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EXPLORE THE INTERACTIVE CONTENT!

This Annual Report is smart. Whenever you see this symbol in the magazine, you can start a video straight from the corresponding page on your smartphone or tablet.

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Hold your device over the page for which you would like to watch additional video content. Tap the screen to scan. Keep still! The device will scan the page and the video will open directly and play.

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TRANSFORMATION MEETS TRADITION
The goal of the new digital lab BI X is to create innovative, digital solutions for the research-driven pharmaceutical company.

THE LITTLE THINGS
Her horses help the scleroderma patient Anna Végh cope with the disease.
Boehringer Ingelheim is one of the world's 20 leading pharmaceutical companies.

**BOEHRINGER INGELHEIM**

**2017 AT A GLANCE**

Founded in 1885 in Ingelheim and family-owned to this day

~ 50,000 employees worldwide

18.1 billion total net sales

3.1 billion expenditure in research and development

17.0% of total net sales

**EUR**

12.6 billion human pharmaceuticals

3.9 billion animal health

678 million biopharmaceuticals

~ 20 leading pharmaceutical companies

Founded in 1885 in Ingelheim and family-owned to this day

~ 50,000 employees worldwide

18.1 billion total net sales

3.1 billion expenditure in research and development

17.0% of total net sales

**EUR**

12.6 billion human pharmaceuticals

3.9 billion animal health

678 million biopharmaceuticals
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 2017, Boehringer Ingelheim achieved net sales of almost 18.1 billion euros. R&D expenditure, exceeding three billion euros, corresponded to 17.0 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.
WHAT AGILITY MEANS FOR US
What role does agility play in the Boehringer Ingelheim tradition?

“Boehringer Ingelheim’s initial success as a family-owned company was based on the industrial production of acids. The move from mass-produced chemical raw materials to patent-protected pharmaceutical specialties required building up a successful own research operation and called for understanding a new customer class – physicians. This example of agility, which turned us into the leading research-driven pharmaceutical company we are today, should serve as an inspiration to us during the current transformation of the healthcare market to also adapt to the needs of those who have to finance our healthcare system.”

CHRISTIAN BOEHRINGER
Chairman of the Shareholders’ Committee
Where will the agile company Boehringer Ingelheim be in 2025?

“Agility to 2025 and beyond will allow Boehringer Ingelheim to increase its contribution to patient health. We will be offering new and innovative therapeutic options and breakthroughs to answer medical needs – on the human as well as the animal side. Using new technology, collaborating with our partners even more intensely in networks and being able to manage ever larger data will enable us to target our medicine more precisely to the individual patient, making our products even more effective and increasing the benefit to society.”

HUBERTUS VON BAUMBACH
Chairman of the Board of Managing Directors

How much influence does agility have on the integration of the new Animal Health Business?

“In Animal Health, we are currently engaged in building a new unit by bringing two successful companies together. This has given us the opportunity to regroup around what is truly core for our business. One of the cornerstones is a common culture where agility is embedded. In such a process, flexibility and adaptability are called for in order to meet the requirements of our customers and to further expand our leading position in this highly competitive market.”

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

How agile must a company be to position itself successfully on the market?

“To be successful in the market it is crucial for a company to be agile. And agility is required in many areas. One is having excellent customer understanding and the agility to react to changing customer perceptions and expectations. Another is the agility to react to changing market conditions. Finally, the agility to respond to competitors’ actions and strategies is important to increase our competitiveness.”

ALLAN HILLGROVE
Member of the Board of Managing Directors with responsibility for the Human Pharma Business Unit
How can agility drive the company’s financial success?

“Agility is a precondition for economic success. For this reason, we not only want to recognise ever faster changing internal and external conditions early, but to also draw the right conclusions. Then it is a matter of acting rapidly, but with the necessary diligence. Thus we will also overcome future challenges, compete successfully and deliver the best services to our customers.”

MICHAEL SCHMELMER
Member of the Board of Managing Directors with responsibility for Finance

What does agility mean for Boehringer Ingelheim’s innovative capability?

“Agility is required every day in the journey from idea to innovation. It is indispensable for the timely integration of new information, allowing us to learn from failures and build on small wins, step by step, to achieve breakthroughs.”

DR MICHEL PAIRET
Member of the Board of Managing Directors with responsibility for the Innovation Unit
“It is about doing the right thing”

Strategic decisions demand great flexibility and courage from the people involved. When the Animal Health organisations of Boehringer Ingelheim and Sanofi merged, two corporate cultures and many different nationalities found their way into a single melting pot that is now Boehringer Ingelheim’s new Animal Health Business Unit. Rogier Biemans, Site Director in Pirbright (UK) and originally from the Boehringer Ingelheim organisation, and Vanessa Mariani, Global Commercial Operations Integration Lead and former Merial employee, discuss how they bring together the best of both worlds.
Rogier, you transferred from the Boehringer Ingelheim site in Weesp in the Netherlands to Pirbright in the UK. Vanessa, you left Atlanta in the USA and came to Ingelheim. How much courage did that take?

**BIEMANS** It wasn’t easy, I can tell you that. Saying goodbye to colleagues is hard. I would have really liked to take some of them with me. I try to stay in touch, but life is moving on. And the people in the UK have been treating me very well.

**MARIANI** For me the move was a game changer. In Atlanta I worked for Merial, now I’m part of Boehringer Ingelheim. I’ve been living in Ingelheim since March 2017 and will stay here until March 2018 on an extended business trip. My husband still lives in Atlanta, so I try to fly home every four weeks.

**BIEMANS** Our jobs also keep us very busy. There’s really no time to miss old ways.

**MARIANI** That’s true. And, after all, it’s really about the people, not the location. I’m still in touch with some colleagues I worked with in Atlanta. But the people here in Ingelheim have been so amazing and welcoming, there’s nothing that I’d change.

Vanessa, how is living in a rather rural area going for you so far?

**MARIANI** Originally I am from Mexico City and I lived in New York City for 15 years. Ingelheim is definitely a change – but I like it. I haven’t really suffered any cultural shock. The only thing that takes a little bit to get used to is Sundays when all the stores are closed in Germany.

Not only has the size of the town taken some time to get used to. The people are also different. What’s special about the Boehringer Ingelheim headquarters?

**BIEMANS** Whenever I visit Ingelheim I feel people are very correct and value rules. The dress code is stricter, the conversations are more formal. But, if you get to know the people, they loosen up.

**MARIANI** I noticed a certain formality here in Ingelheim as well – which I like. I appreciate having a framework and rules. But our lives are so different every day that we have to be flexible. So, despite the formality, we’ve created a space where we can be a lot more relaxed about how we interact with each other or how we approach different situations.

Vanessa, you have spent most of your life in North America. Is working in Germany challenging?

**MARIANI** We work in a global corporate world, so it’s rare to find someone who hasn’t interacted with other cultures. The most positive part about the move to Ingelheim is the culture: the way that I’ve felt welcomed in the Boehringer Ingelheim organisation, in the integration team, in Ingelheim in general. It’s a fantastic experience.

It’s not only a change for you personally, but also for Boehringer Ingelheim and Merial in general – two companies are trying to integrate two businesses and form a single entity, right?

**BIEMANS** This process is still ongoing and will continue throughout the upcoming months. The differences regarding the corporate structure are huge: Merial is a multinational public company, Boehringer Ingelheim is a privately held, global organisation.

