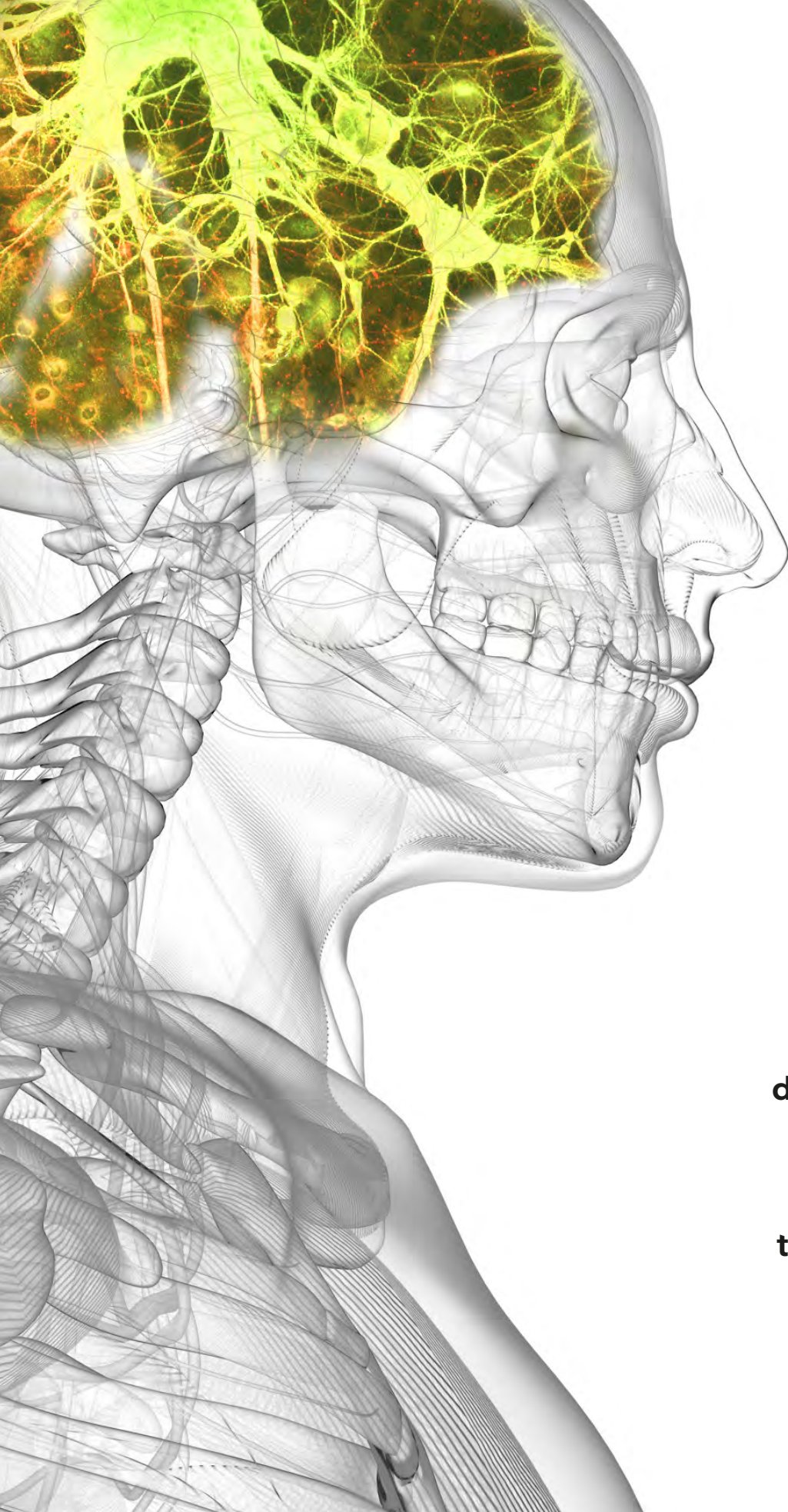


# GRÜNENTHAL REPORT 2022/2023





# **CORPORATE PROFILE**

**Grünenthal is a global leader in pain management and related diseases. We have a long track record of bringing innovative treatments to patients worldwide. As a fully integrated pharmaceutical company we cover the entire value chain – from drug research and development to commercialisation of portfolios with growth products and established brands. We operate in accordance with the highest ethical and regulatory standards, and we focus our efforts on our vision of a World Free of Pain.**

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# LETTER FROM THE CEO

Over the last few years, we have transformed Grünenthal, diversified our portfolio and strengthened our pipeline. Grünenthal is now in a prime position to continue our growth strategy and move closer to our vision of a World Free of Pain.

## Dear Friends and Partners,

Over the past few years, Grünenthal has fundamentally transformed its strategy and culture. We have created solid growth, diversified our portfolio and built an innovation pipeline to provide patients with better treatments to manage their pain. And we have evolved our culture to make Grünenthal more attractive for talents and a great place to work.

2022 was yet another fantastic year for Grünenthal. The company exceeded its financial and non-financial targets. Our revenue reached €1.7 billion, an increase of 13 percent compared to 2021. The adjusted EBITDA reached €438 million, an increase of 18 percent over 2021, and has more than tripled since 2017. These record results were driven by increased demand for pain treatments and excellent sales performance across regions. Its financial success positions Grünenthal well to further invest in advancing the R&D pipeline, continuing the M&A strategy and growing the business in the United States.

## Strategy for growth

Grünenthal's exceptional performance in 2022 is a testament to our people and reflects the demand for better pain treatments. I am pleased with our progress towards our vision of a World Free of Pain.

Key brands such as Qutenza™, Palexia™, Vimovo™, and Zomig™ performed well and grew faster than the market. Especially Qutenza™, a topical non-opioid treatment for various peripheral neuropathic pain conditions, saw a surge in demand, particularly in the U.S., where the product is indicated for treating post-herpetic neuralgia and pain related to diabetic neuropathy of the feet. The neuropathic pain market is significant, with an

estimated size of \$4.5 billion in the United States, which is the largest global neuropathic pain market.<sup>1</sup>

2022 was another very successful year for Grünenthal in terms of acquisitions. In November 2022, Grünenthal acquired Nebido™, a leading brand for testosterone replacement therapy, from Bayer for ~€495 million. The brand immediately contributed to Grünenthal's revenue and profit as of November 2022. Another milestone in Grünenthal's M&A strategy was the announcement to enter into a joint venture agreement with Kyowa Kirin International. The joint venture includes 13 established brands with revenues primarily from pain management products.

## Innovation pipeline

A key priority is the development of resiniferatoxin (RTX). This investigational medicine is being developed for treating pain in patients with knee osteoarthritis, and entered Phase III of clinical development in August 2022. A readout of the data is expected in the second half of 2024. The Phase III programme aims to enable market authorisation in the E.U., U.S. and Japan by 2025/2026. The global osteoarthritis market has significant potential and is expected to grow to ~€11 billion in 2025. Grünenthal's second Phase III programme investigates the use of Qutenza™ in patients with post-surgical neuropathic pain (PSNP) to support an extension of the U.S. label.

In Phase I, trials are ongoing for a Nociceptin/Orphanin FQ peptide receptor (NOP) agonist. This compound is being developed to provide a non-opioid therapy option with a strong analgesic effect without the side effects commonly associated with opioids. Grünenthal is also further developing its Glucocorticoid Receptor Modulator (GRM) in Phase I. The oral



investigational medicine aims to provide a therapy option with broad anti-inflammatory efficacy. Our new GRM compound has the potential to combine the efficacy of traditional glucocorticoids like prednisolone with a significantly improved safety profile allowing for longer-term treatment, an unmet need in many indications.

### Culture and responsibility

Our Impact Initiatives for the Responsible Business programme reached their milestones last year. We made further progress with attracting and developing talents, and launched our Diversity & Engagement strategy. Following excellent employee engagement scores during the 2022 survey, Grünenthal now has 24 entities certified as a Great Place to Work®.

On behalf of the Executive Board Team, I invite you to join us in 2023 as we continue working on getting closer to our vision of a World Free of Pain.



**Gabriel Baertschi**  
Chief Executive Officer



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“ Grünenthal touches the lives of millions of patients every year. And we will continue seeking innovative pain treatments to change lives for the better.

**Gabriel Baertschi**  
Chief Executive Officer

# ABOUT US

We are proud to work for a World Free of Pain.









# BY THE NUMBERS

Pain, especially chronic pain, represents a substantial burden for people and society. Its alleviation remains a significant unmet medical need. Grünenthal is the leading pharmaceutical company focused on pain therapies and research.

**8** We are committed to transforming the future of pain management. As a family-owned company, we have been developing innovative medicines for more than 75 years. Over the past five decades, we have focused on developing, manufacturing and commercialising innovative products for the pain market. From research to distribution, we have capabilities across the entire value chain. We aim to strengthen our pain leadership by developing

highly innovative, non-opioid therapies. In partnership with leading science organisations, we strive to create more value for patients and healthcare systems. Conducting our business responsibly is at the core of our strategy and culture. Acquisitions of carefully selected established brands have been the key driver of our profitability and growth. This strategy helps secure our financial stability and enables us to reinvest in pain research.

**Leadership position in pain-related markets\***

#1

in Latin America\*\* and Europe\*\*\*

**Products sold in around**

100

countries

**Solid revenue base**

1.7

billion euro in 2022

**Focus on innovation**

200

priority patent applications filed in the last 10 years

**Strong and capable team**

4,400

employees worldwide

**Longstanding commitment**

75

years of developing innovative medicines for patients

**Production capacities**

5

manufacturing sites in Europe and Latin America

**International R&D network**

2

R&D sites – one R&D Unit in Aachen (Germany) and an Innovation Hub in Boston, (USA)

\* Including Anti-Calcitonin Gene-Related Peptides (CGRPs). Defined Pain Market incl.: Strong opioids, weak opioids (Codeine, Dextropropoxyphene, Dihydrocodeine, Hydrocodone, Tilidine, Tramadol), NSAIDs & plain Cox2 Inhibitors, oral solid Rx, Antimigraine Triptans, Lidocaine & Capsaicine Patches, Anti-epileptics & Anti-depressants with their respective share in Localized Neuropathic Pain acc. Rx information (Pregabalin, Gabapentin, Carbamazepin, Amitriptylin & Duloxetine)

Accumulated evaluation of countries where Grünenthal is present through its own sales force:

\*\* Brazil, Central America, Chile, Colombia, Ecuador, Dominican Republic, Mexico, Peru

\*\*\* Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, UK.

Source: Based on internal analysis by Grünenthal using data from the following source: IQVIA MIDAS® Quarterly Sales Retail+Hospital, Q4/ 2022, time period year 2022, fixed EUR, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved. Note: data does not account for parallel imports or recent acquisitions or joint ventures.

# OUR EXECUTIVE BOARD TEAM

## Gabriel Baertschi

*Chief Executive Officer*

Drawing on 20 years of experience in the pharmaceutical industry, Gabriel joined Grünenthal in 2016 as Chairman of the Corporate Executive Board and Chief Executive Officer. Under his leadership, Grünenthal has executed a diligent M&A strategy by closing successful acquisitions with a total expected deal value of more than €2 billion since 2017. The company has also transformed its business model, significantly developed its pipeline, and more than tripled its adjusted EBITDA and operating cash flow since 2017.

## Fabian Raschke

*Chief Financial Officer*

In his 15-year career, Fabian has a proven track record of success in projects ranging from completely modernising a company's Finance function to increasing efficiency, driving growth and taking advantage of the full range of financing models. Fabian joined Grünenthal in 2016 as Head Group Controlling, before assuming the role of Chief Financial Officer in 2019. He was pivotal in Grünenthal's move to the capital markets with the first bond placement in 2021. Fabian is also responsible for the realignment of the IT function, supporting our digital road map and substantially increasing our cyber defence capabilities.

## Jan Adams, MD

*Chief Scientific Officer*

Jan has more than 15 years of experience in healthcare and biopharmaceuticals, and took over the role of CSO in 2020. Under his leadership, Grünenthal has transformed its R&D strategy and operating model, significantly strengthening its pipeline of highly innovative non-opioid pain assets. Jan joined Grünenthal in July 2017 as Head of Corporate Strategy and Portfolio Management, and was instrumental in many transformational initiatives working at the interface between Strategy, Business Development, Research, Development and Commercial.

## Victor Barbosa

*Head Global Operations*

Since joining in 2006, Victor has worked across Grünenthal's supply chain and operations teams. With extensive experience in diverse markets, he has been instrumental in redefining the company's organisation for product supply. As Head of Global Operations (GO), Victor is ultimately accountable for Grünenthal's product quality, cost and service to patients and customers worldwide. He leads around 2,000 people in our GO unit, spanning the full value chain of product supply. He is also accountable for Grünenthal's Contract Manufacturing Business.

