

# TOMORROW



Research for a  
Healthier Future



# Boehringer Ingelheim 2021 at a glance

Founded in  
**1885**

in Ingelheim and  
family-owned  
to this day

**52,391**

employees worldwide

thereof  
**10,109**

in Research,  
Development  
and Medicine

**4.1**

billion EUR expenditure in  
Research and Development

equivalent to  
**20.0%**

of total net sales

## Business Units

Human Pharma

**15.3**

billion EUR

Animal Health

**4.3**

billion EUR

Biopharmaceutical  
Contract Manufacturing

**917**

million EUR

### THERAPEUTIC AREAS

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

### BUSINESS SEGMENTS

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

### PORTFOLIO

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

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

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

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

Hubertus von Baumbach  
Chairman of the Board of Managing Directors



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



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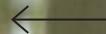
Rachel Nti, Trainee Biology Lab Technician  
at the Biberach Site, Germany



PERSPECTIVES

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

We asked employees from all over the world.



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



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

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



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







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



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

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



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





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



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

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



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

# For a Better



# Tomorrow

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

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

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

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



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

Meet Stefanie Arndt



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

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

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



# 40%

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

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

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

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

#### **Right Time to Invest in Research**

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

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



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

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

### Science is All about Communication

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

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



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

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

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

# 2021 in Focus

## November

### Further development of the sustainability framework

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



## October

### Inauguration of the new biopharmaceutical production facility

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



### Highly automated tablet factory opens

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



### Additional investment in veterinary vaccine capacity

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

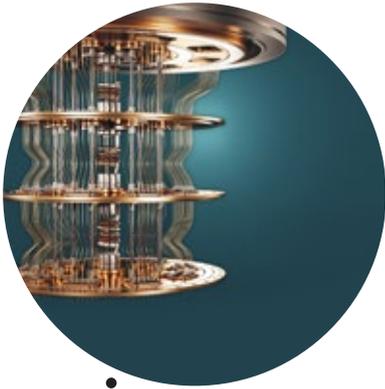


## September

### 75 years of the Biberach site

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





## January

### Advantage through quantum computing

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



## February

### Global Top Employer

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



## March

### PRADAXA® for children

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



## May

### Help with schizophrenia

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



### Treatment of horses in China

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



## June

### JARDIANCE® for heart failure

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



HUMAN PHARMA

# On the Cusp of a Revolution

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

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

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

### Tracking Down Biological Causes

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

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

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



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

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

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

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

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

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

### Looking for Biomarkers

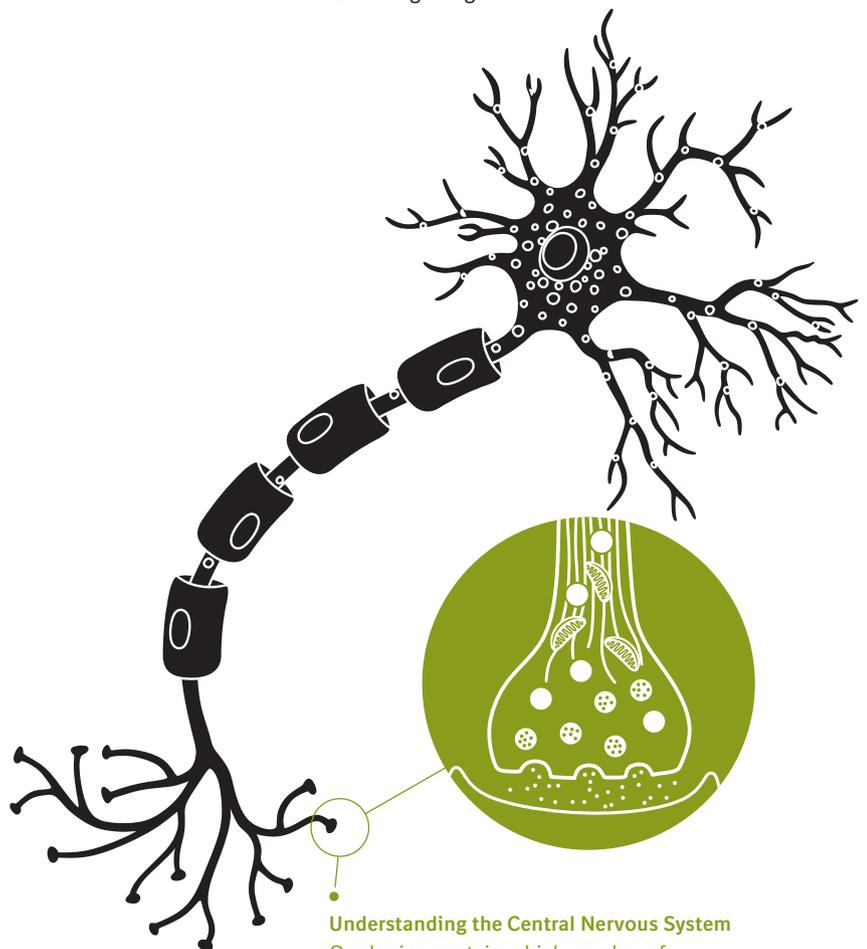
At present, we still distinguish between psychiatric disorders based on the symptoms that can be observed, rather than the underlying dysfunction of a patient’s neural circuits. Experts of Boehringer Ingelheim are discussing the issue with decision makers across the healthcare system – from the medical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

