

# Grünenthal Report 2019/20



Think Innovation. Feel Life.®

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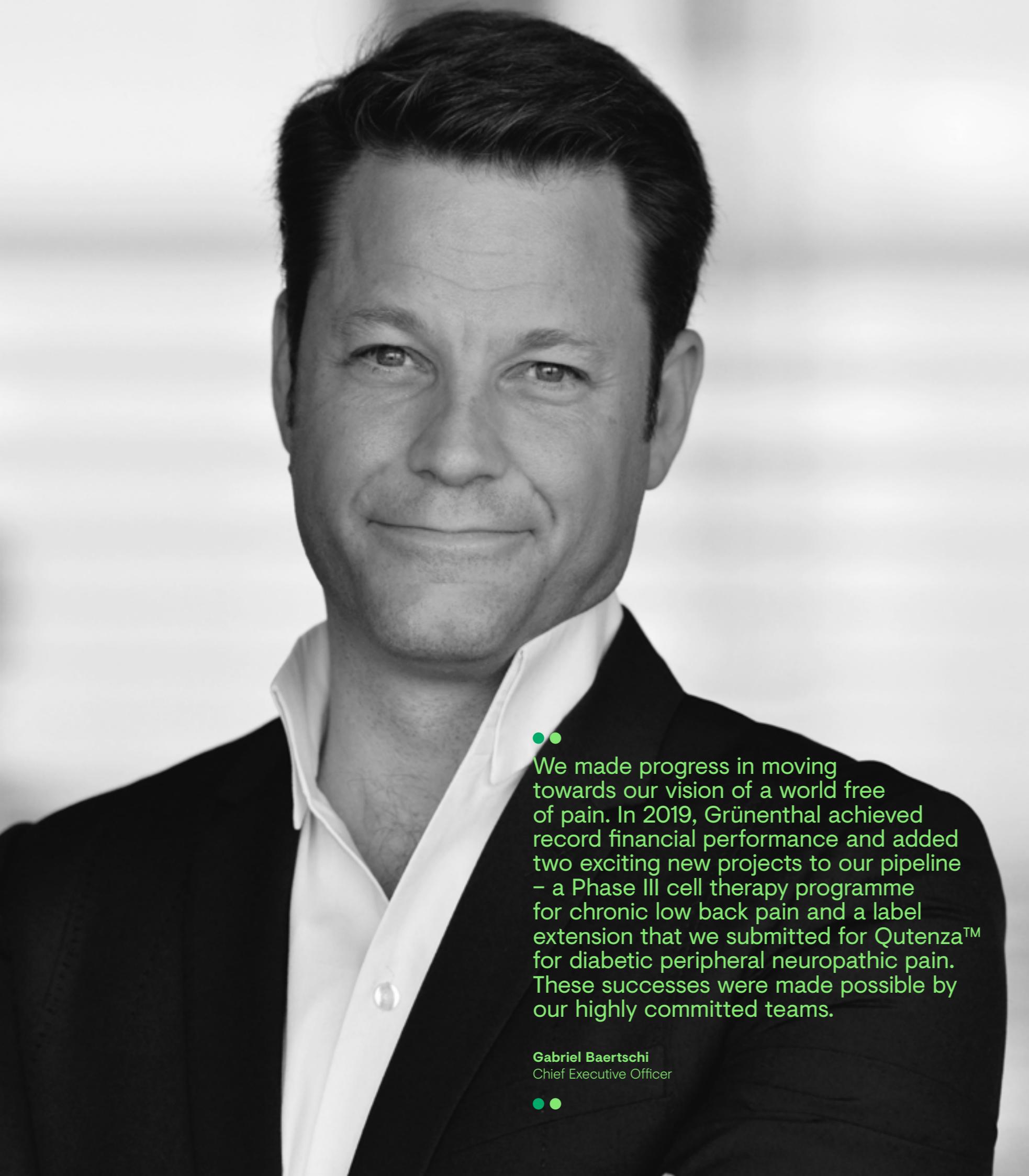
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We made progress in moving towards our vision of a world free of pain. In 2019, Grünenthal achieved record financial performance and added two exciting new projects to our pipeline – a Phase III cell therapy programme for chronic low back pain and a label extension that we submitted for Qutenza<sup>TM</sup> for diabetic peripheral neuropathic pain. These successes were made possible by our highly committed teams.

**Gabriel Baertschi**  
Chief Executive Officer



## Letter from the CEO

Grünenthal achieved its best ever financial performance in 2019. Sales increased by 9 percent and our adjusted EBITDA grew by about 60 percent to reach a total of more than € 340 million. We can look back on this achievement with a deep sense of pride and look forward to the future with great excitement – because our strategy is clearly taking us in the right direction.

Looking beyond financials, we can also be proud of the entrepreneurial steps we took in 2019. We realigned our R&D strategy and implemented a new R&D model to strengthen our position as a science-based, innovation-driven company. This strategy underscores our commitment to addressing areas with high unmet medical needs, with a specific focus on our four core indications: peripheral neuropathic pain, chronic postoperative pain, chronic low back pain, and osteoarthritis. It also emphasises our passion for exploring promising new therapeutic modalities and engaging in collaboration with external partners. The creation of our first Innovation Hub in Boston is a strong example of this approach in action.

Our strategic partnership with Mesoblast,<sup>1</sup> a world leader in cell therapy, is another outstanding example. This is our first cell therapy project, and it encompasses co-development and exclusive commercialisation rights for MPC-06-ID in Europe and Latin America. MPC-06-ID is an innovative investigational treatment for chronic low back pain that is caused by degenerative disc disease. It aims to provide treatment for patients who have not experienced effective relief from available therapeutic options.

Further highlights last year include the successful integration of the two pain-related brands, Nexium<sup>TM</sup> and Vimovo<sup>TM</sup>, which we acquired in 2018 as part of the biggest investment in Grünenthal's history. Both performed above target levels in 2019. On top of this, Qutenza<sup>TM</sup>, Zomig<sup>TM</sup> and Palexia<sup>TM</sup> also made strong contributions to our business performance. And we also achieved impressive sales figures in our Rest of the World region, while our Contract Manufacturing Business also made a valuable contribution.

In addition, we established an innovative start-up called Fern Health that provides a digital concierge service for patients with musculoskeletal pain in the US. We also submitted a supplemental new drug application in 2019, which – if approved – will expand the Qutenza<sup>TM</sup> US label to treat patients with painful diabetic peripheral neuropathy. This would open up a significant opportunity to meet the medical needs of the large population of patients in the US who have been diagnosed with this condition. Beyond this, we have continued implementing our Aim4Prime project in Latin America, which is focusing our efforts on the most differentiated brands and products for pain and women's health in order to add value for patients, promote growth and ensure sustainable success.

Of course, we will only be able to achieve our future ambitions if we have the right culture in place. That is why we introduced a refined set of company Values and Behaviours last year. These define the way we interact and make decisions – and our results for 2019 show that our teams worldwide are embracing this culture and bringing it to life in their daily work.

Grünenthal is now in a strong position in terms of turnover and profit. We are taking advantage of this by reducing our net debt faster than planned and maximising our investment in the future, including exploring possible acquisitions.

Of course, we are facing a high level of unpredictability for the rest of the year – mainly due to the Covid-19 outbreak. However, we are convinced that our excellent results in 2019 provide us with a strong foundation to respond to this challenging situation and make progress throughout 2020.

On behalf of the Corporate Executive Board, I would like to invite you to join us in 2020 as we continue to move closer towards our vision of a world free of pain for patients worldwide.

**Gabriel Baertschi**  
CEO

# 1

## Corporate profile and strategy

Grünenthal is a global leader in pain management and related diseases. Our purpose is to change lives for the better – and innovation is our passion. We are driven to seek effective, life-changing medicines and solutions for patients with severe diseases and high unmet medical needs. We are focussing all of our activities and efforts on moving towards our vision of a world free of pain.

As a science-based, privately-owned pharmaceutical company, we have a long track record of bringing innovative treatments and state-of-the-art technologies to people living with pain worldwide. Strong ongoing partnerships with leading healthcare and development organisations bring our new products to life. We are a fully integrated pharmaceutical company that offers support along the entire value chain – from drug development through to commercialisation.

Grünenthal is headquartered in Aachen, Germany, and has affiliates in 29 countries across Europe, Latin America and the US. Our products are sold in more than 100 countries. In 2019, Grünenthal employed around 4,700 people<sup>1</sup> and achieved sales of € 1.4 billion.

### Key facts and figures

#### Long-standing commitment

**50**

years in pain research

#### Leading market position

**1**

in Latin America and #2 in Europe<sup>2</sup>

#### Strong and capable team

**4,700**

employees worldwide

#### Solid revenue base

**1.4**

billion euro in 2019

#### Commercial presence in

**29**

countries across Europe, Latin America and the US

#### Products sold in more than

**100**

countries

#### Focus on innovation

**250**

priority patent applications filed in the last 10 years

#### International network

**2**

a R&D unit in Aachen and the Innovation Hub in Boston

#### Production capacities

**5**

manufacturing sites in Europe and Latin America

<sup>1</sup> Status: end of December 2019.

<sup>2</sup> In the centrally acting analgesics market - status 2019/Q4. Source: IQVIA Copyright 2019. All rights reserved.

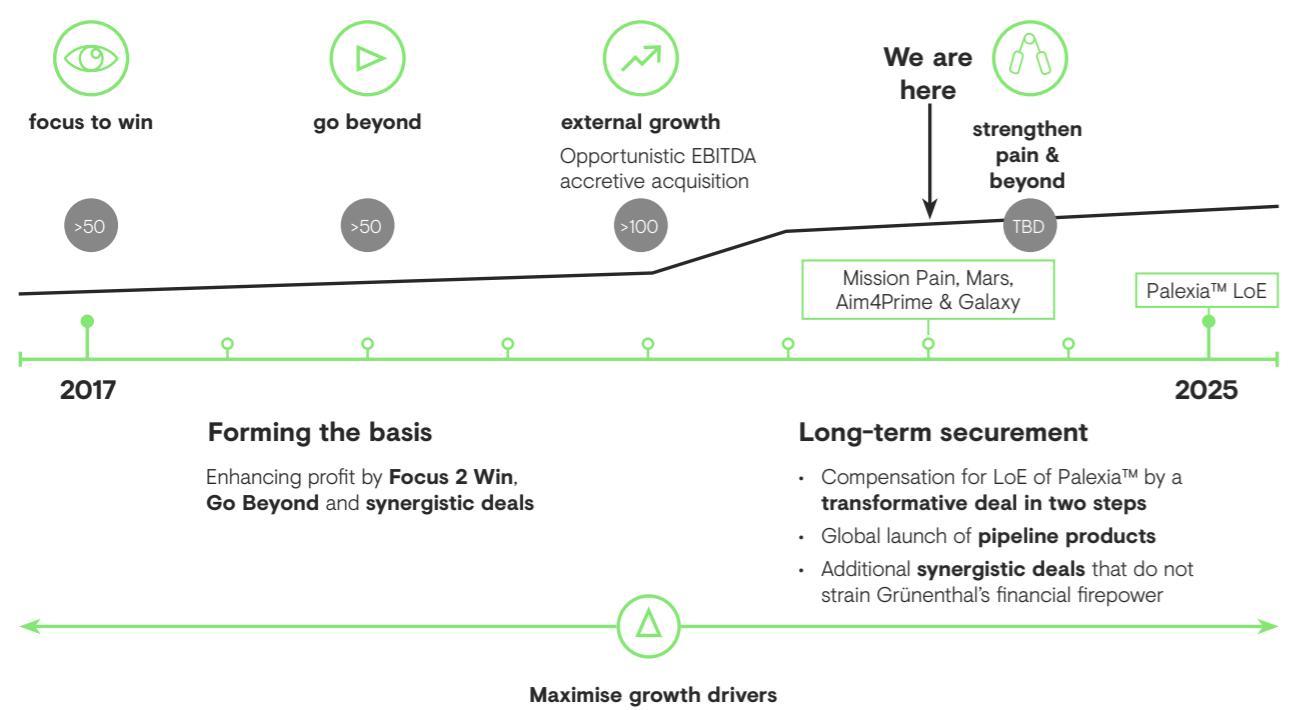
## Our strategy for Grünenthal's long-term success

We operate in a fast-paced, ever-changing market environment. In this context, Grünenthal has a track record of finding answers to current and future challenges, and has integrated these insights into a coherent corporate strategy. Our strategy describes our approach to achieving our vision of a world free of pain. It is built around four priorities: Transformation, Innovation, Growth, and Culture.

These four elements are closely linked. Together, they help us build on our strengths and address headwinds such as expiring patents or some of our key revenue drivers and competition from generics, as well as an increasingly challenging reimbursement environment in many markets, and pharma-typical research and development risks.

We have already achieved significant success, including delivering our best ever financial performance in 2019 – with adjusted EBITDA growing by about 60 percent to reach an estimated total of more than € 340 million.

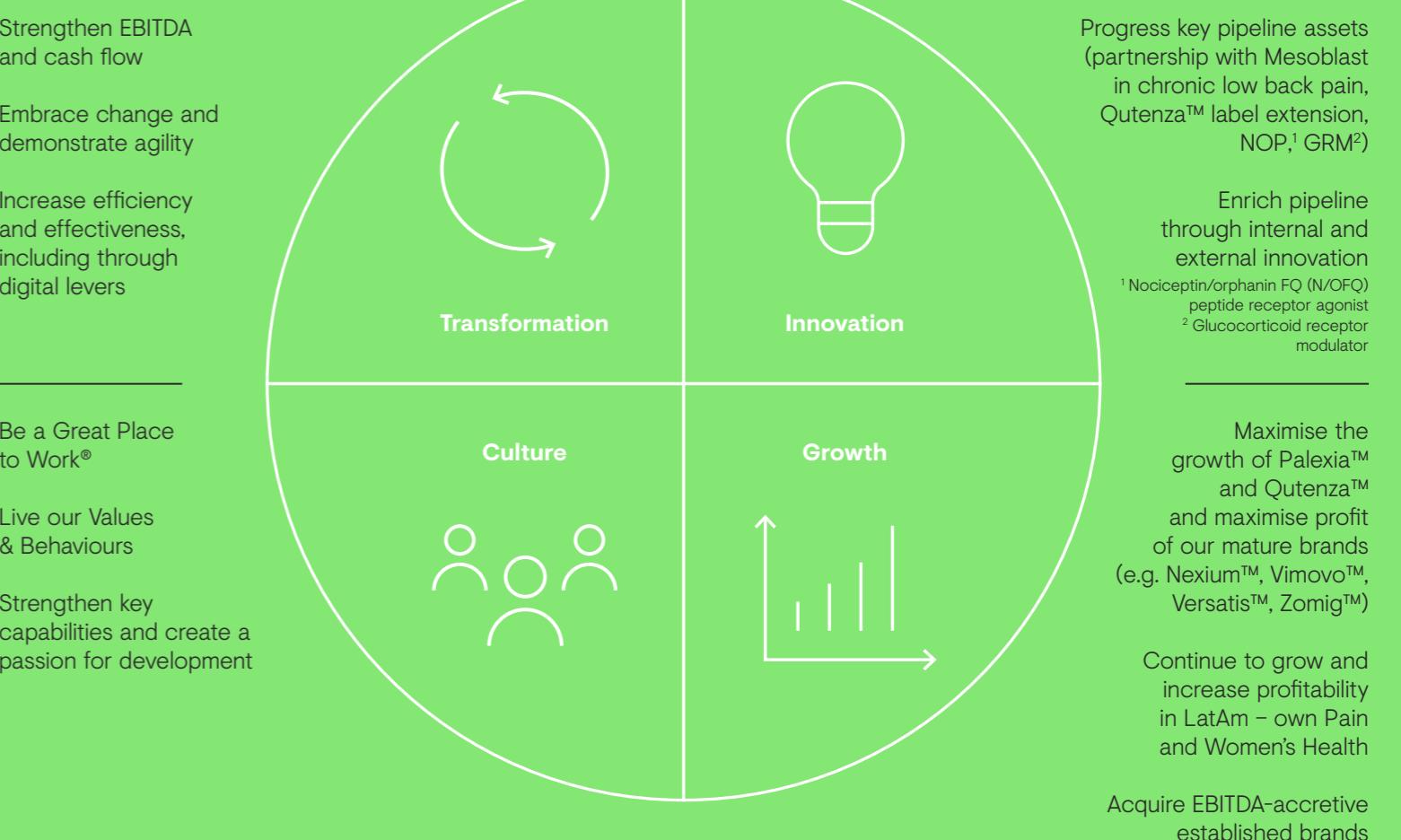
### Back on track for growth and revenue



