

TRANSFORMATION

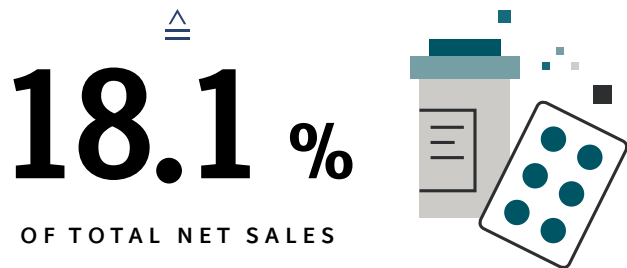
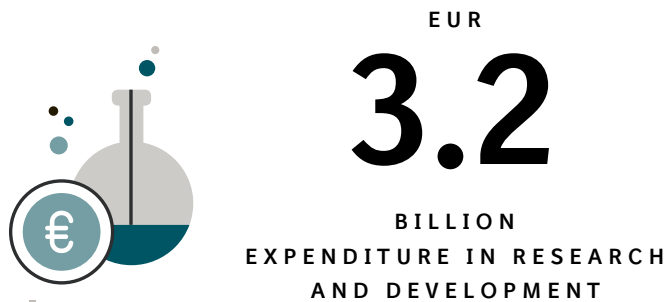
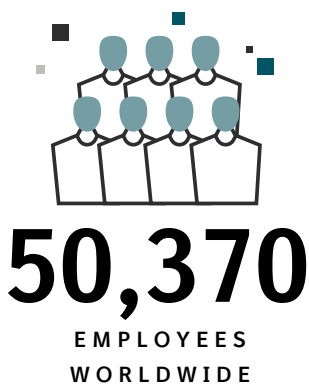
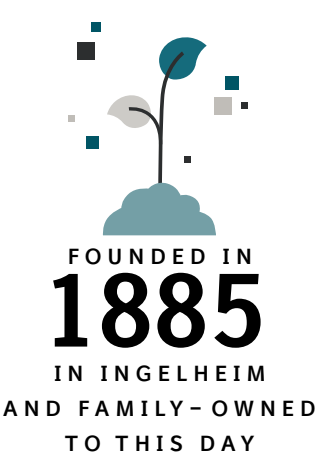
Developing healthcare solutions
for tomorrow



BOEHRINGER INGELHEIM

2018 AT A GLANCE

Boehringer Ingelheim is one of the world's 20 leading pharmaceutical companies.



The core of our Leitbild

Who we are and what we strive for

We are independent, family-owned and intend to remain so

- We are driven by the desire to serve mankind by improving human and animal health.
- We feel responsible for our communities and are respectful of our resources.
- We plan in generations and focus on long-term performance.

We create value through innovation for our customers

- We develop breakthrough therapies and health care solutions in areas of unmet medical need.
- We excel in innovation and deliver the highest quality to drive our competitiveness.
- We believe in partnering for success and the sustainable economic health of the company.

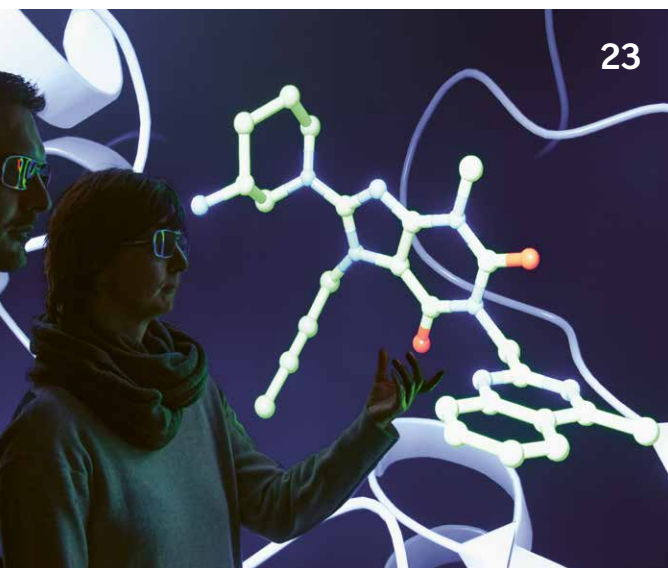
We are powered by our people

- We nurture a diverse, collaborative and open environment, which appeals to the best people.
- We are driven by results, working with integrity and passion.
- We treat each other with respect, trust and empathy, and we grow together.





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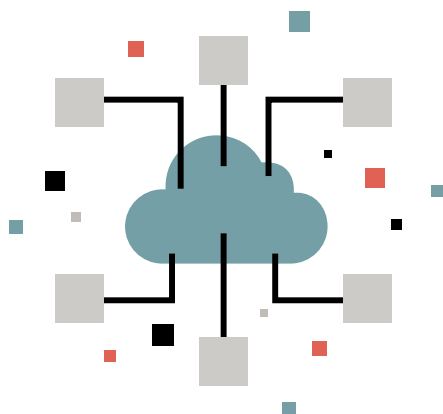


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Time for something new



Digitalisation is changing the healthcare sector. Completely new business models are being created, previously unknown actors are entering the market and processes are being turned upside down. Boehringer Ingelheim is helping to shape this change and has long been an innovator itself. Researchers are developing molecules on their screens using artificial intelligence. Smart production is taking hold, we are improving the health of people and animals with digital assistants. Last but not least, work itself is changing – becoming more agile and creative.



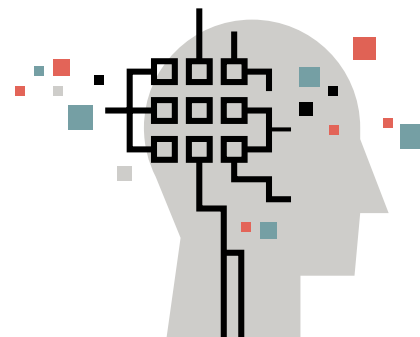
Boehringer Ingelheim clinical studies in the USA? Running soon over PC and smartphone. Study participants sign up with the NORA app and dialogue live with physicians. The physicians explain to them online how they have to take medications or what to do in the event of side effects. Nobody has to present themselves at the study center, everything works virtually, through telemedicine: fast and simple. NORA is part of the digital platform of the US start-up Science37 with which Boehringer Ingelheim joined forces at the beginning of 2019.

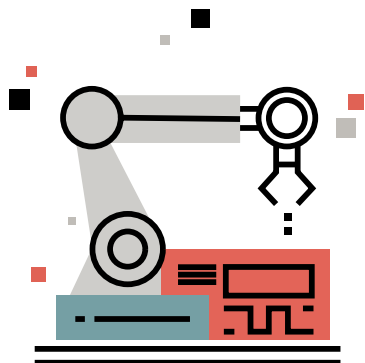
It is just one of many examples that shows how fundamentally digitalisation is changing the healthcare system. Pharmaceutical companies like Boehringer Ingelheim are transforming their processes and products and are becoming increasingly digital. Digital companies, on the other hand, are turning to healthcare. For example, Google is involved in the telemedicine project “Doctor on demand” which allows US patients to obtain a consultation from a doctor using a smartphone app. Via the company Verily, the search engine operator looks for new ways to identify and treat illnesses at an early stage – using large volumes of data, of course, which is the company’s supreme discipline.

Google – and other Silicon Valley companies as well – are thereby venturing into the field of medical technology and pharmaceutical companies like Boehringer Ingelheim. And, instead of simply observing how disruptive technologies are changing established business models, Boehringer Ingelheim is playing an active role in the innovation process.

“Our goal is to use the opportunities of new technologies in the field of research and development – particularly in clinical development –, but also when supporting patients during treatment,” says Hubertus v. Baumbach, Chairman of the Board of Managing Directors of Boehringer Ingelheim. “We believe that we can thus develop even more precise diagnosis and treatment.”

This works because modern medicine is also data processing. What does the internist examining a patient do other than systematically investigate bodily functions and compare them to the norms? What do radiographers do when they look at an X-ray? They try to identify patterns. And a pharmaceutical company like Boehringer Ingelheim? It looks for new active ingredients, with researchers testing thousands of molecule variations and recording every effect in exact detail. Without pharmaceutical research, countless findings from laboratory testing and clinical





“Because digitalisation is making completely new data available, we will be able to provide much more targeted treatments in the future.”

HUBERTUS VON BAUMBACH
Chairman of the Board of Managing Directors

trials would never have been made, even if companies come nowhere near taking full advantage of the foundations provided by this accumulated data. It is clear: medicine derives from data.

Digital technology is now set to relieve people to an ever-increasing degree of the burden of identifying patterns and processing data, explains Matthias Schönermark. The physician is owner of SKC Beratungsgesellschaft, a consultancy firm in Hanover, Germany, that specialises in strategy consultation for pharmaceutical companies, health insurers and medical technology companies. Hubertus v. Baumbach adds: “Because digitalisation is making completely new data available, we will be able to provide much more targeted treatments in the future. The findings from this data treasure will determine the profile of new medicines in the future.”

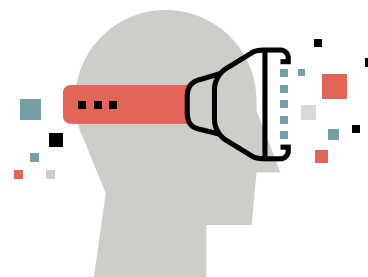
The company, says v. Baumbach, is therefore driving forward fundamental change: “For us, digitalisation is an important topic of the future” (see interview, pages 8 to 10). It is no coincidence that the BI Venture Fund, set up to invest in promising enterprises on behalf of the Group, is constantly seeking digital innovations. With its digital laboratory BIX, the Group has its own incubator for new ideas. Digitalisation has spread throughout the company.

Digital experts in the Group are currently working on a digital “Auscultation Aid” that helps physicians to diagnose rare pulmonary diseases, and on a program to identify pig cough. IT expert and physician Prof. Dr Sylvia Thun, who recently became director of eHealth and interoperability at the Berlin Institute of Health, believes that the age of collective intelligence in the healthcare sector is approaching. “**Artificial intelligence** assists doctors with diagnosis,” says Thun. “Physicians are becoming interconnected and drawing on the knowledge of their colleagues worldwide. This is data-driven medicine.”

↳ [READ MORE IN THE CHAPTER “DIGITAL CARE”, PAGES 11 TO 21.](#)

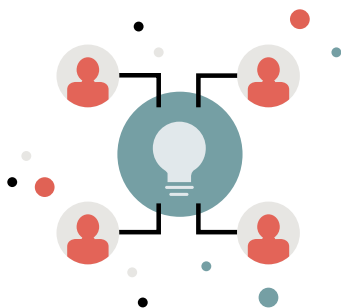
Digitalisation also plays a key role in the development of medicines. Here, the software NTC Studio evaluates patient data, clinical trials and research work and provides the developers with new ideas. Their colleagues build three-dimensional molecule models using artificial intelligence through the “smart assistant” ADAM. They can then modify these models on their screens and test their properties.

↳ [READ MORE IN THE CHAPTER “DIGITAL RESEARCH”, PAGES 22 TO 27.](#)



“Physicians are becoming interconnected and drawing on the knowledge of their colleagues worldwide. This is data-driven medicine.”

PROF. DR SYLVIA THUN
Berlin Institute of Health



As in other industries, digitalisation has also impacted production. Industry 4.0 and “smart factory” are finding their way into the manufacture of medicines. At the new Launch Facility in Ingelheim, Germany, which is expected to commence operations in 2020, intelligent **robotics systems** will soon be filling medicines in minute batch sizes. For this, technicians wear **virtual reality** data glasses to help them align the packaging machines.

↳ [READ MORE IN THE CHAPTER “DIGITAL PRODUCTION”, PAGES 28 TO 36.](#)

Last but not least, digitalisation is changing how people at Boehringer Ingelheim work together. The Animal Health facility in Lyon, France, shows what the digital office of the future can look like. At the recently opened BI CUBE in Ingelheim, employees are training to become “agile facilitators” and bringing modern methods of design thinking to the organisation.

↳ [READ MORE IN THE CHAPTER “DIGITAL WORK”, PAGES 37 TO 41.](#)

Boehringer Ingelheim is thus participating once again in the renewal of its own industry. Innovation, says Hubertus v. Baumbach, has long been a guiding principle for the company. By buying a tartar factory in 1885, the founder Albert Boehringer started to produce tartar and tartaric acid. However, his interest rapidly shifted to the production of citric acid and a little later to the development of a bacterial procedure to set up the production of lactid acid – a venturesome and high-risk decision back then, but one that paid off. The company once again proved to be brave and innovative when it moved away from lactic acid in the early 1970s and again in 1986 when it built a production facility for biopharmaceuticals, the biggest in Europe at the time. Now digitalisation is taking hold in the industry, and Boehringer Ingelheim, where change and progress are deeply embedded in the company’s DNA, is not simply gearing up for the new, digital healthcare sector, says Hubertus v. Baumbach. “We are looking forward to this future.”

GLOSSARY



ARTIFICIAL INTELLIGENCE (AI)

Self-learning computer programs with algorithms that identify patterns autonomously and, in the process, continuously improve, as they avoid repeating errors.



BIG DATA

Mass volumes of unstructured data, such as records of experiment findings, patient data from clinical trials and measurement data from production facilities.



ROBOTICS

Substitution of human work with intelligent machines. Modern industrial robots at Boehringer Ingelheim are “collaborative”. People can work with them.



COLLABORATION

Digital networks where people share information on medicines, clinical pictures, research questions etc. As the number of participants increases, so do the benefits.



VIRTUAL REALITY (VR)

Computer-generated 3D imagery in real time – such as the simulation of a factory that has not yet been built. Incorporation of VR elements into the natural field of vision is called augmented reality.



Hubertus von Baumbach (right) and
Michael Schmelmer

“Digital is a tool, not an end in itself”

Hubertus von Baumbach (CEO) and Michael Schmelmer (CFO) are working together with many employees to advance the company’s digital transformation. In this interview, they expand on how they intend to employ new technical possibilities. Their goal is to achieve real added value in the development of medicines, in production and, above all, for patients, physicians and employees.

Mr v. Baumbach, Mr Schmelmer: digital health is the buzzword which currently has the whole industry talking. Setting aside this buzzword, what concrete added value do the new digital technologies actually deliver?

HUBERTUS v. BAUMBACH (HvB) For us, digitalisation is the generic term for new technologies for employing data – that’s to say, capturing, processing and analysing – and the automated steering of processes. Digitalisation offers us diverse opportunities to improve, in part even fundamentally transform, not only the innovation process, but the complete value chain. Innovations have guaranteed our success and independence over the past 130 years. Today, we still firmly believe in the importance of the power to innovate to the company’s future. We must and will repeatedly question and challenge the existing and the proven. We make corresponding resources available and thereby bear the consequent, entrepreneurial risk. That enables us to turn our vision into reality. We want to create value through innovation.

What does that mean in concrete terms?

This means that we want to develop new therapeutic approaches that will bring measurable and tangible improvements to patients’ lives. We have in particular set our target to develop human pharmaceuticals that are novel and first in their medicinal class. At the same time, we want to create added value for healthcare systems. In doing so, we should not simply reduce the term “value” to “price” or immediate “costs”. Otherwise, we will lose sight of the overall efficiency of the systems. Most of all, we would then neglect the needs of patients.

MICHAEL SCHMELMER (MS) The key challenge for us is to enable Boehringer Ingelheim to seize these opportunities rapidly and efficiently. Digital technologies are transforming processes and business models in almost every area of the company – in some areas these are disruptive transformations, while in others they are more evolutionary.

Can you provide an example?

MS Take the development of medicines, where we have been quite successful in the past. Recently, our diabetes medicine JARDIANCE® received the prestigious International Prix Galien as “Best Pharmaceutical Product”. We are increasingly using digital technologies to push our boundaries and shorten our development cycles. For example, artificial intelligence helps us to register and evaluate patient data in studies faster. We are simply getting better at what we are already doing today – but these are changes which

are somewhat evolutionary in nature. On the other hand, in the areas of production and cooperation with physicians and patients, the changes under way are disruptive. Completely new business models are becoming possible here – and digital platforms are opening up entirely new forms of interaction.

Which of these technologies do you expect to provide the greatest added value?

HvB Artificial intelligence is certainly one of the areas of technology which open up to us particularly promising new opportunities in many areas of our company. The volume of data is growing very fast. AI will in future allow us to reliably structure and analyse this data in a relatively short space of time. Today, this would hardly be possible even with unlimited human resources. But for all our enthusiasm for individual technological innovations, there is no overlooking the fact that digital is a tool rather than an end in

INTERNATIONAL PRIX GALIEN FOR JARDIANCE®

On 28 November 2018, Boehringer Ingelheim's diabetes medication JARDIANCE® (empagliflozin) was awarded with the 2018 International Prix Galien as “Best Pharmaceutical Product”.

The prize is the most prestigious award in the field of pharmaceutical innovation and recognises outstanding efforts and achievements of pharmaceutical research and development.

JARDIANCE® is the first antidiabetic that helps to lower cardiovascular death among patients with type 2 diabetes, in addition to its positive effects on blood sugar, body weight and blood pressure.



“Ultimately, digital health is an attempt to link health sciences even closer to each other.”

HUBERTUS VON BAUMBACH
Chairman of the Board
of Managing Directors

itself. New technology is helping us to transform the company. Appropriate use of these tools will play an even more decisive role in our success, both now and in the future, in order for us to stay true to our entrepreneurial goal and to create new therapeutic options for people and animals.

MS Internal pilot projects and change programmes such as our digital laboratory BI X or our BI CUBE in Ingelheim are certainly also playing an important role. We are developing new, digital processes and products and experimenting with agile work methods there. We thus aim to provide a sense of momentum for our employees' everyday work and for the organisation as a whole.

Does the process of digital transformation also pose such a major challenge because change is unfolding at such a rapid pace? In many areas, there is a considerable fear of disruptors from other industries.

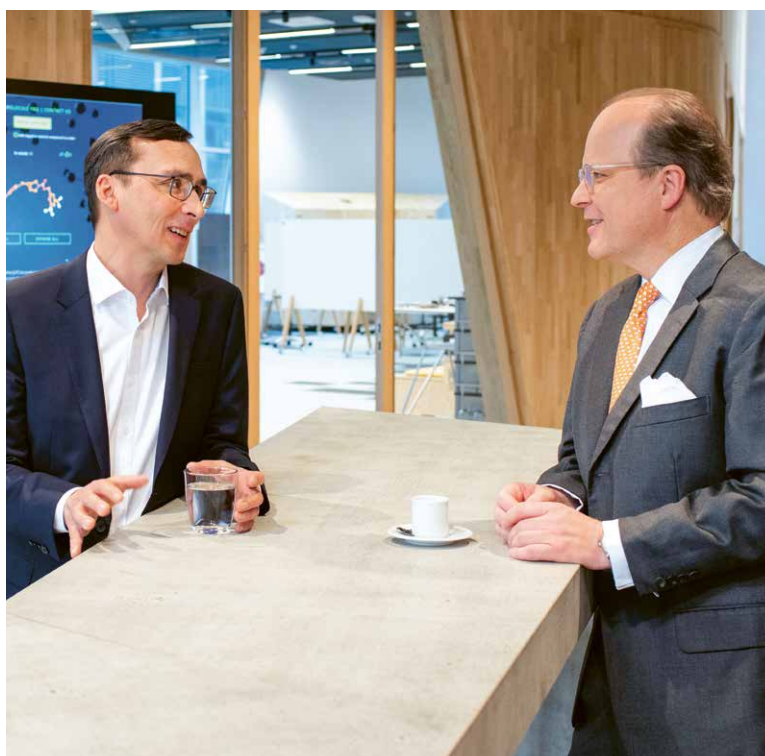
HvB Digitalisation brings acceleration and completely new technological approaches. We experience this in all areas of our lives. As a company, we want to take advantage of these opportunities in order to continue to compete successfully. Being prepared for continual change has always been our guiding principle. We regard change as the motor of the future and would also like to make our contribution to reshape the new, digital healthcare sector. This can, for instance, mean that patients with diseases of the central nervous system will receive the right diagnosis more quickly, thanks to the analysis of specific speech patterns, and the appropriate medicine will then also be available for them.

In epidemiology, digital technology enables us to assess the efficacy, safety and utilisation of our products in close to real time. One of our current studies in patients who suffer from the rare lung disease scleroderma will be concluded in less than six months – compared to five or more years using the traditional registry-based approach. If successful, the medicine will be available to patients more than four years earlier.

MS We are not afraid of disruptors – in fact, we see ourselves as a disruptor for our industry, in the positive sense. So we are absolutely open to external, innovative partners who inspire us and who help us to realise our ideas for better human and animal health. We are cooperating with start-ups, researchers and developers, and integrating physicians and patients in our process of innovation – digital platforms provide fantastic new opportunities. All of that helps us to achieve an even better understanding of our patients' needs and to provide them with targeted offerings.

So Boehringer Ingelheim is ready for the age of digital health?

HvB More than ready. We are already in the process of shaping that future, with all of the opportunities and challenges which it will entail. Ultimately, digital health is an attempt to link health sciences even closer to each other. On the way, things could also gladly move somewhat faster.



Digital Care



Upgrade for a classic



LUCA RICHELDI

The Italian physician has been diagnosing rare pulmonary diseases for decades. He is an expert in his field. With the help of new digital tools he wants to be still faster and better.

For more than 200 years, the stethoscope has been one of the most important devices for physicians. However, when it comes to diagnosing rare pulmonary diseases, it is only of limited suitability. An algorithm should provide urgent assistance.

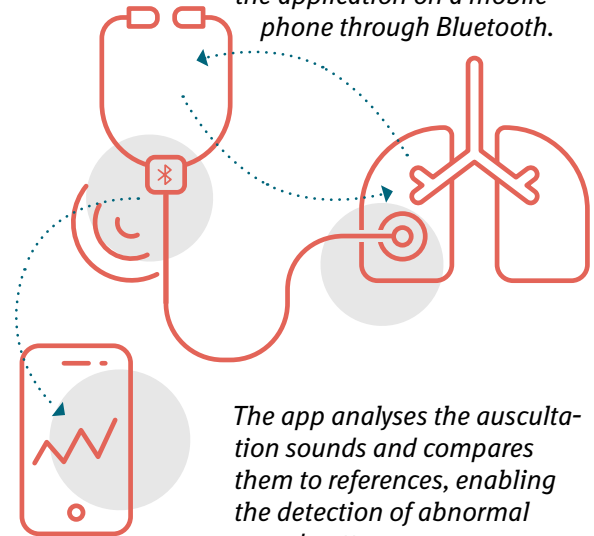
THIS IS HOW THE AUSCULTATION AID WORKS

Luca Richeldi is an unassuming man. He speaks in a quiet and considered way and tends to be reserved – both in his tone and in what he says. He would never claim to be an expert in his field: the diagnosis and treatment of rare pulmonary diseases. Yet, that is exactly what he is. Hailing from Italy, he originally established the chair for rare pulmonary diseases at the University of Modena. Today, he practises at the Gemelli University Hospital in Rome as a professor and director for pulmonary and respiratory diseases – and counts no less a person than the Pope as one of his patients.

His standard diagnostic tool is the stethoscope. Richeldi uses it to listen to his patients' lungs and airways in order to determine the cause of their complaints. However, even the most experienced specialists quickly come up against their limits. "Diagnosing rare pulmonary diseases, such as idiopathic pulmonary fibrosis (IPF), is extremely complicated," he explains. "With the stethoscope, you can hear that something isn't right with the lungs," says Richeldi. "However, inexperienced doctors – in particular – do not necessarily go on to identify IPF, but rather assume that cardiac problems, asthma or other pulmonary diseases are the cause of the very specific sound pattern." It takes an average of 17 months to confirm a diagnosis of IPF after the onset of the initial symptoms. An eternity for patients – and lost time, since the serious disease can often be terminal. The earlier it is identified, the better the treatment outcomes are.

In order to support the identification of IPF at an earlier stage, Boehringer Ingelheim is developing an artificial intelligence-based "Auscultation Aid" which works as follows: a stethoscope with a digital interface is linked via a mobile phone to a cloud-based large sound database. Using artificial intelligence, a patient's lung sound recordings are then compared with reference data from the sound database. This database was created from recorded and confirmed diagnoses of lung diseases, collected in large clinical studies. The auscultation aid immediately sends the physician a result in the form of a "probability score" for a certain lung disease. If this score is higher than a pre-specified threshold value, the tool will provide suggestions to the examining physician for additional diagnostic steps, examinations and procedures.

A digital stethoscope or a standard stethoscope with an easy-to-attach high-quality digital microphone transmits the patient's lung sounds to the application on a mobile phone through Bluetooth.



The app analyses the auscultation sounds and compares them to references, enabling the detection of abnormal sound patterns.

“We firmly believe that this auscultation aid will reduce misdiagnoses and identify rare diseases like IPF much faster.”

ALLAN HILLGROVE
Member of the Board of Managing Directors
with responsibility for Human Pharma

“We firmly believe that this auscultation aid will enable a reduction in misdiagnoses and identify rare diseases like IPF much faster,” says Allan Hillgrove, Member of the Board of Managing Directors with responsibility for the Human Pharma Business Unit at Boehringer Ingelheim. He adds that the device covers a previously unresearched area and will therefore create genuine added value for patients.

At the age of 73, Wolf-Henning Knoblauch from Walldorf, Germany, suffered a stroke. A computer algorithm helped to swiftly make the right diagnosis and thus limit severe aftereffects.



A question of time

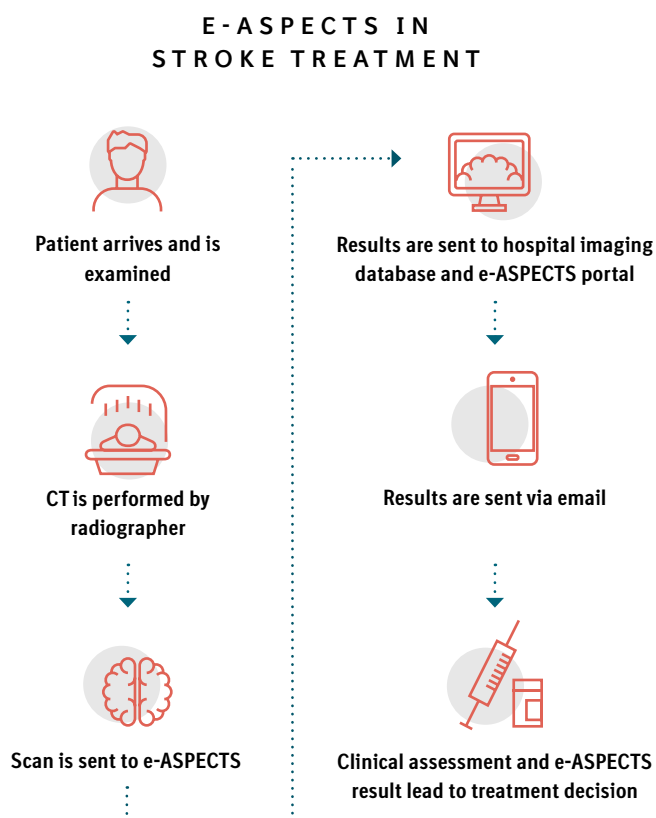
Wolf-Henning Knoblauch was fortunate in misfortune – his stroke was recognised quickly enough, analysed and successfully treated without delay. He thus gained the opportunity to fight his way back into a healthy and active life. Together with the European Stroke Organisation, Boehringer Ingelheim is committed to ensuring that as many patients as possible benefit from such optimal treatment in future. The self-learning software of the medical technology start-up and Boehringer Ingelheim partner Brainomix helps doctors to rapidly assess the nature and extent of brain damage and to select the right therapy.

Faster and better treatment is the key to combating one of the most lethal diseases in Europe: stroke. Disturbance of the flow of blood to the brain is the second most frequent cause of death and the most frequent cause of permanent disability in adults. But the risk can be reduced very considerably if stroke patients are treated quickly enough.

If the supply of blood to the brain is interrupted, around 1.9 million nerve cells will die every minute. This destructive process can be halted by means of medicines and special treatment methods. Specially trained physicians in stroke centres therefore perform a CT scan of the brain as quickly as possible. The goal is for the right treatment to begin no later than four hours after the stroke, on the basis of the information gained from the tomography of the brain.

