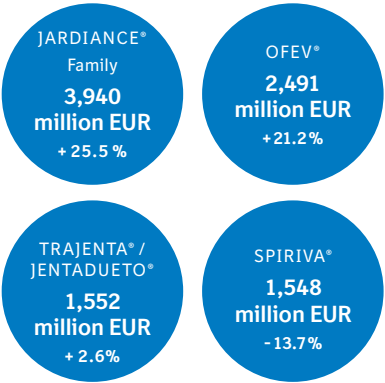
## Financial Highlights

Amounts in million EUR, unless otherwise indicated	2021	2020	Change
<b>Net sales</b>	<b>20,618</b>	<b>19,566</b>	<b>+ 5 %</b>
by region			
Americas	44 %	45 %	
Europe	32 %	30 %	
Asia/Australia/Africa (AAA)	24 %	25 %	
by business			
Human Pharma	74 %	74 %	
Animal Health	21 %	21 %	
Biopharmaceutical Contract Manufacturing	4 %	4 %	
Other sales	1 %	1 %	
Research and development expenses	4,127	3,696	+ 12 %
Personnel expenses	5,692	5,587	+ 2 %
Average number of employees	52,391	51,944	+ 1 %
Operating income	4,705	4,624	+ 2 %
Operating income as % of net sales	22.8 %	23.6 %	
Group profit	3,406	3,062	+ 11 %
Group profit as % of net sales	16.5 %	15.6 %	
Group equity	19,331	17,307	+ 12 %
Investments in tangible assets	968	1,046	- 7 %
Depreciation of tangible assets	609	602	+ 1 %

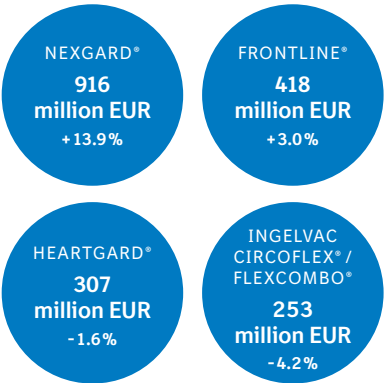
# Summary Report 2021



### Top 4 products – Human Pharma (Net sales 2021)



### Top 4 products – Animal Health (Net sales 2021)



# TOMORROW



Research for a  
Healthier Future



Boehringer  
Ingelheim

# Boehringer Ingelheim

## 2021 at a glance

Founded in

**1885**

in Ingelheim and  
family-owned  
to this day

**52,391**

employees worldwide

thereof

**10,109**

in Research,  
Development  
and Medicine

**4.1**

billion EUR expenditure in  
Research and Development

equivalent to

**20.0%**

of total net sales

### Business Units

Human Pharma

**15.3**

billion EUR

Animal Health

**4.3**

billion EUR

Biopharmaceutical  
Contract Manufacturing

**917**

million EUR

#### THERAPEUTIC AREAS

- Cardiovascular and metabolic diseases
- Oncology
- Respiratory diseases
- Immunology
- Central nervous system
- Retinal health

#### BUSINESS SEGMENTS

- Pets
- Swine
- Poultry
- Cattle/Ruminants
- Horse
- Veterinary Public Health

#### PORTFOLIO

- Joint development, launch, and manufacturing activities for own biopharmaceutical products
- Contract development and manufacturing for clinical and commercial biopharmaceuticals in the external customer business
- Process transfer within the global biopharmaceutical supply network



**Boehringer Ingelheim develops breakthrough  
therapies that transform lives, today and  
for generations to come.**

**Independent and family-owned, we pursue  
our long-term vision to identify tomorrow's  
challenges, relentlessly seeking for solutions  
that target areas of unmet medical need.**

**This is captured in our purpose  
*Transforming Lives for Generations*, which  
inspires all of our more than 52,000  
employees to make a significant difference  
to human and animal lives.**

Hubertus von Baumbach  
Chairman of the Board of Managing Directors

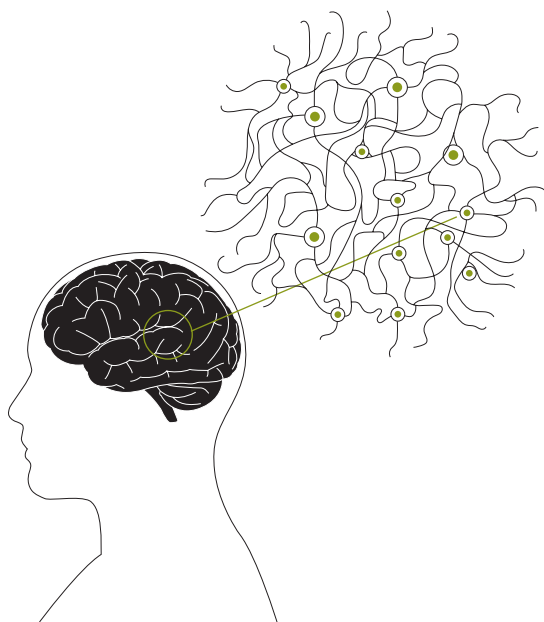


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Sea-ice physicist Stefanie Arndt was part of the MOSAiC expedition into the Central Arctic



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Boehringer Ingelheim is committed to advancing Research into the central nervous system (CNS)

Clive Wood is building a portfolio of first-in-class innovation for cancer patients



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Cover:

Rachel Nti, Trainee Biology Lab Technician  
at the Biberach Site, Germany



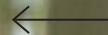




PERSPECTIVES

# **“A better tomorrow” – what does that look like for you?**

**We asked employees from  
all over the world.**



**Orlando Carrasco**  
Value Added Services Manager  
Mexico City, Mexico  
with Boehringer Ingelheim since 2007





**“For me, a better tomorrow is one where our children will have the opportunity to enjoy a cleaner planet and a healthier life, using science and collaboration to fix the challenges and make it happen.”**

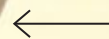
Orlando Carrasco develops programs that empower patients to take control of their diseases and help them to better adapt their lifestyle based on their condition. Along with medications, this helps to improve the quality of life of patients.



**Orlando Carrasco**  
Value Added Services Manager  
Mexico City, Mexico  
with Boehringer Ingelheim since 2007







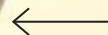
**Aiko Watabe**  
Head of Clinical Operations Japan  
Yokohama, Japan  
with Boehringer Ingelheim since 2010





**“I would like to see a world where people have equal opportunities to learn and grow – and where they have access to what they are entitled to for a healthier life.”**

Aiko Watabe ensures that the delivery of clinical trials and the development of innovative treatments for patients strongly contribute to a healthier future for them.



**Aiko Watabe**  
Head of Clinical Operations Japan  
Yokohama, Japan  
with Boehringer Ingelheim since 2010







←  
**Tony Davison**  
Business Unit Manager New Zealand  
Auckland, New Zealand  
with Boehringer Ingelheim since 1984







**“For me, a better tomorrow is about improving equity and health outcomes for those populations within our community who need support, guidance, and a genuine opportunity to access healthcare – whether that be lifestyle access or access to medicines.”**

Tony Davison’s goal is to achieve equitable access to healthcare for all people in New Zealand. To achieve that, it is critical to have an open mind, as an individual and as a company, and be willing to engage and collaborate differently, such as establishing non-traditional community partnerships.



**Tony Davison**  
Business Unit Manager New Zealand  
Auckland, New Zealand  
with Boehringer Ingelheim since 1984

# For a Better



# Tomorrow

**What would a better tomorrow look like? Dr. Stefanie Arndt is sure that research is crucial. The sea-ice physicist collects samples and data in the Arctic and Antarctica to provide recommendations on how to achieve a better tomorrow. In this essay, Arndt presents her work and calls for a stronger commitment to science.**

Together with a handful of colleagues, I am drifting on an ice floe in the Antarctic Ocean. The helicopter that dropped us off here has already disappeared and our research vessel is several dozen miles away. We are enveloped by the polar day. The ice floe we currently find ourselves on is only around half a mile in size. Below me is around a foot of snow followed by an ice layer that is about three feet thick. And beneath that is an ocean several thousand feet deep.

This is one of the places I work as a sea-ice physicist. I use a thermometer and a magnifying glass to examine the snow that lies on the ice floe. I assess its crystal structures and measure its density. I take samples through a vertical profile. The snow tells us what has happened here over the past year. For instance, if it was warm for a spell, then I will find lenticular ice layers inside the samples.

We can look even further back into the past if we examine Antarctic land ice. It consists of compacted snow whose



**“Scientific work is of fundamental significance when it comes to achieving a better tomorrow.”**

**Meet Stefanie Arndt**



deeper layers are many thousands of years old and thus serve as a climate archive: We are able to determine the composition of the past atmosphere through the microfine air pockets inside this ice.

We cannot save the world through our research, but like the work of so many scientific disciplines, it is of fundamental significance when it comes to achieving a better tomorrow. In the field of climate change, for instance: Only if we are able to gain a precise understanding of how our planet has changed in the past and will continue to do so in the future will we be able to provide recommendations for policy-makers and society. For this purpose, we evaluate the data that nature in the polar regions provides us with and model it at research centers such as the Alfred Wegener Institute in Bremerhaven, Germany, my employer.

I consider it a positive sign that public debate over climate change has strengthened the role of science. My work and that of my colleagues now



# 40%

The sea ice extent has declined by an average of about 40 percent since 1979. On September 12, 2021, its annual minimum was 1.87 million square miles; the previous all-time low was 1.26 million square miles in 2012. The annual extent is quite variable and reaches its minimum in September. The trend indicates a decrease of ten percent per decade.

has a profile and attracts a great deal of attention in the media. People know that the thawing of the polar ice caps is directly associated with man-made emissions of greenhouse gases. Our research vessel, the Polarstern, is one of the world's best icebreakers, and we receive support through public funding. Many people have understood that we must make decisions on the basis of scientific evidence.

I have noticed a similar effect as a result of the COVID-19 pandemic in terms of health research and the role scientific facts play in medicine. While this pandemic is terrible, it has triggered a necessary discussion over the importance of medical research. Broad swaths of societies around the globe are following the advice of virologists and other scientists to whom they would never previously have paid so much attention. Most political decision makers are likewise actively listening to science more than ever before.

Science has a growing reputation – in Germany, Europe, and around the world. But the research environment is not always what it should be. If we want to strengthen the role of science in order to achieve a better tomorrow on a sustainable, ongoing basis, then we must first of all think of young scientists. We need to make it attractive for them to opt for an academic career.

### Right Time to Invest in Research

Unfortunately, that is not how things are at the moment. Many research projects are uncertain because their financing in the form of grants and project funding is frequently only guaranteed on a short-term basis. The personal insecurity for young researchers, who go from one temporary contract to the next and whose personal lives suffer accordingly, is even more serious.

**“If we want to strengthen the role of science in order to achieve a better tomorrow, then we must first think of young scientists. We need to make it attractive for them to opt for an academic career.”**





Stefanie Arndt was most recently with the research ship Polarstern in the Arctic Sea from February to June 2020.

Now is the right time to invest more money in scientific research. This is the only way to tackle fundamental challenges for mankind such as mitigating climate change and coping with pandemics.

### Science is All about Communication

Here, science also needs to be much more open in relation to society and to communicate its findings to the general public in a way that is both exciting and understandable. When we allowed ourselves to become icebound on the Polarstern in the Arctic sea ice in October 2019 in order to drift around 2,100 miles across the Arctic until September 2020, we had a film team on board who subsequently released a successful documentary. We need much more of that kind of activity. I myself was on board of the Polarstern from February to June 2020 and thereafter talked about my experience to the media, at schools, and on many other occasions. After all, science is also about communication.

What is my personal vision of a better tomorrow? I dream of a future where we have found answers to the key challenges of everyday life. There will still be risks such as flooding, drought, and diseases in this tomorrow. But the business sector and science, society and politics will be able to identify these risks, provide people with feasible alternatives, and thus allay their fears. All of this will require a great deal of effort. Let's work on it together.



### DR. STEFANIE ARNDT Sea-Ice Physicist at the Alfred Wegener Institute

Stefanie Arndt, born in 1988, is a post-doctoral researcher and sea-ice physicist. She took part in the MOSAiC expedition, on which 300 scientists from 20 countries joined a ship that was frozen into the ice of the Arctic Sea and drifted with the ice masses for a year from September 2019 to October 2020.

The MOSAiC expedition was the largest polar expedition in history. Its goal was to take the closest look ever at the Arctic as the epicenter of global warming and to gain fundamental insights that are key to a better understanding of global climate change.

# 2021 in Focus

## November

### Further development of the sustainability framework

Under the headline “Sustainable Development – For Generations”, Boehringer Ingelheim announces a comprehensive update of its sustainability framework. Among other measures taken, the company is investing in innovation and partnerships to provide access to healthcare for 50 million people in vulnerable communities.



## October

### Inauguration of the new biopharmaceutical production facility

With the opening of the Large Scale Cell Culture (LSCC) production building in Vienna, Austria, the company completes the single largest capital investment in its history and maintains its leading position in biopharmaceutical contract manufacturing.



### Highly automated tablet factory opens

Boehringer Ingelheim opens the Solids Launch Factory (SOL) at the Ingelheim site. This is where all newly launched medicines in tablet form (solids) are manufactured for the global market.



### Additional investment in veterinary vaccine capacity

Boehringer Ingelheim invests an additional 100 million EUR in its veterinary vaccines production facility in Lyon, France. The goal is to better support government authorities and public health organizations in dealing with emerging cross-border diseases.

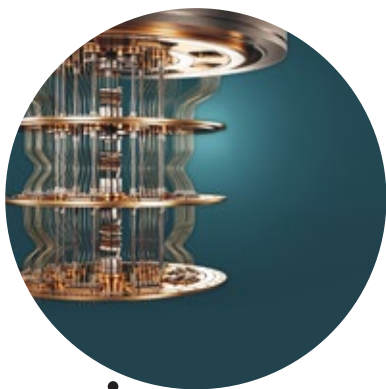


## September

### 75 years of the Biberach site

Boehringer Ingelheim's largest research and development site celebrates its anniversary.





## January

### Advantage through quantum computing

Boehringer Ingelheim and Google Quantum AI are collaborating to develop future use cases for quantum computing in pharmaceutical research and development.



## February

### Global Top Employer

Boehringer Ingelheim is one of 16 companies worldwide to be recognized as a Global Top Employer.



## March

### PRADAXA® for children

PRADAXA® is approved in the European Union as the first treatment option for venous thromboembolism (VTE) in children. Approval in the US followed in June 2021.



## May

### Help with schizophrenia

The US Food and Drug Administration (FDA) grants Breakthrough Therapy Designation for BI 425809, a novel glycine transporter-1 (GlyT1) inhibitor, for the treatment of cognitive impairment associated with schizophrenia (CIAS).



### Treatment of horses in China

Boehringer Ingelheim becomes the first multinational company in China to receive approval for a drug for horses. The product GASTROGARD® is used to treat and prevent gastric ulcers in horses.



## June

### JARDIANCE® for heart failure

With EU approval, JARDIANCE® (empagliflozin) can now be prescribed to treat heart failure with reduced ejection fraction (HFrEF) in patients with or without type 2 diabetes. US approval followed in August 2021. In addition, positive results in July 2021 confirm EMPEROR-Preserved as the first and only successful trial on heart failure with preserved ejection fraction (HFpEF).





HUMAN PHARMA

# On the Cusp of a Revolution

**There are more than 450 million people worldwide living with mental health conditions like depression or schizophrenia. Research into the central nervous system (CNS) seems largely stagnant compared to the constant advances in other medical fields. Boehringer Ingelheim is committed to changing that. Precision psychiatry has the potential to reform clinical practice from the ground up and provide effective treatment for millions of people.**

The CNS research teams at Boehringer Ingelheim have set themselves some ambitious objectives. To better understand these objectives, it's worth considering the maxim that the better our understanding of a disease and what causes it, the more effective and targeted our treatment will be. Or to put it in simpler terms: knowledge comes before treatment.

This has been the fundamental principle driving progress in nearly every medical field in recent decades; as researchers learned more and more about the biological mechanisms underpinning a disease, new and increasingly precise treatments would be developed a short while later. This principle also led to the scientific community differentiating between the various forms of a disease, each of which has a specific and effective treatment.

### Tracking Down Biological Causes

There is one field of medicine which has seen very little progress over the years, however. “When it comes to psychiatry, we still tend to diagnose people based purely on their symptoms rather than the biological cause of the symptoms. This antiquated approach makes it very difficult to develop new therapeutics to provide people with more effective and focused treatments,” said Dr. Hugh Marston, Head of CNS Diseases Research at Boehringer Ingelheim. “It’s something we want to change.” The “we” in that sentence mainly refers to three teams at Boehringer Ingelheim that work together closely: Marston and his Discovery Research team; Dr. Vikas Sharma, Head of Medicine CNS, Retinopathies & Emerging Areas (TA CREA); and Dr. Joachim Scholpp, Head of Translational Medicine & Clinical Pharmacology CNS, Retinal Health & Emerging Areas (TA CREA).

These teams play their part in the drug development pipeline by performing basic research into the biological causes of psychiatric disorders. “Our brains contain a tremendous number of functional neural circuits. Disruption to specific circuits can result in specific symptoms. The journey of finding an effective substance begins with understanding which circuits are defective and how we can recognize that in an individual,” said Scholpp. The goal is to usher in a new era of precision psychiatry, which draws its meaning from the term precision medicine.

Researchers at Boehringer Ingelheim have already discovered nine new drugs for psychiatric indications based on this approach, some of which now have the preclinical development phase in their rear view mirror. One example is the GlyT-1 inhibitor BI 425809,



**“Psychiatrists base their diagnosis on a patient’s symptoms. That makes it extraordinarily difficult to provide people with focused treatment.”**

Dr. Hugh Marston,  
Head of CNS Diseases Research  
at Boehringer Ingelheim

which appears to improve cognition in adults with schizophrenia. It entered Phase III trials in summer 2021.

Another good example of this groundbreaking work is the inhibitor BI 1358894, currently in Phase II. BI 1358894 focuses on parts of the brain which regulate our emotions. “If I’m walking around in the city and hear a loud bang on my left, I would instinctively run in the opposite direction,” explained Marston. “Your brain diverts energy from everything else, like your ability to socialize and your digestive system – it is laser-focused on getting you out of danger.”

People do react differently, though. If your baseline activity is too high or too low, you will reach a trigger point much more quickly than you should. As a result, patients may respond inappropriately to the everyday challenges of life. Magnetic resonance imaging (MRI) can be used to determine whether the neural circuitry is functioning properly. “This disruption causes changes to how a patient processes emotions.

Our inhibitor has the potential to get the emotional system back in balance,” explained Marston. Borderline personality disorder, depression, and post-traumatic stress disorder can involve emotional dysregulation. “That’s why we clinically test BI 1358894 for all three indications,” explained Scholpp.

### Looking for Biomarkers

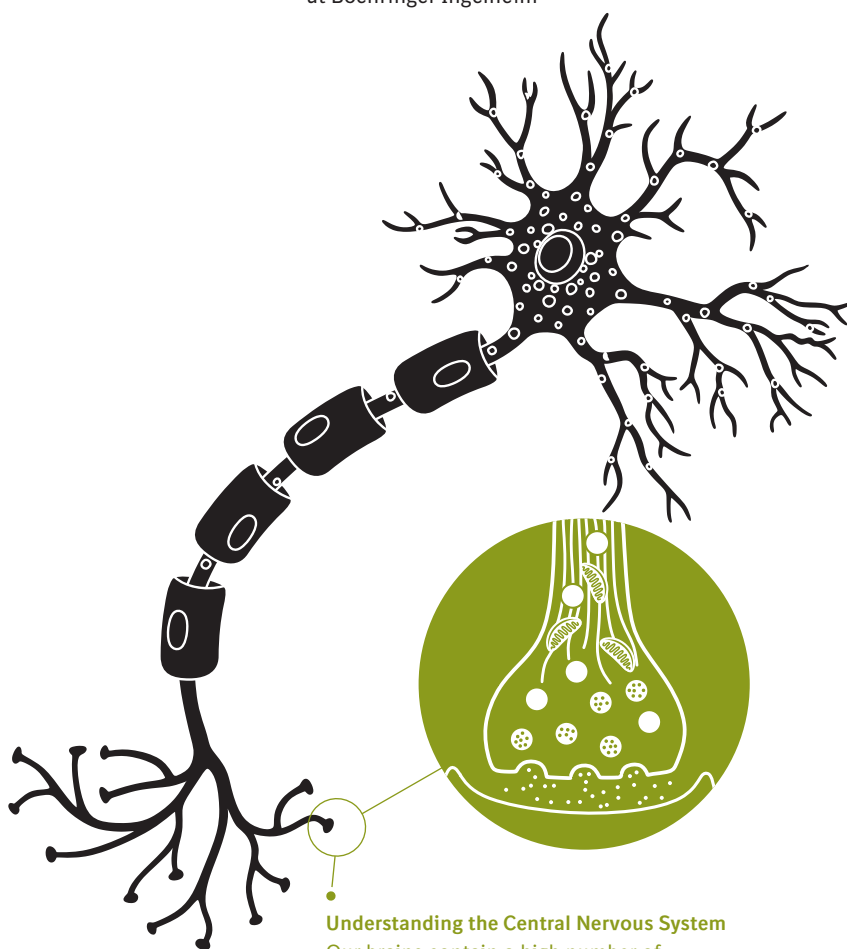
At present, we still distinguish between psychiatric disorders based on the symptoms that can be observed, rather than the underlying dysfunction of a patient’s neural circuits. Experts of Boehringer Ingelheim are discussing the issue with decision makers across the healthcare system – from the medical professionals who have a significant say on treatment guidelines to health insurance providers and regulatory authorities. “Our transdiagnostic approach has the potential to develop medicines that are truly innovative and improve the lives of patients suffering from psychiatric diseases,” said Scholpp.

Marston and his colleagues are also working on another challenge: looking for the biomarkers which would make it easy and cost-effective to detect disruption in neural circuits. “It’s really easy to tell if a patient’s brain is functioning as expected from an MRI. But it’s just not possible to include an MRI for every patient in a clinical routine. That would be incredibly expensive,” said Marston. That’s why the team is looking for other markers and methods which would make it easier to identify dysfunction in the neural circuits. These could include analyzing the concentration of specific substances in the blood or asking patients to fill out a questionnaire about their impulses, or possibly in the future a digital app (see page 21).



**“Our transdiagnostic approach has the potential to develop medicines that are truly innovative and improve the lives of patients suffering from psychiatric diseases.”**

Dr. Joachim Scholpp,  
Head of Translational Medicine & Clinical  
Pharmacology CNS, Retinal Health & Emerging Areas  
at Boehringer Ingelheim



**Understanding the Central Nervous System**  
Our brains contain a high number of functional neural circuits. Disruption to specific circuits can result in symptoms.

# “Genuinely ground-breaking work”

**The focus of Boehringer Ingelheim on understanding the biological mechanisms that cause mental health disorders is visionary, says Dr. Hugh Marston. This approach is one of the reasons why Marston joined the company in 2020.**

**Hugh, you have been involved with psychiatric research since 1987 and joined Boehringer Ingelheim in 2020. What caused you to choose this company specifically?**

Well, it didn't hurt that Boehringer Ingelheim seemed enthusiastic about me joining the company (laughs). Another thing that attracted me was the fact that with the commitment of Boehringer Ingelheim to the area I would have the freedom and resources to do basic research and start to change the mindset in psychiatry. The company had already made a brave decision to stay in psychiatric research and made a significant investment by bringing in a pool of experts. We now have around 50 employees involved in fundamental CNS research and early drug discovery. There aren't many other pharmaceutical companies with a CNS research team of that size and expertise.

**Why do you think that is?**

Psychiatry hasn't really changed in decades. The biological causes of a large number of mental health disorders are still a mystery. Diagnosing patients based solely on their symptoms and selecting a treatment is still more art than science. Take depression,

for example: you might feel temporarily depressed if you experienced the death of someone close to you. But that's not the same as having clinical depression, though it may well be the starting point. Determining the transition from a normal to an abnormal emotional response is difficult.

**Does that mean that we need to improve the way in which we diagnose disorders before we can develop better treatments?**

Yes, and this requires patience and tenacity. Academic researchers are doing important work, but they need more support. Boehringer Ingelheim is fully prepared to get involved. We work together with a lot of partners – like King's College London, where we're probing the brain circuits involved in depression and cognition. We feel like we're on the brink of something really special.

**You already have a few substances in development.**

Yes, I inherited a fascinating pipeline from my predecessor. It's, for instance, incredibly exciting to have a program moving into Phase III development for cognition in schizophrenia that has the potential to break the mold in that area of psychiatry. We are improving

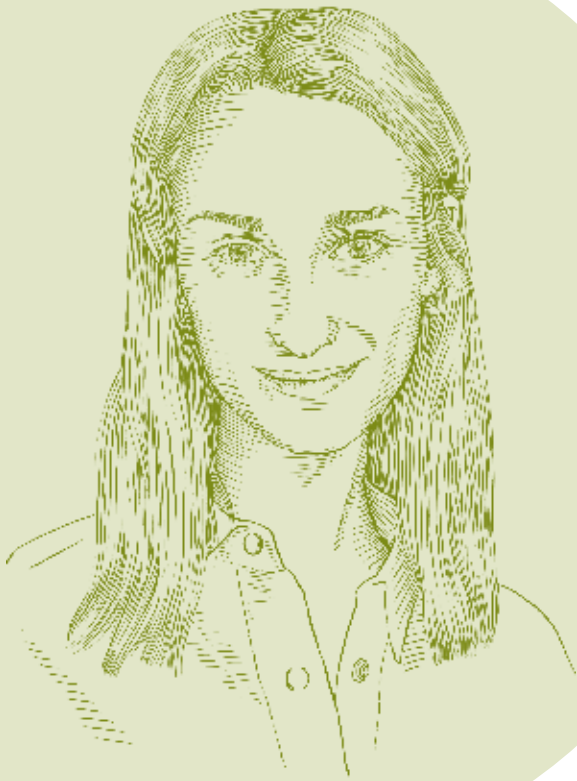
**DR. HUGH MARSTON**  
**Head of CNS Diseases Research**

Hugh Marston studied biology, then gained a PhD in Experimental Psychology at Cambridge before joining Boehringer Ingelheim as Head of CNS Diseases Research in May 2020. Prior to that, he held positions at several pharmaceutical companies, helping to take two compounds to market.

our understanding of mental illnesses by approaching them from a completely new direction, increasingly focusing on the brain circuits that are malfunctioning.

**What is your vision?**

I believe that my grandchildren's generation will live in a world where it will be relatively simple to identify which part of your brain circuitry isn't working quite right, before this majorly disrupts your life. This information will then allow the doctor to select the optimal treatment, quite possibly a combination of drug and digital approaches.



## Staying above Water

**Yammie was diagnosed with schizoaffective disorder when she was 24 – after a year-long journey. Today, she is living a self-determined life. Based on her biography, she knows there is reason for hope, but it all depends on coming up with a correct and timely diagnosis.**

Yammie experienced her first symptoms when she was a small child. “I saw beautiful colors and heard a voice speaking to me,” she recalls. When she was a teenager, Yammie started to feel depressed and frightened. She heard three voices, the psychosis completely took over. “I was driven to despair and had even tried to commit suicide.” She saw psychologists who came up with many different diagnoses. She was already 24 years old, when she got diagnosed with schizoaffective disorder. “It has been a real journey.”

The doctor was not optimistic for Yammie. He expected her symptoms to get worse. He told her she would most likely not be able to go to college, but would probably spend the rest of her life in the hospital.

### **Yammie Reached out for All Kinds of Support**

Nevertheless, the young woman refused to accept that. Instead, she started fighting. She took a course for patients, in which extensive knowledge about the disease and the background was imparted. There, Yammie met Jurgen, a patient dealing with depression. They became friends and helped each other battle their demons. “We didn’t have to pretend that everything was OK. We could be honest with each other and understood what the other was going through,” Yammie explains. Yammie continued her therapy with Jurgen’s help.

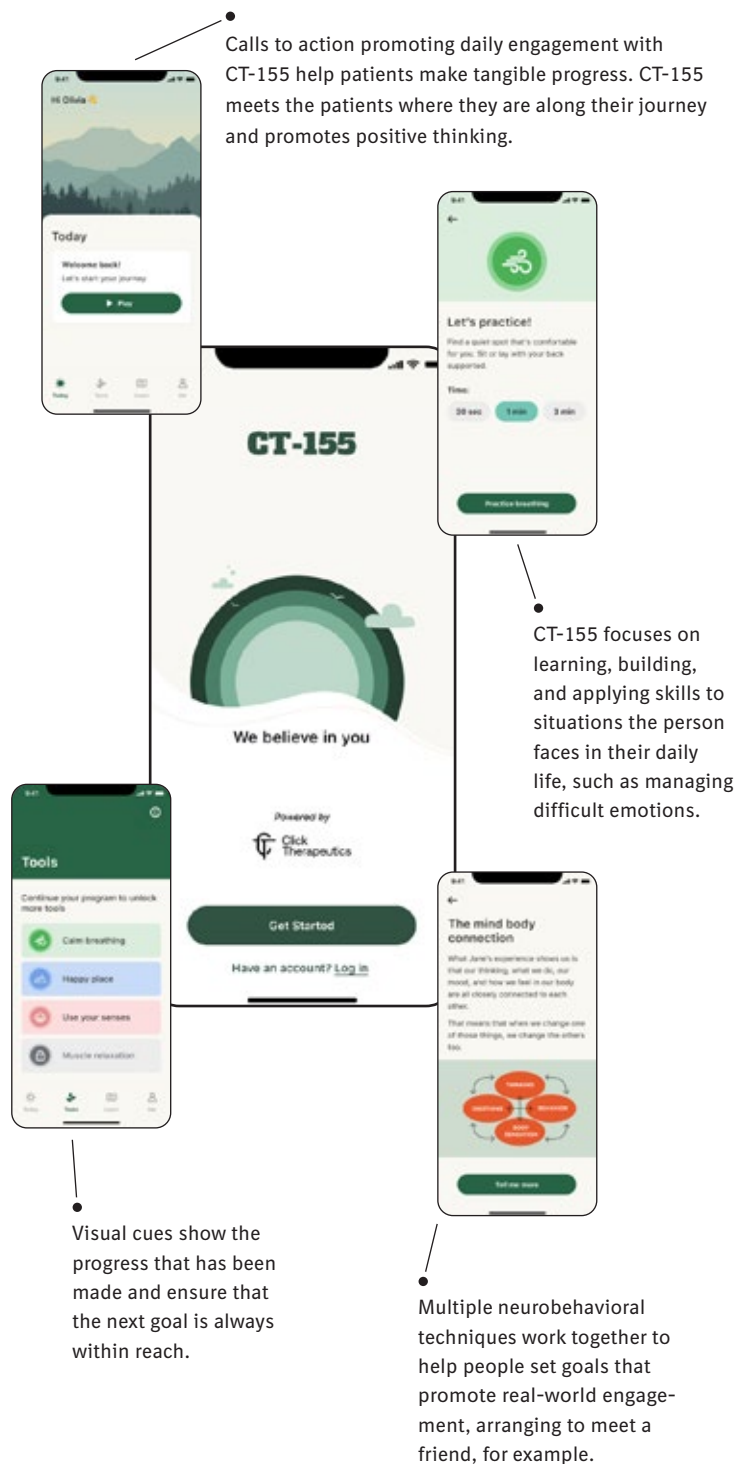
Yammie has now been living a self-determined life for more than four years. “It’s a hard fight from time to time to stay above water – but I have the feeling that I have managed this well, and I’m happy.” This would not have been possible without the correct diagnosis. “A diagnosis can be a curse for some people, but I know it can be a real relief for others. For me, it was a relief because I knew it had a name, and there was treatment for it.”

## Making a Difference with Digital Technology

Digital innovation has the potential to offer new health solutions to patients and the health-care system. Digital Health is growing rapidly, and acceptance by patients, physicians, and health insurance companies is rising fast. In fact, recent surveys have shown that 84 percent of people with mental illnesses who own a smartphone are willing to download an app that helps them with their condition.


Schizophrenia is a complex and multi-faceted condition. Various pharmacological medications for treating the psychotic symptoms, such as hallucinations, delusions, and confusion, are available to people diagnosed with schizophrenia. However, people with schizophrenia can still remain functionally impaired due to insufficient treatment of other core symptoms of the disease, such as cognitive symptoms, anhedonia, or loss of interest and motivation.

Boehringer Ingelheim is collaborating on CT-155, which will address key unmet needs in the treatment of schizophrenia. As an adjunct to pharmacotherapy, CT-155 is intended to offer patients an engaging and accessible psychotherapeutic intervention. This digital therapeutic (DTx) which will prove its therapeutic efficacy in clinical trials and be approved by the health authorities is guided by the underlying science of Cognitive Behavior Therapy and combines multiple therapeutic interventions to help patients modify their behavior and train new skills.





# One Substance to Treat Various Diseases



Understanding the connections between different diseases can provide the key to using the same drug to treat a variety of disorders. By working together across different areas of study, researchers from Boehringer Ingelheim are discovering new treatments for severe diseases and disorders, including heart failure.



Boehringer Ingelheim has been researching the interactions between different diseases for many years. “We draw on this experience to uncover the links between diseases and find more effective ways to treat them,” said Dr. Søren Tullin, Global Head of Cardiometabolic Diseases Research at Boehringer Ingelheim.

An open-door policy helps make this happen. “Our researchers use working groups, office visits, and video calls to stay in touch and share the latest information between divisions,” said Tullin. Thanks to their methodical research, innovative thinking, and a drop of luck, the experts at Boehringer Ingelheim recently demonstrated the beneficial impact that empagliflozin can have for people with heart conditions.

#### **Type 2 Diabetes – a Global Health Problem**

More than 460 million adults worldwide have diabetes, of which approximately 90 percent have type 2 diabetes, the majority thereof caused by being overweight and a lack of exercise. The prevalence of the disease is increasing in many countries – even among children and adolescents. Studies have shown that type 2 diabetes in connection with cardiovascular disease can reduce the lifespan by up to twelve years. The risk of dying from cardiovascular disease is up to two times higher in people with diabetes.

The body functions affected by diabetes interact in complex ways: High blood sugar can lead to fatty deposits in blood vessels, constricting the arteries and lowering the amount of oxygen available to the body. Blocked coronary arteries can lead to a heart attack and heart failure.



**“Our researchers use working groups, office visits, and video calls to stay in touch and share the latest information between divisions.”**

Dr. Søren Tullin,  
Global Head of Cardiometabolic Diseases Research  
at Boehringer Ingelheim

Heart failure takes many forms. One of them is heart failure with reduced ejection fraction (HFrEF). This happens when the muscle of the left ventricle is damaged and unable to pump enough blood into the circulatory system. Another variation is heart failure with preserved ejection fraction (HFpEF), where the left ventricle is stiffer than normal and there is less blood in the ventricle, not allowing the body to get enough oxygen.

#### **Hope on the Horizon for People with Heart Conditions**

Heart failure is a common problem, affecting more than 60 million people worldwide. Approximately half of them suffer from heart failure with preserved ejection fraction, a condition for which treatment options have been limited. “Until recently, we didn’t really have any treatment for patients with heart failure with preserved ejection fraction that had a solid scientific basis,” said Dr. Waheed Jamal, Head of Medicine Therapeutic Area Cardiometabolism & Respiratory at Boehringer Ingelheim.



**“This is a breakthrough in cardiovascular medicine and brings hope for millions of patients suffering from heart failure with preserved ejection fraction.”**

Dr. Waheed Jamal,  
Head of Medicine Therapeutic Area Cardiometabolism &  
Respiratory at Boehringer Ingelheim

That won't be the case for much longer, according to the EMPEROR heart failure trials undertaken by the Boehringer Ingelheim and Lilly Alliance that explore the safety and efficacy of empagliflozin in patients with chronic heart failure with reduced and preserved ejection fraction. The EMPEROR trials found that the drug significantly reduced the risk of cardiovascular death or hospitalization for patients with heart failure with preserved ejection or with reduced ejection fraction, regardless of whether a patient had type 2 diabetes or not. In June 2021, the European Commission and in August 2021, the US Food and Drug Administration (FDA) already granted marketing authorization for JARDIANCE® (empagliflozin) as a treatment for adults with symptomatic chronic heart failure with reduced ejection fraction (systolic heart failure). The marketing authorization as a treatment for adults with heart failure with preserved ejection fraction was granted by the FDA in February 2022. “This is a breakthrough in cardiovascular medicine and brings hope for millions of patients suffering from heart failure with preserved ejection fraction,” said Jamal.

The drug may also have a beneficial effect further afield. Boehringer Ingelheim is now looking into whether it could have a positive impact on other chronic conditions. “Based on what we have seen so far for the SGLT2 inhibitor class, we are hopeful that empagliflozin will be beneficial in a broad range of chronic kidney disease patients studied in our EMPA KIDNEY trial and for the prevention of heart failure following a heart attack in our EMPACT-MI trial.” If the trials continue to be successful, empagliflozin could improve the lives of even more patients worldwide.

#### THE OBESITY PANDEMIC

Obesity is a chronic disease that results from an imbalance between energy intake and expenditure. The global rates of obesity have seen a dramatic increase in the last decade, with some describing it as a pandemic. Worldwide, obesity has nearly tripled since 1975. It is considered an epidemic and the largest chronic disease globally. The World Health Organization (WHO) estimated in 2016 that more than 1.9 billion people, 18 years and over, were overweight and, of these, over 650 million were obese. Obesity is associated with serious complications and is the root cause of multiple associated diseases including type 2 diabetes mellitus, hypertension, chronic kidney disease, non-alcoholic steatohepatitis (NASH), and pain – resulting in tremendous societal burden.

Weight loss not only prevents but also effectively treats the obesity-related comorbidities. As an example, efficient and sustained weight loss results in the long-term remission of diabetes and a highly significant reduction in cardiovascular risk.


Boehringer Ingelheim is working on innovative concepts to meet the high demand for new anti-obesity therapies with a focus on superior and sustainable weight loss, as well as fewer side effects than current therapies.

**> 60 million**

people worldwide are affected by heart failure, a progressive and potentially fatal disease.

**~50%**

of people with heart failure die within five years after diagnosis.



### HEART FAILURE with preserved ejection fraction (HFpEF)

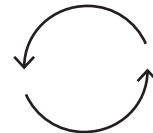
The heart muscle contracts normally but the left ventricle is not able to relax meaning that the heart cannot properly fill with blood during ventricular filling.

### Heart Attack ≠ Heart Failure


A heart attack occurs suddenly and unexpectedly when the flow of blood to the heart is blocked. Damage to the heart muscle from a heart attack may lead to a state where the heart can no longer pump as well as it should and typically results in the death of part of a heart muscle. This raises the risk of heart failure. Heart failure is a condition in which the heart muscle no longer functions properly. It is progressive and can be fatal.



The heart is responsible for pumping the right amount of blood throughout the body. This is important because the blood carries oxygen and nutrients that our organs need to work properly.



Because of the interconnectivity of the heart with other organs, people with heart failure have a high risk of having or developing other conditions such as kidney disease and type 2 diabetes.