## Janneke van der Kamp

*Chief Commercial Officer*

On 1 March, 2023, Janneke joined Grünenthal as our new Chief Commercial Officer. She has broad experience in the pharmaceutical industry, including global leadership roles with a focus on product and portfolio strategy, and substantial experience in launching and growing brands across several disease areas. Her work at Grünenthal will aim to maximise our portfolio, prepare the launch of our pipeline assets, and drive growth from our key brands.

## Leen Hofkens

*Head Global Human Resources*

Since joining in 2018, Leen has been committed to driving a high-performance culture where diverse talents thrive in rich and varied roles, join forces and have a real impact on Grünenthal's success. Leen was instrumental in rolling out the company's Values & Behaviours, which guide our decision making and shape our culture, including our leadership capabilities. Leen also played a key role in strengthening Grünenthal's Performance & Development Management approach and employee engagement activities, as well as driving our diversity and engagement agenda forward.





**Sebastian Köhler**

*General Counsel*

Sebastian joined Grünenthal in 2018 to build and lead the General Counsel area comprising Legal, Responsibility, Compliance, Risk, Audit, Patents, Trademarks, Legal Operations and Corporate Affairs. In this role, he ensures that our business gets best-in-class in-house advice to support the sustainable implementation and evolution of our strategy. Sebastian brings over 10 years of expertise in executive roles and strategic legal consultancy.

**Quentin Le Masne de Chermont**

*Head Corporate Strategy and Portfolio Management*

Before joining Grünenthal in 2019, Quentin spent 8 years consulting companies in the healthcare sector on game-changing business strategies. His career began in research. He now drives our business goals at the intersection of Strategy, Commercial, R&D and Operations. Quentin has additional responsibility for deal assessment of established brand acquisitions.

*from left to right:*

*top row:  
Fabian Raschke,  
Quentin Le Masne de Chermont*

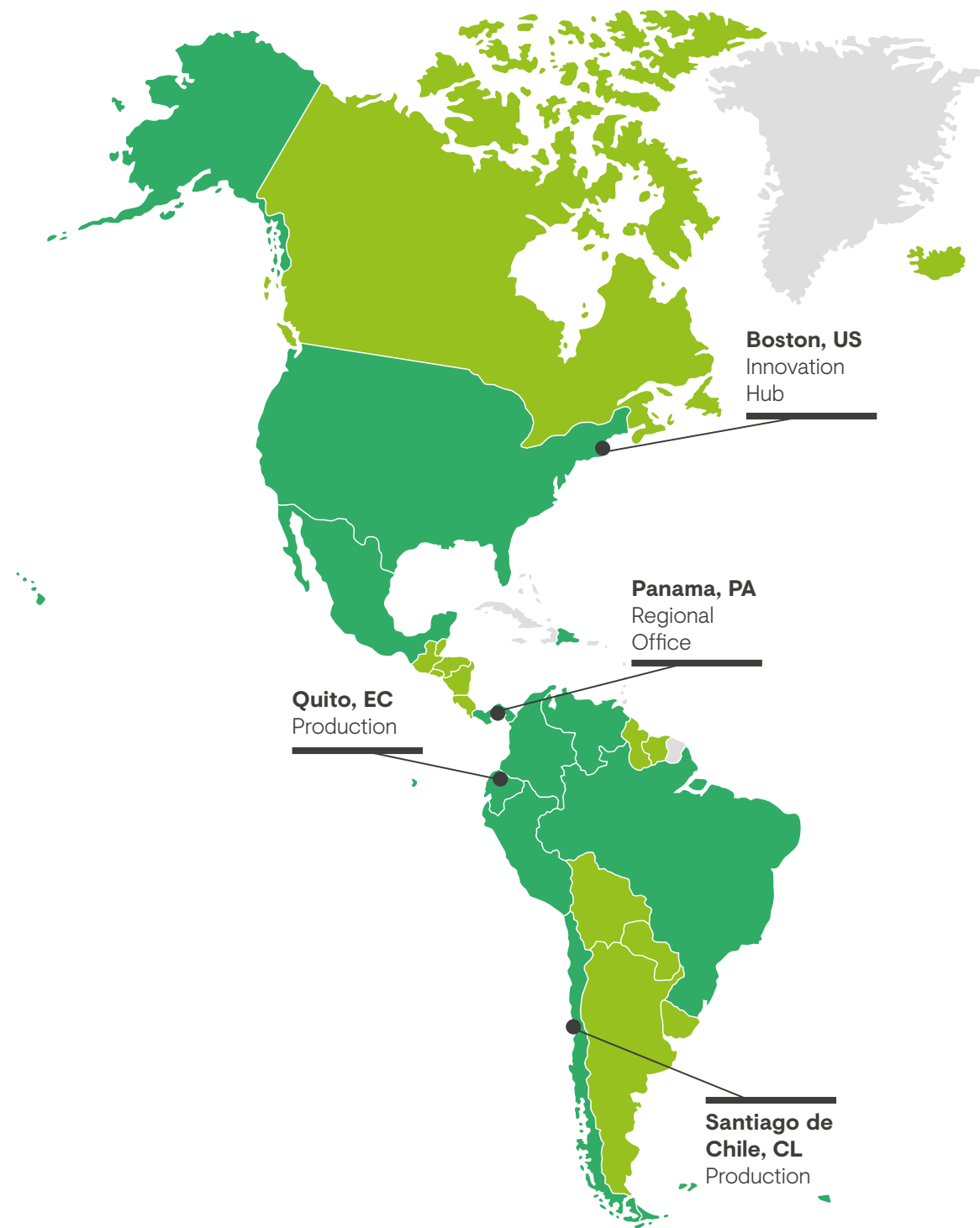
*middle row:  
Janneke van der Kamp,  
Sebastian Köhler, Victor Barbosa*

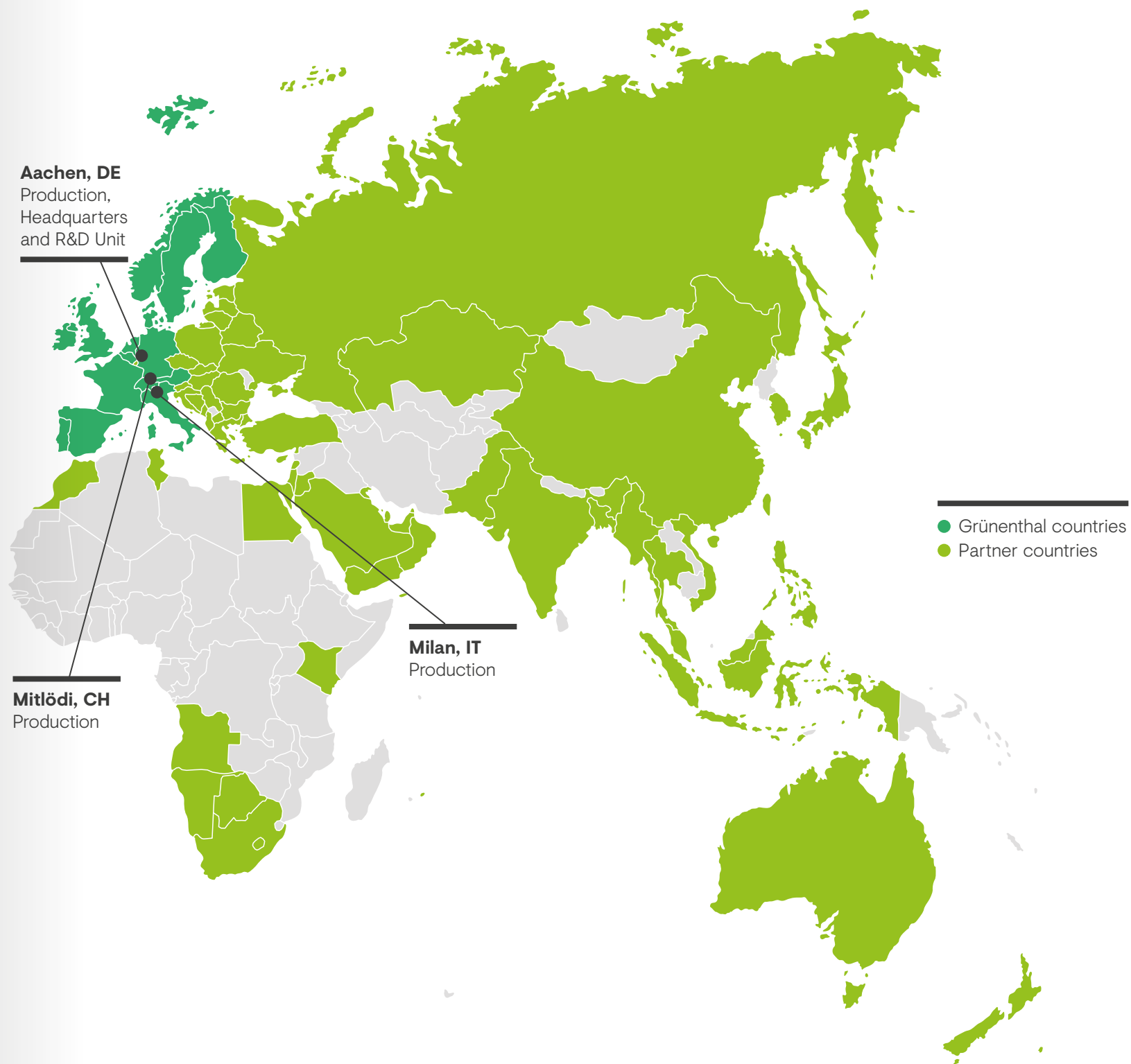
*bottom row:  
Gabriel Baertschi,  
Leen Hofkens, Jan Adams, MD*

# MARKET PRESENCE

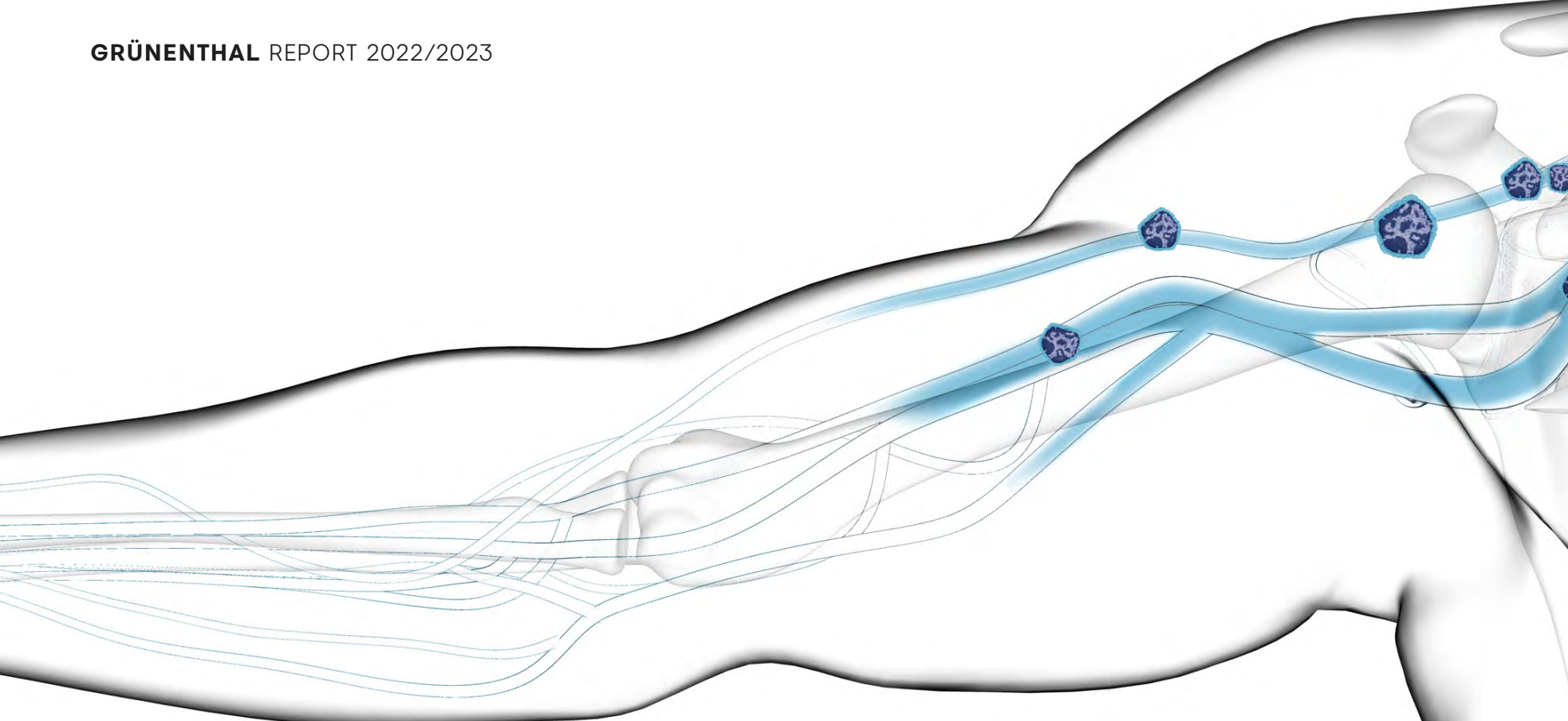
Grünenthal is a global company headquartered in Aachen, Germany. It has affiliates in 28 countries across Europe, Latin America and the US. Patients and customers benefit from Grünenthal products in around 100 countries worldwide.