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



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

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



### Understanding the Central Nervous System

Our brains contain a high number of functional neural circuits. Disruption to specific circuits can result in symptoms.

# “Genuinely groundbreaking work”

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

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

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

**Why do you think that is?**

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

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

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

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

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

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

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

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

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

**What is your vision?**

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



## Staying above Water

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

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

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

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

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

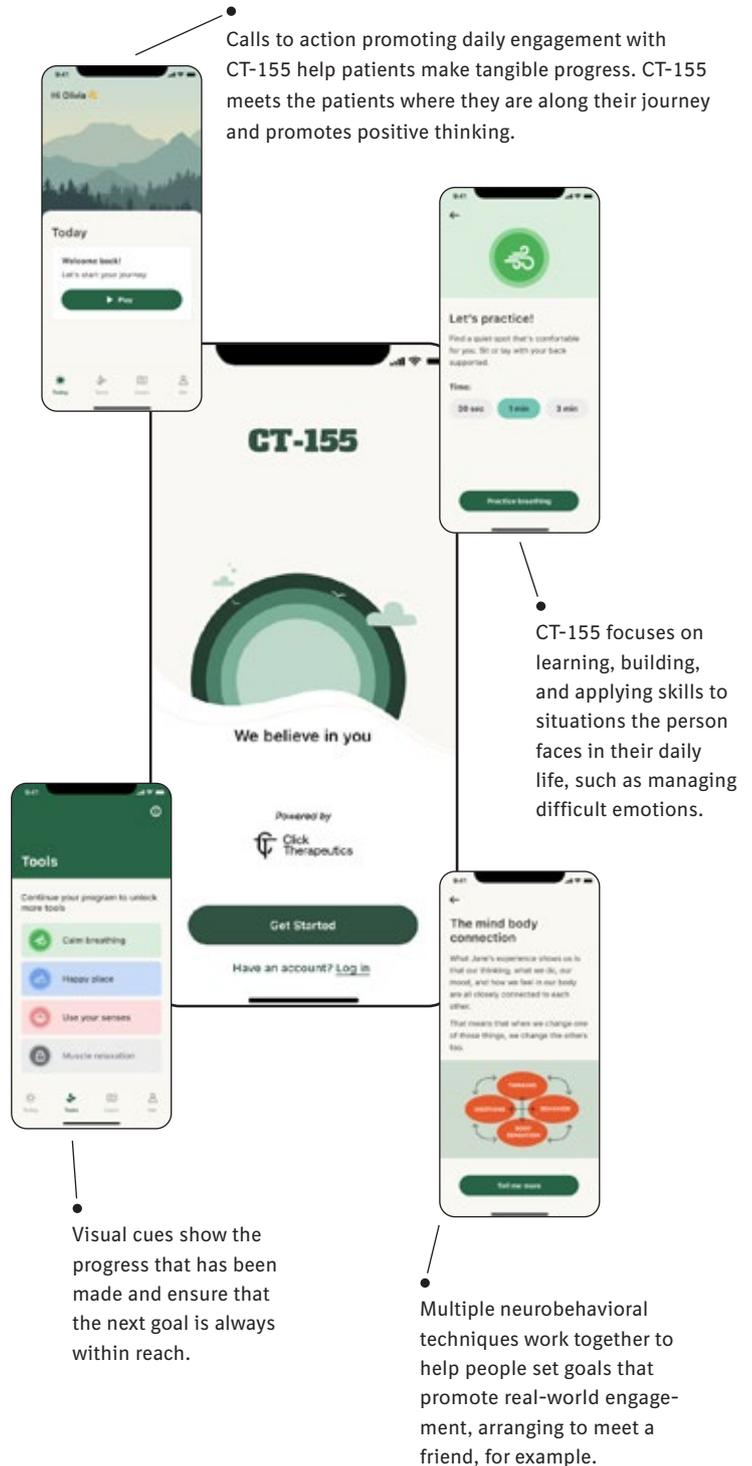
Yammie has now been living a self-determined life for more than four years. “It’s a hard fight from time to time to stay above water – but I have the feeling that I have managed this well, and I’m happy.” This would not have been possible without the correct diagnosis. “A diagnosis can be a curse for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