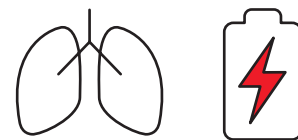


### HEART FAILURE with reduced ejection fraction (HFrEF)

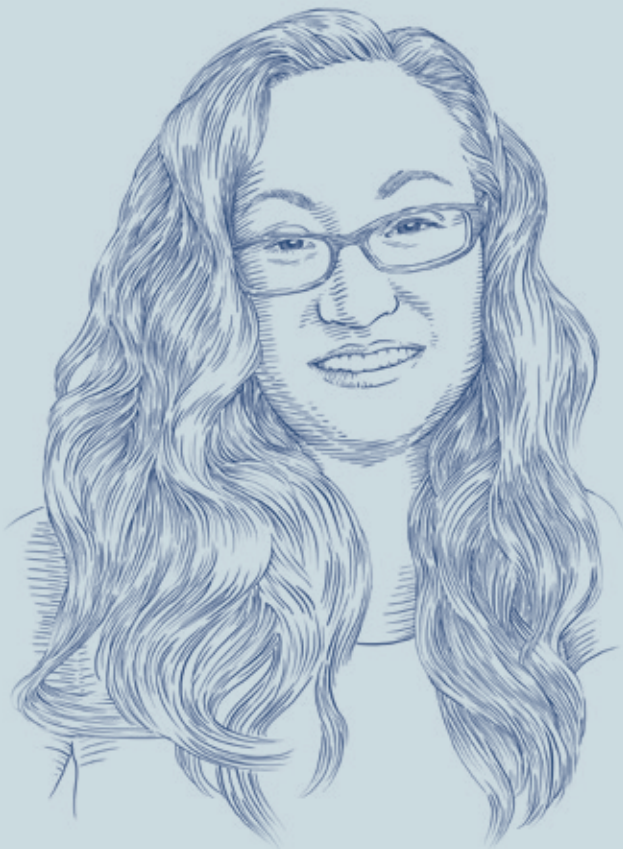
The left ventricle does not contract effectively, and less blood is pumped out to the body compared to a normally functioning heart.

**1/5**

people are expected to develop heart failure in their lifetime.



Heart failure occurs when the heart is unable to supply adequate circulation to meet the body's needs. Symptoms include, amongst others, breathlessness, fatigue, and accumulation of excess fluid leading to swelling, e.g. in the ankles.



Christine Jones

HUMAN PHARMA

# GPP Affects My Entire Life



Meet Christine Jones

**Generalized Pustular Psoriasis (GPP) is a rare heterogeneous and potentially life-threatening skin disease. It causes painful sterile pustules all over the body. So far, little is known about living with this disease.**

Christine Jones lives on the east coast of the United States with her family and several cats. She enjoys vegetarian cooking, music, and volunteering. Christine is living with GPP and shares her experience of living with this disease: “My journey started when my daughter was about six months old. All of a sudden, I noticed that I started to feel very hot and warm in my face. From then on, I’ve never had a day where I’ve had total remission or total clearance.”

Many patients share similar experiences of their journey to diagnosis, fear of flares as well as emotional stress and anxiety. “This really shows us that there is a pressing need for faster diagnosis and treatments that can quickly alleviate symptoms,” says Dr. Emmanuelle Clerisme-Beaty, Head of Clinical Development and Medical Affairs, Dermatology at Boehringer Ingelheim.

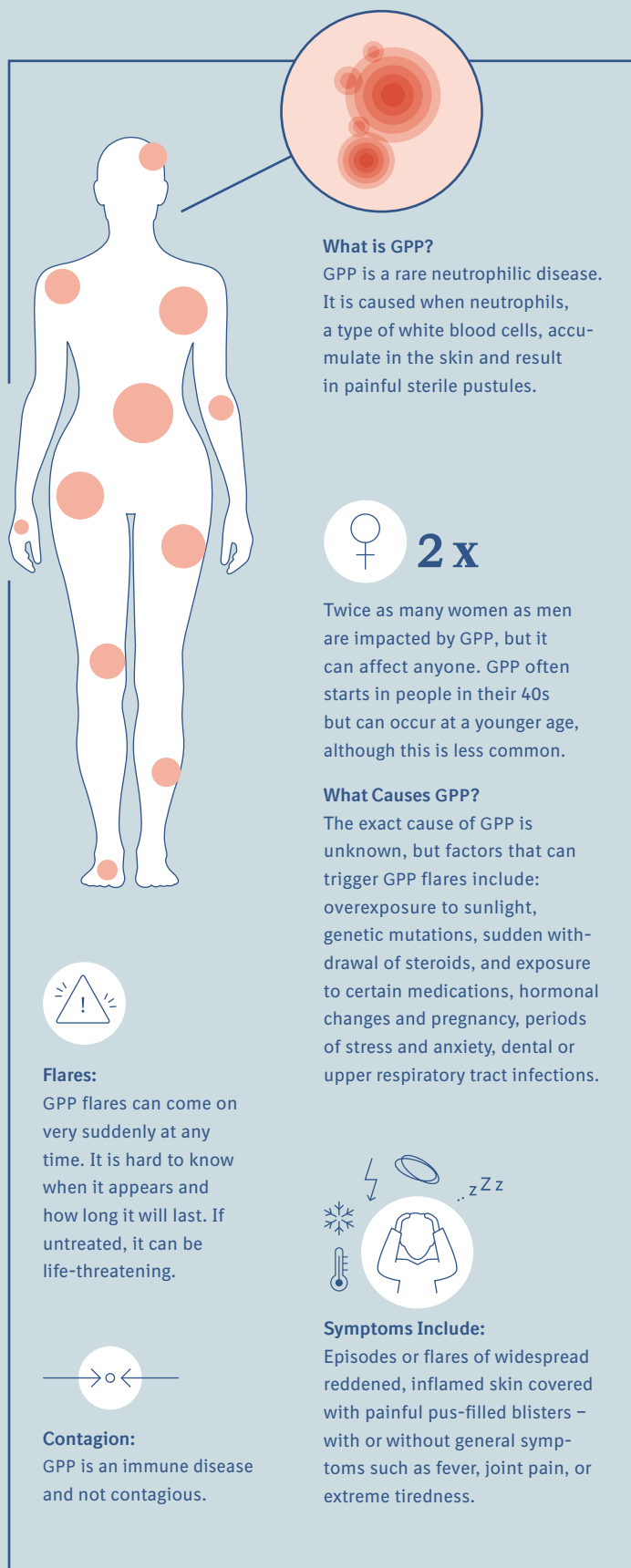
The disease makes many aspects of Christine’s life a lot more difficult, also everyday things like getting up in the morning, taking a shower, putting on clothes, and leaving home. “I have to consider whether a shower is going to be painful, the type of clothing that I put on, whether I can brush my hair,” says Christine.

A particularly difficult aspect of the disease is that it is often visible, even to strangers. Christine explains that there have been times where people have actually refrained from touching or hugging her or even turned their face away. “One thing that is not often discussed is that if you have GPP on different areas of your body, such as private areas, that makes it difficult to even have a physical relationship with somebody,” explains Christine.

One of the most painful experiences Christine remembers is going to the swimming pool with her daughter and having other mothers complain to the lifeguard: “The lifeguard said: ‘Hey, lady, the other mothers here are uncomfortable with you, and we need to ask you to leave.’ And I remember just picking up my daughter, and just running as fast as I could from the pool. And I ran home crying because I was so ashamed and so embarrassed.”

Besides the documented effects of a chronic skin condition, for Christine, the long path to a diagnosis was an additional burden: “There is not enough information for medical professionals, even dermatologists.” Christine tells, she received all sorts of treatments that were not very effective. Her GPP spread and became more debilitating, to the point where she could not work any longer. The journey took for about a year before she received a proper diagnosis.

When asked what Christine wishes for treatment, her answer was very clear: “I would like to not have to deal with ointments and creams and bandaging and worrying about injuring my skin. And a treatment that is easy, effective and doesn’t have scary side effects would really go a long way in helping me focus on what matters most to me: my family, friendships, and career. That would be fantastic!”



**What is GPP?**  
GPP is a rare neutrophilic disease. It is caused when neutrophils, a type of white blood cells, accumulate in the skin and result in painful sterile pustules.

**2x**  
Twice as many women as men are impacted by GPP, but it can affect anyone. GPP often starts in people in their 40s but can occur at a younger age, although this is less common.

**What Causes GPP?**  
The exact cause of GPP is unknown, but factors that can trigger GPP flares include: overexposure to sunlight, genetic mutations, sudden withdrawal of steroids, and exposure to certain medications, hormonal changes and pregnancy, periods of stress and anxiety, dental or upper respiratory tract infections.

**Flares:**  
GPP flares can come on very suddenly at any time. It is hard to know when it appears and how long it will last. If untreated, it can be life-threatening.

**Symptoms Include:**  
Episodes or flares of widespread reddened, inflamed skin covered with painful pus-filled blisters – with or without general symptoms such as fever, joint pain, or extreme tiredness.

**Contagion:**  
GPP is an immune disease and not contagious.





HUMAN PHARMA

# “Kick-starting our immune system into the fight against cancer”

Boehringer Ingelheim is battling cancer on two fronts. Together with partners from all over the world, scientists are not only targeting tumor cells directly, but also attempting to trigger the immune system to fight cancer. Clive Wood, PhD, Head of Discovery Research at Boehringer Ingelheim, explains how specific and powerful T-cells are and how we are giving them a ‘helping hand’.

**Clive, you have been working in the field of immuno-oncology for many years. What fascinates you the most about this research field?**

Our immune system is one of the most complex and powerful systems in our body. It gives the body the ability to distinguish non-self from self – and do it with exquisite specificity – and then eliminate non-self in order to keep us healthy. Unfortunately, many tumors avoid immune detection by directly inhibiting immune cell activity and the small number of specific mutations in a particular tumor can hinder the ability of the immune system to recognize the tumor as non-self. The immune system is then unable to do its job. As an immunologist, I see an opportunity to change this and ‘kick-start’ the immune system into action to attack these so-called cold tumors.

**This approach did not show any significant success for a long time.**

For decades, ideas of using the immune system to fight cancer were considered unrealistic by many and its ability to do so unproven. It was forbidden territory in many companies. I experienced some vehement reactions in the industry against such concepts.

**What turned the tide?**

Some discoveries were made in the late 1990s that led to the approval of antibody therapeutics in 2011 (anti-CTLA4) and 2014 (anti-PD-1) that have opened up this whole new

#### **CLIVE R. WOOD, PhD**

joined Boehringer Ingelheim in 2014 as Global Head of Discovery Research. His career has spanned small biotech and large pharma companies in the US and Europe. His personal R&D contributions have focused on molecular immunology and biologics.

**“We are building a portfolio of first-in-class innovation for cancer patients.”**

immune targeting front in the fight against cancer. They have brought big benefits to some patients, but sadly still to a limited number. There is no longer any question of whether the immune system can succeed in fighting cancer. The focus is now on how to use it to benefit many more patients.

**To lead this battle against cancer, Boehringer Ingelheim is attacking cancer on two fronts.**

Correct. We are developing a new generation of drugs that directly target the drivers of cancer cell growth. And we are working to boost the body’s immune response against cancer by

blocking the tumor’s immune-inhibitory mechanisms and enhancing the recognition of the tumor as non-self. In both areas, we are building a portfolio of first-in-class innovations. The combination of tumor cell-targeted and immune cell-targeted medicines may hold the greatest benefit for most patients.

**You want to turn cold tumors hot.**

That is the basic principle. Hot tumors contain T-cells and have ongoing immune activity. Cold tumors lack T-cells and are a suppressive environment for the immune system. We are very focused on patients with cold tumors – and are excited by the concept of T-cell engagers, for example.

**What are T-cell engagers?**

T-cell engagers support the body’s immune cells in being able to find and destroy cancer. These protein therapeutics are engineered to bind to both T-cells and tumor cells, creating a bridge between them that enables the T-cells to deliver toxins directly to the tumor cells to trigger their destruction. In the absence of the immune system recognizing the tumor as non-self on its own, the T-cell engager is a ‘helping hand’ that guides the T-cell to its target.

**T-cells are very specific.**

Our body has a repertoire of different T-cell receptor specificities, many billions, in fact. When our body is

invaded by a pathogen, a small subset of T-cells with specificities to this invader gets activated and expanded. We need the T-cells of a cancer patient to recognize the tumor cells as ‘invaders’.

**This is where cancer vaccines come into play?**

Exactly. Just like using a conventional vaccine to elicit a protective response against a bacterium or virus, we seek to do the same with tumors. With cancer vaccines, we can tell the body which T-cells are needed to ramp-up the necessary response.

**Oncolytic viruses are yet another powerful tool to turn cold tumors hot and fight cancer.**

Oncolytic viruses have the potential to selectively kill tumor cells, leaving normal cells unharmed. In addition to this direct killing of tumor cells, the oncolytic virus can accelerate the recognition of the tumor cell as non-self. We still have more to learn about how this happens, but fragments of dying cancer cells combined with immune-activating signals in the tumor milieu may enhance immune recognition.

**You are starting to combine oncolytic viruses and cancer vaccines. Why are you doing that?**

Evidence from many different sources suggests that we can boost the immune response by treating with cancer antigens in different ways. Preclinically,

we show that we achieve a stronger response by treating with a cancer vaccine (‘prime’) from AMAL Therapeutics and then later with an oncolytic virus expressing the same antigens (‘boost’). We are testing this now in clinical studies. In addition, we are building other prime-boost candidates. The most recent to enter preclinical development contains six different potential cancer antigens, including one with a specific mutant KRAS.

**You just mentioned AMAL Therapeutics, a Swiss biotech company that Boehringer Ingelheim acquired in 2019. It is one of many partnerships in oncology that Boehringer Ingelheim has initiated in the past years. How important are these collaborations to us?**

To develop breakthrough medicines for patients, we must work together with the best and brightest across the world. External partnerships are very important to our innovation strategy. A number of recent acquisitions have

strengthened our capabilities. These include AMAL Therapeutics in Geneva, Switzerland, and Vira Therapeutics in Innsbruck, Austria, with oncolytic virus technology. In addition, the acquisition of Labor Dr. Merk & Kollegen (today: BI Therapeutics) in Ochsenhausen, Germany, which has amassed considerable expertise in process development, manufacturing, and analytical characterization of viral therapeutics such as oncolytic viruses expands our know-how even further.

**What is the next exciting direction in immuno-oncology?**

We are learning more about additional types of cells in the microenvironment of the tumor and how these possibly influence the ability of the immune system to reject the tumor. Targeting these other cell types may be important for turning cold tumors hot. An exciting example comes from our recent partnership with Northern Biologics. This is a monoclonal antibody targeting a protein of the tumor stroma that is in preclinical development.

**These approaches are as numerous and as diverse as our oncology portfolio. When do you expect Boehringer Ingelheim to offer new treatment options for patients?**

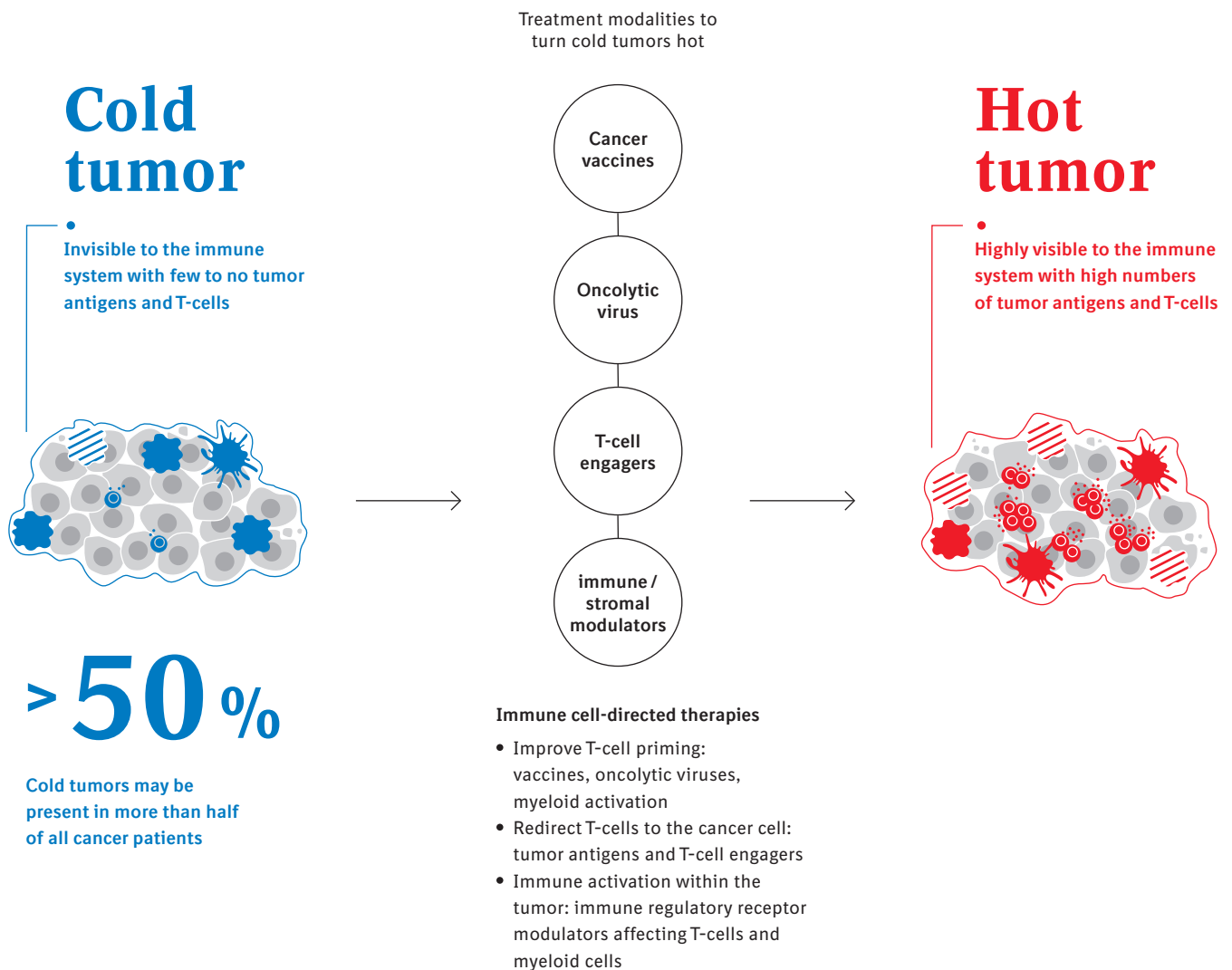
Today, we have a very strong early stage oncology development portfolio, with over fourteen Phase I and preclinical development stage immuno-oncology projects. 2024 onwards will be very exciting for potential launches of new medicines for cancer patients.

**“We must work together with the best and brightest across the world.”**



## TURN COLD TUMORS HOT

Clinical research has shown that the current wave of checkpoint-centric therapies is beneficial in those patients with immunologically active and highly-mutated so-called hot tumors. But they have limited efficacy in those tumor types that lack these properties, commonly known as cold tumors. The objective for the next wave of therapeutics is to alert the immune system to the presence of these cold tumors, and this is where Boehringer Ingelheim is focusing on.



### Components of a tumor



Cancer cell



T-cell



Cytokines with anti-tumor activity



Myeloid-derived suppressor cell (MDSCs)



Dendritic cells

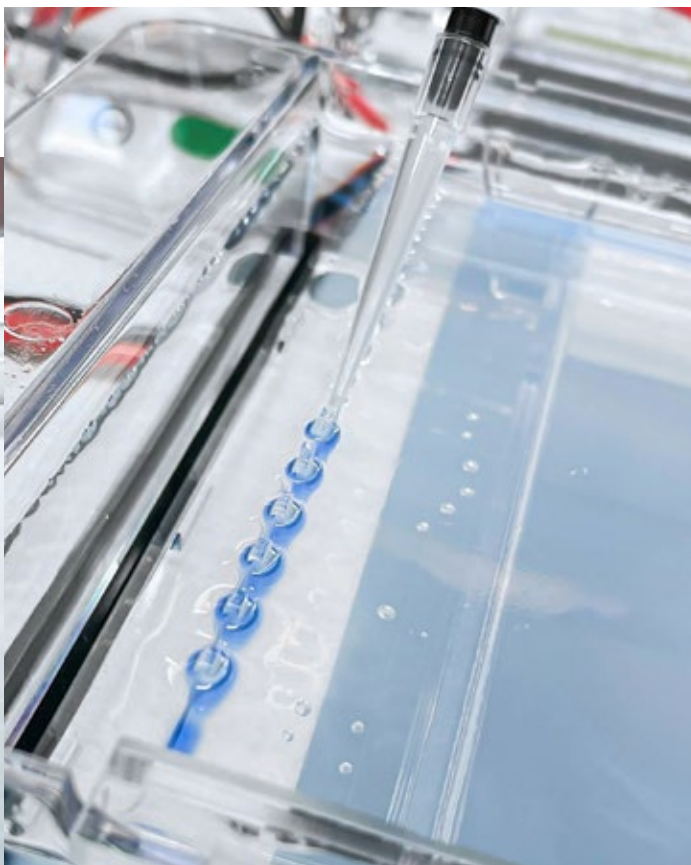


M1 Macrophage



# Prepared for the Next Outbreak

Highly infectious diseases, such as foot-and-mouth disease (FMD), can emerge suddenly and spread with great speed. Boehringer Ingelheim has long-standing experience in this field. Based on this, the company works on innovative R&D technologies and enhanced surveillance in order to support its partners for the next outbreak.



Every livestock owner's worst nightmare came true in the UK in 2001: An outbreak of foot-and-mouth disease (FMD) occurred on February 21. This viral disease spread throughout the country within few days and reached the European mainland on March 13. More than four million animals, in particular cattle and pigs, had to be culled before the end of the epidemic was finally declared almost a year later.

FMD is an example of a disease that recurrently flares up in landscapes of previous infection, but also crosses borders and spreads to new areas. It mainly affects livestock such as cattle, swine, sheep, and goats. However, wild animals such as wild boars, camels, and elephants can also be infected. Animal products, such as meat or milk, are additional sources of contamination and spread of this disease. Humans can neither become infected nor transmit the virus to others. The virus that causes the disease can be transported in the air over a number of miles, thus spreading the disease rapidly and across borders even before the initial outbreak has been recognized.

Veterinarians, public health experts, and infectious disease researchers refer in this context to transboundary and emerging diseases (TEDs). If just one animal in a herd is infected, all animals in the herd may have to be culled to prevent further transmissions and spread. This not only leads to the unnecessary loss of animal life and economic damage; it can also jeopardize food security by disrupting supply chains.

### **Growing Risk of Zoonoses**

Some TEDs are zoonotic. They can pass from animals to humans. While most animal diseases cannot pass to humans, the few that do are of major concern to human health: The majority of new and



Visit [Lelystad](#)



emerging infectious diseases have their origin in animals, such as the human immunodeficiency virus (HIV) and rabies virus. SARS-CoV-2 is presumably another example. The number of zoonoses is increasing around the world. One reason for this is that humans are encroaching ever further onto wild animals' habitats. In addition, global transport flows make it easier for pathogens to spread from their traditional areas of circulation.

### Lelystad Focuses on TEDs

TEDs are constantly evolving. This means that approaches to prevention must be continuously updated. Boehringer Ingelheim's cross-functional Veterinary Public Health (VPH) team is supporting the fight against animal diseases by means of monitoring, modeling, vaccine research, and manufacturing. Furthermore, it is working with governments to plan and implement disease control measures. To be even better prepared for future outbreaks of TEDs, Boehringer Ingelheim is transforming its Lelystad site in the Netherlands into an innovation center. Previously, vaccines against FMD were manufactured here to meet global demand. Lelystad is now part of a Regional Center for Global Innovation and will pursue research and development in support of efforts to curb TEDs worldwide. "With this new site, we will be able to take what is already a strong commitment to the field of animal health to the next level," says Prof. Dr. Eric Haaksma, Head of Animal Health Global Innovation at Boehringer Ingelheim. "We are thus making an important contribution not only to the protection of individual animals and humans but also to entire communities."

#### THE LELYSTAD SITE



Global Innovation site focusing on Research and Development for veterinary vaccines



20 employees

#### FOCUS AREAS



Innovative vaccine solutions for transboundary and emerging diseases



Updating the VPH vaccine portfolio



Vaccine batch production for clinical studies



Scale-up of new vaccine strains



Optimizing yield of virus to produce more vaccines

### Ideal Conditions

The conditions in Lelystad are ideal. "This site already has knowledge, capabilities and expertise that puts us in very good position," says Dr. Jose Coco-Martin, site manager at Lelystad, which is situated around 30 miles to the northeast of Amsterdam. Boehringer Ingelheim has a partnership with the Wageningen University & Research in Lelystad for many years, and its new research center situated adjacent to the university campus will likewise benefit from this. "Our facility in Lelystad also has a high level of security necessary to carry out research into highly infectious pathogens. The colleagues working here know how to operate in this strictly regulated environment with its specific security requirements," Coco-Martin adds.

### Rapid Intervention

Boehringer Ingelheim has many years of experience in producing vaccines to combat FMD and other TEDs such as blue-tongue virus. The company is one of the world's leading manufacturers of FMD vaccines and a longstanding partner of health authorities, governments, and non-governmental organizations (NGOs), including the World Organization for Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO), and the Pan American Health Organization (PAHO). In case of an emergency, it is essential to be well connected. As recently as 2021, together with international partners and the local authorities, employees of Boehringer Ingelheim were able to curb an outbreak of FMD on Rodrigues Island, Mauritius, in just six days. An international team delivered 180,000 doses of vaccine to the island in the Indian Ocean and thus prevented the epidemic from spreading to neighboring islands.



“Lelystad’s expert knowledge and resources will play a key role in our ongoing partnership between the US, Europe, Asia, and Africa to ensure global monitoring of diseases and a rapid response to new threats,” says Elke Abbeloos, the VPH center’s Head of Vaccine Development. “Regardless of how much expertise we have at our disposal, there is always something new to learn about TEDs.”

### **Artificial Intelligence (AI) Identifies Outbreaks of Diseases**

Time is of the essence when an outbreak occurs. To effectively curb an epidemic, it must first of all be detected – and as quickly as possible. For this reason, Boehringer Ingelheim entered into a partnership with the British company Lifebit Biotech in the summer of 2021. “External innovation is an increasingly important aspect of our research and development approach,” remarks Haaksma. Lifebit Biotech uses natural language processing (NLP) and AI to analyze huge volumes of data. Every day, more than 500 million new tweets, three million news articles, and thousands of scientific papers appear online. It is impossible to effectively analyze this flood of scientifically relevant information manually. Lifebit Biotech’s AI monitors these sources in real time and interprets them. It also factors in real data such as loss claims, billing activities, and the data of animal patients, known as real world evidence (RWE). AI-based analysis enables greatly improved monitoring of animal disease-related data worldwide, which in turn speeds up the detection process: an invaluable advantage whenever the next outbreak occurs.



A technician is using the smart glass technology to show partners and colleagues the interpretation of test results in real-time mode.



The results of a virus determination assay, which are distributed in real time mode through the smart glasses.



Mammalian cells susceptible for the viral propagation are withdrawn from the incubator for microscopical examination.



# New Space for Biopharmaceutical Innovation



**Biopharmaceutical molecules play a significant role in the treatment of diseases, such as cancer or autoimmune diseases. As a pioneer in the field, Boehringer Ingelheim has been committed to advancing science and production to achieve medical breakthroughs for patients since the 1980s. With its new manufacturing facility in Vienna, Austria, this commitment is being taken to a new level.**

In 1948, Austria became the first subsidiary of Boehringer Ingelheim outside of Germany. Today, around 2,800 employees work for the company in Vienna, around 1,500 of them in biopharmaceutical manufacturing.



By opening the Large Scale Cell Culture (LSCC) facility in October 2021, Boehringer Ingelheim set a major milestone to serve the growing demand for biopharmaceutical medicines and accelerate access to improved treatment options for patients with severe diseases. The company is an industry-leading manufacturer of biopharmaceuticals. With an investment volume of more than 700 million EUR, the new production plant is the single largest capital investment in the company's history and has created 500 new jobs in Vienna.



**“The flexible structures enable us to supply patients with a variety of highly complex molecule formats.”**

Dr. Christian Eckermann,  
Site Head Biopharma Austria  
at Boehringer Ingelheim

With its new facility, Boehringer Ingelheim now produces biopharmaceuticals based on cell cultures at four sites worldwide. The Vienna site previously specialized in manufacturing based on yeasts and microorganisms.

## PIONEER IN BIOPHARMA- CEUTICAL CONTRACT MANUFACTURING

**1963**

Research on chicken interferon

**1985**

Establishment of the biotechnical center in Vienna, Austria, for the development of genetic engineering substances

**1986**

Opening of the first biotechnical center in Biberach, Germany

**1987**

First own biopharmaceutical product ACTILYSE® receives market authorization for the treatment of acute heart attacks in collaboration with Genentech

**1998**

Entry into global contract manufacturing

**2003 / 2005**

Investments in large-scale production facilities in Biberach and Vienna

**2011**

Acquisition of biopharmaceutical production site in Fremont, USA

**2017**

Opening of biopharmaceutical manufacturing facility in Shanghai, China

Laying of the foundation for the large-scale production facility (LSCC) in Vienna

**2020**

First market authorization in China for a product from contract manufacturing at the production site in Shanghai

**2021**

Opening of the LSCC in Vienna

The plant is designed to allow changeovers from one product to another within a short time as well as the simultaneous production of different products. The facility sets new standards with its technical designs: “We operate one of the most advanced biopharmaceutical production facilities in the world, providing an outstanding degree of automation, digitalization, and flexibility. The flexible structures enable us to supply patients with a variety of highly complex molecule formats,” comments Dr. Christian Eckermann, Site Head Biopharma Austria at Boehringer Ingelheim. For instance, monoclonal antibodies, enzymes, and other recombinant proteins can be produced at the facility.

The bioreactors in LSCC provide a total volume of 185,000 liters, adding an additional 30 percent to Boehringer Ingelheim’s mammalian large scale cell culture capacity. The company manufactures innovative biopharmaceuticals at the facility for both its own product portfolio and for its contract manufacturing business.



Biopharmaceuticals are large and complex molecules that are highly sensitive. Producing them is demanding and takes several weeks.





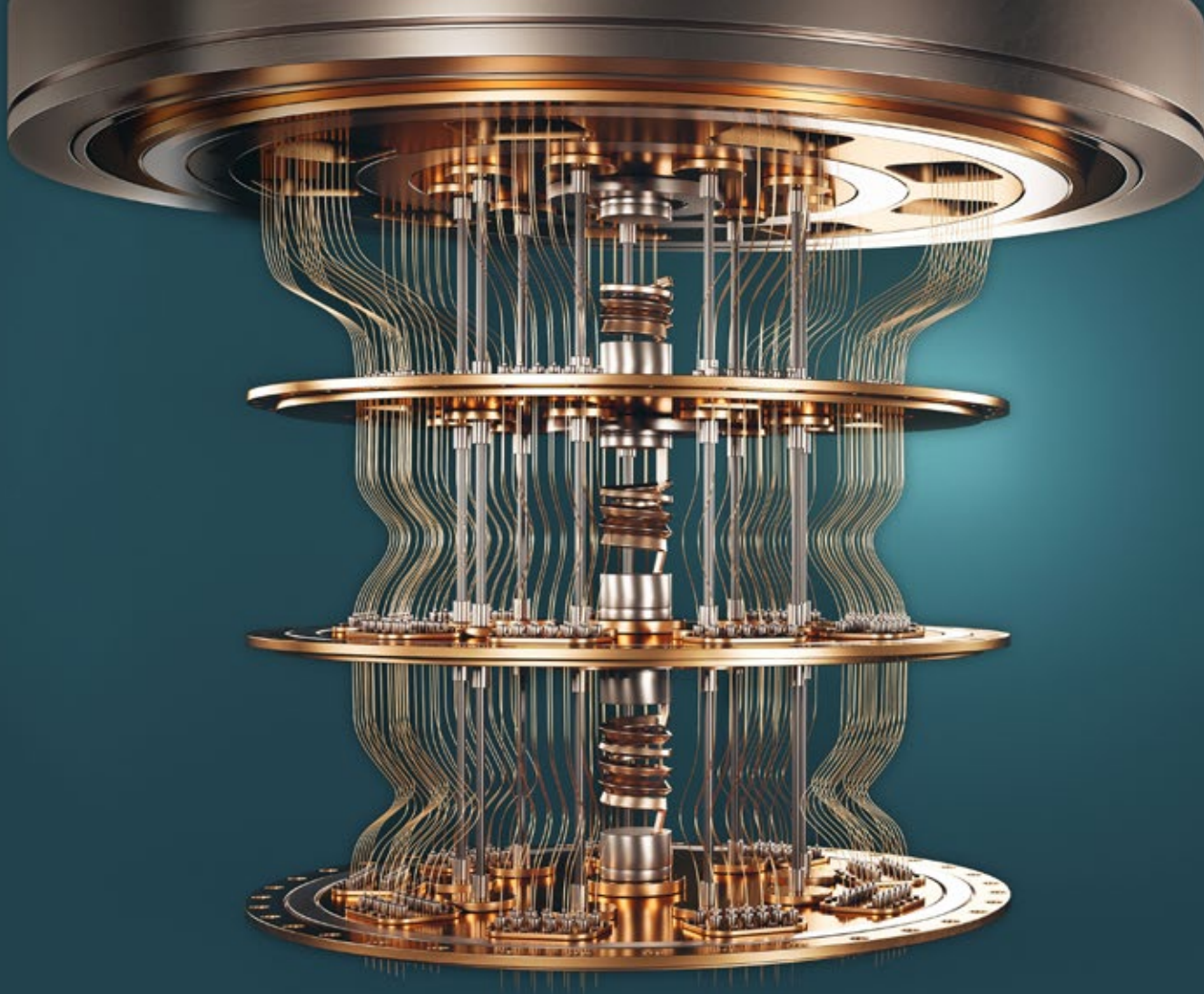
As a pioneer in the field of biopharmaceuticals, Boehringer Ingelheim has manufactured 40 approved biopharmaceutical medicines used by patients all over the world.



The new LSCC plant is one of the most advanced of its kind. The production lines are fully automated and highly digitalized: This provides automation that continuously monitors and regulates the entire production process to drive consistency, compliance, and greater operational excellence. Generated data can be used for production process simulation and optimization applying artificial intelligence technology.



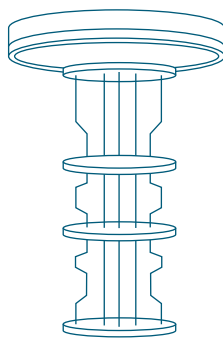




DIGITALIZATION

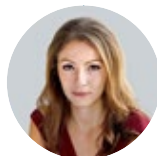
# The Dawn of the Era of Qubits

While traditional computers are becoming increasingly powerful, some tasks are too complex for them to handle. One of these is accurate molecular simulation. Quantum computers hold the prospect of greatly increased computing power. For this reason, Boehringer Ingelheim launched a partnership with Google Quantum AI in early 2021. Elica Kyoseva, Quantum Computing Scientist at Boehringer Ingelheim, and Ryan Babbush, Head of Quantum Algorithms at Google Quantum AI, discuss the potential of quantum computers and the future of pharmaceutical research.



### What is quantum computing?

**Elica Kyoseva:** Quantum computing is the next technological revolution. It will help us solve many of the problems which even the most powerful supercomputers are unable to tackle, such as breaking current cryptography, predicting financial market performance, and, most importantly to Boehringer Ingelheim, solving chemistry problems such as molecular binding. It will enable better ways to discover pharmaceuticals and thus contribute to global medical progress in the future.



**Dr. Elica Kyoseva,**  
Quantum Computing  
Scientist at Boehringer  
Ingelheim

### Why are traditional computers unable to solve these problems?

**Ryan Babbush:** Traditional computers are machines that process information using a gigantic number of binary switches. These switches can be set to either zero or one. Because of the increasing complexity of many problems we want to solve, we are building increasingly powerful traditional computers. But at certain points, they reach their limits.



**Dr. Ryan Babbush,**  
Head of Quantum  
Algorithms at Google  
Quantum AI

**Elica Kyoseva:** Chemical simulations, such as calculating molecular dynamics, quickly become impossible on traditional computers – here is why: Let's assume we've managed to model a molecule, including its electrons, accurately as basis. If we now add one more atom to this molecule, its electrons will interact with all other electrons and nuclei of the system. We need to keep track of all these additional interactions, and to do so computationally, we need to double the resources of our computer. And this goes on for every electron we add to the molecular system. This means the complexity of this calculation increases exponentially both in memory and in time. It becomes obvious here that conventional computers quickly reach their limits in this scenario.

### What is different about quantum computers?

**Elica Kyoseva:** Instead of working with binary switches – bits – they work with qubits, which have quantum mechanical capabilities. The first is

known as superposition: A qubit can exist in two different states at the same time. The second is entanglement, which is the quantum mechanical connection between particles into an inseparable – classically intractable – system. Now why is this important? Because molecules are quantum systems! So, if we want to describe them accurately, we need to reflect those quantum characteristics, which require exponential resources on a classical computer. In contrast, quantum computers expose those characteristics inherently, and hence are the best means to simulate quantum systems – as world-renown physicist Richard Feynman famously noted in the 1980s.

### What additional capability do qubits have?

**Ryan Babbush:** To illustrate the enormous computing power that results: If you combine three classical bits with each other, you produce eight different possibilities: 000, 001, 010, and so on. The three bits together can only be in one of these eight states at any given time. In a quantum mechanical sense, three qubits can assume every possible combination of these states at the same time (superposition).

### As researchers, are you feeling your way forward into a puzzling new world?

**Ryan Babbush:** Quantum mechanics seems to contradict the physical logic that we encounter in everyday life. Yet as researchers, we have a very good understanding of its processes. The theory of quantum physics is nearly 100 years old. The goal is now to apply this knowledge to the field of computing.

### How is that possible?

**Ryan Babbush:** Digital research generally assumes that every scientific principle can likewise be applied to the domain of computers. In the 1980s, people began to think about designing computers based on the laws of quantum mechanics. The first quantum bits (physical qubits) were built in the 1990s, but we have only had hardware that can accurately control larger numbers of qubits

in the last five years or so. The problem is that interactions between the quantum computer and its environment, such as stray photons of light, or vibrations, for example, as well as difficulty in controlling the quantum bits themselves, leads to noise that can corrupt the output of the quantum computation. But it is not clear whether we can manage that sufficiently to perform useful computations. The alternative is to correct errors so we can design a perfect logical qubit. That would be the ideal way to build a fault-tolerant quantum computer. I am optimistic that we will build a useful fault-tolerant quantum computer in about a decade. But this is a huge challenge – in my view, it is comparable to the idea in the 1960s that a person might fly to the moon.

#### **What can quantum computing contribute to the development of medicines?**

**Elica Kyoseva:** Molecules are so complex that traditional computers are unable to accurately model the interactions between their particles, such as electrons. For this reason, we currently use numerous approximations in order to calculate the molecular properties needed for research and development purposes. This means that the calculated properties are approximative and this is one of the reasons why we need further wet lab experiments and patient studies to verify the usefulness of the drug candidates. For all pharmaceutical companies in the world, this costs a great deal of time and resources. Quantum

computers could help to develop better medicines, through providing better accuracy more efficiently.

#### **When do you expect it to be possible for people to use quantum computers to develop medicines?**

**Elica Kyoseva:** There is undoubtedly still much to be done. But I'm optimistic because we're making progress in all three key areas: software, hardware, and concrete use cases. This is one of the reasons for our partnership with Google Quantum AI.

**Ryan Babbush:** For us, the question is when quantum computers will be capable of modeling molecular systems for a company like Boehringer Ingelheim. Looking ahead to the future, again, we have to differentiate between the two approaches to dealing with miscalculations. If we manage to sufficiently suppress the disruptive environmental noise, I think we will reach that point in three to five years. But if fault-tolerant quantum computers are the only means of achieving that goal, we might need up to ten years. I am confident that if not sooner, the advent of fault-tolerant quantum computing will herald a genuinely new era.

#### **DR. ELICA KYOSEVA**

originally from Bulgaria, has been fascinated by physics since her childhood. She holds a doctorate in quantum optics and has conducted research at institutions including the prestigious Massachusetts Institute of Technology in Cambridge, USA. In 2016, she moved to Tel Aviv to continue her research. Since September 2020, she is working as a quantum computing scientist at Boehringer Ingelheim, where she is developing pharmaceutical applications for this future technology.

#### **DR. RYAN BABBUSH**

is a leading researcher in the field of quantum computing and works at Google Quantum AI, a Google research group that is focused on building and deploying useful quantum computing. As its Head of Quantum Algorithms, he leads a team that is focused on discovering and developing the first applications of quantum computers, with a special emphasis on using quantum computers to model otherwise intractable physical systems.