The problem is that there are not many specialised stroke centres and experienced neurologists that can evaluate brain scans. Physicians frequently take too long to decide – often because they need to obtain a second opinion from more experienced colleagues.

The medical software company Brainomix therefore aims to provide every physician with a digital stroke expert as an assistant. Self-learning software, i.e. artificial intelligence, evaluates CT scans.



Wolf-Henning Knoblach today lives an active life visiting friends, driving his car and seeing his children and grandchildren together with his wife.

This digital assistant sends its diagnosis directly to physicians' smartphones in just a few minutes after the completion of the CT scan: an "e-ASPECTS" score indicates the severity of the stroke, while colour markings on the attached images pinpoint the affected region of the brain. "The key advantage of our software is that it does not rely on past experience and previous medical findings alone but rather adds to its learning with each new stroke patient," explains Michael Papadakis, CEO of Brainomix. "So the more physicians and hospitals use our software, the better its assessments will be." New patients will thus very rapidly benefit from new findings in relation to treatment methods and their outcomes.

Brainomix's algorithm is already being used in clinics and stroke centres in many European countries. "Innovative start-ups such as Brainomix, which develop intelligent, digital tools for physicians and patients, are important and exciting partners for Boehringer Ingelheim," says Dr Frank Kalkbrenner, Managing Director of the Boehringer Ingelheim Venture Fund. The venture capital fund invested in this British start-up in early 2018. Kalkbrenner adds: "Digital tools help us to establish holistic, integrated disease management programmes – and thus to offer patients the best possible care."



The well-being of his animals is the top priority for farmer Daniel Woestmann. To identify diseases early, he has upgraded the pig pen with technology.

Eavesdropping in the pig pen

When pigs cough, there is something in the air – or they are seriously ill. Boehringer Ingelheim and the Belgian start-up Soundtalks hang up microphones in the pen to fight infections as early as possible.

As soon as Daniel Woestmann enters the pig pen, things liven up. The animals grunt and squeal; they throng around the feeding area and play around with the cotton rope that the 22-year-old circulates around the pen to collect saliva samples. It is smelly and it is warm – a dry 24 degrees, just the way pigs love it. Above all, however, it is noisy. A cough would not be noticeable here, and so a potential early symptom of a serious illness easily goes unnoticed.

“If a pig coughs, as with people, it doesn’t mean that you need to worry,” says veterinarian Gudrun Finger. If it is dusty, pigs can quickly get a tickle in their throats. “But if coughing occurs more frequently, it’s a red flag, and further examinations are advisable.”

However, for a farmer – particularly one like Daniel Woestmann who produces his own fodder – there is not enough time to pay such close attention to the pigs with so much work to do on the farm. This is precisely where a long-term cooperation between Boehringer Ingelheim and the Belgian start-up Soundtalks comes in: acoustic measurement of the animals’ coughing sounds.

One black microphone is hooked up for four compartments in Woestmann’s pig pen and hangs in the air some two metres above the pigs. It records the sounds of the 130 animals, 24 hours a day, seven days a week. An algorithm filters a crucial factor out of all the noise: the coughing. Datasets are thus created that veterinarians can analyse and link to findings from diagnostic samples. A graph shows the number of coughs in a certain period. High levels of coughing are immediately noticeable. Once a critical level is reached, the programme sends a message to the veterinarians and farmers. “The major advantage is that we can identify danger at an early stage and can help the animals more quickly,” says Dr Joachim Hasenmaier, Member of the Board of Managing Directors

Wireless in future: The new microphones that Soundtalks and Boehringer Ingelheim will launch on the market this year will communicate via the internet.



Veterinarian Gudrun Finger can now give better targeted help to pigs - thanks to digital analysis.

“The major advantage is that we can identify danger at an early stage and can help the animals more quickly.”

DR JOACHIM HASENMAIER
Member of the Board of Managing Directors
with responsibility for Animal Health

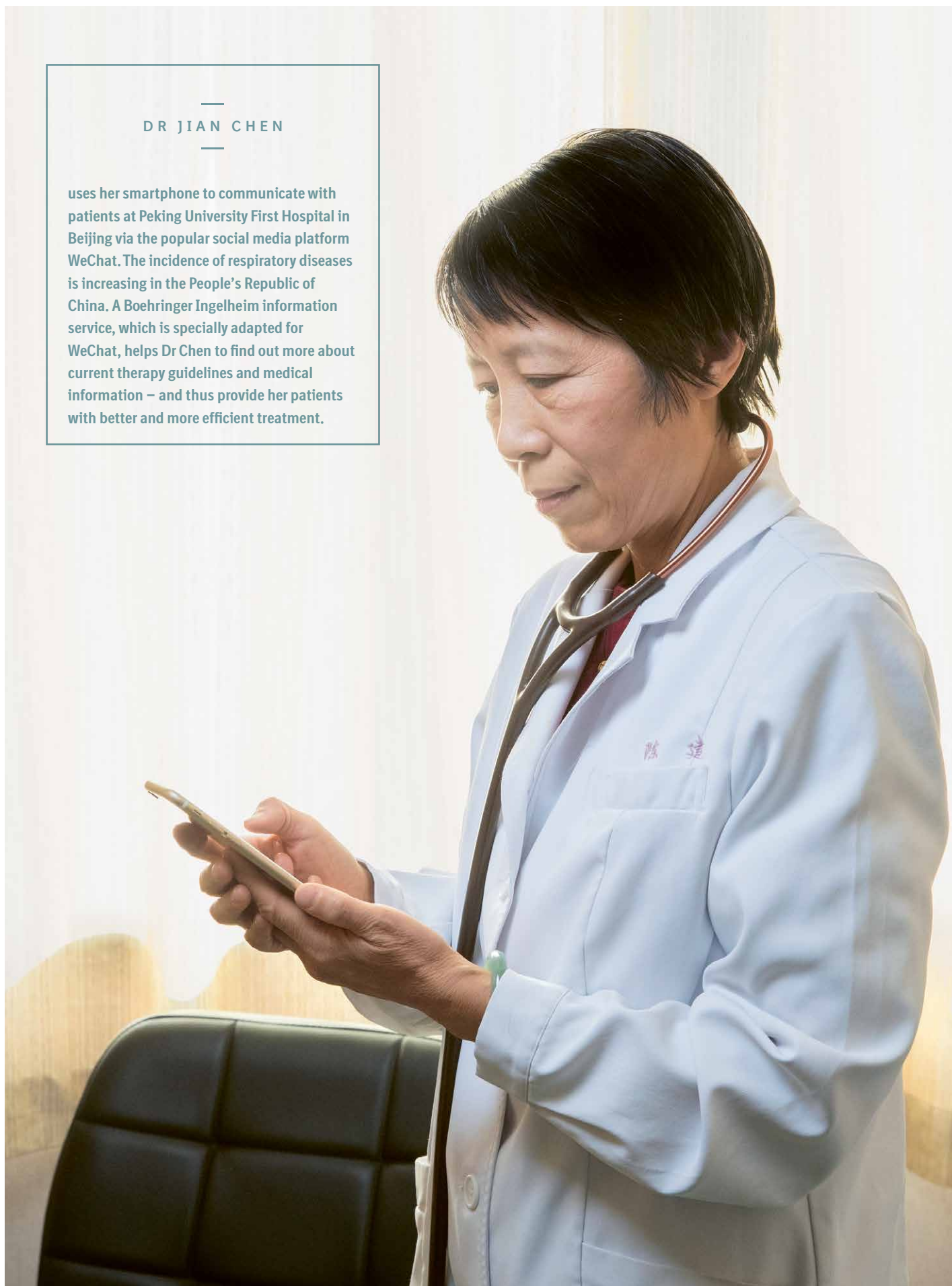
with responsibility for Animal Health. It also makes it possible to obtain objective measurement of the coughing and perform continuous monitoring.

The latest microphones that Soundtalks is putting on the market this year can communicate wirelessly – and, in addition to the pigs’ coughing, can analyse the ambient temperature and humidity level. A “health monitor” for pigs is what Soundtalks head Dries Berckmans calls his tool, which could not have been developed without the cooperation with Boehringer Ingelheim. “We are combining expertise from two different worlds here: the sound engineers and developers on one side, and veterinarians on the other,” says Berckmans.

Pig farmer Daniel Woestmann has long been convinced of the merit of the partnership, and he will continue to use the technology. After all, it is in his interest that his pen remains a hive of activity in the future, too – thanks to strong and healthy animals.

—
DR JIAN CHEN
—

uses her smartphone to communicate with patients at Peking University First Hospital in Beijing via the popular social media platform WeChat. The incidence of respiratory diseases is increasing in the People's Republic of China. A Boehringer Ingelheim information service, which is specially adapted for WeChat, helps Dr Chen to find out more about current therapy guidelines and medical information – and thus provide her patients with better and more efficient treatment.



Help delivered by mobile phone

Dr Jian Chen mainly treats patients with pulmonary diseases at Peking University First Hospital in Beijing. Boehringer Ingelheim assists this specialist by mobile phone – or, more precisely, using the social media channel WeChat.

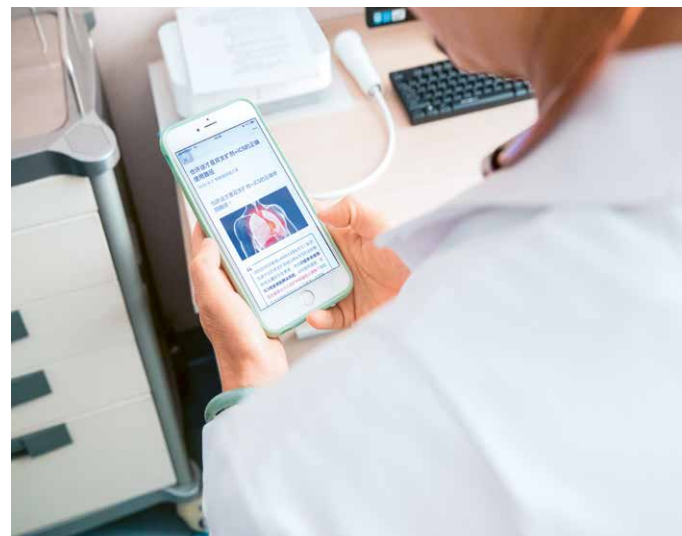
For the pulmonary specialist Chen – like 97 percent of the physicians in the People's Republic of China – her smartphone has become one of her most important tools over the last few years.

The social media service WeChat plays a key role here. Over one billion people use this digital platform every month. Users can send text messages, make telephone calls and shopping payments, use integrated video and messaging services, book train tickets, complete government paperwork digitally and order a taxi. Almost anything is possible on WeChat.

Boehringer Ingelheim uses this digital communication channel to provide optimal support for physicians, such as Dr Chen, in their daily work and professional development. “We set up public accounts on WeChat, which we use to provide physicians and clinics with information and to communicate with them,” says Elena Yang, Head of Digital Marketing and an expert in efficient medical care at Boehringer Ingelheim in

Shanghai. “For instance, physicians can use WeChat to access current information in their area of expertise,” says Yang. “As subscribers to our accounts, they also receive important news on medical guidelines, events and research via a push service.”

The pulmonary specialist Dr Chen finds Boehringer Ingelheim’s “Follow-up WeChat”-service very useful in her everyday work. “I can access the information that I require exactly when I need it,” the physician comments. She recalls a new therapeutic device that recently came onto the market for patients with respiratory diseases. “I was able to use Boehringer Ingelheim’s Respiratory Family WeChat service to watch a video showing how to use this particular device correctly.” Physicians can also use WeChat to share this information and stay up-to-date. “I am notified immediately in case of any changes to important medical guidelines and also receive a summary straight away that indicates the specific changes that this entails for me.”



The smartphone has become a relevant tool in almost every doctor's office. Boehringer Ingelheim provides useful information via the popular service WeChat.

WeChat automatically evaluates which information physicians use frequently or what they indicate to be particularly useful, says Boehringer Ingelheim's Elena Yang. “As a result, we can provide information and services that increasingly fit the actual needs of physicians and their patients – and thus help to ensure continuous improvements in the efficiency and quality of medical care in China.”



THE NEUROSCIENTIST
SIDARTA RIBEIRO

is examining the speech patterns of children and adolescents with a multidisciplinary team, in order to facilitate the earlier diagnosis and treatment of mental illnesses. Intelligent algorithms help the team to analyse these patterns faster and more precisely.

Deciphering hidden signs

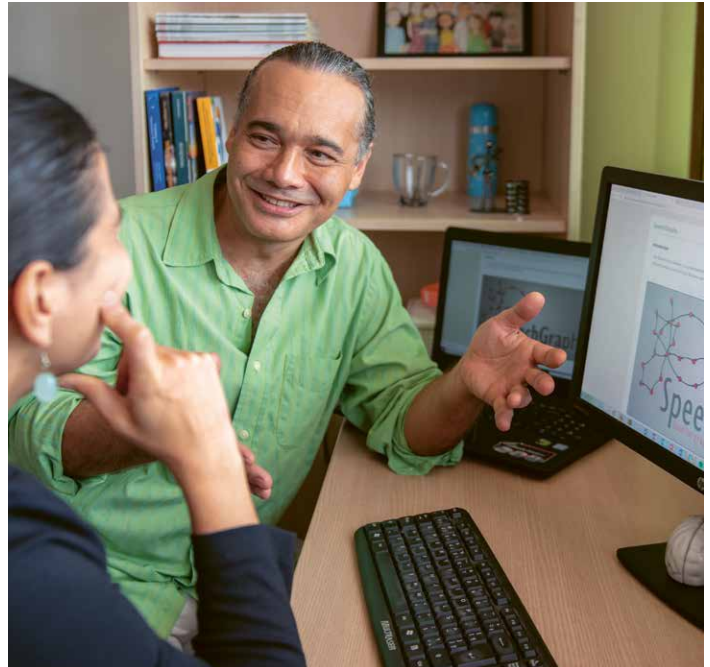
Using artificial intelligence and advanced computational methods, an international academic research team, in collaboration with Boehringer Ingelheim, analyses speech patterns in order to assess whether adolescents are at risk of developing mental illnesses, such as schizophrenia.

Sidarta Ribeiro counts words, chops up sentences into their individual elements and shuffles texts into new texts. A reader seeking to decipher the chaotic-looking results of this word puzzle on Ribeiro's screen would probably consider this pointless and quickly give up. "This is a key part of our project," explains Ribeiro. "Here, we are interested less in the contents of the texts than in the structure of the interplay of words."

Words, syllables, sentences: for the researcher these are primarily data which he can use to feed the intelligent software. The algorithms of this speech detection tool identify patterns and logical contexts in words, sounds and syllables that elude the human ear and eye.

The data that the Brazilian neuroscientist evaluates with a multidisciplinary team come from recordings of conversations which psychologists have conducted with trial participants on the basis of a specific system of questions. "Doctors ask the participants to discuss their most recent dreams, for example," explains Dr Michael Sand, who is responsible for several central nervous system (CNS) clinical programmes at Boehringer Ingelheim. Participants are also asked to describe certain images with emotional context.

The members of Ribeiro's research group, use a specifically designed research software to evaluate the recordings of these conversations. "Studies of



Sidarta Ribeiro uses intelligent software to analyse logical relationships in words, sounds and syllables.

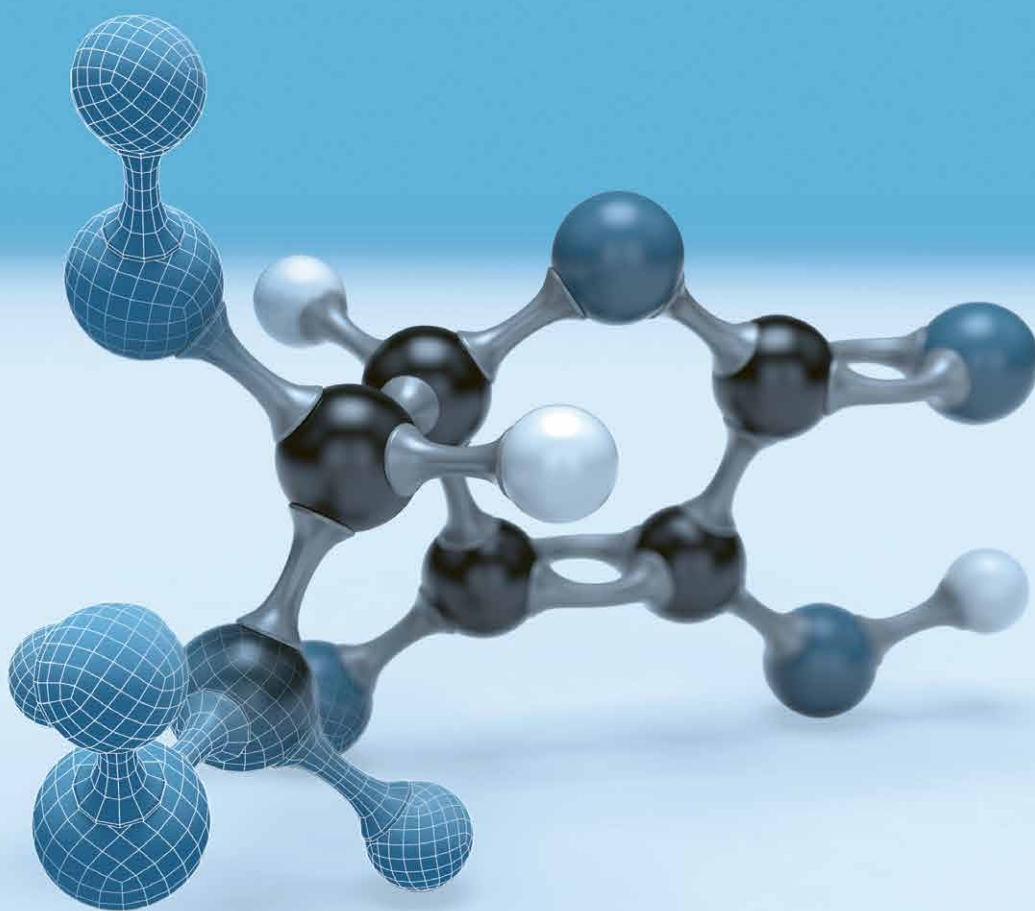
schizophrenia patients have shown that the illness is reflected in their speech patterns," Sand remarks. A change in intonation and a decrease in the level of complexity in their speech may be early signs of the disease.

Boehringer Ingelheim and the research group now plan to use these findings to support early diagnosis of the illness. "In people predisposed to this illness, the onset of schizophrenia typically occurs no earlier than during adolescence", Ribeiro comments. He adds: "Schizophrenia is an illness which gets worse as time goes by". But if it is diagnosed early and properly treated, the process may be slowed down or even stopped.

Ribeiro is optimistic that doctors will in the near future already be able to make reliable predictions for risk groups – with the aid of the intelligent software he also uses in his research. While it used to take days or weeks to analyse speech patterns, now all that it requires is a small number of clicks and a few seconds. "We have become much faster thanks to digitalisation," says Ribeiro. "Hopefully this will soon benefit a lot of people who are at risk of developing the illness."



Digital Research



Better, faster, further

Discovering and developing new medicines is complex and expensive. Scientists explore and select what they think are the most relevant disease mechanisms, then design and test promising candidate molecules that interact with the selected mechanism. Finally, they organise patient studies and evaluate their results. All of that may take years and cost billions of euros with high attrition rates. The digital transformation will revolutionise these processes in line with the motto - better, faster, further. Three examples illustrate the changing nature of research at Boehringer Ingelheim.

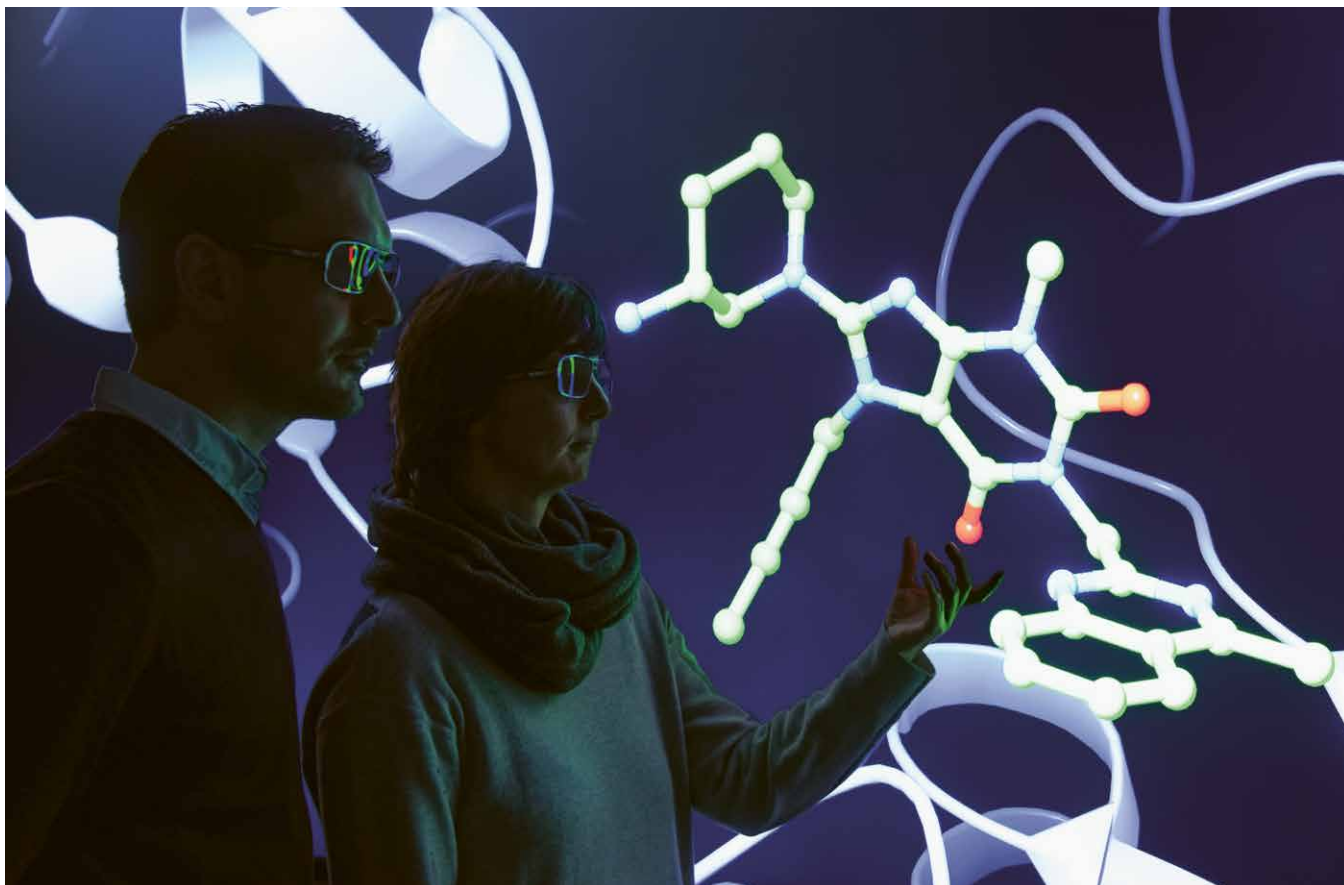


Artificial intelligence-supported software, virtual molecular models and open innovation are currently finding their way into Boehringer Ingelheim's research laboratories. The goal is to develop better medicines. On the basis of highly precise data, scientists at Boehringer Ingelheim can aim higher right from the start: with an exact hypothesis on a certain disease mechanism that takes into account all relevant data from global research results. A smart software makes this kind of precision possible. Computers read the ever-growing flood of data from experiments, external research teams' articles and the values reported in statistics portals in a matter of seconds, evaluate them and reveal links.

Digital processes also help Boehringer Ingelheim researchers to be faster, since drug development often takes too long using analogue processes. Several years can elapse from an idea via initial experiments, prototypes and patient studies to a medicine that is ready for the market. In the worst-case scenario, that may cost human lives since life-saving drugs will not be available in time for treatments.

In addition, digitalisation also takes our scientists further: through open innovation. Digital platforms make new connections and collaborations possible. The borders between internal research teams and external experts are increasingly porous.

"Digital technologies are boosting value creation in our research processes. They help us to identify relevant disease mechanisms, to discover promising molecules and to explore the unexpected far beyond current horizons – through open innovation. The time, quality and knowledge we gain thereby will above all benefit our patients worldwide," explains Dr Michel Pairet, Member of the Board of Managing Directors with responsibility for the Innovation Unit.



Interaction of artificial intelligence and human creativity
in molecule design for new medicines.

“Digital technologies are boosting value creation in our research processes.”

DR MICHEL PAIRET
Member of the Board of Managing Directors
with responsibility for the Innovation Unit

BETTER THROUGH MERGING **COMPLEX DATA** Instantly up-to-date

Before starting a drug discovery project, researchers need to identify the most relevant disease mechanisms they want to address. For this, Boehringer Ingelheim is developing the NTC Studio application in a pilot project. The acronym stands for “NewTherapeutic Concepts”.

NTC merges, that is to say combines and analyses, data from the widest range of internal and external sources. “The volume of information that is relevant for our research comes from all over the world and increases every day,” says the project leader, Dr Jan Kriegel. “Thanks to NTC Studio, researchers have access to many different sources and are always up-to-date with the current state of research.”

The application links results from internal research projects, content from scientific publications and patents, and clinical study data. The programme scours this information for terms which researchers are seeking, groups them and enables the researchers to detect unknown connections from this merged perspective.

In addition, NTC Studio provides the possibility of effective collaboration with researchers who are working, or have worked, on similar projects. Combining the internal know-how of many individual researchers makes it possible over time to build up a valuable fundament of knowledge.

FASTER THANKS TO ARTIFICIAL INTELLIGENCE

Molecules from a machine

A strand of molecules with many branches develops on a smartphone screen. Chemical structures appear, with properties and values listed below – this is research data. The scientist must now decide: should he click on the green box and accept the suggestion? Or click on the red box and reject it? If the researcher accepts the suggestion, he can continue to work on the molecule displayed. If he rejects it, he will instantly receive a new suggestion, generated by means of artificial intelligence. ADAM is the name of this application, which is intended to make life easier for those who develop medicines.

The abbreviation stands for “advanced design assistant for molecules” and denotes the most advanced digital assistant to date within research at Boehringer Ingelheim. Different digital assistants have been helping researchers in processing complex data for some time now.



Smart research assistants like ADAM can be used on various platforms – including smartphones.

Each assistant knows the relevant molecules and data points from all of Boehringer Ingelheim’s current research projects and also has access to historical project data. Within a few seconds, the assistants inform scientists about what is known about a molecule variant at Boehringer Ingelheim, without users having to search for it every time. ADAM constantly updates its algorithms with new information and data from countless current and previous company projects. Use of this know-how raises efficiency in pharmaceutical research. ADAM thereby takes the interaction between man and machine to a completely new level.

SEE WHAT I SEE: THROUGH OTHERS’ EYES

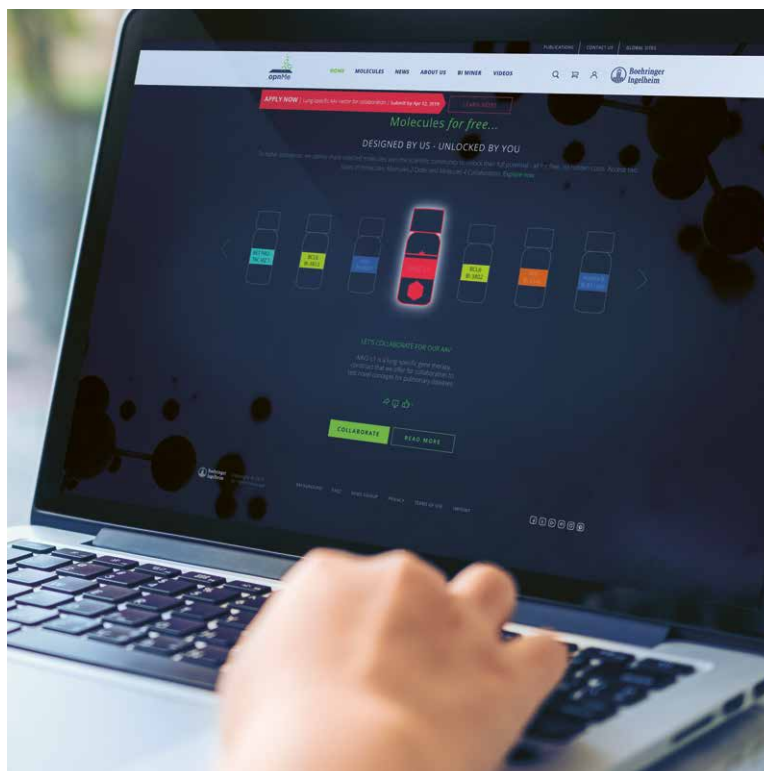


Researchers at Boehringer Ingelheim are working on new medicines worldwide, across national frontiers and continents. With the remote app “[XpertEye](#)”, a researcher in the USA wearing smartglasses can show colleagues in a laboratory in Germany what he is working on, and vice versa. The app enables remote collaboration of an activity – such as repairing equipment, or data analysis. The advantages are obvious: instead of having to travel to the other side of the world to see colleagues, issues in research projects can be resolved by means of electronic communication. Not only is this more sustainable, it also saves time and cost.