**MARIANI** To combine the two businesses, we developed a new vision. We are driven by the conviction that animals enrich human life. It’s vital for the integration process to have a common set of beliefs.

Boehringer Ingelheim and Merial both have their own unique corporate culture. What does corporate culture mean to you?

Vanessa Mariani and Rogier Biemans met in October 2017 in Ingelheim. Both work for Boehringer Ingelheim’s new Animal Health Business Unit.
BIEMANS For me it's how people interact with each other. This relates to the underlying values. At Boehringer Ingelheim there is a structured way of working, people are always correct and respectful. This creates a certain atmosphere that determines how people interact with each other.

MARIANI Culture – whether it’s in society at large or in a corporation – is down to behaviour and everyday life. You can have a written code, but it’s really how you live the underlying values that build a culture.

What are the main differences in the cultures of Merial and Boehringer Ingelheim?

MARIANI I found that Merial was a lot more lax and more open about structuring the daily business, which probably had to do with the fact that it was previously a joint venture. This gave the organisation great freedom to operate.

BIEMANS I agree. At the beginning of this year, we had a global operations conference at the Merial headquarters in Lyon. It was a three-day conference and everybody was waiting for the agenda to be sent out. So we all arrived in Lyon still waiting for the agenda. It was certainly more informal and improvised than Boehringer Ingelheim people were used to.

MARIANI Yes, for many people coming from a more lax environment, a tight framework can be a little bit of a shock.

You’ve both worked in various locations. How does the culture differ in each place?

BIEMANS With Boehringer Ingelheim there’s a common corporate culture, but certain elements are unique for each location. The country hugely influences the way people interact. The type of location also plays a role, whether it’s a production site or an office.
MARIANI I feel that in Animal Health in general, people are very passionate about the industry, about the social purpose their work is fulfilling, about doing the right thing for animals and people. It’s an industry where people work really hard across all locations and countries.

Is doing the right thing specific to Animal Health?

MARIANI I’ve been working in the field for almost 20 years, so from my perspective, it was always very intrinsic for Animal Health. But I’ve found in the time I’ve been here in Ingelheim that it is intrinsic to the overall Boehringer Ingelheim culture. We always ask ourselves, is this the best approach? What is the long-term gain? How does it fit the overall strategy? We try to do the right thing for the right reasons – long-term. It’s refreshing that there’s a link from today to tomorrow, which you don’t always see in other companies.

BIEMANS Again, I agree with you. For example, the products we make in the UK are vaccines against foot-and-mouth disease (FMD). We sell them to governments through the department of Veterinary Public Health in Lyon. These vaccines can change people’s lives. For many people, our products are fundamental – even more fundamental than we sometimes realise.

One of the main differences between English-speaking countries and Germany is how people who work together address each other. In German, we use last names and the more formal word for “you” to retain a certain distance. How do you find that?

BIEMANS In the UK, we hardly use people’s last name, the atmosphere is very relaxed. Animal Health is also a little bit more casual than other areas of the pharmaceutical industry. At production locations in particular it’s less formal. I like that. But in my opinion, boundaries are not established by first or last names. There are other underlying factors.

MARIANI Right. It’s more about creating respect between different parts of the team. My boss, for example, has a “Dr” before of his name. This usually establishes a certain distance, but he is the most approachable person you can find. He works in our team room with us. Whether he’s a doctor or not, an engineer or an architect – what really matters to us is that he’s got commitment. We respect him more for his work than for any title.

BIEMANS I also feel that things are changing in Germany. In the 1980s, it was more formal than today.

Combining two different corporate cultures isn’t easy. Have there been any teambuilding activities to make the transition easier?

MARIANI When the deal between Sanofi and Boehringer Ingelheim was concluded, different countries had “day one events” and integration workshops. In our team here in Ingelheim, we organise quarterly social activities, like going out for dinner.

BIEMANS When I transferred to the UK, the onboarding was good. People are very nice, open and really straightforward. At Pirbright, everyone gets a card for their birthday. We didn’t do that at my previous site in Weesp. I like new ideas, it’s always good to take the best of both worlds and use them.

Are there any stereotypes that arise when working with so many different cultures?

BIEMANS The British are strong on humour; I don’t think that’s a stereotype though. They appreciate a vigorous exchange of views which is sometimes enjoyable and sometimes a little bit too much.

MARIANI Ingelheim is a melting pot of so many different nationalities. You can’t have stereotypes when you work with so many different people; there is just no place for it.

BIEMANS Every individual is different. The fact that one comes from a certain country doesn’t pigeonhole them. There are very formal and informal Germans, there are heated and cool Mexicans.

MARIANI I work with people from Columbia, Spain and other Spanish-speaking countries and we joke about each other’s accents and colloquialisms. But it’s all in good humour.

BIEMANS If you can happily make jokes about each other, you’re communicating at the same level. What matters is the underlying respect.
What’s the goal of the new People Strategy Boehringer Ingelheim has been implementing worldwide since the beginning of 2016?

**LARSEN** We’re faced with the challenge of having to rapidly adapt and position ourselves effectively in a competitive and also increasingly volatile market environment. We’ll only achieve these objectives if our company has the right employees with the right competencies at the right time. We’ve established the strategic basis for this with our People Strategy. With the aid of a structured and holistic approach, we aspire to identify which employees and competencies will be key to our future success.

What changes will the new People Strategy entail for the management and employees?

**LARSEN** We’re supporting individual departments, business areas and subsidiaries in answering: What can we do today to develop the necessary competencies for tomorrow’s challenges? On the basis of a good understanding of what our strengths and weaknesses are, we describe what competencies we need and how we can prepare our employees accordingly. We put special emphasis on also providing the appropriate training. Implementation of our People Strategy will thus sharpen our ability to handle future challenges.

Why is that important?

**LARSEN** Because it takes courage to take new roads together and adapt our organisation to a changing environment. Employees want to know their positions, their roles and their responsibilities in the company today and tomorrow. It’s therefore essential for us in HR to acknowledge that yes, we’ve got to be even more agile and respond accordingly. In the end only a successful business will allow us to create new jobs and keep existing ones. And vice versa only talented, highly motivated people will help us to keep the company flourishing.
Our FOCUS is a framework that helps us concentrate our efforts where they are needed most.
THE CORE OF OUR LEITBILD IS THAT WE ARE AN INDEPENDENT, FAMILY-OWNED COMPANY 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.

Boehringer Ingelheim’s commitment to serve mankind can be met if we are the preferred partner and admired competitor by being:

- Number one in Animal Health
- Number one in biopharmaceutical contract manufacturing
- Number one in value share for our brands in One Human Pharma

By 2025 we aspire to grow our sales to 25 billion euros.

Our FOCUS is a catalyst to unlock our potential. We are Boehringer Ingelheim!

AGILITY:
- We quickly act with an open mind to face internal and external transformation.
- Search and respond to drivers of changes through active experimentation.
- Challenge the status quo and assumptions of your own and others with no political bias.
- Quickly turn data into insights and insights into actions.
- Learn with an open mind and rarely make the same mistake twice.

ACCOUNTABILITY:
- Even in ambiguous circumstances, we always demonstrate ownership for our decisions and actions.
- Role model Boehringer Ingelheim Values by always doing what you say and saying what you think.
- Make timely decisions with well-balanced analysis and intuition, particularly in tough situations.
- Ruthlessly prioritise, then drive execution excellence through discipline and collaboration.
- Actively give and seek feedback; leverage each other’s strengths to deliver results and develop every individual.