# The Next Level of Pharmaceutical Production

**The Solids Launch Factory, a highly automated smart factory, is the latest addition to the production network of Boehringer Ingelheim. It will help bring innovative medicines to market faster than before.**

Anyone standing in front of the Solids Launch Factory (SOL) at the Ingelheim site in Germany quickly understands that this building is different: The futuristic production facility with the large window front on the ground floor and the minimalist white and grey surfaces on the upper floor makes a fresh and clean impression. However, the impressive technology is only revealed once you enter the new building.

**“Smart factories are going to become the new standard for industrial production.”**

Holger Holakovsky, Head of SOL

The SOL consists of three floors: In the basement, there are technical and storage rooms as well as changing rooms. Additional technical, office, and common rooms can be found on the

top floor. The ground floor is where the heart of the new factory is located: the production facilities. Here, everything is equipped with the latest technologies to produce tablets (solids) for the market. A total of around 75 employees work here.

“Within our company’s global production network, we in Ingelheim are responsible for the market launch of all new products,” said Dr. Anja Preißmann, Head of Human Pharma Supply Launch & Innovation. “Thanks to the flexible and innovative design of the SOL and the close links with the Development teams, we can bring our new products to market faster than before. This is not only a competitive advantage for our company, but also of benefit to patients worldwide.”

The special thing about the SOL is its design as a smart factory: All machinery and equipment are fully



## WHAT IS A SMART FACTORY?

A smart factory is an automated factory, where the machinery and equipment are fully connected through digital networks. Due to these digital connections and the software implemented, the smart factory can improve processes through automation and self-optimization.

connected through digital networks and nearly all processes control themselves. Accordingly, the new factory can react independently to changing conditions, based on production data, quality parameters, and environmental conditions. “This is an enormous opportunity for us,” explained Holger Holakovsky, Head of SOL. “We understand more quickly what is happening in the factory and can thus react immediately. Another improvement is that we can predict how processes will develop under different conditions.”



# Thinking in Generations



**For generations, Boehringer Ingelheim has been working to improve the health of humans and animals. Sustainable development is at the heart of the company and is a journey which started with the founding of the family-owned company in 1885. In 2021, all initiatives relevant to sustainable development were incorporated into one company-wide framework entitled “Sustainable Development – For Generations” with three pillars: More Health, More Potential, and More Green.**

Thinking in and for generations has been at the heart of the sustainability approach of Boehringer Ingelheim from the very beginning. Over the years, the understanding of sustainable development has gradually changed and transformed, becoming wider and going deeper. In the founding years of the company, the concept was closely tied to employee well-being. The company founder Albert Boehringer introduced affordable housing, health insurance, and paid annual

leave for his employees. In doing so, he fostered a strong sense of community that has lasted until today.

The global expansion of the company over time led to a growing cultural diversity, which shaped its profile and created awareness for global societal challenges. Boehringer Ingelheim became active in the Animal Health business in 1955. This combined

focus on both Human and Animal Health, as well as the implicit link to environmental impacts, is particularly relevant for the approach Boehringer Ingelheim takes. Related issues include access to healthcare and tackling non-communicable and infectious diseases for both humans and animals, for example.

The 1990s marked a significant turning point for the global sustainable development agenda: Following the Rio Conference in 1992, the creation of a more just, peaceful, and sustainable world became the mission for the approaching 21<sup>st</sup> century. At Boehringer Ingelheim, this led to an increase in initiatives, which have further driven sustainable development at the company, from a variety of different angles.

These diverse initiatives provide the basis for the new company-wide framework. “‘Sustainable Development – For Generations’ is firmly anchored in the company’s heritage and drives it in the future. As a family business, we think in generations, serve mankind, and are respectful of our resources. It is the logical next step to advance our sustainability culture through engaging with our employees and partners,” says Eduardo Liroy, Head of Corporate Sustainable Development at Boehringer Ingelheim. Launched in 2021, this framework increases the existing commitments of Boehringer Ingelheim to sustainable development and classifies them according to three pillars. These encompass existing and new healthcare initiatives (More Health), expand societal initiatives (More Potential), and deepen environmental initiatives (More Green). They are aligned with the United Nations Sustainable Development Goals (UN SDGs) for a more sustainable world. For now and generations to come.



### UNITED NATIONS SUSTAINABLE DEVELOPMENT GOALS

The 17 Sustainable Development Goals (SDGs) are at the heart of the strategy of the United Nations for more peace and prosperity worldwide by 2030. The third goal – good health and well-being – has far-reaching connections to all other goals, turning pharmaceutical companies into essential contributors to achieve all the other SDGs as well.



## More Health – For Humans and Animals

NCD. Three letters, yet 41 million lives lost. Every year, the World Health Organization attributes 41 million deaths to non-communicable diseases (NCDs) such as diabetes, stroke, or cancer. These diseases can be traced back to exposure to certain risks (i.e. air pollution), unhealthy lifestyles, genetic dispositions, etc. An unbalanced diet, insufficient work and exercise habits as well as unfavorable living environments, increase the likelihood of being affected by an NCD. Regardless of the reason, access to healthcare presents a major obstacle in tackling NCDs. This obstacle and other health challenges beyond NCDs call for enabling more health – in the form of sustainable health solutions.

Pharmaceutical companies play an important role here, as Henrik Finnern, Global Lead of the More Health pillar, points out: “NCDs make up 85 percent

### DID YOU KNOW THAT...

since its start in 2016, the Angels Initiative has helped over 6,300 hospitals (and more than 72,300 healthcare providers) in 144 countries worldwide to optimize stroke care. Patients can be treated better and faster, positively impacting the health outcome of around 7.46 million people to date. Improved stroke care was enabled by supporting multi-disciplinary stroke teams with access to consultants, education, standardization tools, best practices, and quality monitoring processes.

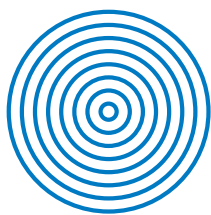
Angels recently received the prestigious Stroke Service Award of the World Stroke Organization for its impact on patient care, with the explanation that “the Angels Initiative achieved more for stroke care in LMICs (Low-Middle Income Countries) than any other international project before”. It is the first time for this award to be given to an industry initiative.



Last Mile Livestock Service Providers (LLSP) demonstrate the administration of veterinary products.

of our medicines portfolio. This is why, together with our researchers, partners, and patients, we continuously develop the initiatives we have been driving for years, while defining new goals for further progress.” Boehringer Ingelheim aims to invest 35 billion EUR in innovation and research by 2030 to help minimize the impact of NCDs. Moreover, the company has committed to expanding NCD healthcare for 50 million people in vulnerable communities. Successful initiatives like Angels (see info box) will be key to achieving these goals.

In addition, infectious diseases remain a critical issue worldwide. Using its expertise in both human and animal health, Boehringer Ingelheim is investing 250 million EUR in partnerships to combat infectious diseases across species. These efforts also build upon existing initiatives, which include Animal Health programs against rabies or the Last Mile Initiative. Stretching across six countries in sub-Saharan Africa, Last Mile has supported over 30,000 farmers to optimize the health and productivity for their livestock.



## More Potential – For Communities and Our People

In 2021, we continue to see vulnerable communities being marginalized and facing growing challenges in areas of health, education, work prospects, living conditions, societal inequalities, and poverty. The COVID-19 pandemic constituted a major setback for the fight against poverty: In 2020, global extreme poverty rose for the first time in 20 years. In these times of increasing challenges, the world is also looking for ways to tap into more potential – for individuals and for communities.

“We believe that all of us can play a role in tackling challenges,” says Robert Shaw, Global Lead of the More Potential pillar, “and Boehringer Ingelheim has a strong commitment to our people. For us, our focus lies on providing the best conditions for our people, communities, and partners along our value chain, to enable them to reach their full potential.”

Therefore, Boehringer Ingelheim continuously increases its efforts in diversity and inclusion, human rights, and ethics. Current company initiatives form a vital part of that mission. One example is the BE SAFE program for workplace safety and employee well-being. After 12 years, the program has reduced accidents by 60 percent, and during the COVID-19 pandemic has engaged employees on mental health awareness. Another example is Boehringer Ingelheim’s

global Diversity & Inclusion (D&I) framework. This approach is aimed at nurturing a diverse, open, collaborative, and inclusive culture and continuously implementing D&I principles throughout our value chain. For example, the company extensively educates and trains leaders and employees on unconscious bias as well as inclusive behaviors and language, which is just one step to ensure that all employees, customers, patients, and stakeholders feel included, heard, and appreciated.

Meanwhile, communities are at the core of the company’s flagship initiative Making More Health (MMH). In 2010, Boehringer Ingelheim and Ashoka, the world’s largest network of social entrepreneurs, jointly created Making More Health, a long-term partnership that seeks to improve healthcare for people, animals, and their communities. The initiative focuses on connecting innovative solutions with business expertise to address complex healthcare challenges and create systemic change. To date, MMH has supported 12 social enterprises and 120 social entrepreneurs, to impact over 10 million people worldwide. Ambitions are increasing. To achieve more potential.

# 50,000,000

By 2030, Boehringer Ingelheim wants to impact this many people in vulnerable communities by empowering employees, partners, and social entrepreneurs.



Learn more about  
Sustainable Development



## Making More Health Together 2021

In November 2021, Boehringer Ingelheim and Ashoka organized Making More Health Together, a convention to co-create sustainable solutions for communities.



In November 2021, Boehringer Ingelheim and Ashoka, the world's largest network of social entrepreneurs, celebrated Making More Health Together 2021 – a two-day virtual event focusing on the empowerment of social entrepreneurship and topics relevant to human and animal health as well as social innovation. Over 1,800 participants from academia, non-profit, industry, and political sectors registered to engage, collaborate, and network towards one common goal: finding more sustainable solutions for the most pressing healthcare issues of our time.

In approximately 40 sessions, participants had the opportunity to learn more about the history behind the creation of MMH, achievements and milestones over the past decade, current projects and new initiatives. Aside from the exciting stories of MMH founders Jean Scheftsik de Szolnok and Arnaud Mourot, Vice President of Ashoka, many social entrepreneurs and Boehringer Ingelheim employees shared their innovative ideas and highlights of the collaboration between and within MMH.

### Transforming Lives Through Better Health

The people who joined this event shared one common goal: to think “out of the box” and create innovative health solutions to their communities’ needs, by making prevention and treatment simpler, cheaper, and more accessible.

“No one can solve today’s immense challenges by themselves. Instead, everyone has skills, expertise, and experiences that can help unlock the tremendous potential collaboration has to create shared value. Events like Making More Health Together can lay the foundation for these partnerships, by bringing together people from different sectors to transform lives through better health,” says Dr. Ilka Wicke, Global Head of Making More Health.

### Stepping Up, to Achieve Even More

During the convention, Boehringer Ingelheim announced two new initiatives aimed at enabling MMH to achieve even more in the future:

**Boehringer Ingelheim Social Engagement:** This builds on the MMH Business Accelerator and provides 50 million EUR in financing for impact to social businesses in vulnerable communities through non-traditional financing options, combined with a partnering approach. With this, the company intends to also enable additional funding from other investors and engage with like-minded partners to catalyze expertise.

**MMH Connect:** The second initiative is an IT platform, designed to better match the skills, know-how, and experience of Boehringer Ingelheim employees with specific social entrepreneurs and projects worldwide, in order to enable more effective matchmaking and better allocate resources.



## More Green

The goal to become even more environmentally sustainable is the driving force behind the More Green pillar, which continuously looks for ways to reduce the company's environmental footprint.

The goals are ambitious: to become carbon neutral in company operations by 2030 (Scope 1 and 2). While Scope 1 includes all direct emissions from company activities under the control of the company, Scope 2 includes indirect emissions derived from purchased energy and used for company operations. Additional goals aim to reduce the water footprint and protect clean water in the communities in which the company operates; to utilize aspects of circularity to reduce overall operational waste to landfill, as well as applying eco-design and green chemistry concepts to all new products. To foster sustainable thinking even further, there is an internal carbon price of 100 EUR per ton CO<sub>2</sub> emissions for investments and the 'More Green Fund' provides another 130 million EUR for global projects to push sustainability in large-scale projects. Moreover, the 'Clean Water' initiative ensures that traces of pharmaceuticals in wastewater remain significantly below any effect level.

"While our goals may seem ambitious today, we compare our work to being on a journey," explains Ingo Weiss, Global Lead of the More Green pillar, "you start at one point and become more determined because you see new possibilities along the way. Optimally, the journey never ends because we know we can always do more."



### OUR COMMITMENT

Through its **More Green** pillar, Boehringer Ingelheim strives to become even more environmentally sustainable, by continuously working towards minimizing the company's environmental footprint.



### OUR MISSION

To protect the health of people, animals, and communities, by investing and implementing more sustainable solutions, emphasizing collaboration, and ensuring alignment with the UN SDGs.



### OUR GOALS

Boehringer Ingelheim aims to reduce company greenhouse gas emissions, energy and resource use even further, by committing to:

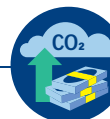
- Becoming carbon neutral in company operations by 2030 (Scope 1 and 2)
- Further reducing the water footprint, particularly at sites affected by water scarcity, as well as protecting clean water in communities in which the company operates
- Utilizing aspects of circularity to reduce overall operational waste to landfill and applying eco-design and green chemistry concepts to all new products



We rely on circular economy, reduce our operational waste to landfill by 80%, and design all new products applying eco-design and green chemistry principles.



We aim to become carbon neutral in company operations by 2030, for example by investing in the construction of a new biomass power plant and increasing renewable electricity purchased worldwide.



Boehringer Ingelheim focuses on environmental sustainability in its larger projects and provides another 130 million EUR for green projects that contribute to the global MORE GREEN goals. We established an internal carbon price of 100 EUR/t CO<sub>2</sub>.



We are the first pharmaceutical company in the EU to receive the 'Green Canteen' certification for a sustainable catering concept at the corporate headquarters.



We minimize water consumption and implement water stewardship programs. We protect clean water, mitigate pharmaceuticals in wastewater from production and combat antimicrobial resistance.

# The Work of Tomorrow

**The way we work is changing significantly. Careers are becoming less standardized and more individual than in the past. As a global employer with more than 52,000 employees around the world, Boehringer Ingelheim encourages agile and flexible career paths.**

Dr. Sven Sommerlatte joined Boehringer Ingelheim as the Head of Human Resources in April 2021. This makes him one of many new employees who joined the company during the COVID-19 pandemic. “One of the many lessons learned from this period is that we can effectively manage the onboarding process virtually,” says the Human Resources expert.



**“In the future, we should invest more time in individual dialogue and less in administration.”**

Dr. Sven Sommerlatte,  
Head of Human Resources  
at Boehringer Ingelheim

In his role Sommerlatte is responsible for driving the company’s HR processes. In doing so, he must keep two things in balance: On the one hand, the company has to provide its employees with options to make their work as varied and as flexible as possible. On the other hand, it is important to continue the development of the company as a whole.

According to Sommerlatte, this will only be possible “if we invest more time in individual dialogue and less in administration in the future.” The company can only make better personnel and career decisions than its competitors if it gets to know the needs of employees and working partners well and supports their development.

## **“Our work is very agile – we don’t follow a rigid plan”**

**Wenhan Zhao (29) works at BI X, the digital laboratory of Boehringer Ingelheim, where she helps shape the company’s digital transformation. From her office at a lofty height, she looks out across Shanghai, China.**

### **What makes the office so special for you?**

Our office is super cool and I like working here. We love the atmosphere and the lively discussions. None of us here has their own desk, and I adapt my working environment to the working situation. Sometimes I work in the open area, the workshop area, or the product room. If I need to concentrate and avoid distractions, I work in the focus room.

### **What kind of projects are you working on?**

One thing I’m currently working on is an app to help stroke patients regain their life via home-based rehabilitation. It uses an Artificial Intelligence (AI) algorithm to recommend individual rehab concepts and special exercises that are then explained in videos.

**Good coordination and communication seem to be important, especially when many work from home.**

### **How do you manage that?**

We’re working with an international team that is based in different time zones and includes experts from different fields. Under these circumstances, good communication is vital. Our work is very agile – we don’t follow a rigid plan and change direction quickly depending on how the product is. I’m mainly self-taught in this area. I actually learn every day. My area of work requires you to acquire knowledge very quickly. Everything is constantly changing and evolving. That makes our work very exciting.





## **“Trust and openness are key to share a managerial role”**

**Timo Bailer (34) worked in a managerial job-share arrangement in Biberach, Germany.**

### **Until recently you worked in a part-time managerial job - how did this idea and decision come up?**

At that time, I was looking for a way to balance my family, my job, and my hobby. My former supervisor also wanted to work less, but he wanted to keep his managerial position. He asked me if I could imagine the two of us sharing his job. We took this proposal to our supervisors, and we were able to convince them that this could be a good solution.

### **How did your daily work routine look like?**

Each of us got a 60 percent position. One of us worked from Mondays to Wednesdays, and the other from Wednesdays to Fridays. Wednesday was our “alignment day”, where we could discuss important issues.

### **What was the most important success criterion for you and your job-share partner?**

We both had a very good relationship based on trust. Our guiding principle was that we would complement rather than monitor each other. Our employees, as well as our peers, have appreciated this style of management and cooperation. This requires openness and trust.

### **Recently you started working full time again. Why?**

For me, the part-time model was the right step at the right time. Of course, you earn less money – but for me, it was worth it. In the second half of 2021, I decided to ramp up and go back to working full-time, to spend more time on my tasks at Boehringer Ingelheim. Following the departure of my job-share partner and former supervisor, I am now in charge of our group.



## **“We have access from anywhere in the world”**

Viktoria Kühl (21) is an apprentice in mechatronics at the site in Ingelheim, Germany.

### **You are doing your apprenticeship during the COVID-19 pandemic. How is that going?**

Fortunately, things are going very well. My apprenticeship covers metalworking and electrical engineering. The apprenticeship has a dual structure, and we rotate between going to vocational school and working at the company. We often attend school from home by webcam, or we work on assignments there. We can try out a lot of things and have lots of room to develop our own ideas.

### **Do you work more on-site or from home?**

I prefer to work on-site as much as possible. Working from home permanently wouldn't be my favorite option, though many of our colleagues are still working remotely. We have the technologies to work well from the site and from home. We connect our laptops to the machines' user interfaces and can get access from anywhere in the world.

### **What fascinates you about your work at the moment?**

I was particularly fascinated by working in the laboratories under clean-room conditions. I currently work in the production facility of Boehringer Ingelheim's chemical division. Among other things, I work with highly complex machines that fill little capsules in various production steps.







# Imprint

**If you have any queries  
or comments, please do not  
hesitate to contact us.**

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With the CO<sub>2</sub> emission certificates we support forest conservation and forest modification in many regions in Germany.



**Value through  
Innovation**

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# 2021



Annual Report

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# Our Company

Making new and better medicines for humans and animals is at the heart of what we do. Our mission is to create breakthrough therapies that change lives. Independent and family-owned, Boehringer Ingelheim has the freedom to pursue its long-term vision, looking ahead to identify the health challenges of the future and targeting those areas of need where we can do the most good.

As a world-leading, research-driven biopharmaceutical company, more than 52,000 employees create value through innovation daily for our three business areas: Human Pharma, Animal Health, and Biopharmaceutical Contract Manufacturing. In 2021, Boehringer Ingelheim achieved net sales of 20.6 billion EUR. Our significant investment of more than 4.1 billion EUR in R&D drives innovation, enabling the next generation of medicines that save lives and improve quality of life.

We realize more scientific opportunities by embracing the power of partnership and diversity of experts across the life-science community. By working together, we accelerate the delivery of the next medical breakthrough that will transform the lives of patients now, and in generations to come.

# The Shareholders' Perspective



*Dear Reader,*

2021 was a year in which the pharmaceutical industry was able to demonstrate its contribution to society. Just 12 months after the WHO's declaration of a pandemic, we saw the first approvals of vaccines, and collaborative efforts across companies provided the tools to protect vulnerable groups.

Importantly, the pharmaceutical industry also maintained the supply of medicines unrelated to COVID-19 and continued to work on innovative medicines, despite logistical and production challenges. However, it has been concerning to see that fewer preventive screenings and check-up examinations were performed as many patients avoided visiting medical centers.

Boehringer Ingelheim has invested substantially in mitigating the effects of the pandemic on patients, employees, partners, and the business. This allowed medicines to continue to be available for patients and animals, despite COVID-19-related supply challenges. At the same time, the company showed significant progress pursuing its ambition of developing breakthrough therapies for humans and animals.

2021 has been a successful year. Our employees have shown true agility in facing these challenges, and they continue to do extraordinary things under difficult circumstances to ensure the supply of much-needed medicines to humans and animals. By advancing medical progress, continuously seeking solutions that target areas of unmet medical need, people at Boehringer Ingelheim are the key to strengthening our long-term competitiveness. On behalf of the Shareholders' Committee, I would like to thank them and everyone who supported us from outside of Boehringer Ingelheim for their extraordinary commitment.

signed by  
Christian Boehringer  
Chairman of the Shareholders' Committee

# The Board of Managing Directors



**Michel Pairet**



**Carinne Brouillon**





**Hubertus von Baumbach**

**Michael Schmelmer**

**Jean Scheftsik de Szolnok**

# Key Aspects 2021

*Dear Reader,*

Our purpose to transform lives has been our driving force for decades, and 2021 was no exception. We were very successful in delivering on this promise last year, thus improving the lives of many patients, humans and animals alike. This led to a very gratifying performance of our organization, across all business areas. While we were able to manage the effects of the COVID-19 pandemic on our operations well, the pandemic has shown us how important pharmaceutical research is for medical progress and societal safety.

We see innovation as the key driver to transform lives and continued to increase our investments in research and development in 2021. Our long-term commitment to innovating for unmet medical needs is proving its value: We have a strong pipeline with more than 100 promising projects at all stages of clinical and preclinical development. The three breakthrough therapy designations granted to us by the US FDA in 2021 are testament to our strategy being the right one; a fourth breakthrough therapy designation followed in February 2022.

Enabled by the high engagement of our employees and the support of a broad network of partners, all three business units recorded profitable growth last year. In Human Pharma, the acceleration of our portfolio continued in 2021. We received priority review for an immunology medication and fast track designation for a treatment of non-alcoholic fatty liver disease. Our innovative medications also showed growth, led by JARDIANCE® and OFEV®, which treatments reached over seven million people worldwide.

Animal Health has had a good year, with sales up in a competitive market. Like in Human Pharma, our focus lies on researching and developing products that transform the lives of animals. We are strengthening our capabilities and increasing our investments to grow our pipeline of products for livestock and companion animals. Meanwhile, we continue to optimize and build a strong base for global research, production, and marketing.

In Vienna, Austria, we inaugurated two additional facilities to our biopharmaceutical production network, which significantly increases our production capacity in mammalian and bacteria-based technology. These milestone investments allow us to meet both growing internal pipeline demand, as well as production demand from our customers, whom we are strongly committed to through our BioXcellence brand.

Last year, we celebrated the 10-year anniversary of our Making More Health social entrepreneurs initiative, as well as our More Green environmental footprint program. Seeing the impact of how our sustainable development activities help improve the environment and the lives of humans and animals, we decided to step up our investment and broaden our commitment. Under a focused umbrella, *Sustainable Development – For Generations*, we are now bringing 19 global sustainability initiatives together across human and animal health, communities and the environment.

A decisive success factor in 2021 has been the personal engagement of each individual employee. Everyone has contributed to our shared purpose of transforming the lives of humans and animals. The fact that we have managed to do this during a second year of the pandemic, fills us with great gratitude towards them, as well as to all our partners.

signed by  
Hubertus von Baumbach

signed by  
Carinne Brouillon

signed by  
Michel Pairat

signed by  
Jean Scheftsik de Szolnok

signed by  
Michael Schmelmer

# Corporate Bodies

## Shareholders' Committee

**Christian Boehringer**

Chairman of the Shareholders' Committee

**Christoph Boehringer**

**Erich von Baumbach**

**Isabel Boehringer**

**Dr. Mathias Boehringer**

**Prof. Dr. Dr. Andreas Barner**



## Board of Managing Directors

**Hubertus von Baumbach**

Chairman of the Board of Managing Directors

**Carinne Knoche-Brouillon**

Member of the Board of Managing Directors,  
Human Pharma

**Dr. Michel Pairet**

Member of the Board of Managing Directors,  
Innovation

**Jean Schefftsik de Szolnok**

Member of the Board of Managing Directors,  
Animal Health

**Michael Schmelmer**

Member of the Board of Managing Directors,  
Finance & Group Functions

## Advisory Board

**Dr. Nikolaus von Bomhard**

Chairman of the Advisory Board  
Chairman of the Supervisory Board  
Münchener Rückversicherungs-Gesellschaft AG

**Dr. Hagen Duenbostel**

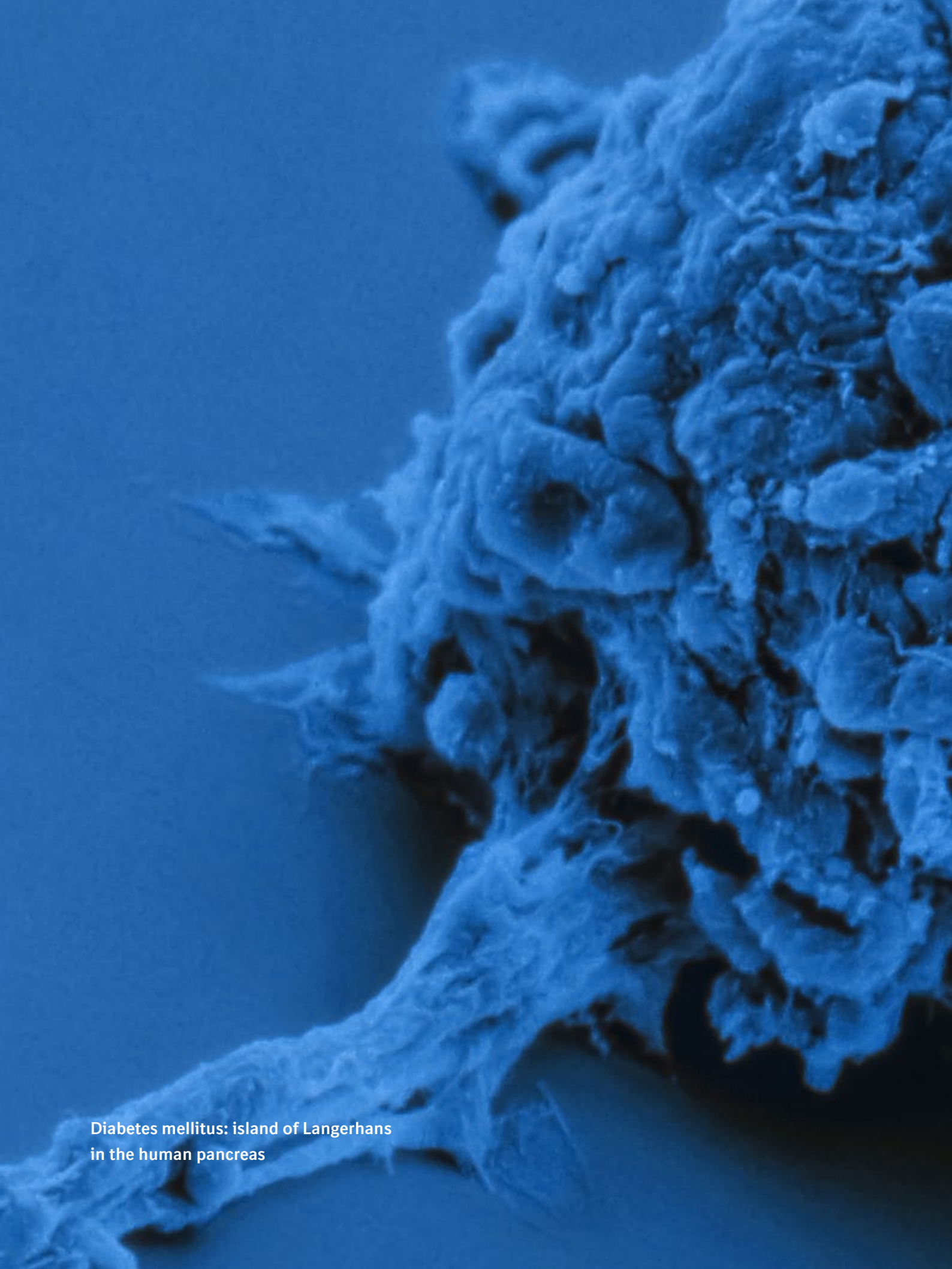
Chief Executive Officer (CEO) KWS SE

**Dr. Frank Mastiaux**

Chief Executive Officer  
EnBW Energie Baden-Württemberg AG

**Jan Rinnert**

Chairman of the Board of Managing Directors, CEO  
Heraeus Holding GmbH



Diabetes mellitus: islet of Langerhans  
in the human pancreas



# Group Management Report

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# Group Management Report

## Information about the Group

### The Group's business model

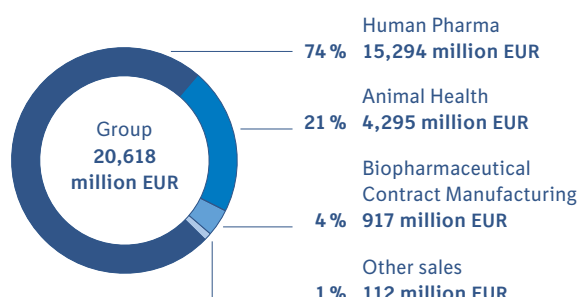
Boehringer Ingelheim develops breakthrough therapies that transform lives, today and for generations to come. Independent and family-owned, we pursue our long-term vision to identify tomorrow's challenges, seeking for solutions that target areas of unmet medical need. This is captured in our purpose Transforming Lives for Generations, which inspires over 52,000 of us to make a significant difference to human and animal lives. Boehringer Ingelheim has stood for innovation for over 135 years. We are among the world's 20 leading companies in this sector and one of Germany's most research-focused companies.

The Human Pharma business is the mainstay of our activities and accounts for a 74 % share of overall sales. This business area is underpinned by an innovative portfolio, and in many cases its products are standard treatments in medicine. Our research focuses on cardiovascular and metabolic diseases, oncology, respiratory diseases, immunology, diseases of the central nervous system (CNS) and retinal health.

**JARDIANCE® with  
two new indications  
in heart failure**

JARDIANCE®, a medicine for treatment of type 2 diabetes, which also reduces the risk of cardiovascular diseases for type 2 diabetics with pre-existing cardiovascular conditions, was the Group's biggest selling Human Pharma product for the third consecutive year. In addition, in 2021, the US public health authority, the FDA, awarded JARDIANCE® a Breakthrough Therapy Designation (BTD) for extended use in the treatment of heart failure. Moreover, this medicine was awarded a new indication through the EU's approval of its use for the treatment of heart failure with reduced ejection fraction (HFrEF) and a first approval in Paraguay for the treatment of heart failure with preserved ejection fraction (HFpEF). OFEV®, which is used for the treatment of the rare respiratory disease idiopathic pulmonary fibrosis (IPF) and increasingly also in a

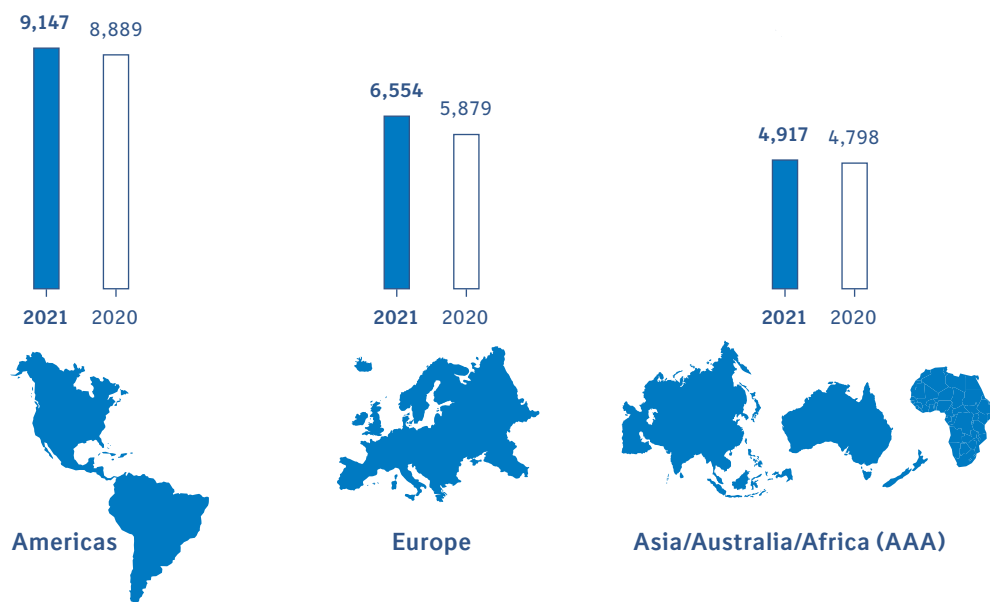
### Net sales by business





## Net sales by region

in million EUR



further indication – systemic sclerosis with interstitial lung disease (SSc-ILD) – registered strong growth. Three other products also played a significant role in Boehringer Ingelheim's success: SPIRIVA®, which is used for the treatment of chronic obstructive pulmonary disease (COPD) as well as asthma, TRAJENTA®, which is used for treatment of type 2 diabetes, and PRADAXA®, which is used to prevent strokes in patients with atrial fibrillation and for the prevention and treatment of thromboembolic disorders.

In its Animal Health business, Boehringer Ingelheim is a significant provider of vaccines and therapeutics. Our portfolio includes products for pets and horses as well as livestock: swine, ruminants and poultry. Our core brands NEXGARD®, followed by FRONTLINE® and HEARTGARD®, are the foundations of our success in the pets segment. In the swine segment, the established swine vaccine INGELVAC CIRCOFLEX®, which is used to treat porcine circovirus type 2, is an important component of the company's product portfolio.

Our biopharmaceutical activities comprise the manufacture of our own human pharmaceutical products (such as ACTILYSE®, METALYSE® and PRAXBIND®) and also – as one of the world's leading providers – process development and commercial production of biopharmaceuticals for third-party industrial customers.

Other sales mainly comprise discontinued operations.

In the 2021 financial year, we achieved the majority of our sales in the Americas (44 %) and Europe (32 %) regions. The Asia/Australia/Africa (AAA) region includes countries such as China and is of strategic significance for the Group's future development, making up 24 % of its sales.

## Research and development

Our goal is to research and develop innovative medicines and therapies for the treatment of diseases for which there are as yet no satisfactory treatments available. Our major emphasis is on the development of medicines and therapies to prevent, detect, and treat chronic diseases. We aim to make a relevant contribution in areas where the need for treatment is high, in the human pharmaceuticals segment as well as in the field of animal health.

**More than  
4 billion EUR  
invested in R&D**

In our global research network, we employed an average of 10,109 people in 2021. We are present in nine countries, with central facilities in Germany (Biberach and Ingelheim am Rhein), the USA (Ridgefield, Connecticut; Duluth, Georgia; and St. Joseph, Missouri), Austria (Vienna), Japan (Kobe), and France (Lyon) as well as China (Shanghai). Through our activities here we are continuing to expand and renew our existing product portfolio, in order to safeguard the Group's organic long-term growth. Accordingly, we have considerably increased our research and development (R&D) expenses in recent years – in the past three years, their growth has even outpaced our revenue trend. A total of around 4.1 billion EUR was invested in the research and development of new medicines. This is above the level in 2020 and corresponds to around 20.0 % of the Group's net sales in 2021 (2020: 18.9 %). Our research and development expenses in Human Pharma amounted to 3.7 billion EUR.

### Research and development

	2021	2020	2019	2018	2017
Expenses in million EUR	4,127	3,696	3,462	3,164	3,078
– as % of net sales	20.0	18.9	18.2	18.1	17.0
Human Pharma expenses in million EUR	3,710	3,283	3,042	2,780	2,714
– as % of Human Pharma net sales	24.3	22.8	21.8	22.1	21.5
Animal Health expenses in million EUR	416	412	419	384	357
– as % of Animal Health net sales	9.7	10.0	10.4	9.7	9.2
Average number of employees	10,109	9,504	9,154	8,552	8,589
Investments in tangible assets in million EUR (without investments in infrastructure)	242	181	183	136	71

In our research, we rely on long-established relationships with academic and public research institutions, biotech companies, and other pharmaceutical companies. In the scientific field, we are collaborating in over 150 projects with more than 120 academic institutions spanning three continents. We are expanding our R&D portfolio through supplementary cooperation and license agreements as well as acquisitions. While the company's own research activities are highly productive and competitive, in Human Pharma we are aiming to source at least 30 % of all new molecules in our pipeline through acquisitions from third parties. Our high scientific standards, the business development relationships which we have forged over time, and the early investments made by the Boehringer Ingelheim Venture Fund play a key role in our success.

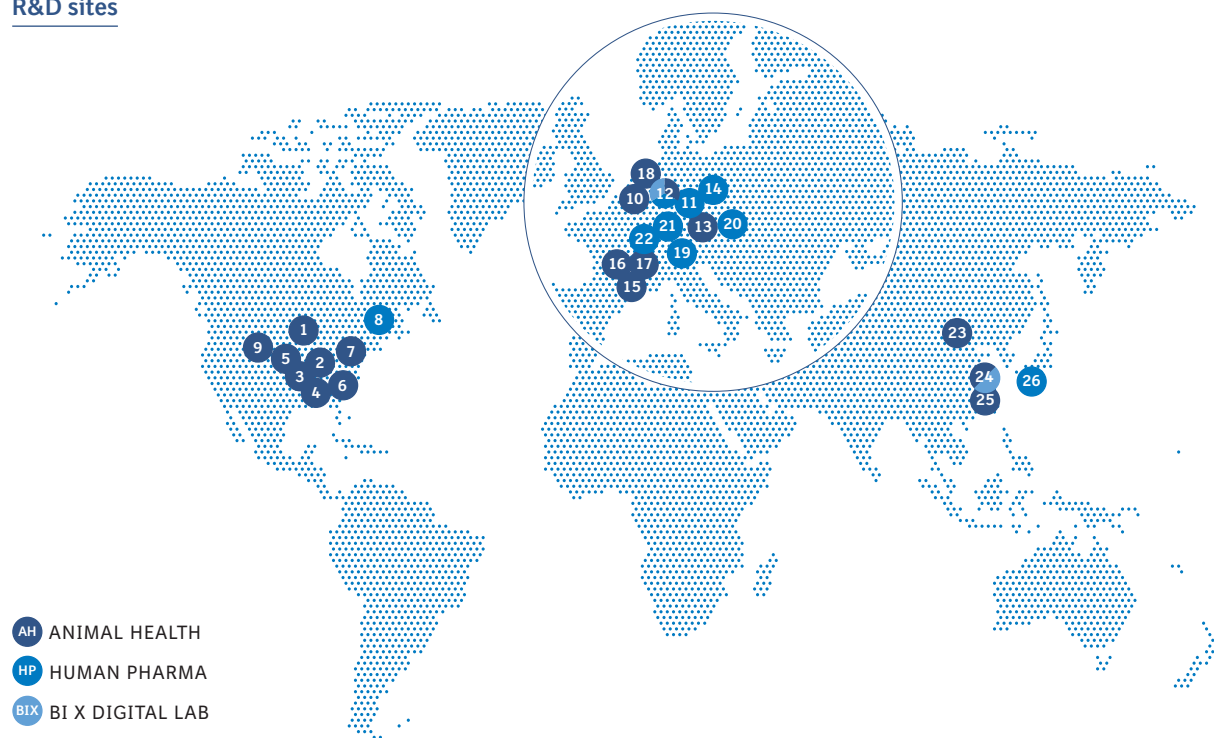
In 2021, Boehringer Ingelheim confirmed its attractiveness as a partner through new acquisitions and partnerships. In our Human Pharma business, we completed our acquisition of NBE-Therapeutics AG at the start of the year. The Swiss biotech company supplements our research activities through an innovative platform for the development of an antibody-drug conjugate pipeline. We also completed our acquisition of contract manufacturer Labor Dr. Merk & Kollegen GmbH. This company was subsequently renamed to Boehringer Ingelheim Therapeutics GmbH. It is an important component of our research activities in the field of immuno-oncology. We further strengthened our activities in the field of oncology – which we have significantly stepped up over the past few years – through our acquisition of Abexxa Biologics, Inc. in September 2021. The research collaboration, established in 2016, aims at developing new antibodies targeting cancer-specific proteins. We also expanded our portfolio of partnerships in the past financial year: We are now working with the well-known Lieber Institute for Brain Development in researching new methods for treating neuropsychiatric diseases. We also entered into a collaboration with the Twist Bioscience Corporation which is headquartered in San Francisco. The collaboration objective is to utilize Twist's proprietary antibody library to identify potential antibody candidates in various therapeutic areas.