Remote collaboration tools such as “[XpertEye](#)” help to resolve specific questions faster and cost-effective.

At your fingertips: new molecules are made available to the global research community through an open innovation online portal.



“The biological processes in the human body are highly complex,” stresses Dr Matthias Zentgraf, of Boehringer Ingelheim’s Research Department. “But there are also frequently recurring questions in drug research. Thanks to digital assistants, we will be able to work much more efficiently here in the near future. ADAM already offers a foretaste of it.”

FURTHER BY MEANS OF OPEN INNOVATION **Designed by us - unlocked by you**

Boehringer Ingelheim’s new open innovation portal “opnMe.com” was launched to enable cooperation in pharmaceutical research far beyond company boundaries. A courier might ring the bell at a university in North America, for instance. Inside the parcel are small tubes carrying some of the most valuable molecules from Boehringer Ingelheim’s research organisation: high-quality compounds developed in-house and patented. The American scientist has ordered them, free of charge, on the opnMe.com portal: here, the company offers 30 molecules that would probably have been kept strictly under lock and key in predigital times.

On opnMe, however, any scientist can order with only a few clicks molecules that are of interest for their own research. Everywhere in the world, they receive them free of charge within a week and can start their own experiments without having to fear infringements of existing patents. Over the past few months, more than 1,700 compounds were delivered to 29 different countries. External researchers thus become accomplices of the company’s in-house drug research.

“opnMe enables us to learn exciting new things about disease biology, at the same time improving our scientific reputation and excellence in drug discovery and development,” says Dr Florian Montel, a medicinal chemist and head of opnMe at Boehringer Ingelheim. “They also demonstrate to the scientific community that Boehringer Ingelheim is open, honest and fair in the field of research accelerating the discovery of new medicines”.

OpnMe.com allows also to commence joint research projects. Scientists interested in accessing them for their research submit an application with a unique and novel research hypothesis. The proposals with the highest potential will be pursued together with scientists from Boehringer Ingelheim. So far, three of these molecules have been offered on opnMe – and Boehringer Ingelheim has received a total of 275 applications. “We have selected the best projects from these and made the molecules available to researchers. As a result, we have started seven new collaborations,” explains Dr Markus Koester, who is in charge of relations with researchers worldwide via opnMe.com.

Collaborative projects in the field of cardiometabolic diseases, infectious diseases and diseases of the respiratory tract are currently underway. Another exciting call will be launched soon: for the first time a pharmaceutical company will offer a lung-specific adeno-associated virus (AAV) to test new genetic



30

well-characterised molecules
are available on opnMe

275

applications for
“Molecules for collaboration”



1,700

compounds shipped
since launch of opnMe

mechanisms for treating respiratory diseases. “This will support our ambition towards scientific leadership in AAV-based gene therapy,” Koester adds.

Through the company opening up, scientists at Boehringer Ingelheim can tap into the knowledge of scientific experts worldwide. According to Montel, opnMe.com goes beyond the frontiers in drug discovery and will eventually accelerate the discovery of next generation medicines for patients in need.

Despite all technological advances, however, one thing will remain irreplaceable in the future: the tireless curiosity, creativity and the genius of enthusiastic scientists.

BRASS: RISKS AND SIDE EFFECTS



When a drug is on the market, Boehringer Ingelheim medical scientists attend to pharmacovigilance. They collect data on possible side effects and thus assess risks with medicines.

They will soon be provided with a digital assistant called BRASS. The experts can enter their own experiences and assessments as well as background information into the application. BRASS can then use various analytical methods to independently develop new findings. In addition, BRASS can also place data in the context of biomedical expertise. However, the decision as to which conclusions to draw from the safety data still lies with the medical profession. Should certain risks be mentioned in the package insert? Are the instructions for use to be supplemented? Although artificial intelligence supports humans in many areas, it cannot replace them.



Learning algorithms help to better understand possible side effects and risks with medicines.

Digital Production



Facility of the future

Boehringer Ingelheim is pushing forward with the digitalisation of its production systems. The goal is to manufacture medicines not only more efficiently and safely, but also in ever-smaller batches tailored to individual patients. The construction of the new Launch Facility - which can produce cancer medicines, for instance, in very small batch sizes - represents a major step on this path. Using a virtual 3D model and virtual reality goggles, employees are already helping to plan for this smart factory.



Here a tablet press emitting tablets at high speed. Is that a robot arm over there automatically testing single tablets? There is a lot of space to move around in between. “I have a very good sense of what it will be like to move around the plant,” says Dr Peter Comes as he removes his virtual reality goggles. He is Head of the solids production in Ingelheim. So far, the ultramodern manufacturing facility which he has just visited only exists on a computer. Using the architect’s model and design drawings for the machines, data specialists have created a dynamic, three-dimensional copy of the Launch Facility which is currently being built at Boehringer Ingelheim’s headquarters. But with these VR goggles, this new facility for the production of tablets comes alive even now. Where construction machinery currently is making a din in front of Comes’ office window, the Launch Facility will mark a new chapter in pharmaceutical production from 2020 onwards.

The Launch Facility is a prime example of the digitalisation of production at Boehringer Ingelheim, but it is far from the only initiative of its kind: many machines at the company’s headquarters and other facilities have long since been networked, and a central registration system will soon collect, compare and evaluate data for entire production lines. The goal is to enable employees to identify irregularities and to eliminate problems in the manufacturing process as early as possible – possibly before they occur and not only when the final inspection reports that medicines deviate more strongly from the norm than the strict tolerance limits permit. At the same time, this final inspection will become significantly easier in future when IT supervises each individual manufacturing phase.

Networked production thinking reduces the volume of rejects and makes processes more efficient, just like quality management. “Our industry is strongly

regulated,” says Dr Anja Preißmann, who is responsible for the production of all human pharmaceuticals at the company’s German facilities. “Our manufacturing system undergoes a large number of extensive audits conducted by German and foreign authorities. Efficiency is a key issue for us here.” One example of the new, paper-free processes is that shift supervisors were previously required to document manually which health checks and safety training courses an employee had completed before being permitted to operate certain types of machinery. In future, they will enter this type of information in the system digitally and can even directly link it to the machine’s control system: if an operator does not fulfil certain preconditions, the machine will not even start.

Boehringer Ingelheim’s production engineers are already using digitalisation in order to optimise existing equipment. To take the example of packaging machines: there is currently a lot of movement once the signal is given that a new batch of tablets is ready for packaging. Specialists then refit one of the lines, which is more than 20 metres in length, for the new job. The machines subsequently fill the blisters with tablets in a matter of seconds, push them into packages together with the package insert, and finally check their weight before they land in boxes for storage and dispatch. Depending on how many of the individual machines need to be reorganised, the set-up of a line can take several hours. During this process, every movement with each tool has to be exact. It takes up to twelve months to train new employees.

At least that’s the way it used to be: in a pilot project on one of the lines, augmented reality goggles are helping new members of staff with the set-up process. They automatically load the appropriate set-up programme by means of a QR code. Each individual work step subsequently appears in the employee’s field of vision via a prism in the top right-hand corner of the goggles. At the same time the employee keeps an eye on his tools and machines and his hands are free for work. “We have found that this enables us to reduce the training period for new employees to six months,” says Head of Human Pharma Supply Germany Preißmann.

“Our manufacturing system undergoes a large number of extensive audits conducted by German and foreign authorities. Efficiency is a key issue for us here.”

DR ANJA PREISSMANN



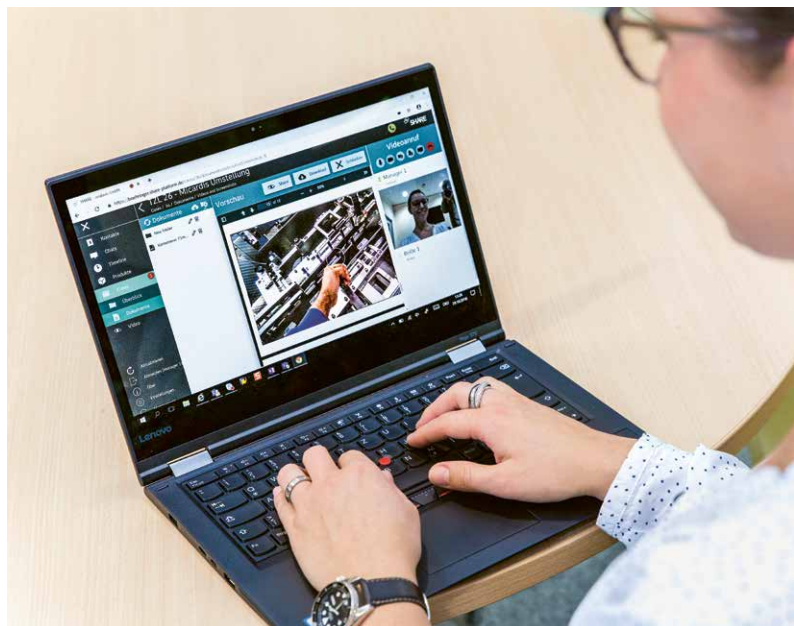
Process optimisation through augmented reality: QR codes and visualisations guide through training procedures.



During maintenance procedures, production engineers can establish a live connection to remote technicians via augmented reality goggles.

In addition to these augmented reality goggles for the set-up of packaging machines, a second, differently configured model is available for emergencies. Previously, when a machine experienced a problem, a technician had to carry out an inspection on site, coming into the facility even during a night shift. Now, in that type of situation the employees can call the technician and put on the AR goggles. Through a camera fitted in the goggles, the technician can see on his laptop at home what the employee on site can see and provide instructions on what needs to be done. “This way, in future we will also be able to provide rapid assistance if our facilities outside Germany run into problems, without the need for a technician to fly over there,” says Preißmann.

The same applies for double checks, where employees currently visit in person on site for important inspections in line with the double-verification approach. This is a laborious process due to strict safety and hygiene regulations: it takes a while to get through the gates inside the facilities, and only a few persons are permitted to enter particularly sensitive



Through a camera fitted in the goggles, the technician can use her laptop to join the engineer's view and provide spoken or written instructions.



A look into the future: the three-dimensional model of the Launch Facility helps to improve the processes even before the plant has been completed.

“We will be ready once individualised medicines for patients will no longer be an exception and become the norm.”

DR ANJA PREISSMANN

areas at any one time. With AR goggles, one of these two employees will soon be able to carry out these checks from the office. The company’s manufacturing experts are currently even considering installing innovative blockchain technology in the goods receipt area. Cameras could scan package deliveries and check their codes against a blockchain database. That would make the purchasing of small batch sizes of packaging material more efficient. “For the digitalisation of our production system, we have already started a number of initiatives,” says Preißmann.

In addition, Preißmann and her colleagues press on into an entirely new world: packaging machines will in future no longer operate along a fixed line as they currently do and will instead work as individual, networked modules. The filling, printing and packaging stations will be digitally configured for various medicines, quantities and different markets. Further stations will be added, if required. Human specialists and collaborating robots work together on the individual modules, and the level of automation can be freely selected.

“With the new facility, our goal is to produce individual packaging sizes at the same cost as huge batches,” says Preißmann. A mechanical engineer is currently developing and building this modularised facility and its components in close cooperation with the company’s experts – this is an individual item. “This type of modularised and automated manufacturing is a real innovation in the pharmaceutical industry,” says Preißmann.

The fact that employees can already view the Launch Facility today using VR goggles is not just a gimmick, by the way. It is intended to help to improve the processes even before the plant has been completed: anyone who has looked around the computer model of the facility will be able to put forward suggestions for improvements. “That provides valuable feedback for us,” says Dr Peter Comes. It is much easier and cheaper to implement proposals during the planning stage than later on in the finished building. This will also boost the machine operators’ attachment to their new workplace, according to Comes: “After all, it will have been built in line with their ideas.”

Back to packaging: Boehringer Ingelheim requires small batch sizes during clinical tests, for instance, where newly developed medicines undergo various testing phases. Developers typically require just a few tablets of a new medicine and then ever more of them over time, as the number of test subjects increases. However, small batches are also increasingly an everyday feature of regular production: even now, Boehringer Ingelheim produces very small quantities in the area of oncology. Cancer medicines are not mass-produced goods and are in part only packaged on the basis of an order for a specific patient in a particular country. Accordingly, the number of units is minuscule – it’s precisely the quantity required.

“It is much easier and cheaper to implement proposals during the planning stage than later on in the finished building.”

DR PETER COMES

This type of order is currently handled via fully automated mass production packaging lines, since individual work steps such as packing tablets in blisters cannot be outsourced. This means that technicians spend several hours refitting the machines. They then run the equipment for this very small order, even if this is just for a few minutes. “In future, we will package this type of order in the new modular packaging line,” says Preißmann. “We will thus be ready once individualised medicines for patients are no longer an exception and become the norm.”



Dr Anja Preissmann is responsible for the production of all human pharmaceuticals at Boehringer Ingelheim's facilities in Germany.

“As complex as a jumbo jet”

ABOUT THE INTERVIEWEE:

Dr Jochen Gerlach is a chemist who has worked at Boehringer Ingelheim since 2012 and is Head of Manufacturing Science at the Vienna biopharmaceuticals facility. The new large-scale cell culture (LSCC) production facility there is scheduled to commence operations in 2021. The investment is around 700 million euros, including infrastructure, and 500 new jobs will be created. Boehringer Ingelheim has been one of the industry's pioneers in biological molecule production since the 1980s.

Biomolecules from an AI-driven factory, constantly enhanced by self-learning algorithms: this is the vision that biopharmaceutical specialists from Vienna are working on with data experts at Boehringer Ingelheim's BI X digital incubator. So far, they have only been dealing with one step in the process – fermentation. If the approach works for the whole process chain, it will open up completely new possibilities. Dr Jochen Gerlach, project owner of Smart Process Design, explains what the initiative has achieved to date – and where the journey is going.

Mr Gerlach, do computers make better researchers?

J O C H E N G E R L A C H (JG) (laughs) No. But they help people to interpret data. The best approach is for people and computers to research together.

Is that the idea behind your Smart Process Design project? To create an intelligent assistant for conducting research into production processes?

JG You could say that. The development of biopharmaceutical production processes in the laboratory is very complex, expensive and demands a high degree of knowledge and experience. We have a software solution in mind that contains a model of the complete production process. It could then analyse this model and make predictions. Our goal is to discover the optimal production process.

Is the production of biopharmaceuticals more complex than the conventional, purely chemical manufacture of medicines?

JG In production we use living organisms that react extremely sensitively to their environment. In addition, biopharmaceutical active ingredients are as a rule highly complex biomolecules. If a standard chemical active ingredient has as complex a structure as a bicycle, then an antibody is equivalent to a jumbo jet. Controlling these two aspects is the challenge for our process developers.

“Major advances have been made in the field of data science. Even large volumes of data can be analysed relatively easily to identify correlations.”

How did you come up with the idea of looking for a technical solution to this issue?

JG At the end of 2017, within the framework of the innovation strategy of biopharmaceuticals in Vienna, we considered how new, digital possibilities could help us to extend our technological and market leadership. The topic of developing and steering production processes crystallised from this. We have ever-increasing data at our disposal, and we knew that major advances have since been made in the field of data science. Even large volumes of data can be analysed relatively easily to identify correlations.

So you turned to BI X.

JG Exactly. After all, BI X is our internal centre of excellence for digitalisation. So we asked our colleagues at BI X whether they could use their data expertise to help us. We refined the idea at an ideation workshop. The plan we came up with was to build and test a prototype for a fermentation step in order to test our hypothesis. That is to say, we hoped to find better production processes if we employed novel data analysis in our biopharmaceutical process development.

What approach have your colleagues taken so far when developing new production processes?

JG In many experiments, they have systematically varied parameters, like temperature, pH value or duration. Many years of experience are of special significance here. It involves collecting as much information as possible in as few experiments as possible. For this, we already use software that subsequently analyses the data. In this way, we arrive at a process variant in which the active ingredient volume is the highest, that is, optimal. We repeat this until we have achieved the predetermined target.

How did you come up with the idea of further enhancing all of this?

JG We have repeatedly observed at production scale that there is still potential for improvement in



Biopharmaceuticals are cultivated in bioreactors with a capacity of up to 15,000 litres.

our production processes. Evidently, the tool we at present use for analysing development data is not capable of discovering the best process variant. The current software cannot learn. It does not improve when I do more experiments, but rather it only ever analyses the one predefined dataset. Furthermore, it only ever uses a single method of data analysis. These are the two things that we have addressed through Smart Process Design.

Learning means gathering experience: should Smart Process Design also be able to do that now?

JG Precisely. Our approach uses the so-called process models that are capable of learning with new data. Every time we generate new data, the model improves and learns new aspects of the production process. We are completely free here as to which machine learning technologies we deploy. Currently, for example, we use neural nets. They are particularly well suited to detecting patterns in large volumes of data. The volume of data is of no significance here. That is particularly important as ever larger amounts of data accumulate in development.

Was it a culture shock, as chemists, biotechnicians and plant technicians, to suddenly find yourself working alongside the digital experts from BI X?

JG (laughs) It's true that there were cultural differences. We had to ensure first that we spoke the same language and understood each other. Our colleagues at BI X had to familiarise themselves with biotechnology, and the scientists here in Vienna had to learn a certain amount about software development.

What will come after the prototype? What is the next step?

JG Shortly before the end of the first project phase, we succeeded in proving our hypothesis in an experiment. Smart Process Design has in fact identified a process variant for our fermentation with significantly higher efficiency. In the next stage, we want to demonstrate that it is also possible to create models for several successive process stages. Then we could at some time model complete production processes and take into account all interdependencies between the process stages.

You would have a model that describes the entire process chain up to the purified end product.

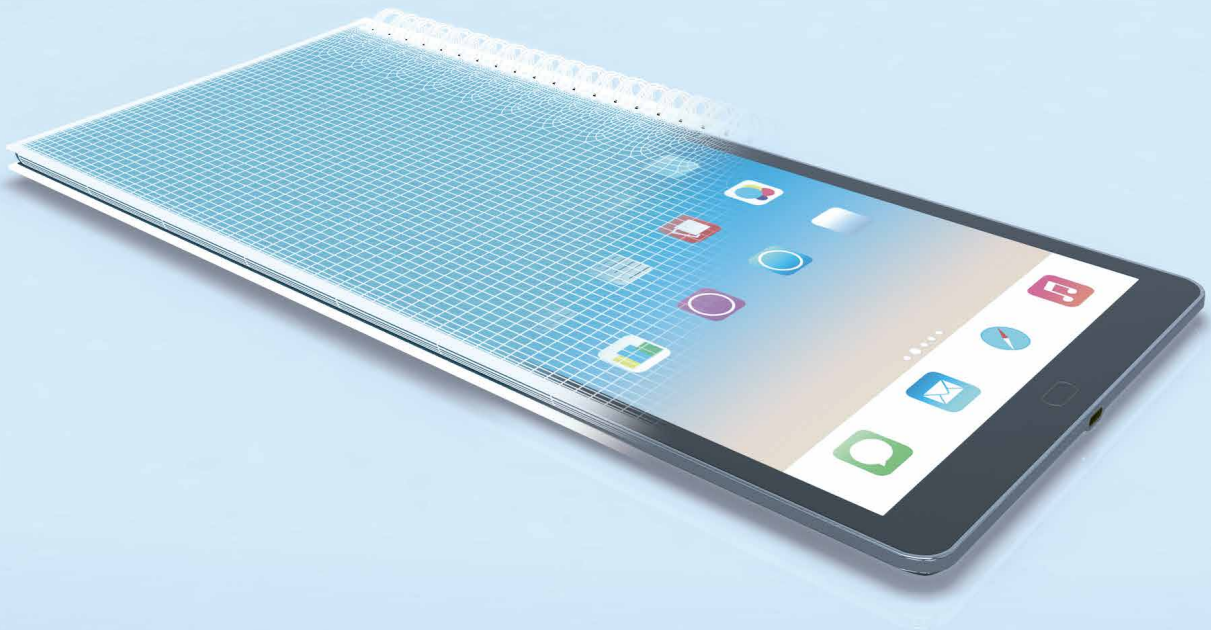
JG Correct. Then we will have come a big step closer to our vision of employing process models in our production plants. We would be in a position to analyse what influence disruptions have on the subsequent process steps – in the computer, while the production process is still running. Model-based instructions are the logical next step. We could change settings in further production in order to offset disruption. When the regulatory issues are clarified, we can steer our production plants predictively.

At some point in time, the self-learning system will perhaps no longer just suggest what you should change, but rather will decide itself.

JG Yes, and you would then have production that is managed by artificial intelligence. That is a very long-term vision. You could say that, with our Smart Process Design, we have taken a first small step on the path towards an AI factory.

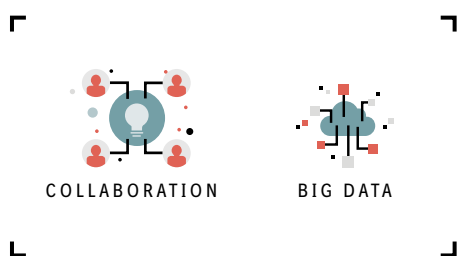
“We have developed a program that is capable of self-learning. Every time we generate new data, the process model improves.”

Digital Work



Everyone at one desk

The digital transformation is changing the world of work. Speed and lateral thinking are needed, partnership and communication are desired. And so offices are changing – in Ingelheim and Biberach, Lyon, Vienna, and in Ridgefield. With the BI CUBE at the company headquarters, agile working even has a place of its own.



Anyone who crosses the campus in Ingelheim cannot fail to notice the new white building beside the canteen: the BI CUBE looks like a UFO, oval-shaped with a flat roof and dark windows. However, there is nothing spaceship-like about the interior. On the contrary, it smells of new wood, and the hall is a landscape of sofas with large cushions and coffee tables. A glass front is all that separates the living-room cosiness in the corridor from the bustling activity in the three work rooms. The glass panes provide a clear view of employees who are cutting out paper figures, writing on whiteboards and sticking up notes on the walls.

The BI CUBE is a place for alternative working: agile and without hierarchies. Boehringer Ingelheim employees share their thoughts, give each other feedback and build on ideas – and thanks to agile methods like scrum and design thinking, they manage to do all of this within the shortest of times. The BI CUBE has a total area of 700 square metres and is equipped with everything needed to support creative working: writable walls, movable furniture, art supplies. If anyone needs more space, the three

conference rooms can be quickly turned into a single large one. “Conventional meetings with PowerPoint battles don’t exist here,” explains Dr Andrea Kreißelmeier, one of some 30 Agile Facilitators at Boehringer Ingelheim. She helps her colleagues to apply agile methods.

The BI CUBE is currently the most visionary building at the company headquarters in Ingelheim – indeed, within the entire Group. It is the expression of a new form of working, since digitalisation is changing processes, approaches and concepts. Smart working is the key word here: “Market development times are getting shorter and shorter, competition more intense, and customers’ needs are continuously changing,” says Kreißelmeier. What is in demand today could well be obsolete tomorrow. “Companies can simply no longer afford to brood over an idea for years.” Like all other companies in the healthcare sector, Boehringer Ingelheim therefore needs shorter channels and flatter hierarchies, and lateral thinkers.

After all, the company has long been competing with more than just other pharmaceutical companies. Large technology companies like Apple, Google and Amazon have also entered the race for healthcare technologies. It is not just about customers here, but also about employee recruitment: digital talent itself is needed everywhere. Collaboration, autonomy and transparency are what they want. For this reason, too, new ways of thinking and innovative approaches are required. Quite simply, alternative working is highly attractive – that applies both to the recruitment of new talent and to existing employees.



In the BI CUBE, employees are cutting out paper figures, writing on whiteboards and sticking up notes on the walls.

The BI CUBE is to be an incubator for the new way of thinking. The architecture and room concept are based on numerous lessons that Boehringer Ingelheim has learned in recent years at various facilities, including the Ridgefield site in the US, the former Merial facility in Lyon and Biberach. The employees at these locations are already practising the “smart working” concept. The basic premise is a flexible work environment rather than individual offices and long corridors. “We are providing answers to the changing digital world by creating an inspiring work environment,” says Uta Dotzauer, Head of Corporate Real Estate. “We understand that in the new digital world, a home for personal collaboration and communication is still required to fill the rapid digital transformation with life.”

The employees in Ridgefield have been practising the concept for five years now. Instead of working in enclosed offices, they work, inter alia, at desk islands in an open space. For meetings, they withdraw to the rooms specifically created for this purpose. Much of the work is done digitally: every employee has a notebook, headset, mobile phone and Skype

access. Stacks of paper? Not here! The advantage is that the employees can theoretically work from any facility. Their computer automatically connects to the Wi-Fi, and off they go. In short, the staff members from Ridgefield are at home anywhere in the world of Boehringer Ingelheim.

In spite of digital tools, however, the employees there today communicate more with each other. This was different when there were still individual offices, recalls Benedikt Kraus, Head of the Infrastructure, Safety, Environment and Engineering (ISEE) department in France: “Even if the doors were open, there was still this barrier. As a result of the new workplace concept, the staff members automatically talk to each other more – and we want to encourage that.” As Kraus knows, open work spaces encourage collaboration. Interaction and communication give rise to new ideas. In the end, that ensures greater productivity.

Everything from scratch

When Boehringer Ingelheim acquired Merial – the animal health business of the French pharmaceutical group Sanofi – at the end of 2016, it provided the company with a major opportunity: the old Merial building in the southern French city of Lyon was no longer fit for purpose, and something new had to be created. As a result, the architects were able to think innovatively. The result was the Boreal building, the first Boehringer property designed for smart working from top to bottom. “We quickly realised in Ridgefield that we were only able to modify rooms to a certain extent,” says Kraus, who has been in charge of the ISEE department in Lyon since June 2018. “We took advantage of the opportunity here to design the entire building in line with the new way of working.”

Whether they are a trainee or a manager, all 750 employees in Lyon practise the “smart working” concept. Each floor consists of various zones: The centrepiece is the Community Center, with

“We are increasingly switching areas to smart working, creating a new way of thinking, a digital pioneering spirit.”

DR ANDREAS NEUMANN
Member of the Board of Managing Directors
with responsibility for Human Resources



The Boreal building in Lyon is the first Boehringer Ingelheim premises designed for smart working from top to bottom. It is increasingly popular among employees.

beverage dispensers and lounge furniture, where staff can drink a coffee together and chat to each other. According to French Head of Animal Health, Erick Lelouche, this is an advantage: “I got talking to more people in the first few weeks here than in all the months in the old building.” The work rooms are divided into clusters. An average of 20 people work in each cluster, and the desks are arranged in both small and big island formations. If someone does not want to be disturbed, they can withdraw to the focus rooms. In addition, each floor has several phone booths and conference rooms. The core of the smart working concept is that nobody has a fixed workstation, but each employee has different options for working so that they are optimally supported in their current work. The employees clear their desks at the end of every day. Everyone has a grey basket and a designated locker for their belongings.

The concept is popular with the employees: “Although I work at a different desk each day, all of our team members sit near each other, so we can communicate more quickly,” says Mathieu Condette, an employee in the ISEE department. “The physical proximity supports our way of working.” Condette is one of the few who still use pen and paper. However,

“I got talking to more people in the first few weeks here than in all the months in the old building.”

ERICK LELOUCHE

this usually creates duplicate work for him, as he admits: He regularly scans all his documents. “I then have to carry less stuff around with me,” says the 38-year-old.