INTRAPRENEURSHIP:
- Together with our customers, we create innovative ideas to respond to changing markets.
- Serve the needs of customers and patients by turning innovative ideas into business results.
- Take smart risks by leveraging all possible opportunities – including resources and talents.
- Demonstrate winning spirit through creating a can-do attitude and positive energy among others.
- Deliver high quality results, despite challenging conditions.
More than a year has now passed since Boehringer Ingelheim acquired its competitor Sanofi’s animal health business, Merial. Its integration is well underway and everything is set for growth: Boehringer Ingelheim intends to make its animal health business the market leader by 2025.
Boehringer Ingelheim has a vision: this research-driven pharmaceutical company wants to create a world where animals no longer suffer from avoidable diseases, because targeted prevention work will help stop them from occurring in the first place. Boehringer Ingelheim is convinced that, when animals are healthy, humans are healthier too.

To realise this vision, Boehringer Ingelheim acquired Merial, the animal health business of the pharmaceutical company Sanofi, in January 2017. The acquisition brings together two highly compatible portfolios to strengthen Boehringer Ingelheim’s competitiveness in the field of animal health: following the integration of Merial, its net sales in animal health have more than doubled and now provide more than one fifth of its total group net sales. With around 10,000 employees in this business unit worldwide, Boehringer Ingelheim now offers animal health products in over 150 markets.

Merial and Boehringer Ingelheim fit together like the pieces of a jigsaw puzzle. While Boehringer Ingelheim was a leader in the livestock segment, Merial brought leadership in companion animals such as cats and dogs.

The combination of these strengths enables Boehringer Ingelheim to take full advantage of the market’s potential. This potential is enormous:

→ Forecasts predict that net sales in the global animal health market will double to 53 billion euros by 2030. This in part reflects a growing world population. By 2050, the world’s population will have reached nine billion and current demand for meat will have doubled or even tripled.

→ Increasing globalisation and stronger links between different countries and continents mean that infectious animal diseases may become even more frequent in future.

→ Another trend is that people are spending increasingly large sums of money on their pets. Their dogs, cats and other domestic animals have long since become members of the family.
Boehringer Ingelheim is optimally positioned with its integrated product portfolio which now features more than 200 products for dogs, cats, horses, pigs, cattle and poultry. Following its acquisition of Merial, Boehringer Ingelheim is now the second-biggest player in the global animal health market. Its goal for the next years is clear: Boehringer Ingelheim aims to become the market leader in animal health by 2025. Today, the company is already the leader in the areas of vaccines and parasiticides. And Boehringer Ingelheim is also the number one in pets, equine and swine and in the field of veterinary public health. It now aims to catch up in poultry and cattle.

Yet competition is fierce on the animal health market. Research and development is a key factor for future success and growth. Around 1,200 scientists and support staff are conducting research at more than 20 sites globally in order to stem the spread of diseases before they even occur. As well as its core segments of vaccines, parasiticides and pharmaceuticals, Boehringer Ingelheim intends to expand its pet health care, diagnostics and live therapeutics segments, so as to be able to offer its customers even broader solutions in the future.

The acquisition brings together two highly compatible portfolios to strengthen Boehringer Ingelheim’s competitiveness in the field of animal health.
While Boehringer Ingelheim has been leader in the livestock segment, Merial brought leadership in companion animals such as cats and dogs.

Boehringer Ingelheim has a long tradition on prevention in animal health. Following the integration of Merial, and thanks to strategic partnerships with external partners such as Novozymes, Boehringer Ingelheim is able to offer even more innovative solutions – now and in the future.

**Partnership with Novozymes**

In order to further boost its expertise in the field of prevention, Boehringer Ingelheim entered into a strategic partnership with Danish biotech company Novozymes in March 2017. Over the next ten years, the new partners want to work together to develop live therapeutic products for poultry hatcheries. While Novozymes will be responsible for the research and development work, Boehringer Ingelheim will market the differentiated solutions, with the first product in line being *floramax*®, a probiotic product from the Novozymes portfolio.

Probiotics are becoming increasingly important as alternatives to antibiotics. As such, they could also play a major role in preventive health: living microbes have a positive impact on the intestinal flora balance of poultry and other animals, thereby providing specific health benefits. In some cases, they produce distinct compounds that will help the immune system to mature – leading to a healthier gut. The first probiotic product from the Boehringer Ingelheim and Novozymes alliance is currently in the test phase and is set for market launch during 2018.

**Nexgard® to combat parasites**

If dogs get fleas, owners soon face a challenge. The pests burrow deep into the dog’s fur and skin and like to jump into their surroundings. Untreated, fleas can cause health problems in dogs and humans, just as ticks can. This makes prevention all the more important.

Thanks to the integration of Merial, Boehringer Ingelheim’s portfolio now includes the *nexgard*® family of medicines: *nexgard®* is administered as a beef-flavoured chew and, at its launch, was the first oral medication to treat both fleas and ticks in dogs. It is currently the best-selling pet medication in the animal health industry. In certain markets, Boehringer Ingelheim recently launched *nexgard® spectra* which adds protection for dogs against certain internal parasites.

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*Data on file*
AGILITY NEEDS COURAGE
Nothing has ever been the same again for Anna Végh since she learned in 2009 that she suffers from scleroderma, a rare autoimmune disease. But Anna did not give up – and has found her way to have a happy life despite her condition.

The little things

Anna is sitting with her mother in a hospital waiting room. This petite young woman with auburn hair is nervous and anxious about what might lie ahead for her. She has been experiencing severe pain for some weeks now. She suffers particularly painful sensations in her stomach and hands as well as when breathing. It is worst in the mornings and evenings.

No one knows what causes this or can explain why Anna’s skin changes and suddenly feels so different; rough and thicker. Her doctor is unable to account for this, her family is frightened and this Hungarian woman living in the small town of Szombathely simply wants to know what is happening with her.

Everyone she knows senses that she is seriously ill. That is why she is now sitting here in the hospital, waiting. As the minutes slowly pass, a poster catches Anna’s eye. Its heading is “Scleroderma” and displays facts about the disease as well as images of people suffering from it. Anna is shocked. She leans over to her mother. “How awful must it be to have that disease?” she asks. Some time later, Anna’s doctor tells her that she is suffering from scleroderma.

That was eight years ago. The very rare disease scleroderma, also known as systemic sclerosis, causes swelling and scarring of connective tissue. In many cases, the lungs and other organs gradually also suffer scarring, which can become life-threatening for patients. The disease affects around two million people worldwide, mainly women between the age of 25 and 55.

“Back then, my world completely fell apart,” Anna recalls. Even though the doctor assured her that many patients maintained a good quality of life with this disease, it felt as though she would never be happy ever again. “I simply couldn’t imagine how someone could lead a nice life with a disease like that”, says Anna, who is now 36 years old. At the time, she did a lot of research in order to find out what she faced. “Everything I found was absolutely terrifying.” She found no
positive examples. Nor did she find anybody else suffering from this disease to talk things over with. “I was completely on my own.”

At the same time, she noted that she was experiencing more and more symptoms. Her mobility declined, she was out of breath more rapidly and had to give up hobbies. Before she fell ill, she had gone to the gym several times a week to exercise on a spinning bike. “But there came a point where I could no longer manage it, I simply didn’t have the strength. That really frustrated me,” says Anna. She also had to get used to regularly taking medicines and attending hospital check-ups as well as being suddenly extremely restricted, even in entirely normal everyday situations. “I couldn’t even use my credit card on my own since it was too much of a strain for my hands to take it out of my purse.”