We have also established long-term partnerships in our Animal Health business. PetMedix Ltd. is a strong partner for antibody-based therapies for pets. The British company has a proprietary, innovative platform which enables the rapid development of antibodies. Our long-term cooperation with Lifebit Biotech Ltd., a provider of biomedical data analyses, aims to utilize an AI platform in order to more rapidly identify global outbreaks of infectious diseases and to report these at an earlier stage.

We are pursuing basic research through a three-year cooperation agreement with Google in the field of quantum computing. As part of our digital transformation strategy, this partnership aims to harness the computing power of this new technology in the service of Boehringer Ingelheim's research and development and thus to pursue innovation in a more rapid and, above all, more precise manner, while at the same time conserving resources.

**Innovation network  
expanded**

## R&D sites



- AH ANIMAL HEALTH
- HP HUMAN PHARMA
- BIX BI X DIGITAL LAB

### Americas

#### USA

1. Ames, Iowa (AH)
2. Athens, Georgia (AH)
3. Colbert, Georgia (AH)
4. Duluth, Georgia (AH)
5. Fulton, Missouri (AH)
6. Gainesville, Georgia (AH)
7. North Brunswick, New Jersey (AH)
8. Ridgefield, Connecticut (HP)
9. St. Joseph, Missouri (AH)

### Europe

#### Belgium

10. Evergem (AH)

#### Germany

11. Biberach (HP)
12. Ingelheim am Rhein (AH, HP, BI X)
13. Katharinenhof-Rohrdorf (AH)
14. Ochsenhausen (HP)

#### France

15. Lyon – Boreal (AH)
16. Lyon – Porte des Alpes (AH)
17. Saint-Vulbas (AH)

#### Netherlands

18. Lelystad (AH)

#### Austria

19. Innsbruck (HP)
20. Vienna (HP)

#### Switzerland

21. Basel (HP)
22. Geneva (HP)

### Asia

#### China

23. Beijing (AH)
24. Shanghai (AH, BI X)
25. Taizhou (AH)

#### Japan

26. Kobe (HP)



Our digital laboratory, BI X, focused in 2021 on establishing its new facility in Shanghai as well as building new capabilities for developing and approving medical software products. The strategy is for BI X to become a center of excellence for developing medical software products throughout our company. As well as the above-mentioned structural development of BI X as an organization, BI X also focused on solutions for doctors and patients in our Human Pharma business in its development of digital products in 2021. For instance, GUARD is a system which helps general practitioners to make the best possible treatment decision for type 2 diabetes patients, based on medical guidelines.

Since 2010, the Boehringer Ingelheim Venture Fund has driven innovation through its strategic investments in young companies which are carrying out research into early-stage science and technology. Our Venture Fund invests in biotech start-up companies with innovative concepts and technologies that have the potential to provide ground-breaking new therapeutic platforms. The Venture Fund also founds companies when it identifies promising research projects in universities and academic institutions. In 2021, we established a Venture Fund Asia alongside our existing venture funds in Germany and the USA.

The Research Institute of Molecular Pathology (IMP) in Vienna is a biomedical research institute which, as a wholly owned Group company, is funded by Boehringer Ingelheim. With more than 200 scientists from approximately 40 countries, the IMP conducts research into molecular and cellular mechanisms that form the basis of complex biological life processes as well as human diseases. The IMP is one of the leading institutions of its kind: As of late 2021, ten of its 15 group leaders had received at least one of the prestigious grants awarded by the European Research Council (ERC). With a success rate of 58% in its ERC applications in the period from 2014 to 2018, the IMP was ranked third among 172 European research institutes and universities in 2020. Six of its 15 group leaders have been elected full members of the European Molecular Biology Organization (EMBO).

With its open innovation platform [opnMe.com](https://opnme.com), Boehringer Ingelheim is contributing to the process of scientific collaboration in the pharmaceutical world: Around 57 molecules in the preclinical stage are currently being made available to academic researchers around the world free-of-charge. These molecules have already enabled new scientific findings, e.g., in the field of oncology.

Boehringer Ingelheim's R&D activities – the preclinical as well as clinical research and development – are the basis for our sustainable success. The Group's positive business development over the past years has been underpinned by an organic process of renewing its portfolio, based on its own research and development activities. In-house R&D – supplemented by external cooperation and partnerships – will also continue to be a top priority in the future. Our high commitment to innovation was confirmed last year by means of three Breakthrough Therapy Designations granted by the FDA: In May 2021, a BTB was issued for our glycine transporter type 1 inhibitor (Gly-T1) BI 425809 as a contribution to research into the treatment of cognitive impairment induced by schizophrenia. In the same month, spesolimab received BTB classification, following its orphan drug designation in 2020. Spesolimab is used for treating the rare inflammatory disease generalized pustular psoriasis (GPP). In addition, JARDIANCE® was awarded a BTB in connection with its extended use for the treatment of patients with heart failure.

**More than 60 new active substances in our Human Pharma portfolio**

### Human Pharma

The promise in 2021 in the Human Pharma business and R&D was to pioneer therapies that transform the lives of patients significantly. We made progress in our focus areas such as cardiovascular and metabolic diseases, oncology, respiratory diseases, immunology, diseases of the central nervous system (CNS), and retinal health.

In 2021, the Human Pharma portfolio included 64 compounds whose development happened in around 250 clinical trials in more than 100 projects.

### Development pipeline end of 2021

Cardiometabolic diseases	Phase
> Metabolic modulator*	Phase I
> Angiotensin II receptor antagonist	Phase I
> Food intake regulator*	Phase I
Hemodynamic modulator 1	Phase I
Hemodynamic modulator 2	Phase I
Transient receptor potential channel inhibitor*	Phase I
> BI 456906*	Phase II
GLP1/GCGR agonist   NASH	Phase II
BI 456906*	Phase II
GLP1/GCGR agonist*   Obesity	Phase II
> BI 685509	Phase II
Hemodynamic modulator   CKD	Phase II
> Tenecteplase (China)	Phase III
Tissue Plasminogen Activator   AIS	Phase III
Empagliflozin / New indication	Phase III
SGLT2 inhibitor   CKD	Phase III
> Empagliflozin / New indication**	Phase III
SGLT2 inhibitor   HF post MI	Phase III
> Empagliflozin / New indication**	Registration
SGLT2 inhibitor   CHF	Registration
Oncology	Phase
> B7-H6/CD3 T-cell engager*	Phase I
DLL3/CD3 T-cell engager*	Phase I
> CD137/FAP antagonist*	Phase I
Ezabenlimab (PD-1 antibody)	Phase I
> HER2 exon20 inhibitor	Phase I
KISIMA* cancer vaccine*	Phase I
> KRAS (G12C) inhibitor*	Phase I
LRP 5/6 antagonist*	Phase I
MDM2-p53 antagonist*	Phase I
MEK inhibitor*	Phase I
> ROR1 ADC*	Phase I
SIRP1α antagonist*	Phase I
SOS1::KRAS inhibitor*	Phase I
STING agonist	Phase I
TRAILR2/CDH17 antibody	Phase I

Development pipeline end of 2021 (continued)

Respiratory diseases	Phase
Cysteine protease inhibitor*	Phase I
‣ BI 1015550 Anti-fibrotic   IPF	Phase II
Immunology	Phase
‣ BI 706321 Kinase inhibitor   CD	Phase II
Spesolimab (BI 655130) IL36R antibody   PPP	Phase II
Spesolimab (BI 655130) IL36R antibody   CD	Phase II
‣ Spesolimab (BI 655130) IL36R antibody   HS	Phase II
Spesolimab (BI 655130) IL36R-antibody   GPP	Registration
Central nervous system diseases	Phase
Phosphodiesterase inhibitor*	Phase I
Digital therapy*	Phase I
BI 1358894* TRPC 4/5 inhibitor   MDD	Phase II
BI 1358894* TRCP 4/5 inhibitor   BoPD	Phase II
BI 425809 GlyT1 inhibitor   CIAS	Phase III

### Development pipeline end of 2021 (continued)

Retinal diseases	Phase
> Ischemia modulator	Phase I
Neuronal damage modulator	Phase I
> BI 836880*	Phase II
VEGF/Ang-2 antibody   wAMD	
> BI 764524	Phase II
Ischemia modulator   DMI	
COVID-19	Phase
> Alteplase	Phase III
TPA   Cov-19 iARDS	

#### Indication abbreviations:

AIS	Acute Ischemic Stroke	Cov-19	COVID-19 induced acute	mBC	Metastatic breast cancer
AtD	Atopic Dermatitis	iARDS	respiratory distress syndrome	MDD	Major depressive disorder
BoPD	Borderline personality disorder	DMI	Diabetic macular ischemia	MI	Myocardial infarction
CD	Crohn's disease	GPP	Generalized pustular psoriasis	NASH	Non-alcoholic steatohepatitis
CHF	Congestive heart failure	HF	Heart failure	PPP	Palmoplantar pustulosis
CIAS	Cognitive impairment associated with schizophrenia	HS	Hidradentis Suppurativa	TPA	Tissue-type Plasminogen Activator
CKD	Chronic kidney disease	IPF	Idiopathis pulmonary fibrosis	wAMD	Moisture of age-related macular degeneration

\* Partnered projects or acquired assets

\*\* Study complete, submissions ongoing

> Key pipeline advances (Dec 2020 – Dec 2021)

### Cardiometabolic diseases

In 2021, we reported positive results of the EMPEROR-Preserved Phase III trial in adults with heart failure with preserved ejection fraction, with and without diabetes. Based on this, the US FDA granted JARDIANCE® the status Breakthrough Therapy to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure and preserved ejection fraction. In addition, we announced positive results of the EMPULSE trial in adults who are in hospital for acute heart failure.

In 2021, we also advanced the GLP-1/glucagon dual agonist, which was already being investigated in a Phase II study for individuals with diabetes, to Phase II clinical trials in adults living with obesity and non-alcoholic steatohepatitis (NASH). In addition, we received Fast Track Designation from the US FDA for adults with NASH.

### Oncology

Cancer is a disease that devastates not only the people diagnosed with it but also their loved ones. In partnership with the wider community, we support awareness, education, improved diagnosis, and care for patients with cancer. We work with patients throughout the development process and beyond to ensure our new treatments make a meaningful difference and reach the patients faster who need them the most. We are advancing a unique pipeline of cancer cell directed agents, immuno-oncology therapies, and combination approaches to help win the fight against cancer.



### Respiratory diseases

Research and development of new therapeutic options for people with respiratory diseases is another focus for Boehringer Ingelheim. Since 2014, OFEV® (nintedanib) has been a treatment option for idiopathic pulmonary fibrosis (IPF) to slow down the decline in lung function. In 2020, a breakthrough in pulmonary fibrosis therapy was achieved leading to two new indications in systemic sclerosis-associated interstitial lung disease (SSc-ILD) and other chronic fibrosing interstitial lung diseases with a progressive phenotype (PF-ILD) building the foundation for approvals in further countries in 2021. OFEV® now is approved as a treatment for IPF in more than 80 countries, in more than 70 countries for SSc-ILD, and in more than 60 countries for PF-ILD. In almost all countries it is the first and only approved treatment option for SSc-ILD und PF-ILD. The ongoing open-label extension trials SENSICIS™-ON and INBUILD™-ON will provide data on longtime safety and efficacy of nintedanib in SSc-ILD and PF-ILD. Additionally, the InPedILD™ study is investigating the dosing and safety profile of nintedanib in children and adolescents. Despite these advances in therapy, there is still a very high unmet therapeutic need in fibrosing pulmonary diseases. Therefore, we are investigating the safety and tolerability of BI 1015550 in patients with IPF in a clinical trial which is making good progress.

### Immunology

Immunological diseases greatly impact the lives of people living with it emotionally and physically. Boehringer Ingelheim is dedicated to discovering and developing first-of-their-kind therapies for these serious inflammatory diseases. With a deep understanding of molecular pathways, we are pioneering scientific breakthroughs that target, repair, and prevent inflammatory diseases of the skin, gut, and joints. Spesolimab is the most advanced investigational compound in Boehringer Ingelheim's immunology pipeline. In 2021, we filed for marketing authorization with the FDA, EMA, Chinese and Japanese authorities for treating patients with a flare of Generalized Pustular Psoriasis. The filing is based on positive Phase II data from our EFFISAYIL-1 trial. In addition, spesolimab has been granted Breakthrough Therapy Designation in China and USA.

### Central nervous system

At Boehringer Ingelheim, we are redefining mental health to enable people to thrive. A decade ago, Boehringer Ingelheim embarked on a research domain criteria (RDoC) inspired approach where we link behavior to the underlying neurobiology to develop targeted therapies that can ease the burden of these conditions, not just the symptoms. One example of this approach is BI 1358894 that we currently further investigate in clinical Phase II trials in people living with borderline personality and major depressive disorder. In 2021, Boehringer Ingelheim initiated the innovative CONNEX Phase III clinical trial for the treatment of Cognitive Impairment Associated with Schizophrenia (CIAS). Based on a successful Phase II trial in the CIAS, the US FDA has granted Breakthrough Therapy Designation for BI 425809, a novel glycine transporter-1 (GlyT1) inhibitor for this indication.

**Retinal diseases**

Retinal diseases such as age-related macular degeneration are the leading cause for legal blindness in the developed world. Although current therapies for some retinal diseases exist, they have limited effectiveness in the real world, and significant unmet treatment needs still exist. In 2021, Boehringer Ingelheim continued developing and advancing the retinal health pipeline. Clinical development of several new compounds was started, with the potential to treat wet age-related macular degeneration and geographic atrophy. Boehringer Ingelheim also transitioned a potential treatment for diabetic macular ischemia (DMI) to a Phase II trial. The work of our scientists is complemented by collaborations with academic and patient organizations, alongside partnerships with biotech companies.

**COVID-19**

As a research-driven biopharmaceutical company, we utilize our different areas of expertise to find medical treatments for COVID-19. In 2020, we initiated three programs to develop new therapy options. We are thus fully concentrating our efforts in this area on the development of alteplase as a potential treatment for COVID-19 patients with severe breathing problems, called acute respiratory distress syndrome (ARDS). Currently, the compound is being investigated in the Phase III part of the TRISTARDS Phase II/III study. These two other programs were discontinued in 2021: the development of BI 764198 for patients hospitalized with COVID-19 with respiratory complications due to the lack of efficacy and the BI 767551 SARS-CoV-2 neutralizing antibody due to the lack of coverage for the delta variant.

The following table shows the relevant changes in current clinical studies (Phase III):

Clinical trial	Phase	Changes in 2021
EMPEROR-Preserved (NCT0357951), a Phase III randomized, double-blind trial investigating once daily empagliflozin compared with placebo in adults with chronic heart failure and preserved ejection fraction, both with and without diabetes, who are receiving current standard of care.	Phase III	<i>Study completed, primary endpoint met and published in New England Journal of Medicine. Empagliflozin demonstrated a 21 percent reduction in the combined risk of cardiovascular death and hospitalization for heart failure in adults with heart failure and preserved ejection fraction. Empagliflozin also reduced first and recurrent hospitalizations for heart failure by 27 percent and significantly slowed kidney function decline.</i>
EMPULSE (NCT04157751), a multicenter, randomized, double-blind, 90-day superiority trial to evaluate the effect on clinical benefit, safety, and tolerability of once daily oral Empagliflozin 10 mg compared to placebo, initiated in patients hospitalized for acute heart failure (de novo or decompensated chronic HF) who have been stabilized.	Phase III	<i>Study completed, primary endpoint met. In the EMPULSE Phase III study, Empagliflozin shows a significant clinical benefit in adults stabilized after acute heart failure in the hospital. Adults hospitalized for acute heart failure were 36 percent more likely to experience clinical benefit when treated with Empagliflozin than with placebo. The benefit was consistent in people with new or existing heart failure, regardless of the ejection fraction or diabetes status.</i>
EFFISAYIL™ 1 (NCT03782792) was a 12-week Phase II trial investigating patients with a GPP flare (N=53). Patient were randomized 2:1 and were treated intravenously with either 900 mg of Spesolimab or placebo. The primary endpoint was a GPP Physician Global Assessment (GPPGA) pustulation subscore of 0 (no visible pustules) at week one. The key secondary endpoint was a GPPGA score of 0/1 (clear/almost clear skin) at week one.	Phase II	<i>Study completed and primary endpoint met. Published in New England Journal of Medicine. Data showed that spesolimab, a novel IL-36 antibody treatment, was effective in rapidly treating adult patients with generalized pustular psoriasis (GPP) experiencing a flare.</i>
CONNEX is a Phase III clinical trial program designed to assess the safety and efficacy of BI 425809 for improving cognition in adults with schizophrenia. The program is comprised of three clinical trials, which are Phase III randomized, double-blind, placebo-controlled parallel group trials, to examine the efficacy and safety of BI 425809 once daily over a 26-week treatment period in patients with schizophrenia.	Phase III	<i>Start of Phase III.</i>
TRISTARDS (NCT04640194) is a seamless, open-label, randomized, parallel-group Phase IIb/III trial which evaluates the efficacy and safety of daily intravenous alteplase for up to five days on top of best available medical management (standard of care) compared with best available medical management alone, in adults with COVID-19 Acute Respiratory Distress Syndrome (ARDS). Primary objective of the trial is the time to clinical improvement or hospital discharge.	Phase III	<i>Start of Phase III.</i>

## Animal Health

In the area of Animal Health, Boehringer Ingelheim concentrates on the discovery and development of treatments and preventive therapies in areas where the medical need is unmet and where our efforts will have the greatest impact – such as targeted therapeutics for oncology and immunology, new chemical entities and new methods of control to counter resistance in parasites, as well as new tools and technologies to improve the prevention of infectious diseases. The current portfolio includes innovative vaccines and antiparasitics for the protection of livestock and pets, as well as pharmaceutical products for the treatment of chronic diseases. Our research increasingly incorporates new approaches and technologies such as the use of stem cells and monoclonal antibodies.

Our innovation strategy is built on a scientific approach to the investigation of the causes and mechanisms of diseases across multiple species – including animals and humans – leading to the discovery of new ways to mitigate those causes or intervene in the disease process. This broad approach enables us to work in close cooperation with our Human Pharma colleagues as well as with external partners in areas outside Animal Health. In our three strategic areas of infectious disease, noninfectious disease, and parasiticides, we use this strategy to target solutions that can be broadly applied across species:

- **Infectious disease (e.g., vaccines):** Focus on areas of innovation, such as mucosal immunity, bacterial disease, and transboundary and emerging diseases.
- **Non-infectious disease (e.g., therapeutics):** Focus on collaboration with Human Pharma and grow our capabilities in key technologies through targeted external partnerships.
- **Parasiticides:** Focus on maintaining our leadership through acceleration of key discovery and development programs for new molecules and investment in innovative technologies for the long term, including solutions that address sustainability.

Our 18 research and development sites are organized into six regional innovation centers located in the USA, Europe, and China. This organization supports the global innovation strategy by ensuring the concentration of critical mass and expertise needed to deliver therapies to customers in our key geographies. Specific sites within each region serve as a focus for competencies in particular segments of our overall strategy. Our footprint strengthens local execution and facilitates regional external networks and partnerships.

### Synergies through collaboration of Human Pharma and Animal Health

A key strategic advantage for Boehringer Ingelheim is that we retain both Human Pharma and Animal Health divisions. By exploiting the synergies between them, we have already successfully introduced such products as VETMEDIN®, SEMINTRA®, METACAM®, and ASERVO® EQUIHALER®. With additional promising compounds in our pipeline, we expect further innovation through this connection, particularly in the area of therapeutics.

External partnerships also play a key role. This is demonstrated by the integration of Global Stem cell Technology NV (later renamed Boehringer Ingelheim Veterinary Medicine Belgium), a company specialized in stem cell therapies for orthopedic and immunological animal diseases, already acquired in 2020. The cooperation led to the first stem cell-based animal health product, ARTI-CELL® FORTE, which was approved by the European Commission. In 2021, we initiated a number of new strategic partnerships, including a partnership with PetMedix, whose platform generates canine therapeutic antibodies for use in developing therapies for immune-mediated conditions such as cancer, allergy, and arthritis. We also are partnering with Lifebit to aid in detecting and early reporting of global infectious disease outbreaks through their AI platform. Furthermore, we continue our work with key research institutions such as the Friedrich-Loeffler-Institut, the Pirbright Institute, and Oxford University Innovation to develop more effective approaches to prevent African Swine Fever, which threatens the swine industry worldwide.



In 2021, we initiated more than 500 research, development and clinical studies worldwide and were awarded more than 126 product authorizations. New regulatory approvals in 2021 include NEXGARD® COMBO in the EU and Canada, which extends one of our flagship parasiticide brands to cats, and NEXGARD® SPECTRA in Brazil – a new market for this broad spectrum product that treats both endo- and ectoparasites. In the USA we received approval for FLEX PARVOPRRS®, a combination vaccine effective against reproductive failure caused by the two most common viral causes of porcine reproductive failure globally. Obtaining approvals for new products and new areas of application and expanding the geographic scope of our sales activities for existing products are additional important aspects of our research and development activities which help us to create value through innovation.

## Production

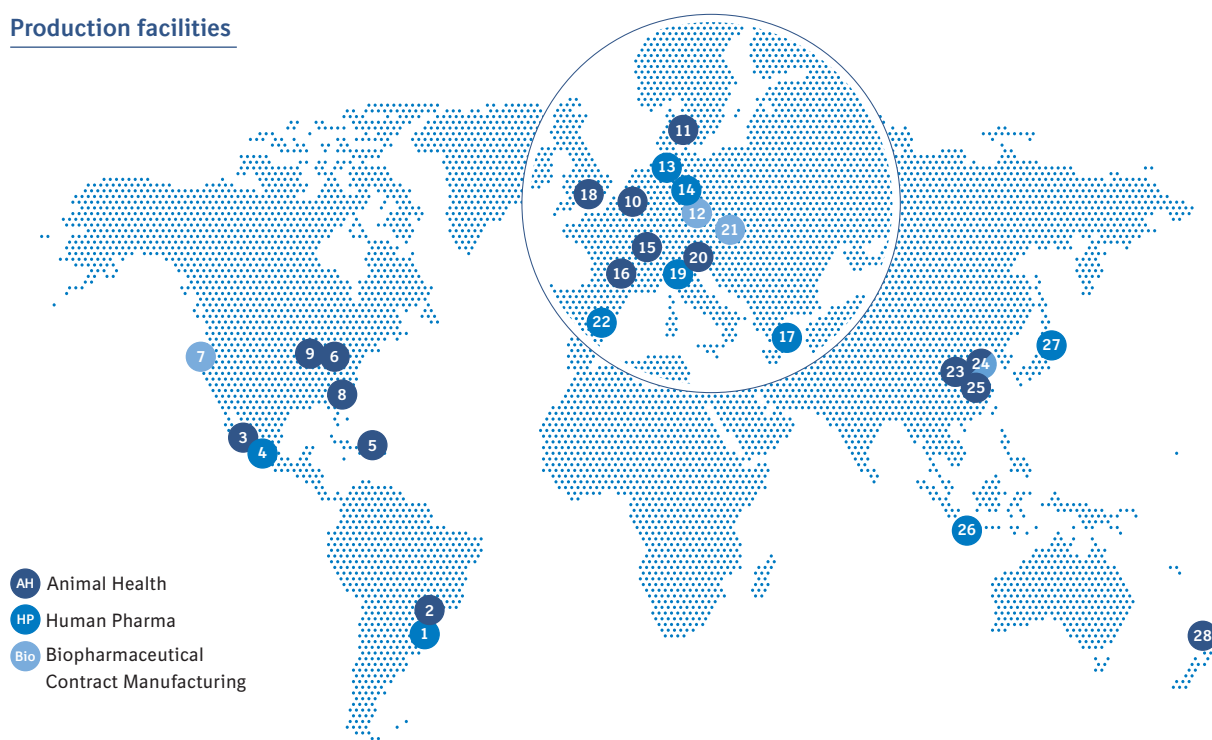
### Human Pharma

In the Human Pharma business, our globally active production facilities are responsible for the steady supply of top-quality medicines for patients. The ongoing development of the company's internal production facilities and our strategic cooperation with external manufacturers have established a modern, flexible market supply network which encompasses the entire value chain, from suppliers of starting materials to worldwide logistics and the distribution of finished pharmaceutical products. Boehringer Ingelheim's production facilities concentrate on products that are strategically important for the company, as well as on state-of-the-art manufacturing technologies. At the same time, partnerships with external manufacturers add specialist technologies to our production network that are not available in-house. They also expand the production capacity of standard technologies for products which have very high capacity requirements or are already far advanced in terms of their life cycle.

In the 2021 financial year, this global network included Boehringer Ingelheim's own plants in nine countries. The Group has four biopharmaceuticals facilities. It also has two facilities for the manufacture of pharmaceutical active substances and one that produces medical devices. Finished pharmaceutical products are manufactured at eight facilities. In the past year, which was once again characterized by unusual logistical challenges due to the COVID-19 pandemic, Boehringer Ingelheim was able to ensure a steady supply of medicines for patients. This was possible thanks to the establishment of key manufacturing steps and technologies at multiple facilities and by further strengthening the resilience concept for every link in the supply chain. The progressing digitalization of our production network and overall supply chain in 2021 played a key role in ongoing development measures to ensure the security of supply. The ongoing implementation of the Group's supply chain strategy optimizes the value chain management from the supplier to the customer ("end-to-end"). The use of digital and automated processes and technologies enables a high level of transparency and efficient management of the global production network supply chain.

Delivery capacity and patient care are top priorities for Boehringer Ingelheim. The company consistently makes important investments in the development and transformation of production capacities in our chemical and pharmaceutical network. At our Ingelheim am Rhein headquarters, we made a key investment in a flexible plant for the industrialization of newly developed medicines and their initial market supply. We made progress with the expansion of production technologies and capacities for pharmaceutical active substances at our Fornovo (Italy) facility, pharmaceutical bulk drugs at our Sant Cugat (Spain) facility, and for finished pharmaceutical products at our Koropi (Greece) and Yamagata (Japan) facilities to ensure the supply of anti-diabetic products (JARDIANCE® in particular) as well as pipeline products. The opening of our

## Production facilities



### Americas

#### Brazil

1. Itapecerica (HP)
2. Paulínia (AH)

#### Mexico

3. Guadalajara (AH)
4. Xochimilco (HP)

#### Puerto Rico

5. Barceloneta (AH)

#### USA

6. Athens, Georgia (AH)
7. Fremont, California (Bio)
8. Gainesville, Georgia (AH)
9. St. Joseph, Missouri (AH)

### Europe

#### Belgium

10. Evergem (AH)

#### Denmark

11. Kalundborg (AH)

#### Germany

12. Biberach (Bio)
13. Dortmund (HP)
14. Ingelheim am Rhein (HP)

#### France

15. Lyon (AH)\*
16. Toulouse (AH)

#### Greece

17. Koropi (HP)

#### Great Britain

18. Pirbright (AH)

#### Italy

19. Forno (HP)
20. Noventa (AH)

#### Austria

21. Vienna (Bio)

#### Spain

22. Sant Cugat (HP)

### Asia/Oceania

#### China

23. Nanchang (AH)
24. Shanghai (HP, Bio)
25. Taizhou (AH)

#### Indonesia

26. Bogor (HP)

#### Japan

27. Yamagata (HP)

#### New Zealand

28. Auckland (AH)

\* Grand Lyon Industrial Biologic Center (LPA St. Priest, Lentilly, Jonage)

biopharmaceutical large-scale cell culture production building at our Vienna facility represented a milestone in the expansion of our capacities in our network for newly developed products. Together with other production facilities in our global biopharmaceutical network, it covers, among other activities, the increased demand for ACTILYSE® and METALYSE®.

### Animal Health

In 2021, Animal Health products were manufactured in a network of 15 production facilities in eleven countries. In addition to the company's own facilities, in 2021 around 110 contract manufacturers turned out medicines for Boehringer Ingelheim. The company's product comprises vaccines, pharmaceutical products and nutraceuticals. These traditional medicines are supplemented with diagnostic products as well as monitoring solutions, including digital applications which are used for livestock monitoring or which link livestock owners with veterinarians. Optimization of the company's production network continues and remains a priority, with the goal of ensuring a reliable, efficient supply of all its products.

In 2021, Boehringer Ingelheim invested in capacity expansion for the strongest revenue contributor, NEXGARD®, at its Barceloneta (Puerto Rico) facility; in the expansion of small animal vaccine production at the company's facility in Athens (Georgia, USA); in the expansion of vaccine capacity in Lyon (France) and St. Joseph (Missouri, USA); and in capacity expansion for foot-and-mouth disease vaccines in Jonage (France) as well as the expansion of its pharmaceutical manufacturing capacities in Toulouse (France). It also invested in the development of modern technologies for the manufacture of our products.

### Biopharmaceutical Contract Manufacturing

Boehringer Ingelheim pursues its biopharmaceutical activities at its facilities in Biberach (Germany), Vienna (Austria), Fremont (California, USA), and Shanghai (China). They comprise the manufacture of own-brand marketable products (such as ACTILYSE®, METALYSE®, and PRAXBIND®), the manufacture of biopharmaceuticals for clinical testing of pipeline products and – as one of the world's leading companies – process development, launch preparation, and commercial production of biopharmaceuticals for third-party industrial customers. Twelve of the top 20 pharmaceutical companies and innovative biotech firms are clients of our Biopharmaceutical Contract Manufacturing business. Boehringer Ingelheim covers the entire biopharmaceutical value chain, from development of the production cell (mammalian cells as well as microorganisms) and the production process, to the manufacture of the active substance and the finished pharmaceutical product, to product launch and global market supply.

# 15

**Animal Health  
production facilities  
in eleven countries**

**One of the leading  
Biopharma provid-  
ers for industrial  
customers**

Capacity utilization of the established network's industrial-scale production facilities remained at a very high level in 2021. At our Biberach facility, the optimized production process was successfully demonstrated in a bioequivalence study along with ramped-up production to meet the growing market demand for ACTILYSE®. To achieve a rapid increase in production volumes, we initiated the transfer of the optimized process to our new large-scale cell culture plant in Vienna. By way of support for the process of submission to the authorities in the EU, the USA, and Japan, Biberach launched preparatory activities for Boehringer Ingelheim's IL36R monoclonal antibody spesolimab which is expected to be introduced to the market in 2022. Our microbial production facility at our Vienna site was approved for a further customer product, a carrier protein for vaccines; our microbial product portfolio has thus increased to 18 biopharmaceuticals. Despite the challenging external conditions associated with the COVID-19 pandemic, our cell culture plants in Biberach, Shanghai, and Fremont and our microbial production in Vienna continued to manufacture and deliver biopharmaceuticals for patients worldwide without incurring interruptions.

The expansion of our cell technology capacity at our Vienna facility was completed in the past year. The local authority authorized its commissioning in compliance with good manufacturing practices (GMP) halfway through the year. Transfer and production activities are currently underway.

Also at our Vienna facility, we completed our microbial expansion project for the production of a recombinant vaccine in 2021. In view of the growing global importance of biotechnologically produced active substances and the significant increase in the number of internal development projects in our own portfolio, these two projects are both of key strategic relevance.

In 2021, our Shanghai facility focused on the market supply of an immuno-oncological antibody for a Chinese customer's cancer therapy. We also further expanded our customer and product portfolio at our facility in Shanghai (China), and filed for this facility's approval for the US market. Its activities focus on the supply of innovative medicines for patients through Chinese and multinational biopharmaceutical companies. Customers greatly benefit from the fact that Boehringer Ingelheim, as a contract development manufacturing organization, is able to cover the entire value chain from a single source and has long-term experience and technical expertise in the preparation of product launches and market supply.

## Employee reporting

In 2021, Boehringer Ingelheim employed 52,391 people on average worldwide. This represents an increase of +0.9% over the previous year.

### Average number of employees by region

	2021	2020
Americas	13,187	13,176
Europe	28,266	27,379
Asia/Australia/Africa (AAA)	10,938	11,389
	<b>52,391</b>	<b>51,944</b>



Our committed employees, who identify with our company's aims and appreciate the respectful work climate at Boehringer Ingelheim, are a major success factor driving our Group's positive growth. With their high level of personal commitment, they help us to fulfill our joint promise of ensuring the supply of vital medicines. This holds particularly true during the worldwide pandemic. Our annual global employee survey provides us with relevant feedback which enables us to continuously improve our work environment.

Boehringer Ingelheim's success is based on innovation as well as its presence in 80 countries. The global nature of our value chain, the international nature of our clientele, and the stringent and greatly varying requirements of national regulators demand great flexibility of our organization as a whole. We are convinced that relationships based on trust as well as mutual openness, respect, and empathy are values that make us strong and competitive. Diversity of thought and a spirit of inclusion in our relationships with one another promote a capacity for innovation in every area of our business.

In addition to competitive salaries, Boehringer Ingelheim offers other benefits to its employees. These benefits include a range of company pension plans, flexible and home-based work options, and numerous health-related benefits. Our human resources department is responsible for promoting a wide range of opportunities for innovation at work – which is a significant aspect of our corporate strategy – and for helping our employees to nurture their personal strengths while developing as individuals. In order to be best prepared for the challenges ahead, we emphasize the acquisition of technical expertise as part of a comprehensive qualification system.

Vocational training has always been of major importance to Boehringer Ingelheim. The company provides young people with career entry opportunities. At the same time, we also retain a talented and well-qualified workforce of young professionals in times of demographic change. However, at our company, vocational training does not just mean passing on expertise. We emphasize getting to know one another and enable young professionals to experience the many aspects of our company and our values. We achieve this goal by means of hybrid learning and teaching.

On average, 749 young people worldwide were enrolled in Boehringer Ingelheim's vocational training program in 2021. At Boehringer Ingelheim's German facilities alone, 201 young people started their careers in 28 different scientific, technical, and commercial fields, through training and dual-study courses. The selection of training and dual-study courses is closely coordinated with our disciplines to ensure that the curricula and training programs meet our needs.

One of the company's important aims is to strengthen the appeal of Boehringer Ingelheim as an employer for our current and future employees. In 2021, Boehringer Ingelheim once again won recognition as a top employer from the auditors of the international independent Top Employers Institute. Awards in 27 countries and three regions not only represent an increase of nine awards compared to the previous year, but also mean that Boehringer Ingelheim is, for the first time, a "Global Top Employer." Of the approximately 1,600 companies which received awards, only 16 were awarded this distinction worldwide. In addition to Germany, Boehringer Ingelheim was also granted this distinction in Argentina, Australia, Austria, Brazil, Chile, China, Colombia, Ecuador, Hungary, Indonesia, Italy, Malaysia, Mexico, the Netherlands, New Zealand, the Philippines, Poland, Romania, Russia, Saudi Arabia, Singapore, South Korea, Spain, Thailand, the United Kingdom, and Vietnam.

**Boehringer  
Ingelheim  
recognized as  
"Global Top  
Employer"**

## Sustainable Development – For Generations

### Sustainable Development as part of our strategy

Sustainability has been firmly anchored in our corporate philosophy since Boehringer Ingelheim's founding in 1885. Our understanding and awareness of sustainability has continuously developed over the generations and influences our decision-making and actions. We have also learned from the global pandemic. This has made it obvious how imperative a holistic approach is to address the intertwined connection between humans, animals, and the environment.

With our focus on human and animal health, Boehringer Ingelheim is well positioned to provide a relevant contribution to a healthier and more sustainable future. In 2021, we updated our sustainability strategy, entitled "Sustainable Development – For Generations." In the process, the focus was on the following: the definition of designated impact areas, a stronger usage of synergies, and unifying our company's global collaborative network as well as ensuring alignment with the UN Sustainable Development Goals. The strategy is based on the following three pillars:

MORE HEALTH – For People and Animals  
MORE POTENTIAL – For Communities and Our People  
MORE GREEN – For Our Planet

Boehringer Ingelheim aims to achieve the following concrete measurable goals by 2030:

**MORE HEALTH:** Expanding access to healthcare for an additional 50 million people in vulnerable communities, investing 35 billion EUR in health innovation and research to tackle non-communicable diseases and an additional 250 million EUR in partnerships to combat emerging infectious diseases.

**MORE POTENTIAL:** Our aim is to positively impact 50 million people in vulnerable communities by empowering and supporting our employees, partners, and innovative social entrepreneurs.

**MORE GREEN:** We will become carbon-neutral in our company operations by 2030 (Scope 1 and 2). We will also significantly reduce the resource footprint across the value chain in the same period, despite our growing business activities.

### MORE HEALTH – For People and Animals

MORE HEALTH follows our ambition to develop better therapies and enable better solutions for global healthcare challenges. The pillar includes a number of projects and initiatives, reflecting the diversity of our patients and the expertise of our partners. These include:

**MORE HEALTH**  
Focus on the  
health of people  
and animals

#### Access to Healthcare

The “Access to Healthcare” initiative seeks to improve the healthcare in vulnerable communities, starting with availability of medicines to access to safe and effective prevention and care. We have achieved several milestones, for example:

- Expanding access to healthcare in less developed regions through the UN Defeat-NCD Partnership.
- We have launched a joint initiative with “PharmAccess” as part of our “In Reach Africa” program in Kenya. Mobile technology improves awareness of hypertension and diabetes and lowers barriers to access.
- The “Pathway” project fund launched in Canada in 2021 intends to improve the lives of 20,000 members of indigenous communities. Above all, the project will address the excessive prevalence of certain non-communicable diseases in these communities.
- A pilot program was launched in Pakistan in 2021 in collaboration with the World Organization of Animal Health, which supports the elimination of rabies by donating the animal vaccine RABISIN® and dog identification collars.

#### Angels

The “Angels” initiative was established in 2016 to improve stroke care worldwide. In 2021, additionally around 2,000 clinics, 26 countries, and 27,000 doctors and nurses joined this continuously growing network. It now includes over 72,300 healthcare professionals and 6,300 clinics in 145 countries and helps ensure that all patients are treated in line with defined standards. The Angels Initiative was featured in the Access To Medicine Report 2021 as a “best practice” example of capacity building and was distinguished with the World Stroke Organization’s Stroke Service Award.

#### LastMile

South of the Sahara, smallholder farmers in Africa often lack access to veterinary treatment. The joint initiative “LastMile” aims to achieve a long-term, sustained improvement in the availability of veterinary products and services. This project was launched in Kenya in 2018 and has since expanded to Cameroon, Nigeria, Mali, Burkina Faso, and Ethiopia. Currently, 22 LastMile Live-stock Service Providers (LLSPs) are working in the field. In 2021, relevant veterinary medicine and farm management modules were added to the LLSP training programs, and four new products were included in the product portfolio. Subsequently, a total of 55 products have now been included. In total, LastMile has assisted many farmers and provided numerous animal trader visits and veterinarian visits.

## MORE POTENTIAL

### Focus on people and communities

#### MORE POTENTIAL – For Communities and Our People

MORE POTENTIAL is focused on providing not only safe, but also the best possible conditions in order for people at Boehringer Ingelheim, in our communities, and at our partners to reach their full potential.

#### BE SAFE

Through the “BE SAFE” program, which was established in 2010, we place a particular emphasis on ensuring a safe workplaces for our employees and partners. We are therefore continuously reviewing and optimizing our work and safety culture and strive to maintain our employees’ long-term good health by preventing accidents, incidents, and occupational health risks. In 2021, Boehringer Ingelheim became an official partner of the EU-OSHA “Healthy Workplaces Lighten the Load 2020-2022” campaign to prevent work-related musculoskeletal disorders (MSDs). In addition, in the spring the internal campaign “Shed a Light” was launched to raise awareness on mental health issues in the workplace and encourage employees to speak up and address this.