Learning from experience

The open office spaces also took a while to get used to. The employees had to learn how to talk normally in a large room: “The employees were almost too quiet out of consideration for their colleagues,” says Head of Animal Health, Lelouche. So the managers led by example and encouraged the staff members to engage in more conversation. The initial difficulties have since been overcome: the employees talk

to each other and make jokes. They move back and forth between the individual zones, sometimes with their notebooks, sometimes without.

Bosses get involved

Boehringer Ingelheim staff members in Biberach have also been using the smart working concept since May 2018, in building D125 – the place where much of what was learned in Ridgefield and Lyon has been incorporated. As is the case with Boreal, there are various room zones in D125, including for co-working, concentrated working and meetings. The “clusters” in Lyon are called “neighbourhoods” in Biberach: there are a total of ten units – including IT, biopharmaceuticals and R&D – each with around 70 staff members. Nobody has a fixed desk here either. “When we first presented the idea of D125, the employees were sceptical,” recalls Sandra Laegner, Head of the German Center of Expertise in Human Resources. “But most of them cannot imagine having individual offices now.”

Many people are curious about the new buildings: The project rooms in the BI CUBE in Ingelheim are usually booked out. In Lyon, staff members regularly visit from other facilities. There is a lot going on in Biberach, too: “We recently had an open

day, and the place was packed with visitors,” says Laegner. The Deputy Head of HR firmly believes that smart working is increasing Boehringer Ingelheim’s attractiveness as an employer. “Employees can work without problems at any facilities. A lot of things are digital, and use of the rooms is flexible.”

The company is now increasingly switching areas to smart working – for example, the VGN administration building, now under construction on the Ingelheim campus. The changes are about nothing less than a new way of thinking, a digital pioneering spirit. And that simply will not happen behind the closed doors of individual offices.

“When we first presented the idea of the D125, the employees were skeptical. But most of them cannot imagine having their individual offices now.”

SANDRA LAEGNER

The BI CUBE is equipped with everything needed to support creative working, like writable walls, movable furniture and art supplies.



IMPRINT

IF YOU HAVE ANY QUERIES OR COMMENTS, PLEASE DO NOT HESITATE TO CONTACT US.

*C. H. Boehringer Sohn AG & Co. KG
Binger Straße 173
55216 Ingelheim
Germany
Telephone + 49 6132 77-0
Fax + 49 6132 72-0*

CONTACT

*Corporate Division Communications and Public Affairs
E-mail press@boehringer-ingelheim.com
Internet www.boehringer-ingelheim.com*

ISSUED BY

C. H. Boehringer Sohn AG & Co. KG

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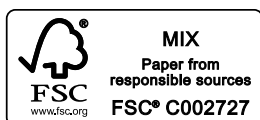
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BOEHRINGER INGELHEIM

2018

Annual Report

FINANCIAL HIGHLIGHTS

SUMMARY REPORT

Amounts in EUR million, unless otherwise indicated	2018	2017	Change
Net sales	17,498	18,056	- 3%
by region			
Europe	30%	32%	
Americas	46%	45%	
Asia, Australia, Africa	24%	23%	
by business			
Human Pharmaceuticals	72%	70%	
Animal Health	23%	22%	
Biopharmaceuticals	4%	4%	
Discontinued Operations	1%	4%	
Research and development	3,164	3,078	+ 3%
Personnel expenses	5,276	4,934	+ 7%
Average number of employees	50,370	49,610	+ 2%
Operating income	3,472	3,487	- 0%
Operating income as % of net sales	19.8%	19.3%	
Group profit / loss	2,075	- 223	- 1,030%
as % of net sales	11.9%	- 1.2%	
Group equity	12,334	10,657	+ 16%
Return on Group equity	19.5%	- 2.0%	
Investments in tangible assets	950	872	+ 9%
Depreciation of tangible assets	552	521	+ 6%

SUMMARY REPORT

2018



Top 4 products – Human Pharmaceuticals

Net Sales 2018	in millions of EUR	change
SPIRIVA®	2,412	- 15%
PRADAXA®	1,486	+ 3%
JARDIANCE®	1,461	+ 45%
TRAJENTA® / JENTADUETO®	1,397	+ 5%

Top 4 products – Animal Health

Net sales 2018	in millions of EUR	Change
NEXGARD®	610	+ 12%
FRONTLINE®	399	- 1%
INGELVAC CIROFLEX®	303	- 9%
HEARTGARD®	299	+ 5%

OVERVIEW

THE CORE OF OUR LEITBILD

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OUR COMPANY

Improving the health and quality of life of patients is the goal of the research-driven pharmaceutical company Boehringer Ingelheim. The focus in doing so is on diseases for which no satisfactory treatment option exists to date. The company therefore concentrates on developing innovative therapies that can extend patients' lives. In animal health, Boehringer Ingelheim stands for advanced prevention.

Family-owned since it was established in 1885, Boehringer Ingelheim is one of the pharmaceutical industry's top 20 companies. Some 50,000 employees create value through innovation daily for the three business areas human pharmaceuticals, animal health and biopharmaceuticals. In 2018, Boehringer Ingelheim generated net sales of around 17.5 billion euros. R&D expenditure of almost 3.2 billion euros, corresponded to 18.1 per cent of net sales.

As a family-owned company, Boehringer Ingelheim plans in generations and focuses on long-term success, rather than short-term profit. The company therefore aims at organic growth from its own resources with simultaneous openness to partnerships and strategic alliances in research. In everything it does, Boehringer Ingelheim naturally adopts responsibility towards mankind and the environment.

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THE SHAREHOLDERS' PERSPECTIVE



Dear Reader,

2018 was a successful year for Boehringer Ingelheim. Success for us means having reached more patients and thereby having delivered a significant contribution to human and animal health. The favourable figures for 2018, which the company documents in this annual report, also testify to this success.

Our primary objective is and remains to maintain Boehringer Ingelheim's independence. In order to be sustainable, we have to continue to remain competitive. For this we need innovations. Our readiness to invest more than the competition average in the research, development and production of innovative medicines, follows this knowledge – and at the same time mirrors the trust we place in Boehringer Ingelheim and all our employees.

Their high degree of commitment is decisive to our success. Shared guiding principles (Leitbild) and the goal of improving the health of humans and animals bind us together worldwide. The individuality of all of them characterises our culture and our values. All of them stand for the family-owned company Boehringer Ingelheim and help us to maintain our independence.

Our express thanks go to our employees who together have all contributed with great engagement and effort to realise our corporate goals.

signed by
Christian Boehringer
Chairman of the Shareholders' Committee

THE BOARD OF MANAGING DIRECTORS



Allan Hillgrove



Michel Pairat



Hubertus von Baumbach



Michael Schmelmer

Andreas Neumann

Joachim Hasenmaier

Dear Reader,

Over 50,000 employees worldwide share our enthusiasm for the task of improving the health of humans and animals through innovation and therapeutic breakthroughs. Today, we want to tell you how we realise this shared vision and what results we were able to achieve in the past year.

The year 2018 was a successful one for Boehringer Ingelheim. The reason for this was our focus on innovation: in a large number of our research projects – currently about 90 all in human pharmaceuticals – we pursue approaches with which we want to be first in the therapeutic class or in the indication. For us it is also decisive to conduct research in areas of unmet medical needs, where patients are dependent on innovations.

This focus – already the principle and foundation of our success at Boehringer Ingelheim for many decades – has provided the basis for the growth of our Human Pharmaceuticals business last year. Although the expiry of market exclusivity had a marked impact on the development of some of our biggest products, overall we were able to grow in line with local markets, and frequently even outgrow them considerably, thanks to the great therapeutic progress offered by our new products such as OFEV® or JARDIANCE®.

In the Animal Health area we have concluded the integration process and further merged both organisations. Prioritising customer needs ahead of our own optimisation has already enabled us to exceed market growth in year two of the new structure.

The Biopharmaceuticals business is also developing very favourably. In particular, progress in expanding capacity in Vienna, Austria, is today already visible to a large extent.

Numerous partnerships that reinforce our innovative core – equally in all business areas and across the whole value chain – have shown how well the specific competences of third parties combine with Boehringer Ingelheim's special capabilities and translate into patient benefit. The accompanying magazine highlights this transformation and takes a detailed look at the possibilities that digitalisation offers us.

Dear Reader, the past financial year was a successful one for Boehringer Ingelheim, also characterised by continual change. As in previous years, the basis for this was the trust of our customers and our partners - and especially the commitment of our employees. Their sense of responsibility and their entrepreneurial spirit have helped us to remain competitive. All of them deserve our thanks.

signed by

HUBERTUS VON BAUMBACH

signed by

JOACHIM HASENMAIER

signed by

ALLAN HILLGROVE

signed by

ANDREAS NEUMANN

signed by

MICHEL PAIRET

signed by

MICHAEL SCHMELMER

CORPORATE BODIES

Shareholders' Committee

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Chairman of the Shareholders' Committee

CHRISTOPH BOEHRINGER

ERICH VON BAUMBACH JR

ISABEL BOEHRINGER

DR MATHIAS BOEHRINGER

PROF. DR DR ANDREAS BARNER

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Finance

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GROUP MANAGEMENT REPORT

INFORMATION ABOUT THE GROUP

The Group's business model

For over 130 years, Boehringer Ingelheim has pursued the goal of improving and preserving the quality of life and health of humans and animals. Headquartered in Ingelheim am Rhein, Germany, the company has been family-owned since its founding in 1885 and is among the 20 leading companies worldwide in its industry. As one of Germany's most research-intensive companies, Boehringer Ingelheim concentrates in particular on researching medicines and offering therapies for diseases for which satisfactory treatment options are currently unavailable and provides the entire value chain, starting from research and development (R&D) through production and commercialisation of its products. Boehringer Ingelheim operates at a global level, with around 50,000 employees in the areas of human pharmaceuticals, animal health and biopharmaceuticals, which generated net sales of almost EUR 17.5 billion in 2018.

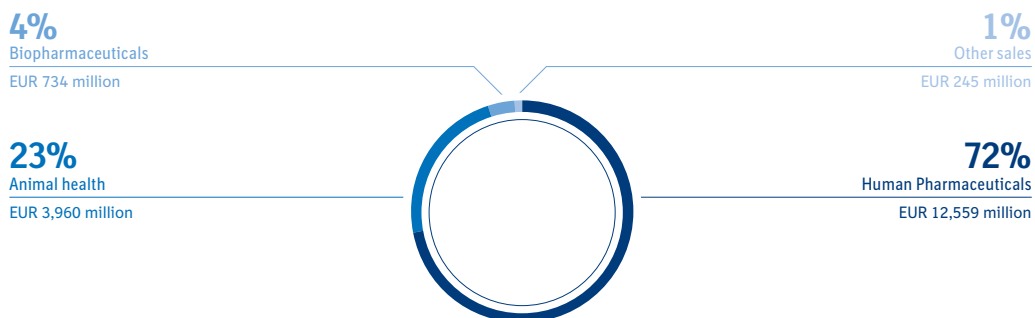
Human pharmaceuticals – in which the company's own medicines are already standard treatments in various therapeutic areas – represent the core focus of Boehringer Ingelheim's activities.

Integration of Merial successfully completed

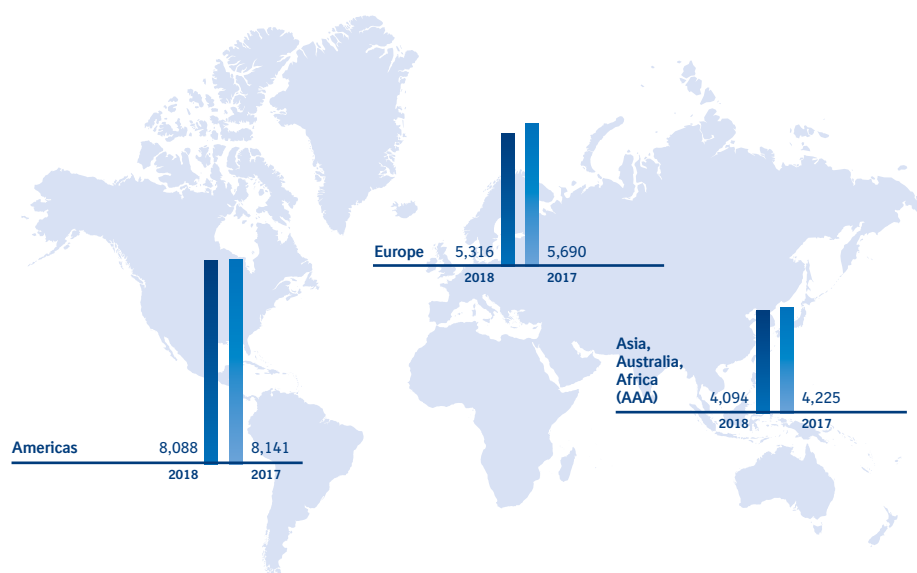
Following the transaction on 1 January 2017, containing a swap of Boehringer Ingelheim's consumer health care business with Sanofi's animal health business (Merial), the integration of the new companies has now been successfully completed. Through the merger of Boehringer Ingelheim's existing animal health activities with Merial, the company's animal health business is now the market leader in Germany and, at the global level, the second-largest provider of veterinary vaccines and medicines.

NET SALES BY BUSINESS

Group: EUR 17,498 million



NET SALES BY REGION (IN EUR MILLION)



Boehringer Ingelheim continues to expand its existing product portfolio through further organic growth, including cooperation with external partners. Through the recent acquisition, the company's global research network has expanded to 13 countries with major facilities in Germany (Biberach, Hanover and Ingelheim), in the US (Ridgefield, Connecticut, Duluth, Georgia, and St. Joseph, Missouri), in Austria (Vienna) as well as in Japan (Kobe) and France (Lyon).

In 2018, the company's biggest revenue contributor in the human pharmaceuticals business was once again SPIRIVA®, which is used to treat chronic obstructive pulmonary disease (COPD) and asthma. The following products also made significant contributions to Boehringer Ingelheim's success: PRADAXA® (used to prevent strokes in patients with atrial fibrillation and for the prevention and treatment of thromboembolic disorders); its type 2 diabetes products JARDIANCE® (winner of the Prix Galien International 2018 for the most innovative pharmaceutical product) and TRAJENTA®; and the medicine OFEV®. The latter medicine was introduced in 2015 and offers people with the rare, fatal respiratory disease idiopathic pulmonary fibrosis (IPF) for the first time a treatment option.

SPIRIVA® still biggest revenue contributor

In the company's animal health business, the antiparasitic NEXGARD® is the strongest product in terms of net sales. Its other antiparasitics HEARTGARD® and FRONTLINE® and its established swine vaccine INGELVAC CIRCOFLEX®, which is used to treat porcine circovirus type 2, also played a key role in the success of the company's animal health business.

The biopharmaceuticals business is another important growth area for Boehringer Ingelheim. Boehringer Ingelheim's biopharmaceutical activities comprise the manufacture of own-brand marketable products (such as ACTILYSE®, METALYSE® and PRAXBIND®), and – as one of the world's leading companies – process development and commercial production of biopharmaceuticals for third-party industrial customers.

In the 2018 financial year, Boehringer Ingelheim once again achieved the majority of its sales in the Americas (46%) and Europe (30%) regions. The region of Asia/Australia/Africa (AAA) is of strategic significance for the Group's future growth, making up 24% of its sales. The three biggest markets, the USA, Japan and Germany, accounted for 52% of sales in 2018.

Research and Development

In line with its mission statement, Boehringer Ingelheim's goal is to research and develop innovative medicines and therapies for the treatment of diseases for which there are currently no satisfactory treatments available. The key emphasis here is on developing pharmaceuticals as well as new approaches and therapies to prevent, detect and treat chronic diseases more effectively. We focus on making a major contribution in areas where the need for treatment is high and on taking a leading position in the human pharmaceuticals business as well as in the field of animal health.

Research and development

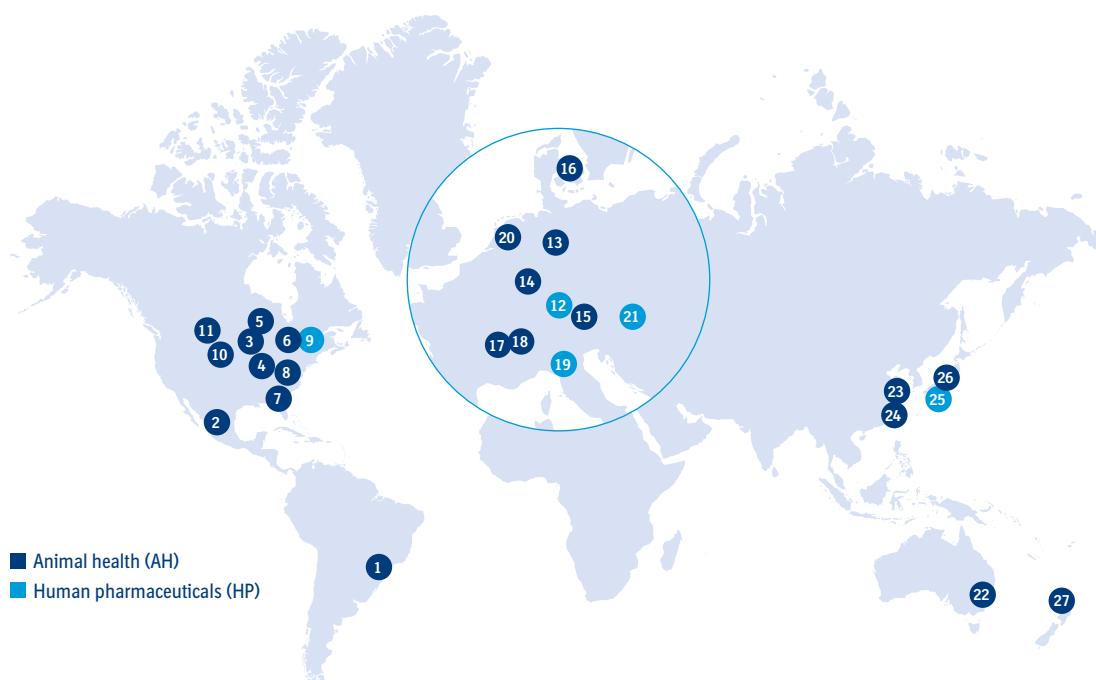
	2018	2017	2016	2015	2014
Expenditure in EUR million	3,164	3,078	3,112	3,004	2,654
– as % of net sales	18.1	17.0	19.6	20.3	19.9
Human Pharmaceuticals expenditure in EUR million	2,780	2,714	2,870	2,780	2,333
– as % of Human Pharmaceuticals net sales	22.1	21.5	23.9	24.8	23.1
Average number of employees	8,566	8,589	8,055	7,895	8,104
Investments in tangible assets (without investments in infrastructure) in EUR million	136	71	92	77	78

We rely on partnerships with academic institutions, other biotech companies, public research institutions as well as a global research network comprising our own facilities in many different countries around the world. Moreover, in the field of development projects and technologies, our research activities are supplemented by important cooperation and licence agreements. Boehringer Ingelheim continued to expand its research network in 2018. Its acquisition of ViraTherapeutics GmbH represents a significant addition in the R&D of immuno-oncological therapies, which are based on the use of oncolytic viruses. In the area of cardiovascular further studies examining the effect of empagliflozin were launched in cooperation with Eli Lilly.

The company's own R&D portfolio, which is already broad, is supplemented by our partnerships. These are a key component of Boehringer Ingelheim's innovation strategy and complement the innovative prowess of our own R&D. They are also evidence of Boehringer Ingelheim's successful collaboration with third parties.

This can also be seen from the online portal opnMe, which gives researchers worldwide the opportunity to order molecules from Boehringer Ingelheim and then to use them without fear of infringing any patents. The researchers have the unique opportunity to start experiments and continue their own research. In addition, joint research projects are being developed from which new findings in drug development can be generated.

R&D SITES



AMERICAS

Brazil

1. Paulínia (AH)

Mexico

2. Guadalajara (AH)

USA

3. Ames (AH)
4. Athens / Colbert (AH)
5. Duluth (AH)
6. Fulton (AH)
7. Gainesville (AH)
8. North Brunswick (AH)
9. Ridgefield (HP)
10. Saint Joseph (AH)
11. Sioux Center (AH)

EUROPE

Germany

12. Biberach (HP)
13. Hanover (AH)
14. Ingelheim (AH)
15. Katharinenhof-Rohrdorf (AH)

Denmark

16. Kalundborg (AH)

France

17. Lyon (AH)
18. Saint Vulbas (AH)

Italy

19. Milan (HP)

The Netherlands

20. Lelystad (AH)

Austria

21. Vienna (HP)

ASIA / OCEANIA

Australia

22. Sydney (AH)

China

23. Shanghai (AH)
24. Taizhou (AH)

Japan

25. Kobe (HP)
26. Tokyo (AH)

New Zealand

27. Auckland (AH)

In the second year of its existence, Boehringer Ingelheim's digital laboratory BI X now has 43 employees. Our experts for digital technologies are currently working on five innovative digital products. Last year, two of these were successfully handed over to their respective business in the past year: PetPro Connect, an app which connects pet owners with vets in the USA, and a collaboration platform for researchers (NTC Studio).

**Digital laboratory BI X
as innovation driver**

Boehringer Ingelheim's R&D activities are the basis for the company's sustainable success. Our innovative capability has played a key role in the Group's positive business development over the past years. In-house R&D – supplemented by external cooperation and partnerships – will also continue to be a top priority in the future.

Respiratory diseases

In the 2018 financial year, we employed an average of 8,566 people at our R&D facilities. A total of almost EUR 3.2 billion was invested in the R&D of new medicines, corresponding to around 18% of the Group's net sales in 2018, which is slightly above the 2017 level, as expected.

Human Pharmaceuticals

Since more than a century, we have been committed to improving the lives of people living with respiratory diseases. The scientific research for new therapeutic concepts to help patients in need continues to be of high importance for Boehringer Ingelheim. In 2018, our focus areas were chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), idiopathic pulmonary fibrosis (IPF), systemic sclerosis with interstitial lung disease (SSc-ILD) as well as other forms of progressive fibrosing interstitial lung diseases (PF-ILD).

Early in 2018, the results of the landmark DYNAGITO® trial were published in The Lancet Respiratory. The data from the 52-week trial show that in people with COPD, tiotropium/olodaterol lowers the rate of moderate-to-severe exacerbations compared to tiotropium monotherapy. These results contribute to our understanding of COPD exacerbations and the role of dual combination bronchodilator LAMA/LABA therapy in the management of COPD. Another focus topic in 2018 was the importance of physical activity for people living with COPD. Here, a number of studies were completed and published which investigated the effect of tiotropium/olodaterol compared to tiotropium monotherapy on physical activity related endpoints. Towards the end of the year, we started to receive the first national approvals for the new and enhanced RESPIMAT® inhaler, which will be launched in the first European countries starting in the first quarter of 2019.

At the European Respiratory Society International Congress 2018, we presented the final data for two important trials in idiopathic pulmonary fibrosis (IPF): the INPULSIS®-ON trial and the INSTAGE® trial. The results of INPULSIS®-ON indicate that safety and efficacy of nintedanib in IPF are maintained over more than four years and are consistent with prior findings from the INPULSIS® study programme. The INSTAGE® trial showed that efficacy and safety of nintedanib in patients with IPF and severe impairment in gas exchange, which are usually excluded from clinical trials, was consistent with that observed in patients with less advanced disease in earlier trials. Both trials were published in high-ranking medical journals (The Lancet Respiratory and The New England Journal of Medicine, respectively). In addition to communicating the new scientific data, a key effort in 2018 was to raise awareness for the need to diagnose and treat IPF as early as possible together with various stakeholders and partners as this remains a key challenge for affected patients.

In 2018, Boehringer Ingelheim became a founding member of the Open Source Imaging Consortium (OSIC), a statement of our commitment to advancing science and supporting innovation for the benefit of patients. The goal of OSIC is to develop digital imaging biomarkers for accurate imaging-based diagnosis, prognosis and prediction of response to therapy in IPF and other fibrosing interstitial lung diseases (ILDs).

In scleroderma (systemic sclerosis, SSc), we continued our efforts to support patients and create awareness for this rare disease with our “More than Scleroderma” campaign. The SENSICIS™ trial investigating the safety and efficacy of nintedanib in patients with systemic sclerosis-associated ILD has been completed. With more than 520 patients recruited, it is the largest randomised and placebo-controlled clinical trial in SSc to date. The results will be presented in 2019.

The INBUILD trial evaluating the efficacy and safety of nintedanib over 52 weeks in patients with Progressive fibrosing interstitial lung disease (PF-ILD) is ongoing. This trial includes a range of patients who have been diagnosed with interstitial lung disease except IPF but exhibit a similar progressive fibrosing phenotype, i.e. deterioration of respiratory symptoms, lung function or worsening of fibrosis on chest imaging, irrespective of the underlying diagnosis. This unique “basket” approach makes INBUILD the only trial including patients with different underlying diseases as varied as chronic hypersensitivity pneumonitis, rheumatoid arthritis associated ILD and sarcoidosis. The approach is based on the underlying hypothesis that the response to lung injury in some of these patients includes the development of fibrosis, which becomes progressive and self-sustaining independent of the initiating trigger. The results are expected in the course of 2019.

At Boehringer Ingelheim, we are committed to fighting cancer to provide patients with new treatment options. We are dedicated to collaborating with the oncology community on a shared journey to deliver leading science. Our goal is first-in-class treatments with breakthrough potential that can transform the lives of patients and help win the fight against cancer. Our focus is on discovering, developing and accelerating novel therapeutic approaches that address unmet needs in lung and gastrointestinal cancers. To this end, we are conducting targeted research into therapies, immuno-oncology products and intelligent combination approaches that offer the greatest chance of success in the fight against cancer. In 2018, we have successfully advanced several of our research programmes into clinical development.

Oncology

To further strengthen our oncology portfolio, we are actively seeking for scientific collaborations, innovative partnerships and strategic acquisitions with the goal to improve our understanding of cancer and transform patient lives. Our commitment to innovation has already resulted in important treatments for lung cancer, afatinib (GIOTRIF®/GILOTRIF®) and nintedanib (VARGATEF®).

Afatinib (GIOTRIF®/GILOTRIF®), a second-generation EGFR inhibitor for the treatment of a specific type of non-small cell lung cancer (NSCLC) patients and metastatic NSCLC of squamous histology, has been available to patients since 2013 and has become the standard of care in many markets in the approved indications. The results of GioTag, a real-world study to investigate how the use of front-line afatinib, followed by the next-line targeted treatment can extend the chemotherapy-free treatment time for patients, were first published in 2018. The study shows that using afatinib (GIOTRIF®/GILOTRIF®) followed by osimertinib, a third-generation EGFR inhibitor, provides a median of 27.6 months of chemotherapy-free regimen in patients with EGFR mutation-positive NSCLC. These results add to the comprehensive ‘LUX-Lung’ trial programme for afatinib of nine trials including head to head randomised trials versus first-generation treatments.

Boehringer Ingelheim’s second marketed cancer drug is VARGATEF® (nintedanib) for the treatment of advanced non-small cell lung cancer (NSCLC) in combination with docetaxel in patients who were previously treated with chemotherapy. In December 2018, results from the real-world study VARGADO showed that nintedanib plus docetaxel could be an option after failure of immunotherapy in these patients. Nintedanib in combination with chemotherapy was also investigated in patients with malignant pleural mesothelioma (MPM) of epithelioid histology, a rare and aggressive type of cancer that is

strongly associated with exposure to asbestos. The data from the respective phase III trial, LUME-Meso, were presented in 2018 and showed that nintedanib in combination with standard chemotherapy did not extend the progression-free survival of patients with MPM.

Cardiovascular and metabolic diseases

Boehringer Ingelheim's therapeutic area of cardiovascular and metabolic diseases contains some of the company's core products.

Within the diabetes portfolio, and specifically with JARDIANCE® (empagliflozin), important research data were published and a range of new clinical trials and collaborations were announced in 2018.

In March, Boehringer Ingelheim and diabetes alliance partner Eli Lilly announced plans to expand the clinical trial programme for empagliflozin in chronic heart failure with the EMPERIAL trials. These trials will evaluate the effect of empagliflozin on exercise ability and heart failure symptoms in people with chronic heart failure independent of whether they have type 2 diabetes.