(x) Aspired EBITDA effect p.a. (€ mn)

LoE = loss of exclusivity

## Our strategic priorities



Progress key pipeline assets (partnership with Mesoblast in chronic low back pain, Qutenza™ label extension, NOP,<sup>1</sup> GRM<sup>2</sup>)  
Enrich pipeline through internal and external innovation

<sup>1</sup> Nociceptin/orphanin FQ (N/OFQ) peptide receptor agonist

<sup>2</sup> Glucocorticoid receptor modulator

Maximise the growth of Palexia™ and Qutenza™ and maximise profit of our mature brands (e.g. Nexium™, Vimovo™, Versatis™, Zomig™)

Continue to grow and increase profitability in LatAm – own Pain and Women's Health

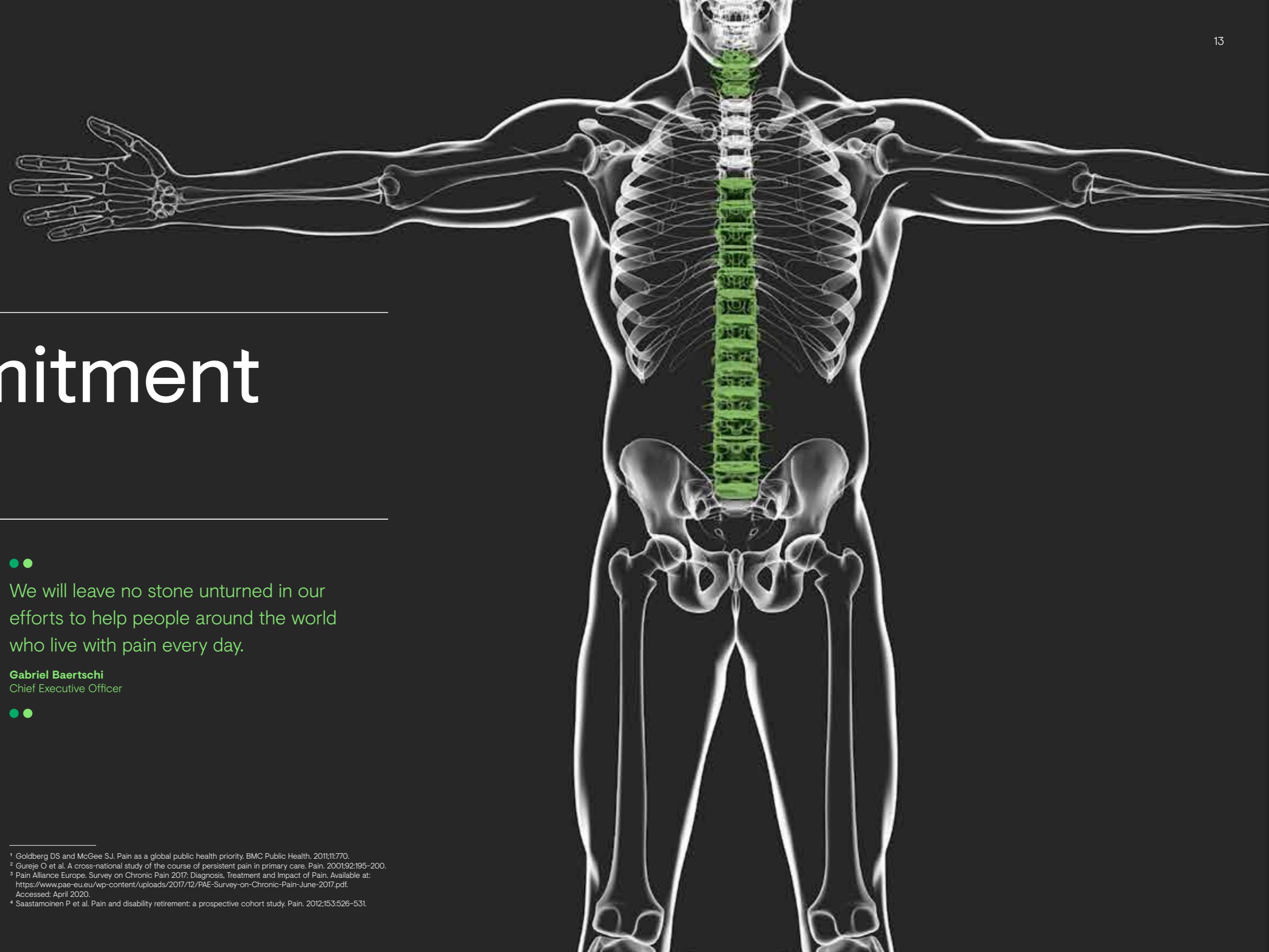
Acquire EBITDA-accretive established brands

# 2

## Our commitment to pain

Pain is a huge burden. It impacts patients – as well as their families, friends, caregivers and society as a whole. It is estimated that about 1 in 5 people worldwide suffers from chronic pain,<sup>1</sup> which equates to around 1.4 billion people. Pain is one of the most common reasons people seek medical help,<sup>2</sup> which places an enormous economic burden on healthcare systems. For many conditions there is no standard of care, and even in cases where these do exist, they may have limited efficacy.<sup>3</sup> Chronic pain is one of the major reasons why people leave the labour market prematurely, and is also a significant contributor to disability retirement. Around the world,<sup>4</sup> many people live with pain every day.

Given the prevalence and debilitating effects of pain, Grünenthal considers it to be a disease in its own right rather than just a symptom. As a global leader in pain research and management for nearly 50 years, we are fully aware that patients are still hugely underserved in this area. We are driven to seek new solutions to relieve pain. We are also fully committed to transforming this field. We are redefining and shaping the future of pain management through our own research, as well as by drawing on external innovation, collaboration and networks.



We will leave no stone unturned in our efforts to help people around the world who live with pain every day.

**Gabriel Baertschi**  
Chief Executive Officer



<sup>1</sup> Goldberg DS and McGee SJ. Pain as a global public health priority. BMC Public Health. 2011;11:770.

<sup>2</sup> Gureje O et al. A cross-national study of the course of persistent pain in primary care. Pain. 2001;92:195–200.

<sup>3</sup> Pain Alliance Europe. Survey on Chronic Pain 2017: Diagnosis, Treatment and Impact of Pain. Available at: <https://www.pae-eu.eu/wp-content/uploads/2017/12/PAE-Survey-on-Chronic-Pain-June-2017.pdf>. Accessed: April 2020.

<sup>4</sup> Saastamoinen P et al. Pain and disability retirement: a prospective cohort study. Pain. 2012;153:526–531.

## Why pain matters

**1 in 5**

or 1.4 billion people worldwide  
are affected by chronic pain<sup>5</sup>

**21**

% of chronic pain patients  
suffer for more than 20 years<sup>6</sup>

**78**

% of chronic pain patients state  
that their treatment was not  
as good as they expected<sup>7</sup>

**500**

million sick days per year  
in Europe are caused by  
musculoskeletal pain alone<sup>8</sup>

**60**

% of permanent work  
incapacity in Europe is related  
to musculoskeletal pain alone<sup>9</sup>

**34**

billion euros are lost by the  
European economy due to  
chronic pain every year<sup>10</sup>

### Societal Impact of Pain (SIP)

Societal Impact of Pain (SIP) is an international platform created in 2009 as a joint initiative of the European Pain Federation (EFIC) and Grünenthal. It aims to raise awareness of the impact that pain has on our societies, as well as our health and economic systems. It does this by facilitating the exchange of information and best-practice sharing across all European Union member states, and by developing and fostering Europe-wide policy strategies and activities for improved pain care. The scientific framework of the SIP platform is under the responsibility of EFIC. Cooperation partners for SIP include the Pain Alliance Europe and the Active Citizenship Network.

[www.sip-platform.eu](http://www.sip-platform.eu)

<sup>5</sup> Goldberg DS and McGee SJ. Pain as a global public health priority. BMC Public Health. 2011;11:770.

<sup>6</sup> Breivik H et al. Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. Eur J Pain. 2006;10:287-333.

<sup>7</sup> Pain Alliance Europe. Survey on Chronic Pain 2017: Diagnosis, Treatment and Impact of Pain. Available at: <https://www.pae-eu.eu/wp-content/uploads/2017/12/PAE-Survey-on-Chronic-Pain-June-2017.pdf>. Accessed: April 2020.

<sup>8</sup> Wiffen P. Pain: there is a lot of it. Eur J Hosp Pharm. 2013;20:1.

<sup>9</sup> Bevan S et al. Reducing Temporary Work Absence Through Early Intervention: The case of MSDs in the EU. The Work Foundation. 2013.

<sup>10</sup> Wiffen P. Pain: there is a lot of it. Eur J Hosp Pharm. 2013;20:1.

# 3

## Research & Development

### 3.1 Being a leading innovator in pain

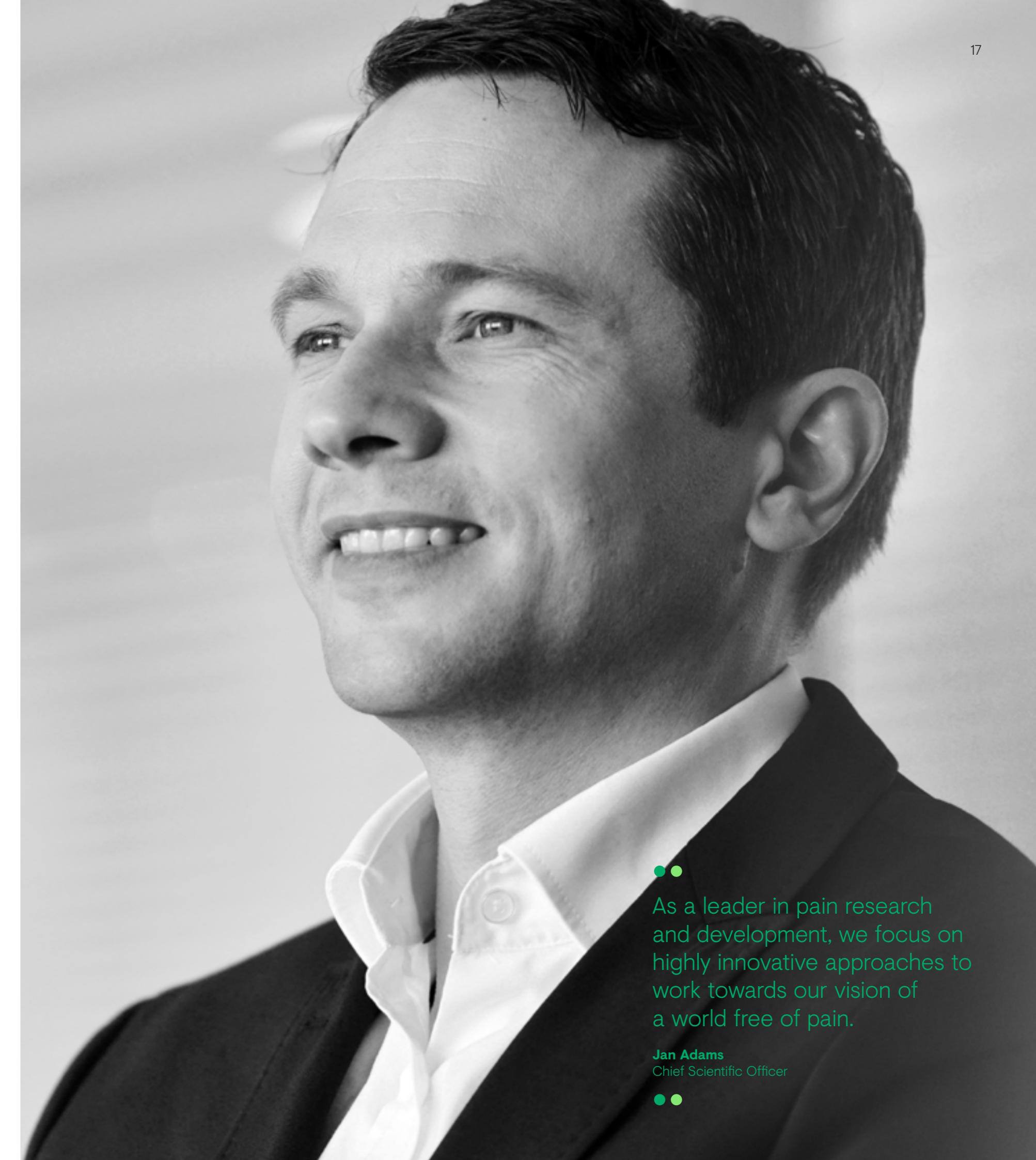
In 2019, Grünenthal made decisive steps in Research & Development (R&D) to drive progress towards our vision of a world free of pain.

In an extensive and cross-functional process, we redefined our strategy for pain. Our R&D activities now focus on four strategic indications: peripheral neuropathic pain, chronic postoperative pain, chronic low back pain, and osteoarthritis. In all of these indications, there are still significant unmet medical needs that we aim to address through highly innovative medicines that truly make a meaningful difference to patients.

As well as redefining our therapeutic area strategy, we also transformed our R&D organisation and operating model to be much more flexible and focused on differentiating capabilities. We put particularly strong emphasis on human and clinical validation, translational sciences and deep disease understanding. In addition to our internal small-molecule capabilities, we leverage partnerships to draw from a wide range of therapeutic modalities, such as biologics and peptides, as well as cell and gene therapy. This enables us to pursue our priorities with a solution-agnostic mindset.

In addition, we continue to embrace the external innovation ecosystem and open ourselves up to even more collaboration with external partners around the world. We are committed to entering strategic partnerships with leading institutions and scientists to shape the field in pain research. In this spirit, we offer our expertise in pain R&D and our end-to-end capabilities to interested partners. The recent opening of our Boston Innovation Hub marks an important milestone in getting us even closer to the global research community.

We also made significant advances in progressing and strengthening our pipeline. With our new collaboration with Mesoblast and a submission to the US Food and Drug Administration (FDA) to expand the label for Qutenza™, we added two major late-stage opportunities to our portfolio. This allowed us to mitigate the setbacks we faced from terminating our Neridronate and Neosaxitoxin programmes. We also made good progress in our preclinical and drug discovery projects.



As a leader in pain research and development, we focus on highly innovative approaches to work towards our vision of a world free of pain.

**Jan Adams**  
Chief Scientific Officer



## 3.2 Embracing external innovation

Today, innovation and value creation take place in a decentralised and networked manner that involves interaction between pharma companies, start-ups, biotechs and academia. Grünenthal has a strong track record of forming successful research and development partnerships. As a key part of Grünenthal's strategic realignment, we want to move even closer to scientific communities around the globe by implementing Innovation Hubs in global research hotspots. In line with this, we opened our Boston Innovation Hub in 2019.