#### Diversity & Inclusion

Through our core values of empathy, respect, passion, and trust, we foster a diverse, collaborative, open, and inclusive work environment, which is key for innovation, value creation, and sustainable growth. Boehringer Ingelheim is convinced that valuing diversity is not only the right thing to do for our people and communities, but also the smart thing to do for our business, since it helps us to understand and fulfill the different needs and requirements of our patients, customers, and partners around the globe. In 2021, we continued our focus on awareness and education. This included updating training programs on topics such as unconscious bias and inclusive behavior.

#### Human Rights

Boehringer Ingelheim is continuously stepping up efforts in the areas of human rights and ethics. The approach is aligned with the United Nations’ Guiding Principles on Business and Human Rights. Subsequently, our Human Rights Policy is an integral component of our guidelines for cooperation with external partners, e.g., in the code of conduct.

#### Making More Health

In 2010, Boehringer Ingelheim and Ashoka, the world’s largest network of social entrepreneurs, jointly established the “Making More Health” (MMH) initiative. This long-term partnership focuses on enabling innovative solutions to tackle complex healthcare challenges for people, animals, and their communities. This approach links interdependent issues such as economic development, infrastructure, education, culture, and healthcare issues. It emphasizes collaboration with communities as equal partners and engages Boehringer Ingelheim employees to share their knowledge and skills. Highlights include:

- **Social innovation:** To date, over 120 innovators worldwide working in the areas of human and animal health have been supported.
- **Community activation:** Since 2014, programs have been initiated in India, Kenya, Nigeria, and Ghana which have already impacted 150,000 lives and proven to be game changers. This includes clean water and hygiene projects, implementing innovative farming models, and providing animal health and business skills training courses as well as inclusion programs for marginalized community groups, such as people with albinism.



- **Cross-sector collaboration:** “Making More Health” emphasizes a “win-win” collaborative approach to bridge the gap between business and society. One such initiative is the “Business Accelerator” funding program. The initiative provides funding and expertise to support social start-ups in Sub-Saharan Africa, enabling them to scale up and sustain their business models. Many of these social enterprises have now progressed to a stage where more substantial funding is necessary.

Subsequently, the new initiative “Boehringer Ingelheim Social Engagement” was launched in 2021 with an investment of 50 million EUR to offer in addition to corporate donations alternative financing opportunities for social entrepreneurs. This includes, for example, the provision of subordinate loans, whose terms and conditions would be adjusted to the local needs and requirements of the social enterprises.

Also in 2021, the “MMH Connect” IT platform was launched, which aims to enable and match 20,000 Boehringer Ingelheim employees to support effective and innovative partnerships with social enterprises by 2030, where they will be able to contribute their skills while also developing as individuals.

The “Making More Health Together 2021” convention, a two-day virtual event, brought together over 1,800 participants from across academia and the non-profit, industry and political sectors. In more than 40 interactive sessions, the participants discussed how to resolve the world’s most pressing health-related issues.

#### **MORE GREEN – For Our Planet**

A healthy planet is a prerequisite for healthy people, animals, and communities. Environmental challenges should not be seen in isolation, as they have tangible effects on the health of whole societies. The sustainable use of natural resources and the promotion of a strong environmental awareness are subsequently key components of our environmental sustainability program, in order to help protect the health of current and future generations and safeguard their prospects for a healthy future.

The MORE GREEN Fund supports internal projects in the areas of decarbonization, water management, and the circular economy and has already provided funding for approximately 40 new environmental projects worldwide since 2020. Boehringer Ingelheim pays particular attention to ecological aspects in its major projects and has set aside an additional 130 million EUR for this purpose.

In 2021, Boehringer Ingelheim was the first pharmaceutical company in the EU to receive the “GreenCanteen” certification for the sustainable catering concept at the Ingelheim headquarters.

**MORE GREEN**  
Focus on the  
environment

### Carbon Footprint

We are continuously working on reducing our greenhouse gas emissions, having committed to becoming carbon-neutral in our operations (Scope 1 and 2) by 2030, using 100 % renewable electricity and continuing to make substantial investments in sustainable technology. One of the tools used in this process is the introduction of an internal carbon price of 100 EUR per ton to create an additional economic incentive for green innovation. Further recent examples of our activities include:

- The construction of a new biomass power plant in Ingelheim.
- The transition to renewable electricity solutions at numerous locations, including sites in Germany, Austria, Spain and the USA. Since 2020, the company's share of renewable electricity purchased worldwide has increased from 30 % to over 50 %.
- The certification of carbon neutrality for the sites Dortmund and Sant Cugat.
- Our partnership with ClimateSeed supports biodiversity and protects drinking water by offsetting carbon emissions through, among others, reforestation projects in Africa, India, Indonesia, and Germany.

### Resource Use

Circular economy aspects are implemented in stages of the value chain to minimize waste and to apply eco-design and green chemistry concepts in new products. Through continuous optimization measures, we have reduced our annual volume of waste to landfills and resource use since 2010. We are thus optimizing the environmental footprint of future Boehringer Ingelheim products.

### Water Stewardship

Access to clean water has a major impact on social and cultural justice, environmental sustainability, and the local economy. For this reason, Boehringer Ingelheim implements programs related to water and related risks at all production sites. Sites in established water scarcity areas implement a recognized "Water Stewardship" program, such as that of the "Alliance for Water Stewardship" (AWS). In 2021, the AWS certification of our Promeco production facility in Xochimilco (Mexico) was renewed and the AWS certification process for our production facility in Fremont (California, USA) was initiated.

Furthermore, we have evaluated the wastewater at the production sites regarding possible residues of active pharmaceutical ingredients (API) and other trace substances. On this basis, "Clean Water" initiative ensures that traces of pharmaceuticals in wastewater remain significantly below any effect level. The initiative also works with industrial networks and suppliers to cover the entire value chain.

In this context, Boehringer Ingelheim finances joint projects with "Making More Health" in Kenya, which aim to improve access to clean water.

# Report on economic position

## Macroeconomic environment

World economic output recovered in 2021 following its COVID-19-related collapse in 2020. According to the International Monetary Fund (IMF), the global economy grew by +5.9%. In the first six months of the year, many economies experienced an upswing due to the easing of the measures which had been introduced in order to contain the pandemic and on account of the increased level of consumer demand. This growth slowed in the second half of the year due to factors including industrial enterprises' continuing global supply and capacity bottlenecks as well as rising commodity prices and freight costs. The trade policy situation between the USA and China remained tense. There was a further increase in tensions in 2021, which was reflected in factors such as increased import duties. Also the conflict between Russia and Ukraine is closely monitored. There were also signs of rising inflation.

Unlike other sectors, pharmaceutical markets tend to be shaped by long-term economic output and, in particular, by societies' demographic trends. Their performance is also influenced by the continuous global improvement in access to healthcare. The global pharmaceutical market – not including COVID-19 vaccines – thus increased to 1.3 trillion USD in the past year. This corresponds to a +5% average annual rate of growth over the past five years (source: IQVIA). However, developing countries' growth contribution decreased relative to the situation at the start of this decade. In the pharmaceutical industry, social distancing measures resulted in delays in clinical studies and thus impacted the schedules of research activities or had to be compensated by additional costs where possible. Largely stable core business by comparison with other industries allowed pharmaceutical companies to remain a key driver of investment in research and development, including in the fight against the SARS-CoV-2 virus.

In 2021, healthcare systems around the globe were further pressured by the COVID-19 pandemic, the burden of chronic diseases, aging populations, and increased budget pressure. In order to address these challenges, governments and healthcare authorities are expanding the use of cost-containment actions including mandatory price reductions, external reference pricing, lengthy as well as complex negotiation processes which delays access to innovative new medicines. Also the patient is increasingly involved in the cost for treatments, by different forms of co-payments. Such measures are increasingly putting pressure on the pharmaceutical companies and thus might limit their future ability to invest in the development of new treatment options and to improve access to innovative medicines. The pharmaceutical industry is working together with governments and healthcare authorities to address these challenges and thus to maintain and improve sustainable patient access, to reduce access delays and continuously bring innovation to the patients. An important prerequisite for achieving this objective remains a reliable legal framework that promotes innovation and ensures the protection of intellectual property.

The animal health market – consisting of the pet and livestock segments – continued its positive growth trend in 2021. This mainly reflects population growth, many people's rising living standards in the emerging markets and animals' improved life expectancy due to continuous advances in veterinary care. In the pet segment, pets' growing popularity due to the COVID-19 pandemic prompted an increased level of demand for products. The livestock segment is benefiting from growing demand for animal products. The increasing prevalence of zoonoses (infectious diseases which are transmissible from animals to humans and from humans to animals)

**Growing Human  
Pharma market  
allowed increased  
investment in R&D**

**Animal health  
market continues  
positive growth  
trend**

is reinforcing the importance of the animal health industry. In general, consolidation through mergers on both the supplier and customer sides is ongoing. This is resulting in increased competition. In the future, growth in the Animal Health business will largely be driven by therapeutic innovation. In order to grow with the market, investments need to be continuous, sustainable, and competitive.

In 2022, according to the IMF, the global economy will grow by 4.9%. The advanced economies which have broad access to COVID-19 vaccines are expected to have made up for their pandemic-related decline in economic output by the end of 2022. Moreover, there are many different scenarios with regard to the inflation trend and when inflation might return to a pre-pandemic level. However, according to the IMF there are also a large number of risks associated with world economic growth: Vaccine-resistant mutations of the COVID-19 pathogen and uneven access to vaccines are resulting in increasing gaps between developing countries, emerging markets, and the advanced economies. In addition, ongoing climate change is increasing the risk of natural disasters and thus of the related health and economic impacts.

### Currency trends

Boehringer Ingelheim's global presence means that currency trends influence its revenue figures. The US dollar (USD), the Japanese yen (JPY) and the Chinese renminbi (CNY) are particularly worthy of note here. Following a low of 1.22 EUR/USD (January) at the start of the year, the US dollar had reached a high of 1.13 EUR/USD (December) by the end of the year. The Japanese yen fluctuated between a high of 126.31 EUR/JPY (January) and a low of 132.63 EUR/JPY (June). At the start of the year, the Chinese renminbi was at a low of 7.87 EUR/CNY (January) and had reached a high of 7.20 EUR/CNY by the end of the year (December). Significant transactional currency risks are hedged through suitable currency instruments.

### Currency development

Average rate – basis: 1 EUR	2021	2020	Effect on net sales (in million EUR)
US dollar	1.18	1.14	-268
Japanese yen	129.86	121.78	-92
Chinese renminbi	7.63	7.87	+33

### Earnings position

A stable and competitive earnings position and solid financing guarantee Boehringer Ingelheim's independence and are therefore central to our activities. It is on this basis that we pursue our guiding principle of "Value through Innovation" and contribute to improvements in human and animal health by means of innovative therapies.



Boehringer Ingelheim's positive growth trend remained intact in 2021. We recorded net sales of 20,618 million EUR, which represents a +5.4 % increase relative to the previous year's net sales figure of 19,566 million EUR. Exchange rate effects adversely affected the sales trend in 2021. Adjusted for these effects, the Group achieved a growth rate of +7.5 %.

**20.6**  
billion EUR in net sales

Growth in all  
regions

We achieved sales growth in every region. As in previous years, with sales of 9,147 million EUR and a 44 % share of overall sales the Americas region was Boehringer Ingelheim's key sales market and grew by +2.9 % (currency-adjusted +6.6 %). The Europe region registered the strongest level of sales growth in the past financial year, with a rate of +11.5 % (currency-adjusted +11.3 %). Its sales volume amounted to 6,554 million EUR, which represents a 32 % share of Group sales. This positive trend was mainly driven by the global licensing business which is allocated to this region, as well as in the markets in Germany, Spain, the United Kingdom, and the countries of Eastern Europe. In our Asia/Australia/Africa (AAA) region, sales increased by +2.5 % (currency-adjusted +4.3 %) to 4,917 million EUR. Especially due to institutional price adjustments in a core market and, to some degree, the continuing effects of the COVID-19 pandemic on the course of business, the AAA region was unable to emulate the growth rates which it had registered in previous years.

#### Net sales by region (in million EUR)

	2021	2020	Change	currency-adjusted
Americas	9,147	8,889	+2.9 %	+6.6 %
Europe	6,554	5,879	+11.5 %	+11.3 %
Asia/Australia/Africa (AAA)	4,917	4,798	+2.5 %	+4.3 %

In our Human Pharma business, in 2021, we once again made our products available to more patients thanks to new approvals in additional countries; we also further strengthened established products. These include the products of the JARDIANCE® family and OFEV® especially. Global licensing business also provided a significant growth contribution. Our R&D pipeline is developing positively. Important milestones were reached here in 2021. Our Animal Health business grew in 2021, particularly in our pet segment. In our Biopharmaceutical Contract Manufacturing business, the commissioning of our large-scale cell culture plant in Vienna was a key milestone for us and a highlight of the 2021 financial year.

#### Key figures (in million EUR)

	2021	2020	Change
Net sales	20,618	19,566	+5.4 %
Operating income	4,705	4,624	+1.8 %
Return on net sales	22.8 %	23.6 %	
Income before taxes	4,368	4,305	+1.5 %
Income after taxes	3,406	3,062	+11.2 %

The materials ratio (taking into consideration the change in inventory) rose slightly to 13.5% (2020: 12.9%). Personnel expenses increased by +1.9%, primarily due to the additional employees hired in the areas of research, development, medicine, and biopharmaceutical medicine production, which are of strategic significance for Boehringer Ingelheim.

Amortization of intangible assets and depreciation of tangible assets in 2021 were – 242 million EUR lower compared with the previous year. This was particularly attributable to a high volume of impairment losses on intangible assets in the 2020 financial year. On the other hand, the continuing high level of investment activity and acquisitions resulted in increased amortization of intangible assets and depreciation of tangible assets.

We achieved growth in all of our businesses in the 2021 financial year, and our operating income increased to 4,705 million EUR. The positive sales trend for our businesses enables us to make long-term investments in research and development – we increased our research and development expenditure as a percentage of net sales to 20.0% in the 2021 financial year. Our return on sales fell to +22.8% (2020: +23.6%). This was due to higher prices on our procurement markets, our increased number of employees in strategically important areas, and our investments. Financial income and holding income were both influenced by one-off effects. While the previous year's holding income had included the profit from the sale of an investment and was thus lower in 2021 for this reason especially, financial income improved, in particular, due to the new method which was introduced in 2021 for the measurement of long-term obligations. Income before taxes therefore rose particularly due to the higher operating income.

Income after taxes was likewise higher than in the previous year. This reflected the improved pre-tax profit as well as lower income taxes. It must be noted in this regard that, under the provisions of German commercial law, shareholders' personal taxes arising from Group business activities may not be recognized as tax expenses. Instead, these taxes are presented as part of withdrawals from Group equity. When taking this specificity into account, the actual tax ratio is markedly higher than the figure shown in the profit and loss statement.

# 3.4

billion EUR  
Group profit

Despite challenging market conditions in some business areas and the heightened cost pressure, Boehringer Ingelheim registered a positive performance in the 2021 financial year. Following a Group profit of 3,062 million EUR in the previous year, in 2021, this figure rose by +344 million EUR to 3,406 million EUR.

## Development of the businesses

In the past year, Boehringer Ingelheim's activities were divided into the Human Pharma, Animal Health, and Biopharmaceutical Contract Manufacturing businesses.

### Net sales by business (in million EUR)

	2021	2020	Change	currency-adjusted
Human Pharma	15,294	14,415	+ 6.1 %	+ 8.4 %
Animal Health	4,295	4,121	+ 4.2 %	+ 6.2 %
Biopharmaceutical Contract Manufacturing	917	837	+ 9.6 %	+ 9.5 %
Other sales	33	33	+ 0.0 %	+ 1.2 %
Discontinued operations	79	160	- 50.6 %	- 49.2 %

### Human Pharma

The Human Pharma business is the mainstay of Boehringer Ingelheim's activities and accounts for a 74 % share of the Group's net sales. Sales in our Human Pharma business increased by + 6.1 % (currency-adjusted + 8.4 %) in the 2021 financial year to 15,294 million EUR. This growth was mainly driven by the established products of the JARDIANCE® family as well as OFEV®. The growing volume of licensing business – in particular SKYRIZI® which we have licensed to AbbVie, which is responsible for the marketing of this product – also made a key contribution to the positive development of our Human Pharma business.

### Human Pharma: Net sales Top 5 products (in million EUR)

	2021	2020	Change	currency-adjusted
JARDIANCE® Family	3,940	3,140	+ 25.5 %	+ 28.6 %
OFEV®	2,491	2,055	+ 21.2 %	+ 25.4 %
TRAJENTA® / JENTADUETO®	1,552	1,512	+ 2.6 %	+ 5.1 %
SPIRIVA®	1,548	1,793	- 13.7 %	- 11.9 %
PRADAXA®	1,318	1,492	- 11.7 %	- 10.3 %

The strongest revenue contributor in 2021 was JARDIANCE®, which is used to treat type 2 diabetes. The JARDIANCE® family generated net sales of 3,940 million EUR, which was thus + 25.5 % (currency-adjusted + 28.6 %) higher than in the previous year.

**JARDIANCE® and OFEV® drive growth**

OFEV®, Boehringer Ingelheim's second biggest-selling product in 2021, is mainly used to treat idiopathic pulmonary fibrosis and two additional indications, SSc-ILD and PF-ILD. OFEV® recorded net sales of 2,491 million EUR and thus achieved a growth rate of + 21.2 % (currency-adjusted + 25.4 %).

Unlike in the previous year, TRAJENTA® and JENTADUETO® – which are used to treat type 2 diabetes – returned to sales growth. Sales increased by + 2.6 % (currency-adjusted + 5.1 %) in 2021 to 1,552 million EUR.

SPIRIVA®, which is used for the treatment of chronic obstructive pulmonary disease (COPD), registered declining sales figures. This reflects the stage that this product has now reached in its life cycle. In line with expectations, the net sales volume of 1,548 million EUR in 2021 was – 13.7% (currency-adjusted – 11.9%) lower than in the previous year.

Sales of the anticoagulant PRADAXA® fell by – 11.7% (currency-adjusted – 10.3%) year-over-year. However, with a sales volume of 1,318 million EUR PRADAXA remained one of Boehringer Ingelheim's five biggest-selling medicines in the 2021 financial year.

Sales growth of + 136.3% (currency-adjusted likewise + 136.3%) was registered for the licensing income provided by SKYRIZI®. This product, which is marketed globally by our partner AbbVie, is based on risankizumab, a medication for treatment of plaque psoriasis which was mainly developed by Boehringer Ingelheim. In 2021, this medicine was also approved in several markets for the treatment of Crohn's disease and psoriasis arthritis. The sales volume in the 2021 financial year thus also reflects related one-off milestone payments.

The Human Pharma business achieved growth in every region year-over-year. In terms of the regional distribution of this revenue, the USA remained our strongest revenue contributor, with a growth rate of + 2.1% (currency-adjusted + 5.9%) to 5,777 million EUR. This represents an almost 38% share of the Human Pharma business's overall sales volume.

We achieved net sales of 5,221 million EUR in our EUCAN region (Europe, Canada, Australia, and New Zealand) in 2021, a growth rate of + 13.9% (currency-adjusted + 13.2%). The EUCAN region thus once again gained in importance, with a 34% share of sales (+ 2% points higher than in the previous year).

The company's emerging markets also registered an improved volume of sales in the past financial year, with a growth rate of + 4.2% (currency-adjusted + 5.9%). Overall, sales in these countries rose to 2,959 million EUR. However, single-digit growth in the emerging markets fell short of our expectations. The Chinese market was particularly challenging. Sales fell here by – 4.5% (currency-adjusted – 7.3%) due to the inclusion of core products in the country's national reimbursement drug list and the use of volume-based procurement mechanisms.

Japan accounted for almost 9% of total net sales in the Human Pharma business. Sales here rose by + 0.5% (currency-adjusted + 7.1%) to 1,337 million EUR.

#### Human Pharma: Net sales by region (in million EUR)

	2021	2020	Change	currency-adjusted
USA	5,777	5,658	+ 2.1%	+ 5.9%
EUCAN	5,221	4,585	+ 13.9%	+ 13.2%
Emerging Markets	2,959	2,841	+ 4.2%	+ 5.9%
Japan	1,337	1,331	+ 0.5%	+ 7.1%

#### Animal Health

In the past financial year, the Animal Health business achieved net sales totaling 4,295 million EUR and thus provided almost 21% of the Group's sales. Animal Health increased its sales volume by + 4.2% (currency-adjusted + 6.2%) and thus stepped up its pace of growth relative to the previous year. This growth was driven by the pet segment.



**Animal Health: Net sales Top 4 products (in million EUR)**

	2021	2020	Change	currency-adjusted
NEXGARD®	916	804	+ 13.9 %	+ 16.6 %
FRONTLINE®	418	406	+ 3.0 %	+ 4.8 %
HEARTGARD®	307	312	– 1.6 %	+ 1.4 %
INGELVAC CIRCOFLEX® / FLEXCOMBO®	253	264	– 4.2 %	– 2.7 %

This segment accounts for the biggest-selling medicines in our Animal Health business: The antiparasitics NEXGARD® and FRONTLINE® registered growth rates of + 13.9 % (currency-adjusted + 16.6 %) and + 3.0 % (currency-adjusted + 4.8 %) in 2021. In the past year, NEXGARD® achieved a sales volume of 916 million EUR and thus remained the biggest-selling product in our Animal Health portfolio. FRONTLINE® was our second-biggest seller, with a revenue of 418 million EUR.

**Pet segment  
drives growth**

The medicine HEARTGARD® suffered a – 1.6 % decline (currency-adjusted + 1.4 %) in sales in the past financial year. This product is used to prevent heartworm disease. It contributed 307 million EUR to the Animal Health business' sales volume.

Our swine vaccine INGELVAC CIRCOFLEX® also registered a declining sales volume in 2021: revenue fell by – 4.2 % (currency-adjusted – 2.7 %) to 253 million EUR – not least due to the continuing challenges associated with African swine fever in key markets.

In our Animal Health business, we surpassed the previous year's sales volume in every region. In the USA, we achieved currency-adjusted growth of + 3.9 % and registered a positive course of business in the 2021 financial year, particularly in our pet segment including horses. This compensated for a slightly lower sales figure in the swine segment.

The EUCAN region likewise registered strong sales growth in the pet segment. On the other hand, growth in the swine and poultry segments failed to match our expectations. Overall sales growth in the EUCAN region amounted to + 8.1 % (currency-adjusted + 7.0 %).

The TCM region (The Chinese Market) improved its sales volume by + 17.1 % (currency-adjusted + 15.1 %) year-over-year. This growth was mainly driven by the swine segment.

The ALAMEA (Asia, Latin America, Middle East, Africa) region registered sales growth of + 2.5 % (currency-adjusted + 6.6 %). Sales in the pet segment were higher than those in the livestock segment.

**Animal Health: Net sales by region (in million EUR)**

	2021	2020	Change	currency-adjusted
USA	1,819	1,815	+ 0.2 %	+ 3.9 %
EUCAN	1,345	1,244	+ 8.1 %	+ 7.0 %
ALAMEA	789	770	+ 2.5 %	+ 6.6 %
TCM	342	292	+ 17.1 %	+ 15.1 %

**Continued strong growth in the Biopharmaceutical Contract Manufacturing**

**Biopharmaceutical Contract Manufacturing**

In the Biopharmaceutical Contract Manufacturing business, revenue was +9.6% (currency-adjusted +9.5%) higher than in the previous year due to strong demand for our business partners' market products. The order situation for the entire business has developed positively, resulting in a high level of capacity utilization.

**Other sales/discontinued operations**

Under discontinued operations we aggregate activities of minor strategic importance for Boehringer Ingelheim. Net sales decreased as expected.

**Financial position**

Boehringer Ingelheim's financial management strategy aims to safeguard the company's financing by means of its operating cash flow as far as possible, to minimize financial risks, and to optimize the cost of capital.

Cash inflow from operating activities amounted to +3,846 million EUR and is attributable to the positive business performance in the 2021 financial year. It was –117 million EUR lower than in the previous year (2020: +3,963 million EUR), mainly due to an increase of receivables and higher tax payments.

(in million EUR)	2021
<b>Financial funds as of 1.1.</b>	<b>6,105</b>
Cash flow from operating activities	3,846
Cash flow from investing activities	–6,002
Cash flow from financing activities	–1,499
<b>Change in financial funds from cash relevant transactions</b>	<b>–3,655</b>
Change in financial funds due to exchange rate movements and valuation adjustments	96
<b>Financial funds as of 31.12.</b>	<b>2,546</b>

Cash outflow from investment activities increased significantly to –6,002 million EUR (2020: –326 million EUR). In the 2021 financial year, cash holdings and funds previously invested in current assets were invested in long-term securities. In addition, the previous year included one-off payments from share and business divestitures.

**High capital expenditure volume to enable business development**

Further milestones were achieved in the context of the large investments in tangible assets in 2021. The expansion of the production facilities in Vienna (Austria) for Biopharmaceutical Contract Manufacturing was successfully completed. In 2021, more than 150 million EUR were invested again at the Vienna site. In Germany, the construction of the Biological Development Center (BDC) and the expansion of the research site in Biberach were further promoted last year. The investments amounted to around 115 million EUR, supplementing a number of high investments in Boehringer Ingelheim's global research and development network.

In Animal Health, Boehringer Ingelheim invests in a new antigen production center in Jonage (France) for Veterinary Public Health in response to the growing demand for medicines to treat foot-and-mouth and bluetongue disease. The total investment for this project is over 230 million EUR, of which approximately 60 million EUR were paid in the past financial year.

Cash outflow from financing activities in the amount of – 1,499 million EUR mainly comprises tax refunds for shareholders' personal taxes associated with the Group's activities. These amounts are not to be reported in the Group's tax expense due to commercial law regulations.

Overall, after taking into consideration changes due to exchange rate movements and valuation-related changes, the Group's financial funds decreased by a total of – 3,559 million EUR to 2,546 million EUR as of December 31, 2021, in particular due to the transfer of cash and short-term securities to long-term financial assets.

## Net assets position

(in million EUR)	31.12.2021	31.12.2020	Change	Change in %
<b>Assets</b>				
Intangible and tangible assets	10,113	9,345	768	
Financial assets	12,964	8,553	4,411	
<b>Fixed assets</b>	<b>23,077</b>	<b>17,898</b>	<b>5,179</b>	<b>+ 28.9%</b>
Inventories	4,237	3,863	374	
Trade accounts receivable	5,178	4,302	876	
Other receivables and other current assets	1,407	950	457	
Securities	250	1,499	– 1,249	
Cash and cash equivalents	2,296	4,606	– 2,310	
<b>Current assets</b>	<b>13,368</b>	<b>15,220</b>	<b>– 1,852</b>	<b>– 12.2%</b>
Other assets	4,174	3,769	405	
<b>Total assets</b>	<b>40,619</b>	<b>36,887</b>	<b>3,732</b>	<b>+ 10.1%</b>
<b>Equity and liabilities</b>				
<b>Group equity</b>	<b>19,331</b>	<b>17,307</b>	<b>2,024</b>	<b>+ 11.7%</b>
Provisions for pensions and similar obligations	6,190	5,581	609	
Tax provisions and other provisions	10,765	9,739	1,026	
Accounts payable and loans	2,224	1,912	312	
- thereof residual term over 1 year:	85	77	8	
<b>Liabilities</b>	<b>19,179</b>	<b>17,232</b>	<b>1,947</b>	<b>+ 11.3%</b>
Other liabilities and difference from capital consolidation	2,109	2,348	– 239	
<b>Total equity and liabilities</b>	<b>40,619</b>	<b>36,887</b>	<b>3,732</b>	<b>+ 10.1%</b>

As of December 31, 2021, Boehringer Ingelheim's total assets amounted to 40,619 million EUR, an increase of +3,732 million EUR as compared with the previous year. This increase was mainly attributable to investments in tangible assets and acquisitions, as well as to the positive cash flow of the financial year. Inventories and receivables also rose. Moreover, positive currency effects have increased all balance sheet items.

Intangible and tangible fixed assets increased due to acquisitions and the continuously high volume of capital expenditure in the strategic expansion of the company's business, including

in Human Pharma research in Germany, Biopharmaceuticals in Vienna (Austria) and Fremont (California, USA), and Animal Health in France. In addition, positive currency effects have increased the volume of fixed assets. Funds which were previously held as cash or invested in short-term investments were invested in long-term securities. Together with the investment of further funds resulting from cash flow over the course of the financial year in long-term securities and investments, this significantly increased the volume of long-term financial assets.

Working capital (inventories and receivables) rose due to the increased production costs as a result of higher price levels on the procurement markets, the buildup of safety stocks for Biopharmaceutical Contract Manufacturing and Animal Health as well as positive currency effects. Moreover, trade accounts receivable rose in the USA as of the reporting date due to an increased volume of receivables from wholesalers, and in Germany due to an increase in the volume of receivables arising from license agreements. The rise in other receivables and other assets resulted from increased tax prepayments and sales tax receivables in Germany, Mexico, and the USA in particular. Other assets increased due to higher deferred tax assets resulting from temporary differences between the valuations in the consolidated companies' tax balance sheets and the valuations in the consolidated balance sheet (for pension provisions especially) as well as the positive market trend for plan assets for pensions and similar obligations. This item also increased due to currency effects.

**19.3**  
billion EUR  
equity

**48%**  
equity ratio

Equity amounted to 19,331 million EUR as of December 31, 2021. The equity ratio improved to around 48 % (December 31, 2020: 47 %) in spite of the higher balance sheet total. In addition to equity, the pension provisions and long-term liabilities are also available to the Group as capital in the long term. These three items totaled 25,606 million EUR as of December 31, 2021, representing a 63 % share of total assets. Consequently, as in previous years, long-term disposable capital continues to cover all intangible and tangible fixed assets as well as working capital.

Pension provisions rose in Germany in particular due to a further decline in the discount rate as well as currency effects. The increase in other provisions correlates to the change in the level of revenue, since this includes provisions for discounts in the USA, for commissions and for royalty payments. In addition, positive currency effects resulted in higher tax provisions and other provisions. The volume of liabilities has risen due to increased debt financing in Brazil, Greece, and China, advance payments by customers in the Biopharmaceutical Contract Manufacturing business, liabilities to shareholders, and positive currency effects. Other liabilities have declined, mainly due to the release of the difference arising from capital consolidation as well as deferred income.

The net assets position likewise reflects Boehringer Ingelheim's positive development in the 2021 financial year. Boehringer Ingelheim remains a soundly financed company, making considerable capital expenditure in the development of its business and research activities in order to ensure its long-term growth and thus its independence.



# Report on opportunities and risks

## Opportunities and risk management

When assessing the risks in the context of holistic opportunities and risk management, we also endeavor to take into account the resulting opportunities.

Opportunity management is based on the strategies and objectives of the company and of individual businesses and operating business units and is an integral part of the Group-wide planning and management systems. Those responsible for the businesses and functions bear direct responsibility for the early and systematic identification, analysis, and use of opportunities.

For Boehringer Ingelheim as a research-driven biopharmaceutical company, its current research and development activities are naturally considered an opportunity. Relevant projects have already been outlined in the research and development chapter. We also consider digitalization to be an opportunity and see new technological possibilities in the areas of research and (particularly clinical) development, as well as in the support of patients during therapy. In the current COVID-19 pandemic, we are giving greater priority to this opportunity for digitalization in many different areas, but especially in sales and administration.

The aim of the risk management system implemented at Boehringer Ingelheim is to identify business-specific risks as early as possible (particularly risks that jeopardize the continued existence of the company), to assess them, and to reduce them to a reasonable level by means of suitable measures. The persons responsible for the key businesses and functions are also included in the process of calculating and assessing risks. The Group-wide risk and information system ensures that all identified risks are analyzed and assessed carefully. Following appropriate classification, adequate risk management measures are initiated and their implementation is consistently monitored.

In the year under review, internal auditing performed targeted routine audits as well as extraordinary audits around the world. In addition to adherence to legal requirements and internal Group guidelines, the main focal points were the functionality of systems, the effectiveness of internal controls for the prevention of loss of assets, and the efficiency of structures and processes. Corresponding adjustments or optimizations were initiated as necessary.

## Individual risks

The key risks which Boehringer Ingelheim is exposed to are broken down into the following specific categories: financial risks, legal risks, information technology risks, production and environmental risks, personnel risks, and sector-specific risks.

Risks are identified below as being “concrete” when they appear to be controllable by means of specific management procedures. The term “abstract” is used in the case of risks that cannot be completely controlled, even by means of targeted management procedures, regardless of the probability of their occurrence.

### Financial risks

Relevant financial risks are themselves broken down as follows: currency risks, geopolitical risks, credit and country-specific risks as well as financial investment and shareholding risks.

#### Currency risks

The global orientation of our business activities is subject to risks and opportunities due to exchange rate volatility in relation to the US dollar and the Japanese yen above all – but also with regard to emerging markets' currencies, especially the Chinese renminbi. The Group monitors and quantifies these risks at regular intervals, making them predictable for future business by means of relevant hedging strategies and appropriate financial instruments, such as forward exchange contracts. The resultant risks are subsequently designated as being concrete and controllable and therefore limited.

#### Geopolitical risks

The business of Boehringer Ingelheim as a global company can be adversely affected by geopolitical developments. Significant risks may arise, for example, from geopolitical tensions or from changing economic and political conditions, which may have an impact on production sites and on sales markets. Global geopolitical developments are under constant observation by Boehringer Ingelheim, in order to be able to take appropriate measures at an early stage to address these abstract and low risks and to maintain a successful global business.

#### Credit and country-specific risks

Boehringer Ingelheim is exposed to various credit and country-specific risks as a result of its international business activities. From the portfolio of trade accounts receivable and trade accounts payable, we have not identified any extraordinary risks for the Group beyond the usual level in the industry since the start of the COVID-19 pandemic, also compared with previous years. The same applies to possible default risks for receivables, which are largely hedged against economic and political risks. We will continue to carefully track credit and country-specific risks, so as to be in a position to respond to negative changes in a timely manner. These risks, which we consider moderate, are therefore regarded as concrete.

#### Financial investment and shareholding risks

The Group pursues a conservative investment strategy in its management of its financial assets. Its primary objective is the long-term preservation of their real value. This is reflected in the orientation of our portfolio, which mainly comprises money market and bond investments. This results in a concrete, controllable, and limited level of risk for most of our financial investments. The net book value of some of the strategic investments in related companies is affected by market and business circumstances, which leads to a higher level of volatility in the fair market value. All specific risks have been covered by respective impairments in the consolidated financial statements.

**Legal risks**

The business activities of the Group are exposed to legal risks. A distinction is made between regulatory, liability, and patent protection risks.

**Regulatory risks**

Boehringer Ingelheim is exposed to risks arising from legal disputes and proceedings as well as official investigations. As the legal or administrative decisions in ongoing or future proceedings cannot be predicted, we regard the resultant risks as being abstract and high.

**Liability risks**

The marketing and sale of pharmaceuticals are exposed to a potential product liability risk. Boehringer Ingelheim currently has product liability insurance for the company's risk profile. There is absolutely no guarantee, however, that this insurance coverage can be maintained at reasonable cost and acceptable conditions, or that it is sufficient to protect Boehringer Ingelheim against a claim or loss, or against all potential claims or losses. In case it is foreseeable that the product liability insurance does not cover or only partially covers a specific liability risk, the remaining risk exposure has been covered by a provision. We therefore see a moderate risk for the Group here.

Furthermore, product liability claims could tie up substantial financial resources and management capacity and be detrimental to the company's image in the event that the market considers the product to be unsafe or ineffective as a result of unexpected side effects. We see this as an abstract and moderate risk.

**Patent protection risks**

Protection of innovations through trademark and patent rights is of particular importance to Boehringer Ingelheim as a research-driven biopharmaceutical company. These commercial protective rights are increasingly the target of attacks and breaches. We have taken the necessary precautions to allow us to detect threats at an early stage and, by commencing appropriate countermeasures, defend our legal position using all legal means available to us so that these factors are regarded as concrete and moderate risks.

**Information technology risks**

Boehringer Ingelheim uses globally networked IT systems in core areas of its operations for business and production processes as well as internal and external communication. It also makes use of cloud-based third-party systems and services. These systems are used to process, store, and transmit confidential and personal data. The availability, integrity, and confidentiality of these systems and the data processed are thus highly significant.

External cyberattacks or any manipulation of systems may result in the loss of information and expertise as well as temporary interruptions to business and production processes. This risk is considered to be high and concrete in view of the continuously evolving global environment and the growing frequency of cyberattacks.

The COVID-19 pandemic has elevated the risk of such threats and attacks, since people are increasingly working from home and employees thus have access to sensitive data via less secure IT environments.

Boehringer Ingelheim is countering this risk by means of continuous IT process analysis and improvements as well as further preventive and reactive measures. This helps to identify and ward off current threats and to minimize potential damage.

#### **Production and environmental risks**

Our quality management system and compliance processes are continuously optimized in close cooperation with the relevant authorities in order to ensure compliance with cGMP standards (current good manufacturing practices). Risks in this area continue to be of high significance to the Group and are classified as abstract. Boehringer Ingelheim implemented risk-mitigating measures in the past year in order to counter COVID-19-specific threats to its production activities. These include the physical segregation of production teams when possible, the obligation to wear a mask, an increase in the supply of disinfectants, and in-house initiatives for testing the COVID-19 status of employees. In order to protect facility-based functions, employees whose presence is not site-dependent were asked to work from home.

In order to ensure the supply of our products to the market, we have implemented measures that guarantee reliable and high-quality supplies for internal and external customers. In addition to supplier management on the procurement side, this also involves building up internal standby capacities. Overall, this represents a concrete and moderate risk.

Risks in the areas of the environment, health, safety, and sustainability (EHS&S) are preemptively minimized by ensuring global adherence to our high safety standards. Appropriate emergency plans have been drawn up for possible incidents of any kind and are practiced and subjected to comprehensive quality testing at regular intervals. As a result of these measures, these risks are classed as concrete and limited.

#### **Personnel risks**

Boehringer Ingelheim, as other companies, is exposed to demographic change and the resultant risk of being affected by a lack of appropriately qualified personnel. This potential risk can have a substantial impact on the company's business activities. It has therefore been included in the long-term planning process for many years and has gained strategic significance as a result.

Boehringer Ingelheim counters the risk by means of a comprehensive personnel concept. In the context of global personnel management, this also presents the Group with opportunities. Regardless of their ethnic background, gender, or religion, we offer all of our company's employees development opportunities based on their professional abilities, social skills, personal aptitudes, and willingness to take on responsibility in accordance with the needs of the company. In view of the measures described above, the risk is regarded as concrete and moderate.

Boehringer Ingelheim is likewise exposed to human resources risks as a result of the COVID-19 pandemic. If the pathogen were to spread, this would have a significant impact both in and outside of our production activities. The company is therefore closely monitoring the situation in the vicinity of its sites. It also emphasizes working from home, using digital applications rather than in-person meetings, and curbing employee travel to a large extent. In view of these measures, this is considered to be a concrete and moderate risk.

#### **Industry-specific risks**

Boehringer Ingelheim is subject to the industry-specific business risks of the pharmaceutical industry. These risks have partly materialized in the past financial year and are becoming increasingly important for Boehringer Ingelheim due to their effects. They continue to be classed as abstract and high. In addition to the loss of exclusivity of products established on the market and risks associated with the development and registration of new medicines, these risks increasingly include changing and restrictive requirements relating to pricing and reimbursement on many sales markets. Frequently, the prices of pharmaceutical products are subject not only to state monitoring and regulation, but also to price pressure from cheaper generic drugs which is induced by state reimbursement systems. Boehringer Ingelheim is keeping a close eye on the various changes in its sales markets and takes appropriate measures in response to current developments.

### **Overall statement on the risk situation**

From a current perspective, we are not aware of any risks that alone or in conjunction with other risks could lead to a lasting impairment of the company's assets or financial or earnings position and could jeopardize the continued existence of Boehringer Ingelheim.