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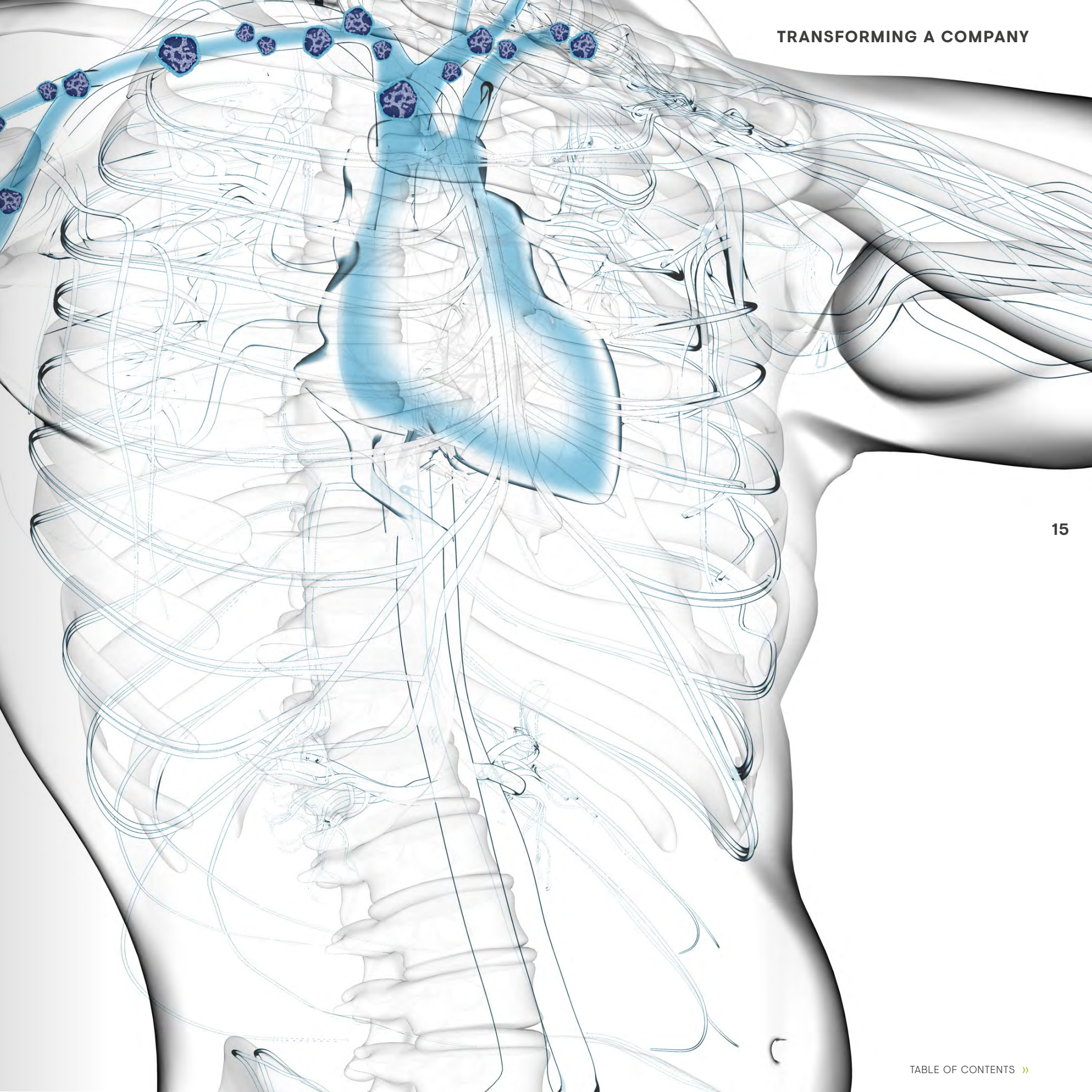


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# TRANSFORMING A COMPANY

Our path to a World Free of Pain.







# STORY OF TRANSFORMATION

Since 2017, Grünenthal has made radical and far-reaching changes that put us in a strong position to achieve future growth and reach more patients with life-changing treatments.

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## Our vision and strategic approach

To emphasise our focus on making life better for people around the globe, we launched our shared vision of a World Free of Pain in 2017. Grünenthal now touches the lives of millions of patients every year, with innovative treatments that reduce suffering and give patients the quality of life they deserve.

Looking ahead, we are striving to achieve this vision by pursuing two key strategic approaches. First, we are targeting organic growth by focusing our research and development activities on pain management. Second, we are tapping into inorganic growth opportunities by acquiring assets that strengthen our established brand portfolio – no matter which therapeutic area. These deals deliver significant EBITDA contributions that enable us to continue investing in innovative pain treatments.



**Proud  
to Work  
for a World  
Free of Pain**



Transformation milestones since 2017

---



**Financial growth**

More than tripled company value, entered debt capital market and received favourable credit ratings.



**R&D transformation**

Built promising R&D pipeline with three Phase III projects, two Phase I projects and innovative pre-clinical platforms.



**M&A**

Closed successful acquisitions outperforming benchmark M&A in the pharmaceutical market, with total expected deal value of more than €2.0 bn since 2017.



**Patient supply**

Continued reliable supply of medicines despite strong headwinds in recent years.



**Latin America**

Focused promotion on innovative products in Pain and Women's Health for better profitability and sustainable growth.



**US entry**

Fully represented in the USA: Established our research site Boston Innovation Hub and our commercial affiliate Averitas Pharma.



**Inclusive culture and responsible business**

Became workplace with winning culture, ensured highest standards for conducting business responsibly.

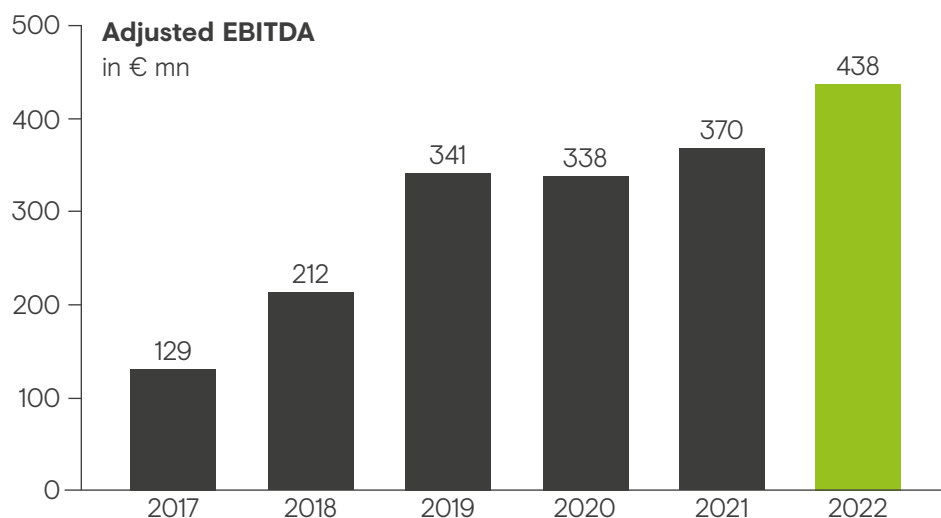
“ There are many ingredients needed to transform a company. A talented and high-performing team is the true key to success.

**Gabriel Baertschi**  
Chief Executive Officer

## Financial growth

Our company has achieved remarkable progress with its financial performance since 2017. Grünenthal's profitability, measured by adjusted EBITDA, has more than tripled during the last half-decade. Our company value is now more than three times higher, in terms of our equity market value and operating cash flow. In 2021, Grünenthal successfully closed its first-ever bond transaction of €950 million, with strong investor demand. Three major independent credit rating agencies regularly assess Grünenthal and have confirmed our solid financial position.

## Grünenthal's business results 2017-2022



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## Driving innovation

Since 2017, we have dramatically expanded our innovation pipeline. Several exciting candidates are making their way through the development process. This includes resiniferatoxin (RTX), an investigational medicine developed for the treatment of pain in patients with knee osteoarthritis. Our innovative approach has already led to tangible outcomes. For example in the USA we achieved a label extension for Qutenza™. Under the extended label, this non-opioid treatment option is now available to patients with Diabetic Peripheral Neuropathy of the feet in adults, a progressive and debilitating complication of diabetes that affected more than five million Americans in 2020<sup>18</sup>. This is a powerful example of how our experts achieve tangible breakthroughs for patients' quality of life.

This growing pipeline of innovative investigational medicines reflects the success of our R&D strategy launched in 2019. It has created a modern operating model that enables our scientists to pursue high-potential assets in a modality-agnostic manner. Since adopting this new setup, we have become a more diverse and international organisation, with a global approach that includes partnerships with organisations who share our passion for scientific progress. As part of this approach, we set up our Innovation Hub in Boston in 2020. It establishes a centre of excellence for pain research, where our experts can identify and develop promising external innovation opportunities by collaborating with institutions in the Boston area, one of the world's largest life science hotspots.

**Pipeline development 2019-2023**

2019	PRE-CLINICAL	PHASE I	PHASE II	PHASE III	APPROVAL
Qutenza™ DPN					
Qutenza™ PSNP					
Resiniferatoxin (RTX)					
MPC-06-ID*					
NOP	█				
GRM	█				
NOP Back-up	█				
Ion channel programme					

2023	PRE-CLINICAL	PHASE I	PHASE II	PHASE III	APPROVAL
Qutenza™ DPN	████████████████████				
Qutenza™ PSNP	██				
Resiniferatoxin (RTX)	██				
MPC-06-ID*	██				
NOP	████████████████████████████████				
GRM	████████████████████████████████				
NOP Back-up	████████████████████████████				
Ion channel programme	████████████████████████████				

\* Collaboration with Mesoblast

### The right deals

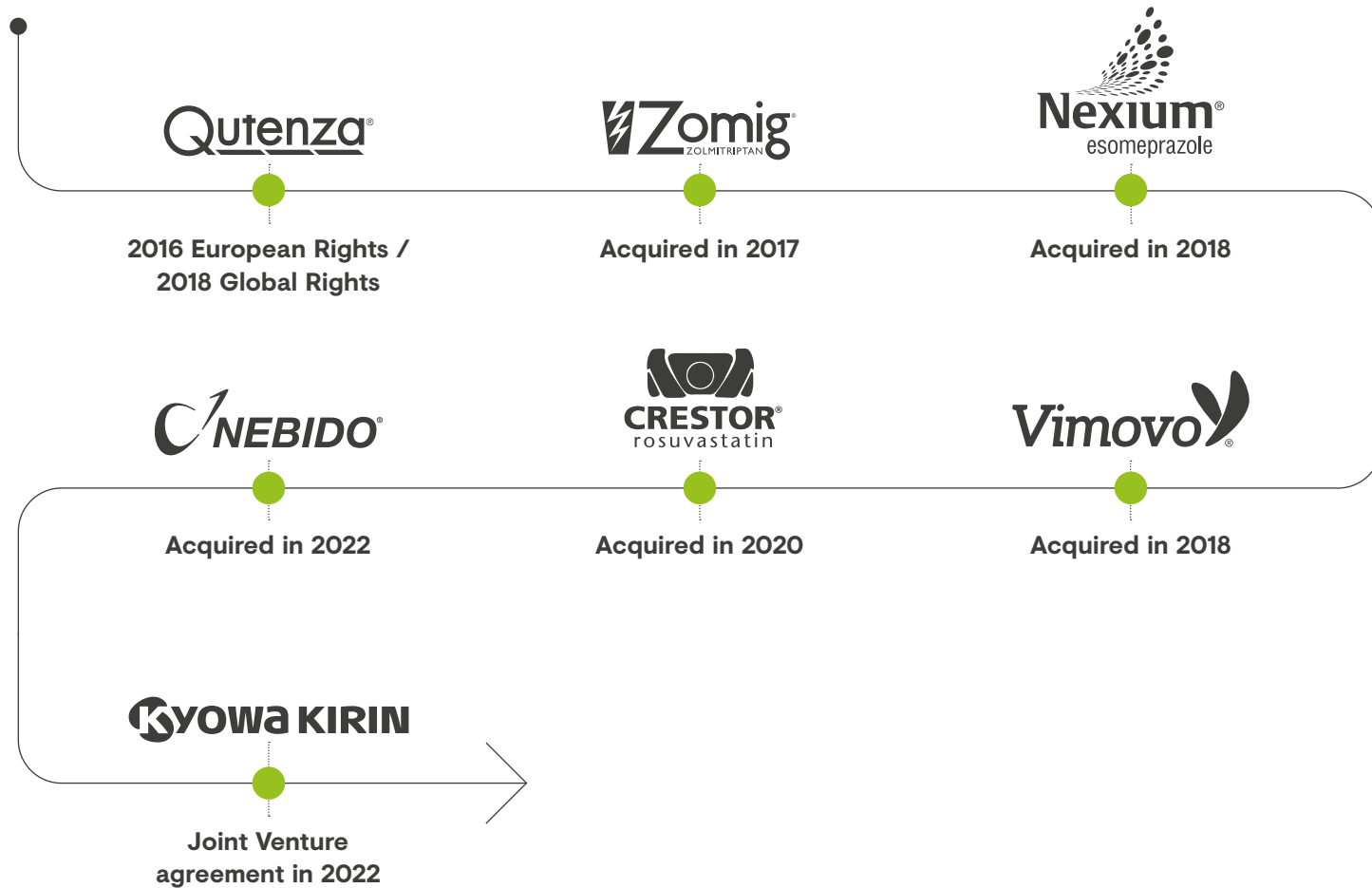
Mergers and Acquisitions (M&A) are a key driver of our growth strategy. Our M&A strategy has increased profitability and diversified Grünenthal's brand portfolio. Since 2017, Grünenthal has closed successful acquisitions with a total expected deal value of more than €2.0 billion; of which approx. €1.8 billion relate to acquisitions of established brands, incl. Zomig™, Nexium™ and Vimovo™, Crestor™ as well as Nebido™. We also

expanded our portfolio of established brands through a joint venture collaboration with Kyowa Kirin, which gives Grünenthal access to 13 life-changing brands across six therapeutic areas.