In April, the diabetes alliance initiated EMPA-KIDNEY. The clinical trial investigates the effects of empagliflozin on the progression of kidney disease and the occurrence of cardiovascular death in people with established chronic kidney disease, with and without diabetes. The study will be independently conducted, analysed and reported by the Medical Research Council Population Health Research Unit at the University of Oxford (MRC PHRU). In summer of 2018, data from the EASE phase III programme investigating the use of empagliflozin in combination with insulin therapy in adults with type 1 diabetes were published. Both randomised controlled trials met their primary endpoint. Based on the totality of the EASE data, Boehringer Ingelheim has initiated regulatory discussions for empagliflozin as adjunct to insulin for adults with type 1 diabetes. The European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion in July to update the labels of JARDIANCE® (empagliflozin), SYNJARDY® (empagliflozin and metformin) and GLYXAMBI® (empagliflozin and linagliptin) to include additional important data from the landmark EMPA-REG OUTCOME® trial on heart failure and kidney endpoints. The labels now also include results on the relative risk reduction in hospitalisation for heart failure by 35% and the relative risk reduction for new-onset or worsening of kidney disease by 39% with empagliflozin, compared with placebo, in people with type 2 diabetes and established cardiovascular disease.

At the European Association for the Study of Diabetes (EASD) congress in October, results from CARMELINA®, the first of two cardiovascular outcome trials for the DPP-4 inhibitor linagliptin (TRAJENTA®), were presented. CARMELINA® studied the impact of linagliptin on cardiovascular and kidney safety in adults with type 2 diabetes at high risk for heart and/or kidney disease. The study met its primary endpoint, with linagliptin demonstrating a similar cardiovascular safety profile compared to placebo when added to standard of care. CARMELINA® also included a key secondary composite endpoint, showing a similar kidney safety profile compared to placebo. The results of the second cardiovascular outcome trial CAROLINA® are expected for 2019. CAROLINA® evaluates the impact of treatment with linagliptin compared to the sulphonylurea, glimepiride, on top of standard of care, on cardiovascular safety in patients with early type 2 diabetes and increased cardiovascular risk or established cardiovascular complications.

Shortly after the EASD congress the American Diabetes Association (ADA) and the EASD published a Consensus Report recommending SGLT2 inhibitors, such as empagliflozin, to help manage cardiovascular outcomes in patients with type 2 diabetes. Empagliflozin is the only SGLT2 inhibitor recommended in the ADA 2018 Standards of Medical Care in Diabetes for reducing the risk of cardiovascular death in people with type 2 diabetes and established cardiovascular disease. Following this announcement, the American College of Cardiology (ACC) published a new Expert Consensus Decision Pathway (ECCDP) also recommending empagliflozin as the preferred SGLT2 inhibitor for its proven benefit in reducing the risk of cardiovascular death in adults with type 2 diabetes and established cardiovascular disease. Worldwide, more than 50 treatment guidelines have now been updated to include findings from the EMPA-REG OUTCOME TRIAL® in their endorsement of type 2 diabetes treatments with proven cardiovascular benefits.

In October 2018, the journal *Circulation* published an analysis based on data from the EMPA-REG OUTCOME® trial which suggests that treatment with empagliflozin positively impacts life expectancy in adults with type 2 diabetes and established cardiovascular disease. Using actuarial methods, and assuming that the demonstrated beneficial effects of empagliflozin remain consistent with long-term use, empagliflozin was estimated to extend life expectancy by 1 to 4.5 years on average, depending on age, when compared with placebo.

At the American Heart Association (AHA) Scientific Sessions in November, initial effectiveness results from the first real-world evidence study with empagliflozin (EMPRISE) were presented, reinforcing the clinical results from the landmark EMPA-REG OUTCOME® trial.

Finally, to conclude a highly successful year for the diabetes products, JARDIANCE® (empagliflozin) was awarded the 2018 International Prix Galien “Best Pharmaceutical Product” award – the most prestigious honour in the field of pharmaceutical research and innovation, recognising the outstanding efforts and achievements of pharmaceutical R&D.

It was also a successful year for PRADAXA®. In October, the company presented primary results from two key trials, RE-SPECTESUS® and RE-SPECT CVT® at the World Stroke Congress in Montreal, Canada. RE-SPECTESUS® was the first trial to investigate dabigatran etexilate versus acetylsalicylic acid (ASA). Full results of both trials are expected to be published in 2019. Both primary analyses will contribute to the scientific community’s understanding of the diseases and add to the wealth of evidence supporting the established safety profile of PRADAXA®.

Some of the most important neuropsychiatric diseases, such as Schizophrenia or Alzheimer’s disease as well as depression, continue to be the centre of Boehringer Ingelheim’s research in central nervous system diseases. Many companies and institutions have pulled out of CNS projects in the past years, the reason being that for many players in the field, setbacks seem to be more frequent than successes. At Boehringer Ingelheim, we remain true to our motto “#Commitment Never Stops” and we are optimistic that we can develop effective therapies for the treatment of neuropsychiatric diseases.

Diseases of the
central nervous
system (CNS)

In such highly complex diseases like Schizophrenia, we focus on investigating the impaired glutamatergic signalling pathway present in a range of CNS diseases. Based on findings from a clinical trial in schizophrenia, we are investigating in particular how a specific mechanism of action could be used to prevent further deterioration after a first psychotic episode and to prevent relapses in schizophrenia.

Studies on the effect of GlyT1 inhibition on cognitive impairment in Alzheimer's disease and Schizophrenia are on track and we expect phase II clinical results within 2019.

Beyond that, clinical trials in depression investigating the effect of a substance that should influence the hyperactivity of certain brain regions, which are responsible for the impaired processing of negative stimuli, were started. Further substances are being investigated in earlier stages of development.

Immunology

Boehringer Ingelheim has been continuously developing its immunology R&D activities for some years now and is ramping up its capacities for a series of dermatological and gastroenterological indications.

Initial clinical testing results published in September 2018 in the field of dermatology suggest positive therapeutic potential for the active substance BI 655130, an interleukin 36 receptor antagonist, for a rare form of psoriasis known as generalised pustular psoriasis. Patients with these and other clearly visible inflammatory skin diseases, such as palmoplantar pustulosis (PPP) or neurodermitis (atopic dermatitis), frequently face considerable disruptions in their lives since these skin changes are not only painful, but also visible.

These and a series of other active substances, such as an ROR-gamma inhibitor, are currently at the clinical development stage and are showing initial signs of offering strong therapeutic potential for patients with various immunological diseases. Boehringer Ingelheim's development programme includes substances for the treatment of chronic inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, and also lupus nephritis, for which there is a strong and as yet unmet medical need for more effective therapies.

Last year, the development of the substance risankizumab for the treatment of psoriasis, which originally resulted from our research activities, was completed in partnership with AbbVie. AbbVie has now submitted this substance to the regulatory authorities. This development and marketing partnership with AbbVie offers the best means of ensuring that the first interleukin inhibitor to emerge from Boehringer Ingelheim's research programme can be made available to the greatest possible number of patients.

With its broad-based pipeline and its substantial investments in immunology, Boehringer Ingelheim expects to significantly contribute to the better treatment of patients with immune diseases in the foreseeable future and will assume sole responsibility for development and marketing activities.

Animal Health

In its R&D work in the field of animal health, Boehringer Ingelheim concentrates on innovative vaccines and antiparasitics for the protection of livestock and pets, as well as on pharmaceutical products for the treatment of chronic diseases.

At our facilities in Europe, Asia, Oceania and North, Central and South America, we focus on research into new drugs and the development of future therapeutic solutions. Since many vaccines are based on local pathogens and pathogen variants, it is imperative that we are present in all key market regions with local R&D and production facilities.

In the past year, we invested approximately EUR 38 million in new R&D plants and the expansion of existing facilities. In Lyon Porte-des-Alpes, France, we completed the construction of a EUR 70 million research building for over 200 employees, in order to bring our R&D activities and vaccine production together at a single facility. Another milestone was the spatial consolidation of our research activities in China through a EUR 19 million investment in the expansion of our research centre there. These investments demonstrate our commitment to strengthen animal health by means of innovative, preventive medicines and our intention to sustainably expand our leading position in this field.

In 2018, we initiated more than 400 clinical studies worldwide and received more than 300 product authorisations. In addition to our internal R&D, we analyse external projects or products and integrate them in our portfolio where appropriate. Obtaining approvals and expanding the geographical distribution of existing products are other important aspects of our R&D activities.

Biopharmaceuticals

In 2018, we decided to pursue our biosimilars activities, including potential partnerships, within the US market and to end development activities for other markets. We are concentrating on launching our approved biosimilar CYLTEZO® (adalimumab-adbm) on the US market.

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 (AH)
7. Columbus (HP)
8. Fremont (Bio)
9. Gainesville (AH)
10. St. Joseph (AH)

EUROPE

Denmark

11. Kalundborg (AH)

Germany

12. Biberach (HP, Bio)
13. Dortmund (HP)
14. Ingelheim (HP)

France

15. Lyon (AH)
16. Saint-Herblon (AH)
17. Toulouse (AH)

Greece

18. Koropi (HP)

Italy

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

The Netherlands

21. Lelystad (AH)

Austria

22. Vienna (Bio)

Spain

23. Malgrat (HP)
24. Sant Cugat (HP)

United Kingdom

25. Pirbright (AH)

ASIA / OCEANIA

China

26. Nanchang (AH)
27. Shanghai (HP, Bio)
28. Taizhou (AH)

Indonesia

29. Bogor (HP)

Japan

30. Yamagata (HP)

New Zealand

31. Auckland (AH)

Production

Human Pharmaceuticals

In the Human Pharmaceuticals business, production is responsible for the reliable supply of innovative, top-quality medicines at competitive prices for patients and customers. 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 distribution of finished pharmaceutical products.

In 2018, this global network included 20 of Boehringer Ingelheim's own plants in 10 countries. The group now has four biopharmaceuticals facilities. It also has three plants for the manufacture of active pharmaceutical ingredients as well as 13 plants which manufacture finished pharmaceutical products. Boehringer Ingelheim's own production facilities concentrate on products which are of strategic importance for the company as well as state-of-the-art and in some cases unique manufacturing technologies. Partnerships with external manufacturers expand production capacities and focus on products which are already far advanced in terms of their life cycle.

Within the scope of the company's redesigned network, the increasing amounts produced for the company's antidiabetic product portfolio have now been transferred to facilities throughout the world, which are thus assuming an increasingly important role. For instance, production capacity has been increased for active pharmaceutical ingredients in Forno (Italy) and for finished pharmaceutical products in Koropi (Greece) and Xochimilco (Mexico). The company also initiated additional important investments in the development and transformation of capacities in its internal and external network. At its Ingelheim headquarters, the company began to implement a key investment in the industrialisation of newly developed medicines and the initial market supply of these medicines. At its Sant Cugat facility in Spain, the company made further progress in the construction of a plant to supply the market with RESPIMAT® technology-based inhalation medicines. At the same time, with the end of the product life cycle for AGGRENOX® the company closed its Biberach site's dedicated production plant.

Alongside the continued development of the company's production network, the ongoing development of its value chain management is another current area of focus. The implementation of the company's supply chain strategy has set in motion a process of transformation spanning the entire value chain, from the supplier to the customer ("end-to-end"). The goal is a highly integrated and flexible delivery chain which is fully transparent and can be efficiently controlled through modern digital technology.

Animal Health

Following the acquisition of Merial in 2017, teams from the two companies have been working together to create an environment that promises future success. In 2018, Boehringer Ingelheim Animal Health operated a network of 16 facilities in 11 countries which are dedicated to the manufacture of vaccines, finished pharmaceutical products and nutraceuticals. This industrial set-up is complemented by contract manufacturers, primarily in North and Central America as well as in Europe. We have defined a new network strategy in order to balance internal and external production subsequently to the integration of Merial and focus on core products in full alignment with business requirements. In addition to our production facility in Paulínia (Brazil), in the past year we invested in a new production line for our strong revenue contributor NEXGARD® at our Barceloneta (Puerto Rico) facility. Moreover, our production of vaccines for the foot-and-mouth disease has been expanded at a global level. Boehringer Ingelheim established a collaboration with two Chinese partners, aiming for the triplication of production of the much sought-after vaccine.

20

facilities in
10 countries for human
pharmaceuticals

16

Animal Health facilities
in 11 countries

One of the leading
companies for
industrial customers

Biopharmaceuticals

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 and – as one of the world’s market leaders – process development, launch preparation and commercial production of biopharmaceuticals for third-party industrial customers. 15 out of the top 20 pharmaceutical companies and innovative biotech firms are clients of Boehringer Ingelheim’s biopharmaceuticals business. Boehringer Ingelheim covers the entire biopharmaceutical value chain, from genetic development of the production cell, followed by manufacturing the active substance and filling the finished pharmaceutical product, down to the product launch and the global market supply.

2018 saw an overall increase to almost full use of capacity at its network of industrial-scale production facilities. Besides many other products, Boehringer Ingelheim fulfilled at its Biberach (Germany) facility the increasing level of market demand for ACTILYSE® for the Chinese market in particular. At the company’s facility in Fremont, California (USA), a third large-scale bioreactor was launched in 2018 and the market product of a customer was transferred. It will thus be possible to meet rising product demand within the network from both Biberach (Germany) and Fremont, California (USA). Moreover, at our large-scale cell culture plant in Biberach (Germany) and our large-scale microbial plant in Vienna (Austria), two further customer products were successfully approved by the international authorities. The expansion project (a new industrial-scale biopharmaceutical production facility) at Boehringer Ingelheim’s site in Vienna (Austria) reached a further milestone, as the topping-out ceremony for this facility took place in the autumn of 2018. The company’s commercial filling facility in Shanghai (China) was also successfully put into operation. For the local market and countries outside China, production and delivery began as scheduled, from GMP hospital products to finished pharmaceutical products. In addition, an application for approval of a customer product by the Chinese authorities was successfully completed. This was another important milestone in terms of the Chinese authorities’ recognition of our Shanghai facility as a contract manufacturer (CMO).

Occupational safety and environmental protection

The protection of the employees and the environment, as well as the sustainable use of natural resources and the promotion of environmental awareness, are major components of our group’s mission statement and are of prime importance to Boehringer Ingelheim. Compliance with social and environmental aspects has been firmly anchored in our corporate philosophy for many years now to ensure that we can achieve sustainability for future generations.

Group-wide, we have long established binding standards in terms of environmental protection and health and safety at work. These internal guidelines reflect the respective country-specific requirements. In many cases, they go far beyond the standards prescribed by law. In particular, we follow international standards and guidance documents and work in close cooperation with the relevant associations. Within Boehringer Ingelheim, the corporate department Environment, Health, Safety & Sustainability (EHS&S) is responsible for this particular strategic focus.

For Boehringer Ingelheim, 2018 continued to be characterised by the integration of Sanofi's animal health division (Merial) into our Group. In addition to safety and environmental risk assessments for the new facilities, integration audits were implemented and a training platform ("EHS Academy") was established in order to provide our employees with EHS&S training and develop their awareness of this field.

Technical support and regular EHS&S audits, both at Boehringer Ingelheim's internal facilities and at the premises of suppliers and contract manufacturers, ensure compliance with our own as well as international standards. The company continuously reviews the status of environmental protection and health and safety at work. Potential for improvement is identified on this basis.

To us, close coordination with stakeholders both within and outside the company is extremely important in advancing current topics that are relevant to our company. We are taking a stand and are formulating related position papers in order to achieve continuous and sustainable improvements worldwide, for the sake of our company. These topics range from the use of improved refrigerants and the use of certified natural resources to the careful handling of plastics.

Boehringer Ingelheim supports the United Nations (UN) sustainable development goals (SDGs) as well as the development of corresponding ISO standards, and is making its own contribution to sustainability. At the 24th UN Climate Change Conference in Katowice, Poland (Conference of the Parties, COP24) in 2018, EHS&S representatives of Boehringer Ingelheim participated once again.

As our contribution towards reducing global greenhouse gas emissions, we continue to pursue the goal of reducing our entire CO₂e emissions by 20% by 2020 as compared with 2010 values. To achieve this goal and make further future-oriented reductions in our environmental footprint overall, our international BE GREEN initiative has been stepped up and further activities are planned.

The roll-out of the BE SAFE safety initiative, which aims to further reduce the number of workplace accidents, also continued in 2018. Successful workshops with a focus on behaviour-based safety were held at several of the company's worldwide facilities. The "High Five for Safety" initiative defines five simple rules of behaviour which shall ensure improved occupational safety.

Activities for further
CO₂ reduction

760
additional employees
in 2018

Employee reporting

In 2018, Boehringer Ingelheim employed 50,370 people on average worldwide. This represents an increase of 1.5% on the previous year. The number of staff increased in all of its regions.

Average number of employees by region

	2018	2017
Americas	12,986	12,890
Europe	26,758	26,300
Asia/Australia/Africa (AAA)	10,626	10,420
	50,370	49,610

A major success factor for the positive growth of the Group is its engaged and motivated staff. Accordingly, we are particularly committed to actively developing and supporting our employees. In order to be best prepared for the challenges ahead and as part of a comprehensive training system, we emphasise the acquisition of technical expertise and also promote social skills.

With the integration of various experiences, cultural backgrounds and personalities, Boehringer Ingelheim creates an openness to different approaches and opinions, living up to its corporate vision “Value through Innovation”. As a global company, it is important to us that the diversity of the markets is reflected in our workforce. Creating a working environment that embraces diversity and differences is one of the pillars of the corporate culture of Boehringer Ingelheim and is a contributing factor to the company’s success.

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. As a significant segment of our corporate strategy, it is part of our Talent Management department’s remit to ensure the employability of our staff, promote a wide range of opportunities for innovation at work, and motivate our employees to nurture their own talents and develop as individuals.

631
apprentices
in Germany

Vocational training has always been of major importance to Boehringer Ingelheim. As part of its understanding of social responsibility, the company offers career opportunities to a great number of young people. At the same time, we also tie a talented and well-qualified workforce of young professionals to the company against a backdrop of demographic change. In 2018, 204 young professionals started their careers with Boehringer Ingelheim in Germany in over 25 different scientific, technical and commercial fields, in training and dual-study courses. As of 31 December 2018, 631 young people were enrolled on our vocational training programme in Germany.

One of the company’s aims is to strengthen the appeal of Boehringer Ingelheim as a top employer for our current and future employees. Boehringer Ingelheim was the recipient of various awards for its efforts in this area in 2018. We received top marks from the auditors of the international, independent Top Employers’ Institute in the categories of salaries (“Compensation & Benefits”) and employee development (“Performance Management”). We received this distinction for our facilities in Germany as well as for our facilities in China, Taiwan, Brazil, Russia, Spain, Poland and for the first time, Singapore. The number of country organisations that were awarded this rating was unprecedented. This is

evidence of the strong appeal and development opportunities at our company – both for employees and for potential recruits.

Social responsibility

Taking social responsibility is also an important aspect of our corporate culture. Our commitment to the well-being of our patients, employees and their families is the focus of a range of projects. In addition, we support people in need through various initiatives in countries and regions where we are active as a company. All of our company's activities also focus on protecting and maintaining the environment.

As in previous years, Boehringer Ingelheim continues to assist in providing support and in the integration of people who have fled their home country. It pursues a broad range of measures in this area: Boehringer Ingelheim employees in Germany are conducting workshops for refugees. In addition, the company has a partnership with the Deutsche Universitätsstiftung. Through this partnership, Boehringer Ingelheim sponsors the WELCOME scholarship programme, which supports students from crisis regions. The company also helps candidates from crisis regions and areas people are fleeing from to join our company by offering them apprenticeships or the opportunity to complete an introductory training year or an internship. Upon successfully completing internships, employees were once again offered permanent positions in the past year.

A major pillar of our social commitment is our Making More Health (MMH) initiative. Since its start in 2010, this has continuously developed as a social entrepreneurship movement, both within our company and externally. Socially entrepreneurial and sustainable activities are not limited to individual projects relating to various regions and issues. Instead, this initiative focuses on creatively connecting with local and international partners from different sectors. Networking across all traditional visible and invisible borders is a central element of a successful social movement, in order to identify, promote and implement innovative solutions for far-reaching and complex challenges in the health care sector. "Co-creation" as a bridge between social and commercial entrepreneurship brings together social entrepreneurs and non-profit organisations from the health care sector with Boehringer Ingelheim employees and their resources. To date, within the MMH network, Boehringer Ingelheim and Ashoka – one of the world's largest non-profit organisations – have together helped around 90 social entrepreneurs to reach approximately 9 million people worldwide in the area of health care.

Making More Health as
worldwide initiative

The MMH initiative also aims to promote employees' commitment to social entrepreneurship in order to advance health care projects in many different countries, by working with local, external partners as well as colleagues from throughout Boehringer Ingelheim. MMH leadership programmes in rural southern India (Insights India); participation in online social intrapreneurship courses; opportunities to collaborate with social entrepreneurs in our MMH network as Executives in Residence; and an internal competition promoting employees' own projects have honed our staff's social entrepreneurial thinking and activities. We have also strengthened our networking philosophy through partnerships with non-profit organisations and social enterprises in the health care sector. A large number of local projects have taken place in which our employees are actively involved. Above all, improving health means understanding people's environment and their everyday challenges and offering solutions where they are needed. Health awareness, affordability, accessibility of health services and acceptance play a key role here. MMH plays a role in the university sector, with the goal of helping students and lecturers to learn more about socially entrepreneurial thinking and practical activities through the development of health care-related projects.

With the Angels Initiative, together with the European Stroke Organisation (ESO), the World Stroke Organisation (WSO), the Stroke Alliance for Europe (SAFE) and many other national stroke associations and companies, Boehringer Ingelheim has established a unique health initiative. The goal of this initiative is to improve stroke care in Europe and in emerging markets. More than 2,500 hospitals are already part of the Angels Initiative. In November 2018, this initiative received the prestigious “Health Collaboration” award in the “Service Delivery” category from the European Federation of Pharmaceutical Industries and Associations (EFPIA).

In 2018, Boehringer Ingelheim established and introduced a “LastMile” programme with support from the Global Alliance for Livestock Veterinary Medicines (GALVmed) and funding from the Bill & Melinda Gates Foundation. This integrated, solution-oriented initiative aims to respond to critical challenges in the field of animal health by ensuring the consistent availability of medical resources for animals in hard-to-access areas of sub-Saharan Africa. This initiative currently focuses on ruminants such as sheep, goats and cattle but is to be expanded to include poultry. Through this project, Boehringer Ingelheim helps small farmers in Africa to gain access to veterinary medicines. This underlines Boehringer Ingelheim’s strong social commitment: we aim to have a positive impact on human and animal lives in areas where there is a particularly vital need for this.

Boehringer Ingelheim values and respects its employees’ differences and actively promotes a diverse, cooperative and open working environment. We are conscious of the fact that the diversity of our markets and customers has to be reflected in our workforce. For us, diversity makes for the right mix, but it is inclusion which brings out the best results from this mix. We therefore focus on encouraging an inclusive environment where this kind of diversity can thrive. Boehringer Ingelheim participated in the 6th German Diversity Day under the motto “Fly the Flag for Diversity” at its two largest German facilities, Ingelheim and Biberach. It has been an official member of the “Diversity Charter” since early 2016 and a PROUT EMPLOYER acknowledged by the PROUT AT WORK foundation since 2017.

REPORT ON ECONOMIC POSITION

Macroeconomic environment

In line with 2017, an worldwide economic growth rate of slightly below 4% was likewise registered in 2018. In the eurozone, economic output grew less strongly than in 2017, while the growth rate for the emerging markets and developing countries was on the same level as in the previous year, slightly below 5%. Due to the growth slowdown in the major economies a reduction in global growth is expected over the next few years. The continuously expanding emerging markets and developing countries will be unable to make up for this.

In the USA, as a result of increasing private consumption as well as investments in intellectual property and production wells in the oil and gas industry, the second-longest growth phase of the past 160 years continued. Strongly expansionary fiscal policy in the form of a tax reform at the start of 2018 also stimulated economic output, while at the same time increasing the funding deficit. The tariff increases resolved by the USA at the start of 2018, and the counter-tariffs introduced by the affected trading partners in response, had a negative impact on economic growth, although the economic repercussions were relatively limited due to the low proportion of overall trade volume.

Japan, the world's third-largest economy, recorded a decline in its gross domestic product in the first quarter of the year, despite its consistently low unemployment rate. This followed eight consecutive quarters of growth. Nevertheless, the economy managed to grow throughout the year, however, not as strongly as in 2017. This is attributable to the high rate of utilisation of existing capacities as well as a decrease in the growth of exports.

The Chinese economy continues to undergo a process of structural transformation, whereby the service sector is asserting itself in comparison with the manufacturing sector. The Chinese economy's rate of growth remains strong, driven by the government's high growth targets. However, it has weakened slightly compared with the previous years. This is also attributable to restrictive market access conditions for foreign companies in China, as well as external trade and political tensions with the USA.

Economic performance steadily increased in the Asian region as a whole due to strong economic growth in the emerging markets and developing countries in particular. On a global scale however, some emerging markets and developing countries provided grounds for concern. In Argentina and Turkey, relatively serious current account deficits, significant debt levels and high inflation rates triggered a devaluation of these countries' currencies. However, this has so far been limited to these countries, since other emerging markets hold high foreign currency reserves.

In terms of economic momentum, the eurozone recorded a negative development in 2018. This was due to an attenuation of foreign trade, which ended the export-driven boom of the past few years for now. A lack of qualified personnel and technical capacities resulted in supply-side bottlenecks in manufacturing industries in particular. In addition, factors such as the ongoing discussion over the introduction of tariffs on certain product groups as well as the EU's post-Brexit economic relationship with the United Kingdom negatively affected sentiment in the eurozone. On the other hand, the unemployment rate remained unchanged in the eurozone, despite the economic downturn. Inflation picked up over the course of the year due to rising energy prices and wage costs.

The German economy continued to grow over the past year, though this trend weakened appreciably from the summer to the end of the year. Reasons for this included production losses due to strikes and illness as well as problems in the German automotive industry. The weaker level of demand in the eurozone and the world economy's loss of impetus present enduring problems. These are having an additional adverse effect on foreign demand, which has already been negatively affected by economic conditions.

Inflation in Germany averaged 1.9% in 2018 and was thus close to the ECB's target level of 2%. Prices increased strongly compared with previous years due to an above-average increase in the price of food and luxury food items such as tobacco and beer, and sharply increased prices of heating oil and petrol.

The global economic upturn is expected to weaken in 2019. On the one hand, this reflects the fact that many of the advanced economies have already exhausted their production capacities and are also experiencing recruitment difficulties. On the other hand, it is expected that the USA's restrictive monetary policy will result in significantly worse financing terms in Latin America, which will decelerate the pace of economic growth. In addition, the positive effect of the USA's tax reform will gradually recede into the background.

Currency development

Average rate - basis: EUR 1	2018	2017	Effect on net sales (in EUR million)
USD	1.18	1.13	– 300
JPY	130.41	126.66	– 45
CNY	7.81	7.63	– 14
GBP	0.88	0.88	– 5
CAD	1.53	1.46	– 15
BRL	4.31	3.60	– 68

The global pharmaceuticals market registered growth of 5% in the 2018 financial year (IQVIA: The Global Use of Medicine in 2019 and Outlook to 2023). This trend was driven by rising demand in the industrialised countries for cancer medicines, products for the treatment of autoimmune diseases and anti-diabetic medicines. Due to the ageing population in the industrialised countries, the industry's growth remained stable and surpassed the growth of the previous year 2017.

Earnings position

Long-term and sustainably successful development forms the basis for securing the company's independence over the long term. Combined with stable earnings and sound financing, this is at the core of Boehringer Ingelheim's strategic focus. As in previous years, we based our approach on these principles.

Boehringer Ingelheim recorded net sales of EUR 17,498 million in the 2018 financial year, which corresponds to a decrease of 3.1% as compared with the previous year's level of EUR 18,056 million. The exchange rate developments on the foreign exchange markets and the associated exchange rate effects had a negative impact on sales growth in the biggest markets.

EUR
17.5
billion net sales

Currency adjusted, the Group's growth rate stood at + 0.6%. Leaving aside the discontinued operations (interim contracts and agreements which were signed in early 2017 following the exchange of businesses with Sanofi) which had contributed significantly to sales in 2017, operating sales from the company's core business areas – adjusted for currency effects – grew by 4.0%.