## Report on expected developments

Boehringer Ingelheim can look back on a successful 2021 financial year in which we surpassed our ambitious targets, both in terms of absolute figures and our contribution to the well-being of patients, pets, and livestock. Despite the volatile global economic situation, we were able to ensure the company's sustainable development and profitable growth.

The continuing COVID-19 pandemic, fragile global supply chains, general inflation trend, and a more difficult industry environment mean that we will continue to face challenges in 2022. However, the uncertainty of the past two years – in the context of a global pandemic – would appear to be gradually giving way to more predictable challenges and opportunities. We therefore have an optimistic view of the ongoing volatility, even if it remains difficult to make forecasts for the coming financial year.

In 2022, we expect to see ongoing global economic recovery, and we assume that the vaccines and medicines already approved, plus other therapies currently undergoing the approval process, will help to curb the COVID-19 pandemic. On the strength of our experience of the past few years and the measures which we have implemented, we are confident that we will be able to handle any temporary setbacks without encountering any substantial supply problems.

The largest source of uncertainty over the next five years will be the potential impact of economic factors on governments' budget planning and whether this will affect policymaking in terms of expenditure on healthcare and medicines. Assuming that it is possible to curb the COVID-19 pandemic, we expect to see moderate market growth for prescription pharmaceuticals. However, we are also witnessing growing global institutional efforts to bring down the prices of medicines. In view of this trend, financial flexibility remains critical for us, in order to ensure long-term growth and innovation.

In our Animal Health business, following strong market growth in 2021, we now expect to see a normalization of the market growth trend in the new financial year. Research and innovation will play a particularly important role here. Together with our business partners, we intend to continue to provide our customers with innovative solutions. The development of the African swine fever situation will remain a critical factor in 2022. Our priorities in our Biopharmaceuticals business are supplying the market with our own products and contract manufacturing for our business partners. The increasing level of capacity utilization of our new large-scale cell culture plant in Vienna will be another core area of focus in 2022.

For 2022, we expect Boehringer Ingelheim to achieve a slight year-on-year increase in net sales on a comparable basis (adjusted for currency and extraordinary effects).

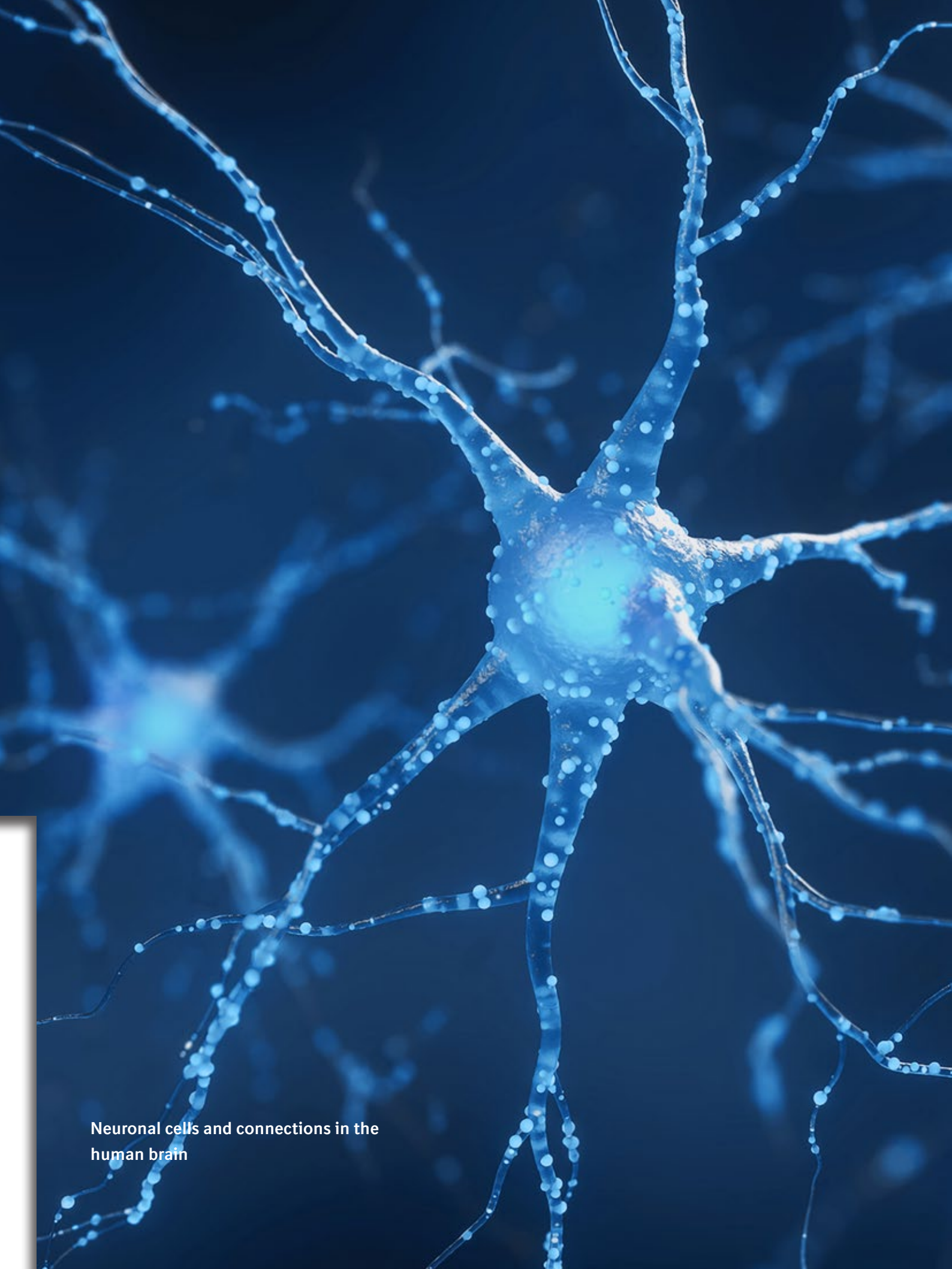
Our consistently high R&D expenditure, which once again increased in 2021, is in line with our strategic focus on continuing to drive growth and the flow of new products. In 2021, we once again achieved our goal of obtaining some of our R&D through external innovation and partnerships. We will continue to actively pursue this strategy in 2022. We invest in our own and external R&D after close investigation of the therapeutic benefit and the associated prospects for success. The flow of innovative medicines in our research and development pipeline shows short-, medium-, and long-term growth potential. We expect to see a further increase in R&D investments in new medicines in 2022, and intend to reach new milestones in research and development as well as individual market approvals.

In addition to patent expiry and attacks on patents, the major challenges facing the research-driven pharmaceutical industry are the increasing amount of investment in R&D as well as bigger hurdles and increased costs associated with product approvals. Also of particular note is the previously mentioned growing cost pressure in healthcare systems. In the last two years of the pandemic, research-driven pharmaceutical companies displayed an unprecedented level of networking and energy to develop solutions extremely quickly, thus proving the societal value of research and innovation, with the support of policymakers. Additional concrete steps are needed so that the contribution of pharmaceutical companies to the increased efficiency of the overall healthcare system is remunerated appropriately. Animal health research likewise requires major investments in both preventive research and diagnostic options.

In conjunction with the long planning and development cycles for new products, growing public cost pressure means that business is less predictable. It requires us to quickly recognize and seize opportunities in both Human Pharma and Animal Health on the one hand, while continuously monitoring and adjusting costs and strategies on the other. In 2021, we implemented measures in all our business areas to accelerate the speed of our response to changes, to reduce the complexity of the organization, and to optimize the cost base. In this way, we are creating potential for capital expenditure and securing the company's long-term success.

For 2022, we expect Boehringer Ingelheim to achieve slightly lower operating income due to our increased level of investment in research and development on a comparable basis (adjusted for currency and extraordinary effects).

As a family-owned company, Boehringer Ingelheim's primary aim remains the creation of "Value through Innovation". This safeguards our competitiveness and our long-term entrepreneurial independence. We are confident that we will achieve our ambitious targets in all of our business areas, thanks to our great innovative strength which rests on a comprehensive portfolio of prospective products, our global presence, and the support of our highly qualified and motivated employees. We remain committed to our "Ambition 2025" for our company as a whole. We will research and develop innovative products in human and veterinary medicine and bring them to the market in areas of high medical need, and we will break new ground with therapeutic approaches. The aim of our endeavors is to make new medicines available to both humans and animals so they can be treated more effectively with new therapies.



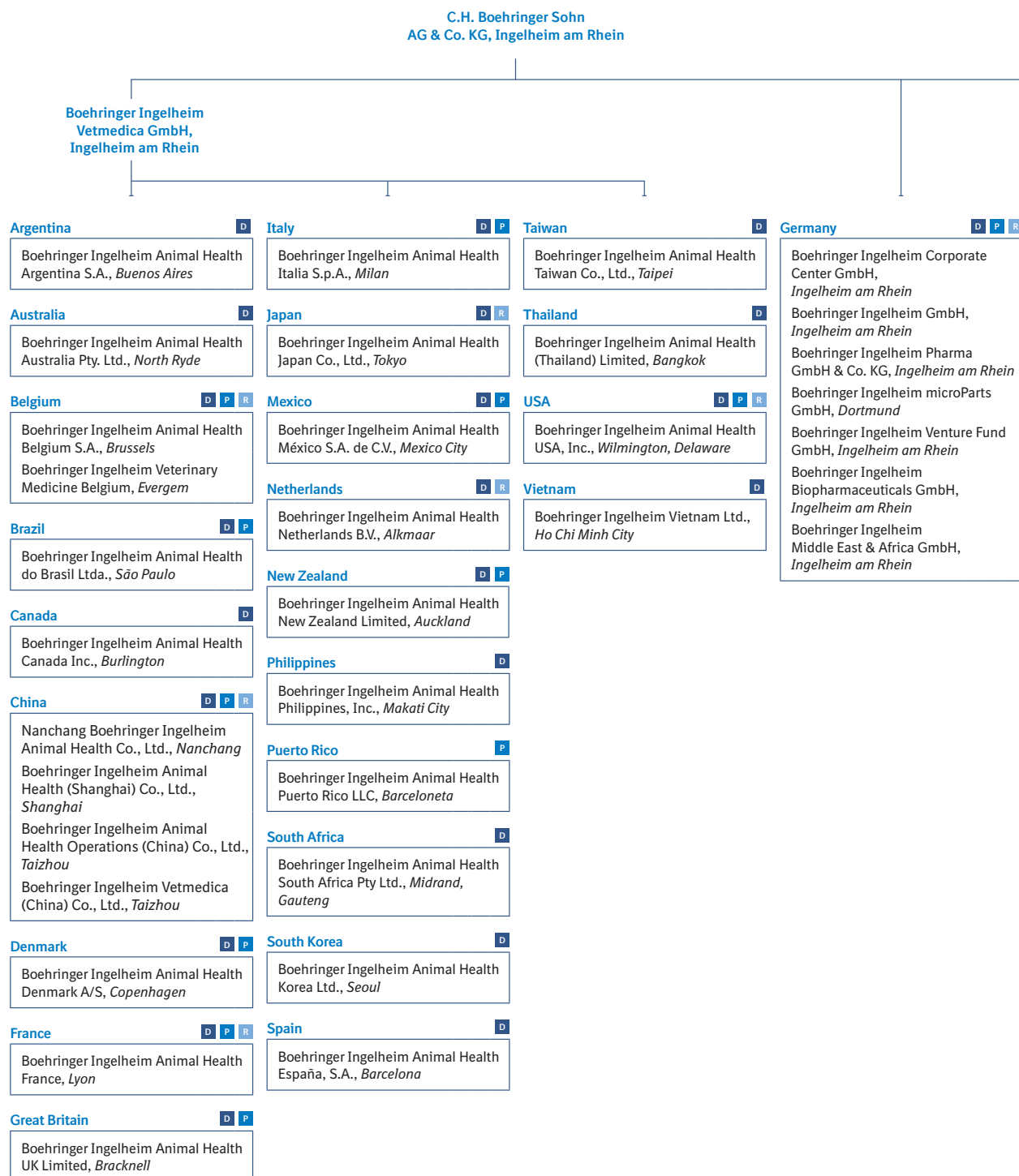
Neuronal cells and connections in the human brain

# Consolidated Financial Statements

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# Overview of selected consolidated companies



D Distribution  
P Production  
R Research and development





# Consolidated balance sheet

Assets (in million EUR)	Notes <sup>1)</sup>	31.12.2021	31.12.2020
Intangible assets	(3.1)	4,624	4,295
Tangible assets	(3.2)	5,489	5,050
Financial assets	(3.3)	12,964	8,553
<b>Fixed assets</b>		<b>23,077</b>	<b>17,898</b>
Inventories	(3.4)	4,237	3,863
Accounts receivable and other assets	(3.5)	6,585	5,252
Securities		250	1,499
Cash and cash equivalents		2,296	4,606
<b>Current assets</b>		<b>13,368</b>	<b>15,220</b>
Prepaid expenses		342	330
Deferred tax assets		3,543	3,194
Exceeding amount of plan assets		289	245
<b>Total assets</b>		<b>40,619</b>	<b>36,887</b>

Equity and liabilities (in million EUR)	Notes <sup>1)</sup>	31.12.2021	31.12.2020
Shareholders' capital		178	178
Group reserves		19,479	17,672
Balance sheet currency conversion difference		- 327	- 544
<b>Equity attributable to the parent company</b>		<b>19,330</b>	<b>17,306</b>
Non-controlling interests		1	1
<b>Group equity</b>		<b>19,331</b>	<b>17,307</b>
<b>Difference from capital consolidation</b>		<b>1,159</b>	<b>1,283</b>
Provisions	(3.6)	16,955	15,320
Accounts payable and loans	(3.7)	2,224	1,912
<b>Liabilities</b>		<b>19,179</b>	<b>17,232</b>
Deferred income		319	385
Deferred tax liabilities		631	680
<b>Total equity and liabilities</b>		<b>40,619</b>	<b>36,887</b>

1) For explanations, see relevant section in the notes to the consolidated financial statements.

# Consolidated profit and loss statement

(in million EUR)	Notes <sup>1)</sup>	2021	2020
<b>Net sales</b>	(4.1)	<b>20,618</b>	<b>19,566</b>
Changes in finished goods and work in process		240	328
Other own work capitalized		11	2
Other operating income	(4.2)	2,726	3,358
<b>Total revenues</b>		<b>23,595</b>	<b>23,254</b>
Cost of materials	(4.3)	- 2,826	- 2,567
Personnel expenses	(4.4)	- 5,692	- 5,587
Amortization of intangible assets and depreciation of tangible assets	(4.5)	- 1,134	- 1,376
Other operating expenses	(4.6)	- 9,238	- 9,100
<b>Operating income</b>		<b>4,705</b>	<b>4,624</b>
Financial income	(4.7)	- 337	- 523
Holding income	(4.8)	0	204
<b>Income before taxes</b>		<b>4,368</b>	<b>4,305</b>
Income taxes <sup>2)</sup>	(4.9)	- 962	- 1,243
<b>Income after taxes</b>		<b>3,406</b>	<b>3,062</b>
Net income	(4.10)	3,406	3,062
Non-controlling interests		0	0
<b>Group profit</b>		<b>3,406</b>	<b>3,062</b>

1) For explanations, see relevant section in the notes to the consolidated financial statements.

2) Due to legal requirements, the shareholders' personal taxes arising from group business activities are shown as withdrawals from the group reserves.

# Consolidated cash flow statement

(in million EUR)	2021
Income after taxes (including non-controlling interests)	3,406
Amortization, depreciation, write-downs and reversal of write-downs of intangible, tangible and financial assets	1,144
Change in provisions for pensions and similar obligations (including change of plan assets)	578
Change in other provisions	608
Other non-cash income and expenses	- 111
Gain from disposals of consolidated companies	- 26
Gains/losses from disposals of fixed assets	- 40
Grants received	- 16
Change in inventories	- 336
Change in accounts receivable and other assets not related to investing or financing activities	- 915
Change in accounts payable and other liabilities not related to investing or financing activities	78
Interest income/interest expenses	39
Other income from investments	- 3
Income/expenses from income taxes	962
Income taxes paid	- 1,522
<b>Cash flow from operating activities</b>	<b>3,846</b>
Payments to acquire intangible fixed assets	- 175
Payments to acquire tangible fixed assets	- 968
Payments to acquire financial fixed assets	- 4,469
Payments to acquire plan assets	- 21
Payments relating to purchase price adjustments of consolidated entities	- 40
Investments in consolidated companies	- 487
Proceeds from disposals of intangible fixed assets	3
Proceeds from disposals of tangible fixed assets	54
Proceeds from disposals of financial fixed assets	41
Proceeds from disposals of consolidated entities	43
Interest received	14
Income from dividends	3
<b>Cash flow from investing activities</b>	<b>- 6,002</b>

## Consolidated cash flow statement (continued)

(in million EUR)	2021
Cash receipts from grants	16
Interest paid	- 34
Cash receipts from shareholders of the parent company	4
Cash payments to shareholders of the parent company <sup>1)</sup>	- 1,531
Proceeds from loans	110
Cash repayments of loans	- 64
<b>Cash flow from financing activities</b>	<b>- 1,499</b>
<b>Change in financial funds from cash relevant transactions</b>	<b>- 3,655</b>
Change in financial funds due to exchange rate movements and valuation adjustments	96
<b>Financial funds <sup>2)</sup> as of 1.1.</b>	<b>6,105</b>
<b>Financial funds <sup>2)</sup> as of 31.12.</b>	<b>2,546</b>

1) This line mainly contains the shareholders' personal taxes arising from group business activities, which according to legal requirements are not included in the Group's tax expenses.

2) Cash and cash equivalents and securities within current assets.

(+) = source of funds, (-) = use of funds

# Statement of changes in group equity

(in million EUR)	Shareholders' capital <sup>1)</sup>	Group reserves <sup>2)</sup>	Balance sheet currency conversion difference	Equity attributable to the parent company	Non-controlling interests	Group equity
<b>Balance as of 31.12.2019</b>	<b>178</b>	<b>14,709</b>	<b>-207</b>	<b>14,680</b>	<b>1</b>	<b>14,681</b>
Withdrawals	0	- 99	0	- 99	0	- 99
Net income	0	3,062	0	3,062	0	3,062
Currency effects	0	0	- 337	- 337	0	- 337
<b>Balance as of 31.12.2020</b>	<b>178</b>	<b>17,672</b>	<b>-544</b>	<b>17,306</b>	<b>1</b>	<b>17,307</b>
Withdrawals	0	- 1,588	0	- 1,588	0	- 1,588
Net income	0	3,406	0	3,406	0	3,406
Reduction from recognition of deferred tax liabilities recognized directly in equity	0	- 11	0	- 11	0	- 11
Changes in consolidated companies	0	0	5	5	0	5
Currency effects	0	0	212	212	0	212
<b>Balance as of 31.12.2021</b>	<b>178</b>	<b>19,479</b>	<b>-327</b>	<b>19,330</b>	<b>1</b>	<b>19,331</b>

1) The shareholders' capital consists of the equity of C.H. Boehringer Sohn AG & Co. KG and C.H. Boehringer Sohn Grundstücksverwaltung GmbH & Co. KG. The shareholders' capital consists only of the limited partner's capital contribution.

2) The shareholders' personal taxes arising from group business activities are shown as withdrawals from the group reserves.



# Notes to the consolidated financial statements

## 1 Principles and methods

### 1.1 General principles

The consolidated financial statements of Boehringer Ingelheim for the 2021 financial year were prepared in accordance with Section 264a of the German Commercial Code (HGB), in line with the legal requirements to prepare consolidated financial statements under Section 290 et seq. HGB.

In accordance with Section 297 (1) HGB, the consolidated financial statements consist of the consolidated balance sheet, the consolidated profit and loss statement, the notes to the consolidated financial statements, the consolidated cash flow statement, and the statement of changes in equity.

The consolidated financial statements were prepared in euros in accordance with Section 298 (1) in conjunction with Section 244 HGB.

To improve the clarity and transparency of the consolidated financial statements, subtotals have been added in the consolidated profit and loss statement; furthermore, individual items of the consolidated balance sheet and the consolidated profit and loss statement have been combined. These items are presented and explained separately in the notes. The additional disclosures required for the individual items can also be found in the notes.

### 1.2 Registry information

The parent company is registered under the name C.H. Boehringer Sohn AG & Co. KG, with its headquarters in Ingelheim am Rhein, in the commercial register of Mainz district court under the number HRA 21732.

### 1.3 Information on the group of consolidated companies

The parent company of the Boehringer Ingelheim Group is C.H. Boehringer Sohn AG & Co. KG, Ingelheim am Rhein. Boehringer AG, Ingelheim am Rhein, is the sole unlimited partner of this company.

The Boehringer Ingelheim Group consists of a total of 180 affiliated companies in Germany and abroad. 151 subsidiaries have been included in the consolidated financial statements of C.H. Boehringer Sohn AG & Co. KG under full consolidation rules. C.H. Boehringer Sohn Grundstücksverwaltung GmbH & Co. KG is a special purpose entity in which C.H. Boehringer Sohn AG & Co. KG bears a majority of the risks and opportunities in economic terms. C.H. Boehringer Sohn AG & Co. KG holds a majority of the voting rights in the other subsidiaries, either directly or indirectly.

In accordance with Section 296 (2) HGB, 26 subsidiaries were not included in the consolidation in the reporting year, as they are individually and collectively insignificant to the Group's net assets, financial, and earnings position. The total amount of the sales, equity, and net income for the year of the subsidiaries not included in consolidation accounts for less than one percent of the aggregated Group financial statements totals. For two further subsidiaries there are ongoing restrictions on control due to the terms of the articles of association. In accordance with Section 296 (1) No. 1 HGB, these companies were not consolidated either.

The total number of subsidiaries increased by four compared to the previous year:

- Nine companies were acquired.
- Two companies lost their separate legal identities by merger.
- Two affiliated companies were liquidated.
- One affiliated company was sold.

The following subsidiaries were exempted from the reporting and disclosure obligations of Section 264 (3) HGB:

- Boehringer Ingelheim GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Europe GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Finanzierungs GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Secura Versicherungsvermittlungs GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Grundstücks-GmbH, Ingelheim am Rhein
- Boehringer Ingelheim R&D Beteiligungs GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Animal Health France Participations GmbH, Ingelheim am Rhein
- Boehringer Ingelheim FinanzInvest GmbH, Ingelheim am Rhein

The following subsidiaries were exempted from the reporting and disclosure obligations of Section 264b HGB:

- C.H. Boehringer Sohn AG & Co. KG, Ingelheim am Rhein
- C.H. Boehringer Sohn Grundstücksverwaltung GmbH & Co. KG, Ingelheim am Rhein
- Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein
- Boehringer Ingelheim Veterinary Research Center GmbH & Co. KG, Ingelheim am Rhein

Boehringer Ingelheim participates in one joint venture, which has not been included in the consolidated financial statements using either the proportionate method or the equity method, since it is not material. Furthermore, Boehringer Ingelheim holds an interest in 19 associated companies, which have not been accounted for using the equity method either due to their lack of significance. The resulting effect on the Group's total assets and net income is less than one percent.

## 1.4 Consolidation methods

For inventories and fixed assets, receivables, liabilities, and income and expense items, transactions between the companies included in consolidation were eliminated as part of debt consolidation procedures in accordance with Section 303 HGB, procedures to eliminate intercompany profits in accordance with Section 304 HGB and income and expenses consolidation procedures in accordance with Section 305 HGB.

The revaluation method was applied when including subsidiaries in the consolidation for the first time in accordance with Section 301 HGB. Companies were included in the consolidation for the first time on the date on which the company became a subsidiary.

The book value of the shares held by the parent company was offset against the corresponding equity of the subsidiary. Equity was carried at the amount of the fair value of the assets, liabilities, prepaid expenses, deferred income, and special reserves included in the consolidated financial statements as of the time of consolidation. Any remaining positive balance was recorded as goodwill; any remaining negative balance was recorded as a difference from capital consolidation.

## 1.5 Currency translation

Assets and liabilities resulting from foreign currency transactions were translated using the average spot exchange rate as of the balance sheet date. The realization principle (Section 298 (1) in conjunction with Section 252 (1) No. 4 half-sentence 2 HGB) and the historical cost principle (Section 298 (1) in conjunction with Section 253 (1) sentence 1 HGB) were applied to items with a remaining term of more than one year.

In these consolidated financial statements, the financial statements of foreign subsidiaries domiciled in a state outside the eurozone that are denominated in a foreign currency have been converted into euros using the modified closing rate method, in accordance with Section 308a HGB.

Using the modified closing rate method, the asset and liability items of the annual financial statements prepared in foreign currency were translated into euros using the average spot exchange rate as of the balance sheet date, with the exception of equity, which was translated using the historical rate. Items included in the profit and loss statement were translated into euros using the annual average rate. The resulting translation differences were reported within consolidated equity below the reserves in “Balance sheet currency conversion difference”.

The exchange rates for the Group’s most important currencies changed as follows during the reporting year (basis: 1 EUR):

	Spot rate		Average rate	
	31.12.2021	31.12.2020	2021	2020
US dollar	1.13	1.23	1.18	1.14
Japanese yen	130.38	126.49	129.86	121.78
Chinese renminbi	7.19	8.02	7.63	7.87

## 2 Accounting policies

### 2.1 Fixed assets

Acquired tangible and intangible assets are carried at cost, less scheduled straight-line amortization and depreciation determined under consideration of the technical and economic circumstances. This is based on the following useful lives:

Goodwill	10 years
Other intangible assets	2 to 19 years
Buildings	20 years
Technical facilities and machines	10 years
Other facilities, operating equipment	3 to 10 years

Only straight-line depreciation and amortization are used in the consolidated financial statements. Additional write-downs are recorded to reflect impairments when the value of assets has been considered permanently impaired. Manufacturing costs include materials and labor manufacturing costs, an appropriate portion of materials and labor overheads, and the depreciation of fixed assets (to the extent caused by production). Manufacturing costs do not include financing costs.

All capitalized intangible assets have finite useful lives.

In the current financial year, goodwill increased overall by 445 million EUR due to the acquisition of three companies. Of this amount, 384 million EUR related to the acquisition of NBE Therapeutics S.A.

Financial assets primarily include investment securities, shareholder rights, and loans and were carried at the lower of cost or fair market value, if impaired. In the event that the reasons for the impairment losses recognized in previous financial years were no longer applicable, corresponding reversals were recorded.

### 2.2 Current assets, prepaid expenses, deferred income, and exceeding amount of plan assets

Inventories are carried at the lower of cost or fair market value.

Raw materials, consumables, and supplies are capitalized at the lower of average acquisition prices or fair market value on the balance sheet date.

Finished goods and work in progress are measured at manufacturing cost on the basis of individual calculations, taking into account the directly attributable costs of materials, direct labor costs, special direct costs, an appropriate share of material and production overhead costs, and production-related depreciation.

Goods for resale are valued at the lower of either acquisition cost or fair market value.

All identifiable risks in inventories arising from above-average storage periods, diminished marketability, and lower replacement costs were taken into account by recording appropriate valuation adjustments.

Inventories are valued loss-free – that is, deductions were made from the expected sales prices to reflect costs yet to be incurred.

Receivables and other assets were recognized at cost less allowances for specific risks and general credit risk. Low-interest or non-interest-bearing receivables with a term of more than one year were discounted.

Securities classified as current assets solely include other securities and have been recognized at the lower of cost or the fair market value/ the stock market price as of the reporting date.

Cash and cash equivalents, consisting of cash, balances at banks, and checks, were recognized at the lower of cost or fair market value.

Prepaid expenses recorded in accordance with Section 250 (1) HGB include expenses paid in advance in respect of a defined period of time after the balance sheet date.

Deferred income recorded in accordance with Section 250 (2) HGB includes proceeds that represent income in respect of a defined period of time after the balance sheet date.

The fair market value of pension plan assets and the corresponding present value of pension obligations have been offset according to German GAAP. The exceeding amount of plan assets has been capitalized separately.

## 2.3 Group reserves

Group reserves include the retained earnings of the consolidated subsidiaries from prior and current years and consolidation entries that affect earnings.

## 2.4 Difference from capital consolidation

The difference from capital consolidation reported on December 31, 2021 was primarily a result of the business swap of Boehringer Ingelheim's consumer healthcare business and Sanofi's animal health business, which was completed on January 1, 2017. This resulted in a difference from capital consolidation of 1,986 million EUR. The difference is amortized over an estimated period of 15 years. The remaining balance of the difference amounted to 1,159 million EUR as of December 31, 2021.

The difference from capital consolidation was primarily influenced by the current year release of 118 million EUR. Furthermore, the difference from capital consolidation decreased by a further 6 million EUR due to the sale of the US company Newport Laboratories Inc. The income from the release of the difference arising from capital consolidation is included in other operating income. The release is made corresponding to the amortization of those assets of the acquired company identified in the purchase price allocation and not previously recognized in that company's balance sheet.



## 2.5 Provisions

Tax provisions and other provisions include all uncertain liabilities and expected losses from executory contracts. They were carried at the amount required to settle the obligation based on reasonable prudent commercial judgment (that is, including future cost and price increases). Provisions with a remaining maturity of more than one year were discounted using the matched-term, average market interest rate. In the case of pension provisions this interest rate results from the average market interest rate over the last ten years and in the case of other provisions from the average market interest rate over the last seven years (in accordance with the “Rückstellungsabzinsungsverordnung”, German Regulation on the Discounting of Provisions).

Since environmental protection measures are in some cases expected to result in a permanent burden, the relevant provisions have been calculated on the basis of a perpetual annuity, while taking into consideration cost and price increases as well as interest effects. The valuation method was adjusted in the year under review, since the method previously used no longer gives a true and fair view of the net assets and earnings position of the group under consideration of declining interest rates and rising inflation rates. Instead of the average rate of change in the consumer price index over the past ten years, the current costs are now adjusted for inflation on the basis of the average rate of change in the producer price index for industrial products since the introduction of the euro in 2002. The ultimate forward rate (UFR) provided by the European Insurance and Occupational Pensions Authority (EIOPA) is now used for discounting, instead of the seven-year average interest rate over a term of 50 years, in accordance with the “Rückstellungsabzinsungsverordnung” (German Regulation on the Discounting of Provisions). The effects of this valuation adjustment on the balance sheet and profit and loss statement are explained in note 3.6.

## 2.6 Accounts payable

Accounts payable and loans were recognized at settlement amount.

## 2.7 Deferred taxes

To calculate deferred taxes arising from temporary or quasi-permanent differences between the carrying amounts of assets, liabilities, prepaid expenses, and deferred income in the commercial balance sheet and their carrying amounts for tax purposes or tax loss carryforwards, the amounts of the resulting tax benefits and expenses at the time that the differences will reverse were measured using tax rates specific to the respective consolidated company (4% – 35%). Deferred tax balances are not discounted. Differences due to consolidation measures in accordance with Sections 300 to 305 HGB were also measured using the company-specific tax rates applicable at the time of the expected reversal of the difference. Deferred tax assets on loss carryforwards were taken into account if it is likely that they will be used within the next five years.

Deferred tax assets and liabilities were reported without offsetting.

## 3 Notes to the consolidated balance sheet

### 3.1 Intangible assets

(in million EUR)	Acquired concessions / similar rights	Goodwill	Advance payments	Total
<b>Acquisition / manufacturing costs</b>				
<b>Balance as of 1.1.2020</b>	7,116	86	12	<b>7,214</b>
Currency conversion difference	- 276	0	0	- 276
Changes in consolidated companies	99	84	0	183
Additions	162	0	8	170
Disposals	- 116	0	0	- 116
Reclassifications	15	0	- 11	4
<b>Balance as of 31.12.2020</b>	<b>7,000</b>	<b>170</b>	<b>9</b>	<b>7,179</b>
Currency conversion difference	244	2	0	246
Changes in consolidated companies	70	445	0	515
Additions	168	0	7	175
Disposals	- 69	0	0	- 69
Reclassifications	9	0	- 9	0
<b>Balance as of 31.12.2021</b>	<b>7,422</b>	<b>617</b>	<b>7</b>	<b>8,046</b>
<b>Accumulated amortization</b>				
<b>Balance as of 1.1.2020</b>	2,323	9	0	<b>2,332</b>
Currency conversion difference	- 110	0	0	- 110
Changes in consolidated companies	0	0	0	0
Additions	762	12	0	774
Write-ups	0	0	0	0
Disposals	- 116	0	0	- 116
Reclassifications	4	0	0	4
<b>Balance as of 31.12.2020</b>	<b>2,863</b>	<b>21</b>	<b>0</b>	<b>2,884</b>
Currency conversion difference	104	0	0	104
Changes in consolidated companies	- 23	0	0	- 23
Additions	469	56	0	525
Write-ups	0	0	0	0
Disposals	- 68	0	0	- 68
Reclassifications	0	0	0	0
<b>Balance as of 31.12.2021</b>	<b>3,345</b>	<b>77</b>	<b>0</b>	<b>3,422</b>
<b>Book value as of 31.12.2020</b>	<b>4,137</b>	<b>149</b>	<b>9</b>	<b>4,295</b>
<b>Book value as of 31.12.2021</b>	<b>4,077</b>	<b>540</b>	<b>7</b>	<b>4,624</b>

### 3.2 Tangible assets

(in million EUR)	Land and buildings	Technical facilities and machines	Other facilities / operating equipment	Advance payments / construction in progress	Total
<b>Acquisition / manufacturing costs</b>					
<b>Balance as of 1.1.2020</b>	<b>4,082</b>	<b>4,065</b>	<b>2,370</b>	<b>1,296</b>	<b>11,813</b>
Currency conversion difference	-156	-95	-66	-25	-342
Changes in consolidated companies	0	1	0	0	1
Additions	57	69	129	791	1,046
Disposals	-34	-63	-83	-1	-181
Reclassifications	158	30	113	-305	-4
<b>Balance as of 31.12.2020</b>	<b>4,107</b>	<b>4,007</b>	<b>2,463</b>	<b>1,756</b>	<b>12,333</b>
Currency conversion difference	150	126	75	17	368
Changes in consolidated companies	-6	-5	7	0	-4
Additions	68	119	226	555	968
Disposals	-64	-70	-133	-1	-268
Reclassifications	268	364	477	-1,109	0
<b>Balance as of 31.12.2021</b>	<b>4,523</b>	<b>4,541</b>	<b>3,115</b>	<b>1,218</b>	<b>13,397</b>
<b>Accumulated depreciation</b>					
<b>Balance as of 1.1.2020</b>	<b>2,337</b>	<b>2,909</b>	<b>1,813</b>	<b>0</b>	<b>7,059</b>
Currency conversion difference	-94	-63	-48	0	-205
Changes in consolidated companies	0	0	0	0	0
Additions	184	228	190	0	602
Write-ups	0	0	0	0	0
Disposals	-31	-59	-79	0	-169
Reclassifications	12	-45	29	0	-4
<b>Balance as of 31.12.2020</b>	<b>2,408</b>	<b>2,970</b>	<b>1,905</b>	<b>0</b>	<b>7,283</b>
Currency conversion difference	100	105	62	0	267
Changes in consolidated companies	-2	-3	4	0	-1
Additions	161	224	224	0	609
Write-ups	0	-1	0	0	-1
Disposals	-56	-66	-127	0	-249
Reclassifications	0	0	0	0	0
<b>Balance as of 31.12.2021</b>	<b>2,611</b>	<b>3,229</b>	<b>2,068</b>	<b>0</b>	<b>7,908</b>
<b>Book value as of 31.12.2020</b>	<b>1,699</b>	<b>1,037</b>	<b>558</b>	<b>1,756</b>	<b>5,050</b>
<b>Book value as of 31.12.2021</b>	<b>1,912</b>	<b>1,312</b>	<b>1,047</b>	<b>1,218</b>	<b>5,489</b>

### 3.3 Financial assets

(in million EUR)	Investments in affiliated companies	Loans to affiliated companies	Investments in related companies	Loans to related companies	Investment securities	Other loans	Total
<b>Acquisition / manufacturing costs</b>							
<b>Balance as of 1.1.2020</b>	<b>6</b>	<b>0</b>	<b>954</b>	<b>4</b>	<b>8,191</b>	<b>35</b>	<b>9,190</b>
Currency conversion difference	0	0	-3	0	-1	-1	-5
Changes in consolidated companies	0	0	0	0	0	0	0
Additions	0	0	227	1	33	4	265
Disposals	0	0	-838	0	-27	-8	-873
Reclassifications	0	0	0	0	0	0	0
<b>Balance as of 31.12.2020</b>	<b>6</b>	<b>0</b>	<b>340</b>	<b>5</b>	<b>8,196</b>	<b>30</b>	<b>8,577</b>
Currency conversion difference	1	0	4	0	1	1	7
Changes in consolidated companies	0	0	-15	0	0	0	-15
Additions	15	0	68	0	4,374	12	4,469
Disposals	0	0	-11	-3	-21	-8	-43
Reclassifications	0	0	0	0	7	-7	0
<b>Balance as of 31.12.2021</b>	<b>22</b>	<b>0</b>	<b>386</b>	<b>2</b>	<b>12,557</b>	<b>28</b>	<b>12,995</b>
<b>Accumulated depreciation</b>							
<b>Balance as of 1.1.2020</b>	<b>0</b>	<b>0</b>	<b>16</b>	<b>0</b>	<b>9</b>	<b>3</b>	<b>28</b>
Currency conversion difference	0	0	-1	0	-1	0	-2
Changes in consolidated companies	0	0	0	0	0	0	0
Additions	0	0	3	0	0	0	3
Write-ups	0	0	0	0	0	0	0
Disposals	0	0	-5	0	0	0	-5
Reclassifications	0	0	0	0	0	0	0
<b>Balance as of 31.12.2020</b>	<b>0</b>	<b>0</b>	<b>13</b>	<b>0</b>	<b>8</b>	<b>3</b>	<b>24</b>
Currency conversion difference	0	0	1	0	0	0	1
Changes in consolidated companies	0	0	0	0	0	0	0
Additions	0	0	6	2	4	0	12
Write-ups	0	0	-1	0	0	0	-1
Disposals	0	0	-3	0	0	-2	-5
Reclassifications	0	0	0	0	0	0	0
<b>Balance as of 31.12.2021</b>	<b>0</b>	<b>0</b>	<b>16</b>	<b>2</b>	<b>12</b>	<b>1</b>	<b>31</b>
<b>Book value as of 31.12.2020</b>	<b>6</b>	<b>0</b>	<b>327</b>	<b>5</b>	<b>8,188</b>	<b>27</b>	<b>8,553</b>
<b>Book value as of 31.12.2021</b>	<b>22</b>	<b>0</b>	<b>370</b>	<b>0</b>	<b>12,545</b>	<b>27</b>	<b>12,964</b>

As in the previous year, the “Other loans” item does not include any loans to shareholders.

### 3.4 Inventories

(in million EUR)	31.12.2021	31.12.2020
Raw materials and supplies	941	811
Unfinished goods	2,059	1,891
Finished goods and goods for resale	1,225	1,152
Advance payments to suppliers	12	9
	<b>4,237</b>	<b>3,863</b>

### 3.5 Accounts receivable and other assets

(in million EUR)	31.12.2021	Residual term over 1 year	31.12.2020	Residual term over 1 year
Trade accounts receivable	5,178	5	4,302	7
Receivables from affiliated companies	42	0	21	0
Receivables from related companies	24	0	21	0
Other assets	1,341	290	908	161
	<b>6,585</b>	<b>295</b>	<b>5,252</b>	<b>168</b>

The “Other assets” item includes receivables from shareholders of 5 million EUR (previous year: 23 million EUR).

Receivables from affiliated companies almost exclusively consist of receivables from loans.

Receivables from related companies primarily consist of trade accounts receivable.

### 3.6 Provisions

(in million EUR)	31.12.2021	31.12.2020
Pension provisions and similar obligations	6,190	5,581
Tax provisions	1,772	1,746
Other provisions	8,993	7,993
	<b>16,955</b>	<b>15,320</b>



## Provisions for pensions and similar obligations

The provisions for pensions and similar obligations were determined on the basis of actuarial calculations using the projected unit credit method, taking into account future adjustments in salaries and pensions.