## Making a Difference with Digital Technology

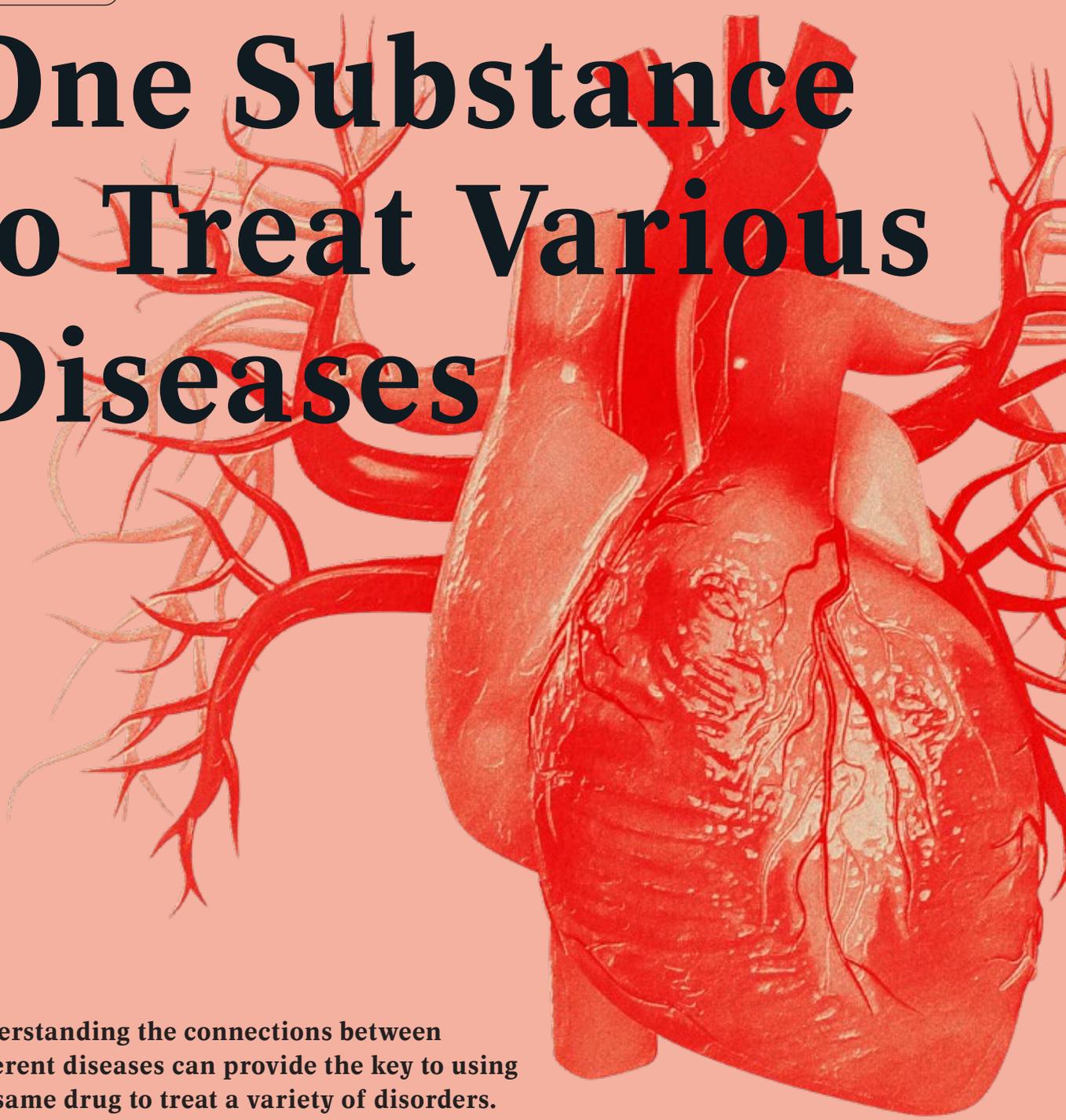
Digital innovation has the potential to offer new health solutions to patients and the health-care system. Digital Health is growing rapidly, and acceptance by patients, physicians, and health insurance companies is rising fast. In fact, recent surveys have shown that 84 percent of people with mental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