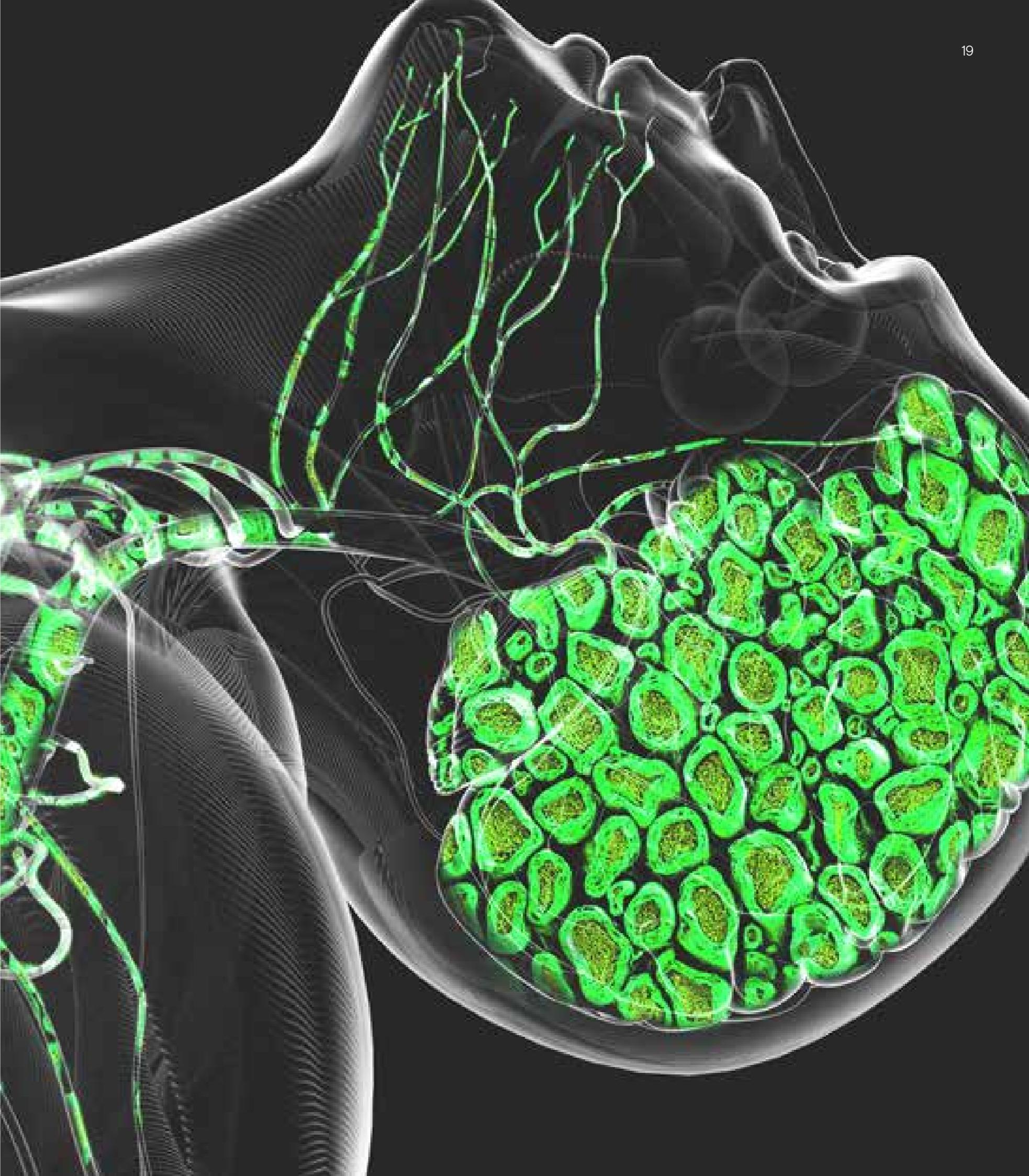
Innovation Hubs are centres of excellence for pain research, and an open invitation to scientists and institutions who are dedicated to addressing pain to team up with us as we work towards our vision of a world free of pain. They feature teams of high-profile scientists and medical doctors who operate virtually to initiate projects and drive them forward. Although each of our Innovation Hubs is equipped to conduct these projects independently – from target identification through to clinical proof of concept – they naturally work together with the R&D unit at our headquarters in Aachen to offer our partners the best of both worlds.

Grünenthal is looking forward to further leveraging its end-to-end R&D capabilities – such as deep disease understanding, clinical and technical development capabilities, market access and commercialisation – in many more promising R&D projects with partners from around the world.



We are committed to entering strategic R&D partnerships to drive progress in pain research and create solutions for patients' unmet medical needs in pain.

Gabriel Baertschi  
Chief Executive Officer



## 3.3 Progressing our pipeline: our lead programmes

To move closer to our vision of a world free of pain, we are currently pursuing a range of programmes across different modalities, targets and mechanisms of action. Here are some selected highlights from our development pipeline.



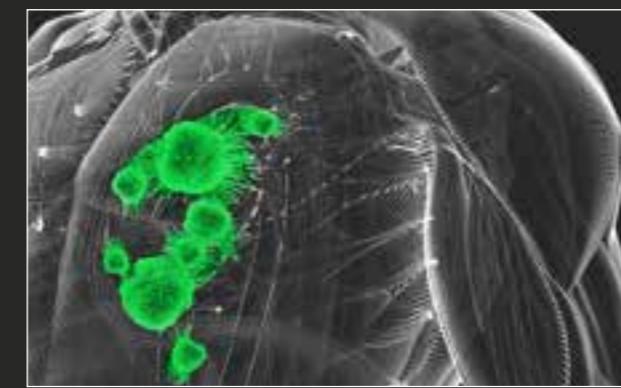
### Nociceptin/orphanin FQ (N/OFQ) peptide receptor agonist (NOP)

Despite different treatment options being available, many patients with neuropathic pain still suffer from treatment non-response or insufficient pain relief. With our NOP receptor agonist programme, we are pursuing the development of a selective oral treatment with a unique mechanism of action for chronic peripheral neuropathic pain. This programme is based on many years of intense and groundbreaking research at Grünenthal in the field of NOP receptors, and creates a unique opportunity for a transformative first-in-class treatment. In 2020, we aim to bring the front-runner compound into clinical development.



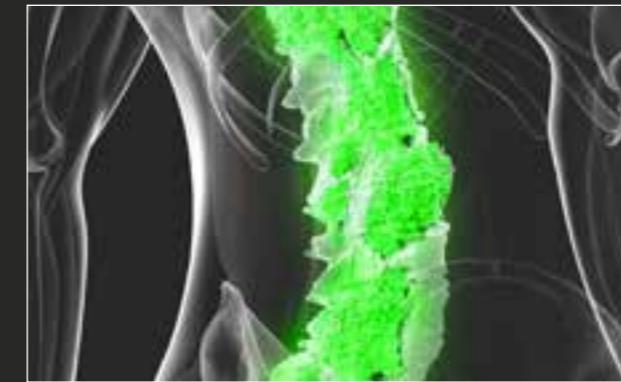
We follow a holistic and solution-agnostic approach to deliver highly effective pain treatments, building our programmes on a firm foundation of human pathophysiology and solid human target validation.

**Gillian Burgess**  
Head of Research



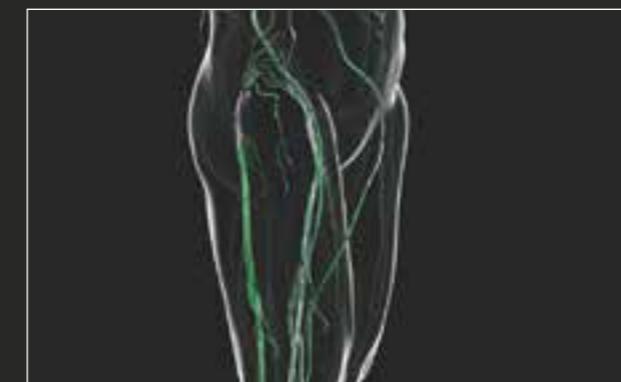
### Glucocorticoid receptor modulator (GRM)

Glucocorticoids such as cortisone are known to be highly efficacious anti-inflammatory drugs. However, they come with several significant side effects that limit their use, particularly in chronic indications. With our GRM programme, we are pursuing the development of clinical candidates for oral treatment with broad anti-inflammatory efficacy but significantly fewer side effects than glucocorticoid-based therapies. Our team is aiming to bring our front-runner compound into clinical development during 2020.



### MPC-06-ID (Mesoblast collaboration)

More than 7 million patients in Europe suffer from chronic low back pain associated with degenerative disc disease.<sup>1-4</sup> Many patients still suffer from significant pain after exhausting available conservative treatment options. Together with Mesoblast, we are pursuing the development of a highly innovative mesenchymal precursor cell (MPC) therapy for patients with chronic low back pain associated with degenerative disc disease who have not found effective relief from available treatment options. In 2020, we expect to receive the first results from an ongoing Phase III study in the US. Based on these findings, we will progress towards a second European Phase III trial.



### Qutenza™

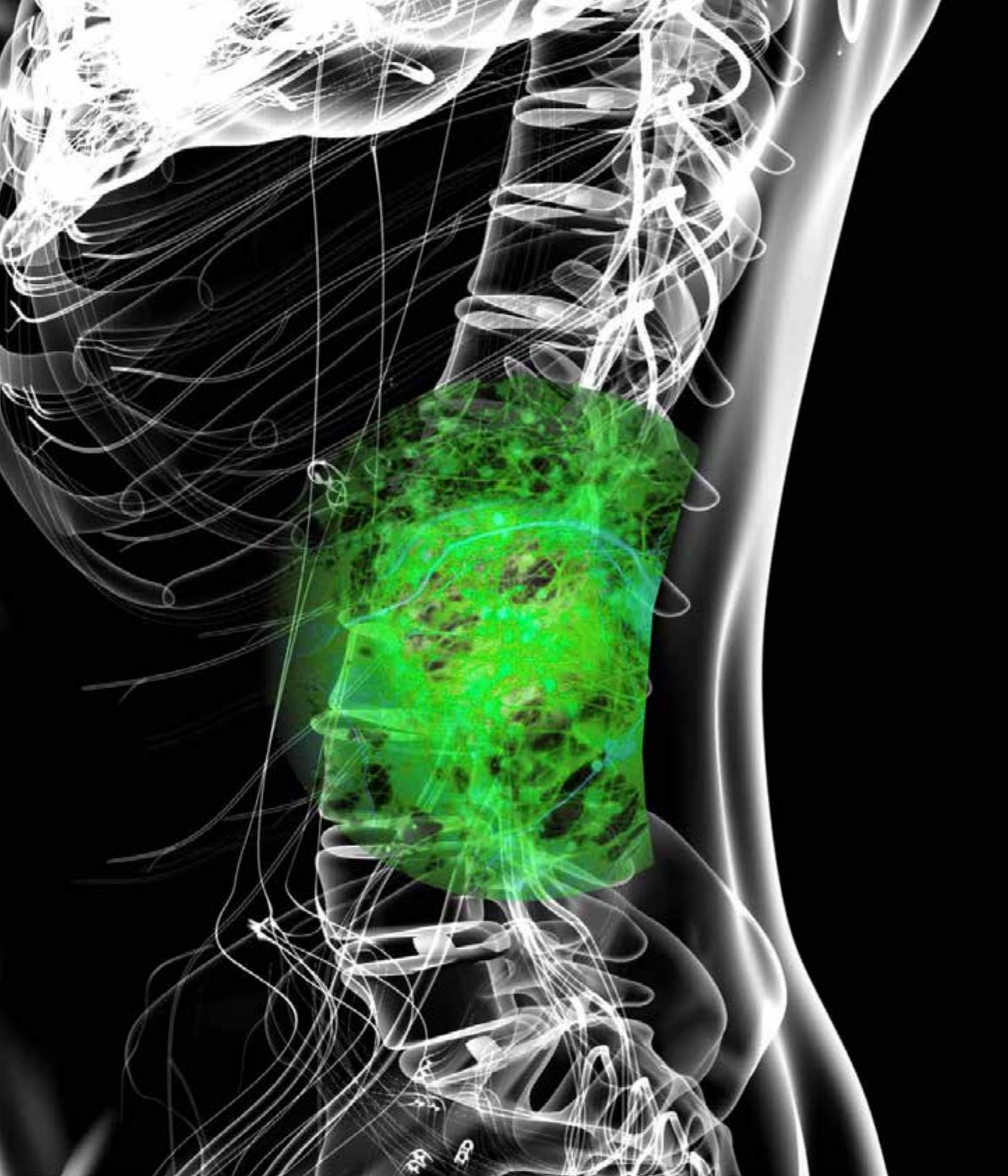
Qutenza™ is a cutaneous patch (capsaicin 179 mg/8%) that is approved for the treatment of peripheral neuropathic pain in Europe and for the treatment of neuropathic pain associated with postherpetic neuralgia in the US. Currently, the US FDA is reviewing our supplemental new drug application to expand the label for Qutenza™ to include treatment of pain associated with diabetic peripheral neuropathy. We expect a decision from the FDA by 19 July 2020. We are also considering additional lifecycle management ideas to further demonstrate the benefits of Qutenza™.

<sup>1</sup> Andersson GB. Epidemiological features of chronic low-back pain. Lancet. 1999;354:581-585.

<sup>2</sup> Freburger JK et al. The rising prevalence of chronic low back pain. Arch Intern Med. 2009;169:251-258.

<sup>3</sup> Malanga GA et al. Epidemiology. In: Cole AJ & Herring SA, eds. The Low Back Pain Handbook: A Guide for the Practicing Clinician. 2nd ed. Philadelphia. PA: Hanley and Belfus; 2003:1-7.

<sup>4</sup> DePalma MJ et al. What is the source of chronic low back pain and does age play a role? Pain Med. 2011;12:224-233.



### 3.4 At the forefront of science: our partnership with Mesoblast in chronic low back pain

As a global leader in pain research, we are deeply committed to making a meaningful difference to patients. To achieve this, we focus on truly innovative approaches and we believe that we can only be successful if we team up with other innovators that share our vision of a world free of pain.

For this reason, we are very excited to have entered a strategic partnership with Mesoblast in 2019. This collaboration marks a major milestone for Grünenthal as it represents access to our first cell therapy programme. It grants Grünenthal exclusive commercialisation rights in Europe and Latin America.

Mesoblast is a world leader in cellular medicines. Together, we aim to develop and commercialise MPC-06-ID, a highly innovative Phase III cell therapy with the potential to transform treatment of chronic low back pain associated with degenerative disc disease in patients who have exhausted available conservative treatment options. This patient population often suffers from particularly severe pain.

More than 7 million people in Europe alone are thought to suffer from degenerative disc disease,<sup>1,4</sup> which often causes significant pain and can finally result in loss of function.<sup>5</sup> Most existing therapies provide only limited symptomatic relief. As a result, patients typically suffer for several years without being able to sufficiently address their pain.<sup>6</sup>

Phase II data for MCP-06-ID showed that a single intra-discal injection using a unit dose of 6 million allogeneic MPCs resulted in meaningful improvements in pain intensity and functionality for patients for at least two years.<sup>7</sup>

Currently, a first Phase III study is ongoing in the US. We expect to see the first results by mid-2020. Together with Mesoblast, we are jointly preparing a second Phase III study for Europe, which we aim to initiate in 2021.



**Through our partnership with Mesoblast, we are striving to deliver the first allogeneic mesenchymal stem cell therapy for patients with chronic low back pain associated with degenerative disc disease.**

**Jan Adams**  
Chief Scientific Officer



<sup>1</sup> Andersson GB. Epidemiological features of chronic low-back pain. Lancet. 1999;354:581-585.

<sup>2</sup> Freburger JK et al. The rising prevalence of chronic low back pain. Arch Intern Med. 2009;169:251-258.

<sup>3</sup> Malanga GA et al. Epidemiology. In: Cole AJ & Herring SA, eds. The Low Back Pain Handbook: A Guide for the Practicing Clinician. 2nd ed. Philadelphia, Pa.: Hanley and Belfus; 2003:1-7.

<sup>4</sup> DePalma MJ et al. What is the source of chronic low back pain and does age play a role? Pain Med. 2011;12:224-233.

<sup>5</sup> Rider SM et al. Molecular mechanisms of intervertebral disc degeneration. Spine Surg Relat Res. 2018;3:1-11.