Grünenthal's experts around the globe join forces across functions to maximise the return on our investments by integrating new products and businesses into our company quickly and

effectively. This begins with our due diligence approach, where we evaluate possible targets with a focus on potential synergies in our production, logistics and commercial activities. Our teams actively strive to reduce costs and generate additional value from all brands at every stage in the product life cycle. And we strongly focus on identifying deals for brands that will make an immediate positive contribution to profitability and cash flow.

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### Commercial success

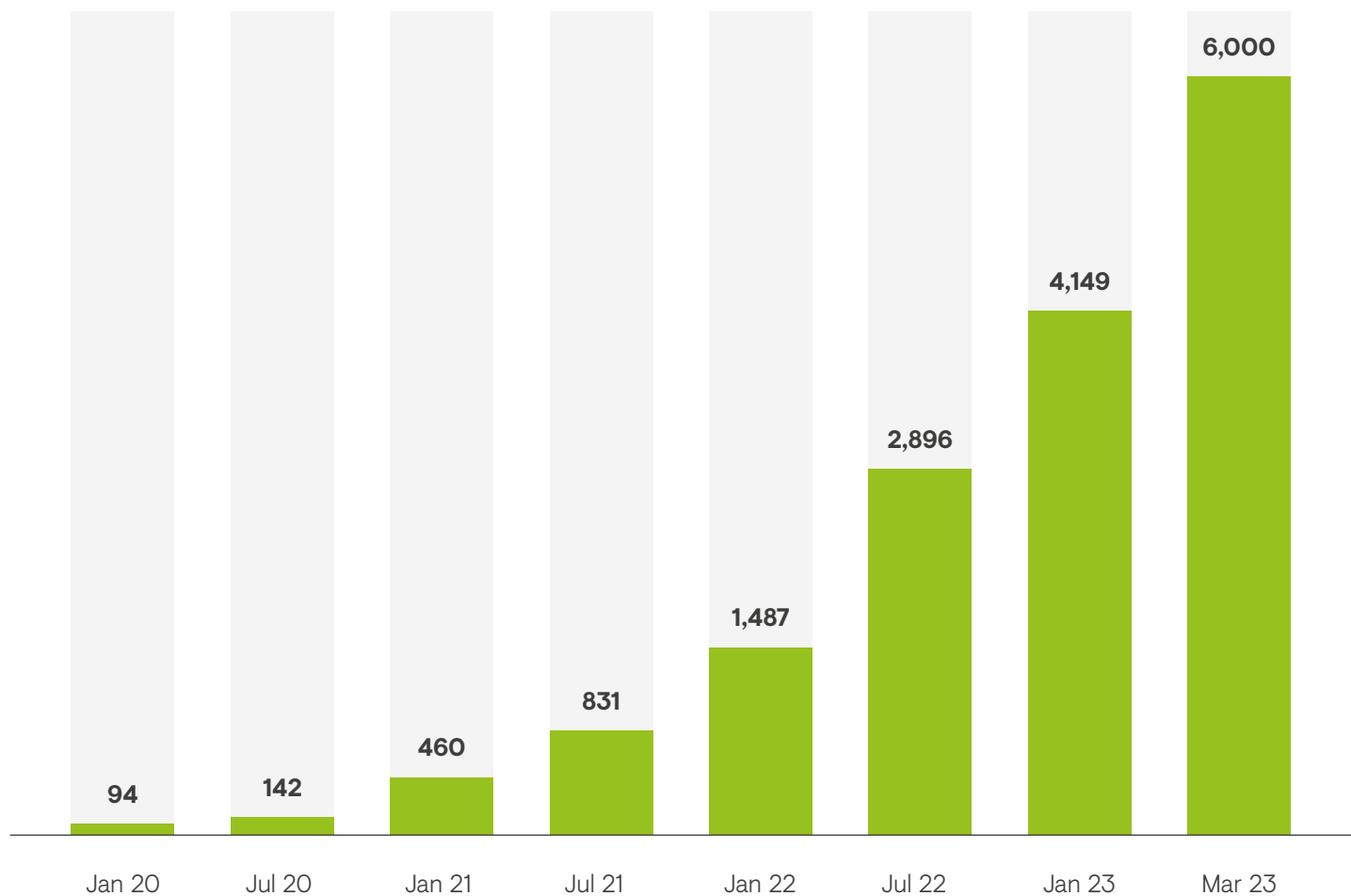
We continue to see strong commercial performance across our portfolio and geographies. In Europe, our established brands have grown faster than the market and our growth brand Qutenza™ has shown strong performance in key markets such as France.

In 2018, we extended our commercial footprint to the United States and entered the market with the non-opioid topical system Qutenza™. We built an entire organisation from scratch and have seen strong growth since then. One third of Grünenthal's revenue comes from Latin America, with a very diverse product portfolio. Since 2017,

we have been focusing on innovative pain products (+30% growth) and profitable diversified products (+23% growth), a successful strategy that has led to increased profitability in the region.

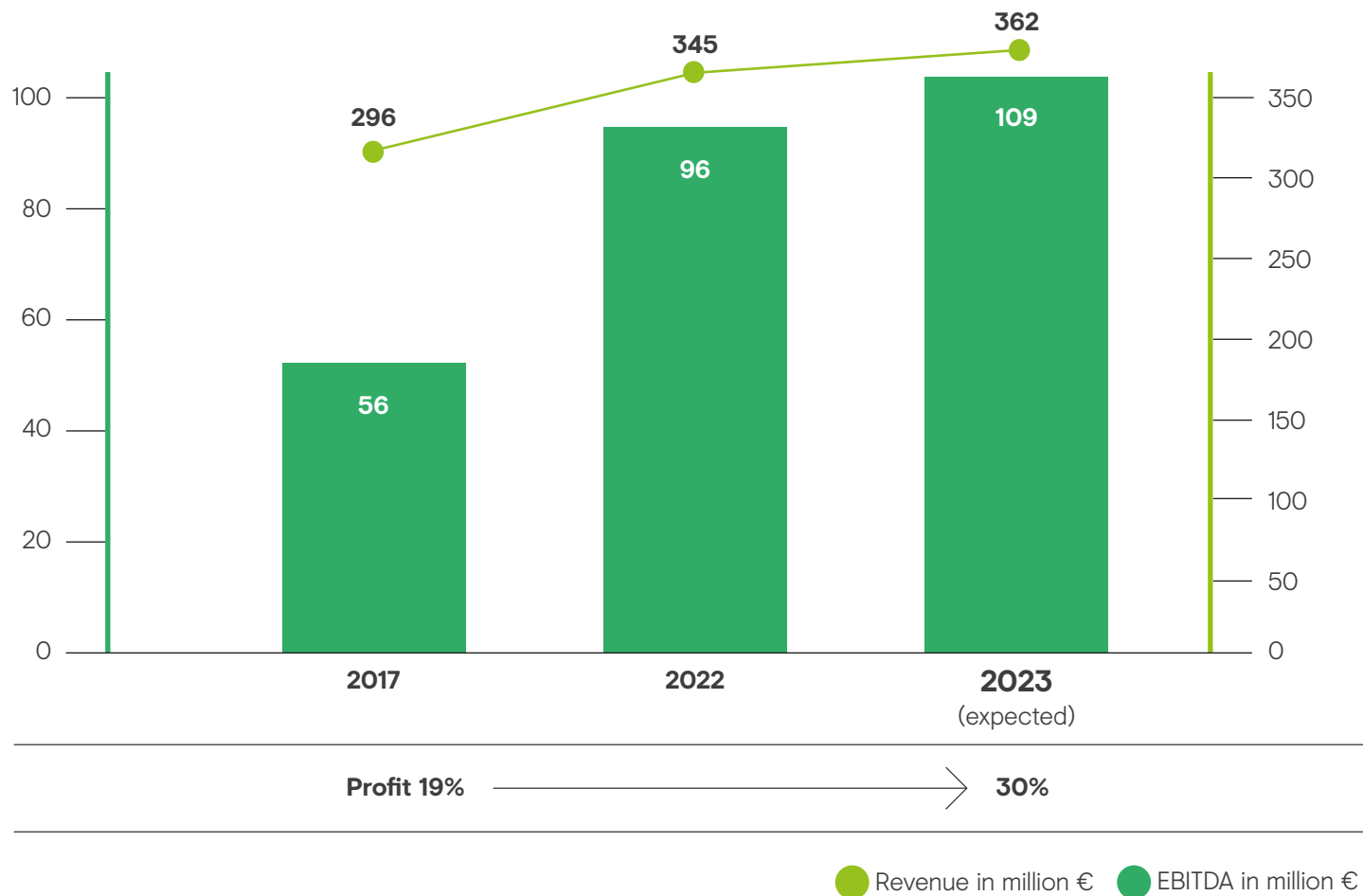
### Qutenza™ US overview

In-market topical systems (TS) volume



As we look to the future, we continue to evaluate opportunities to further expand our portfolio and our geographic footprint. As part of this ambition, in 2022 we entered into a commercial partnership with Shionogi to commercialise RTX in Japan.

### Performance Latin America



## Reaching patients worldwide

Global Operations (GO) started its journey in 2017, when it was founded as a new business area to enable end-to-end processes for our product supply worldwide. As a second step in 2020, GO implemented a strategic growth plan, GO2025, which aims to create the optimal setup to seamlessly integrate further products into our portfolio and supply them to patients. As part of GO2025, our GO team aims to drive Grünenthal's profitability by ensuring excellence in our processes and continuously innovating the way we operate.

GO has the clear mission to ensure safe, efficient and reliable product supply to patients. In line with this, our manufacturing and operations teams successfully

kept our business running at all times – despite the pandemic, global supply challenges and disrupted supply chains.