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

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



# One Substance to Treat Various Diseases



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

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

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

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

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

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



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

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

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

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

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



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

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

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

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

### **THE OBESITY PANDEMIC**

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

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

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



**> 60 million**

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

**~50%**

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

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

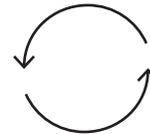
The heart muscle contracts normally but the left ventricle is not able to relax meaning that the heart cannot properly fill with blood during ventricular filling.

**Heart Attack ≠ Heart Failure**

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



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



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



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

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

**1/5**

people are expected to develop heart failure in their lifetime.



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



Christine Jones

HUMAN PHARMA

# GPP Affects My Entire Life



Meet Christine Jones

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

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

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

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

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

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

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

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

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

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

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

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

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

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



HUMAN PHARMA

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

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

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

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

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

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

**What turned the tide?**

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

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

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

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

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

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

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

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

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

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

**What are T-cell engagers?**

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

**T-cells are very specific.**

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

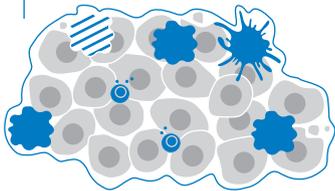
## TURN COLD TUMORS HOT

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

Treatment modalities to turn cold tumors hot

### Cold tumor

Invisible to the immune system with few to no tumor antigens and T-cells

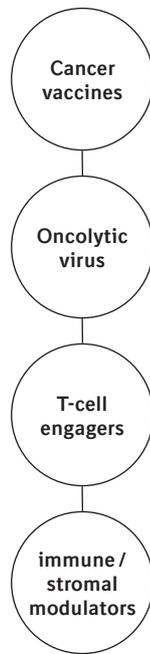
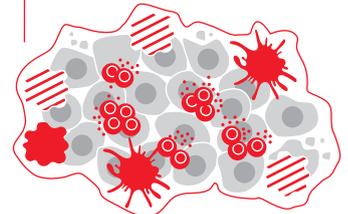


> 50%

Cold tumors may be present in more than half of all cancer patients

### Hot tumor

Highly visible to the immune system with high numbers of tumor antigens and T-cells



#### Immune cell-directed therapies

- Improve T-cell priming: vaccines, oncolytic viruses, myeloid activation
- Redirect T-cells to the cancer cell: tumor antigens and T-cell engagers
- Immune activation within the tumor: immune regulatory receptor modulators affecting T-cells and myeloid cells

#### Components of a tumor



Cancer cell



T-cell



Cytokines with anti-tumor activity



Myeloid-derived suppressor cell (MDSCs)