<sup>6</sup> Grünenthal Internal Data on File.

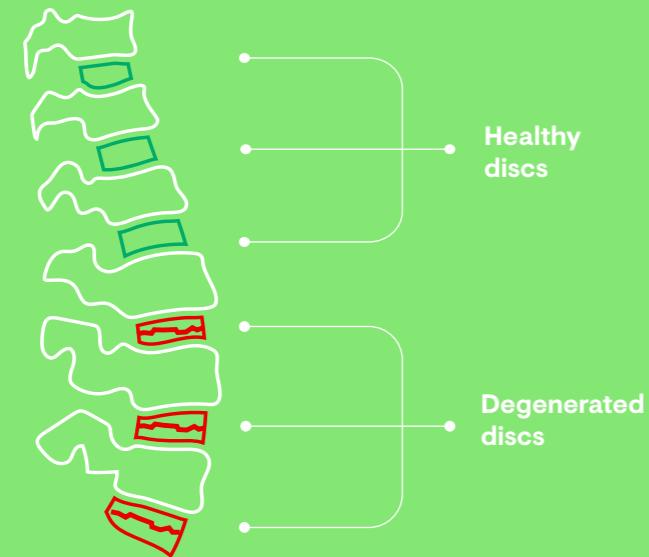
<sup>7</sup> Mesoblast. Trial Results: MPC-06-ID Phase 2 Chronic Low Back Pain Due to Disc Degeneration Clinical Trial. Available at: <https://www.mesoblast.com/clinical-trial-results/mpc-06-id-phase-2>. Accessed: April 2020.

# Exploring the role of cell therapy in degenerative disc disease

## What is degenerative disc disease (DDD)?

DDD is a common condition which involves inflammation and degeneration of the intervertebral discs due to various factors, including age, trauma or genetic predisposition.<sup>1</sup>

The lack of 'cushioning' can result in spinal instability, mechanical stress and bony changes of the spine, which can eventually cause significant pain and loss of function.<sup>2</sup>



Clinical studies are exploring whether therapies involving MPCs could deliver meaningful, lasting improvements to people with chronic low back pain due to DDD.



**More than 7 million people in Europe** are thought to suffer from chronic low back pain caused by DDD.<sup>1,3-5</sup>

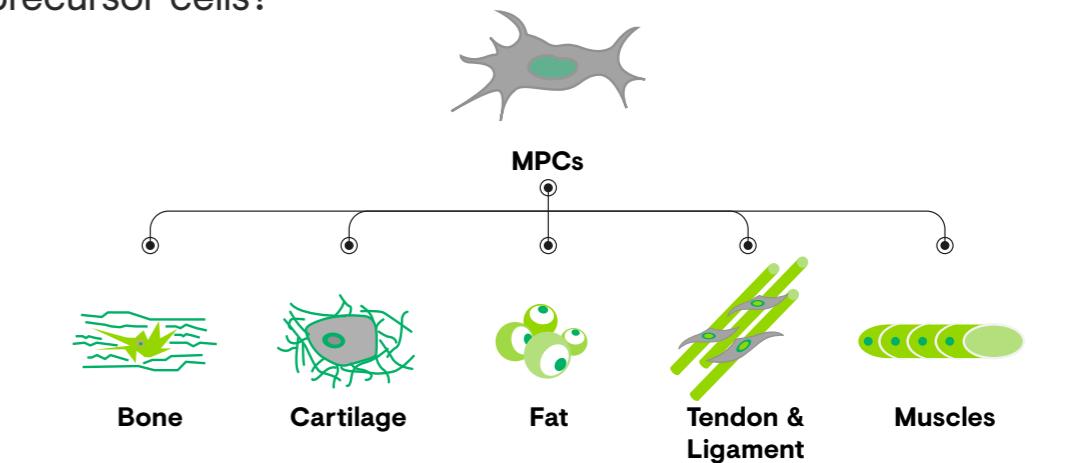
**MPCs have the potential to deliver meaningful lasting improvements to patients with DDD beyond symptomatic treatment.**

<sup>1</sup> Freburger JK et al. The rising prevalence of chronic low back pain. Arch Intern Med. 2009;169:251-258.  
<sup>2</sup> Rider SM et al. Molecular mechanisms of intervertebral disc degeneration. Spine Surg Relat Res. 2018;33:1-11.

<sup>3</sup> Andersson GB. Epidemiological features of chronic low-back pain. Lancet. 1999;354: 581-585.  
<sup>4</sup> Malanga GA et al. Epidemiology. In: Cole AJ & Herring SA, eds. The Low Back Pain Handbook: A Guide for the Practicing Clinician. 2nd ed. Philadelphia, Pa.: Hanley and Belfus, 2003:1-7.  
<sup>5</sup> DePalma MJ et al. What is the source of chronic low back pain and does age play a role? Pain Med. 2011;12:224-233.

<sup>6</sup> Grünenthal internal data on file.

## What are mesenchymal precursor cells?

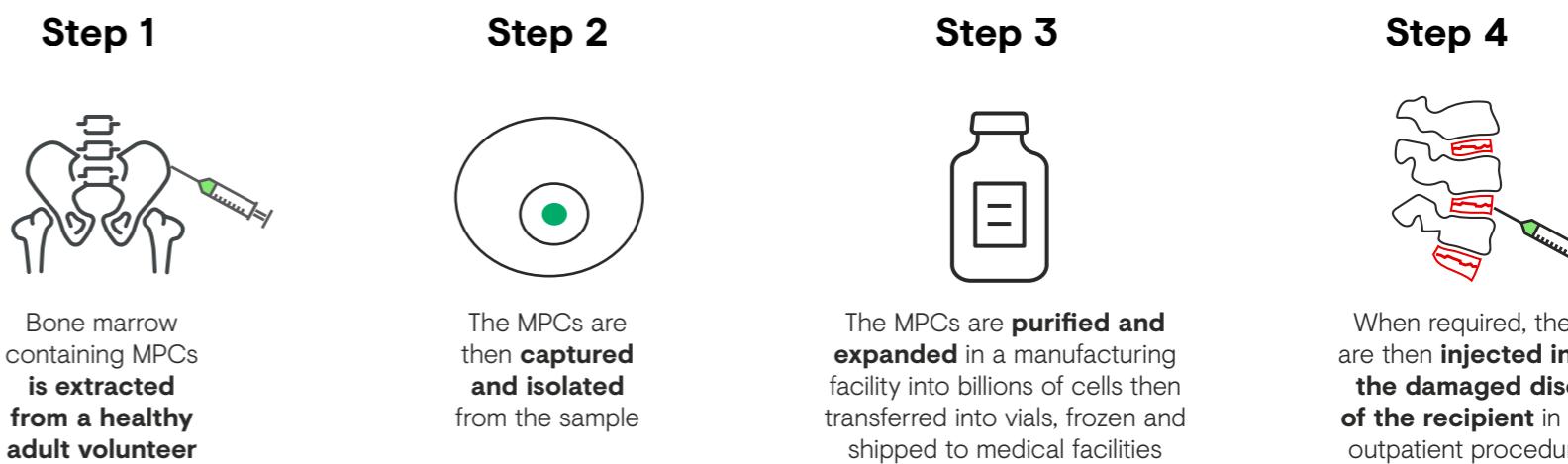


MPCs can differentiate into tissues such as **bone, cartilage, fat, tendon and muscle.**<sup>7</sup>

Clinical trials are currently evaluating the use of donor MPCs in treating people with DDD.

## How could MPCs be used in treating DDD?

The process of extraction and delivery



## Potential treatment effect

Scientists believe that the injection of MPCs into a damaged disc can trigger three biological reactions:



These biological effects can provide relief for up to 2 years and maybe even longer.<sup>8</sup>

<sup>7</sup> National Institutes of Health (U.S. Department of Health and Human Services). Stem Cell Information: Stem Cell Basics IV. Available at: <https://stemcells.nih.gov/info/basics/4.htm>. Accessed April 2020.  
<sup>8</sup> Mesoblast. Trial Results: MPC-06-ID Phase 2 Chronic Low Back Pain Due to Disc Degeneration Clinical Trial. Available at: <https://www.mesoblast.com/clinical-trial-results/mpc-06-id-phase-2>. Accessed April 2020.

# 4

## People and culture

### Driving a vibrant, high-performing culture

Our business success is made possible by our people. As a player in a fast-paced, ever-changing market environment, we continuously question the way we do things and embrace change as an integral part of our daily work. Our employees demonstrate this agility every day. With their ambition, talent and commitment, our teams drive our efforts to strengthen our position as a cutting-edge pharmaceutical company. We offer our employees an exciting working environment and wide-ranging individual development opportunities. It is our goal to maintain high levels of engagement with our current workforce and to strengthen our company as a Great Place to Work®.

We promote a vibrant, high-performance culture. Every employee is required to have high-quality objectives that are aligned with our strategy. Performance is monitored in our Performance & Development Management process that focuses on results – as well as on how those results were achieved. Outstanding results are recognised and rewarded. To celebrate exceptional contributions, we have created the Grünenthal Global Excellence Award, which was presented for the first time in 2019.

At the end of December 2019, Grünenthal employed approximately 4,700 people worldwide.



Guided by our Values & Behaviours, we continuously strive to strengthen our Grünenthal culture. We create an environment where people can thrive, join forces and have real impact on our shared success, their own development and our vision. Together, we work towards a world free of pain.

**Leen Hofkens**  
Head Global HR



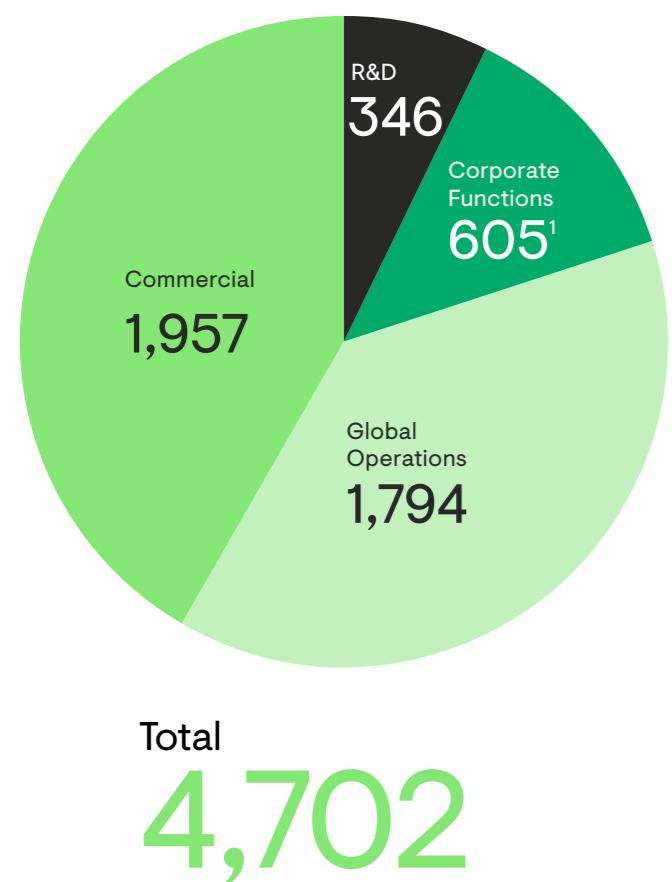
## We invest in talent

To achieve our strategic priorities, we continue to attract, develop and retain a talented and diverse workforce that is united in the pursuit of our vision. We aim to continuously drive employee engagement and bring our values and behaviours to life – by embedding them in our key people processes, ensuring they guide our decision-making and anchoring them within our organisation for the long term. We are growing our talents from within, while also identifying and recruiting emerging talents from outside of our company if they share our values, fit our culture and want to contribute to pursuing our vision of a world free of pain.

We encourage leaders to spend time supporting their employees in their development. In 2019, we strengthened our Performance & Development Management approach and now have individual development plans in place for the majority of our employees. In 2020, we will focus on further improving the effectiveness of our approach by fostering regular and actionable feedback on performance, while also helping employees to take ownership of their development and put their plans into action. In this way, we will strengthen and build the capabilities we need across our organisation – today and tomorrow.

### Employees by function

**Actual Headcount**  
December 2019



## Growing leadership capabilities and continuing to build a diverse workforce

As part of our efforts to achieve our strategic priorities, we aim to harness different perspectives, talents and ideas, while also ensuring that we develop a strong and diverse group of leaders. Between 2016 and 2019, nearly two-thirds of vacancies on our Senior Level were filled internally. With employees from 23 nationalities joining forces in 29 different countries, and with women in 33 percent of our leadership positions<sup>2</sup>, our workforce reflects the diverse markets and societies in which we operate.

## Engaging our employees

We want to make sure our employees understand and fully support our strategy. We offer several internal platforms on the global and country levels that provide all employees worldwide with opportunities to gather information and enter into dialogue with our Corporate Executive Board.

We also care about the wellbeing of our employees and offer relevant benefits across the countries we operate in. For example, we regularly hold Health Day events at our headquarters in Germany, which include a range of activities related to mental and physical health. We also have our own internal childcare centre. It is located at our headquarters in Aachen and supports working parents in balancing their family life with their career.

We use employee opinion surveys and leadership feedback surveys to measure employee satisfaction and engagement, as well as the progress we have made towards our aim of maintaining high levels of engagement and strengthening our company as a Great Place to Work®. In this context, we implemented a new 180-degree leadership feedback survey in 2019. The next Great Place to Work® evaluation is planned for 2020.

## Highlights 2019

**729**

new hires worldwide,  
including 139  
in Germany

**26**

% of our talent  
moved into a  
new role

**59**

% of vacancies  
on our Senior  
Level were filled  
internally between  
2016 and 2019

## 180-degree leadership feedback survey

Our first 180-degree survey involved over 30 percent of our employees who gave feedback on how leaders manage the team's performance and development. Over 90 percent of all feedback highlighted that priorities are clear and that employees understand how these priorities link to our functional objectives and global strategy. The vast majority of managers also received positive feedback on the way they keep their teams focused, and encourage cross-functional collaboration; 86 percent of all employee feedback stated they would recommend their manager to other colleagues. Giving regular, actionable feedback and reducing micromanagement remain areas of potential improvement for some of our managers. In 2020, we will offer this survey tool to an even larger group of managers in all functions and regions.



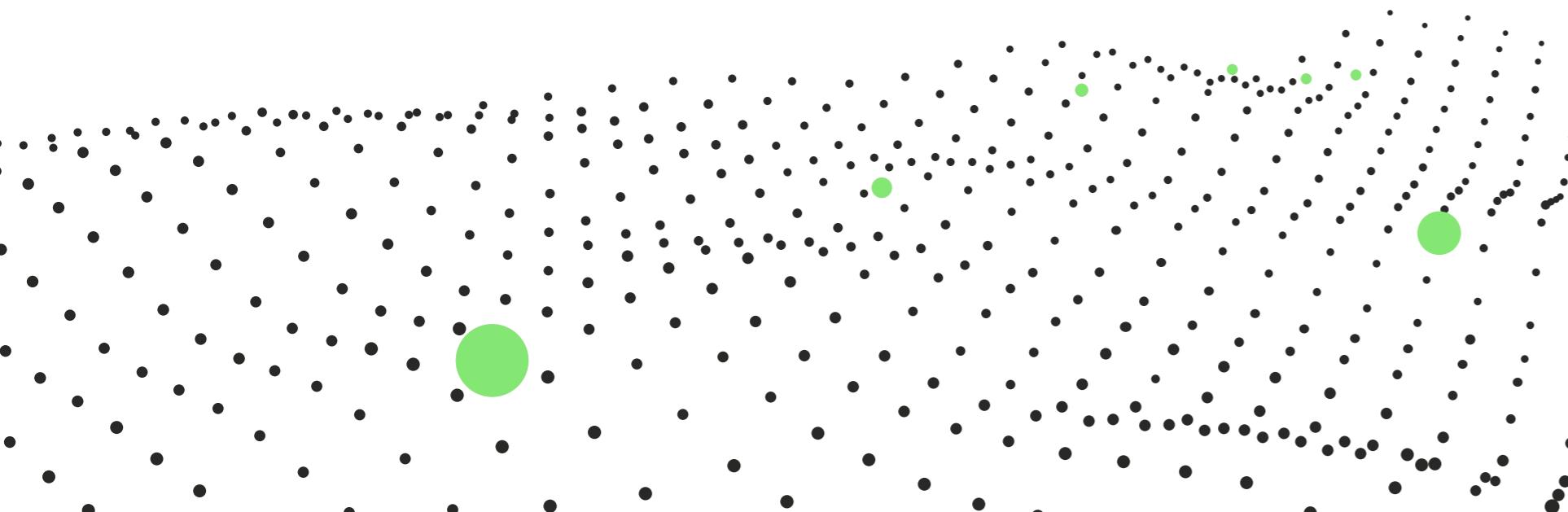
## A unique place to work

At Grünenthal, we are passionate about encouraging our people to innovate in every possible way – whether they're building our pipeline by focusing on our strategic indications and the latest science, challenging the status quo, improving our processes or implementing new ideas to drive performance along the value chain.