### 2020 until end of 2023



**€114 million investment** in our manufacturing capabilities

### 2017 until end of 2022



**25 end-to-end integrations** into our Global Operations (finalised or in progress)

### Cost-effective integration of acquired products

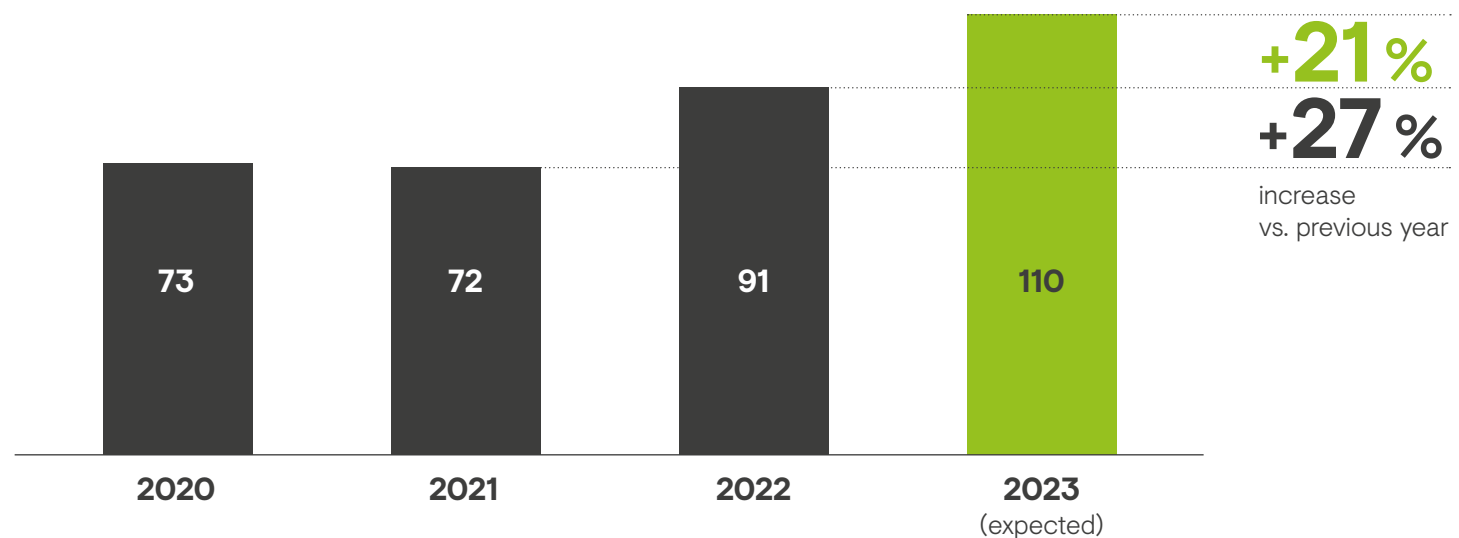
Successful acquisitions depend on integrating new brands into our supply chain

quickly and effectively. Our GO team ensures that we get maximum value for our investments. We are often able to achieve substantial cost reductions in production. Here are some examples:

- **Nexium™ and Vimovo™:** approx. €10.2 million per annum through in-house packaging
- **Zomig™:** approx. €3.7 million annually expected through in-house bulk production and packaging
- **Crestor™:** approx. €15 million per annum expected through in-house bulk production and packaging

## Grünenthal's growth is reflected in the development of production volume

Manufacturing site in Aachen, Germany  
Volume in million packs



## Enhancing reputation

### Dialogue with our communities

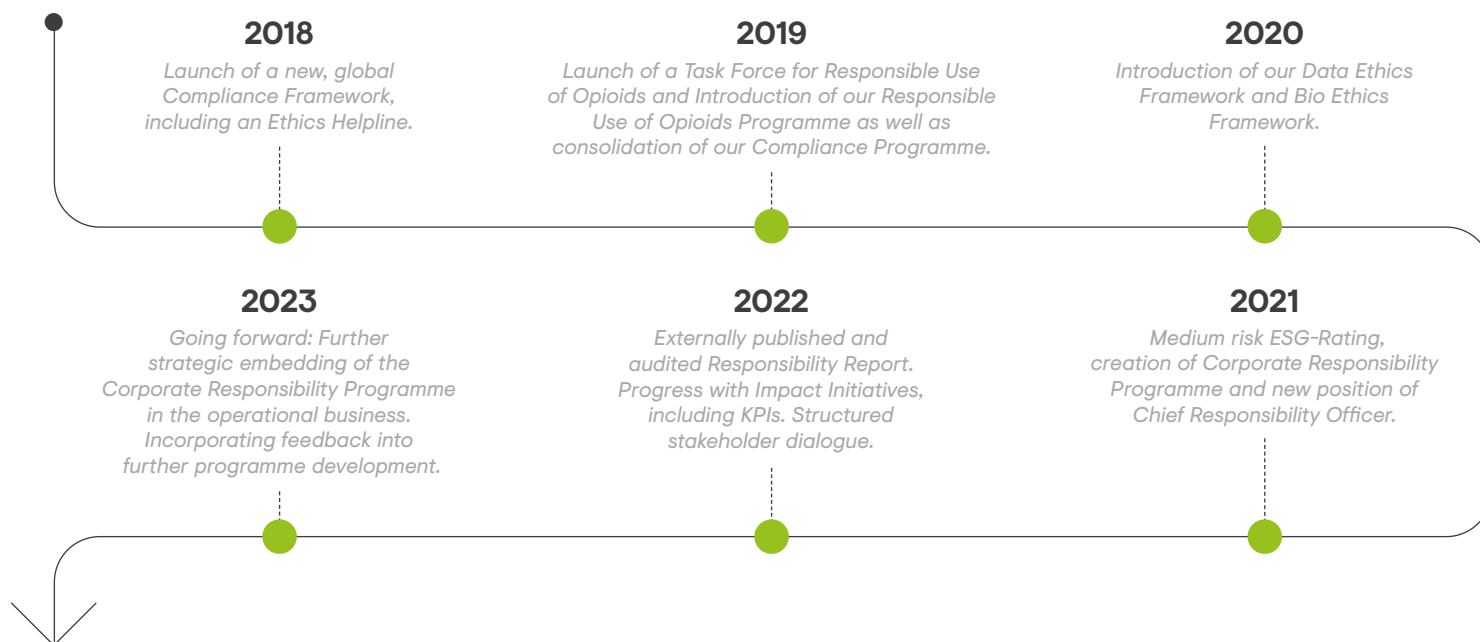
Interactions with external partners and stakeholders play an important role in defining our position as a science-driven and patient-focused company. We actively seek dialogue with our stakeholders, for example local politicians, to understand our communities' needs and reaffirm our commitment to the regions where we are based. Since 2018, we have reshaped our Grünenthal brand and corporate design to strengthen the way we approach our target groups worldwide. This includes a more engaging social media presence that boosts our capacity to share clear and inspiring insights into how our company improves quality of life for pain patients worldwide. Our communities include those that have been affected by the Thalidomide tragedy, which will always

remain a part of our company's history. In November 2021, Dr. Michael Wirtz, shareholder of Grünenthal, apologised to those affected and their families on behalf of his family. We welcome this gesture as a further step on the chosen path of dialogue between affected people, Grünenthal and the shareholder family.

### Ensuring the highest standards for conducting our business responsibly

As a global leader in pain management, we conduct business in a responsible way and aspire to proactively create a positive impact on society and the environment. In 2020, we stepped up our efforts to lead progress for a better world by launching our holistic Corporate Responsibility Programme. It centres around four dedicated Fields of Action with 12 material topics, each with specific ambitions that sharpen our focus

on delivering improvements every day. An independent ratings agency ranked Grünenthal in the top 3 percent for our pharmaceutical subindustry in 2022. This reflects the real-world action that Grünenthal is taking to protect its long-term future, as well as the long-term future of communities and the environment.





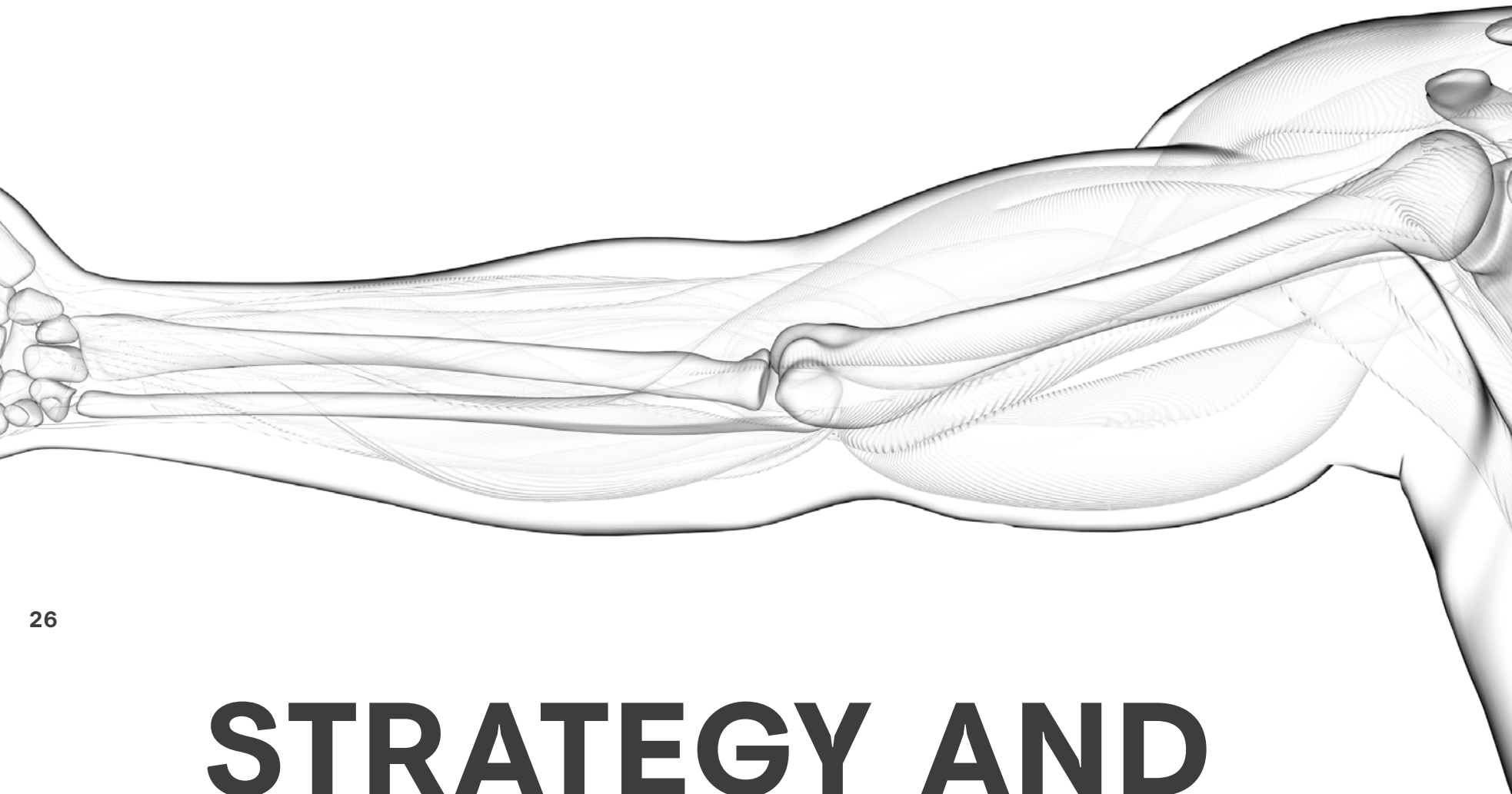
## Winning culture

Talented people are the decisive factor in our company's success and they make a real-world impact on improving patients' lives. Our global team has joined forces to transform Grünenthal during the last five years, and we are now a more agile business that is ready to seize opportunities for growth. To do this, Grünenthal has taken a wide range of steps to keep strengthening its culture since 2017, and this is reflected in the highly motivated team that pushes our company forward every day.

The spirit of continuous improvement has been a decisive factor in our transformation since 2017 – and it will continue to move our company forward in the future too. Our people are always searching for ways to increase flexibility, improve efficiency and optimise our way of working. In this way, we make sure Grünenthal is ready to take advantage of opportunities to further boost business success and keep making life better for patients worldwide.

*Grünenthal Executive Board Team  
at internal Group Conference  
thanking all employees for their  
commitment*

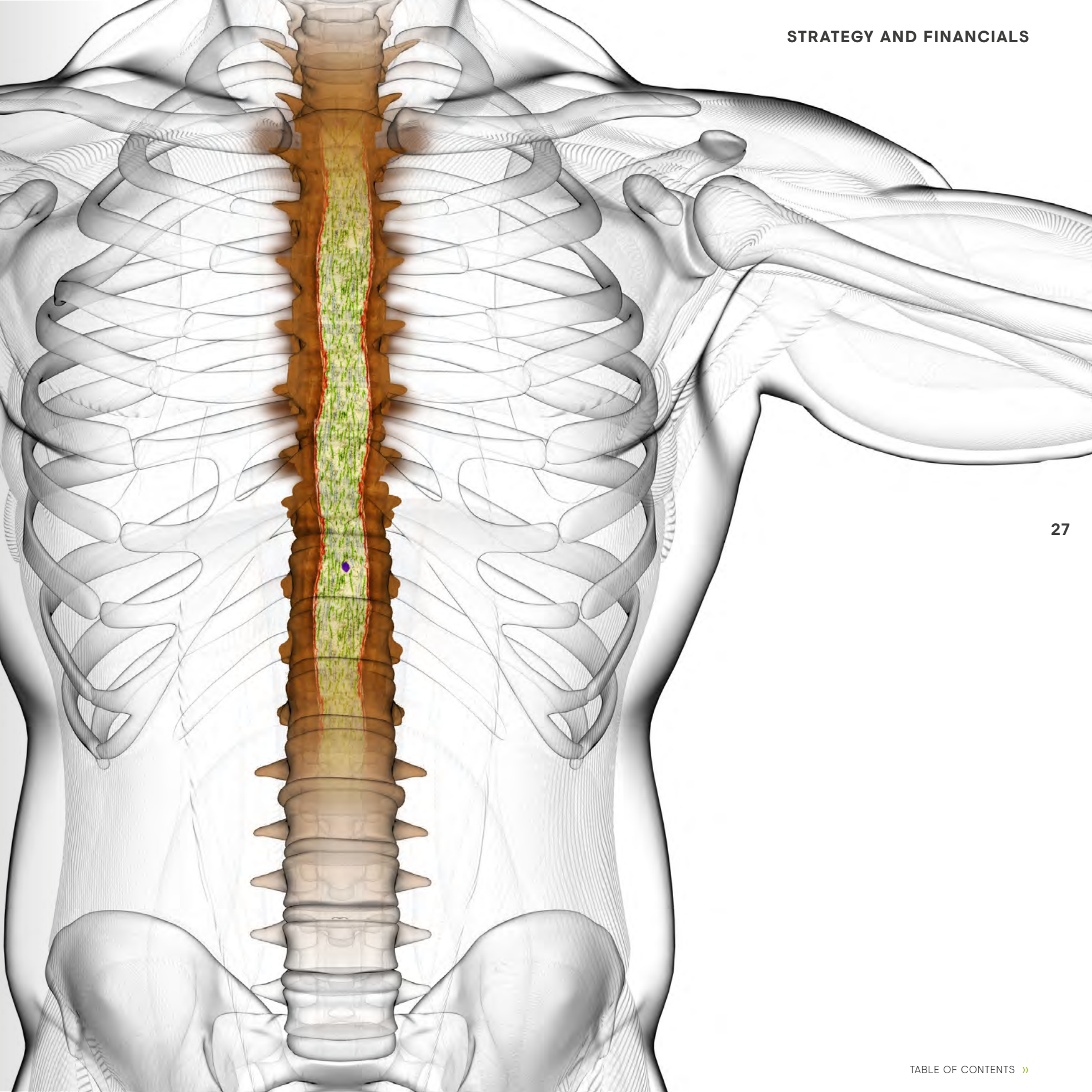




# STRATEGY AND FINANCIALS

We have a strong corporate strategy for further transforming our company. Our results prove that we are heading in the right direction.