Dendritic cells



M1 Macrophage

# Prepared for the Next Outbreak

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



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

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

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

### **Growing Risk of Zoonoses**

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



Visit [Lelystad](#)



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

### Lelystad Focuses on TEDs

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

#### THE LELYSTAD SITE



Global Innovation site focusing on Research and Development for veterinary vaccines



20 employees

#### FOCUS AREAS



Innovative vaccine solutions for transboundary and emerging diseases



Updating the VPH vaccine portfolio



Vaccine batch production for clinical studies



Scale-up of new vaccine strains



Optimizing yield of virus to produce more vaccines

### Ideal Conditions

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

### Rapid Intervention

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

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

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

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



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



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



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

# New Space for Biopharmaceutical Innovation



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

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



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



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

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

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

## PIONEER IN BIOPHARMA- CEUTICAL CONTRACT MANUFACTURING

**1963**

Research on chicken interferon

**1985**

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

**1986**

Opening of the first biotechnical center in Biberach, Germany

**1987**

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

**1998**

Entry into global contract manufacturing

**2003 / 2005**

Investments in large-scale production facilities in Biberach and Vienna

**2011**

Acquisition of biopharmaceutical production site in Fremont, USA

**2017**

Opening of biopharmaceutical manufacturing facility in Shanghai, China

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

**2020**

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

**2021**

Opening of the LSCC in Vienna

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

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



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

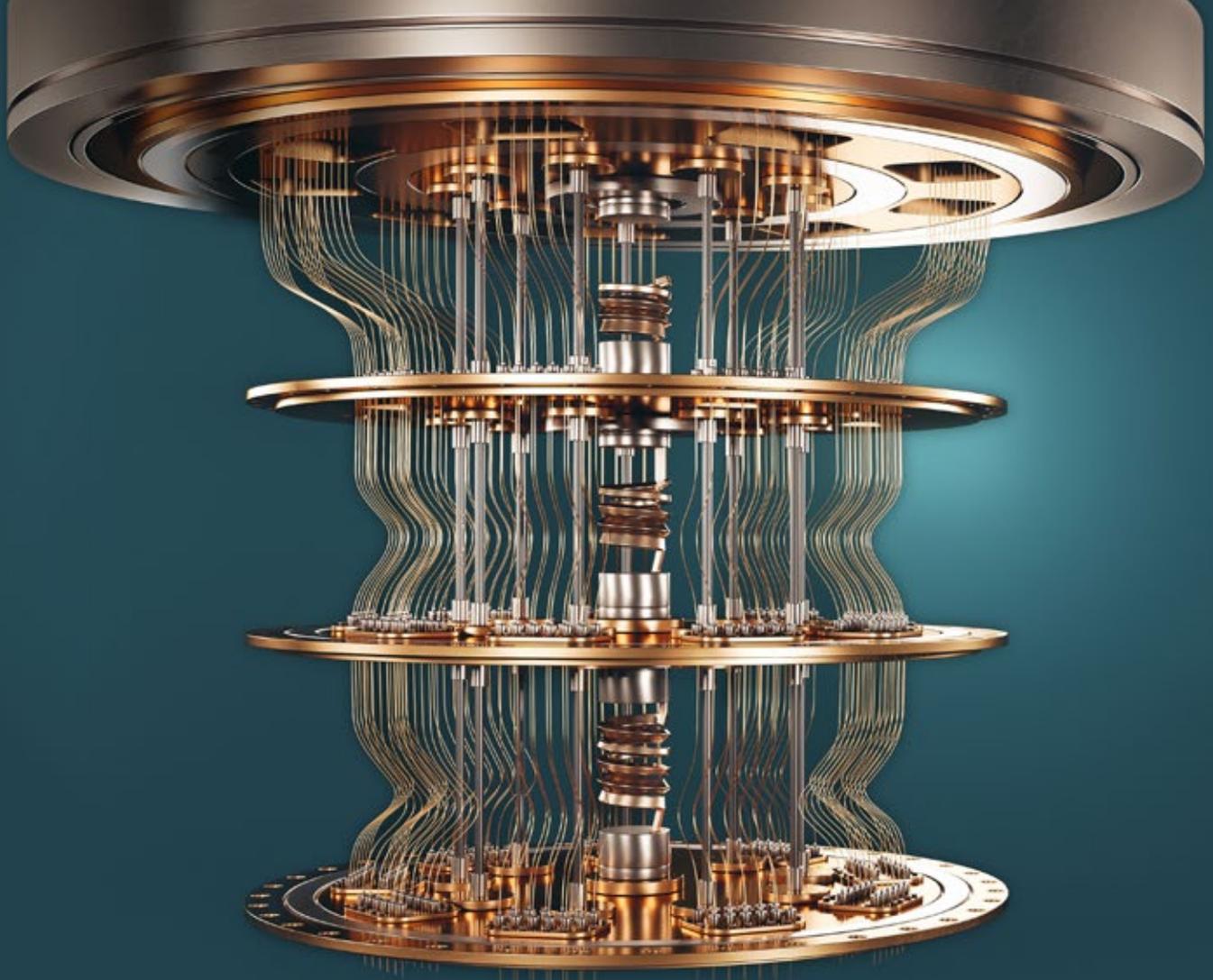


As a pioneer in the field of biopharmaceuticals, Boehringer Ingelheim has manufactured 40 approved biopharmaceutical medicines used by patients all over the world.



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

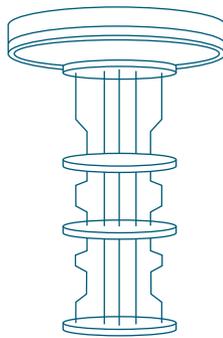




DIGITALIZATION

# The Dawn of the Era of Qubits

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



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



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

### What is quantum computing?

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

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

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

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

### What is different about quantum computers?

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

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

### What additional capability do qubits have?

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

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

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

### How is that possible?

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

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

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

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

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

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

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

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

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

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

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

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

# The Next Level of Pharmaceutical Production

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

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

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