Our people join forces across teams, functions and international locations. They work hard, challenge and support each other, and seek opportunities to learn while demonstrating integrity in everything they do.

Each employee is empowered to make an impact on the results we achieve and on the lives of the patients we serve.

Join forces  
Make an impact  
Innovate for a world free of pain



# Our culture

Culture is one key pillar of our strategy, which supports progress towards our vision of a world free of pain. Five Values that are supported by specific Behaviours guide our decision making and give a clear indication of how we behave – as individuals and as an organisation. By bringing these values to life every day, we create our unique culture: “We are Grünenthal”.

# We are Grünenthal

Values &  
Behaviours

We **are**  
patient-centric

We **live**  
entrepreneurship

We **join**  
forces

We **act**  
with integrity

We **drive**  
performance



# 5

## Markets and products

### Extending our reach

We continuously grow and expand our market presence and product portfolio, and we collaborate with commercial partners and multiple stakeholders from the pain management field and beyond in order to make our medicines available to patients.

Grünenthal's field teams currently comprise approximately 1,400 people distributed across Europe, Latin America and the US. Their overall focus is on pain and mature brands, while our teams in Latin America focus on other therapeutic areas as well, e.g. women's health. In 2019, our field teams visited nearly 300,000 stakeholders, including physicians, pharmacists, nurses, and administrative staff within the healthcare system.

In addition, Grünenthal has built a strong network of commercial partners in countries where we do not maintain our own local commercial organisation.

In 2019, we achieved some important milestones on our journey towards implementing our strategy across our pain franchise. Patients suffering from various types of pain remains a significant unmet need, as does healthcare professionals' desire for new ways to help patients find relief. At Grünenthal, we are proud to have a portfolio of products that aims to help break the endless cycle of pain, where patients and their doctors continuously work to find the right dose, the right combination of treatments and the right timing to take medication to give relief.

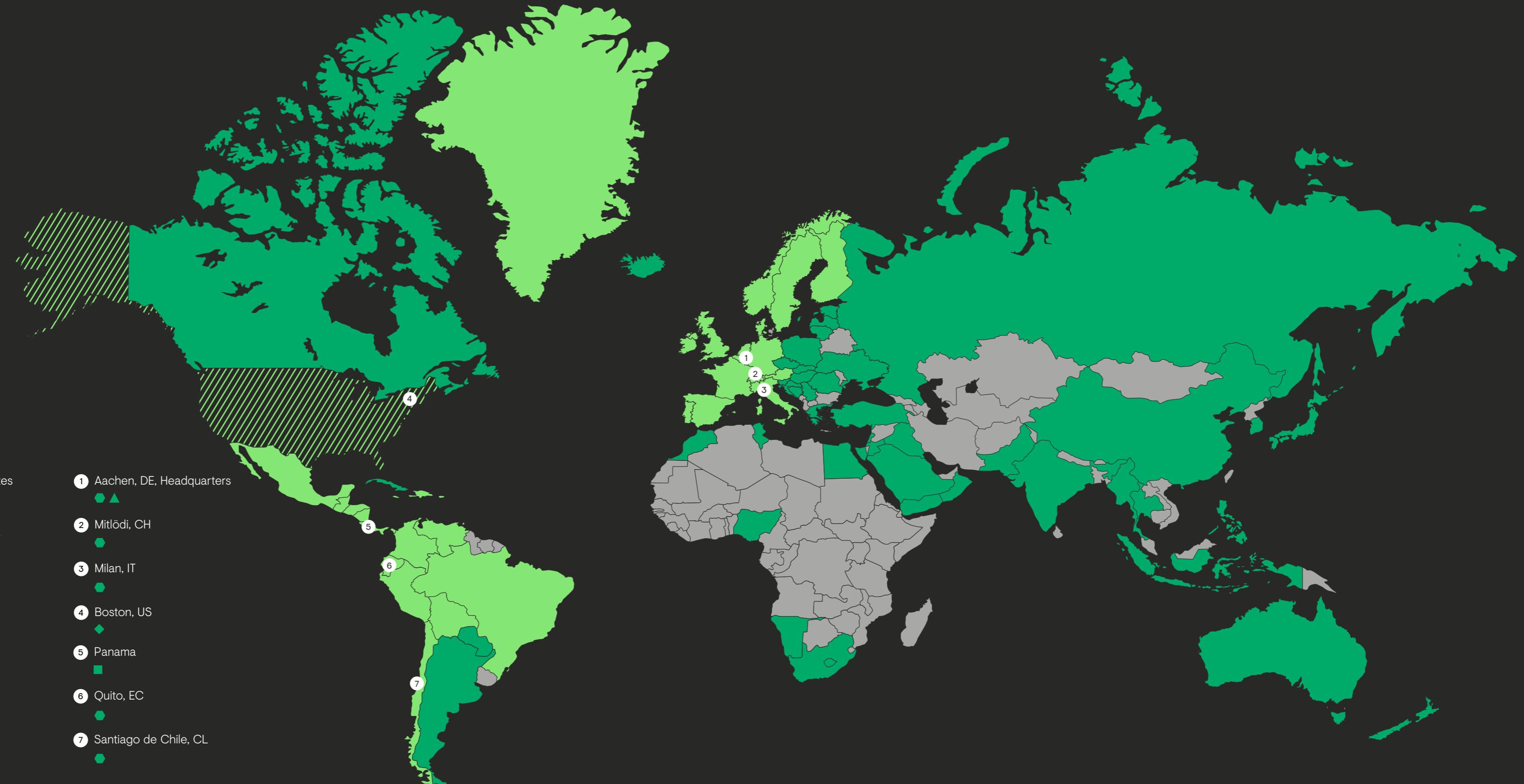
Last year we reached more than 10 million patients treated with Palexia™ (tapentadol) worldwide since its launch, showcasing another example of how the Grünenthal product portfolio is making a meaningful difference to patients' lives globally.

Additionally, 2019 saw the expansion of our commitment to bringing Qutenza™ (capsaicin 179 mg/8%) to patients suffering with peripheral neuropathic pain, including post-surgical neuropathic pain, painful chemo-induced peripheral neuropathic and post-herpetic neuralgia (and it is currently under review in the US by the FDA for painful diabetic peripheral neuropathic pain). The numbers of patients whose pain is successfully treated with Qutenza™ continues to grow in Europe, and we are excited to support the expansion of Qutenza™ operations in the US. In the US, we have set up a new scientifically skilled field force to relaunch Qutenza™ for the management of postherpetic neuralgia, a painful condition that affects the nerve fibres and the skin as a complication of shingles, which is the indication for Qutenza™ currently approved by the FDA. The Averitas team is piloting a new scheme to support commercialisation of Qutenza™ and will provide the basis for expansion.

Elsewhere in the world we signed partner agreements to commercialise Nexium™ (esomeprazole) and Vimovo™ (naproxen/esomeprazole). These agreements are part of our overall strategic approach that aims to ensure that these medicines get to the right patients by working closely with strong partners in countries where Grünenthal does not currently have a presence.

And in early August 2019, we successfully launched Versatis™ (lidocaine) in Mexico – making it the first product exclusively indicated to relieve localised neuropathic pain in this country. This condition affects nearly 7 million Mexican patients who were not previously able to access effective treatment.<sup>1</sup>

## Market presence – the Grünenthal world



## 5.1 Integrating Nexium™ and Vimovo™

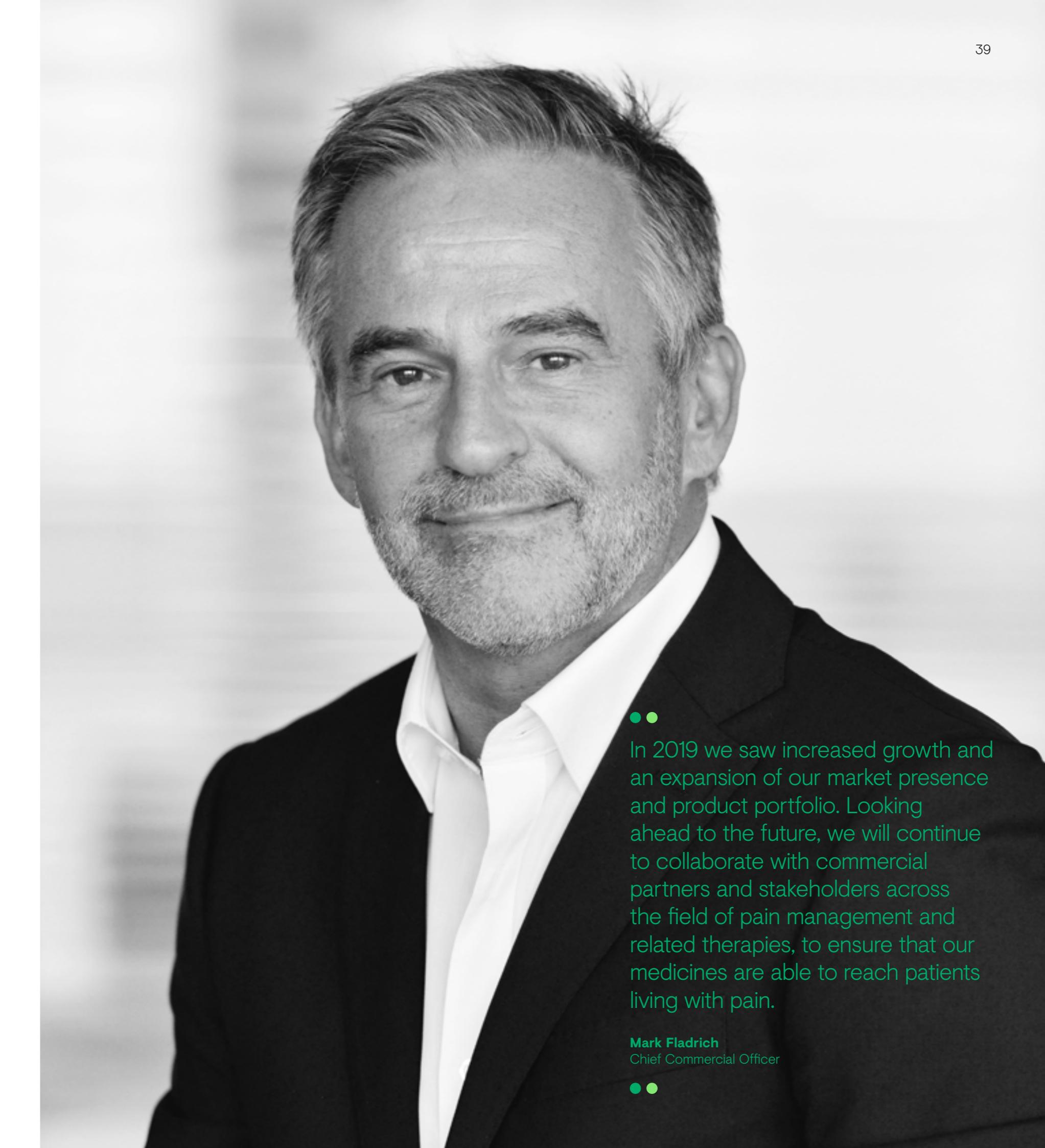
In late 2018, we agreed the biggest deal in our company's history – to acquire the European rights to Nexium™ and the global rights to Vimovo™ (excluding the US and Japan). This marked the start of a critical period of transition and integration.

Our Integration Management Office is closely coordinating the overall process. It is responsible for steering all aspects of the integration, including commercial, operational and regulatory considerations.

The operational integration of Nexium™ and Vimovo™ will be a major factor in making sure Grünenthal gets full value for this historic investment. Our integration teams are making sure that the supply and distribution of these products are successful across all affiliates, contract manufacturers and partner businesses worldwide.

In 2019, we achieved some major milestones in the integration process. In October, our colleagues in Brazil became the first country team to successfully transfer marketing authorisation for Vimovo™ from AstraZeneca to Grünenthal. Alongside this key achievement, we also submitted nine transfer applications for marketing authorisation for Nexium™ across Europe in 2019.

Overall, we took key steps to prepare for the core transition year in 2020. More than 50 employees from across our company worked together to support the integration of Vimovo™ and Nexium™ in 2019. This team will continue to join forces across functions to help make this historic investment a true success for Grünenthal. In this spirit, we are going to further invest in this integration project by hiring new talent, installing new manufacturing equipment and increasing our production volumes.



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In 2019 we saw increased growth and an expansion of our market presence and product portfolio. Looking ahead to the future, we will continue to collaborate with commercial partners and stakeholders across the field of pain management and related therapies, to ensure that our medicines are able to reach patients living with pain.

**Mark Fladrich**  
Chief Commercial Officer

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## 5.2 Working to reach more patients in the US

Marv Kelly, General Manager at Grünenthal US, shares his insights into the company's ambitious plans in the US – the world's largest pharmaceutical market.

### How can we summarise Grünenthal's recently established presence in the US?

Our ambitious set-up is completely different to the approach that other companies have adopted when entering the US. We are striving to achieve long-term growth in this market by providing innovations that change patients' lives – and we are aiming to do this by investing in three pillars:

1. **Product:** Building a specialty pharmaceutical business called Averitas Pharma to optimise opportunities related to our Qutenza™ brand.
2. **Platform:** Developing a digital health platform called Fern Health as part of a future-facing approach to pain management.
3. **Pipeline:** Establishing Grünenthal Therapeutics, an Innovation Hub in Boston, Massachusetts, to deliver innovative medicines for pain patients through partnerships and collaboration.

### What are the current market conditions in the US?

56 percent of the world's patients with a diagnosis for neuropathic pain live in the US,<sup>1</sup> and the number of people diagnosed with this condition is expected to grow by 30 percent between 2019 and 2030.<sup>2</sup> For this reason, there are significant opportunities for Grünenthal to provide new therapies that meet high unmet medical needs for people who suffer from neuropathic pain in this market.



I would like our company to make a difference to the lives of as many pain patients as possible by leveraging our global knowledge and exploring potential new therapeutic areas.

**Marv Kelly**  
General Manager US



## What differentiates Grünenthal from other providers?

Grünenthal has a strong portfolio of life-changing treatments for pain patients. The cutaneous patch Qutenza™ (8% capsaicin) is just one example. Grünenthal is the sole owner of commercial rights for this treatment worldwide. A single local topical treatment with Qutenza™ can provide up to three months of pain relief from post-shingles nerve pain (PHN), and the one-hour treatment can be repeated every 90 days.

The product is currently indicated for neuropathic pain associated with PHN in the US; however, we filed a supplemental New Drug Application to the US FDA in 2019 to extend Qutenza™ to treat neuropathic pain associated with diabetic peripheral neuropathy. The FDA has accepted the file for review and a final decision will be made under the Prescription Drug User Fee Act by 19 July 2020. If successful, this will be a key moment in our long-term strategic plan to expand the label for Qutenza™ in the US to provide much-needed relief for patients with a broader range of neuropathic pain conditions.