With sales of EUR 8,088 million and a share of around 46% of overall sales, the Americas region remains Boehringer Ingelheim's key sales market. The slight decline in sales resulted from negative currency effects in North and South America, which ordinary sales growth in North America could not offset. On a currency-adjusted basis, sales in the Americas region increased by 5.6% as compared with the previous year. The Europe region registered net sales of EUR 5,316 million and thus contributed 30% of the Group's net sales. This corresponds to a 6.6% decline in sales compared with 2017. This decrease was largely a consequence of lower than previous-year sales from discontinued operations. Currency effects had no significant impact here. The Asia/Australia/Africa (AAA) region realised only a slight growth of 0.5% on a currency-adjusted basis, as net sales declined particularly in Japan. Net sales of EUR 4,094 million were achieved in this region, corresponding to a share of almost 24% of the Group's total revenues.

Net sales by region (in EUR million)

	2018	2017	Change	currency adjusted
Americas	8,088	8,141	-0.7%	+5.6%
Europe	5,316	5,690	-6.6%	-6.0%
Asia/Australia/Africa (AAA)	4,094	4,225	-3.1%	+0.5%

In general, sales growth conformed to expectations. Supported by good results from clinical trials as well as by our external partners, we have been able to place promising new products on the market and successfully push ahead with well-established products. On the other hand, we are experiencing an increasingly difficult market situation with constantly challenging market access and growing price pressure in our key markets. Overall, the company has asserted itself well despite the difficult conditions and has laid the foundations for future growth.

The materials ratio (taking into consideration the change in inventory) has improved to 16.1% (2017: 20.9%). This resulted from the negative impact in the previous year of sales from the Merial companies' inventories which were assessed at market value. In addition, the relatively low-margin service and production agreements from discontinued operations (consumer health care business) was no longer included. Personnel expenses increased due to the increased number of employees, plus expenses for pension plans and similar obligations. Depreciation and amortisation also increased. This was mainly attributable to the write-down on intangible assets in the animal health business as well as impairment losses on tangible assets in France and Spain. In 2018, the operating income included extraordinary effects which totalled EUR – 420 million (2017: EUR – 309 million), mainly due to restructuring measures and integration costs. Overall, despite the positive operating trend for our core business, operating income was thus in line with the previous year's level which, considering extraordinary effects, met our expectations. Boehringer Ingelheim recorded an operating income of EUR 3,472 million, corresponding to a return on sales of 19.8%, which is 0.5 percentage points above the previous year's return on sales.

Key figures (in EUR million)	2018	2017	Change
Net sales	17,498	18,056	– 3.1%
Operating income	3,472	3,487	– 0.4%
Return on net sales	+ 19.8%	+ 19.3%	
Income before taxes	3,176	2,856	+ 11.2%
Income after taxes	2,075	– 229	n.a.

Income before taxes increased by EUR 320 million or 11.2%, mainly due to improved holding income. The financial result reflects increased interest expenses due to pension commitments and similar obligations as well as losses from plan assets; in the previous year, it included gains from plan assets. The other financial result improved.

While tax expenses in 2017 were negatively affected by significant extraordinary effects resulting from the disposal of the consumer health care business as well as the tax reform in the USA, these negative factors were no longer applicable in 2018. We can therefore report a clearly positive income after tax once again.

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 recognised as tax expenses. Instead, these taxes are presented as part of withdrawals from Group equity. Taking this specificity into account, the actual tax ratio is markedly higher than the figure shown in the profit and loss statement.

EUR
2.1
billion income
after taxes

Despite difficult market conditions and adverse currency effects, Boehringer Ingelheim registered a positive development of the operating business in the 2018 financial year. Following the previous year, which was shaped by integration processes and extraordinary tax effects, we concluded the past year with income after taxes of EUR 2,075 million (2017: EUR – 229 million).

Development of the businesses

In the past financial year, Boehringer Ingelheim's business activities were divided into the areas of Human Pharmaceuticals, Animal Health and Biopharmaceuticals.

Net sales by businesses (in EUR million)

	2018	2017	Change	currency adjusted
Human Pharmaceuticals	12,559	12,621	-0.5%	+3.3%
Animal Health	3,960	3,901	+1.5%	+5.6%
Biopharmaceuticals	734	678	+8.3%	+8.3%
Other sales	40	43	-7.0%	-4.3%
Discontinued Operations	205	813	-74.8%	-73.1%

Human Pharmaceuticals

With around 72% of total Group revenue, Human Pharmaceuticals is the main pillar of Boehringer Ingelheim's business activities. Net sales from this business amounted to EUR 12,559 million in 2018. This is equivalent to a change of -0.5% (+3.3% currency adjusted) compared with the previous year. The positive currency-adjusted sales growth has resulted, in particular, from the successful placement of innovative products as well as the solid market position of established medicines. In 2018, the emerging markets and the US market were once again the key growth drivers for the human pharmaceuticals business. On the other hand, in many significant markets, price pressure – particularly on established medicines – and a relatively strong euro represent a difficult environment in which Boehringer Ingelheim has nonetheless managed to assert itself.

Our product SPIRIVA®, which is used to treat chronic obstructive pulmonary disease (COPD), was once again the biggest contributor to sales in 2018. It generated revenues of EUR 2,412 million in the reporting period, which was below the previous year's level (EUR 2,828 million) as a result of increasing price pressure.

Boehringer Ingelheim's second-strongest product in terms of sales, the anticoagulant PRADAXA®, registered sales of EUR 1,486 million in the past year, an increase compared with 2017 (+3.3%).

In the 2018 financial year, the type-2 diabetes medicine JARDIANCE® – winner of the Prix Galien International 2018 for the most innovative pharmaceutical product – once again recorded strong growth. We achieved sales of EUR 1,461 million with JARDIANCE® in the reporting period, which corresponds to an increase of 44.9% compared with the previous year's EUR 1,008 million.

3.3%
growth (currency
adjusted) for human
pharmaceuticals

Net sales (in EUR million)

	2018	2017	Change
SPIRIVA®	2,412	2,828	- 14.7%
PRADAXA®	1,486	1,438	+ 3.3%
JARDIANCE®	1,461	1,008	+ 44.9%
TRAJENTA® / JENTADUETO®	1,397	1,333	+ 4.8%

With regard to the regional distribution of sales in the human pharmaceuticals business, the USA, with a share of 41%, was once again by far the largest market. Here, Boehringer Ingelheim generated sales of EUR 5,104 million, which corresponds to an increase of 0.2% compared with the previous year (+ 4.7% currency-adjusted).

Our second-biggest market, the EUCAN region (Europe, Canada, Australia, New Zealand), accounted for 32%, with revenues of EUR 3,971 million. Sales increased by 0.2% compared to 2017 (EUR 3,965 million). Exchange rate effects did not have any significant influence on the sales trend here.

In Japan, sales declined by 18.0% to EUR 1,160 million (2017: EUR 1,415 million), partly due to the expiry of a cooperation agreement for the product MICARDIS®.

Net sales by region (in EUR million)

	2018	2017	Change
USA	5,104	5,096	+ 0.2%
Europe/Canada/Australia/New Zealand (EUCAN)	3,971	3,965	+ 0.2%
Emerging Markets	2,324	2,145	+ 8.3%
Japan	1,160	1,415	- 18.0%

**Strong sales increase in
growth markets**

In the growth markets, sales increased by 8.3% to EUR 2,324 million (+ 16.5% currency-adjusted). Sales in the previous year had amounted to EUR 2,145 million here. In China, growth of almost 28% was achieved compared with 2017, resulting in sales of EUR 658 million.

Animal Health

Sales of products in the animal health business once again increased in 2018. They amounted to EUR 3,960 million and were thus 1.5% (+ 5.6% currency-adjusted) higher than in 2017.

Net sales (in EUR million)

	2018	2017	Change
NEXGARD®	610	546	+ 11.7%
FRONTLINE®	399	401	- 0.5%
INGELVAC CIRCOFLEX®	303	333	- 9.0%
HEARTGARD®	299	284	+ 5.3%

As in the 2017 financial year, in the 2018 reporting period three antiparasitics and the vaccine INGELVAC CIRCOFLEX® were the company's four best selling medicines.

Growth driven by
antiparasitics

The product NEXGARD® once again generated the strongest sales with revenues of EUR 610 million (2017: EUR 546 million), thus recording growth of 11.7% compared with the previous year.

This is followed by another antiparasitic, FRONTLINE®, which registered a decrease of 0.5% from EUR 401 million (2017) to EUR 399 million due to adverse currency effects.

The product INGELVAC CIRCOFLEX®, which is used as a vaccine against porcine circovirus type 2, achieved EUR 303 million in sales in the 2018 financial year, which represents a decline of 9.0% on the previous year (EUR 333 million).

Net sales by region (in EUR million)

	2018	2017	Change
North America	1,726	1,664	+ 3.7%
Europe	978	970	+ 0.8%
Africa/Asia/Middle East/Oceania (METAsia)	971	954	+ 1.8%
Latin America	285	313	- 8.9%

Biopharmaceuticals

In the 2018 financial year, the biopharmaceuticals business maintained its position in the industrial customers segment. The order situation for the entire business has developed positively, resulting in high capacity utilisation for biopharmaceutical production. Sales increased from EUR 678 million in 2017 to EUR 734 million (+ 8.3%).

Once again
strong growth in
Biopharmaceuticals

Financial position

(in EUR million)	2018
Financial funds as of 1.1.	8,130
Cash flow from operating activities	2,988
Cash flow from investing activities	– 1,403
Cash flow from financing activities	– 208
Change in financial funds from cash relevant transactions	1,377
Change in financial funds due to change of consolidated companies or exchange rate movements	– 53
Financial funds as of 31.12.	9,454

Boehringer Ingelheim's financial management instruments and methods are aimed at securing liquidity, minimising financial risks and optimising the cost of capital with an appropriate capital structure. Our financial activities are therefore geared towards supporting the business strategy.

Cash flow from operating activities amounted to EUR 2,988 million, which represents an increase of EUR 364 million in comparison to the previous year (EUR 2,624 million). Cash flow from investing activities declined considerably to EUR 1,403 million (2017: EUR 5,115 million), as the prior year was strongly affected by the cash settlement for the swap of businesses with Sanofi and tax payments resulting from the sale of our consumer health care business.

Significant investments

Investments are of particular importance to Boehringer Ingelheim from a strategic point of view. Continuous investment is a requirement for long-term development of the company and forms the basis for the profitable growth of our business activities. A total of EUR 1,073 million was invested in tangible and intangible assets in the year under review, representing an unchanged high level and a slight increase compared to 2017 (EUR 1,023 million). Furthermore, EUR 367 million have been deposited in plan assets for pension and similar obligations mainly in the USA.

After the topping-out ceremony in autumn 2018 for the expansion of production in Vienna (Austria) for the strongly growing biopharmaceutical business represents the biggest single investment in the history of Boehringer Ingelheim and is well underway, with a further 500 jobs to be created. In 2018 alone, about EUR 180 million has been invested into the facility that has been a significant site for the Group for decades.

An important investment also took place in the business of human pharmaceuticals. Despite the disposal of our chemical production site in Malgrat, Spain beginning of 2019, whose new proprietor will in future be incorporated into our production network as an external strategic partner, Spain remains an important site of the Boehringer Ingelheim Group. In 2018, more than EUR 45 million has been invested into a project that comprises the production of cartridges used in RESPIMAT® products and their filling as well as the packaging for the global distribution in Sant Cugat, Spain.

A further important investment was made in the animal health business. In March 2018, groundbreaking for a new production facility, which will focus on the production of avian vaccines, has begun in Lyon Porte-des-Alpes (France) and is expected to offer employment to more than 40 people. This investment follows to the rising demand of vaccines for the foot-and-mouth disease, resulting from higher poultry consumption.

The cash outflow from financing activities in the amount of EUR 208 million mainly includes payments to the shareholders and interest paid. Overall, after taking currency effects and changes within the group of consolidated companies into consideration, this led to an increase in the Boehringer Ingelheim Group's financial funds of EUR 1,324 million to EUR 9,454 million.

Net assets position

(in EUR million)	31.12.2018	31.12.2017	Change	Change in %
Assets				
Intangible and tangible assets	9,400	9,239	161	
Financial assets	6,058	5,830	228	
Fixed assets	15,458	15,069	389	+ 2.6%
Inventories	3,312	3,087	225	
Trade accounts receivable	3,540	3,146	394	
Other receivables and other current assets	1,033	1,360	- 327	
Cash and cash equivalents	4,303	3,071	1,232	
Current assets	12,188	10,664	1,524	+ 14.3%
Other assets	3,242	2,653	589	
Total assets	30,888	28,386	2,502	+ 8.8%
Equity and liabilities				
Group equity	12,334	10,657	1,677	+ 15.7%
Provisions for pensions and similar obligations	4,712	4,289	423	
Tax provisions and other provisions	9,040	8,439	601	
Accounts payable and loans	2,142	2,004	138	
- of which greater than 5 years:	20	134	- 114	
Liabilities	15,894	14,732	1,162	+ 7.9%
Other liabilities and difference from capital consolidation	2,660	2,997	- 337	
Total equity and liabilities	30,888	28,386	2,502	+ 8.8%

In the 2018 financial year, Boehringer Ingelheim's total assets amounted to EUR 30.888 million, which is an increase of EUR 2,502 million as compared with the previous year. A significant reason for this was the development of the financial funds which rose by EUR 1,232 million as a result of the positive cash flow. An increase in deferred tax assets, working capital (trade receivables and inventories) and fixed assets contributed to the rise as well.

Despite depreciation, amortisation and impairments, a high investment activity, the initial consolidation of the ViraTherapeutics GmbH and positive currency effects led to a slight increase in tangible and intangible assets of around 2%. The financial assets also went up by around 4% due to a reversal on an impairment loss in the previous year.

Inventories and trade receivables grew significantly by 10% (EUR 619 million) as a result of higher working capital in the USA, the emerging markets (especially in China) and in Japan. Other receivables and other current assets decreased mainly due to lower tax prepayments in the USA, France and Germany. The increase in other assets arose from higher deferred tax assets based on temporary differences in fixed assets as well as higher plan assets for pensions and similar obligations in the USA.

Increased equity ratio
in spite of higher
balance sheet total

The increase in Group equity by EUR 1,677 million is the result of the Group profit in 2018 as well as positive currency effects that surpassed withdrawals by the shareholders. Group equity as of 31 December 2018, amounted to EUR 12,334 million. The equity ratio improved to about 40% (31 December 2017: 38%). In addition to equity, pension provisions and long-term liabilities are also at the Group's disposability in the long term. The total of these three items amounted to EUR 17,066 million in 2018, representing a share of 55% of the total assets. Consequently, long-term disposable capital covers all intangible and tangible assets as well as the working capital.

Pension provisions increased due to a higher actuarial interest rate and the utilisation of updated mortality tables. Provisions for discounts and guarantees in the USA and tax provisions in Germany went up in comparison to the previous reporting year as well. While the trade accounts payable and liabilities to banks slightly decreased in 2018, other liabilities increased due to higher tax liabilities in Germany. Other liabilities declined mainly due to the reversal of the difference from capital consolidation and lower deferred tax liabilities from temporary differences in fixed assets.

Boehringer Ingelheim's positive development in the 2018 financial year is also reflected in its net asset position. Boehringer Ingelheim remains a soundly financed and profitable company.

REPORT ON OPPORTUNITIES AND RISKS

Opportunities and risk management

When assessing the risks in the context of holistic opportunities and risk management, we also endeavour to take into account the resulting opportunities. Opportunities management is based on the strategies and objectives of the company, 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 and innovative pharmaceutical company, the current R&D activities are considered a relevant opportunity. Relevant projects have already been illustrated in the research and development chapter.

The aim of the risk management system implemented at Boehringer Ingelheim is to identify business-specific risks and, in particular, risks that jeopardise the continued existence of the company as early as possible, 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 as well included in the process of calculating and assessing risks. The Group-wide risk and information system ensures that all identified risks are analysed and assessed carefully. Following an appropriate classification into various categories, 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 optimisations were initiated as necessary.

Individual risks

The most important risks to which Boehringer Ingelheim is exposed are broken down into the following specific categories: financial risks, legal risks, production and environmental risks, personnel risks and industry-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 broken down as follows: currency 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 opportunities and risks due to exchange rate volatility, particularly with regard to the US dollar and Japanese yen. 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.

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 sector. 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 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 defensive investment strategy in the management of its financial assets. This is reflected in the orientation of its portfolio, which is focused on European Economic and Monetary Union (EMU) government bonds with top credit ratings and short-term investments at selected banks. This results in a concrete, controllable and thus limited risk – but therefore only limited opportunities – for the major part of the 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 volatility of 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 a moderate and abstract risk.

Patent protection risks

Protection of innovations through trademark, brand and patent rights is of particular importance to Boehringer Ingelheim as a research 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 moderate risks are regarded as concrete.

Production and environmental risks

Our quality management system and compliance processes are continuously optimised 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.

In order to guarantee 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. As a result, we see the risk as concrete.

Risks in the areas of environment, health, safety and sustainability (EHS&S) are pre-emptively minimised by ensuring global adherence to our high safety standards. Appropriate emergency plans have been drawn up for possible incidents of any kind and are practised 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 company employees development opportunities based on their vocational skills, social expertise, personal aptitudes and willingness to take on responsibility in accordance with the needs of the company. In view of the counter-measures described above, the risk is regarded as moderate and concrete.

Industry-specific risks

Boehringer Ingelheim is exposed to business risks specific to the pharmaceutical industry. Some of these risks materialised in the past financial year and are increasing in significance as a result of their impact on Boehringer Ingelheim. They will continue to be classed as significant and abstract.

In addition to the loss of exclusivity of products established on the market and risks associated with the development and registration of new products, the industry-specific 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 caused by the state reimbursement systems. Boehringer Ingelheim is therefore 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 net assets, financial or earnings position that could jeopardise the continued existence of Boehringer Ingelheim.

REPORT ON EXPECTED DEVELOPMENTS

Boehringer Ingelheim can look back on a successful 2018 financial year in which we achieved our ambitious targets – both in absolute figures and in comparison with our competitors – and laid the foundations for sustainable development and long-term growth.

We demonstrated the consistent focus of our business on innovation-oriented fields by the strategic exchange of Sanofi's animal health business (Merial) and Boehringer Ingelheim's consumer health care business. The transaction was successfully closed on 1 January 2017. Through this transaction, we improved the competitiveness of our animal health business in the industry's important growth markets. The animal health business is growing in the second year following integration of the Merial business. We have successfully managed the demanding task of incorporating this organisation with many products, new customers and processes. We expect this to provide the Group with further growth momentum in the future.

Further sales growth expected

The increasingly difficult market environment and increased unpredictability of doing business poses major challenges for the entire pharmaceutical industry and will continue to require significant attention from Boehringer Ingelheim in 2019, too. With regard to competitiveness, it is even more important, therefore, that we retain our scope for growth and innovation as well as our financial ability to act so that we can continue to be successful on the market in the future. In view of the many change processes in healthcare systems, which are faced with ageing populations and increasing price pressure in many major markets, we only expect to see low growth impetus for the pharmaceutical industry in the coming year. On a comparable basis (adjusted for currency and extraordinary effects), we expect to see a slight increase in net sales for Boehringer Ingelheim in 2019.

R&D expenses remain continuously high, in line with our strategy to drive growth and promote new products in the future primarily with products from our own R&D facilities. We invest in this area with care after close investigation of the therapeutic benefit and the associated prospects for success. The replenishment of innovative medicines in our research pipeline shows short-, mid- and long-term growth potential. For 2019, we envisage a slight increase in our investments in the R&D of new pharmaceuticals.

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. In this context, the increasing cost pressure in healthcare systems as outlined above must also be particularly emphasised. The systems are increasingly unwilling to substantially and adequately reward high investments in the development of new medicines and the value contribution to increasing the efficiency of the system as a whole. As a result, there is significant price pressure in all major markets for prescription medicines. In conjunction with longer planning and development cycles for new products, this makes business less predictable and requires us to recognise and seize opportunities quickly on the one hand, while subjecting costs and strategies to continual monitoring and adjustments on the other hand. To this end, we have launched initiatives over the past few years to accelerate our reaction to changes and to reduce organisational complexities as well as to lower our cost base in order to create potential for investments and to secure the company's long-term success. With the difficult market environment on the one hand, and the potential resulting from the measures we have introduced as well as promising new product launches on the other hand, we plan to see a 2019 operating income which is on a comparable basis (adjusted for currency and extraordinary effects) slightly above last year's level.

As a family-owned company, Boehringer Ingelheim's primary aim is to maintain the group's independence and competitiveness. As such, long-term and sustainable organic growth still takes precedence over short-term profit targets. We are confident that we will achieve our ambitious targets in all of our businesses thanks to our great innovative strength based on a comprehensive portfolio of prospective products, our global presence and the support of our highly qualified and motivated employees. We will stand by our vision "Value through Innovation" and develop and bring to market innovative products in areas of high unmet medical need and therapeutic approaches where we aim to be first. The aim of our endeavours is to make new medicines available that will allow the treatments of humans and animals more effectively than is currently possible.

Boehringer Ingelheim
well positioned
for the future

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OVERVIEW OF SELECTED CONSOLIDATED COMPANIES



D Distribution

P Production

R Research and Development

C.H. BOEHRINGER SOHN
GRUNDSTÜCKSVERWALTUNG GMBH & CO. KG,
INGELHEIM AM RHEIN

BOEHRINGER INGELHEIM
INTERNATIONAL GMBH,
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ARGENTINA D P	COLOMBIA D	ITALY D P R	SOUTH AFRICA D
Boehringer Ingelheim S.A., <i>Buenos Aires</i>	Boehringer Ingelheim S.A., <i>Santa Fé de Bogotá</i>	Boehringer Ingelheim Italia S.p.A., <i>Milan</i> Bidachem S.p.A., <i>Fornovo S. Giovanni</i>	Ingelheim Pharmaceuticals (Proprietary) Ltd., <i>Randburg</i>
AUSTRALIA D P	CZECH REPUBLIC D	JAPAN D P R	SOUTH KOREA D
Boehringer Ingelheim Pty. Ltd., <i>North Ryde</i>	Boehringer Ingelheim, spol. s.r.o., <i>Prague</i>	Nippon Boehringer Ingelheim Co., Ltd., <i>Tokyo</i> Boehringer Ingelheim Seiyaku, <i>Yamagata</i> Boehringer Ingelheim Japan, Inc., <i>Tokyo</i>	Boehringer Ingelheim Korea Ltd., <i>Seoul</i> Boehringer Ingelheim Vetmedica Korea Ltd., <i>Seoul</i>
AUSTRIA D P R	DENMARK D	MEXICO D P R	SPAIN D P
Boehringer Ingelheim RCV GmbH & Co. KG, <i>Vienna</i> Forschungsinstitut für molekulare Pathologie Gesellschaft mbH, <i>Vienna</i>	Boehringer Ingelheim Danmark A/S, <i>Copenhagen</i>	Boehringer Ingelheim Mexico S.A. de C.V., <i>Mexico City</i> Boehringer Ingelheim Vetmedica S.A. de C.V., <i>Guadalajara</i>	Boehringer Ingelheim España S.A., <i>Barcelona</i>
BELGIUM D	ECUADOR D	NETHERLANDS D	SWEDEN D
SCS Boehringer Ingelheim Comm.V., <i>Brussels</i>	Boehringer Ingelheim Del Ecuador Cia. Ltda., <i>Quito</i>	Boehringer Ingelheim B.V., <i>Alkmaar</i>	Boehringer Ingelheim Aktiebolag, <i>Stockholm</i>
BRAZIL D P	FINLAND D	NEW ZEALAND D	SWITZERLAND D
Boehringer Ingelheim do Brasil Química e Farmaceutica Ltda., <i>São Paulo</i> Solana Agro Pecuária Ltda., <i>Arapongas</i>	Boehringer Ingelheim Finland Ky, <i>Espoo</i>	Boehringer Ingelheim (N.Z.) Ltd., <i>Auckland</i>	Boehringer Ingelheim (Schweiz) GmbH, <i>Basel</i>
CANADA D	FRANCE D	NORWAY D	TAIWAN D
Boehringer Ingelheim (Canada) Ltd., <i>Toronto</i>	Boehringer Ingelheim France S.A.S., <i>Paris</i>	Boehringer Ingelheim Norway KS, <i>Asker</i>	Boehringer Ingelheim Taiwan Ltd., <i>Taipei</i>
CHILE D	GREAT BRITAIN D	PHILIPPINES D	THAILAND V
Boehringer Ingelheim Ltda., <i>Santiago de Chile</i>	Boehringer Ingelheim Ltd., <i>Bracknell</i>	Boehringer Ingelheim (Philippines), Inc., <i>Manila</i>	Boehringer Ingelheim (Thai) Limited, <i>Bangkok</i>
CHINA D P R	GREECE D P	POLAND D	TURKEY D
Boehringer Ingelheim Shanghai Pharmaceuticals Co., Ltd., <i>Shanghai</i> Boehringer Ingelheim Biopharmaceuticals (China) Co., Ltd., <i>Shanghai</i> Boehringer Ingelheim (China) Investment Co., Ltd., <i>Shanghai</i> Boehringer Ingelheim International Trading (Shanghai) Co., Ltd., <i>Shanghai</i> Boehringer Ingelheim Vetmedica (China) Co., Ltd., <i>Taizhou</i>	Boehringer Ingelheim Ellas A.E., <i>Athens</i>	Boehringer Ingelheim Sp. z o.o., <i>Warsaw</i>	Boehringer Ingelheim İlaç Ticaret A.S., <i>Istanbul</i>
HONG KONG D	INDIA D	PORTUGAL D	USA D P R
Boehringer Ingelheim (Hong Kong) Ltd., <i>Hong Kong</i>	Boehringer Ingelheim India Private Ltd., <i>Mumbai</i>	Unifarma-Uniao Internacional de Laboratórios Farmacêuticos, Lda., <i>Lisbon</i>	Boehringer Ingelheim Pharmaceuticals, Inc., <i>Wilmington, Delaware</i> Boehringer Ingelheim Fremont, Inc., <i>Wilmington, Delaware</i> Boehringer Ingelheim USA Corporation, <i>Wilmington, Delaware</i>
INDONESIA D P	ISRAEL D	RUSSIAN FEDERATION D	VIETNAM D
PT Boehringer Ingelheim Indonesia, <i>Jakarta</i>	Boehringer Ingelheim Israel Ltd., <i>Tel Aviv</i>	OOO Boehringer Ingelheim, <i>Moscow</i>	Boehringer Ingelheim Animal Health Vietnam Limited Liability Company, <i>Ho Chi Minh City</i>

CONSOLIDATED BALANCE SHEET

Assets (in EUR million)	Notes ¹⁾	31.12.2018	31.12.2017
Intangible assets	(3.1)	5,120	5,372
Tangible assets	(3.2)	4,280	3,867
Financial assets	(3.3)	6,058	5,830
Fixed assets		15,458	15,069
Inventories	(3.4)	3,312	3,087
Accounts receivable and other assets	(3.5)	4,573	4,506
Cash and cash equivalents		4,303	3,071
Current assets		12,188	10,664
Prepaid expenses		377	334
Deferred tax assets		2,784	2,307
Exceeding amount of plan assets		81	12
Total assets		30,888	28,386
Equity and liabilities (in EUR million)	Notes ¹⁾	31.12.2018	31.12.2017
Shareholders' capital		178	178
Group reserves		12,453	10,868
Balance sheet currency conversion difference		– 298	– 388
Equity attributable to the parent company		12,333	10,658
Non-controlling interests		1	– 1
Group equity		12,334	10,657
Difference from capital consolidation		1,511	1,729
Provisions	(3.6)	13,752	12,728
Accounts payable and loans	(3.7)	2,142	2,004
Liabilities		15,894	14,732
Deferred income		463	514
Deferred tax liabilities		686	754
Total equity and liabilities		30,888	28,386

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

CONSOLIDATED PROFIT AND LOSS STATEMENT

(in EUR million)	Notes ¹⁾	2018	2017
Net sales	(4.1)	17,498	18,056
Changes in finished goods and work in process		244	– 291
Other own work capitalised		13	16
Other operating income	(4.2)	1,872	3,411
Total revenues		19,627	21,192
Cost of materials	(4.3)	– 3,058	– 3,474
Personnel expenses	(4.4)	– 5,276	– 4,934
Amortisation of intangible assets and depreciation of tangible assets	(4.5)	– 1,089	– 963
Other operating expenses	(4.6)	– 6,732	– 8,334
Operating income		3,472	3,487
Financial income	(4.7)	– 654	– 330
Holding income	(4.8)	358	– 301
Income before taxes		3,176	2,856
Income taxes ²⁾	(4.9)	– 1,101	– 3,085
Income after taxes		2,075	– 229
Net income/loss	(4.10)	2,075	– 229
Non-controlling interests		0	6
Group profit/loss		2,075	– 223

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.