Holger Holakovsky, Head of SOL

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

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

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

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



## WHAT IS A SMART FACTORY?

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

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

# Thinking in Generations



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

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

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

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

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

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

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



**UNITED NATIONS SUSTAINABLE DEVELOPMENT GOALS**

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



## More Health – For Humans and Animals

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

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



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

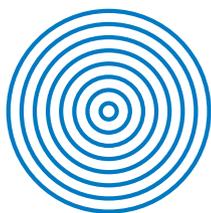
of our medicines portfolio. This is why, together with our researchers, partners, and patients, we continuously develop the initiatives we have been driving for years, while defining new goals for further progress.” Boehringer Ingelheim aims to invest 35 billion EUR in innovation and research by 2030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

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

### DID YOU KNOW THAT...

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

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



## More Potential – For Communities and Our People

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

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

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

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

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

# 50,000,000

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



Learn more about  
Sustainable Development

## Making More Health Together 2021

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



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

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

### Transforming Lives Through Better Health

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

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

### Stepping Up, to Achieve Even More

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

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

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



## More Green

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

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

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

### OUR COMMITMENT

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

### OUR MISSION

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

### OUR GOALS

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

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

### OUR GOALS (Detailed)

- We rely on circular economy, reduce our operational waste to landfill by 80%, and design all new products applying eco-design and green chemistry principles.
- We aim to become carbon neutral in company operations by 2030, for example by investing in the construction of a new biomass power plant and increasing renewable electricity purchased worldwide.
- Boehringer Ingelheim focuses on environmental sustainability in its larger projects and provides another 130 million EUR for green projects that contribute to the global MORE GREEN goals. We established an internal carbon price of 100 EUR/t CO<sub>2</sub>.
- We are the first pharmaceutical company in the EU to receive the 'Green Canteen' certification for a sustainable catering concept at the corporate headquarters.
- We minimize water consumption and implement water stewardship programs. We protect clean water, mitigate pharmaceuticals in wastewater from production and combat antimicrobial resistance.

# The Work of Tomorrow

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

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



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

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

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

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

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

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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





# Imprint

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

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