## And what services make Grünenthal stand out in the US?

Fern Health is a great example of our future-facing and patient-centric approach. It is a digital concierge platform that offers personalised care programmes for patients with musculoskeletal pain. With its modern format, it aims to improve treatment outcomes for patients with this condition while also decreasing the related costs for the healthcare system. The mobile app was launched in June 2019.

Fern Health is unique because it combines digital technology with a human touch. Patients begin their journey by discussing their condition with one of Fern's care coordinators, who act as trusted advisors by helping them to navigate the range of available treatment options and make the best decision. In the next step, the platform uses published clinical evidence to create a personalised treatment plan that is tailored to reflect the patient's specific lifestyle and needs. Importantly, the plans are solution-agnostic and leverage all of the available options – from acupuncture or physiotherapy through to pharmacological therapy to surgery.

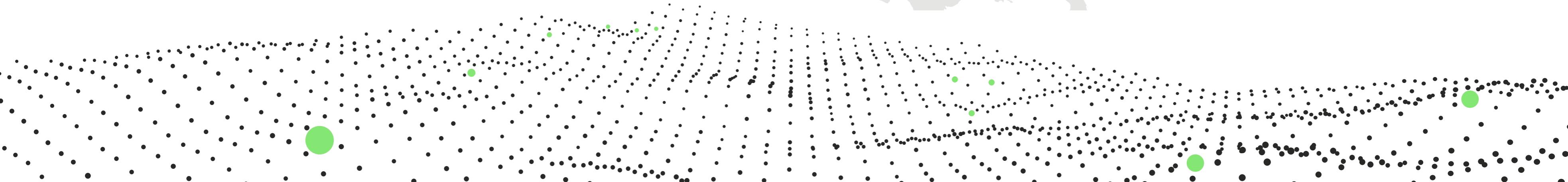
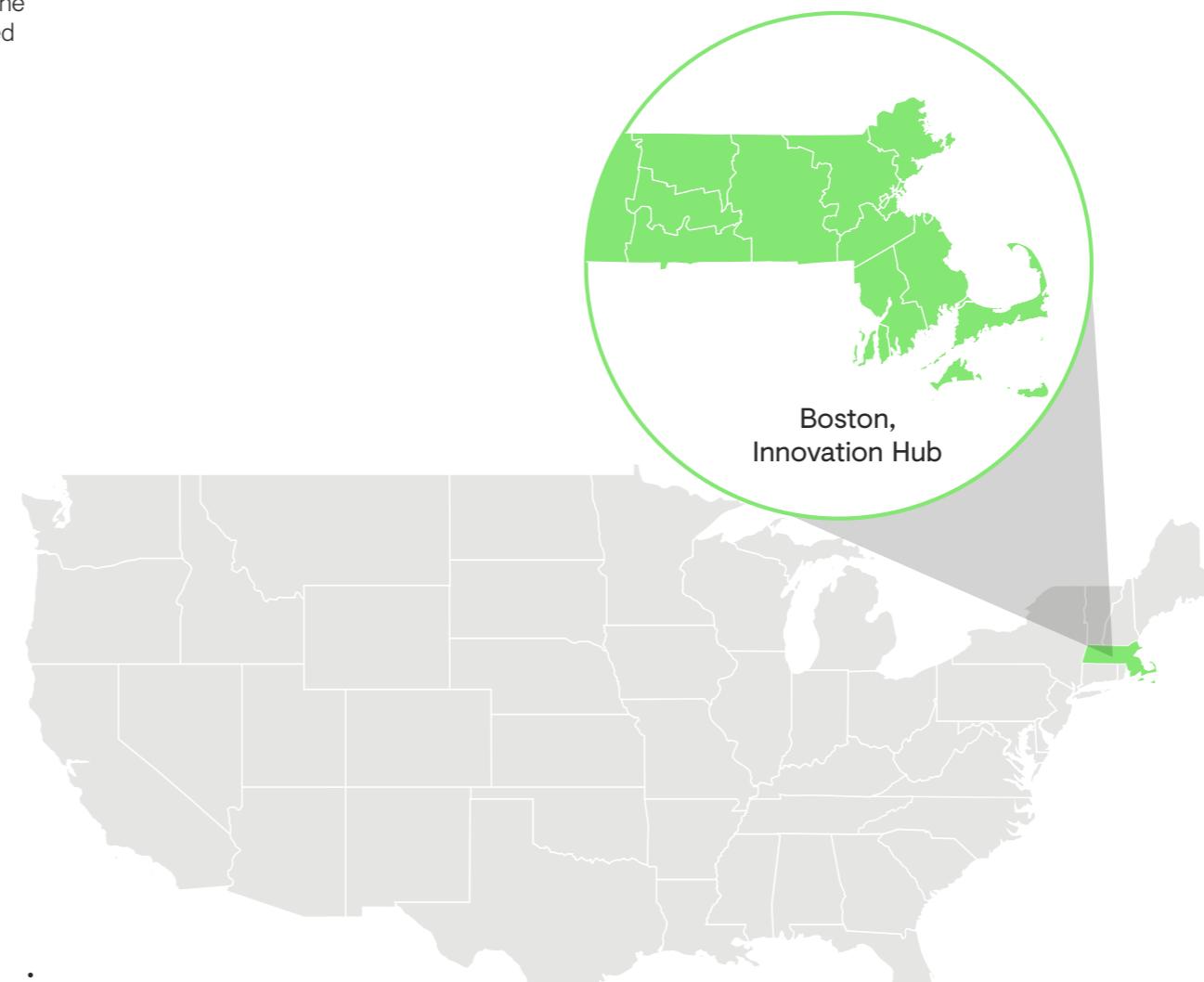
## What about the new Innovation Hub in Boston?

The Innovation Hub in Boston, Massachusetts, aims to develop partnerships that will deliver a pipeline of therapies – from drug discovery through to proof of concept. Known as Grünenthal Therapeutics, the hub rounds off Grünenthal's US presence by creating a collaborative scientific site where our teams can join forces with world-leading researchers, universities and companies. It is a critical part of Grünenthal's investment in the future and aims to identify innovative modalities such as cell and gene therapy that can lead to the creation of a pipeline of high-calibre pain treatments that can make an important contribution to improving the standard of care for patients.

## What would you like Grünenthal to achieve in the US going forward?

I would like our company to make a difference to the lives of as many pain patients as possible by leveraging our global knowledge and exploring potential new therapeutic areas. We have a uniquely multifaceted team that is going to collaborate across functions to achieve results that benefit people who are living with pain every day. Colleagues in the Averitas commercial model can make new products available on the market, while the team at our Boston Innovation Hub will help us to understand the needs of patients and healthcare professionals by interacting with pioneers from the scientific community, and the insights from Fern Health can be used to improve everything we do – within Averitas and at our Innovation Hub.

Overall, this interconnected set-up, built around our three pillars, will enable us to provide patients with comprehensive and life-changing medicines for managing pain. There is a lot for patients in the US to be excited about. And we are excited too.



## 5.3 Initiatives and grants

Grünenthal has launched a number of initiatives and grants to support healthcare professionals and patients in managing pain.

### Change Pain

Change Pain is an initiative endorsed by the European Pain Federation (EFIC) and Grünenthal. Its objective is to raise awareness on unmet needs in the management of pain and support education on pain aimed at improving patients' outcomes. Since the initiative was launched in 12 European countries in 2009, a great number of tools have been developed to support better diagnosis of pain, and more than 65,000 healthcare professionals have been involved in educational activities, either by completing web-based learning modules or attending workshops across Europe.

In 2018 and 2019, we organised a CHANGE PAIN Steering Committee meeting. This brought together representatives from the Latin American Federation of Associations for the Study of Pain (FEDELAT), EFIC, the International Association for the Study of Pain (IASP), the European Federation of National Associations of Orthopaedics and Traumatology (EFORT) and a group of key international external experts specialised in the management of acute and chronic pain with the objective to explore tangible ways of increasing the impact of the CHANGE PAIN initiative on patients' outcomes, as well as to discuss future collaborations centred around patients' unmet needs.

In October 2019, more than 100 delegates attended a Change Pain Masterclass. The masterclass was also live-streamed, and the online attendance exceeded the expected 300 connections – with more than 500 online participants. The Change Pain Masterclass, the first event of its kind for Grünenthal, consisted of three keynote presentations, 12 plenary sessions and 21 workshops. A Change Pain Masterclass for Latin America was held in Mexico in November 2019, based on the Change Pain Masterclass curriculum, presentations and materials. 'Meeting in a box' content based on the original Change Pain Masterclass will enable Grünenthal affiliates to organise their own educational events in 2020 and beyond in order to raise awareness about unmet needs in the management of pain.

[www.change-pain](http://www.change-pain)

### My pain feels like...

Many patients have a difficult time describing their pain in a way that allows doctors to identify the type of pain and optimally understand the impact on their daily lives. As a result, patients endure a drawn out 'trial and error' treatment approach that can last months or even years.

The main goal of 'My pain feels like...' is to improve the communication between patients and doctors. The focus is on nerve pain (also called neuropathic pain), which affects millions of people worldwide. One part of the initiative is the 'My pain questionnaire', which supports patients in reflecting their pain symptoms, describing them more precisely, and preparing for doctors' appointments. Another component is the so called 'pain box', a psychophysical experiment in which people can experience symptoms of localised neuropathic pain. The 'pain box' was developed at the Montescano Pain School in Italy to teach doctors how localised neuropathic pain feels, and improve empathy and understanding for patients.

[www.mypainfeelslike.com](http://www.mypainfeelslike.com)

### EFIC-Grünenthal Grant

These biennial grants are provided by Grünenthal and the EFIC and total € 200,000. These grants support young scientists early in their career in carrying out innovative clinical pain research in any member country of EFIC.

Individual research grants are worth up to € 40,000 per project for a duration of up to two years. Research grants are intended for clinical and human experimental pain research, including innovative educational initiatives aimed at improving diagnosis and treatment of pain. The decision on awarding grants is made independently from Grünenthal by a working group for grants and prizes for the EFIC.

In 2018, The EFIC-Grünenthal Grant received 59 applications from 16 countries – which promises to deliver interesting winning projects that benefit pain patients over the long term. The winners were announced in May 2019.

[www.e-g-g.info](http://www.e-g-g.info)

### Brain, Mind and Pain (BMP) Grant

The Brain, Mind, and Pain Patient-Centred Innovation Grant was initiated by the Pain Alliance Europe in 2017 and is supported by Grünenthal. Its main aim is to encourage patient-centred innovation that leads to improvements in the life conditions of pain patients.

The second edition of the 2019-2020 BMP Grant has the theme 'STOP Stigma! Reduce stigma to improve quality of life for brain, mind, and pain patients'. The application of proposals ended on 31 December 2019.

The projects will be evaluated by an independent jury and the announcement of the winners will be made public on 24 June 2020. More information at:

[www.pae-eu.eu](http://www.pae-eu.eu)

## 5.4 Global brands

Brand name, examples	Active ingredient/ Technology	Indication range <sup>1</sup> , Please note that the below indications are EU only. Indications and formulations may vary from country to country	Sales 2019 <sup>2</sup> in € m	Brand name, examples	Active ingredient/ Technology	Indication range, Please note that the below indications are EU only. Indications and formulations may vary from country to country	Sales 2019 in € m
<b>Palexia™</b>	Tapentadol	<b>Film-coated IR tablet:</b> Relief of moderate to severe acute pain in adults which can be adequately managed only with opioid analgesics  <b>Oral solution:</b> <b>OS 4 mg:</b> Relief of moderate to severe acute pain in children <sup>4</sup> from 2 years of age and in adults, which can be adequately managed only with opioid analgesics <b>OS 20 mg:</b> Relief of moderate to severe acute pain in children <sup>4</sup> from 2 years of age with a body weight of more than 16 kg and in adults, which can be adequately managed only with opioid analgesics  <b>Prolonged-release tablet:</b> Management of severe chronic pain in adults which can be adequately managed only with opioid analgesics	<b>284.6</b>  Partner sales of Nucynta in the US: <b>170.6</b>	<b>Zomig™</b>	Zolmitriptan	<b>Film-Coated Tablet and Orally Dissolving Tablet:</b> In adults aged 18 years and older for acute treatment of migraine headache with or without aura  <b>Nasal Spray:</b> In adults and adolescents aged 12 years and older for the acute treatment of migraine headache with or without aura and in adults for the treatment of cluster headache	<b>73.3</b>
<b>Nucynta™ (US)<sup>3</sup></b>				<b>Nexium™</b>	Esomeprazole	<b>Tablets:</b> Indicated in adolescents from the age of 12 years and in adults for: Gastroesophageal reflux disease (GERD) - treatment of erosive reflux esophagitis - long-term management of patients with healed esophagitis to prevent relapse - symptomatic treatment of GERD  Indicated in adults for: In combination with appropriate antibacterial therapeutic regimens for the eradication of <i>Helicobacter pylori</i> and: - healing of <i>Helicobacter pylori</i> associated duodenal ulcer and - prevention of relapse of peptic ulcers in patients with <i>Helicobacter pylori</i> -associated ulcers  Patients requiring continued NSAID therapy - Healing of gastric ulcers associated with NSAID therapy - Prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk	<b>146.1<sup>5</sup></b>
<b>Qutenza™</b>	Capsaicin	Treatment of peripheral neuropathic pain in adults either alone or in combination with other medicinal products for the treatment of pain	<b>28.2</b>				
<b>Vimovo™</b>	Fixed-dose combination of Esomeprazole and Naproxen	Symptomatic treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis, in patients who are at risk for developing non-steroidal anti-inflammatory drug (NSAID)-associated gastric and/or duodenal ulcers and where treatment with lower doses of naproxen or of other NSAIDs is not considered sufficient	<b>33.0<sup>5</sup></b>				
<b>Versatis™</b>	Lidocaine	Symptomatic relief of neuropathic pain associated with previous herpes zoster infection (post-herpetic neuralgia) in adults	<b>130.1</b>				

<sup>1</sup> Status: April 2020. Please note that indications and formulations may vary from country to country.  
Please refer to the respective local product information or Summary of Product Characteristics (SmPC).

<sup>2</sup> Including revenues from licenses.

<sup>3</sup> In the US the product is marketed under the Nucynta brand by a partner. Grünenthal is the licensor.

<sup>4</sup> In children restricted to hospital use where appropriate equipment to enable respiratory support is available and for a maximum treatment duration of 3 days.

<sup>5</sup> Acquisition closed end of November 2018.