Anna nevertheless learned how to cope with this disease. “I noticed that there were many important things which I was still capable of doing”, she says. She kept her job as a quality manager. “It was important for me that my colleagues continued to treat me normally and that I was able to do my job.” Nor did her social life change as a result of the disease. “My family is still the most important thing for me.” Her mother, brother and sister never leave her side during tests and consultations with doctors. Her friends also give her a lot of strength. “It was important to know that the disease can’t take them away from me.”

In the meantime, Anna has become happy once again, and maybe even happier than she was before her diagnosis:

“The horses sense my mood without me having to say anything.”

Anna has decided to go public with her story in order to encourage other sufferers. “I would like to make it clear
“I would like to make it clear to them that they are not alone.” She has not forgotten that poster in the waiting room. “Seeing those horror scenarios makes it only worse – instead, we should be hearing more about people who live happy lives in spite of the disease.” People like Anna.

Anna long looked for a stud farm that keeps horses in paddocks. The huge amount of space the horses enjoy also gives her a sense of freedom when she rides across the paddocks.

MORE THAN SCLERODERMA

Scleroderma, or systemic sclerosis (SSc), is a rare, so far incurable disease. It is characterised by hardening of the skin and connective tissue. It affects around two million people worldwide¹ and three times more women than men, mainly in mid-life. Lung diseases are a common manifestation of systemic sclerosis. This is particularly serious as most patients develop pulmonary fibrosis to some extent. Boehringer Ingelheim – a leader in respiratory medicine – has been conducting active research into the potential fatal consequences of fibrotic lung diseases for years. With its global initiative “More than Scleroderma: The Inside Story”, Boehringer Ingelheim is pursuing the goal of educating society as a whole and providing information about the disease to those interested. To this end, the company collects inspiring stories from patients all over the world and publishes brief portraits of their lives on the website www.boehringer-ingelheim.com. These portraits may be video interviews or photo series. Sufferers can read about how other patients cope with the disease. At the same time, they learn about the progression of the disease and its in part serious effects. But the initiative is not seeking to scare people – on the contrary: the goal is to show patients that the disease will not determine their lives and that each of them can find their own way of coping with it. Eight portraits of patients from seven countries are currently featured on the website.

¹ University of Michigan, Scleroderma Program: www.med.umich.edu/scleroderma/patients/scleroderma.htm
AGILITY NEEDS CREATIVITY
Transformation meets tradition

Wild sketches, brightly painted office walls, fur-covered stools – BI X, Boehringer Ingelheim’s new digital lab, looks like the work spaces of a start-up in San Francisco or Berlin.
The goal: innovative digital solutions for the research-driven pharmaceutical company. BI X thereby marks the beginning of the transformation of the whole company. The digitisation of Boehringer Ingelheim is in full swing.
“Even projects that fail can indirectly lead to success later, if we learn something from them.”

Anyone looking for the new BI X digital lab on the Boehringer Ingelheim campus in Ingelheim, Germany, stands a good chance of getting lost. It is a 15-minute walk from the main gate. The building is located on the edge of a little wood and is rather unassuming, almost old-fashioned from the outside. Only inside does it look like a start-up. Although there are also desks, people work wherever it suits them at the time: in the foyer, in the lounge corner or at the large wooden table in the kitchen. Anyone who has a spontaneous idea can instantly jot it down with a marker pen on the writable walls. Even the large windows with their views of greenery have bright post-it notes stuck on them so that no ideas are lost. The technology is impressive too. In almost every room there is a giant touchscreen. In addition there are unconventional tools such as small building blocks in case quick, tangible models are called for.

BI X is a whole new world for Boehringer Ingelheim. While elsewhere on the Ingelheim site, people predominantly dress in traditional businesswear, lab coats and overalls, Dr Daniel Hach opens the doors to BI X in trainers and a T-shirt. The 32-year-old was one of the first people employed by the digital lab and is responsible as part of a four-man management team for day-to-day operations. At our visit in October 2017, we meet Michael Schmelmer1, who was then head of BI X as well as Boehringer Ingelheim’s Chief Information Officer (CIO).

The company, founded in summer 2017, is still comparably small with a staff of around 30. However, new faces join the team every month. By mid-2018, around 50 talented tech specialists should be working at the digital lab. The company seeks out experienced experts who bring with them in-depth knowledge of the industry and of methodical digitisation, as well as pioneers with the necessary passion for implementing initiatives and visions with conviction.

Formally, BI X is a subsidiary of Boehringer Ingelheim, but the digital lab is de facto a start-up. The synergies with the parent company create benefits and make everyday work easier: “As an independent company, BI X benefits greatly from the freedom of a start-up, but also from the tried-and-tested processes of a globally leading pharmaceutical company – for example, when it comes to contracts or approval processes,” says Schmelmer. “This gives our people more time for what they are meant to be doing.” And it is specifically this way of working that distinguishes BI X so clearly from the rest of the company. The tech experts work in accordance with the latest agile planning methods.

The fact that this does not always lead to instant success is all part of the plan. “Failure is allowed at BI X,” states Schmelmer. “At BI X, we consciously work on high-risk projects that are hard to implement. On average, only half of our projects are successful.” Set-backs are all part of the learning process:
WANTED: INNOVATIONS. 
THE FIRST BI X PROJECTS

BI X developments go through three cycles, Michael Schmelmer¹ explains. The first phase is all about ideas that are very closely aligned with the business of the parent company. For example, the BI X team has developed software for researchers to make it easier to analyse data and the latest scientific insights from the whole world and to identify possible relationships. For example, certain protein concentrations could be recognised as a possible therapeutic approach and medication development speeded up. The team is currently in the second wave of generating ideas. They are developing new approaches that are still connected to Boehringer Ingelheim’s business but are disruptive and thereby capable of opening up new business areas. The BI X team has, for instance, developed an app for the digital early detection of Alzheimer’s disease. The aim is to determine by only analysing speech whether a person is showing early signs of the disease. “Alzheimer’s research is linked to the traditional businesses at Boehringer Ingelheim, but the app offers a service that does not yet exist in this form. What’s more, nobody else has done anything like it before,” Michael Schmelmer says. In the third wave, the team wants to go still further and take on assignments with the potential to shake up the market, as Schmelmer puts it. “But that will come with time, once BI X is more mature. We will start with topics that we can gauge, and once the processes are in place, when the team knows how BI X works, then we can address more high-risk matters.” However, what kind these might be is not something that Schmelmer wants to reveal yet.

¹ CFO of Boehringer Ingelheim since 1 January 2018
“Successful implementation is not the only thing that counts. Even projects that fail can indirectly lead to success later, if we learn something from them.”

Learning from mistakes is part of BI X’s DNA. The mission statement is literally writ large in the foyer. “We take on challenges every day. We take risks and make mistakes with pride. We play by our own rules. We are BI X,” the manifesto states. The members of staff developed the mission statement together, which is a new approach for Boehringer Ingelheim: “I like the fact that the team decides for itself what it wants to achieve and how it wants to work, who its members are and what their plans are,” says Schmelmer. In large corporations in particular, it is not usual that staff from all levels in the organisation make strategy decisions together. It is also not always easy for Schmelmer to accept the decision-making freedom of the staff at BI X: “It’s a learning process for me to be hands-off. But I try not to intervene in the day-to-day running of BI X.”