CASH FLOW STATEMENT

(in EUR million)	2018
Income after taxes (including non-controlling interests)	2,075
Amortisation / reversal of write-downs of intangible assets and depreciation / reversal of write-downs of tangible assets	1,081
Change in provisions for pensions and similar obligations (without acquiring or generating of plan assets)	711
Change in other provisions	414
Other non-cash income and expenses	-515
Gain from disposals of consolidated companies	-4
Gain/loss from disposals of fixed assets	-1
Grants received	-7
Change in inventories	-229
Change in accounts receivable and other assets not related to investing or financing activities	-478
Change in trade accounts payable and other liabilities not related to investing or financing activities	8
Interest income/interest expenses	93
Other income from investments	-13
Income/expenses of extraordinary magnitude or significance	-87
Income taxes	1,101
Income taxes paid	-1,161
Cash flow from operating activities	2,988
Payments to acquire intangible fixed assets	-123
Payments to acquire tangible fixed assets	-950
Payments to acquire financial fixed assets ¹⁾	-43
Payments to acquire or generate plan assets	-367
Investments in consolidated companies	-99
Proceeds from disposals of intangible fixed assets	0
Proceeds from disposals of tangible fixed assets	12
Proceeds from disposals of financial fixed assets ¹⁾	33
Cash receipts relating to the purchase price adjustment of consolidated companies	7
Cash receipts of extraordinary magnitude or significance	96
Interest received	18
Income from dividends	13
Cash flow from investing activities	-1,403

CASH FLOW STATEMENT

(in EUR million)	2018
Cash receipts from grants	7
Interest paid	-62
Cash payments from shareholders of the parent company	62
Cash payments to shareholders of the parent company	-217
Proceeds from loans / cash repayments of loans	2
Cash flow from financing activities	-208
Change in financial funds from cash relevant transactions	1,377
Changes in financial funds due to change of consolidated companies	5
Changes in financial funds due to exchange rate movements	-58
Financial funds²⁾ as of 1.1.	8,130
Financial funds²⁾ as of 31.12.	9,454

¹⁾ Excl. investment securities.

²⁾ Cash and cash equivalents and investment securities within fixed assets.

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

STATEMENT OF CHANGES IN GROUP EQUITY

(in EUR million)	Shareholders' capital ¹⁾	Group reserves ²⁾	Balance sheet currency conversion difference	Equity attributable to the parent company	Non-controlling interests	Group equity
Balance as of 31.12.2016	178	11,220	-71	11,327	0	11,327
Withdrawals	0	-145	0	-145	0	-145
Net loss	0	-223	0	-223	-6	-229
Changes in consolidated companies	0	16	-21	-5	5	0
Currency effects	0	0	-296	-296	0	-296
Balance as of 31.12.2017	178	10,868	-388	10,658	-1	10,657
Contributions	0	62	0	62	0	62
Withdrawals	0	-544	0	-544	0	-544
Net income	0	2,075	0	2,075	0	2,075
Changes in consolidated companies	0	-8	-2	-10	2	-8
Currency effects	0	0	92	92	0	92
Balance as of 31.12.2018	178	12,453	-298	12,333	1	12,334

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 2018 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 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, 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, personally liable, managing shareholder of this company.

Besides C.H. Boehringer Sohn AG & Co. KG, there is C.H. Boehringer Sohn Grundstücksverwaltung GmbH & Co. KG, Ingelheim am Rhein, whose general partner is controlled by C.H. Boehringer Sohn AG & Co. KG.

The Boehringer Ingelheim Group consists of a total of 176 affiliated companies in Germany and abroad. The consolidated financial statements of C.H. Boehringer Sohn AG & Co. KG include 152 fully consolidated subsidiaries. C.H. Boehringer Sohn Grundstücksverwaltung GmbH & Co. KG is consolidated as a special purpose entity because the majority of the risks and rewards from its business activities is attributable to C.H. Boehringer Sohn AG & Co. KG. In the remaining subsidiaries, C.H. Boehringer Sohn AG & Co. KG, directly or indirectly, holds a majority of the voting rights.

In accordance with Section 296 (2) HGB, 21 affiliated companies 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 affiliated companies not included in consolidation accounts for less than 1% of the aggregated Group financial statements totals. For two further affiliated companies, there are ongoing restrictions on control due to the terms of the articles of association. These companies were also not consolidated in accordance with Section 296 (1) No. 1 HGB.

The total number of affiliated companies decreased by five compared to the previous year:

- One new company was founded.
- One company was acquired.
- Six companies lost their separate legal identity through merger.
- One affiliated company was liquidated.

ViraTherapeutics GmbH, Innsbruck, was acquired on 10 September 2018.

The following subsidiaries were exempt from the duty to prepare and disclose annual financial statements and management reports in accordance with Section 264 (3) HGB:

- Boehringer Ingelheim GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Europe GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Secura Versicherungsvermittlungs GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Grundstücksgesellschaft mbH, Ingelheim am Rhein
- Boehringer Ingelheim Finanzierungs GmbH, Ingelheim am Rhein
- Boehringer Ingelheim R&D Beteiligungs GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Venture Fund GmbH, Ingelheim am Rhein
- Boehringer Ingelheim Invest GmbH, Ingelheim am Rhein

The following subsidiaries were exempt from the duty to prepare and disclose annual financial statements and management reports in accordance with 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, Hanover

Two joint ventures have been included at cost instead of either using the proportionate method or the equity method due to their lack of significance.

In accordance with Section 311 (2) HGB, associated companies were not valued using the equity method due to their lack of significance.

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 acquisition 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 at 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 and deferred income and special reserves included in the consolidated financial statements as at 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 at the balance sheet date. The realisation principle (Section 298 (1) in conjunction with Section 252 (1) No. 4 half-sentence 2 HGB) and the historical cost convention (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 in accordance with Section 308a HGB using the modified closing date rate method.

Using the modified closing date 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 at 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 average rate. The resulting translation difference was 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: EUR 1):

	Closing rate		Average annual rate	
	31.12.2018	31.12.2017	2018	2017
US dollar	1.15	1.20	1.18	1.13
Japanese yen	125.85	135.01	130.41	126.66
Chinese renminbi	7.88	7.80	7.81	7.63
Pound sterling	0.89	0.89	0.88	0.88

2 Accounting policies

2.1 Fixed assets

Acquired intangible assets and tangible fixed assets are carried at cost, less scheduled straight-line amortisation and depreciation, considering technical and economic circumstances. This is based on the following useful lives:

Intangible assets	2 to 15 years
Buildings	20 years
Technical equipment and machinery	10 years
Other equipment, operating and office equipment	3 to 10 years

Only straight-line depreciation and amortisation 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 labour manufacturing costs, an appropriate portion of materials and labour overheads, and the depreciation of fixed assets (to the extent caused by production). Manufacturing costs do not include financing costs.

All capitalised intangible assets have finite useful lives.

A useful life of ten years was applied to the goodwill for ViraTherapeutics GmbH, acquired this year, as past experience of products and sales markets together with the business conditions of ViraTherapeutics GmbH indicates that this presents a true and fair view.

Financial assets primarily include investment securities, shareholder rights and loans and were carried at the lower of cost or fair market value, if impaired. Once the reasons for the impairment made in previous financial years no longer existed, appropriate write-ups were made.

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

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

Raw materials, consumables and supplies are capitalised 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 labour costs, special direct costs, and an appropriate portion 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, i. e. deductions were made from the expected sales prices to reflect costs yet to be incurred.

Receivables and other assets were recognised 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.

Cash and cash equivalents, consisting of cash, balances at banks and cheques were recognised 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 include proceeds that represent income relating to a defined period of time after the balance sheet date.

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

2.3 Difference from capital consolidation

The difference from capital consolidation reported on 31 December 2018 was primarily a result of the business swap of Boehringer Ingelheim's consumer health care business and Sanofi's animal health business, which was completed on 1 January 2017. This resulted in a difference from capital consolidation of EUR 1,986 million. The difference is amortised over an estimated period of 15 years. The remaining balance of the difference amounted to EUR 1,495 million at 31 December 2018.

The difference from capital consolidation reported on 31 December 2018 also included an amount arising from the acquisition of a US company in 2011. The original difference amounted to EUR 157 million. The difference is amortised over an estimated period of ten years. The remaining balance of this difference amounted to EUR 16 million at 31 December 2018.

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 amortisation of those assets of the acquired company identified in the purchase price allocation not previously recognised in that company's balance sheet.

2.4 Group reserves

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

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 judgement (i. e. 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 last ten years average and in the case of other provisions, from the last seven years average (in accordance with the Rückstellungsabzinsungsverordnung – German Regulation on the Discounting of Provisions).

2.6 Accounts payable and loans

Accounts payable and loans were recognised 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 group financial statements 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% - 39%). 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 EUR million)	Acquired concessions/ similar rights	Goodwill	Advance payments	Total
Acquisition/manufacturing costs				
Balance as of 1 January 2017	1,815	6	12	1,833
Currency conversion difference	- 625	- 1	- 1	- 627
Changes in consolidated companies	5,635	0	- 1	5,634
Additions	137	0	14	151
Disposals	- 290	0	- 1	- 291
Reclassifications	4	0	- 4	0
Balance as of 31 December 2017	6,676	5	19	6,700
Currency conversion difference	182	0	0	182
Changes in consolidated companies	80	24	0	104
Additions	102	0	21	123
Disposals	- 145	0	0	- 145
Reclassifications	13	0	- 14	- 1
Balance as of 31 December 2018	6,908	29	26	6,963
Accumulated amortisation				
Balance as of 1 January 2017	1,280	3	0	1,283
Currency conversion difference	- 72	0	0	- 72
Changes in consolidated companies	- 164	0	0	- 164
Additions	442	0	0	442
Write-ups	0	0	0	0
Disposals	- 161	0	0	- 161
Reclassifications	0	0	0	0
Balance as of 31 December 2017	1,325	3	0	1,328
Currency conversion difference	36	0	0	36
Changes in consolidated companies	0	0	0	0
Additions	537	0	0	537
Write-ups	0	0	0	0
Disposals	- 58	0	0	- 58
Reclassifications	0	0	0	0
Balance as of 31 December 2018	1,840	3	0	1,843
Book value as of 31 December 2017	5,351	2	19	5,372
Book value as of 31 December 2018	5,068	26	26	5,120

3.2 Tangible assets

(in EUR million)	Land and buildings	Technical facilities and machines	Other facilities/operating equipment	Advance payments/construction in progress	Total
Acquisition/manufacturing costs					
Balance as of 1 January 2017	2,962	3,147	2,153	468	8,730
Currency conversion difference	-170	-101	-77	-34	-382
Changes in consolidated companies	802	536	18	162	1,518
Additions	50	88	135	599	872
Disposals	-134	-132	-175	-58	-499
Reclassifications	117	179	64	-360	0
Balance as of 31 December 2017	3,627	3,717	2,118	777	10,239
Currency conversion difference	34	24	18	1	77
Changes in consolidated companies	0	1	0	0	1
Additions	62	88	124	676	950
Disposals	-19	-52	-101	-1	-173
Reclassifications	221	192	69	-481	1
Balance as of 31 December 2018	3,925	3,970	2,228	972	11,095
Accumulated depreciation					
Balance as of 1 January 2017	1,698	2,296	1,691	0	5,685
Currency conversion difference	-88	-65	-58	0	-211
Changes in consolidated companies	376	318	12	0	706
Additions	141	218	162	0	521
Write-ups	0	0	0	0	0
Disposals	-72	-109	-148	0	-329
Reclassifications	1	-1	0	0	0
Balance as of 31 December 2017	2,056	2,657	1,659	0	6,372
Currency conversion difference	22	18	15	0	55
Changes in consolidated companies	0	0	0	0	0
Additions	162	232	158	0	552
Write-ups	-3	-5	0	0	-8
Disposals	-13	-48	-95	0	-156
Reclassifications	-1	3	-2	0	0
Balance as of 31 December 2018	2,223	2,857	1,735	0	6,815
Book value as of 31 December 2017	1,571	1,060	459	777	3,867
Book value as of 31 December 2018	1,702	1,113	493	972	4,280

3.3 Financial assets

(in EUR million)	Investments in affiliated companies	Loans to affiliated companies	Investments in related companies	Advance payments	Investment securities	Other loans	Total
Acquisition/manufacturing costs							
Balance as of 1 January 2017	7	0	965	18	5,000	196	6,186
Currency conversion difference	0	0	-1	-2	-1	-20	-24
Changes in consolidated companies	0	0	16	-16	0	0	0
Additions	0	0	16	0	107	14	137
Disposals	0	0	-5	0	-30	-17	-52
Reclassifications	0	0	0	0	0	0	0
Balance as of 31 December 2017	7	0	991	0	5,076	173	6,247
Currency conversion difference	0	0	0	0	2	3	5
Changes in consolidated companies	0	0	0	0	0	0	0
Additions	5	0	31	0	117	7	160
Disposals	0	0	-21	0	-29	-145	-195
Reclassifications	0	0	0	0	0	0	0
Balance as of 31 December 2018	12	0	1,001	0	5,166	38	6,217
Accumulated amortisation							
Balance as of 1 January 2017	0	0	75	0	16	3	94
Currency conversion difference	0	0	-1	0	-1	0	-2
Changes in consolidated companies	0	0	0	0	1	0	1
Additions	0	0	324	0	1	0	325
Write-ups	0	0	-1	0	0	0	-1
Disposals	0	0	0	0	0	0	0
Reclassifications	0	0	0	0	0	0	0
Balance as of 31 December 2017	0	0	397	0	17	3	417
Currency conversion difference	0	0	0	0	0	0	0
Changes in consolidated companies	0	0	0	0	0	0	0
Additions	0	0	2	0	1	0	3
Write-ups	0	0	-256	0	-3	0	-259
Disposals	0	0	-2	0	0	0	-2
Reclassifications	0	0	0	0	0	0	0
Balance as of 31 December 2018	0	0	141	0	15	3	159
Book value as of 31 December 2017	7	0	594	0	5,059	170	5,830
Book value as of 31 December 2018	12	0	860	0	5,151	35	6,058

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

3.4 Inventories

(in EUR million)	31.12.2018	31.12.2017
Raw materials and supplies	626	575
Unfinished goods	1,602	1,547
Finished goods and goods for resale	1,071	951
Advance payments to suppliers	13	14
	3,312	3,087

3.5 Accounts receivable and other assets

(in EUR million)	31.12.2018	Residual term over 1 year	31.12.2017	Residual term over 1 year
Trade accounts receivable	3,540	0	3,146	1
Receivables from affiliated companies	24	0	29	0
Receivables from related companies	27	0	28	0
Other assets	982	67	1,303	79
	4,573	67	4,506	80

The “Other assets” item included receivables from shareholders of around half a million euro (previous year: EUR 87 million).

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

Receivables from related companies primarily consisted of trade accounts receivable.

3.6 Provisions

(in EUR million)	31.12.2018	31.12.2017
Pension provisions and similar obligations	4,712	4,289
Tax provisions	1,812	1,750
Other provisions	7,228	6,689
	13,752	12,728

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 (e.g. for Germany, mortality tables 2018 G 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 31 December 2018)	Germany	USA	Japan
Discount rate	3.21	4.20	1.23
Salary increase	3.50	4.00	4.18
Pension increase	1.88	3.00	0.00

Discounting 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 11 March 2016. The interest rates used to discount significant foreign pension obligations (USA and Japan) were determined with comparable parameters, in line with the German Regulation on the Discounting of Provisions of 11 March 2016.

The difference calculated in accordance with Section 253 (6) HGB amounts to EUR 767 million.

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 EUR 1,845 million. The related amount of pension obligations and similar obligations was EUR 6,477 million. 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, EUR 81 million in losses from plan assets and EUR 562 million in interest expense relating to pension and similar obligations are included under “Interest expense relating to pensions and similar obligations and other provisions” within the financial result.

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 Co-operation 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, as well as provisions for litigation, legal claims and compensation for damages.

3.7 Accounts payable and loans

(in EUR million)	Residual term less than 1 year	greater than 1 year	of which greater than 5 years	31.12.2018	31.12.2017	Residual term less than 1 year
Bank loans	412	8	0	420	439	373
Other accounts payable	1,685	37	20	1,722	1,565	1,381
<i>of which:</i>						
- Trade accounts payable	852	3	0	855	880	875
- Advance payments received	142	22	13	164	131	131
- Accounts payable to affiliated companies	4	5	5	9	6	1
- Accounts payable to related companies	1	0	0	1	1	1
- Other liabilities*	686	7	2	693	547	373
	2,097	45	20	2,142	2,004	1,754
* Of which:						
- from taxes (EUR million)				225	189	
- social security liabilities (EUR million)				40	37	

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 EUR 255 million (previous year: EUR 22 million). These are presented within the "Other liabilities" item.

Accounts payable to affiliated companies include loans amounting to EUR 4 million (previous year: EUR 5 million) and trade accounts payable amounting to EUR 5 million (previous year: EUR 1 million).

4 Notes to the consolidated profit and loss statement

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

4.1 Net sales

by businesses (in EUR million)	2018	2017
Human Pharmaceuticals	12,559	12,621
Animal Health	3,960	3,901
Biopharmaceuticals	734	678
Other sales	40	43
Discontinued Operations	205	813
	17,498	18,056

by geographic region (in EUR million)	2018	2017
Europe	5,316	5,690
<i>of which: Germany</i>	888	982
Americas	8,088	8,141
<i>of which: USA</i>	6,924	6,861
Asia/Australia/Africa	4,094	4,225
<i>of which: Japan</i>	1,323	1,601
	17,498	18,056

4.2 Other operating income

Other operating income includes income from currency translation of EUR 783 million (previous year: EUR 1,040 million).

4.3 Cost of materials

(in EUR million)	2018	2017
Costs of raw material, supplies and goods for resale	2,172	2,431
Expenditure on services	886	1,043
	3,058	3,474

4.4 Personnel expenses

(in EUR million)	2018	2017
Wages and salaries	4,260	4,078
Social benefits and retirement benefits	1,016	856
<i>of which: retirement benefits</i>	305	154
	5,276	4,934

All interest effects of the measurement of the provisions for pensions and similar obligations were shown as a separate item of financial income.

Average headcount	2018	2017
Production	16,380	16,361
Administration	5,964	5,826
Marketing and Sales	18,762	18,123
Research and Development	8,566	8,589
Apprentices	698	711
	50,370	49,610

The allocation of employees among their different functions was restated for 2017 as many former Merial employees were not allocated to their respective function in the first year that Merial was consolidated, but rather reported within Administration.

4.5 Amortisation of intangible assets and depreciation of tangible assets

Amortisation of intangible assets and depreciation of tangible fixed assets include extraordinary write-downs of EUR 116 million (previous year: EUR 16 million).

4.6 Other operating expenses

Other operating expenses include expenses from currency translation of EUR 779 million (previous year: EUR 2,060 million).

In addition, other items included in operating expenses are mainly the charges made to record provisions for legal risks and restructuring, as well as 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.

4.7 Financial income

(in EUR million)	2018	2017
Interest expense relating to pensions and similar obligations and other provisions	- 665	- 321
Other interest expense and similar expenditure	- 149	- 153
Interest expense and similar expenditure	- 814	- 474
Amortisation of and loss on disposal of financial fixed assets and short-term investments	- 1	- 1
Income from other investment securities and from long-term loans	104	104
Other interest income and similar income	57	41
	- 654	- 330

4.8 Holding income

(in EUR million)	2018	2017
Write-downs on financial fixed assets	- 2	- 324
Write-ups of financial fixed assets	256	1
Income from related companies	104	22
<i>of which: from disposal of related companies</i>	91	10
	358	- 301

4.9 Income taxes

(in EUR million)	2018	2017
Current income taxes	1,588	2,333
Deferred taxes	- 487	752
	1,101	3,085

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

The total balance of deferred tax assets at the balance sheet date amounted to EUR 2,784 million (previous year: EUR 2,307 million). Deferred tax assets primarily arise on the difference between the book values of provisions for pension obligations and for discounts, tax goodwill, intangible fixed assets, inventories and on tangible fixed assets. Deferred tax liabilities of EUR 686 million (previous year: EUR 754 million) were recorded. These primarily relate to differences between the book values of intangible fixed assets, tangible fixed assets, inventories and provisions.

4.10 Net income

The net income for 2018 was positively influenced by prior-period operating income (mainly from the reversal of other provisions and tax refunds for prior years) of EUR 352 million (previous year: EUR 724 million) and negatively influenced by prior-period operating expenses (mainly due to additional payment of taxes for prior years) of EUR 511 million (previous year: EUR 170 million).

5 Notes to the cash flow statement

The cash flow statement shows the changes in cash and cash equivalents (cash and long-term investment securities that can be sold at any time) of the Boehringer Ingelheim Group resulting from cash inflows and outflows in the reporting year. In accordance with the German Accounting Standard on the cash flow statement (DRS 21), the cash flow statement has been broken down according to cash flows from operating activities and cash flows from investing and financing activities.

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, cash and cash equivalents are carried at the closing rate. The effect of exchange rate changes on cash and cash equivalents has been shown separately.

The financial funds also include financial assets with a remaining maturity exceeding three months on the date of acquisition which can be converted into cash in the short term.

The financial funds as of 31 December 2018 comprised the following items:

(in EUR million)	2018
Cash and cash equivalents	4,303
Financial assets	5,151
	9,454

The financial funds included EUR 492 million in restricted funds at the balance sheet date.

6 Other disclosures

6.1 Contingent liabilities

(in EUR million)	31.12.2018	31.12.2017
Liabilities from guarantees	21	21
Warranties and the granting of securities for third-party liabilities	235	159
	256	180

The risk of utilisation 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 EUR million)	31.12.2018	31.12.2017
Rental and lease obligations	512	445
Residual other financial commitments	1,465	1,392
<i>of which: pension-related</i>	10	0

There are rental and lease obligations of EUR 512 million (previous year: EUR 445 million), EUR 12 million of which (previous year: EUR 11 million) relate to long-term rental obligations with non-consolidated affiliated companies.

The purpose of the lease agreements is the lower capital commitment compared to acquired 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 utilise the properties fully, of which there are no indications at this time.

Residual other financial commitments include future expenditure-effective investments of EUR 1,125 million (previous year: EUR 1,120 million).

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 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 organisational processes are set out in internal guidelines. There is a strict separation between trading, processing, documentation and control.

Risk positions are regularly tracked, analysed and measured in a special Group-wide financial report. The positions entered into are periodically re-evaluated 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 EUR 49 million were recognised for currency forwards not included in hedge accounting for which there was a negative fair value within one currency as at the balance sheet date. In line with the impairment principle, positive fair values within one currency were not recognised.

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

(in EUR million)	Nominal value		Fair value	
	31.12.2018	31.12.2017	31.12.2018	31.12.2017
Foreign exchange forward contracts	3,906	4,105	-27	-23

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

The following accounting policies apply to the recognition of valuation groups 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 recognised 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 at 31 December 2018, hedges for highly probable forecasted net cash flows were recognised as follows:

January to December 2019:

Net cash flow (in EUR million)		Foreign exchange forward contracts (in EUR million)		
	Nominal value		Nominal value	Fair value
USD	1,460	USD	– 1,453	– 39
JPY	720	JPY	– 481	– 6
AUD	127	AUD	– 113	2
MXN	103	MXN	– 62	– 2
CAD	266	CAD	– 116	1
GBP	153	GBP	– 109	1

January to December 2020:

Net cash flow (in EUR million)		Foreign exchange forward contracts (in EUR million)		
	Nominal value		Nominal value	Fair value
USD	1,505	USD	– 880	– 34
JPY	711	JPY	– 361	– 8
AUD	24	AUD	– 16	0
MXN	14	MXN	– 11	– 1
CAD	44	CAD	– 16	0
GBP	56	GBP	– 39	0

January to December 2021:

Net cash flow (in EUR million)		Foreign exchange forward contracts (in EUR million)		
	Nominal value		Nominal value	Fair value
USD	1,495	USD	– 384	– 13
JPY	709	JPY	– 188	– 5

January to February 2022:

Net cash flow (in EUR million)		Foreign exchange forward contracts (in EUR million)			
Nominal value		Nominal value			Fair value
USD	186	USD	− 51	USD	− 2
JPY	88	JPY	− 26	JPY	− 1

For the year 2019, there were also hedge accounting valuation units from long and short positions of derivatives. The offsetting nominal values amount to +/- EUR 64 million from Japanese yen.

Furthermore, as at 31 December 2018, valuation units for foreign currency receivables were recognised as follows:

Receivables (in EUR million)		Foreign exchange forward contracts (in EUR million)			
Nominal value		Nominal value		Fair value	
RUB	100	RUB	− 53	RUB	3
PLN	54	PLN	− 15	PLN	0

The amount of the hedged foreign currency risk correlates to the relative change in the exchange rate between the planning date and the realisation date of the forecast transactions. If all currencies were to appreciate or depreciate against the euro by 10.0%, there would be a foreign currency risk of plus or minus EUR 782 million without hedging.

6.4 Research and development expenses

(in EUR million)	2018	2017
Research and development expenses	3.164	3.078

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

6.5 Shareholdings

The list of companies included in the consolidated financial statements and the 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.

6.6 Subsequent events

Since the end of the 2018 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 Total auditor fees

Total fees charged to the Group by the auditor for the financial year amounted to EUR 7.3 million. EUR 1.6 million of this relates to audits of financial statements, EUR 1.7 million to tax advisory services and EUR 4.0 million to other services.

Ingelheim am Rhein, 5 March 2019

Boehringer AG

Board of Managing Directors

Hubertus von Baumbach

Joachim Hasenmaier

Allan Hillgrove

Dr Andreas Neumann

Dr Michel Pairet

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 2018, and 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 2018, and notes to the consolidated financial statements, including a summary of significant accounting policies. 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 2018.

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 2018 and of its financial performance for the financial year from 1 January to 31 December 2018, in accordance 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 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 the German Generally Accepted Standards of 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 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 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 consolidated financial statements that comply, in all material respects, with the requirements of German commercial law and 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. 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 the German Generally Accepted Standards of 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 judgement and maintain professional scepticism 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 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 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 / Main, 5 March 2019

KPMG AG

Wirtschaftsprüfungsgesellschaft

Original German version signed by

Kneisel

Wirtschaftsprüfer

[German Public Auditor]

Krauß

Wirtschaftsprüfer

[German Public Auditor]

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PRODUCT PORTFOLIO

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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 characterised 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 hyperresponsiveness, 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.