In addition to local biometric data (in Germany, for example, 2018 G mortality tables published by Prof. Dr. Klaus Heubeck which have been adjusted for Group-specific death probabilities and invalidity rates), pension obligations in the significant countries were calculated on the basis of the following actuarial parameters:

(in % as of December 31, 2021)	Germany	USA
Discount rate	1.87	3.50
Salary increase	3.50	4.90
Pension increase	1.88	0.00

Discount rates were determined by reference to average market rates for 15-year maturities in accordance with the German Regulation on the Discounting of Provisions of March 11, 2016. The interest rates used to discount significant foreign pension obligations (USA) were determined with comparable parameters, in line with the German Regulation on the Discounting of Provisions of March 11, 2016.

The difference calculated in accordance with Section 253 (6) HGB amounts to 634 million EUR (previous year: 803 million EUR).

The plan assets intended solely to cover pension and similar obligations that are unavailable to all other creditors (plan assets as defined in Section 246 (2) sentence 2 HGB) were measured at fair market value, which is essentially derived from stock market prices, and offset against the underlying pension and similar obligations. The fair market value of the plan assets on the balance sheet date was 2,189 million EUR. The related amount of pension obligations and similar obligations was 8,090 million EUR.

## Tax provisions

The tax provisions also include provisions for double taxation risks, which have resulted following the implementation of the action plans of the Organisation for Economic Cooperation and Development (OECD) as part of their international initiative known as the “Action Plan on Base Erosion and Profit Shifting” (BEPS).

## Other provisions

Other provisions mainly include provisions for discounts and guarantees, personnel-related provisions, provisions for outstanding invoices, provisions for litigation, legal claims, compensation for damages, and environmental provisions. Please refer to our comments on the impacts of the change of valuation method on environmental provisions in note 2.5. The use of the new method has resulted in a 195 million EUR reduction in the related provisions as of December 31, 2021 – relative to the situation as of December 31, 2020. This reduced operating income in the past financial year by 42 million EUR as a one-off effect, while financial income increased by 237 million EUR.

## 3.7 Accounts payable

(in million EUR)	Residual term less than 1 year	over 1 year	thereof over 5 years	31.12.2021	31.12.2020	Residual term less than 1 year
Bank loans	308	4	0	312	251	243
Other accounts payable	1,831	81	37	1,912	1,661	1,592
thereof:						
– Trade accounts payable	963	2	0	965	928	924
– Advance payments received	267	21	10	288	219	196
– Accounts payable to affiliated companies	6	5	5	11	8	3
– Accounts payable to related companies	1	0	0	1	0	0
– Other liabilities*	594	53	22	647	506	469
	2,139	85	37	2,224	1,912	1,835
*thereof:						
– from taxes (in million EUR)				243	201	
– social security liabilities (in million EUR)				29	29	

As in the previous year, there were no liabilities secured by mortgages or similar collateral rights on the balance sheet date.

At the end of the year, there were liabilities to shareholders of 204 million EUR (previous year: 163 million EUR). These are presented within the “Other liabilities” item.

Accounts payable to affiliated companies include loans amounting to 4 million EUR (previous year: 4 million EUR) and trade accounts payable amounting to 7 million EUR (previous year: 4 million EUR).

## 4 Notes to the consolidated profit and loss statement

The structure of the consolidated profit and loss statement is based on the total cost format. Other taxes are included in other operating expenses.

### 4.1 Net sales

by business (in million EUR)	2021	2020
Human Pharma	15,294	14,415
Animal Health	4,295	4,121
Biopharmaceutical Contract Manufacturing	917	837
Other sales	33	33
Discontinued operations	79	160
	<b>20,618</b>	<b>19,566</b>

by region (in million EUR)	2021	2020
Americas	9,147	8,889
Europe	6,554	5,879
Asia / Australia / Africa (AAA)	4,917	4,798
	<b>20,618</b>	<b>19,566</b>

### 4.2 Other operating income

Other operating income includes income from currency translation of 1,746 million EUR (previous year: 1,964 million EUR).

### 4.3 Cost of materials

(in million EUR)	2021	2020
Costs of raw material, supplies, and goods for resale	2,164	2,005
Expenditure on services	662	562
	<b>2,826</b>	<b>2,567</b>

## 4.4 Personnel expenses

(in million EUR)	2021	2020
Wages and salaries	4,668	4,586
Social benefits and retirement benefits	1,024	1,001
<i>thereof: retirement benefits</i>	228	261
	<b>5,692</b>	<b>5,587</b>

Interest effects of the measurement of the provisions for pensions and similar obligations are shown under financial income.

Average headcount	2021	2020
Production	17,373	16,940
Marketing and sales	17,560	18,468
Research and development	10,109	9,504
Administration	6,600	6,310
Apprentices	749	722
	<b>52,391</b>	<b>51,944</b>

## 4.5 Amortization of intangible assets and depreciation of tangible assets

Amortization of intangible assets and depreciation of tangible assets include impairment losses of 33 million EUR (previous year: 369 million EUR).

## 4.6 Other operating expenses

Other operating expenses include expenses from currency translation of 1,765 million EUR (previous year: 2,150 million EUR).

In addition, other items included in operating expenses are mainly the charges made to record provisions for third-party services for research, development, medicine and marketing purposes, administrative expenses, fees and contributions, commissions, rent, freight, and expenses for repairs carried out by third parties as well as legal risks and restructuring.

## 4.7 Financial income

(in million EUR)	2021	2020
Interest expenses and similar expenses	- 430	- 559
Amortization of and loss on disposal of financial fixed assets and short-term investments	- 5	- 7
Income from other investment securities and from long-term loans	83	12
Other interest income and similar income	15	31
	<b>- 337</b>	<b>- 523</b>

The “Interest expenses and similar expenses” item includes the interest result from provisions for pensions and similar obligations and other provisions in the amount of 377 million EUR (previous year: 499 million EUR) as well as other interest expenses and similar expenses in the amount of 53 million EUR (previous year: 60 million EUR).

Gains and losses from plan assets and interest expense relating to pension and similar obligations were offset in accordance with Section 246 (2) sentence 2 HGB. In total, 86 million EUR in earnings from plan assets and 682 million EUR in interest expense relating to pension and similar obligations are included under “Interest expenses and similar expenses”.

## 4.8 Holding income

(in million EUR)	2021	2020
Write-downs of financial assets	- 8	- 3
Write-ups of financial assets	1	0
Income from related companies	7	207
<i>thereof: from disposal of related companies</i>	3	194
	<b>0</b>	<b>204</b>

## 4.9 Income taxes

(in million EUR)	2021	2020
Current income taxes	1,308	1,529
Deferred taxes	- 346	- 286
	<b>962</b>	<b>1,243</b>

Current income taxes primarily include the corporation and trade tax expenses of the consolidated companies.



The total balance of deferred tax assets as of the balance sheet date amounted to 3,543 million EUR (previous year: 3,194 million EUR). Deferred tax assets primarily arise on the difference between the carrying amounts of provisions for pension obligations and for discounts, tax goodwill, intangible assets, inventories, and tangible assets. Deferred tax liabilities of 631 million EUR (previous year: 680 million EUR) were recorded. These primarily relate to differences between the carrying amounts of intangible assets, tangible assets, inventories, and provisions.

#### 4.10 Net income

The net income for 2021 was positively influenced by non-period income (primarily from the reversal of other provisions) of 609 million EUR (previous year: 634 million EUR) and was negatively influenced by non-period expenses (in particular additional expenses related to other provisions) of 281 million EUR (previous year: 226 million EUR).

## 5 Notes to the consolidated cash flow statement

The consolidated cash flow statement shows the changes in financial funds of the Boehringer Ingelheim Group resulting from cash inflows and outflows in the reporting year. Financial funds contain cash and cash equivalents as well as securities which can be converted into cash in the short-term.

The changes in the balance sheet items of the affiliated companies included were translated using average rates for the year. As on the balance sheet, financial funds are carried at the spot rate. The effect of exchange rate changes on the financial funds has been shown separately.

The financial funds as of December 31, 2021 comprised the following items:

(in million EUR)	2021
Cash and cash equivalents	2,296
Securities	250
	<b>2,546</b>

The financial funds included 15 million EUR in restricted funds as of the balance sheet date.

## 6 Other disclosures

### 6.1 Contingent liabilities

(in million EUR)	2021	2020
Liabilities from guarantees	71	44
Warranties and the granting of securities for third-party liabilities	56	55
	<b>127</b>	<b>99</b>

The risk of utilization of these contingent liabilities is assessed as low on account of the good net assets, financial, and earnings position.

### 6.2 Other financial commitments and off-balance sheet transactions

(in million EUR)	31.12.2021	31.12.2020
Rental and lease obligations	477	470
Residual other financial commitments	1,265	1,845
	<b>1,742</b>	<b>2,315</b>

Within the rental and lease obligations, 17 million EUR (previous year: 23 million EUR) relate to long-term rental agreements with subsidiaries not included in the consolidation.

The purpose of the lease agreements is the lower capital commitment compared to buying property and the absence of the resale risk. Risks could arise from the term of the lease should it not be possible to continue to utilize the properties fully. There are no such indications at this time.

The residual other financial commitments include investments with future effects on cash flows of 868 million EUR (previous year: 1,090 million EUR).

### 6.3 Derivative financial instruments and valuation units

Due to its extensive international structure, the Boehringer Ingelheim Group is highly dependent on developments in the world's currencies and interest rates. To hedge these risks, particularly those emerging from delivery of goods, services, and financing, currency forwards and options are generally used for currency risks. Interest rate swaps and options are used for interest rate risks.

The use of derivative financial instruments and the organizational processes are set out in internal guidelines. There is a strict separation between trading, processing, documentation, and control.

Risk positions are regularly tracked, analyzed, and measured in a special Group-wide financial report. The positions entered into are periodically reevaluated and monitored. The fair value of the derivative financial instruments is calculated using generally accepted market valuation methods (currency forwards based on the present value method) taking into account the market data as of the balance sheet date.

Provisions of 93 million EUR were recognized for currency forwards not included in hedge accounting for which there was a negative fair value within one currency as of the balance sheet date. In line with the impairment principle, positive fair values within one currency are not recognized.

On the balance sheet date, the derivative financial instruments not included in hedge accounting valuation units were as follows:

(in million EUR)	Nominal value		Fair value	
	31.12.2021	31.12.2020	31.12.2021	31.12.2020
Foreign exchange forward contracts	6,923	5,183	- 41	41

To the extent that the requirements for hedge accounting of foreign currency forward exchange contracts with highly probable forecast transactions in accordance with Section 254 HGB are met, the foreign currency forward exchange contracts are not recognized in the balance sheet in line with the net hedge presentation method.

The following accounting policies apply to the recognition of valuation units in accordance with Section 254 HGB:

Economic hedges are accounted for in the financial statements by the use of valuation units. The valuation units are recognized for each foreign currency based on the net amount of highly probable forecasted transactions and currency forwards that match the forecasted net cash flow in terms of maturity, nominal amount and foreign currency (macro hedge). The highly probable forecasted transactions (incoming and outgoing payments for planned sales and purchases) are derived from company planning. Ex-post analysis of planning has shown that the planned transactions are highly probable.

The opposing changes in value of the hedged item and the hedging instrument are fully offset as the critical terms (maturity, nominal amount, and foreign currency) match. An effective hedge can therefore be assumed both prospectively and retrospectively. The critical term match method is exclusively used to measure the prospective and retrospective effectiveness of hedges. Excess amounts under hedging transactions are not included in the valuation units.

As of December 31, 2021, hedges for highly probable forecasted net cash flows were recognized as follows:

### January to December 2022:

Net cash flow (in million EUR)		Foreign exchange forward contracts (in million EUR)		
	Nominal value		Nominal value	Fair value
USD	2,379	USD	1,483	USD –51
JPY	712	JPY	560	JPY 31
AUD	157	AUD	112	AUD –3
MXN	123	MXN	47	MXN –4
CAD	296	CAD	215	CAD –8
GBP	277	GBP	115	GBP –2

### January to December 2023:

Net cash flow (in million EUR)		Foreign exchange forward contracts (in million EUR)		
	Nominal value		Nominal value	Fair value
USD	1,899	USD	1,620	USD –34
JPY	693	JPY	489	JPY 15
AUD	30	AUD	15	AUD 0
MXN	21	MXN	7	MXN 0
CAD	46	CAD	30	CAD –1
GBP	103	GBP	33	GBP –1

### January to December 2024 (USD) and January to May (JPY):

Net cash flow (in million EUR)		Foreign exchange forward contracts (in million EUR)		
	Nominal value		Nominal value	Fair value
USD	1,914	USD	708	USD –7
JPY	362	JPY	83	JPY 1

### January to May 2025:

Net cash flow (in million EUR)		Foreign exchange forward contracts (in million EUR)		
	Nominal value		Nominal value	Fair value
USD	954	USD	245	USD 0

Furthermore, as of December 31, 2021, valuation units for foreign currency receivables were recognized as follows:

Receivables (in million EUR)		Foreign exchange forward contracts (in million EUR)	
	Nominal value		Fair value
RUB	125	RUB	49 RUB – 2

As of December 31, 2021, valuation units for foreign currency receivables resulting from loans were recognized as follows:

Receivables (in million EUR)		Foreign exchange forward contracts (in million EUR)	
	Nominal value		Fair value
CAD	20	CAD	20 CAD – 1
CHF	7	CHF	7 CHF 0
CNY	50	CNY	50 CNY – 2
MXN	313	MXN	313 MXN – 11
RUB	12	RUB	12 RUB 0
THB	39	THB	39 THB – 1
USD	64	USD	64 USD – 1

The amount of the hedged foreign currency risk correlates to the relative change in the exchange rate between the planning date and the realization date of the forecasted transactions. If all currencies were to appreciate or depreciate against the euro by 10.0%, there would be a foreign currency risk of + / – 1,060 million EUR without hedging.



## 6.4 Research and development expenses

(in million EUR)	2021	2020
Research and development expenses	4,127	3,696

Non-capitalized research and development expenses include, among other items, the costs associated with clinical studies.

## 6.5 Total auditor fees

Total fees charged to the Group by the auditor for the financial year amounted to 9.2 million EUR. 1.7 million EUR of this relates to audits of financial statements, 1.1 million EUR to other assurance services, 2.0 million EUR to tax advisory services and 4.4 million EUR to other services.

## 6.6 Subsequent events

Since the end of the 2021 financial year, we have not become aware of any events that are of material significance to the Group or that could lead to a reappraisal of its net assets, financial and earnings position.

## 6.7 Shareholdings

The list of companies included in the consolidated financial statements and the complete list of shareholdings presented in accordance with Section 313 (2) HGB are included in the audited consolidated financial statements submitted to the German Federal Gazette.

Ingelheim am Rhein, March 1, 2022  
Boehringer AG

Board of Managing Directors

Hubertus von Baumbach

Carinne Knoche-Brouillon

Dr. Michel Pairet

Jean Schefftsik de Szolnok

Michael Schmelmer

# Independent auditor's report

To C.H. Boehringer Sohn AG & Co. KG, Ingelheim am Rhein

## Qualified Audit Opinion on the Consolidated Financial Statements and Audit Opinion on the Group Management Report

We have audited the consolidated financial statements of C.H. Boehringer Sohn AG & Co. KG, Ingelheim am Rhein and its subsidiaries (the Group), which comprise the consolidated balance sheet as at 31 December 2021, the consolidated profit and loss statement, cash flow statement and statement of changes in group equity for the financial year from 1 January to 31 December 2021, and notes to the consolidated financial statements, including the recognition and measurement policies presented therein. In addition, we have audited the group management report of C.H. Boehringer Sohn AG & Co. KG for the financial year from 1 January to 31 December 2021.

In our opinion, on the basis of the knowledge obtained in the audit,

- except for the effects of the matter described in section “Basis for the Qualified Audit Opinion on the Consolidated Financial Statements and the Audit Opinion on the Group Management Report” the accompanying consolidated financial statements comply, in all material respects, with the requirements of German commercial law and give a true and fair view of the assets, liabilities, and financial position of the Group as at 31 December 2021, and of its financial performance for the financial year from 1 January to 31 December 2021 in compliance with German Legally Required Accounting Principles, and
- the accompanying group management report as a whole provides an appropriate view of the Group's position. In all material respects, this group management report is consistent with the consolidated financial statements, complies with German legal requirements and appropriately presents the opportunities and risks of future development.

Pursuant to Section 322 (3) sentence 1 HGB [Handelsgesetzbuch: German Commercial Code], we declare that, except for the qualification of the audit opinion on the consolidated financial statements mentioned, our audit has not led to any reservations relating to the legal compliance of the consolidated financial statements and of the group management report.

## Basis for the Qualified Opinion on the Consolidated Financial Statements and the Audit Opinion on the Group Management Report

Contrary to Section 314 (1) number 6 letters a) and b) HGB the total remuneration granted to the members and the former members of the board of managing directors as well as the pension provisions recognized and not recognized for the former members of the board of managing directors are not disclosed in the notes to the consolidated financial statements.

We conducted our audit of the consolidated financial statements and of the group management report in accordance with Section 317 HGB and in compliance with German Generally Accepted Standards for Financial Statement Audits promulgated by the Institut der Wirtschaftsprüfer [Institute of Public Auditors in Germany] (IDW). Our responsibilities under those requirements and principles are further described in the “Auditor's Responsibilities for the Audit of the Consolidated Financial Statements and of the Group Management Report” section of our auditor's report. We are independent of the group entities in accordance with the requirements of German commercial and professional law, and we have fulfilled our other German professional responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinions on the consolidated financial statements and on the group management report.

## Other Information

Management is responsible for the other information. The other information comprises the annual report, with the exception of the audited consolidated financial statements and group management report and our auditor's report.

Our opinions on the consolidated financial statements and on the group management report do not cover the other information, and consequently we do not express an opinion or any other form of assurance conclusion thereon.

In connection with our audit, our responsibility is to read the other information and, in so doing, to consider whether the other information

- is materially inconsistent with the consolidated financial statements, with the group management report audited for content or our knowledge obtained in the audit, or
- otherwise appears to be materially misstated.

## Responsibilities of Management for the Consolidated Financial Statements and the Group Management Report

Management is responsible for the preparation of the consolidated financial statements that comply, in all material respects, with the requirements of German commercial law and that the consolidated financial statements, in compliance with German Legally Required Accounting Principles, give a true and fair view of the assets, liabilities, financial position, and financial performance of the Group. In addition, management is responsible for such internal control as they, in accordance with German Legally Required Accounting Principles, have determined necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, management is responsible for assessing the Group's ability to continue as a going concern. They also have the responsibility for disclosing, as applicable, matters related to going concern. In addition, they are responsible for financial reporting based on the going concern basis of accounting provided no actual or legal circumstances conflict therewith.

Furthermore, management is responsible for the preparation of the group management report that, as a whole, provides an appropriate view of the Group's position and is, in all material respects, consistent with the consolidated financial statements, complies with German legal requirements, and appropriately presents the opportunities and risks of future development. In addition, management is responsible for such arrangements and measures (systems) as they have considered necessary to enable the preparation of a group management report that is in accordance with the applicable German legal requirements, and to be able to provide sufficient appropriate evidence for the assertions in the group management report.

## Auditor's Responsibilities for the Audit of the Consolidated Financial Statements and of the Group Management Report

Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and whether the group management report as a whole provides an appropriate view of the Group's position and, in all material respects, is consistent with the consolidated financial statements and the knowledge obtained in the audit, complies with the German legal requirements and appropriately presents the opportunities and risks of future development, as well as to issue an auditor's report that includes our opinions on the consolidated financial statements and on the group management report.

Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with Section 317 HGB and in compliance with German Generally Accepted Standards for Financial Statement Audits promulgated by the Institut der Wirtschaftsprüfer (IDW) will always detect a material misstatement. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements and this group management report.

We exercise professional judgment and maintain professional skepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the consolidated financial statements and of the group management report, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinions. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal controls.
- Obtain an understanding of internal control relevant to the audit of the consolidated financial statements and of arrangements and measures (systems) relevant to the audit of the group management report in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of these systems.
- Evaluate the appropriateness of accounting policies used by management and the reasonableness of estimates made by management and related disclosures.
- Conclude on the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Group's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in the auditor's report to the related disclosures in the consolidated financial statements and in the group management report or, if such disclosures are inadequate, to modify our respective opinions. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the Group to cease to be able to continue as a going concern.

- Evaluate the overall presentation, structure and content of the consolidated financial statements, including the disclosures, and whether the consolidated financial statements present the underlying transactions and events in a manner that the consolidated financial statements give a true and fair view of the assets, liabilities, financial position and financial performance of the Group in compliance with German Legally Required Accounting Principles.
- Obtain sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the Group to express audit opinions on the consolidated financial statements and on the group management report. We are responsible for the direction, supervision and performance of the group audit. We remain solely responsible for our audit opinions.
- Evaluate the consistency of the group management report with the consolidated financial statements, its conformity with German law, and the view of the Group's position it provides.
- Perform audit procedures on the prospective information presented by management in the group management report. On the basis of sufficient appropriate audit evidence we evaluate, in particular, the significant assumptions used by management as a basis for the prospective information, and evaluate the proper derivation of the prospective information from these assumptions. We do not express a separate opinion on the prospective information and on the assumptions used as a basis. There is a substantial unavoidable risk that future events will differ materially from the prospective information.

We communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

Frankfurt am Main, 1 March 2022

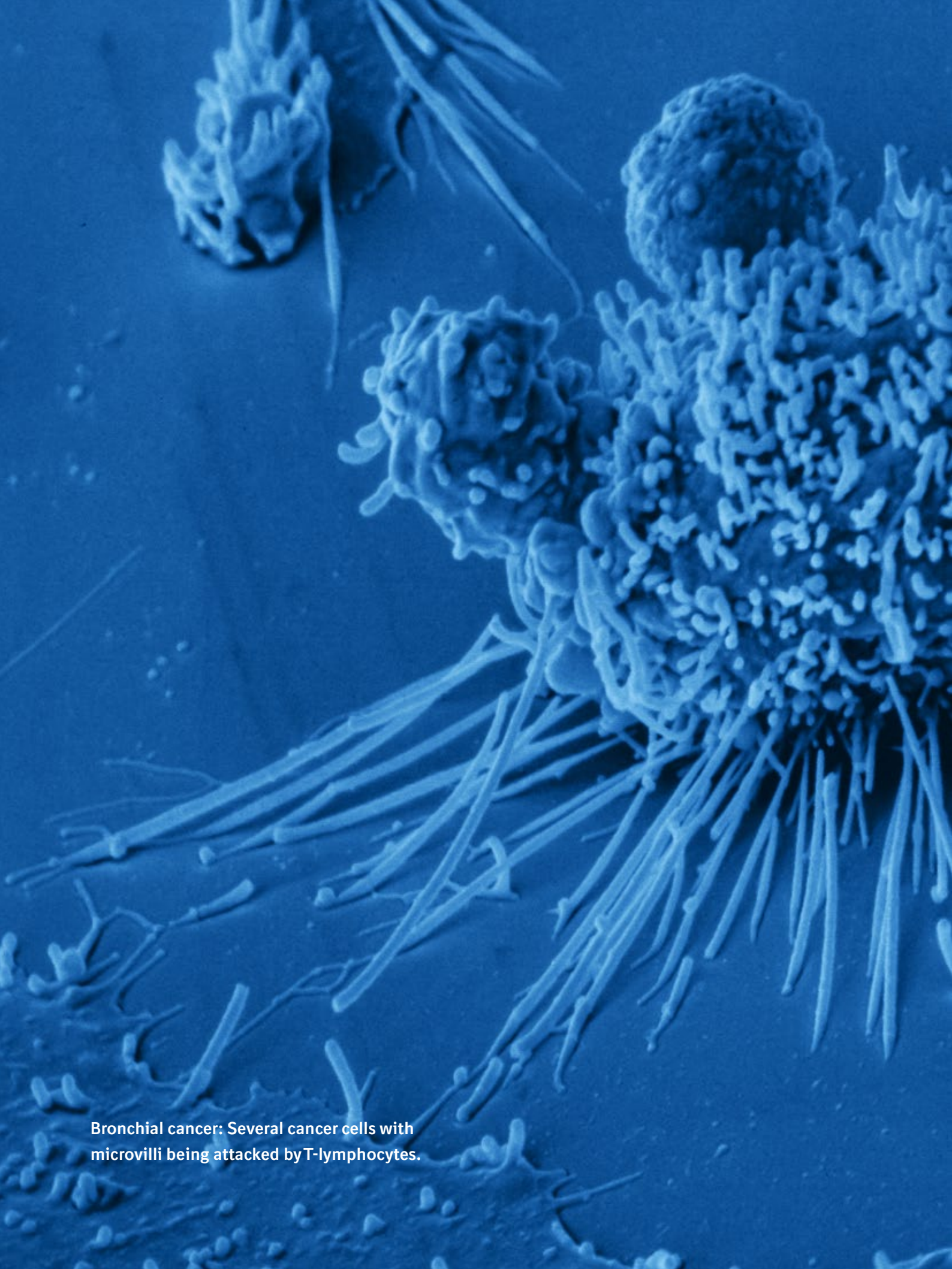
KPMG AG  
Wirtschaftsprüfungsgesellschaft

[Original German version signed by:]

Kneisel	Bernau
Wirtschaftsprüfer	Wirtschaftsprüferin
[German Public Auditor]	[German Public Auditor]







Bronchial cancer: Several cancer cells with microvilli being attacked by T-lymphocytes.



# Product Portfolio

## A Selection

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# Respiratory Diseases

Respiratory diseases are very common. Chronic obstructive pulmonary disease (COPD) and bronchial asthma are among the most prevalent chronic diseases and a frequent cause of morbidity and premature deaths worldwide.

Idiopathic pulmonary fibrosis (IPF) is a rare disease which is severely debilitating and ultimately lethal.

## COPD

COPD is a chronic disease of the lungs that causes coughing, excessive mucus production and dyspnea and ultimately destroys the lung tissue. The alveoli and thus gas exchange are the most affected. This leads to a limitation of airflow, causing shortness of breath and other respiratory symptoms. The airflow limitation is only partially reversible and usually worsens over time, leading to disability and ultimately to death. Symptoms such as excess cough and breathlessness are the main reasons why COPD is very stressful for patients. Lung emphysema and chronic bronchitis are the main manifestations of COPD.

COPD is caused by continuous damage to the lungs resulting from inhaling pollutants, primarily cigarette smoke. However, other factors also need to be considered including indoor and outdoor air pollution. The course of COPD, which is a disease that occurs in the second half in a human's life, is characterized by an accelerated loss of lung function compared to normal ageing and by occasional sudden worsening of symptoms and function referred to as acute exacerbations. This can lead to a downward spiral of worsening symptoms and thus further inactivity.

## Bronchial asthma

Bronchial asthma is a chronic inflammatory disorder of the airways. The inflammation is accompanied by airway hyper-responsiveness, which leads to a narrowing of the airways and recurrent episodes of wheezing, breathlessness and coughing. These symptoms occur particularly at night or in the early hours of the morning. It is now known that asthma can be triggered by genetic and environmental factors (e.g. allergens and viral infections). Unlike COPD, asthma can occur very early in childhood; it can also be present in adolescents or adults. Asthma is often underestimated as an easy-to-manage condition. However, almost one in two patients with asthma still experience symptoms while receiving maintenance therapy, putting them at increased risk of potentially life-threatening asthma exacerbations. In addition, patients often adjust their daily lives to accommodate their conditions and avoid physical exertion in day-to-day activities, which has a negative impact on quality of life.

Indications	Brand Names	Active Ingredients	
Chronic obstructive pulmonary disease (COPD)	SPIRIVA® SPIRIVA® HANDIHALER® SPIRIVA® RESPIMAT®	<i>tiotropium bromide</i>	Maintenance treatment of patients with COPD (including chronic bronchitis and emphysema), maintenance treatment of associated dyspnoea and for prevention of exacerbations.
Bronchial asthma	SPIRIVA® RESPIMAT®	<i>tiotropium bromide</i>	An add-on maintenance bronchodilator treatment in patients aged six years and older with severe asthma who experienced one or more severe asthma exacerbations in the past year.*  *SPIRIVA® RESPIMAT® is approved for use in asthma in the EU, Japan, the USA and many other countries. The label varies by country. Please refer to the local product information.
Chronic obstructive pulmonary disease (COPD)	SPIOLTO® RESPIMAT® STIOLTO® RESPIMAT® INSPIOLTO® RESPIMAT®	<i>tiotropium bromide, olodaterol hydrochloride</i>	Maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).
Chronic obstructive pulmonary disease (COPD)	STRIVERDI® RESPIMAT®	<i>olodaterol hydrochloride</i>	Maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
Reversible broncho-spasms associated with obstructive airway diseases	COMBIVENT® RESPIMAT®	<i>ipratropium bromide, salbutamol, sulphate</i>	A combination of a short-acting anticholinergic and beta-adrenergic for the management of reversible bronchospasms associated with obstructive airway diseases in patients requiring more than one bronchodilator.
Chronic obstructive pulmonary disease (COPD)  Chronic bronchitis  Bronchial asthma	ATROVENT®	<i>ipratropium bromide</i>	Prevention and treatment of shortness of breath in patients with chronic obstructive pulmonary disease (COPD) and mild to moderate bronchial asthma in adulthood and childhood as a supplement to beta-agonists in cases of acute asthma.
Chronic obstructive airway disorders	BERODUAL® BRONCHODUAL® DUOVENT®	<i>ipratropium bromide, fenoterol hydrobromide</i>	Prevention and treatment of symptoms in chronic obstructive airway disorders with reversible airflow limitation such as bronchial asthma and especially chronic bronchitis with or without emphysema.



# Respiratory Diseases (continued)

## Idiopathic pulmonary fibrosis (IPF)

IPF is a chronic progressive lung disease associated with a markedly reduced life span and affecting as many as 14–43 people per 100,000 worldwide. IPF is characterized by progressive scarring of lung tissue and a loss of lung function over time. Development of scarred tissue is called fibrosis. Over time, as the tissue thickens and stiffens with scarring, the lungs lose their ability to take in and transfer oxygen into the bloodstream, and vital organs do not get enough oxygen. As a result, individuals with IPF experience shortness of breath, even when resting, and often have difficulty coping with the demands of everyday life due to their limited physical capacity.

Acute IPF exacerbations are defined as rapid deteriorations of symptoms and lung function within days or weeks. These events can occur at any point in the course of the disease, even at first presentation, and are associated with high mortality. All patients with IPF are at risk of acute IPF exacerbations.

## Systemic sclerosis associated interstitial lung disease (SSc-ILD)

Systemic sclerosis (SSc), also known as scleroderma, is a rare incurable autoimmune disease affecting connective tissue. The disease is estimated to affect 15 to 24 people in every 100,000 in Europe and 2.5 million worldwide. SSc impacts four times as many women as men, and the onset of the disease typically occurs at a young age – between 25 and 55 years. It can cause scarring (fibrosis) of the skin as well as major organs such as the heart, lungs, digestive tract and kidneys and can have life-threatening complications. Approximately 25% of patients develop significant pulmonary involvement within three years of diagnosis.

When SSc affects the lungs, it can cause interstitial lung disease (ILD), known as SSc-ILD. It is a key driver of mortality among people with SSc, accounting for approximately one third of deaths.

## Other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype beyond idiopathic pulmonary fibrosis (IPF)

Interstitial lung diseases are a heterogeneous group of more than 200 mostly rare conditions of the lung that run the risk of developing pulmonary fibrosis. Fibrosis is a pathological multiplication of the connective tissue leading to usually chronic and irreversible scarring of the lung tissue. The course of interstitial lung disease may develop into a progressive fibrosing ILD, leading to a decline function associated with increased morbidity and mortality. Idiopathic pulmonary fibrosis (IPF) is a phenotype of a chronic fibrosing ILD. The course of the disease and symptoms are similar to chronic PF-ILDs, despite the underlying ILD diagnosis. On average, 18–32% of ILD patients will develop progressive pulmonary fibrosis.

Indications	Brand Names	Active Ingredients	
			Symptomatic treatment of acute asthma attacks. Prophylaxis of exercise-induced asthma bronchiale.  Symptomatic treatment of allergic and non-allergic asthma bronchiale and other conditions with reversible airway narrowing, e.g. chronic obstructive bronchitis.
Bronchial asthma	BEROTEC®	<i>fenoterol hydrobromide</i>	
			
Bronchial asthma			Prophylactic treatment of patients with bronchial asthma. Prophylaxis and symptomatic treatment of allergic rhinitis.
Allergic rhinitis	ALESION®	<i>epinastine hydrochloride</i>	
Idiopathic pulmonary fibrosis (IPF)			In more than 80 countries for the treatment of patients with idiopathic pulmonary fibrosis (IPF).  In more than 70 countries as therapy for SSc-ILD to slow down the rate of decline in pulmonary function.
Systemic sclerosis associated interstitial lung disease (SSc-ILD)			
Chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype	OFEV®	<i>nintedanib</i>	In more than 60 countries for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype beyond IPF.

# Cardiovascular and Metabolic Diseases

Cardiovascular disease (CV), including heart disease and stroke, is a major global health concern and the leading cause of death and disability worldwide. Currently, it is responsible for nearly one in three deaths worldwide. One key risk factor for developing cardiovascular disease is the presence of diabetes: people with type 2 diabetes are two to four times more likely to develop cardiovascular disease than people without diabetes, and as a result, their life expectancy is up to 12 years shorter. Proper control of diabetes and other treatable risk factors like heart failure is therefore vital for the prevention of cardiovascular events.

## Stroke

Stroke is the rapidly developing loss of brain functions caused by a disrupted blood flow to the affected brain tissue. This can be due to ischemia (lack of blood supply) caused by thrombosis or embolism, or due to bleeding (hemorrhagic stroke). As a result, the affected area of the brain is unable to function and the damage quickly becomes permanent, if untreated. A stroke is an acute event requiring emergency diagnosis and intervention. Worldwide, stroke is one of the leading causes of death and long-term disability.

Symptoms of a transient ischemic attack (TIA) are similar to stroke, but last for only a few minutes or hours and do not result in permanent neurological damage. As a TIA may precede a stroke, emergency medical care and subsequent preventive treatment may be necessary.

## Atrial fibrillation

Atrial fibrillation (AF) is the most common sustained heart rhythm condition, affecting approximately 2% of the total population. One in four adults over 40 develops AF in their lifetime. Patients with AF are at higher risk of developing blood clots in their upper left heart chamber, which can cause a stroke if the clot breaks loose and travels to the brain. AF leads to a five-fold increase in the risk of stroke, resulting in up to three million patients worldwide suffering AF-related strokes each year. For patients with AF, the risk of stroke can be reduced by appropriate anticoagulation therapy.

## Prevention and treatment of venous thromboembolism

Venous thromboembolism (VTE) is an umbrella term that encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT occurs when a thrombus (blood clot) forms in a deep vein, most commonly in the leg, and partially or completely blocks the flow of blood. As the thrombus grows, a portion may break away from the main clot and travel in the circulatory system to the lungs. The lodging of a blood clot in the arteries of the lung is called a PE. VTE is a serious disorder with potentially fatal consequences.

Patients undergoing orthopedic surgery are at considerable risk of developing DVT, and chronic venous insufficiency and/or pulmonary hypertension may develop in the longer term.

Indications	Brand Names	Active Ingredients	
Stroke prevention in atrial fibrillation			Prevention of strokes and blood clots in patients with atrial fibrillation.
Primary prevention of venous thromboembolic events after orthopedic surgery			Primary prevention of venous thrombo-embolic events (VTE) in adults after elective total hip or knee replacement surgery.
Treatment and secondary prevention of venous thromboembolic events	PRADAXA® PRADAXAR® PRAZAXA®	 <i>dabigatran etexilate</i>	Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and secondary prevention of recurrent DVT and PE in adults.  Treatment of venous thromboembolic events (VTE) and prevention of recurrent VTE in pediatric patients from birth to less than 18 years of age.
Specific reversal of PRADAXA® (dabigatran etexilate)	PRAXBIND®	 <i>idarucizumab</i>	PRAXBIND® is a specific reversal agent for dabigatran and is indicated in adult patients treated with PRADAXA® (dabigatran etexilate) when rapid reversal of its anticoagulant effects is required: for emergency surgery / urgent procedures; in life-threatening or uncontrolled bleeding.
Hypertension			Treatment of hypertension. For the reduction of the risk of myocardial infarction (heart attack), stroke or death from cardiovascular (CV) causes in patients 55 years of age or older at high risk of developing major CV events who are unable to take ACE inhibitors (US).
Cardiovascular morbidity and mortality prevention	MICARDIS®	 <i>telmisartan</i>	For the reduction of cardiovascular morbidity in patients with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke or peripheral arterial disease), or patients with type 2 diabetes mellitus with documented target organ damage (EU).
Hypertension	MICARDISPLUS® MICARDIS® PLUS MICARDIS® HCT CO-MICARDIS®	 <i>telmisartan, hydrochlorothiazide</i>	Treatment of hypertension alone or with other antihypertensive agents, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Not indicated for initial therapy (US).  Treatment of essential hypertension. MICARDISPLUS® fixed dose combination is indicated in adults whose blood pressure is not adequately controlled on telmisartan alone (EU).

# Cardiovascular and Metabolic Diseases (continued)

To prevent VTE events and their consequences after orthopedic surgery, patients should receive some kind of thromboprophylaxis. Patients who have already suffered from VTE require anticoagulant treatment for secondary prevention of a recurrent thromboembolic event.

## Reversing anticoagulation

Anticoagulation therapy offers important benefits for patients at risk of thromboembolic events. However, even though rare, there may be situations when rapid reversal of anticoagulation is medically necessary, e.g. if a patient taking an anticoagulant is involved in a severe car accident and needs emergency surgery.





## Hypertension and cardiovascular diseases

Hypertension (high blood pressure) is a chronic disease in which the blood pressure is chronically elevated. Hypertension is also one of the major risk factors for stroke, heart attacks, heart failure and chronic renal failure. The primary goal of antihypertensive treatment is to prevent such cardiovascular events and to reduce the risk of cardiovascular mortality.

## Acute myocardial infarction

An acute myocardial infarction, or heart attack, occurs when a thrombus (blood clot) suddenly prevents blood flow to an area of the heart muscle. Unless the blood flow is restored quickly, the affected section of heart muscle becomes permanently damaged. Heart attacks are one of the most common causes of death in industrialized countries.



Indications	Brand Names	Active Ingredients	
Hypertension	TWYNSTA® MICAMLO® MICARDIS® AMLO MICARDIS® DUO	 <i>telmisartan, amlodipine</i>	Treatment of hypertension alone or with other antihypertensive agents. As initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals (US).  Add-on therapy in adult patients with not adequately controlled blood pressure on amlodipine, and replacement therapy in adult patients receiving telmisartan and amlodipine from separate tablets (EU).
Acute ischemic stroke			
Acute myocardial infarction			
Acute massive pulmonary embolism			
Catheter clearance due to thrombotic occlusion	ACTILYSE® ACTILYSE® CATHFLO®	<i>alteplase</i>	Fibrinolytic treatment of acute ischemic stroke, acute myocardial infarction, acute massive pulmonary embolism. Fibrinolytic treatment of occluded catheters.
Secondary prevention of stroke or transient ischemic attacks (TIA)	AGGRENOX®	 <i>dipyridamole, acetylsalicylic acid</i>	Prevention of stroke following an initial first stroke, or transient ischemic attacks (TIA).
Acute myocardial infarction	METALYSE®	 <i>tenecteplase</i>	Fibrinolytic treatment of acute myocardial infarction.

# Cardiovascular and Metabolic Diseases (continued)

## Diabetes, heart failure, and the cardio-renal-metabolic system

Type 2 diabetes is a chronic, progressive condition associated with elevated blood sugar levels. People with type 2 diabetes have a high burden of comorbidities and risk factors, which include heart failure, kidney disease, hypertension, and obesity. Cardio-renal-metabolic conditions affect more than one billion people worldwide and are a leading cause of death.