Digitisation is of strategic importance to Boehringer Ingelheim. With BI X, the company hopes to offer even better treatment options to its patients in future. The goal is to combine the expertise of a global research-driven pharmaceutical company with technological know-how and to integrate this newly acquired knowledge into the classic pharma business on a lasting basis. Boehringer Ingelheim sees powerful development potential here for the whole organisation, with the customers in mind. “Without the support of the top management and the whole company’s combined aspiration, however, that would not be possible,” says Schmelmer.

The birth of BI X came in spring 2016. Out of the idea of structuring digital initiatives for Boehringer Ingelheim, the desire to do more grew rapidly. For this, a small team of digital-thinking colleagues and external strategists was formed to jointly develop the BI X concept. Hach, still an external consultant then, was on board. “We discussed a lot about what Boehringer Ingelheim needed in terms of its digital transformation,” he recalls. “For the first few weeks, we just collected ideas. It quickly became clear that we wanted action.” It was all about basics in the beginning: what was needed in terms of office space, technologies and staff? How should the company look like? And was Ingelheim really the right place for this? It quickly became clear that BI X would need to be near the parent company’s headquarters. The BI X team found a suitable building in the former guest restaurant, which was at the time only being used occasionally for internal training sessions. Modification took four months, with the BI X team moving in in June 2017.

The team includes Maria Apsolon from Estonia, who joined BI X as a software specialist in October 2017. As a front-end developer, she digitally implements the design of developed ideas. She is currently working on a platform with which pharmaceutical researchers can collect, structure and exchange data. When she started at BI X she was the only front-end developer. “We work hard and a lot. But it’s worth it, as we’re developing products that make a difference.” What in her opinion makes BI X stand out above all is the special way of working.

The tech experts work flexibly, using the scrum method. “At the start of a
project phase, which generally lasts two weeks, there is only one clearly defined, measurable goal. The individual project steps are flexible, however, and only emerge in the course of the process,” Apsolon says. For each project, the staff are divided into new teams comprising data scientists, scrum masters, front-end and back-end developers and user experience designers. They all get together for a daily stand-up at which each member of staff briefly explains their priorities for that day. At the end of the project phase, the team looks back together at the results and decides whether or not the direction of the project needs adjusting. Progress can be seen by all members of staff in the foyer, where the status of the project is displayed on three large screens. “Each team sets its own goals for the respective week,” Schmelmer says. “There’s an immense performance culture here – everyone wants to make a difference and you can really feel it.”

As a counter balance to their hard work, the team enjoys regular time-outs. Once a week, the team goes out for dinner together, trying out the various restaurants in the area. If something is not going quite right with a project, that is when the table football in the foyer comes in: “If we have different ideas of how something should be done, we just go with whatever the winner decides,” jokes Apsolon.

The front-end developer is the only Estonian on the team. Her colleagues come from countries like the USA, Spain, Austria, the Netherlands, Hungary and Bulgaria. The BI X office language is English. And it is no accident that so many different nationalities come together to work here. Boehringer Ingelheim has focused on diversity and inclusion for years. The company is certain that diversity is a major driver for innovation and growth.

International talent, however, is in international demand. Undoubtedly, only very few people would off the top of their heads name Ingelheim as their preferred job location. “That’s one of the greatest challenges facing BI X because we need the right people in order to be successful,” says Schmelmer. He wants to draw talented staff to the location with the exciting content of the work: “With us, people can actually bring about change. They will be working on solutions that could potentially save lives.”

The BI X team’s plans are almost limitless: “In the current year, we want to implement as many projects as possible, and Boehringer Ingelheim will help us to build up these ideas,” Hach says. But this initial support also has impact in the other direction too, with BI X spreading the entrepreneurial spirit and innovative working techniques from the digital lab throughout the entire company. After all, one thing is clear: the qualities associated with a start-up – agile, flexible and result-driven work – will also be factors for success in the future for a traditional company like Boehringer Ingelheim.

### INTO THE FUTURE WITH BITS AND BYTES

Boehringer Ingelheim aims to fully exhaust the digital potential and thereby build on multiple initiatives. Here is a selection.

**BI X**

As an independent subsidiary, BI X promotes smart healthcare solutions in the business areas Human Pharmaceuticals, Animal Health and Biopharmaceuticals. In order to develop a digital business idea, the business areas can turn to BI X. The digital lab helps them to clearly define the idea and delivers prototypes for new products. Failure is expressly allowed here. What is decisive is trying out new technologies and thereby possibly also reaching the goal indirectly.

**Business Model & Healthcare Innovation**

The innovation team located in the One Human Pharma business unit works closely with experts from the various therapeutic areas. The experts can thus recognise needs early and work jointly with partners on targeted solutions. Here they concentrate intensively on digital healthcare solutions based on modern information and communication technology (see interview with Dr Oliver Reuß, page 48).

**Accelerate**

With its IT initiative Accelerate, Boehringer Ingelheim employs the innovative potential of all its employees worldwide. On it everyone can submit proposals for digital innovations. An interdisciplinary jury decides on these. The submitters must then implement their proposals within the desired timeframe, which is mainly about three months. Subsequently, they report on their experiences, even if projects have in the meantime failed, for it is important that everybody learns from each other (see text on the Hololens project, page 33).
ON THE MOVE – WORLDWIDE

In the past year, Boehringer Ingelheim has driven various projects covering the most varied topics. However, there is something they all have in common: open-minded employees with a sense of responsibility, who have consistently and inventively sought answers to change – and found them.
THE POWER OF INFLUENCERS

We are already used to them in social networks, but actively harnessing the power of influencers is still a new phenomenon in companies. Boehringer Ingelheim Japan has taken up the concept and tailored it for a research-driven pharmaceutical company. More than 150 young employees, known as Change Champions, started pushing ahead with the new global principles of working together, rolled out in 2017: agility, accountability and intrapreneurship – AAI (see page 14). The AAI Change Champions are connected with each other in informal networks and work as facilitators, influencers, storytellers and front-runners. Without any instructions from above, they develop goals, own initiatives and seek dialogue with their colleagues. This practical approach has developed a very favourable dynamic that has inspired all sides. So it is no surprise that the second generation of AAI Change Champions is already in the starting blocks.
AFRIKA KOMMT!

The “Afrika kommt!” (Africa is coming) initiative allows specialists from Africa to exchange views with managers from major German corporations and to effect change together. As one of the founding members, the research-driven pharmaceutical company Boehringer Ingelheim has since 2008 supported this initiative to foster diversity. The pharmacist Simon Manyara from Kenya participated in the programme at Boehringer Ingelheim’s site in Ingelheim, Germany, for eight months. Since his fellowship, Simon has continued to support various projects within Corporate Strategy and Development at Boehringer Ingelheim.