# ACHIEVING OUR VISION OF A WORLD FREE OF PAIN

As a company dedicated to developing and commercialising innovative pain products, we are committed to our vision of a World Free of Pain. Our corporate strategy is designed to bring this vision to life.

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## The 5 pillars of our corporate strategy

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### 1. Innovation

Be a leading innovator in pain treatments to address critical, unmet medical needs, with a focus on non-opioid treatments.



### 2. Growth

Drive the commercial success of our growth brands and evolve our go-to-market model towards digital and omnichannel approaches.



### 3. Acquisitions

Complement our portfolio with deals for established brands, irrespective of therapeutic area.



### 4. Efficiency

Drive profitability through efficiencies across the value chain and manufacture at the best safety, quality and cost level.



### 5. People

Invest in building capabilities of our people, and operate in line with the highest ethical and regulatory standards.

Our corporate strategy is built on five pillars: innovation, growth, acquisitions, efficiency and people. All five elements are essential and closely linked. Our results in recent years show that our strategy is transforming our company and moving us in the right direction.

## Innovation

As a science-driven company, we focus on developing novel non-opioid treatments for pain therapy. We develop promising candidates through proof of concept and beyond, and take a world-leading role in creating pain treatments that address unmet medical needs. Grünenthal focuses on four key pain indications: peripheral neuropathic pain, chronic post-surgical pain, chronic low back pain and osteoarthritis. One of our most recent in-house developments is our ion channel programme. These potential non-opioid treatments aim to address peripheral neuropathic and

nociceptive pain indications. You can explore further specific examples of our innovative R&D projects in the chapter A World Free of Pain.

In addition, we selectively source early-stage and late-stage projects to complement Grünenthal's R&D pipeline. With our acquisition of Mestex AG in 2021, Grünenthal secured global rights for resiniferatoxin (RTX). This attractive late-stage asset could offer an innovative non-opioid therapy option for millions of patients affected by pain associated with osteoarthritis of the knee. This condition affects over 360 million people worldwide.<sup>2</sup>

Sharing the costs and risks of late-stage development with partners is vital to our R&D strategy. In March 2022, Grünenthal entered an agreement with NovaQuest Capital Management for the global clinical Phase III programme for RTX. This agreement significantly contributes to securing the development

costs for RTX while also opening up the potential for Grünenthal to advance promising pipeline assets into the clinic. This was the first time that Grünenthal has agreed a strategic collaboration of this type.

In August 2022, we enrolled the first patient into our global clinical Phase III programme for RTX. If the drug is approved by regulators, we envisage a potential market entry in 2025/2026. In 2022, we also took a significant step towards providing RTX to patients outside of our core markets the EU, the US and Latin America by entering into a collaboration with Shionogi. They will serve the Japanese market as our exclusive partner.

## Growth

Grünenthal is well-positioned to maximise business opportunities and build successful brands now and in the future. This includes expanding the commercial success of Qutenza™ in the US. The label extension for the treatment of neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults represents a unique growth opportunity, allowing us to help more patients in the US than under the original label for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN).

We will also continue to maximise the value of Palexia™ in Europe. This product is still growing after more than a decade on the market because of its differentiated profile. At the same time, we will prepare for and manage the upcoming loss of exclusivity of Palexia™ in Europe.

Across all brands, we have continued to evolve our go-to-market model towards a digital and omnichannel approach. This has been accelerated by the Covid-19 pandemic, and we have rapidly and substantially expanded our use of channels that enable remote interaction.

## Acquisitions

We keep growing our business through targeted acquisitions of established brands based on clearly defined acquisition criteria:

- Established brands with high brand loyalty and predictable, stable sales.
- Synergistic products with significant overlaps to our existing infrastructure

and regulatory expertise, ideally in territories where Grünenthal has a commercial footprint.

- Acquisitions that enhance our portfolio diversification in products in areas with high medical needs.
- Immediate positive EBITDA and cash flow contributions, with an acquisition at attractive multiples, guaranteeing short payback periods and fast deleveraging.

We enforce a disciplined acquisition strategy supported by robust due diligence. Leveraging our many years of experience, we ensure fast and effective integration of acquisitions while maintaining an uninterrupted market supply. Partners benefit from our commercial, regulatory and manufacturing expertise to achieve valuable synergies.

Since 2017, Grünenthal has closed successful acquisitions with a total expected deal value of more than €2.0 billion, of which approx. €1.8 billion relate to acquisitions of established brands, including Zomig™, Nexium™ and Vimovo™, Crestor™ as well as Nebido™. In 2022, these brands contributed €278 million to Grünenthal's adjusted EBITDA, representing 63 percent of our total adjusted EBITDA. Some Grünenthal acquisitions are also made through collaborations and joint venture arrangements, like our latest joint venture collaboration with Kyowa Kyrin, encompassing a portfolio of established brands.

These acquisitions and collaborations will further contribute to our solid EBITDA growth in 2023. In addition to this, synergies play an important role after the integration of acquired brands. In 2022, manufacturing synergies for Nexium™,

Vimovo™ and Zomig™ reached around €12 million.

## Efficiency

We continuously identify potential ways of boosting efficiency throughout our value chain. Key ongoing projects include operational excellence programmes, leveraging digital technologies and automation, technical product re-development, and direct spend optimisation. These improvements are integrated end-to-end in our manufacturing process for our own medicines as well as for products that we manufacture for other pharmaceutical companies as a trusted supplier.

At all times, we apply strict measures for controlling costs and follow a prudent financial policy supported by the long-term commitment of our shareholders.

## People

Our people are the key to our success – and our company's culture is the backbone of everything we achieve. We continued to make substantial progress on our cultural journey last year. In 2022, we were certified as a Great Place to Work® in 24 entities spread across 19 countries. Looking ahead, we will maintain our drive towards a high-performance culture, while continuing to strengthen opportunities for personal and professional development.

We strongly believe diversity is the foundation of an innovative business. In 2022, we launched our first Diversity and Engagement Strategy. It provides a plan and specific global commitments that aim to truly empower, inspire, support and

engage all our people, partners and communities. This will enable us to achieve outstanding business results and build the capabilities we need for the future.

We remain committed to maintaining the highest ethical and regulatory standards in our business operations and our role as an advocate for the responsible use of our products – including medically necessary opioids. In order to ensure highly effective compliance processes, we have instilled a culture that gives our company an ethically minded and fully engaged workforce.

Grünenthal's second ESG rating in July 2022 confirmed the company's improved ESG risk management, putting it in the top three percent of the global pharmaceutical subindustry.

You can learn more about our approach in the chapters People and Culture and Responsible Business.



# STRONG BRANDS THAT CREATE VALUE AND FUND FUTURE DRUG DEVELOPMENT

We have the expertise and strategy to maximise value from our brands – developed or acquired – to drive growth and fund innovation.

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Our success builds on our portfolio's complementary mix of established and growth brands.

The established brands bring together all mature and off-patent products. They are characterised by high brand awareness, predictable and stable sales, and high profitability. These include Nexium™, Crestor™ and Nebido™, and brands we have developed over a longer period, like Tramal™.

The growth brands include innovative and patent-protected products like Qutenza™, and brands that continue

to have valuable growth potential like Palexia™ and Vimovo™.

Combining these two product categories provides us with a well-balanced and resilient business. In addition, the profit that we generate with our established and growth brands gives our company financial stability. This enables us to fund the development of urgently needed innovative pain therapies.

## Enriching our portfolio

Our M&A strategy is designed to enrich our portfolio of brands. We achieve this

through early-stage and late-stage asset R&D deals in the therapeutic area of pain, and through the acquisition of established brands irrespective of therapeutic area.

## Acquisition of early-stage and late-stage development assets in pain

We will continue to selectively source early-stage and late-stage projects in pain to complement Grünenthal's R&D pipeline. Our 2021 acquisition of Mestex AG, with its late-stage asset RTX, is one example of this approach.

€2 bn

total expected deal value of closed successful acquisitions since 2017





33

“ Combining both established and growth brands in our portfolio provides us with a well-balanced and resilient business. The profits we generate give us the financial stability to fund the development of new pain therapies that patients urgently need.

**Quentin Le Masne de Chermont**  
Head Corporate Strategy and Portfolio Management

### Acquisitions of established brands

We also seek to acquire established brands, irrespective of their therapeutic area – brands that offer stable sales performance with the potential to support funding for our R&D projects and secure our financial stability. As a fully integrated pharmaceutical company with extensive experience in established brands, we can enhance the performance of acquired products to create significant value for Grünenthal and its partners. Dedicated teams ensure fast and effective integration. We use our commercial expertise to maximise market performance while achieving synergies through our cost-efficient manufacturing.

Acquisitions of established brands represent a unique opportunity that matches our strengths and capabilities, directly impacting our financial stability. We typically acquire established brands that benefit from high brand loyalty. Our acquisitions of Crestor™ from AstraZeneca and Nebido™ from Bayer are recent examples. We believe there will be more opportunities like this in the future.

In November 2022, we entered a joint venture collaboration with Kyowa Kirin International, a Japan-based global specialty pharmaceutical company. This collaboration covers an established medicines portfolio that includes 13 brands across six therapeutic areas, primarily focused on pain. The portfolio fits very well with our geographic footprint and therapeutic areas, and we believe we can expand the reach of the medicines to help even more people in need.

Grünenthal will own a 51 percent majority share in the joint venture and intends to acquire the remaining shares at the beginning of 2026.

Backed by the trust of our shareholders, we are a proven and reliable partner with the ability to execute acquisitions quickly and pragmatically.

### Further acquisitions

Alongside investing in R&D assets and established brands, we are also open to acquiring selected companies and growth brands – as we did with Qutenza™. Since 2017, we have closed successful acquisitions with a total expected deal value of more than €2 billion.



## The power of partnerships

Working with partners is the best way to achieve our vision of a World Free of Pain.

### R&D partnerships in pain management

At Grünenthal, we never stop searching for new partnerships with organisations and individuals that share our vision of a World Free of Pain. We believe collaboration is the key to developing life-changing treatments for patients. In this spirit, we actively seek R&D collaborations for non-opioid treatments that focus on our core pain indications: chronic low back pain and osteoarthritis, and that have the potential to make a real difference for patients – independent of the modality and their stage of development. A recent example is the partnership with NovaQuest Capital Management. Over many decades, our experts have built strong networks by sharing knowledge and collaborating – while always focusing on improving patients' lives together.

### Commercial out-licensing partnerships

Through our commercial partner business, we give patients access to our products in territories where we do not have our own presence. This includes Africa, Asia, Australia, Canada, Central Eastern Europe and the Middle East. We are working on finding the most appropriate partners for Qutenza™ and RTX in the Asia Pacific (APAC) region and Canada. In addition, Grünenthal is currently pursuing out-partnering opportunities for established brands, such as Crestor™ and Nebido™, in countries where we do not have our own commercial footprint. This will give patients across the globe access to our medicines.

### Commercial in-licensing partnerships

Our exceptional commercial capabilities and regulatory expertise make us a natural partner for businesses that want to bring projects to the market successfully. We are proud of our robust in-market capabilities for commercialising brands. We do this by using in-person promotion, as well as via a range of digital channels.