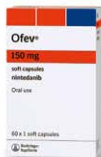
INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
- Chronic obstructive pulmonary disease (COPD)	SPIRIVA® SPIRIVA® HANDIHALER® SPIRIVA® RESPIMAT®	<i>tiotropium bromide</i>	Maintenance treatment of patients with COPD (including chronic bronchitis and emphysema), maintenance treatment of associated dyspnoea 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 bronchospasms 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 characterised 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.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
– Bronchial asthma	BEROTEC®	<i>fenoterol hydrobromide</i>	<p>Symptomatic treatment of acute asthma attacks.</p> <p>Prophylaxis of exercise-induced asthma bronchiale.</p> <p>Symptomatic treatment of allergic and non-allergic asthma bronchiale and other conditions with reversible airway narrowing, e.g. chronic obstructive bronchitis.</p> 
– Bronchial asthma – Allergic rhinitis	ALESION® FLURINOL®	<i>epinastine hydrochloride</i>	<p>Prophylactic treatment of patients with bronchial asthma. Prophylaxis and symptomatic treatment of allergic rhinitis.</p> 
– Idiopathic pulmonary fibrosis (IPF)	OFEV®	<i>nintedanib</i>	<p>Treatment of patients with idiopathic pulmonary fibrosis (IPF).</p> 

CARDIOVASCULAR AND METABOLIC DISEASES

Cardiovascular (CV) disease is the leading cause of death worldwide and is still increasing in prevalence. 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 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 ischaemia (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 ischaemic 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 orthopaedic surgery are at considerable risk of developing DVT, and chronic venous insufficiency and/or pulmonary hypertension may develop in the longer term. To prevent VTE events and their consequences after orthopaedic 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.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> – Stroke prevention in atrial fibrillation – Primary prevention of venous thromboembolic events after orthopaedic surgery – Treatment and secondary prevention of venous thromboembolic events 	PRADAXA® PRADAXAR® PRAZAXA®	<i>dabigatran etexilate</i>	 <p>Prevention of strokes and blood clots in patients with atrial fibrillation.</p> <p>Primary prevention of venous thromboembolic events (VTE) in adults after elective total hip or knee replacement surgery.</p> <p>Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and secondary prevention of recurrent DVT and PE in adults.</p>
<ul style="list-style-type: none"> – Specific reversal of PRADAXA® (dabigatran etexilate) 	PRAXBIND®	<i>idarucizumab</i>	 <p>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.</p>
<ul style="list-style-type: none"> – Hypertension – Cardiovascular morbidity and mortality prevention 	MICARDIS®	<i>telmisartan</i>	 <p>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 (USA).</p> <p>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).</p>
<ul style="list-style-type: none"> – Hypertension 	MICARDISPLUS® MICARDIS® PLUS MICARDIS® HCT CO-MICARDIS®	<i>telmisartan; hydrochlorothiazide</i>	 <p>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).</p> <p>Treatment of essential hypertension. MICARDISPLUS® fixed dose combination is indicated in adults whose blood pressure is not adequately controlled on telmisartan alone (EU).</p>
<ul style="list-style-type: none"> – Hypertension 	TWYNSTA® MICAMLO® MICARDIS® AMLO MICARDIS® DUO	<i>telmisartan, amlodipine</i>	 <p>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 (USA).</p> <p>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).</p>






CARDIOVASCULAR AND METABOLIC DISEASES (CONTINUED)

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 anti-hypertensive 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 industrialised countries.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> - Acute ischaemic stroke - Acute myocardial infarction - Acute massive pulmonary embolism - Catheter clearance due to thrombotic occlusion 	ACTILYSE® ACTILYSE® CATHFLO®	<i>alteplase</i>	 <p>Fibrinolytic treatment of acute ischaemic stroke, acute myocardial infarction, acute massive pulmonary embolism. Fibrinolytic treatment of occluded catheters.</p>
<ul style="list-style-type: none"> - Secondary prevention of stroke or transient ischaemic attacks (TIA) 	AGGRENEX® ASASANTIN® ASASANTIN® RETARD	<i>dipyridamole, acetylsalicylic acid</i>	 <p>Prevention of stroke following an initial first stroke, or transient ischaemic attacks (TIA).</p>
<ul style="list-style-type: none"> - Acute myocardial infarction 	METALYSE®	<i>tenecteplase</i>	 <p>Fibrinolytic treatment of acute myocardial infarction.</p>
<ul style="list-style-type: none"> - Hypertension 	CATAPRESAN® CATAPRES® CATAPRESSAN® CATAPRES-TTS®	<i>clonidine; clonidine hydrochloride</i>	 <p>Treatment of hypertension.</p>
<ul style="list-style-type: none"> - Hypertension 	MOTENS®	<i>lacidipine</i>	 <p>Treatment of hypertension.</p>

CARDIOVASCULAR AND METABOLIC DISEASES (CONTINUED)

Diabetes






Type 2 diabetes is a chronic, progressive condition associated with elevated blood sugar levels that can cause long-term complications if not treated. An estimated four million deaths worldwide every year are linked directly to the long-term effects of diabetes. Type 2 diabetes is the most common form of the disease and accounts for up to 95% of all cases in the developed world. Currently, more than 425 million people in the world live with diabetes, which represents an enormous burden on health care systems globally. Without effective prevention and management strategies, it is estimated that the number of cases will reach 629 million by 2045.

In addition, type 2 diabetes is one of the major risk factors for cardiovascular disease. Life expectancy of people with type 2 diabetes at high cardiovascular risk decreases, on average, by up to 12 years.

Overall, around half of deaths in people with type 2 diabetes are caused by concomitant cardiovascular disease, indicating a high unmet medical need.

In addition to cardiovascular disease, serious complications of diabetes include:

- Nephropathy, culminating in renal failure requiring dialysis
- Retinopathy with potential loss of vision
- Peripheral neuropathy with the risk of developing foot ulcers and potentially requiring foot or leg amputations
- Autonomic neuropathy, which can cause gastrointestinal, genitourinary and cardiovascular symptoms and sexual dysfunction.

INDICATIONS	BRAND NAMES*	ACTIVE INGREDIENTS	
- Type 2 diabetes mellitus	TRAJENTA® TRADJENTA® TRAZENTA® TRAYENTA®	linagliptin	 <p>Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control, used in monotherapy (if metformin is not tolerated or contraindicated) or in combination therapy.</p>
- Type 2 diabetes mellitus	JENTADUETO® TRAYENTA DUO® TRAJENTA DUO® TRAJENTAMET®	linagliptin, metformin hydrochloride	 <p>Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control when treatment with metformin does not lead to sufficient control or when patients are treated with TRAJENTA® (linagliptin) and metformin.</p>
- Type 2 diabetes mellitus	JARDIANCE® JARDIANZ®	empagliflozin	 <p>Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control and to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.*</p> <p><i>*USA indication, December 2016. The label varies by country. Please refer to the local product information.</i></p>
- Type 2 diabetes mellitus	SYNJARDY® JARDIANCE DUO®	empagliflozin, metformin hydrochloride	 <p>Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control when treatment with both empagliflozin and metformin hydrochloride is appropriate.*</p> <p><i>*USA indication, December 2016. The label varies by country. Please refer to the local product information.</i></p>
- Type 2 diabetes mellitus	GLYXAMBI®	empagliflozin, linagliptin	 <p>Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus when both empagliflozin and linagliptin are appropriate treatments.*</p> <p><i>*USA indication, March 2015. The label varies by country. Please refer to the local product information.</i></p>

* 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, forming a cluster or tumour. 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.

Lung cancer is more than just one disease. 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 tumour 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®	<i>afatinib</i>	 <p>First-line treatment of patients with meta-static non-small cell lung cancer (NSCLC) whose tumours 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>
– Non-small cell lung cancer (NSCLC)	VARGATEF®	<i>nintedanib</i>	 <p>Combination therapy with docetaxel for the treatment of adult patients with locally advanced, metastatic or local non-small cell lung cancer (NSCLC) of adenocarcinoma tumour 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 tremor (shaking) 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 neurotransmitter dopamine in distinct areas of the human brain.


Restless legs syndrome (RLS)



Restless legs syndrome (RLS) is a common neurological disorder characterised 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 tumours. Babies of infected mothers are at risk of getting the virus during pregnancy, childbirth or breastfeeding.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> – Parkinson's disease (PD) – Restless legs syndrome (RLS) 	SIFROL® MIRAPEX® MIRAPEXIN® PEXOLA®	<i>pramipexole</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.</p>
<ul style="list-style-type: none"> – Sleep disorders 	LENDORMIN®	<i>brotizolam</i>	 <p>Short-term treatment of disorders of initiating and maintaining sleep. Insomnia requiring pharmacological intervention.</p>

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> – 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 labour. Prolonged release tablets for once-daily dosing within combination therapy.</p>
<ul style="list-style-type: none"> – 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). This vaccine provides significant reduction of mortality in the acute phase of PCVD as well as improved growth rates in the chronic phase of the disease. INGELVAC CIRCOFLEX® protects with minimal systemic adverse reactions or injection site swellings and can be used during gestation and lactation. Our INGELVAC® PRRS products are licensed for active immunisation against the respiratory and reproductive form of porcine reproductive and respiratory syndrome (PRRS).

INGELVAC MYCOFLEX® provides proven safety, efficacy and rapid onset of long-lasting immunity against *Mycoplasma hyopneumoniae* (M. hyo.) with a single dose. INGELVAC MYCOFLEX® contains the IMPRANFLEX® adjuvant which allows for fresh mixing with INGELVAC CIRCOFLEX® to form FLEXCOMBO®.

INGELVAC PROVENZA® protects against multiple IAV-S strains and decreases nasal shedding, providing protection before pigs are most vulnerable.

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.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
- Infectious respiratory diseases	INGELVAC CIRCOFLEX®	recombinant vaccine (porcine circovirus type 2, PCV 2)	For the active immunisation 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 viraemia.
			
- Infectious respiratory diseases	INGELVAC® PRRS MLV INGELVAC PRRSFLEX® EU REPROCYC® PRRS EU	attenuated live vaccine (PRRS virus type 2, type 1)	Depending on the product, for the active immunisation of pigs at various ages against porcine reproductive and respiratory syndrome virus (PRRSV).
			
- Infectious respiratory diseases	INGELVAC MYCOFLEX®	inactivated vaccine (Mycoplasma hyopneumoniae)	For the active immunisation of pigs from the age of three weeks to reduce lung lesions following infections with Mycoplasma hyopneumoniae.
			
- Infectious respiratory diseases	INGELVAC PROVENZA®	attenuated live influenza vaccine (LAIV)	For the vaccination of pigs one day of age or older against influenza virus strains H1N2 and H3N2.
			
- Infectious enteric diseases	ENTERISOL® ILEITIS	attenuated live vaccine (Lawsonia intracellularis)	For the active immunisation 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.
			

LIVESTOCK - CATTLE/RUMINANTS

Our cattle/ruminants business is a global leader in antiparasitic 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 immunisation 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®	ivermectin	 <p>Depending on formulation, the product is for the treatment of nematodes, lice, mites, ticks, flies, lungworms and liver flukes.</p>
- Internal and external parasites of cattle	LONGRANGE®	eprinomectin, long-acting	 <p>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.</p>
- Internal and external parasites of ruminants	EPRINEX®	eprinomectin	 <p>Depending on formulation, the product is for the treatment of nematodes, lice, mites, ticks, flies and lungworms in cattle and sheep.</p>
- Bacterial causes of respiratory disease and interdigital dermatitis (footrot)	ZACTRAN®	gamithromycin	 <p>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).</p>
- Reproductive infectious diseases in cattle	BOVELA®	bovine viral diarrhoea (BVD) types 1 and 2	 <p>Reduces hyperthermia and minimises the reduction of leukocyte count caused by bovine viral diarrhoea virus (BVDV-1 and BVDV-2); reduces virus shedding and viraemia caused by BVDV-2 and prevents the birth of persistently infected calves caused by transplacental infection.</p>

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 minimise 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® PRESponse®	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>The PYRAMID®/PRESponse® 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®	meloxicam	 <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 and inactivated vaccines for broilers, layers and breeder hens, providing protection against the most critical viral and bacterial diseases like avian influenza, infectious bronchitis, Newcastle disease, infectious bursal disease, egg drop syndrome and avian coryza. This portfolio of preventive products 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®	<i>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, gallibacterium anatis</i>	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. 
- Infectious bursal disease and Marek's disease	VAXXITEK®HVT + IBD	<i>serotype 3, live Marek's disease vector, live vHVT013-69 recombinant virus (and diluent)</i>	To prevent mortality and to reduce clinical signs and lesions of infectious bursal disease. The onset of protection is from two weeks and the protection extends to nine weeks. To reduce mortality, clinical signs and lesions of Marek's disease. The onset of protection is four days. A single vaccination is sufficient to provide reliable protection during the risk period. 
- Newcastle disease (ND)	AVINEW®	<i>live Newcastle disease virus, VG/GA-AVINEW strain</i>	In broiler chickens from one day of age: active immunisation 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 immunisation against egg drop caused by Newcastle disease before vaccination with an inactivated vaccine (strain Ulster 2C) prior to the beginning of lay. 
- Marek's disease	PREVEXXION™ RN	<i>live herpes virus chimera, serotype 1, strain RN1250</i>	The vaccine is recommended for in ovo vaccination of 18 to 19-day-old embryonated chicken eggs to protect against the very virulent Marek's disease. 
- Newcastle and Marek's diseases	NEWXXITEK™ HVT+ND	<i>live Marek's disease vectored virus, serotype 3, that contains a gene insert from Newcastle disease; the vaccine includes a diluent</i>	The vaccination of 18 to 19-day-old embryos and one-day-old chickens is effective against Marek's disease and Newcastle disease. 




VETERINARY PUBLIC HEALTH (VPH)

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

Our foot-and-mouth vaccines portfolio works for the active immunisation of cattle, sheep or pigs to reduce clinical signs and mortality following exposure to foot-and-mouth disease (FMD) virus.

RABISIN® is an inactivated vaccine against rabies, available as a clear colourless suspension for injection.

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

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
- Foot-and-mouth disease (FMD)	AFTOPOR® AFTOVAXPUR® AFTOVAX® AFTOBOV® OLEOSA AFTOVAXPUR® DOE	<i>mix of inactivated FMD virus antigens out of the widest range of vaccine strains</i>	<p>FMD vaccines with highly potent and purified antigens (AFTOPOR®, AFTOVAXPUR®, AFTOBOV® OLEOSA) have potential marker properties that allow differentiation between infected and vaccinated animals (DIVA) for endemic or emergency situations.</p> <p>AFTOVAXPUR® DOE is suitable for emergency situations only.</p> 
- Rabies	RABISIN® RABORAL V-RG®	<i>Rabisin: inactivated and adjuvanted rabies glycoproteins Raboral V-RG: vaccina-vectored rabies vaccine</i>	<p>RABISIN® is used for the active immunisation 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 next re-vaccination dose.</p> <p>RABORAL V-RG® is an oral rabies recombinant vaccine that protects raccoons and coyotes against rabies, thereby reducing the risk of exposure to rabies to humans and domestic animals. It is only sold to government agencies conducting rabies control programs.</p> 
- Bluetongue	BTV PUR®	<i>Mix of inactivated bluetongue virus</i>	<p>Active immunisation of sheep to prevent viraemia and to reduce clinical signs caused by bluetongue virus serotypes 1, 2, 4 and/or 8 (combination of maximum 2 serotypes).</p> <p>Active immunisation of cattle to prevent viraemia 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 BTV2) after the primary vaccination course for BTV-1, BTV-2 (cattle), BTV-4 and BTV-8 serotypes.</p> 

COMPANION ANIMALS - HORSE

Our main horse products focus on the prevention and treatment of parasite infestations, management solutions for chronic diseases, and vaccines. Our equine portfolio also includes a range of flagship products for the treatment of joint disease, colic and respiratory disease, for pain management, and nutraceuticals.





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 customised 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 USA 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.

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</i> <i>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>

COMPANION ANIMALS - PETS

Our pets portfolio offers diverse solutions for some of the most important needs of canine and feline health including industry-leading parasiticides, vaccines, and therapeutics to address major chronic diseases: heart failure, kidney diseases, hypertension, epilepsy and osteoarthritis.

For more than 20 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.¹ FRONTLINE® continues to bring innovation to the category, with the recent launch of FRONTLINE TRI-ACT®, which features repellency and insecticidal efficacy on many disease-carrying flying insects and which decreases the risk of transmission of vector-borne pathogen.²

NEXGARD® contains the active ingredient afoxolaner and was the first oral medication that treats both fleas and ticks in dogs. Because of its efficacy and palatable, beef-flavoured soft chew formulation, NEXGARD® is currently the best-selling pet medication in the animal health industry.³

NEXGARD SPECTRA® combines the flea and tick efficacy of afoxolaner in NEXGARD® with a broad-spectrum deworming ingredient, milbemycin oxime, in the same beef-flavoured chew. NEXGARD SPECTRA® is not only effective in treating fleas and ticks, but also protects dogs against deadly parasites such as heartworm and lungworm as well as gastrointestinal parasites.

HEARTGARD® plus contains the active ingredients ivermectin and pyrantel in a soft beef chew. When given monthly, ivermectin is effective in preventing deadly 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.⁴

BROADLINE® offers pet owners all-in-one convenience providing confidence that their cat has the broadest possible protection. It protects cats against the broadest spectrum of internal and external parasites, including adult fleas, flea eggs, flea larvae, ticks, heartworms, hookworms, roundworms and tapeworms.

As the first of a new class of heart treatments termed inodilators, VETMEDIN® has been shown to significantly improve clinical signs and extend life expectancy in dogs with congestive heart failure originating from dilated cardiomyopathy or valvular insufficiency (mitral and/or tricuspid regurgitation). Recent studies have also shown that when used preclinically in appropriate asymptomatic cases of either dilated cardiomyopathy in Doberman pinschers or valvular insufficiency, VETMEDIN® significantly delays the onset of clinical signs of congestive heart failure.

¹⁾ Data on file.

²⁾ A novel combination of fipronil and permethrin (Frontline Tri-Act®/Frontect®) reduces risk of transmission of *Babesia canis* by *Dermacentor reticulatus* and of *Ehrlichia canis* by *Rhipicephalus sanguineus* ticks to dogs. Jongejan et al. *Parasites & Vectors* (2015) 8:602.

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® FRONTECT®	<i>fipronil</i> <i>fipronil/S-methoprene</i> <i>fipronil/permethrin</i>	<p>FRONTLINE® is indicated for the treatment and prevention of fleas, ticks and chewing lice in dogs and cats, and aids in the control of sarcoptic mange in dogs.</p> <p>FRONTLINE PLUS®/ FRONTLINE COMBO® is indicated for the treatment and prevention of fleas, ticks and chewing lice in dogs and cats. Also breaks the flea life cycle by preventing the development of immature stages. It aids in the control of sarcoptic mange in dogs.</p> <p>FRONTLINE TRI-ACT®/FRONTECT® is indicated for the treatment and prevention of flea and tick infestations where repellent (anti-feeding) activity is necessary against sandflies, biting flies and/or mosquitos. For dogs only.</p> 
- Antiparasitic: canine external parasites	NEXGARD®	<i>afoxolaner</i>	 <p>NEXGARD® is delivered in a highly palatable beef-flavoured chew that kills adult fleas and is indicated for the treatment and prevention of flea infestations and the treatment and control of tick infestations in dogs and puppies for one month.</p>
- Antiparasitic: canine internal and external parasites	NEXGARD SPECTRA®	<i>afoxolaner</i> , <i>milbemycin oxime</i>	 <p>NEXGARD SPECTRA® is delivered in a highly palatable beef-flavoured chew that kills adult fleas and is indicated for the treatment and prevention of flea and tick infestations. Prevents heartworm disease and treats and controls hookworm, roundworm, whipworm and lungworm infestations in dogs and puppies.</p>
- Antiparasitic: canine internal parasites	HEARTGARD® PLUS	<i>ivermectin</i> , <i>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</i> , (s)- <i>methoprene</i> , <i>eprinomectin</i> , <i>praziquantel</i>	 <p>Protects cats against the broadest spectrum of internal and external parasites including adult fleas, flea eggs, flea larvae, ticks, heartworms, hookworms, roundworms, and tapeworms.</p>
- Congestive heart failure	VETMEDIN®	<i>pimobendan</i>	 <p>Treatment of canine congestive heart failure originating from dilated cardiomyopathy or valvular insufficiency (mitral and/or tricuspid regurgitation).</p> <p>Treatment of dilated cardiomyopathy in the preclinical stage (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter) in Doberman Pinschers.</p> <p>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.</p>

COMPANION ANIMALS - PETS (CONTINUED)

METACAM® is a non-steroidal anti-inflammatory drug (NSAID). It is available as an oral suspension, tablets and injectable solution for dogs and as an oral suspension and injectable solution for cats. In dogs, the indications include the alleviation of inflammation and pain in both acute and chronic musculoskeletal disorders as well as the reduction of pain following surgery. In cats, the indications include the alleviation of inflammation and pain in acute and chronic musculoskeletal disorders, as well as for the alleviation of mild to moderate postoperative pain. The variety of formulations offers veterinarians and owners the flexibility to use the formulation they prefer in individual cases to manage the various levels of inflammation and pain associated with the licensed indications.

SEMINTRA® is the first-ever licensed angiotensin receptor blocker (ARB) for veterinary use. It provides a proven, convenient and safe compliance solution for cats, cat owners and vets. 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 (CKD) 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.

Our pet vaccine product portfolio includes the PUREVAX® feline vaccines formulated to provide effective protection without the use of adjuvants and RECOMBITEK®, providing targeted protection for dogs through recombinant technology.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
– Pain and inflammatory diseases	METACAM®	<i>meloxicam</i>	 <p>In dogs, METACAM® is used to reduce post-operative pain and inflammation following orthopaedic (e.g. fracture operation) and soft tissue surgery.</p> <p>In cats, METACAM® is used to reduce postoperative pain and inflammation, e.g. after ovariohysterectomy (spay operation), orthopaedic and minor soft tissue surgery.</p> <p>Moreover, it is used for the alleviation of pain and inflammation in acute and chronic musculoskeletal disorders (dogs and cats).</p>
– Chronic kidney disease (CKD) in cats – Hypertension in cats	SEMINTRA®	<i>telmisartan</i>	 <p>4mg/ml – Management of chronic kidney disease (CKD) in cats: for reduction of proteinuria associated with CKD in cats.</p> <p>10mg/ml – Hypertension: indicated for the treatment (EU)/control (US) of feline systemic hypertension.</p>
– Feline vaccines portfolio	PUREVAX®	<i>feline herpes virus</i> <i>feline calicivirus</i> <i>feline panleukopenia virus</i> <i>chlamydomphila felis</i> <i>recombinant vectored feline leukemia virus</i> <i>recombinant vectored rabies virus</i>	 <p>PUREVAX® is the only fully adjuvant-free feline vaccine range and provides:</p> <ul style="list-style-type: none"> • Optimised safety profile with adjuvant-free protection for all components; • Powerful immune response without adjuvant, thanks to its innovative canarypox technology for FeLV and rabies; • An easy fit to all cat lifestyles, allowing compliance with feline vaccination guidelines; • Sustained protection up to three years for the rabies component.
– Canine vaccines portfolio	RECOMBITEK® (*in the US and others)	<i>recombinant vectored canine distemper virus,</i> <i>canine parvovirus,</i> <i>canine adenovirus type 2,</i> <i>canine parainfluenza virus,</i> <i>coronavirus,</i> <i>leptospira Canicola,</i> <i>leptospira grippotyphosa,</i> <i>leptospira icterohaemorrhagiae,</i> <i>leptospira Pomona,</i> <i>recombinant borrelia burgdorferi,</i> <i>bordetella bronchiseptica</i>	 <p>RECOMBITEK® offers a complete line of canine vaccines with:</p> <ul style="list-style-type: none"> • Proven efficacy against distemper in the presence of maternal antibodies;* • Concentrated Parvo with demonstrated protection against major circulating strains CPV-2a, 2b, 2c;* • Prevention of disease and shedding against leptospirosis;* • Targeted, advanced science – without the need for adjuvants. <p>RECOMBITEK® lyme: The only vaccine that contains OspA in a non-adjuvant formulation.</p> <p>RECOMBITEK® oral bordetella: Effective and safe protection made easy.</p> <p>*Data on file</p>

C.H. Boehringer Sohn AG & Co. KG, Ingelheim

COMPARISON OF BALANCE SHEET AND FINANCIAL DATA 2009 – 2018

(in EUR million)

Assets (as of December 31)	2009	2010	2011	2012	2013
Intangible assets	745	736	710	682	582
Tangible assets	3,219	3,314	3,442	3,103	2,887
Financial assets	1,699	3,168	3,953	4,222	4,737
Fixed assets	5,663	7,218	8,105	8,007	8,206
Inventories	1,801	1,850	1,998	2,095	2,083
Accounts receivable and other assets (incl. prepaid expenses, deferred taxes and exceeding amount of plan assets)	3,663	4,047	4,652	4,814	5,131
Liquid funds	3,877	3,118	3,903	2,374	2,879
Current and other assets	9,341	9,015	10,553	9,283	10,093
Total assets	15,004	16,233	18,658	17,290	18,299
Equity and Liabilities (as of December 31)	2009	2010	2011	2012	2013
Shareholders' capital	178	178	178	178	178
Group reserves (incl. balance sheet currency conversion difference)	3,964	5,408	5,812	4,763	5,619
Group profit	1,759	888	1,476	1,237	1,324
Equity attributable to the parent company	5,901	6,474	7,466	6,178	7,121
Non-controlling interests	179	0	0	0	1
Group equity	6,080	6,474	7,466	6,178	7,122
Difference from capital consolidation	0	0	157	134	104
Provisions (incl. deferred taxes)	5,731	6,598	7,402	7,749	7,817
Liabilities (incl. deferred income)	3,193	3,161	3,633	3,229	3,256
Total liabilities (incl. deferred taxes and deferred income)	8,924	9,759	11,035	10,978	11,073
Total equity and liabilities	15,004	16,233	18,658	17,290	18,299
Summary of selected financial data	2009	2010	2011	2012	2013
Net sales	12,721	12,586	13,171	14,691	14,065
Operating income	2,239	1,896	2,272	1,853	2,114
Operating income as % of net sales	17.6	15.1	17.3	12.6	15.0
Income after taxes	1,764	888	1,476	1,237	1,324
Income after taxes as % of net sales	13.9	7.1	11.2	8.4	9.4
Return on equity (in %)	37.4	15.0	22.8	16.6	21.4
Equity ratio (in %)	39.3	39.9	40.0	35.7	38.9
Cash flow from operating activities	2,391	2,056	2,570	2,170	1,819
Financial funds	5,384	6,113	7,711	6,467	7,514
Personnel expenses	3,221	3,358	3,664	4,024	4,071
Personnel expenses as % of net sales	25.3	26.7	27.8	27.4	28.9
Average number of employees	41,534	42,224	44,094	46,228	47,492
Research and development expenses	2,215	2,453	2,516	2,795	2,743
R&D expenses as % of net sales	17.4	19.5	19.1	19.0	19.5
Investments in tangible assets	630	519	458	562	558
Depreciation of tangible assets	470	498	535	793	640

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C.H. Boehringer Sohn AG & Co. KG
 Binger Straße 173
 55216 Ingelheim
 Germany
 Telephone + 49 6132 77-0
 Fax + 49 6132 72-0

CONTACT

Corporate Division Communications and Public Affairs
 E-mail press@boehringer-ingelheim.com
 Internet www.boehringer-ingelheim.com

ISSUED BY

C.H. Boehringer Sohn AG & Co. KG

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PHOTOS

Andreas Pohlmann (page 2)
 Andreas Reeg (page 4 / 5)

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2014	2015	2016	2017	2018
592	606	550	5,372	5,120
3,070	3,264	3,045	3,867	4,280
5,312	5,933	6,092	5,830	6,058
8,974	9,803	9,687	15,069	15,458
2,237	2,483	2,610	3,087	3,312
5,546	6,463	6,837	7,159	7,815
3,294	4,536	7,005	3,071	4,303
11,077	13,482	16,452	13,317	15,430
20,051	23,285	26,139	28,386	30,888

2014	2015	2016	2017	2018
178	178	178	178	178
6,884	7,844	9,296	10,703	10,080
1,047	1,577	1,853	– 223	2,075
8,109	9,599	11,327	10,658	12,333
2	4	0	– 1	1
8,111	9,603	11,327	10,657	12,334
91	71	52	1,729	1,511
8,840	10,543	12,233	13,482	14,438
3,009	3,068	2,527	2,518	2,605
11,849	13,611	14,760	16,000	17,043
20,051	23,285	26,139	28,386	30,888

2014	2015	2016	2017	2018
13,317	14,798	15,850	18,056	17,498
2,140	2,269	2,872	3,487	3,472
16.1	15.3	18.1	19.3	19.8
1,046	1,576	1,849	– 229	2,075
7.9	10.7	11.7	– 1.3	11.9
14.7	19.4	19.3	– 2.0	19.5
40.4	41.2	43.3	37.5	39.9
2,015	2,232	2,888	2,624	2,988
8,507	10,200	11,989	8,130	9,454
4,116	4,518	4,570	4,934	5,276
30.9	30.5	28.8	27.3	30.2
47,743	47,501	45,692	49,610	50,370
2,654	3,004	3,112	3,078	3,164
19.9	20.3	19.6	17.0	18.1
548	591	645	872	950
449	475	516	521	552

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