LEARNING TO UNDERSTAND PATIENTS BETTER

What is important to the patient? What are the unfulfilled needs and how can research be tangibly applied to help address those needs? In order to get to the bottom of such questions, Boehringer Ingelheim launched the Scorecard Project in the USA in March 2017. Eight cross-disciplinary teams now look far beyond the therapeutic areas of a traditional research-driven pharmaceutical company – and they work in very close cooperation with the patients themselves to improve clinical trials and gain a better understanding of patients’ needs. This is done by employing questionnaires and one-on-one patient interviews, as well as moderated online discussions on a digital consultation platform.
V I R T U A L  P I G S

Pigs are romping about Boehringer Ingelheim’s corporate site in Ingelheim, Germany. But the animals can only be seen by people wearing special goggles. A Microsoft Hololens allows interactive 3-D images to be projected onto the immediate environment. Hand movements can herd the pigs and, when touching them, you can even hear a gentle grunt. A tool like this could in future help farmers administer medicines to their animals. However, this is still a long way off. The aim of Boehringer Ingelheim and the Fraunhofer Institute for Software and System Technology (ISST) was to test in a three-month pilot project the opportunities this new technology can offer. An employee from the IT department had requested further research into this innovative, dynamic digital approach via the company’s special “Accelerate” internal platform. Boehringer Ingelheim agreed to the request and supported the development of the pilot project with 50,000 euros.
TOGETHER FOSTERING SOCIAL INNOVATION

During two days in October 2017, 267 participants from a variety of countries gathered at the Boehringer Ingelheim Campus in Ingelheim, Germany. Their joint objective was to drive the future success of the Making More Health (MMH) initiative. Founded in 2010 by Boehringer Ingelheim and Ashoka, MMH fosters social innovation around the world, explores unconventional partnerships and business models, and encourages Boehringer Ingelheim employees. The MMH Convention gave the participants the opportunity to network, inform themselves about innovative local and international MMH projects, and unleash new cooperations. Three pillars provided the framework: co-creation as a bond between social responsibility and business; social innovation of 85 social entrepreneurs in the MMH network; and the fostering of entrepreneurial and intrapreneurial thinking. This changemaker programme is an innovative way to develop leadership skills. The convention delivered an exhibition, different workshops, success stories, panel discussions and interviews.
ACCELERATING THE DEVELOPMENT OF IMMUNO-Oncology Therapies

The combination of immuno-oncology therapy concepts is an essential part of Boehringer Ingelheim’s cancer research. The strategy focuses on turning tumours that are hidden to the immune system visible and therefore enable the body’s immune system to recognize and attack these tumours – an approach that can be commonly described as “turning cold tumours into hot tumours”. The researchers are focusing on novel approaches that might result in breakthrough treatments for patients with difficult-to-treat conditions such as lung cancer or gastrointestinal cancers.

Despite recent treatment advances, lung cancer still is the number one cancer killer. Gastrointestinal tumours have been of increasing importance over the last years and are among the most frequent cancers in Asia. To bring the results of oncology research to patients quickly, Boehringer Ingelheim is collaborating with Sarah Cannon Cancer Research Institute, US, to conduct clinical trials. The expertise of this partner supports the research-driven pharmaceutical company in identifying the right patients and in optimally supporting them in clinical trials so that meaningful results of high quality may be achieved in a timely manner. Boehringer Ingelheim’s goal remains always to accelerate the development of innovative cancer treatments for patients with high therapeutic need.
An open, unbiased way of thinking requires a corresponding (working) environment. That is why Boehringer Ingelheim has reshaped its Ridgefield site in the USA. The Inclusive Campus has now been completely redesigned with diversity and inclusion in mind – from its workstations and parking places to its bathroom facilities. Another example is a re-designed auditorium, with wheelchair access and technology to support employees with hearing impairments. The project was instigated and implemented by the Ridgefield workforce. This is a clear example of the changes that teams are able to bring about when everyone pulls together.

It is often difficult to correctly interpret the symptoms of the rare disease idiopathic pulmonary fibrosis (IPF). However, a fast diagnosis is decisive. In Denmark, a virtual reality game is helping doctors to hone their awareness – for example, by interpreting various lung noises in the virtual world, or by investigating healthy lung tissue or that of an IPF sufferer. Boehringer Ingelheim’s brand and communication team in Denmark developed the game in record time last year so that it could be employed for the first time at the annual conference for Danish lung specialists.
TWELVE CITIES IN TWELVE MONTHS

Today’s modern workers desire flexibility and a healthy work-life balance. Innovative companies, like Boehringer Ingelheim, identify this transformation and turn to programmes such as Remote Year for support and inspiration. Remote Year is an organised development programme that brings together a mix of international professionals, freelancers and entrepreneurs to live and work as a community in twelve global cities over a whole year. Remote Year promises to provide personal and professional growth, giving participants the opportunity to learn from one another and immerse themselves in different local cultures and business ecosystems. Anne-Madeleine Kleinwächter, Global Senior Manager Leadership Development at Boehringer Ingelheim, is the first Boehringer Ingelheim employee to take part in this programme. Anne-Madeleine’s itinerary covers both emerging and mature markets and consists of cities as e.g.: Prague, Lisbon, Kyoto, Kuala Lumpur, Chiang Mai, Buenos Aires and Mexico City. Picture: Anne-Madeleine with colleagues at work in Kyoto, Japan.
AMBITIOUS CONSTRUCTION PROJECT

Speed is the name of the game. Boehringer Ingelheim’s new manufacturing facility for the RESPIMAT® pocket inhaler in Sant Cugat, Spain, is to go into production by September 2019. The ground-breaking ceremony took place in June 2017. The path to this point involved several hurdles, but the project and engineering teams were ultimately able to stay on schedule and to obtain planning permission from the local authorities. In the future, Boehringer Ingelheim will manufacture up to 20-25 million cartridges for the RESPIMAT® inhaler every year and also package the finished product in Sant Cugat.
WHEN TWO BECOME ONE

2017 was a year of change for Boehringer Ingelheim’s animal health business. Two former competitors became one. Previous strangers became colleagues and supervisors. In order to make the transition as seamless as possible, the staff of Boehringer Ingelheim Animal Health in the Philippines organised the “Camp ONE” project, a team-building activity not only calling for mental agility. Everybody understood that the merger would mean that everyone would have to operate outside their comfort zone. The project was a success: the new animal health business in the Philippines already enjoyed a significant increase in sales in the second half of the year.

INITIATIVE FOR STROKE PATIENTS

It all began in October 2014 in Dubai in the United Arab Emirates. After the first stroke center was set up there, with the support of Boehringer Ingelheim, the “META Stroke Initiative” quickly expanded to the rest of the META region, consisting of Middle East, Turkey and the Africa region. Because every second counts in the treatment of stroke patients’ lives, the initiative aims at creating stroke centers of excellence all over the region, spreading knowledge and experience locally. As a result of the initiative, the thrombolysis rate was increased from 0.001 per cent when the initiative was established to 3 per cent in 2017. The initiative focuses on more than 19 countries, with its board including 14 specialists from eight of those countries. Together with Boehringer Ingelheim and the health authorities, its objective is to heighten public awareness about stroke. The initiative meanwhile succeeded in increasing the number of treated stroke patients from around 1,400 in 2015 to more than 10,000 in 2017. The incidence of stroke is on the rise around the world. The “META Stroke Initiative” is part of the Boehringer Ingelheim-initiated “Angels Initiative” that cooperates with leading stroke organisations and experts. The goal is to improve acute stroke care for patients worldwide.