Scan here to see the  
Grünenthal statement on the  
responsible use of opioids

## Global brands

Brand name, examples	Active ingredient/ Technology	Indication range, Please note that the below indications are EU only. Indications and formulations may vary from country to country	Sales 2019 in € m	Brand name, examples	Active ingredient/ Technology	Indication range, Please note that the below indications are EU only. Indications and formulations may vary from country to country	Sales 2019 in € m
<b>Nexium™</b>	Esomeprazole	<p><b>Intravenous:</b> Indicated in adults for: Gastric antisecretory treatment when the oral route is not possible, such as: - GERD in patients with esophagitis and/or severe symptoms of reflux - healing of gastric ulcers associated with NSAID therapy - prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk Prevention of rebleeding following therapeutic endoscopy for acute bleeding gastric or duodenal ulcers</p> <p>Indicated in children and adolescents aged 1–18 years for: Gastric antisecretory treatment when the oral route is not possible, such as: - GERD in patients with erosive reflux esophagitis and/or severe symptoms of reflux</p> <p><b>Granules for oral suspension:</b> Children 1–11 years old: GERD - treatment of endoscopically proven erosive reflux esophagitis - symptomatic treatment of GERD</p> <p>Children over 4 years of age: In combination with antibiotics in treatment of duodenal ulcer caused by <i>Helicobacter pylori</i></p> <p>Adults and adolescents from the age of 12 years: Reference is made to the Nexium gastro-resistant tablet SmPC</p> <p>Nexium oral suspension may also be used by patients having difficulty swallowing dispersed Nexium gastro-resistant tablets</p>	95.4	<b>Tramal™</b>	Tramadol	Treatment of moderate to severe pain	69.6
				<b>Zaldiar™</b>	Fixed-dose combination of Tramadol and Paracetamol	Symptomatic treatment of moderate to severe pain; use should be restricted to patients whose moderate to severe pain is considered to require a combination of tramadol and paracetamol	65.2
				<b>Transtec™</b>	Buprenorphine	Moderate to severe cancer pain and severe pain which does not respond to non-opioid analgesics. Not suitable for the treatment of acute pain	28.2
				<b>Intac™</b>	Proprietary hot melt extrusion technology platform	Technology to raise barriers to non-oral routes of abuse of active pharmaceutical ingredients (APIs) with abuse potential	
Top growth products		Sales 2018 in € m	Sales 2019 in € m	Growth			
<b>Nexium™</b>		12.6 <sup>1</sup>	146.1	>+100%			
<b>Vimovo™</b>		2.3 <sup>1</sup>	33.0	>+100%			
<b>Qutenza™</b>		23.3	28.2	+21%			
<b>Zomig™</b>		63.9	73.3	+15%			
<b>Palexia™</b>		269.7	284.6	+6%			

<sup>1</sup>Figures from Q4 2018

# 6

# Manufacturing and Global Operations

## Lean manufacturing principles and excellence along the entire value chain

Our Global Operations (GO) organisation provides the backbone for Grünenthal's ambitious plans for business growth. It creates value by applying lean principles and searching for continuous improvement opportunities along the entire value chain – from the raw materials we buy through to the logistics network we use to bring our medicines to patients around the world. Our global GO team supports our company's growth by minimising costs, increasing efficiency and ensuring the highest quality standards.

Grünenthal operates five specialised production sites in Germany, Switzerland, Italy, Ecuador and Chile. These sites manufacture our products and also support Grünenthal's external customers, who account for around 50 percent of our overall production capacity. Our employees are passionate about making our internal and external customers happy – and making sure patients around the world can rely on our leading solutions to improve their quality of life.

## Protecting patients against falsified pharmaceutical products

In February 2019, we began operating in line with the requirements of a new piece of EU legislation called the Falsified Medicines Directive (FMD). It aims to protect patients by preventing counterfeit medicines from being dispensed by pharmacies. The changes related to the FMD are widely viewed as one of the largest transformations in the history of our industry. Grünenthal was one of the first 20 companies to receive certification in line with this new legislation, which demonstrates our dedication to ensuring patients' safety.

We are now implementing our FMD-compliant approach across our sites worldwide to protect people around the globe from falsified pharmaceutical products. Here are some examples of our achievements:

- We have processed more than 63 million serial numbers.
- We have successfully connected 31 European countries via our EU Hub connection, as well as 11 customers for our Contract Manufacturing Business and 14 suppliers.
- Several pharmacies have reported that our efforts have been successful, and we are continuing to work with authorities and system vendors to further improve serialisation. Through a well-implemented monitoring process, we have been able to ensure that up to 90 percent of all technical and process-based errors have been reduced from February 2019 to today.

Moving forward, we are now preparing for changing requirements outside of the EU. Approaches around the world are not always comparable to the European FMD. For example, some countries request end-to-end verification, in which goods are not tracked between the Marketing Authorisation Holder and the pharmacy, while others follow a track-and-trace approach where every movement is reported. We are currently preparing a solution for Russia and countries in the Middle East and North Africa, as well as for Brazil. Our US business operates fully in line with the FDA regulatory requirements for serialisation, track and trace.

## Expanding our Contract Manufacturing Business

Our Contract Manufacturing Business, Grünenthal PRO, offered services to 45 active pharmaceutical ingredient (API) customers and 25 finished product customers in 2019. Grünenthal's sites that are involved in this business are fully integrated from API production through to finished products. They provide a strong service portfolio including controlled drugs handling, regulatory services, production process design, export to 100 countries worldwide and special technologies such as hormones, hot melt extrusion or biopharma packaging. Together with all relevant services across our end-to-end supply chain, we work to make sure our customers are satisfied in every way.

We took steps to further expand Grünenthal's Contract Manufacturing Business in 2019. These include:

- Our site in Quito, Ecuador, achieved re-certification in line with European standards for Good Manufacturing Practice (GMP) for the fourth time. The certification covers solids, semi-solids and liquids. It puts us in a unique selling position as we can export to any country in Latin America and also supply to European countries in line with the respective quality expectations.
- Our site near Milan, Italy, has become the second site in Grünenthal's global manufacturing network to be successfully inspected by the US FDA – following our site in Switzerland. The inspection focused on the biopharma assembly and packaging operations of our site.
- Grünenthal's production site for hormones in Santiago, Chile, is now certified by the Agência Nacional de Vigilância Sanitária (ANVISA), the Brazilian Health Regulatory Authority. This is a major milestone in our company's ambitious plans for Latin America. The site acts as Grünenthal's centre of excellence for producing women's health products and contraceptives, including pills and gels.

## Investing in Latin America to consolidate world-class operations in the region

In 2019, Grünenthal's Supervisory Board gave the green light for an investment of more than € 100 million over five years in a programme that aims to ensure world-class infrastructure and process technologies at our production site for solids in Santiago, Chile. At the same time, we also reinforced our strategy of establishing our site in Quito, Ecuador, as a regional manufacturing and distribution centre for liquids and semi-solids. We have thus started to transfer all liquids and semi-solids dosage forms from our site in Santiago to Quito. We also significantly invest in the robustness of our products, to guarantee patient supply in an ever increasing and demanding regulatory landscape.

In the next few years, we aim to secure Grünenthal's strength in Latin America for the long term. We will do this by lifting our manufacturing operations to world-class level, improving our ability to enter new attractive markets in countries like Brazil and Mexico, and by maximising our Contract Manufacturing Business. In this way, we are demonstrating our strong commitment to ensuring the same approach to product quality, regulatory compliance and product development standards across all of our sites worldwide.

## Master Data Management

Our Master Data Management project was launched in 2019 to provide a strong pulse of high-quality data that keeps our company moving forward around the world. It will create a single source of truth that gives everybody in Grünenthal access to important information in a way that is transparent and streamlined across functions and regions. At the end of last year, the project team achieved a Material Master Data Accuracy rate of 94 percent, which represents a substantial improvement within just 12 months. This is the first step on an ongoing journey that aims to ensure Grünenthal's success in the digital age by providing a solid foundation of consistent data.



Our Global Operations team plays a key role in driving Grünenthal towards its ambitious growth plans – and making sure patients around the world can fully rely on our life-changing medicines.

**Victor Barbosa**  
Head Global Operations



# 7

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# Responsibility

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Our company culture is based on a strong commitment to upholding the highest ethical standards in everything we do.

**Sebastian Köhler**  
General Counsel



## 7.1 Code of Conduct

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### Building trust through high ethical standards

At Grünenthal, we share the responsibility to act with integrity and conduct all of our research and business activities in compliance with applicable laws and regulations. Building trust through high ethical standards gives confidence to all of our stakeholders, including patients, customers, employees, partners, suppliers, investors and the communities we serve. Our compliance system provides a clear framework for our decisions and actions. It is built around our Code of Conduct, which we relaunched in 2018.

Our compliance framework covers our interactions with healthcare providers, patients, business partners, data privacy matters, competition and antitrust rules as well as financial compliance. Grünenthal's compliance organisation is part of the Legal, Compliance, Risk and Audit team, which is led by our General Counsel.

### You see it, you say it

Building a culture of compliance also means challenging any unethical, dishonest or otherwise unacceptable behaviour and speaking up when noticing anything that does not meet our high ethical standards. That is why everyone – employees and external stakeholders alike – is asked to promptly report any compliance problems, concerns or misconduct. Concerns or questions can be reported personally or anonymously via our Ethics Helpline, which offers full confidentiality.

[www.ethicshelpline.grunenthal.com](http://www.ethicshelpline.grunenthal.com)

## 7.2 Our commitment to the responsible use of opioids

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It is widely accepted that access to appropriate and effective pain treatment is a basic human right, as stated in the 2011 Declaration of Montreal from the International Association for the Study of Pain (IASP). In line with this, we believe opioids should be one of the treatment options available because these medicines can play an important role in managing severe pain.

However, opioids may also carry a risk of inappropriate use including misuse, abuse, addiction and diversion. That is why it is essential for physicians to carefully consider the relative benefits and risks of all available treatment options before prescribing opioids. At Grünenthal, we believe physicians prescribing opioids should adopt an individual approach to opioid therapy, including agreeing a clear and realistic therapeutic objective with the patient.

Grünenthal is committed to contributing to solving the challenges related to opioids worldwide. In particular, the opioid crisis in the US requires urgent attention from policymakers and pharmaceutical companies. We are actively engaged in a range of measures and initiatives that aim to relieve the tragic impact that opioid use disorder has on individuals, families and society. In 2019, for example, we introduced a mandatory statement that must be included in all informative, educational and promotional materials that mention opioids. This statement reinforces our long-standing principle that all communications from our company describe the benefits and risks of our products in a factual, accurate, precise and balanced way. The statement was rolled out across our company through an educational campaign that emphasised our responsibilities related to these medicines and aimed to foster a shared ethical mindset

that goes far beyond compliance with laws and regulations.

We will continue to further enhance our efforts to minimise the risk of inappropriate use of prescription opioids, while striving to ensure that patients with a clear need are not denied access to effective and appropriate treatments. Above all, we will continue to work tirelessly to bring innovative solutions to the market that bring us closer to our vision of a world free of pain for patients.

[www.grunenthal.com/about-us/our\\_positions](http://www.grunenthal.com/about-us/our_positions)

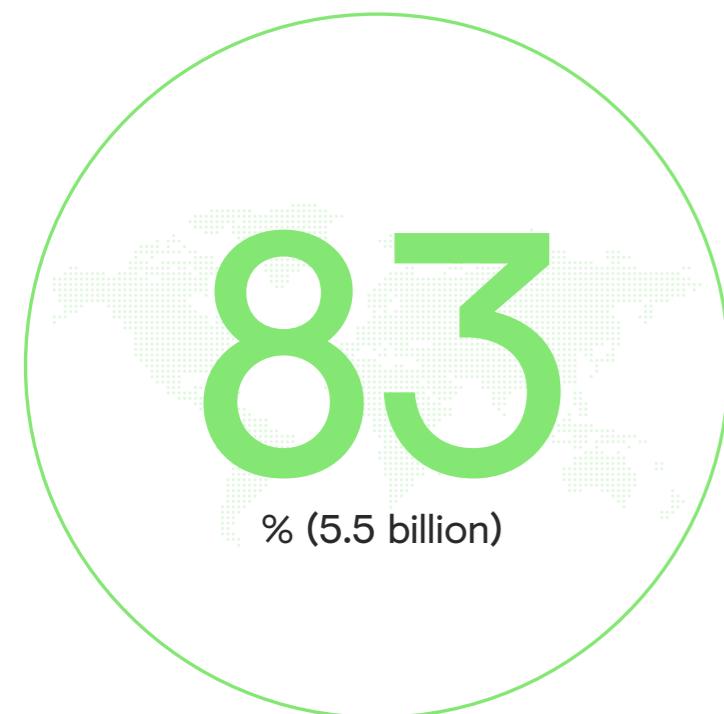
# The Grünenthal charter on the responsible medical use of opioids in pain

Pain represents a huge burden in society:

# 1.5 billion

people suffer from chronic pain around the world<sup>1</sup>

Access to adequate pain medicines is a key element in the treatment of pain patients – it is widely accepted as a basic human right<sup>2</sup> and remains a serious public health issue, especially in low-income countries<sup>3</sup>



The World Health Organisation (WHO) estimates that 5.5 billion people (83 percent of the world's population) live in countries with low to non-existent access to controlled medicines and have inadequate access to treatment for moderate to severe pain<sup>4</sup>

A wide spectrum of therapies are available to help manage pain, depending on its severity. One option for moderate to severe pain is the use of opioids.

Opioids can carry a risk of inappropriate use<sup>5</sup>:



It is essential that physicians prescribe opioids after careful consideration of the benefits and risks of all available treatment options.



At Grünenthal, we believe physicians prescribing opioids should adopt an individual approach to opioid therapy, including agreeing a clear and realistic therapeutic objective with the patient.

We share the broad consensus in the pain community that:



Grünenthal will continue its efforts to minimise the risk of inappropriate and illegitimate use of prescription opioids, while striving to ensure that patients with a clear need are not denied access to effective and appropriate treatments.

We are working to bring innovative solutions to relieve pain and to contribute to redefining the future of pain management through our own research, as well as by drawing on external innovation, collaborations and networks. In our research and development, we are also investigating non-opioid modes of action.

Our commitments in this are:

- We recognise the unfulfilled medical needs of pain patients, the challenges faced by healthcare professionals and the increasing pressure on social and healthcare systems caused by the inappropriate and illegitimate use of prescription opioids
- We put patient needs at the core of the development and therapeutic use of our medicines, demonstrating our belief that access to pain management is a fundamental human right
- We are committed to developing novel analgesics with better safety profiles, including opioids and non-opioids
- We believe that opioids remain an option for appropriate pain patients, and strive to reduce the risks of non-medical inappropriate use of our products to the greatest degree possible
- We recognise the importance of working with the medical community to ensure compliance to policies and guidelines regulating the correct medical use of opioids in pain treatment
- We are committed to developing and distributing our products in line with the highest ethical and scientific standards

<sup>1</sup> Global Industry Analysts, Inc. Global Pain Management Market to Reach US\$60 Billion by 2015, According to a New Report by Global Industry Analysts, Inc. 2011. Available at: <http://www.prweb.com/pdfdownload/8052240.pdf>. Accessed: April 2020.

<sup>2</sup> International Association for the Study of Pain. Declaration of Montreal, 2010. Available at: <https://www.iasp-pain.org/DeclarationofMontreal>. Accessed: April 2020.

<sup>3</sup> Bhadelia A et al. Solving the global crisis in access to pain relief: lessons from country actions. Am J Public Health. 2019;109(1):58–60.

<sup>4</sup> World Health Organisation. Controlled substances and WHO: Access to Analgesics and to Other Controlled Medications. Available at: [https://www.who.int/medicines/access/controlled-substances/control\\_substances\\_who/en/](https://www.who.int/medicines/access/controlled-substances/control_substances_who/en/). Accessed: April 2020.

<sup>5</sup> Brennan F et al. Access to pain management as a human right. Am J Public Health. 2019;109(1):61–65.

For more information on the Grünenthal charter on the responsible medical use of opioids in pain:

[www.grunenthal.com/en/about-us/responsibility/responsible-use-of-opioids](http://www.grunenthal.com/en/about-us/responsibility/responsible-use-of-opioids)



## 7.3 Environment, health and safety

### Driving progress towards a sustainable future

The world's limited resources are becoming increasingly depleted and the environmental footprint of humankind is already more than the planet can sustain. That is why we are committed to driving progress towards environmental responsibility and sustainable development.

Our company's efforts to promote sustainable development include defining concrete goals that are relevant for our operations and introducing management systems in line with leading international standards for environment, health and safety. We collect and analyse data from our production sites and use it to continuously improve efficiency and occupational safety, while also reducing energy consumption and minimising waste.

In February 2020, the company announced that electric and hybrid engines will be included in the fleet of Grünenthal's cars for managers at its site in Aachen, Germany. The decision is part of the Grünenthal's ongoing commitment to promoting sustainability by reducing the environmental footprint of its operations.

### Occupational safety

In 2018, there were 57 work-related accidents across Grünenthal, which was our lowest ever figure. In 2019, the number of accidents rose to 63, which is an increase of 11 percent.