“ Win-win outcomes and compromises during negotiations are very important for successful long-term partnerships. Our partnerships often continue far beyond the negotiation, integration and implementation phases.

**Susanne Ziemons**  
Head M&A and Licensing



# PRODUCT PORTFOLIO PERFORMANCE

Our product portfolio comprises a complementary mix of innovative growth brands and established brands with high levels of brand awareness.

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In 2022, our growth brands comprised our patent-protected brands Palexia™, Qutenza™ and Vimovo™. Operational revenue from Palexia™ (excluding licensing revenue), our highest-selling product, accounted for around 20 percent of total revenue in 2022. Qutenza™ has become an even more powerful potential growth driver following a US label extension in July 2020, a ramp-up of our US commercial infrastructure and promotional activities in 2021/2022. These measures have significantly increased the patient population that can benefit from this treatment.

Our established brands include Nebido™, Nexium™, Versatis™, Tramal™, Zaldiar™/Iprim™, Crestor™, Zomig™/AscoTop™ and Transtec™/Norspan™.

## **Diversified product mix**

Revenue from pain products accounted for 59 percent of our revenue in 2022. In recent years, we have diversified our product portfolio beyond the pain segment through successful acquisitions of established brands.

## **Revenue distribution by geography**

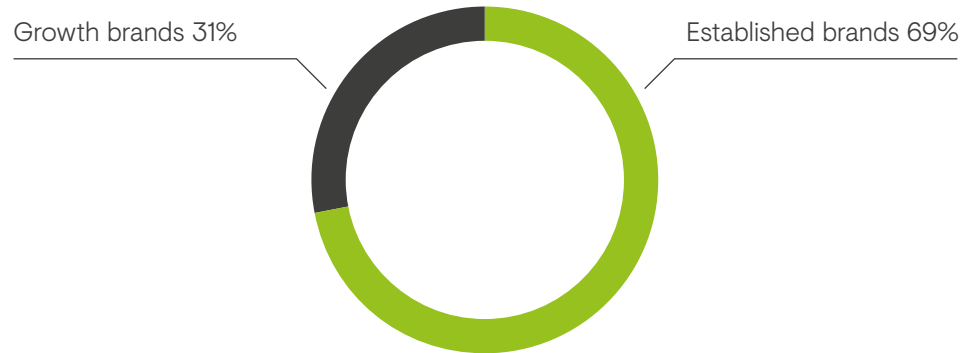
Diversifying products and geographies enables us to manage our business risks more effectively, making us less dependent on a single product or market.



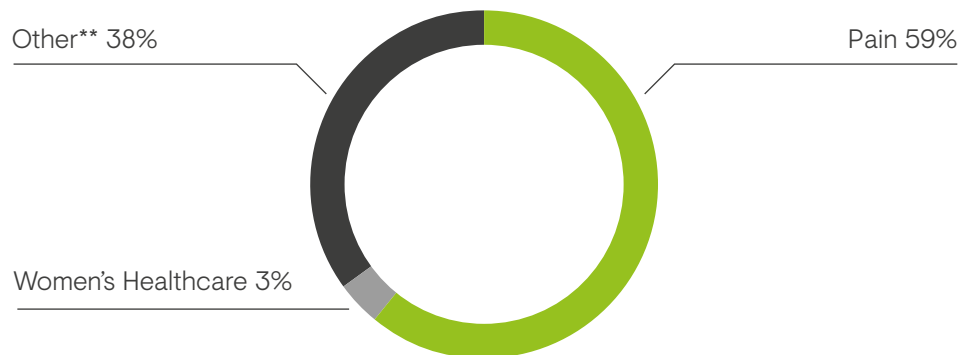


## Revenue split as of December 31, 2022

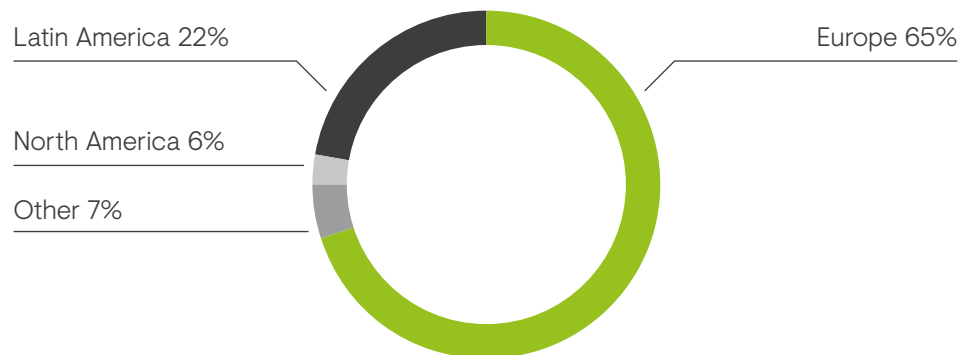
### Revenue by product typology\*



### Revenue by therapeutic area



### Revenue by geography



\* Based on operational revenue of products

\*\* Includes Nexium™, Andromaco branded generics, contract manufacturing, partner business in APAC, and R&D cost reimbursements



# STRONG FINANCIAL PERFORMANCE

Revenue and profit hit record levels in 2022, with key investments to ensure our company's future.

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## Financial results exceeded expectations

2022 was another year of record results for Grünenthal. Revenue reached €1,654 million, an increase of 13 percent compared to 2021. Adjusted EBITDA reached €438 million last year, which is an increase of 18 percent compared to 2021. With this result, we have more than tripled our profitability since 2017. Grünenthal has also more than tripled its operating cash flow since 2017, putting our company in a solid position to further invest in advancing the R&D pipeline, continuing the M&A strategy and growing the business in the United States.

## Excellent business performance and partnerships

The 2022 results were made possible by excellent business performance, as well as revenue from strategic partnerships for our late-stage asset resiniferatoxin

(RTX). The Japanese company Shionogi will obtain exclusive commercialisation rights for RTX in Japan. In addition, the life science investment firm NovaQuest Capital Management is now sharing the clinical development and approval risks of developing this asset with us.

Operational revenue from growth brands and established brands increased significantly, leading to our company's best ever financial performance. We exceeded our targets for 2022, which shows that Grünenthal is making excellent progress with its ambitious strategy for business growth.

Key brands such as Qutenza™, Palexia™, Vimovo™ and Zomig™ grew faster than the market. Palexia™'s operational revenue reached €333.7 million (+€17 million; +5%), Vimovo™'s operational revenue reached €66.6 million (+€20 million; +44%) and Zomig™'s operational revenue reached €70.2 million (+€8 million; +12%). Operational revenue from Qutenza™ reached €76.0 million (+€33 million; +77%). The surge in demand

for this topical non-opioid treatment for various neuropathic pain conditions was particularly evident in the U.S., where the product is indicated for treating post herpetic neuralgia and pain related to diabetic neuropathy of the feet. The neuropathic pain market is significant, with an estimated size of \$4.5 billion in the United States, which is the largest global neuropathic pain market.<sup>1</sup>

For information about the sales performance of our other brands, please see the table in the chapter A World Free of Pain.

## Growing through acquisitions

We made several important investments in our company's future during 2022. Grünenthal acquired Nebido™ from Bayer for around €495 million in November, for example. This leading brand for testosterone replacement therapy immediately contributed to revenue and profit as of November 2022. If we had

are patient-centric  
ive entrepreneurship  
oin forces  
net with integrity  
rive performance

nal  
ours



acquired Nebido™ on January 1, 2022, the brand would have contributed an additional €102 million of revenue and €80 million of EBITDA during the full year. We also entered a joint venture agreement with Kyowa Kirin International (KKI) in 2022, which involves 13 established brands primarily in pain management. Grünenthal will own a 51 percent share in the new company and intends to acquire the remaining 49 percent at the beginning of 2026. This will contribute to Grünenthal's revenue performance (top-line) from 2023 onwards and profitability (bottom-line) from 2026. Due to license fees and a royalty agreement with the seller, there will be a limited EBITDA impact until Grünenthal purchases the remaining shares and integrates the product portfolio into its network in 2026.

## Outlook

Our prudent approach to finance will remain unchanged in 2023.

Our strong liquidity profile is supported by high cash generation, existing cash on the balance sheet and €500 million of Revolving Credit Facility (RCF).

In April 2023, we successfully placed a new €300 million bond, following the issuance of our debut bonds in 2021.

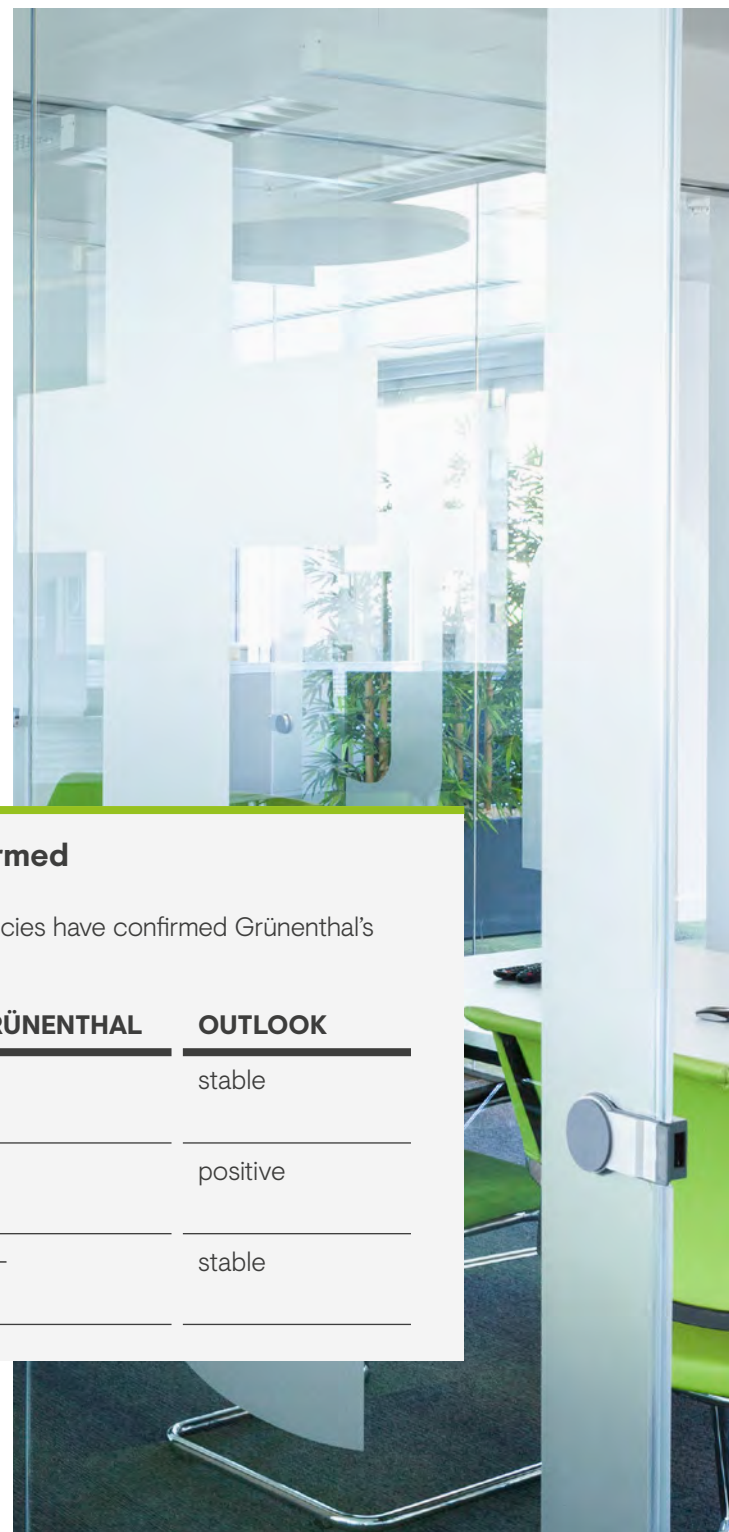
The new financing will enhance the company's capital structure and provide additional flexibility for the implementation of its strategy and in making progress towards its vision of a World Free of Pain.

Going forward, we will continue to finance our M&A strategy with an optimal funding mix.

We will adhere to our disciplined approach to acquisitions of established products with attractive multiples and

which are EBITDA accretive in order to maintain acceptable leverage levels. Our financial policy is supported by our family shareholders and their long-term commitment to the sustainable growth of the Group and a balanced dividend policy.

Following this record year for our company's financial performance, we anticipate a slight increase in revenue for 2023 – primarily driven by growth for Qutenza™ and the recent Nebido™ acquisition, as well as the joint venture with KKI. Profitability is expected to remain almost unchanged due to the expected entry of alternative tapentadol products for Palexia™, and also because of continuous investments in the US that will aim to unlock the full sales potential for Qutenza™.