Heart failure is a progressive, debilitating, and potentially fatal condition that occurs when the heart cannot supply adequate circulation to meet the body's demands for oxygenated blood, or to do so requires increased blood volume leading to fluid accumulation (congestion) in the lungs and peripheral tissues. It is a widespread condition affecting over 60 million people worldwide and expected to increase as the population ages.

A collaborative multidisciplinary team approach to optimize patient care by coordinating treatment of related comorbidities, including the use of emerging medications with broad cardiovascular, renal, and metabolic effects, can help improve outcomes for people with these serious chronic conditions.

Indications	Brand Names**	Active Ingredients	
Type 2 diabetes mellitus	JARDIANCE® JARDIANZ®	 empagliflozin	Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control and to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.*  <i>*US indication, December 2016. The label varies by country. Please refer to the local product information.</i>
Heart failure	JARDIANCE® JARDIANZ®	 empagliflozin	Treatment of adults with heart failure with reduced ejection fraction (with or without type 2 diabetes).*  <i>*The label varies by country. Please refer to the local product information.</i>
Type 2 diabetes mellitus	SYNJARDY® JARDIANCE DUO® JARDIANZ DUO® SYNJARDY® XR	 empagliflozin, metformin hydrochloride	Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control when treatment with both empagliflozin and metformin is appropriate.*  <i>*US indication, December 2016. The label varies by country. Please refer to the local product information.</i>
Type 2 diabetes mellitus	GLYXAMBI® TRAJENTA® JARDIANZ DPP®	 empagliflozin, linagliptin	Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when both empagliflozin and linagliptin are appropriate treatments.*  <i>*US indication, March 2015. The label varies by country. Please refer to the local product information.</i>
Type 2 diabetes mellitus	TRAJENTA® TRAJENTA® TRAJENTA® TRAJENTA®	 linagliptin	Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control, used in monotherapy (if metformin is not tolerated or contraindicated) or in combination therapy.
Type 2 diabetes mellitus	JENTADUETO® TRAJENTA DUO® TRAJENTA DUO® TRAJENTAMET® JENTADUETO® XR	 linagliptin, metformin hydrochloride	Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control when treatment with metformin does not lead to sufficient control or when patients are treated with TRAJENTA® (linagliptin) and metformin.

\*\* Diabetes portfolio in collaboration with Eli Lilly and Company.



# Oncology

Cancer is a threat to global health. In 2018, an estimated 18 million new cases of cancer were diagnosed worldwide and 9.6 million people died from cancer, nearly one in six global deaths (WHO World Cancer Factsheet 2018). The most common diagnosed cancer types were lung cancer (nearly 12%), breast cancer (nearly 12%), colorectal cancer (10%), prostate cancer (7%) and stomach cancer (6%).

## Lung cancer

Lung cancer refers to malignant abnormal cell growth inside the lung tissue. It is the most common cancer with an estimated 2.1 million new cases per year worldwide (2018). Smoking is the primary cause of the disease, contributing to almost 90% of the cases. Recently, however, the incidence of lung cancer among non-smokers has increased. Lung cancer has a poor prognosis, with 1.8 million deaths per year, representing nearly 20% of all cancer deaths. Lung cancer symptoms are unspecific so that the disease may take many years to appear. Late diagnosis in an advanced stage of the disease results in an often dismal prognosis, with only 10–15% of lung cancer patients surviving five years or more following diagnosis.

There are different subtypes such as small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). More than ten different molecular genetic aberrations (mutations) present in the tumor have been identified. By focusing on molecular changes that are specific to the respective subtype of lung cancer, targeted therapies have become more effective than other treatments. They show a survival benefit and are at the same time less harmful to normal cells, thereby reducing side effects.

Indications	Brand Names	Active Ingredients
Non-small cell lung cancer (NSCLC)	GIOTRIF® GILOTRIF®	<div></div> <p><i>afatinib</i></p> <p>First-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating epidermal growth factor receptor (EGFR) mutations.</p> <p>For the treatment of patients with locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum-based chemotherapy.</p>
		<div></div> <p><i>nintedanib</i></p> <p>Combination therapy with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumor histology after first-line chemotherapy.</p>



# Diseases of the Central Nervous System

Mental and neurological diseases such as depression and Parkinson's disease significantly impact patients and their families and are also a substantial burden to society.

## Parkinson's disease

Parkinson's disease (PD) is a degenerative disorder of the central nervous system. Patients usually notice motor symptoms like hand shaking (tremor) as their first sign of the disease, which may progress to include shaking of the arms, legs or head. Other motor symptoms that may develop over time include stiffness that often results in loss of facial expression and a gradual slowing or loss of motion, or "freezing". About 30–40% of patients also suffer from non-motor symptoms associated with PD, such as depression and sleep disorders. The primary symptoms are the result of a lack of the neuro-transmitter dopamine in distinct areas of the human brain.


## Restless legs syndrome (RLS)

RLS is a common neurological disorder characterized by an uncontrollable urge to move the legs, primarily occurring in the evening and night hours. It is usually accompanied by unpleasant and sometimes painful sensations in the legs as well as disturbed sleep resulting in daytime tiredness or sleepiness. The sensations are felt deep within the legs and are described as creeping, crawling or aching.



# Infectious Diseases

## HIV infection / AIDS

Acquired immune deficiency syndrome (AIDS) is a set of symptoms and infections resulting from the damage to the human immune system caused by the human immunodeficiency virus (HIV). If untreated, infection with HIV progressively reduces the effectiveness of the immune system and leaves individuals susceptible to opportunistic infections and tumors. Babies of infected mothers are at risk of getting the virus during pregnancy, childbirth or breastfeeding.

Indications	Brand Names	Active Ingredients
Parkinson's disease (PD)  Restless legs syndrome (RLS)	SIFROL® MIRAPEX® MIRAPEXIN® PEXOLA® MIRAPEX® ER SIFROL® ER	<div></div> <p><i>pramipexole, pramipexole dihydrochloride monohydrate</i></p>
		Symptomatic treatment of idiopathic Parkinson's disease. It may be used as monotherapy or in combination with levodopa. Symptomatic treatment of idiopathic moderate to severe restless legs syndrome.

Sleep disorders	LENDORMIN®	 <i>brotizolam</i>	Short-term treatment of disorders of initiating and maintaining sleep. Insomnia requiring pharmacological intervention.
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Indications	Brand Names	Active Ingredients	
HIV/AIDS	VIRAMUNE® VIRAMUNE XR®	 <i>nevirapine</i>	<p>For the combination therapy of HIV-1 infection and (in several countries) for the prevention of mother-to-child transmission of HIV-1 in pregnant women who are not taking antiretroviral therapy at time of labor.</p> <p>Prolonged release tablets for once-daily dosing within combination therapy.</p>
HIV/AIDS	APTIVUS®	 <i>tipranavir</i>	<p>Indicated for combination antiretroviral treatment of HIV-1 infected patients, co-administered with 200 mg of ritonavir, who are treatment-experienced and infected with HIV-1 strains resistant to more than one protease inhibitor.</p>

# Livestock – Swine

## Infectious respiratory diseases

INGELVAC CIRCOFLEX® is the first single-dose piglet vaccine for the control of porcine circovirus disease (PCVD). INGELVAC CIRCOFLEX® contains IMPRANFLEX® adjuvant which allows for fresh mixing with INGELVAC MYCOFLEX® to form FLEXCOMBO® with the TwistPak system. Our INGELVAC® PRRS products are licensed for active immunization against the respiratory and reproductive form of porcine reproductive and respiratory syndrome (PRRS).

## Infectious enteric diseases

ENTERISOL® ILEITIS is the first and only oral live vaccine against ileitis, globally the most prevalent enteric disease in swine caused by *Lawsonia intracellularis*. It is licensed to improve weight gain and to reduce growth variability associated with the disease. ENTERISOL® ILEITIS helps to reduce the total antimicrobial use in pork production.

## Integrated Health Management (IHM)

With FARMERA® and SOUNDTALKS™ we will empower pig producers, breeders, retailers, and consumers to improve health, animal welfare, and efficiency by giving insights, predictions, and recommendations through our IHM solutions.

Indications	Brand Names	Active Ingredients	
Infectious respiratory diseases	INGELVAC CIRCOFLEX®	<i>recombinant vaccine (porcine circovirus type 2, PCV2)</i>	 <p>For the active immunization of pigs over the age of two weeks against porcine circovirus type 2 to reduce mortality, clinical signs – including weight loss – and lesions in lymphoid tissues associated with porcine circovirus diseases (PCVD). In addition, vaccination has been shown to reduce PCV 2 nasal shedding, viral load in blood and lymphoid tissues, and duration of viremia.</p>
Infectious respiratory diseases	INGELVAC® PRRS MLV INGELVAC PRRSFLEX® EU REPROCYC® PRRS EU	<i>attenuated live vaccine (PRRS virus type 2, type 1)</i>	 <p>Depending on the product, for the active immunization of pigs at various ages against porcine reproductive and respiratory syndrome virus (PRRS).</p>
Infectious respiratory diseases	INGELVAC MYCOFLEX®	<i>inactivated vaccine (Mycoplasma hyopneumoniae)</i>	 <p>For the active immunization of pigs from the age of three weeks to reduce lung lesions following infections with Mycoplasma hyopneumoniae.</p>
Infectious enteric disease	ENTERISOL® ILEITIS	<i>attenuated live vaccine (Lawsonia intracellularis)</i>	 <p>For the active immunization of pigs from the age of three weeks against intestinal lesions caused by Lawsonia intracellularis infection and to reduce growth variability and loss of weight gain associated with the disease.</p>
Respiratory diseases	SOUNDTALKS™*	<i>sound monitors, gateways and algorithms</i>	 <p>SOUNDTALKS™ is sound monitoring technology that detects early symptoms of respiratory distress in swine thanks to its 24/7 monitoring and algorithms.</p>
Data capture forms and tools	FARMERA®	<i>mobile app. Digital data management and communication platform for swine production</i>	 <p>FARMERA® allows being more efficient, effective, and proactive by enabling evidence-based decision making with real-time information when managing health and production in production companies.</p>

\* SOUNDTALKS™ is a trademark of SoundTalks, N.V.






# Livestock – Cattle/Ruminants

Our cattle/ruminants business is a global leader in anti-parasitic brands such as IVOMEC®, LONGRANGE® and EPRINEX®. These world renowned parasiticides treat and protect grazing animals from the harmful effects of internal and external parasites.

ZACTRAN® treats cattle with bacterial pneumonia and sheep with digital dermatitis infections.

BOVELA® is for active immunization of cattle of three months of age in terms of reproductive infectious diseases.





Indications	Brand Names	Active Ingredients	
Internal and external parasites of cattle	IVOMEC®	 <i>ivermectin</i>	Depending on formulation, the product is for the treatment of nematodes, lice, mites, ticks, flies, lungworms and liver flukes.
Internal and external parasites of cattle	LONGRANGE®	 <i>eprinomectin, long-acting</i>	The Theraphase® technology used to develop this formulation of eprinomectin allows a single treatment to last up to 100-150 days – long enough to break the parasite life cycle and effectively reduce parasite burdens on the pasture. LONGRANGE® is effective in the control of most internal and external parasites of cattle: gastrointestinal roundworms, lungworms, grubs, mites.
Internal and external parasites of ruminants	EPRINEX®	 <i>eprinomectin</i>	Depending on formulation, the product is for the treatment of nematodes, lice, mites, ticks, flies and lungworms in cattle and sheep.
Bacterial causes of respiratory disease and interdigital dermatitis (footrot)	ZACTRAN®	 <i>gamithromycin</i>	Depending on species indication (and country of registration), the product is for the treatment and metaphylaxis control of respiratory disease in cattle caused by key bacteria (Mannheimia, Pasteurella, Histophilus and Mycoplasma) and footrot disease in sheep caused by key bacteria (Fusobacterium and Dichelobacter).
Reproductive infectious diseases in cattle	BOVELA®	 <i>bovine viral diarrhoea (BVD) types 1 and 2</i>	Reduces hyperthermia and minimizes the reduction of leukocyte count caused by bovine viral diarrhoea virus (BVDV-1 and BVDV-2); reduces virus shedding and viremia caused by BVDV-2 and prevents the birth of persistently infected calves caused by transplacental infection.

# Livestock – Cattle/Ruminants (continued)






Our vaccine PYRAMID®/PRESPOSE® is part of our expanding portfolio of respiratory and reproductive vaccines to prevent diseases that affect livestock.

METACAM® is a non-steroidal anti-inflammatory drug (NSAID), helping to minimize losses from inflammation and tissue damage in animals suffering from disease, hence addressing the need for maintained profitability and the concern for farm animal well-being.

Indications	Brand Names	Active Ingredients
Infectious respiratory diseases and reproductive disorders in cattle	PYRAMID® PRESPOSE®	 <p>family of multivalent vaccine combinations including different modified live viruses: bovine viral diarrhoea (BVD) types 1 and 2, infectious bovine rhinotracheitis (IBR), parainfluenza 3 (PI3) and bovine respiratory syncytial virus (BRSV), and bacteria: <i>Pasteurella multocida</i>, <i>Mannheimia haemolytica</i>, <i>L. canicola</i>, <i>L. grippotyphosa</i>, <i>L. hardjo</i>, <i>L. icterohaemorrhagiae</i> and <i>L. pomona</i></p> <p>The PYRAMID®/PRESPOSE® family of vaccines provides broad coverage for BVD types 1 and 2, IBR, BRSV, PI3 and Mannheimia haemolytica with only a single dose. They contain the MetaStim®* adjuvant system to enhance the animal's response for greater protection (US and Canada only).</p> <p>*MetaStim® is a registered trademark of Zoetis Services LLC</p>
Pain and inflammatory disorders	METACAM®	 <p><i>meloxicam</i></p> <p>For the treatment of mastitis in lactating cows and for the control of pain associated with dehorning or surgery. It is also indicated for use in calves affected by diarrhoea and in cattle suffering from respiratory disease.</p>

# Livestock – Poultry

Our poultry vaccine portfolio consists of a significant range of live, inactivated, and vectored vaccines for broilers, layers, and breeder hens, providing protection against the most acute viral and bacterial diseases like avian influenza, infectious bronchitis, Newcastle disease, infectious bursal disease, egg drop syndrome, and avian coryza. This portfolio of preventive solutions helps producers worldwide to provide safe, affordable, abundant, and sustainable high-quality poultry meat and eggs.

Indications	Brand Names	Active Ingredients
Various viral and bacterial diseases in poultry	GALLIMUNE® GALLIVAC® VOLVAC®	 <p><i>monovalent or polyvalent attenuated live and inactivated vaccine containing antigens for vaccination against avian influenza, Newcastle disease, avian coryza, egg drop syndrome, infectious bronchitis, infectious bursal disease, avian rhinotracheitis, salmonella and gallibacterium anatis</i></p>
Infectious bursal disease (IBD), Marek's disease (MD) and Newcastle disease (ND), or infectious laryngotracheitis (ILT)	VAXXITEK® HVT + IBD VAXXITEK® HVT + IBD + ND VAXXITEK® HVT + IBD + ILT	 <p><i>serotype 3, live Marek's disease vector, live vHVT013-69 recombinant virus which contains a gene of IBD virus and, for the trivalent vaccines, a gene of IBD virus and of ND or ILT viruses (and diluent)</i></p>
Newcastle disease (ND)	AVINEW®	 <p><i>live Newcastle disease virus, VG/GA-AVINEW strain</i></p>
Marek's disease	PREVEXXION® RN PREVEXXION® RN+HVT PREVEXXION® RN+HVT+IBD PREVEXXION® RN & VAXXITEK® HVT+IBD	 <p><i>live herpes virus chimera, serotype 1, strain RN1250 (and diluent)</i></p>
Newcastle and Marek's diseases	NEWXXITEK™ HVT + ND	 <p><i>live Marek's disease vectored virus, serotype 3, that contains a gene insert from Newcastle disease (and diluent)</i></p>

For vaccination of healthy chickens against diseases caused by the included antigens. For the prevention of the most common diseases in broiler chickens and diseases responsible for losses in egg production in layers.

The vaccination of 18- to 19-day-old embryos or one-day-old chickens is effective against standard and variant infectious bursal disease, Marek's disease, and for the trivalent vaccines against Newcastle disease or infectious laryngotracheitis.

In broiler chickens from one day of age: active immunization against Newcastle disease to reduce mortality and clinical signs associated with the disease.

In future layer and future breeder pullets from the age of four weeks: priming for active immunization against egg drop caused by Newcastle disease before vaccination with an inactivated vaccine (strain Ulster 2C) prior to the beginning of lay.

The vaccination of 18- to 19-day-old embryos and / or one-day-old chickens is recommended to protect against the very virulent Marek's disease.

The vaccination of 18- to 19-day-old embryos or one-day-old chickens is effective against Marek's disease and Newcastle disease.



# Veterinary Public Health (VPH)

We work together with governments and private partners toward improving control and eradicating diseases such as foot-and-mouth disease, bluetongue virus and rabies.

Our foot-and-mouth (FMD) vaccines portfolio including AFTOPOR®, AFTOVAXPUR® and AFTOVAX® provides active immunization of cattle, sheep or pigs to reduce clinical signs and mortality following exposure to FMD virus.

RABISIN® is an inactivated vaccine against rabies, available as a clear colorless suspension for injection. RABORAL V-RG® is an oral recombinant vaccine that protects wildlife against rabies.

BTVPUR ALSAP® is a multi-strain vaccine used for active immunization of sheep and cattle to prevent viremia and to reduce clinical signs caused by bluetongue virus.

Indications	Brand Names	Active Ingredients	
Foot-and-mouth disease (FMD)	AFTOPOR®	<i>mix of inactivated FMD virus antigens with the widest range of vaccine strains</i>	 <p>AFTOPOR® and AFTOVAXPUR® are highly potent vaccines with purified antigens, recommended in endemic or emergency situations. Both have potential marker properties that allow differentiation between infected and vaccinated animals (DIVA).</p>
	AFTOVAXPUR® AFTOVAX® AFTOVAXPUR® DOE		
Rabies	RABISIN®	<i>Rabisin: inactivated and adjuvanted rabies virus; Raboral V-RG: vaccinia-vectored rabies vaccine</i>	 <p>RABISIN® is used for the active immunization of dogs and cats to reduce mortality and clinical signs due to rabies infection. Immunity has been demonstrated one month after vaccination and has been shown to persist up to the first booster dose, (1 year after primary vaccination) and up to 3 years following booster vaccination.</p>
	RABORAL V-RG®		
Bluetongue	BTVPUR ALSAP®	<i>mix of inactivated bluetongue virus</i>	 <p>Active immunization of sheep to prevent viremia and to reduce clinical signs caused by bluetongue virus serotypes 1, 2, 4 and /or 8 (combination of maximum 2 serotypes).</p> <p>Active immunization of cattle to prevent viremia caused by bluetongue virus serotypes 1, 2, 4 and /or 8, and to reduce clinical signs caused by bluetongue virus serotypes 1, 4 and /or 8 (combination of maximum 2 serotypes).</p> <p>Onset of immunity has been demonstrated three weeks (or five weeks in sheep for BTV-2) after the primary vaccination course for BTV-1, BTV-2 (cattle), BTV-4 and BTV-8 serotypes.</p>

# Companion Animals – Horses

Our equine portfolio is highly comprehensive, covering the key aspects of equine health, including parasite control, vaccination, and the management of chronic diseases. We have a range of flagship and market leading equine products and have recently enhanced our joint disease and respiratory portfolios with the addition of new innovative products. We also have a line of nutraceuticals which can be bought without prescription.

PRASCEND® is indicated for the treatment of pituitary pars intermedia dysfunction (PPID), which is also known as equine Cushing's disease. Clinical signs of PPID are hypertrichiosis, laminitis, change in body conformation and lack of performance. Treatment with PRASCEND® is life-long.

VETERA® vaccines are the first US vaccine portfolio to include multiple convenient combinations of disease protection for horses from as young as four months of age. The vaccines protect against as many as nine infectious organisms including influenza, herpes, the West Nile virus, tetanus and others. This enables customized protection for each horse with limited needle injections.

GASTROGARD®/ULCERGARD® is indicated for the treatment and prevention of equine gastric ulcers, which is one of the most common diseases in horses. GASTROGARD® is supplied in an easy-to-use oral paste form and has been the first choice for treatment of gastric ulcers since its launch in 1999. ULCERGARD® in the US is the preventive of choice for horses with an increased risk of developing gastric ulcers.

EQVALAN®/ZIMECTERIN® contains ivermectin, a leading ingredient that controls a wide variety of important internal parasites, including bots and benzimidazole-resistant small strongyles, in an easy-to-administer oral paste. EQVALAN®/ZIMECTERIN® is approved for adult horses and foals as young as six weeks of age.

EQVALAN® DUO/GOLD, ZIMECTERIN® GOLD combines ivermectin with praziquantel, an ingredient that specifically controls tapeworms.

ARTI-CELL® FORTE is the world's first licensed veterinary stem cell product which is a ready-to-use intra-articular injection of chondrogenic induced mesenchymal cells for the treatment of lameness linked to non-infective joint inflammation in horses. ARTI-CELL® FORTE is one of the latest additions to the equine portfolio and is available in a range of countries within the EU as of 2019.

ASERVO® EQUIHALER® is the first inhalation product for the treatment of severe equine asthma. This product is a novel glucocorticoid pro-drug (ciclesonide inhalation solution) delivered in an inhaler specifically designed for use in horses, and implementing the Soft Mist™ technology derived from the RESPIMAT® inhalers in human pharma. This exciting new introduction gained final authorization and product availability in the EU, US and Canada in 2020; further approvals in other countries are expected in due course.

Indications	Brand Names	Active Ingredients	
Pituitary pars intermedia dysfunction (PPID)	PRASCEND®	<i>pergolide mesylate</i>	 <p>Symptomatic treatment of clinical signs associated with pituitary pars intermedia dysfunction (PPID, also known as equine Cushing's disease).</p>
Combination vaccine against up to nine common diseases in horses	VETERA®	<i>Eastern, Western and Venezuelan encephalomyelitis, tetanus, West Nile virus, equine herpes virus, equine influenza viruses</i>	 <p>For vaccination of healthy horses as an aid in the prevention of diseases caused by the included antigens (US and Canada only).</p>
Equine gastric ulcers	GASTROGARD® ULCERGARD®	<i>omeprazole</i>	 <p>For treatment and prevention of gastric ulcers and prevention of recurrence of gastric ulcers in horses and foals four weeks of age and older.</p>
Internal parasites	EQVALAN® ZIMECTERIN® EQVALAN® GOLD EQVALAN® DUO ZIMECTERIN® GOLD	<i>ivermectin ivermectin, praziquantel</i>	 <p>For treatment and prevention of parasitic infestations in horses and donkeys due to large and small strongyles, ascarids.</p> <p>GOLD/DUO includes treatment against tapeworms.</p>
Reduction of mild to moderate recurrent lameness associated with non-septic joint inflammation in horses	ARTI-CELL® FORTE	<i>chondrogenic induced equine allogeneic peripheral blood-derived mesenchymal stem cells</i>	 <p>For treatment of mild to moderate lameness linked to non-infective joint inflammation in horses. It contains stem cells which are obtained from equine blood. Stem cells can develop into other types of cells. The stem cells in the active substance (mesenchymal stem cells) are treated so that they develop into cartilage cells.</p>
Severe equine asthma	ASERVO® EQUIHALER®	<i>ciclesonide inhalation solution</i>	 <p>For the alleviation of clinical symptoms of severe equine asthma characterized by coughing, nasal discharge, nasal flaring, increased breathing effort at rest, or abnormal lung sounds.</p>

# Companion Animals – Pets

Our pet portfolio offers diverse solutions for some of the most important needs of canine and feline health including industry-leading parasiticides, vaccines, pain therapy and therapeutics to address major chronic diseases: heart failure, kidney diseases, hypertension, epilepsy, diabetes mellitus, and osteoarthritis.

For 25 years, FRONTLINE® has been a leader in flea and tick control on dogs and cats, and is one of the most trusted brands in animal health.<sup>1</sup> FRONTLINE® continues to bring innovation to the category, with the recent launch of FRONTLINE® SHIELD in the US, which features repellency and insecticidal efficacy on many disease-carrying flying insects and which decreases the risk of transmission of vector-borne pathogens.<sup>2</sup>

NEXGARD® contains the active ingredient afoxolaner and was launched in 2014 as the first oral medication to treat both fleas and ticks in dogs. Because of its efficacy and palatable, beef-flavored soft chew formulation, NEXGARD® is currently the best-selling pet medication in the animal health industry.<sup>3</sup>

NEXGARD SPECTRA® combines the flea and tick efficacy of afoxolaner in NEXGARD® with a broad-spectrum deworming ingredient, milbemycin oxime, in the same beef-flavored chew. NEXGARD SPECTRA® is not only effective in treating flea, tick and mite infestations, as well as gastrointestinal parasites infections, it also protects dogs against deadly parasites such as heartworm and lungworm.

HEARTGARD® PLUS contains the active ingredients ivermectin and pyrantel in a soft beef chew. When given monthly, ivermectin is effective in preventing heartworm disease. Pyrantel is effective in the treatment and control of roundworms as well as hookworms. HEARTGARD® was launched in 1987 as the first monthly heartworm preventative and is still the best-selling heartworm preventative in the world.<sup>4</sup>

BROADLINE® and the recently launched NEXGARD® COMBO offer cat owners all-in-one convenience providing confidence that their cat has the broadest possible protection. They protect cats against the broadest spectrum of internal and external parasites, including fleas, ticks, heartworms, hookworms, roundworms, lungworms, vesical worms, and tapeworms.

Boehringer Ingelheim has the most complete, trusted, and proven range of products and services in pain management. Choosing this portfolio gives veterinarians the freedom to tailor treatment to each patient and provides access to value-added veterinary services.

METACAM® offers an extensive range of formulations and indications, making it the complete non-steroidal anti-inflammatory drug (NSAID) for dogs, cats, and guinea pigs. It enables veterinarians to better achieve their goals in pain management and gives each owner and pet exactly the product they need. Ample long-term studies support the product's safety and efficacy and have led to multiple indications across diverse species.

The liquid formulation of METACAM® for dogs makes it easy to titrate to the lowest effective dose while the liquid formulation for cats is easy to administer. An improved dog administration syringe aimed to achieve better accuracy was introduced in 2020.

1) Data on file.

2) *Babesia canis* transmitted by *Dermacentor reticulatus* ticks, *Ehrlichia canis* transmitted by *Rhipicephalus sanguineus* ticks, and *Leishmania infantum*, transmitted by phlebotomine sandflies.

3) Data on file.

4) Data on file.



Indications	Brand Names	Active Ingredients	
Antiparasitic: canine / feline external parasites	FRONTLINE® FRONTLINE COMBO® FRONTLINE PLUS® FRONTLINE TRI-ACT® FRONTLINE® SHIELD	<i>fipronil</i> <i>fipronil, s-methoprene</i> <i>fipronil, permethrin, pyriproxifen</i>	 <p>FRONTLINE PLUS®/FRONTLINE COMBO® is indicated for the treatment and prevention of flea, tick, and lice infestations. It also breaks the flea life cycle by preventing the development of flea immature stages.</p> <p>FRONTLINE TRI-ACT®/FRONTLINE® and FRONTLINE® SHIELD are indicated for the treatment and prevention of flea and tick infestations in dogs. They also provide repellent activity against mosquitoes, sandflies, and ticks, reducing the risk of transmission of vector-borne pathogens.</p>
Antiparasitic: canine external parasites	NEXGARD®	<i>afoxolaner</i>	 <p>NEXGARD® is a highly palatable beef-flavored chew. It is indicated for the treatment and prevention of flea and tick infestations in dogs. It is also indicated for the prevention of <i>Borrelia burgdorferi</i> infections (US), and the treatment of <i>Demodex</i>, <i>Sarcoptes</i>, and <i>Otodectes</i> mite infestations in non-US geographies.</p>
Antiparasitic: canine internal and external parasites	NEXGARD SPECTRA®	<i>afoxolaner, milbemycin oxime</i>	 <p>NEXGARD SPECTRA® is delivered in a highly palatable beef-flavored chew. It is indicated for the treatment and / or prevention of flea, tick, and mite infestations. It also prevents heartworm disease, angiostrongylosis, and thelaziosis. It treats hookworm, roundworm, and whipworm infestations in dogs.</p>
Antiparasitic: canine internal parasites	HEARTGARD® PLUS	<i>ivermectin, pyrantel</i>	 <p>For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae for a month (30 days) after infection, and for the treatment and control of roundworms and hookworms.</p>
Antiparasitic: feline internal and external parasites	BROADLINE®	<i>fipronil, (s)-methoprene, eprinomectin, praziquantel</i>	 <p>Protects cats against the broadest spectrum of internal and external parasites including adult fleas, flea eggs, flea larvae, ticks, heartworms, lungworms, hookworms, roundworms, vesical worms, and tapeworms.</p>
Antiparasitic: feline internal and external parasites	NEXGARD® COMBO	<i>esafoxolaner, eprinomectin, praziquantel</i>	 <p>Spot-on formulation containing esafoxolaner to provide the new generation flea and tick control in cats. Protects cats against the broadest spectrum of internal and external parasites including fleas, ticks, ear mites, heartworms, lungworms, hookworms, roundworms, vesical worms, and tapeworms.</p>
Pain and inflammatory diseases	METACAM®	<i>meloxicam</i>	 <p>METACAM® is used to reduce specific types of post-operative pain and inflammation as well as musculoskeletal disorders in dogs and cats.</p>

# Companion Animals – Pets (continued)

PREVICOX® was designed specifically for dogs and is the most selective veterinary COX-2 inhibitor. PREVICOX® provides safe, sustained pain relief with a fast onset of action. Long-term safety and efficacy have been established in large field studies and PREVICOX® has been shown to be more efficacious than competition in acute models of osteoarthritis.

VETMEDIN® is an inodilator which has become the standard of care when treating dogs with congestive heart failure caused by dilated cardiomyopathy or valvular insufficiency (mitral and/or tricuspid regurgitation). When used in combination with furosemide, it significantly improves clinical signs and extends life expectancy in these patients. Recent studies have also shown that when used in preclinical asymptomatic cases of either dilated cardiomyopathy in Doberman pinschers or valvular insufficiency, VETMEDIN® significantly delays the onset of clinical signs of congestive heart failure, a first in veterinary cardiology.

SEMINTRA® is the first-ever licensed angiotensin receptor blocker for veterinary use. Specifically designed for cats, SEMINTRA® is the scientifically advanced treatment in one simple solution that safely and effectively harnesses the protective benefits of the cat's renin-angiotensin-aldosterone system to protect kidneys and other key organs. SEMINTRA® is available as 4mg/ml and 10mg/ml oral solution. SEMINTRA® (4mg/ml) was first launched in 2013 for the reduction of proteinuria associated with chronic kidney disease in cats. In 2018, SEMINTRA® (10mg/ml) was launched for the control (US) / treatment (EU) of feline systemic hypertension. It is the first vet-licensed product for feline hypertension in the US.

Since its launch in 2009 PROZINC® has become the proven insulin choice for feline patients and their owners for convenient management of feline diabetes. With the approval of PROZINC® for canine patients, we have the opportunity to become the first-choice solution for successful management of diabetes in both dogs and cats. Large clinical studies in Europe, the US, and Japan have confirmed that the majority of dogs can be managed with one injection of PROZINC® insulin per day – a major breakthrough for dogs, owners, and veterinarians.

Our pet vaccine product portfolio includes the PUREVAX® feline vaccines formulated to provide effective protection without the use of adjuvants. For a more cat-friendly vaccination, PUREVAX® has been launched in reduced 0.5 ml volume in 2021 in the US and France. RECOMBITEK® offers a complete line of advanced canine vaccines providing targeted protection through recombinant technology, and RABISIN® and IMRAB® provide trusted vaccines to fight rabies, with decades of proven efficacy and safety.

Indications	Brand Names	Active Ingredients
Pain and inflammatory diseases	PREVICOX®	 <i>firocoxib</i> For the relief of pain and inflammation associated with osteoarthritis as well as specific types of post-operative pain in dogs.
Congestive heart failure	VETMEDIN®	 <i>pimobendan</i> Treatment of canine congestive heart failure originating from dilated cardiomyopathy or valvular insufficiency (mitral and / or tricuspid regurgitation). Treatment of dilated cardiomyopathy in the preclinical stage (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter) in Doberman Pinschers. Treatment of dogs with myxomatous mitral valve disease (MMVD) in the preclinical stage (asymptomatic with a systolic mitral murmur and evidence of increased heart size) to delay the onset of clinical symptoms of heart failure.
Chronic kidney disease (CKD) in cats Hypertension in cats	SEMINTRA®	 <i>telmisartan</i> Management of chronic kidney disease (CKD) and feline systemic hypertension (US and EU) in cats.
Diabetes	PROZINC®	 <i>protamine zinc</i> For the treatment of diabetes mellitus in cats and dogs to achieve reduction of hyperglycemia and improvement of associated clinical signs.
Feline vaccines portfolio	PUREVAX®	 <i>feline herpes virus, feline calicivirus, feline panleukopenia virus, chlamydia felis, recombinant vectored feline, leukemia virus, recombinant vectored rabies virus</i> PUREVAX® is the only fully adjuvant-free feline vaccine range and leverages its innovative canarypox technology for FeLV and rabies. It also offers sustained protection on rabies for up to three years.
Canine vaccines portfolio	REKOMBITEK®	 <i>recombinant vectored canine, distemper virus, canine parvovirus, canine adenovirus type 2, canine parainfluenza virus, canine coronavirus, leptospira Canicola, leptospira grippotyphosa, leptospira icterohaemorrhagiae, leptospira Pomona, recombinant borrelia burgdorferi, bordetella bronchiseptica</i> REKOMBITEK® features a complete line of canine vaccines including: REKOMBITEK® lyme: The only vaccine that contains OspA in a non-adjuvant formulation. REKOMBITEK® oral bordetella: Effective and safe protection made easy.
Rabies vaccines portfolio	RABISIN® IMRAB®	 <i>inactivated and adjuvanted rabies glycoproteins</i> Sustained rabies protection up to three years after first year booster. Consistently high seroconversion rate. Rabies protection for six species.

\* In the US and others.

# Comparison of balance sheet and financial data 2012 – 2021

## Assets (as of December 31)

in million EUR	2012	2013	2014	2015	2016
Intangible assets	682	582	592	606	550
Tangible assets	3,103	2,887	3,070	3,264	3,045
Financial assets	4,222	4,737	5,312	5,933	6,092
<b>Fixed assets</b>	<b>8,007</b>	<b>8,206</b>	<b>8,974</b>	<b>9,803</b>	<b>9,687</b>
Inventories	2,095	2,083	2,237	2,483	2,610
Accounts receivable and other assets (incl. prepaid expenses, deferred taxes and exceeding amount of plan assets)	4,814	5,131	5,546	6,463	6,837
Financial funds	2,374	2,879	3,294	4,536	7,005
<b>Current and other assets</b>	<b>9,283</b>	<b>10,093</b>	<b>11,077</b>	<b>13,482</b>	<b>16,452</b>
<b>Total assets</b>	<b>17,290</b>	<b>18,299</b>	<b>20,051</b>	<b>23,285</b>	<b>26,139</b>

## Equity and liabilities (as of December 31)

in million EUR	2012	2013	2014	2015	2016
Shareholders' capital	178	178	178	178	178
Group reserves (incl. balance sheet currency conversion difference)	4,763	5,619	6,884	7,844	9,296
Group profit	1,237	1,324	1,047	1,577	1,853
<b>Equity attributable to the parent company</b>	<b>6,178</b>	<b>7,121</b>	<b>8,109</b>	<b>9,599</b>	<b>11,327</b>
Non-controlling interests	0	1	2	4	0
<b>Group equity</b>	<b>6,178</b>	<b>7,122</b>	<b>8,111</b>	<b>9,603</b>	<b>11,327</b>
<b>Difference from capital consolidation</b>	<b>134</b>	<b>104</b>	<b>91</b>	<b>71</b>	<b>52</b>
Provisions (incl. deferred taxes)	7,749	7,817	8,840	10,543	12,233
Liabilities (incl. deferred income)	3,229	3,256	3,009	3,068	2,527
<b>Total liabilities (incl. deferred taxes and deferred income)</b>	<b>10,978</b>	<b>11,073</b>	<b>11,849</b>	<b>13,611</b>	<b>14,760</b>
<b>Total equity and liabilities</b>	<b>17,290</b>	<b>18,299</b>	<b>20,051</b>	<b>23,285</b>	<b>26,139</b>

## Summary of selected financial data

in million EUR	2012	2013	2014	2015	2016
Net sales	14,691	14,065	13,317	14,798	15,850
Operating income	1,853	2,114	2,140	2,269	2,872
Operating income as % of net sales	12.6	15.0	16.1	15.3	18.1
Income after taxes	1,237	1,324	1,046	1,576	1,849
Income after taxes as % of net sales	8.4	9.4	7.9	10.7	11.7
Equity ratio (in %)	35.7	38.9	40.4	41.2	43.3
Cash flow from operating activities	2,170	1,819	2,015	2,232	2,888
Financial funds	2,374	2,879	3,294	4,536	7,005
Personnel expenses	4,024	4,071	4,116	4,518	4,570
Personnel expenses as % of net sales	27.4	28.9	30.9	30.5	28.8
Average number of employees	46,228	47,492	47,743	47,501	45,692
Research and development expenses	2,795	2,743	2,654	3,004	3,112
R&D as % of net sales	19.0	19.5	19.9	20.3	19.6
Investments in tangible assets	562	558	548	591	645
Depreciation of tangible assets	793	640	449	475	516

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2017	2018	2019	2020	2021
5,372	5,120	4,882	4,295	4,624
3,867	4,280	4,754	5,050	5,489
5,830	6,058	9,162	8,553	12,964
<b>15,069</b>	<b>15,458</b>	<b>18,798</b>	<b>17,898</b>	<b>23,077</b>
3,087	3,312	3,563	3,863	4,237
7,159	7,815	8,924	9,021	10,759
3,071	4,303	2,195	6,105	2,546
<b>13,317</b>	<b>15,430</b>	<b>14,682</b>	<b>18,989</b>	<b>17,542</b>
<b>28,386</b>	<b>30,888</b>	<b>33,480</b>	<b>36,887</b>	<b>40,619</b>

2017	2018	2019	2020	2021
178	178	178	178	178
10,703	10,080	11,781	14,066	15,746
-223	2,075	2,721	3,062	3,406
<b>10,658</b>	<b>12,333</b>	<b>14,680</b>	<b>17,306</b>	<b>19,330</b>
-1	1	1	1	1
<b>10,657</b>	<b>12,334</b>	<b>14,681</b>	<b>17,307</b>	<b>19,331</b>
<b>1,729</b>	<b>1,511</b>	<b>1,471</b>	<b>1,283</b>	<b>1,159</b>
13,482	14,438	15,172	16,000	17,586
2,518	2,605	2,156	2,297	2,543
<b>16,000</b>	<b>17,043</b>	<b>17,328</b>	<b>18,297</b>	<b>20,129</b>
<b>28,386</b>	<b>30,888</b>	<b>33,480</b>	<b>36,887</b>	<b>40,619</b>

2017	2018	2019	2020	2021
18,056	17,498	18,997	19,566	20,618
3,487	3,472	3,782	4,624	4,705
19.3	19.8	19.9	23.6	22.8
-229	2,075	2,721	3,062	3,406
-1.3	11.9	14.3	15.6	16.5
37.5	39.9	43.8	46.9	47.6
2,624	2,988	3,344	3,963	3,846
3,071	4,303	2,195	6,105	2,546
4,934	5,276	5,367	5,587	5,692
27.3	30.2	28.3	28.6	27.6
49,610	50,333	51,015	51,944	52,391
3,078	3,164	3,462	3,696	4,127
17.0	18.1	18.2	18.9	20.0
872	950	1,073	1,046	968
521	552	585	602	609



With the CO<sub>2</sub> emission certificates we support forest conservation and forest modification in many regions in Germany.