AGILITY NEEDS CREATIVITY
SHOWING POSITIVE HEALTH IMPACT

Communicating results from highly-scientific registration trials and transforming its complex data in layman’s terms is becoming ever more challenging. In order not to lose sight of the overall picture in big data, Boehringer Ingelheim has set in train the development of the in-house app “Health Impact – Care for Patients” (HI-CAP). It enables the measurement of how many patients worldwide have been helped by the research-driven pharmaceutical company’s products. A committed team of statisticians and data experts have taken on the task. The result is an app that converts the abstract concept of public benefit into accessible visuals. The HI-CAP calculator, which is based on R shiny technology, gives an estimated number of prevented events of interest or life-years gained by those patients who have been taking a Boehringer Ingelheim medication. These calculations with all assumptions are transparent and scientifically sound. Initially, the HI-CAP calculator will be used by Boehringer Ingelheim’s internal specialists from Medical Affairs and Marketing. HI-CAP is far more than simply an innovative gadget. The app translates highly complex technical details based on clinical trial results and drug sales data – broken down by country – into easily understood graphic elements and shows the great contribution from Boehringer Ingelheim to benefiting patients’ health.
An eye for the big picture

When the Boehringer Ingelheim Science Department was founded 100 years ago, future Nobel Prize winner Heinrich Wieland ensured that this was done in a future-oriented way. Today, the company's scientific activities are bundled in the Innovation Unit, which continues to embody the company's spirit of research. Although scientists such as Michael Mark do things quite differently now compared to Wieland's time, there are still lots of similarities.
Michael Mark noticed one thing straight away: “Everyone gave such a friendly welcome”, he says, looking back on his first day at Boehringer Ingelheim in Biberach, in Germany’s Upper Swabian region. The then 28-year-old pharmacology graduate joined the research department in 1985.

His feeling of belonging has remained to this day, Mark says. In other respects, a lot has happened since then. The company has grown enormously and Mark has participated in countless research projects, advancing to become Head of the Cardiometabolic Research Department within the Innovation Unit. He has never for one minute regretted choosing Boehringer Ingelheim. “The job appealed to me straight away – it was exactly what I wanted. Here, I was able to discover new mechanisms of action and develop new medicines – there’s nothing more appealing to a trained pharmacist.”

Today, Mark is responsible for the work of 80 researchers in Biberach as well as 40 people in Ridgefield, Connecticut, USA. He organises the various research projects internally and in partnership with collaboration partners, reviews ideas put forward by the working groups, withdraws staff from projects or increases their number if a substance is looking particularly promising. “At Boehringer Ingelheim, we are able to work on fundamental issues with the necessary foresight”, Mark says. “We get the time required and, above all, the responsibility.”

It is not least the spirit of Heinrich Wieland that has a lasting effect here. The company’s Science Department celebrated its centenary in 2017 and the great chemist and later Nobel Prize winner was there from the very beginning.

Born in 1877, Wieland was a cousin of Helene, the wife of company founder Albert Boehringer. From 1904 onwards, he advised Boehringer’s company on the development of new medicines. At the time, he was about the same age as Mark was when he started at Biberach.

A gifted chemist, Wieland pushed the boundaries of research into plant-based alkaloids. He developed the cardiovascular medicine CADECHOL® for Boehringer Ingelheim and later LOBELIN®, an emergency treatment for respiratory arrest and other shock conditions. He conducted regular basic research with his students and assistants at the University of Munich – to a degree that would hardly have been possible for the medicine developers at the Ingelheim-based company on their own.
We are able to work on fundamental issues with the necessary foresight.

At the start of the 20th century, in addition to pursuing their academic careers, young chemists usually worked as advisors to pharmaceutical companies in order to make a living as external lecturers. But Wieland was much better connected and integrated at Boehringer Ingelheim than most of his colleagues in the industry. He was thus a kind of founding father to today’s researchers at the company – who also include Mark.

When he thinks of the great Heinrich Wieland today, Mark sometimes wishes he could engage in finding solutions with the same freedom and straightforward manner as was possible then. “Drug development is more complex now, involving many different disciplines. Regulations are of course necessary, not least to ensure patient safety”, says Mark. On the other hand, researchers today naturally have many more opportunities at their disposal. In his team, Mark works with scientists from nine countries with differing education and expertise, including specialists in human medicine and molecular biology. He can employ gene analysis and modern microscopes, has access to all available scientific databases, and will probably even soon be able to simulate effects and side effects using software – as promised by the nascent discipline of systems biology. With regards to all research activities, Boehringer Ingelheim also builds on collaborations with external partners, universities as well as start-up companies (please see the guest contribution of Rui-Ping Xiao from Peking University on page 50).

Mark came to his current field of research thanks to his PhD supervisor. The well-known pharmacologist Hermann Ammon was working on diabetes research, so his young protégé – during and after his doctoral studies – worked on the mechanisms of insulin release. At Boehringer Ingelheim in Biberach, Mark directly linked in with these studies and initially focussed on glinides, the substance class that stimulates insulin secretion from the pancreas. From this emerged repaglinide, which was put on the market as Prandin¹ in 1997. After a protracted phase, during which Mark and his colleagues focussed on lipid metabolism and atherosclerosis, a new phase in diabetes research began in 1999. As one of the first projects, Mark initiated the search for DPP-4 inhibitors. These are substances that inhibit the breakdown of a specific hormone from the intestine, eventually lowering blood sugar. As a result of his work, the active substance linagliptin (TRAJENTA²) was launched in 2011 and is now one of the best-selling medicines in the Boehringer Ingelheim portfolio.

¹ licensed to Novo Nordisk
² jointly marketed with Eli Lilly and Company
The next significant medicine in which Mark’s work played a major role is the SGLT2 inhibitor called jardiance® with its active substance empagliflozin. Reading scientific articles in the late 1990s, it occurred to Mark that phlorizin, which was initially isolated from the root bark of apple trees, lowers blood sugar levels as it causes glucose to be excreted in the urine. While this mechanism had been known for a long time, Mark and his team were among the first to use this knowledge to develop a medicine to treat diabetes. They therefore applied knowledge about a rare genetic mutation, the carriers of which also excrete sugar in their urine. “We knew from these people that this mechanism has no apparent disadvantages. Accordingly, the SGLT2 inhibitors should be efficacious and well-tolerated long-term,” says Mark. Although many experts were sceptical, the team was able to pursue the idea and jardiance® is also a major success today.

For jardiance®, the diabetes researchers drew on a plant-based source material – one that Wieland would probably have been aware of. Wieland represented the last generation of Boehringer Ingelheim developers to work with natural active substances. His best student, Georg Scheuing, who headed the Science Department from 1926 onwards, guided the company to synthetic substances, which was a major step forwards. Mark and his colleagues approached the development of jardiance® in a similar way to what Wieland did in his time. They had an idea of how a substance could work and pursued it until the application for diabetic patients. “In modern pharmaceutical research, we constantly ask ourselves which patients and which diseases need improved therapies. What applications are possible? And then we search for therapeutic approaches in full knowledge of the disease and with understanding of the fundamental biological mechanism, as well as with expertise in how to arrive at the suitable molecules.”

In modern pharmaceutical research, we constantly ask ourselves which patients and which diseases need improved therapies. What applications are possible?

The fact that individual scientists, such as Wieland and his successor Georg Scheuing, developed entire medicines practically on their own would no longer be possible in today’s world, Mark says. “The fields of research are simply too big and the individual topics too complex, making the specialist knowledge and expertise of many necessary.” But Mark is convinced that even today we need “champions who believe in their idea and want to follow it through”.

Currently, he and his colleagues are working on treatments for the complications of diabetes, addressing the damage that it causes to the eyes, kidneys and vascular system. Wherever possible, he also wants to investigate the root causes of diabetes development as well as what can be done to avoid this disease. Here, as with diseases of the liver – a further focus of cardio-metabolic research – the lipid metabolism plays a major role and Boehringer Ingelheim is already one step ahead, Mark believes: “We have never looked at diabetes and glucose metabolism in isolation but always as being part of the body’s entire metabolic events.”