Early in 2019, we decided to take measures to continue our journey towards zero accidents in the workplace. We have intensified our analysis of accidents at work and are also analysing the reasons for near-accidents. In this way, we aim to take appropriate measures to prevent these situations from occurring again. Every occupational accident is discussed with the entire Global Manufacturing Leadership Team, and findings are applied at all of our production sites worldwide.

As one of our main initiatives, we started implementing a Behavioural Safety Observation approach across all of our production sites. Every manufacturing employee spends 20 minutes each month observing the safety behaviour of her or his work colleagues in a chosen area and providing constructive feedback. In addition to this initiative, all of our manufacturing sites introduced specific local activities to strengthen safety awareness. Of course, safety is a permanent topic on meeting agendas at all of our sites.

In this way, we are striving to improve safety awareness among our entire workforce – and to avoid unsafe situations and move closer to achieving our goal of zero accidents at work. We are convinced that these measures are having a positive impact and will actively help to protect our employees.

## 7.4 Social responsibility

Caring for the world around us is a key part of our company culture. We have a long track record of supporting projects that have a positive impact on people and communities, ranging from palliative care and charity activities through to environmental protection. We actively engage in projects that increase quality of life for people around the globe. Here are just a few examples.

### The Grünenthal Foundation for Thalidomide-affected People

The Grünenthal Foundation for Thalidomide-affected People runs support projects for people affected by a thalidomide-containing product from Grünenthal or its licensees. It aims to permanently improve their lives in a pragmatic way by providing specific, needs-based support. Since the Foundation was established, it has provided support for more than 2,000 individual cases – ranging from barrier-free bathrooms and kitchens through to specially adapted wheelchairs and cars, voice-controlled software for the remote use of computers and other devices, as well as investments in adapted hospital rooms.

One of the projects involved supporting home improvements that give disabled people greater freedom in their day-to-day lives. Contributions from the foundation helped remodel kitchens, for example. The new facilities feature state-of-the-art technologies that make a range of everyday tasks easier – from sensors that activate the hot and cold-water taps, through to remote controls for appliances and innovative designs that make cupboards and drawers easier to access.

The Grünenthal Foundation is open to all people suffering from Grünenthal's thalidomide products or its licensees who are acknowledged by an official institution that applies similar eligibility criteria as the Contergan Foundation, a German federal foundation under public law, or the UK Thalidomide Trust.

### From the stars to the stables

During 2019, Grünenthal Italy has contributed to 'Dalle stelle alle stalle: un mondo di cavalli, natura e bambini'.

This initiative, literally 'From the stars to the stables: a world of horses, nature and children', was launched by the 'Amici del Centro Vittorio di Capua' association and provides support for the Centre for Equestrian Rehabilitation at the ASST Grande Metropolitan Hospital Niguarda in Milan.

This facility offers a programme of initiatives that aim to guarantee continuity of care for patients after they have been discharged, in order to offer a modern rehabilitation approach that is as smooth and effective as possible. It also promotes and raises awareness about equestrian rehabilitation practices in Italy and around the world.

Sessions at the Centre for Equestrian Rehabilitation typically last around 90 minutes and include riding or working with a horse, as well as work on the ground. The support from Grünenthal Italy has enabled the centre to develop its activities, treating more than 100 patients in a year.



The Grünenthal Foundation organises activities for children in rural areas in Ecuador



Grünenthal employees contributing to repairs at care centres in Colombia

## Supporting communities in rural Ecuador

Our team in Ecuador organises activities and provides donations for people in rural areas, with a strong focus on meeting children's needs. For example, our employees donated school backpacks and winter kits to children aged 5 to 16 in La Condencia last year. Many children in this community live in houses made of cane and have to travel for one hour to reach school. The winter kits included a waterproof poncho, rubber boots and umbrella to help children make this important journey – even in the winter months.

On top of this, our team also supported dental examinations and oral care sessions for people living in Cayambe and Toacaso, and donated special games that promote children's physical and mental development.

These activities are part of our long-standing commitment to supporting the development of communities in rural Ecuador. The Grünenthal Foundation has been carrying out social projects in this country for many years, in close collaboration with our employees. Alongside the special initiatives in 2019, our team also organises a full range of activities aiming to encourage shared moments of recreation with children and elderly people in vulnerable situations across Ecuador.

## A donation with a difference

In 2019, our team in Colombia visited four care centres that are specialised in providing services for elderly people with limited economic resources. Our employees joined forces with the staff at these centres by putting on overalls and contributing to repairs, painting and maintenance projects that were in need of additional support.

The Grünenthal team spent time getting to know the residents and staff members, while also delivering donations and getting involved in a few games of bingo. Our employees benefited from this opportunity to share their time, happiness and positive energy – in a way that goes beyond physical donations and makes a meaningful emotional contribution to the lives of elderly care patients.

## Making hospital more comfortable for young patients

Grünenthal employees in Spain took part in a special team-building activity in 2019 to sharpen their focus on our company value, 'We are patient-centric'. This is one of five values that provide clarity about how we want to work together to achieve successful outcomes for our company and for patients.

The team organised a quiz where employees competed against each other to win points that were later transformed into donations to the Hospital Universitario La Paz in Madrid and the Hospital de la Santa Creu i Sant Pau in Barcelona. These hospitals were selected with support from the Spanish Society of Paediatric Palliative Care.

The activity aimed to support our teams in driving progress towards our vision of a world free of pain. As a result of this activity, Grünenthal Spain has contributed to making young patients a little more comfortable during hospital stays.

# 8

## Financials

Transforming our business to facilitate future growth

2019 was a record year for Grünenthal in terms of financial performance. Sales increased by 9 percent and our adjusted EBITDA<sup>1</sup> grew by about 60 percent to reach a total of more than € 340 million. Our increased revenue was mainly driven by the full-year impact of Nexium™ and Vimovo™, which were acquired late in 2018 as part of the biggest investment in Grünenthal's history. The continuous organic growth of Palexia™ also made a strong contribution, and this was mainly achieved in Europe and via our partner business in Australia. External growth led to a significant increase in sales in Europe and in our global partner business (Rest of the World).

Our strong operating business performance was supported by our continuous cost management. At the same time, we continued our investment in growth activities like establishing our own commercial organisation in the US and building up Fern Health. These positive developments were made possible thanks to the extraordinary commitment of our employees, even in the face of major headwinds such as generic competition and an increasingly challenging reimbursement environment.

<sup>1</sup> Adjusted EBITDA, short for Earnings Before Interest, Taxes, Depreciation and Amortisation before special items, is a key driver of free cash flow and has been defined as our most important performance indicator.



2019 was our best ever year in terms of financial performance, and we are in a strong position to build on this success in the future.

**Fabian Raschke**  
Chief Financial Officer

It is part of the nature of R&D activities that some products do not reach market launch. In 2019, for example, we decided not to proceed with development projects including Neosaxitoxin and Neridronate. In 2019, we transformed our R&D organisation, which led to some one-time restructuring costs. Impairments and restructuring costs had a negative impact on our Income Before Taxes (IBT). Despite these one-time charges, we were able to reduce our net debt faster than planned. This creates new financial headroom to continue our strategy.

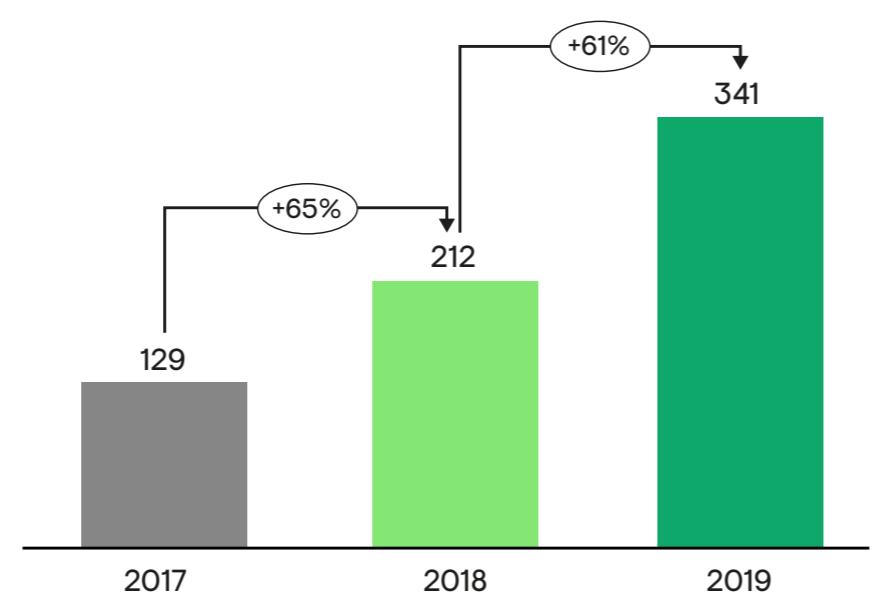
### Profit and loss statement<sup>1</sup>

in € million	Actual 2018	Actual 2019
<b>Sales<sup>2</sup></b>	<b>1,280</b>	<b>1,394</b>
Cost of Goods Sold (COGS)	-416	-419
<b>Gross profit<sup>3</sup></b>	<b>864</b>	<b>975</b>
Marketing, Sales & Medical costs	-431	-439
Research & Development costs	-192	-184
Other costs	-118	-290
Depreciation Fixed Assets <sup>4</sup>	98	207
<b>EBITDA</b>	<b>221</b>	<b>270</b>
<b>Adj. EBITDA</b>	<b>212</b>	<b>341</b>
<b>IBT</b>	<b>102</b>	<b>27</b>

### Our strategy is achieving clear success

The successful implementation of our strategy is making a strong and valuable contribution to our company's performance, while opening up new opportunities for us.

**Adjusted EBITDA 2017-2019 (in € million)**



### Outlook for 2020

Before the Covid-19 outbreak, we expected a largely unchanged market environment in 2020.

Given the nature of our portfolio, we anticipated a slight decrease in revenue and adjusted EBITDA on a like-for-like basis. So far, the financial impact of Covid-19 has been very limited for Grünenthal, but this impact may become more significant depending on the duration of the crisis and the way it develops.<sup>5</sup>

Despite these challenges, we aim to continue to explore opportunities to tap into further growth for our business through acquisitions that directly boost our adjusted EBITDA and cash flow.

## 8.1 Business development and licensing

### Shaping our future by making deals

We believe collaboration is the key to developing life-changing medicines for patients with unmet medical needs. That is why we actively seek committed partnerships with like-minded organisations who share our passion for creating innovative treatments. Building this strong network opens up opportunities for experts from across disciplines to exchange knowledge and drive progress towards our company's vision of a world free of pain.

Grünenthal is known for its tireless commitment to innovation in pain, and we have worked over the last 50 years to build this reputation as a leader in pain research and management. Our experts have been using their deep understanding and experience to find breakthrough solutions for patients for many decades. However, we never stop searching for new R&D collaborations in pain and have the potential to make a real difference to people's lives.

Of course, our partnerships also extend beyond R&D. As a privately-owned, mid-sized pharmaceutical company with strong R&D and commercial capabilities, we are a natural partner for businesses looking to bring projects successfully to market. In particular, partners value our high-quality products and state-of-the-art production and product supply. For this reason, we also engage in trustful relationships including sales partnerships, licensing agreements and acquisitions for development projects as well as marketed products. We are especially interested in out-license agreements in countries where we have not yet established a presence through our own subsidiaries.

Inorganic growth is a key pillar of our strategy. We have invested € 1.4 billion in build-muscle deals such as the acquisitions of Nexium™, Vimovo™ and Zomig™. Furthermore, Grünenthal remains focused on acquiring products or portfolios that immediately strengthen our adjusted EBITDA.



**2019 was a successful year for Grünenthal, and we are excited to continue our company's long track record of changing patients' lives for the better.**

**Gabriel Baertschi**  
Chief Executive Officer



<sup>1</sup> Management view.

<sup>2</sup> Sales is Grünenthal's income from its commercial effort to market pharmaceuticals either directly to wholesalers, pharmacies and hospitals or in cooperation with a partner.

<sup>3</sup> Gross profit reveals how much money a company earns taking into consideration the costs that it incurs for producing its products and/or services.

<sup>4</sup> Depreciation is part of COGS, Marketing, Sales and Medical costs, R&D costs.

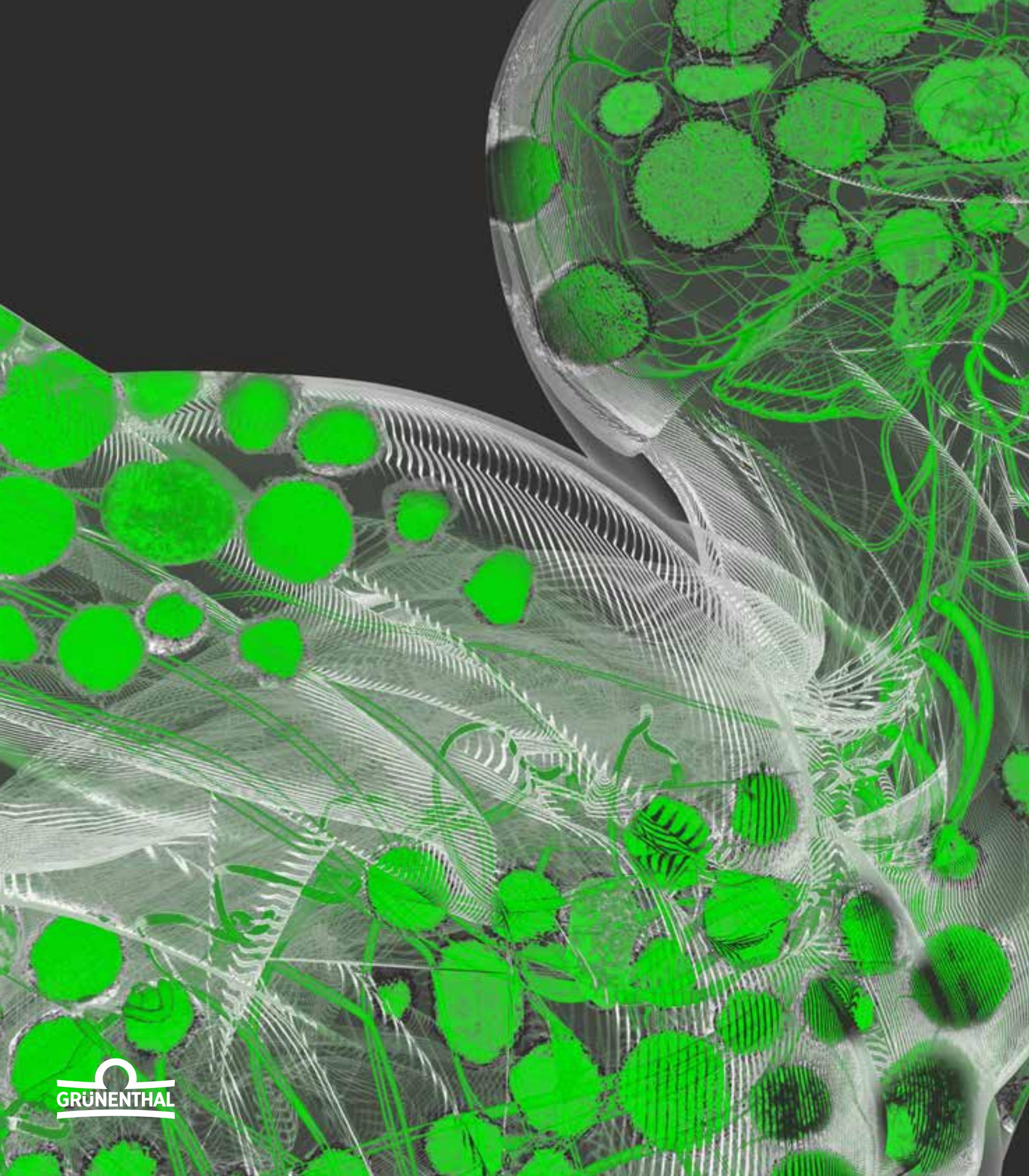
<sup>5</sup> Status April 2020



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