Something else has also remained fundamentally unchanged since the Wieland era. Boehringer Ingelheim has close ties with the scientific community, supports basic research and draws on these factors to attract talented people to work for the company. Mark calls it talent management – supporting promising young scientists, supervising them and preparing them for new tasks, or playing an active role in international research networks. So, in the final analysis, he is not all that different from Wieland, who regularly recommended some of his best students and promising scientists to Boehringer Ingelheim. And he was himself the PhD supervisor of Ernst Boehringer, younger son of the company’s founder.

³ jointly marketed with Eli Lilly and Company
For Boehringer Ingelheim Heinrich Wieland developed lobelin®, an emergency medication for respiratory arrest and other shock conditions.

From his office in Biberach, Germany, Michael Mark is responsible for the work of 120 research colleagues.

Phlorizin, from which the SGLT2 inhibitor empagliflozin (JARDIANCE®) was derived, originally comes from the root bark of the apple tree. Today, the diabetes medicine JARDIANCE® is a great success.
FOCUS ON PATIENTS
Which products and services can Boehringer Ingelheim in future offer beyond medicines?

This idea is being addressed by Dr Oliver Reuß and his team of doctors, biologists and business managers.

Dr Reuß, why is Boehringer Ingelheim even considering technologies outside the conventional medicine business?

**DR REUSS** Our aim is to provide patients with more comprehensive care than before. Until now, we’ve primarily provided medicines, that’s to say ways to treat illness. For several years now, however, increasing focus has been on services and technologies that go beyond that, putting patients at the centre of things and offering them additional benefit.

How do you work in practice?

**DR REUSS** On the one hand, we work together closely with the human pharmaceuticals therapeutic areas and define solutions when we identify new needs. On the other hand, we also establish contacts outside Boehringer Ingelheim, as innovative ideas often come from start-ups. Special partners, known as accelerators, put us in contact with these start-ups so that we can gauge the potential of a partnership very early on. This way we’re able to incorporate their entrepreneurial spirit into our company. In this context, it’s exciting that the Boehringer Ingelheim Venture Fund recently received additional funding for digital healthcare concepts.

What kinds of projects are these specifically?

**DR REUSS** Let me give you an example. We’re currently working on a smart add-on for the classic stethoscope: a small digital microphone fitted inside the stethoscope can be linked to a smartphone. Algorithms analyse the patient’s lung sounds and help the doctor to identify respiratory disorders. One example of this is idiopathic pulmonary fibrosis – a rather rare and not always so easily diagnosed disease, but one which requires early treatment.

Aren’t the major technology companies the pioneers in the digital environment? What opportunities does Boehringer Ingelheim expect here?

**DR REUSS** Of course, there’s mega-hype in this field and lots of digital concepts centred on the patient. There’s a huge selection of sensor technologies enabling the patient to measure, for instance, their own blood pressure or blood sugar levels simply, and sometimes on an ongoing basis. Other approaches involve Blockchain in order to enable the secure handling of patient data. Until now, this technology has primarily been used in the financial sector in the context of bitcoin. And, of course, artificial intelligence is a huge topic.

But across all these fields, we as a pharmaceutical company primarily consider the overall challenges for patients, doctors and the healthcare system when it comes to the development of new medicines. As such, we are in a position to identify potential solutions and to develop them ourselves or with partners. Additionally, our knowledge of regulatory affairs and our global presence are absolutely necessary for marketing a new product. This is our core competence and we utilise this competitive advantage.
At the turning point

In recent decades, China has become a leading economic power. The country is currently outstanding in research, too. Those involved now can help shape the future.

Lots of people have asked me why I left the USA to return to China eight years ago in 2010. I had worked there for twenty years as a senior investigator at the National Institute on Aging (NIH). The answer is simple: in 2010, scientific research was at an historical turning point in China and I wanted to be part of history when my home country progresses into one of the leading research locations on the planet. So, when Peking University invited me to become the head of its new Institute of Molecular Medicine, I seized the opportunity and accepted. And the institute, with its research into cardio-metabolic diseases and regenerative medicine, has in fact become one of the leading institutions in the world over the past few years.

In general, the international significance of my homeland’s scientific community has grown considerably over recent years. China is now ranked second for research after the USA in terms of the number of patents and scientific publications in international journals. According to forecasts, this trend is set to continue. The Chinese government is thus increasingly investing resources to further promote science and technology in the country.

When I graduated in medicine from Tong-Ji Medical University in Wuhan in 1987, the standing of the sciences in the country was not so good. Universities simply lacked resources to finance their research. It was clear to me then that if I wanted to achieve anything as a scientist, I would have to leave my homeland. That was the case for lots of Chinese researchers at the time. Thousands of talented people, like me, left for the USA or Europe in order to continue to research or teach there. But then the Chinese government increased its research spending by over 20 per cent – on a sustainable basis. As a result, the situation today is completely different with more and more scientists returning home to China.

In the USA, I specialized in cardiovascular disease. At the National Institute on Aging, I developed treatments to strengthen the heart muscle after a heart attack, for example. I was able to continue my research in this field at Peking University. At the Institute of Molecular Medicine, we are now also conducting basic research into metabolic disorders. We are looking at the consequences for major diseases, such as type-2 diabetes and its complications like high blood pressure and high cholesterol, which can have a disastrous impact on the whole body. That is why we are looking for ways to treat these complications.

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AGILITY NEEDS FORESIGHT
thankfully has opportunities to pursue this costly but necessary form of research. As a scientist, however, you might get to the stage where you need further support from the private sector. After all, even the best research is fruitless if it fails to reach people. This is where strong industry partners come in, bringing the strength and zest to develop the results further, making them ready for the market.

We have found such a partner in Boehringer Ingelheim. Since May 2017, Peking University has been a cooperation partner of the Research Beyond Borders programme with which Boehringer Ingelheim promotes highly promising research outside the company’s traditional therapeutic areas. The strategic partnership primarily concerns regenerative medicine. Currently, there are five projects investigating different topics, such as cell regeneration of the heart and the pancreas. However, the joint research agenda also covers topics such as cancer and diabetes research, as well as gene therapy. Two further projects are also to be launched in the near future. Thanks to the partnership, Boehringer Ingelheim has access to our research results and helps us to implement them in practice.

At the same time, Boehringer Ingelheim supports Peking University in several ways: the company is currently financing four of our postdoc positions, with other posts in the pipeline. However, even more important than financial support is the wealth of specialist expertise that we are able to draw on as participants of the Research Beyond Borders programme. Boehringer Ingelheim has, for example, an extensive expertise on cancer research, which has significantly enriched our research.

Over the course of my career as a researcher, I have already worked with many different partners from the world
In 2015, Boehringer Ingelheim established its Research Beyond Borders (RBB) team in the field of Discovery Research. The team has 28 employees based in Biberach (Germany), Ridgefield, Connecticut and Boston, Massachusetts (USA), Beijing and Shanghai (China), Kobe (Japan) and Vienna (Austria). From these locations, the team’s scouts search the international scientific community for promising ideas and actively establish contact with researchers at external research institutions and universities.

RBB’s goal is to identify novel scientific approaches and technologies within and beyond the company’s current therapeutic areas, which could be future focus areas. Examples are regenerative medicine, gene therapy and microbiome research. In the meantime, RBB has concluded over 30 partnerships with universities and scientific institutes. RBB is also planning collaborations with biotech companies and start-ups.