## Solid financial position confirmed

Leading independent credit rating agencies have confirmed Grünenthal's solid financial position.

RATING AGENCY	GRÜNENTHAL	OUTLOOK
<b>Fitch Ratings</b> (March 2023)	BB	stable
<b>Moody's Investors Service</b> (April 2023)	B1	positive
<b>Standard &amp; Poor's</b> (April 2022)	BB-	stable





### Profit and loss statement\*

IN € MILLION	ACTUAL 2021	ACTUAL 2022
<b>Revenue**</b>	<b>1,467</b>	<b>1,654</b>
Cost of sales***	-438	-519
<b>Gross profit#</b>	<b>1,029</b>	<b>1,134</b>
Marketing, Sales & Medical costs##	-424	-479
Core Research & Development cost	-140	-164
Other Costs	-300	-238
Depreciation Fixed Assets###	151	155
<b>EBITDA</b>	<b>316</b>	<b>408</b>
<b>Adjusted EBITDA+</b>	<b>370</b>	<b>438</b>
<b>Earnings before taxes</b>	<b>115</b>	<b>203</b>

- \* **Management view** Profit and loss statements (P&L) can be displayed in Accounting and Management view. Both P&Ls include the same information, but are designed to serve different needs. The Accounting P&L is used for reporting according to German Commercial Code (HGB) while the Management P&L is used for internal steering and tracking. Both views are similar for Revenue, Cost of sales and thus Gross profit. But they differ in terms of the recognition of depreciation on acquired product rights and medical affairs costs. Depreciation of acquired products rights are recognised in Management view as part of "other costs" whereas Accounting view shows it as part of "selling expenses". Medical commercial R&D costs comprise post approval product costs, e.g. for the maintenance of registration, for clinical studies for Phase IIIb/IV and the support of investigator initiated studies as well as structural costs. These costs are part of "Marketing, Sales & Medical costs" in Management view whereas shown as "Research & Development costs" in Accounting view
- \*\* **Revenue** primarily comprises sales of products and revenue from licensing, as well as milestone payments. It also includes service income from our contract manufacturing business, such as customer refunds for the purchase of machines required to produce a certain product or for customisation of product formulations
- \*\*\* **Cost of sales** are any costs that can be directly associated with products sales
- # **Gross profit** reveals how much money a company earns taking into consideration the costs that it incurs for producing its products and/or services
- ## **Marketing, Sales & Medical costs** consists of all costs to promote, sell and distribute our products to the customer. This excludes depreciation on acquired products which is part of "other costs"
- ### **Depreciation** of machines, IT equipment and several other items is an incremental part of CoGs, Marketing, Sales and Medical costs, R&D costs. In order to derive the Earnings before interest, taxes, depreciation and amortisation (EBITDA), it needs to be added back
- + **Adjusted EBITDA**, short for adjusted Earnings Before Interest, Taxes, Depreciation and Amortisation, is a key performance indicator for the Grünenthal Group. It is calculated by adjusting the operating result for amortisation, depreciation and impairment and special effects, in particular from restructuring and acquisition-related expenses

“ The trust investors place in Grünenthal encourages us to continue our growth strategy.

**Fabian Raschke**  
Chief Financial Officer

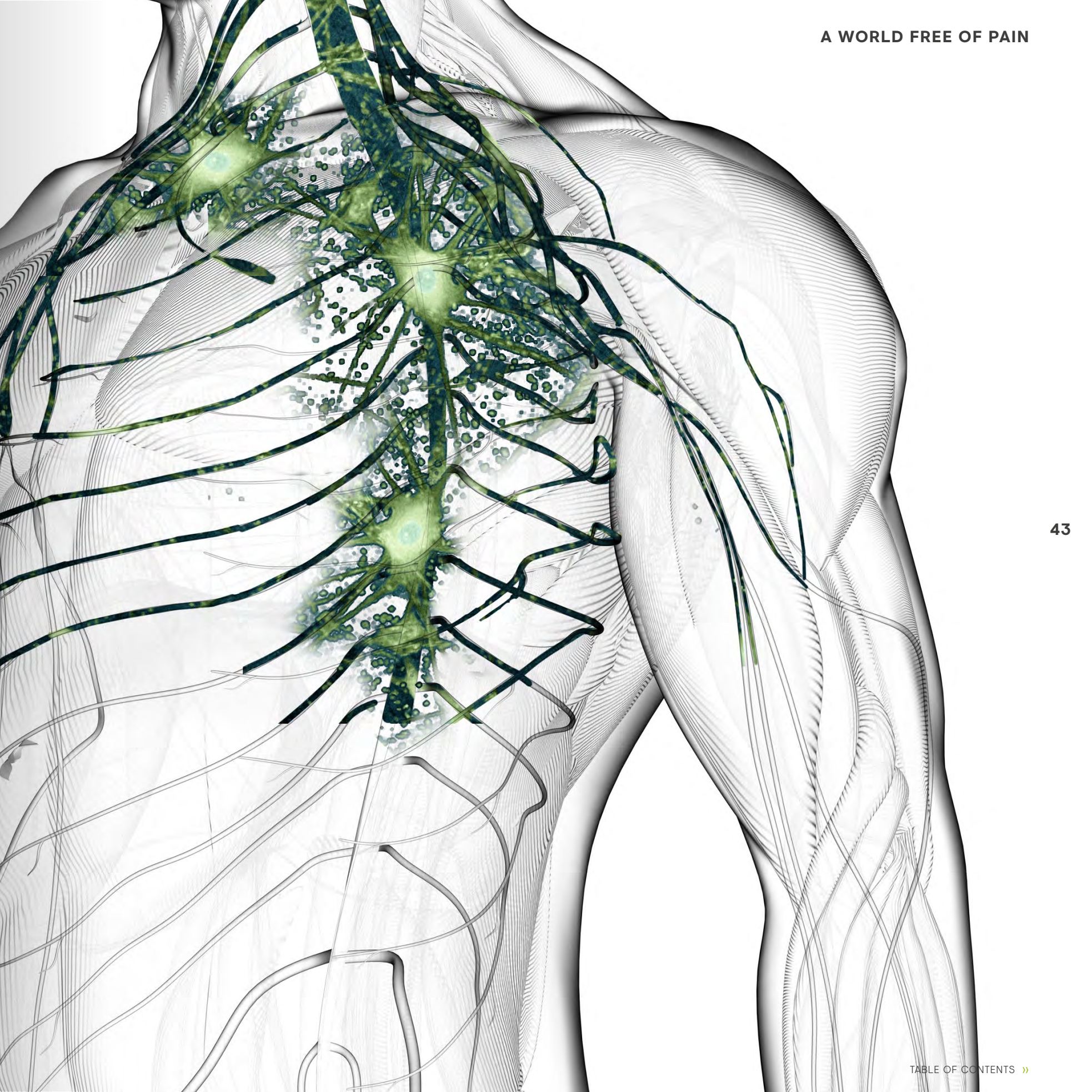


# A WORLD FREE OF PAIN

For more than 50 years, we have been a leading innovator in pain treatments that address critical unmet medical needs and bring us closer to our vision of a World Free of Pain.









# UNDERSTANDING PAIN

More than 1.5 billion individuals suffer from chronic pain<sup>3</sup>  
– almost one in five people worldwide.

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This disease is one of the most common reasons for seeking medical help. It is also a frequent cause of people withdrawing from the labour market early and a significant contributor to disability retirement.<sup>4</sup> It is associated with multiple conditions, and many patients struggle to find effective relief from available medicines.

## Chronic pain

At Grünenthal, we consider pain a disease in its own right rather than just a symptom. We have dedicated the last 50 years to delivering innovative treatment options for people affected by pain. That dedication led to developing six important treatment options

for pain patients – and we are now a global leader in pain research and management.

This success story began in the 1970s with Tramal™ (Tramadol), which is still one of the most frequently prescribed opioid analgesics in the world. Palexia™ (Tapentadol) is another example. It was the first innovative molecule in the opioid analgesic class to be approved for over 25 years. Our non-opioid product Qutenza™ leverages Nobel Prize-winning science and is at the heart of pain leadership.

We know patients are still seriously underserved in this therapeutic area. That is why we are determined to

develop the next generation of pain medicines. Our R&D activities focus on four strategic indications that are characterised by a substantial unmet medical need in large patient populations:

- Peripheral neuropathic pain
- Chronic post-surgical pain
- Chronic low back pain
- Osteoarthritis

Our innovators have been driving progress towards our vision of a World Free of Pain for more than half a century. With every research project we launch and every medicine we create, we seek to relieve pain and make life better for patients and their families.





# A GLOBAL DISEASE

Pain is generating an increasingly large burden worldwide.<sup>5</sup> It impacts patients, their families, caregivers, and society as a whole.

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Chronic pain refers to pain that lasts longer than three months.<sup>6</sup> In chronic pain syndromes, pain can be the sole or a leading complaint or can be secondary to an underlying disease.<sup>7</sup> The condition is influenced by multiple interconnected biological, psychological and social factors. This might include injury, illness

or nerve damage, poor sleep, anxiety or depression.<sup>8</sup>

In 2019, chronic pain was recognised as a health condition in its own right by the International Association for the Study of Pain and the World Health Organization.<sup>9</sup> Patients need better solutions to manage their pain as many current pain

treatments do not provide sufficient relief or have severe side effects. Grünenthal continues to invest in researching innovative, non-opioid pain medicines and ensures that more patients can benefit from its medicines.

## Some of the most common types of chronic pain are<sup>9</sup>:

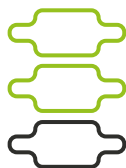
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Migraine



Pain associated with osteoarthritis



Low back pain or lumbar pain



Neck pain



Musculoskeletal pain

**1 in 5**

people suffer from chronic pain worldwide.<sup>3</sup>

**60%**

of permanent work incapacity in Europe is related to musculoskeletal pain alone.<sup>10</sup>

**13%**

Lower back pain prevalence in Southern Latin America in 2017.<sup>11</sup>

**78%**

of chronic pain patients state that they were not satisfied with the efficiency of the treatment they received.<sup>12</sup>

**53–90%**

of adults with chronic pain experience a clinically significant degree of insomnia.<sup>13</sup>

**\$560–635 bn**

estimated medical costs and lost productivity per year caused by chronic pain in the US.<sup>8</sup>

**€300 bn**

estimated total cost of the consequences of chronic pain across Europe.<sup>14</sup>

# DEVELOPING LIFE-CHANGING TREATMENTS

We meet the unmet medical needs of patients worldwide by driving innovation in the therapeutic area of pain.

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“ The scientific community has made great progress in understanding pain and its pathophysiology in recent years. Grünenthal strives to play a leading role in translating these insights into novel therapies.

**Jan Adams, MD**  
Chief Scientific Officer



Existing pain therapies work for some patients – but not for all of them. One European survey revealed that 40 percent of patients were unsatisfied with their pain management.<sup>15</sup> This shows the clear need for innovative treatment options that provide better outcomes for more patients.

Grünenthal is uniquely positioned in the therapeutic area of pain. Since the 1970s, we have focused on developing innovative pain therapies and have become a leading company. Our scientists have developed several life-changing pain medicines for patients. And in 2022, we made significant progress in strengthening our pipeline and moving forward with high-priority projects.

	RESEARCH/ PRE-CLINICAL	PHASE I	PHASE II	PHASE III
<b>Qutenza™</b> (Capsaicin 8%)	Post-surgical neuropathic pain (PSNP)			
<b>RTX</b> (Resiniferatoxin)	Osteoarthritis			
<b>MPC-06-ID*</b> (Rexlemestrocel-L)	Chronic low back pain (degenerative disc disease)			
<b>GRM</b> (Glucocorticoid Receptor Modulator)	Chronic inflammatory diseases			
<b>NOP</b> (Nociceptin/Orphanin Peptide Receptor Agonist)	Chronic pain			
<b>NOP Back-up</b> (Nociceptin/Orphanin Peptide Receptor Agonist)	Chronic pain			
<b>Ion channel programme</b>	Acute and chronic pain			

\* Collaboration with Mesoblast



# OUR KEY PROJECTS IN R&D

We are pursuing a range of programmes that aim to move us closer towards achieving our vision of a World Free of Pain.

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In April 2021, we acquired the Swiss biotech company Mestex AG and its innovative investigational medicine resiniferatoxin (RTX). This is a potential intra-articular treatment for pain associated with osteoarthritis (OA) of the knee, a condition which currently cannot be cured. RTX is a highly potent TRPV1 agonist with a well-validated mechanism of action. Initial data indicates a long-lasting and significant analgesic effect, functional improvements compared to placebo and a favourable safety profile.

In 2022, Phase III trials started to investigate the efficacy and safety of intra-articular injections of RTX in adults with knee osteoarthritis who have exhausted available treatment options and still suffer from moderate to severe pain. These studies are part of a global

development programme that aims to meet requirements for approval in the EU, the US and Japan. Grünenthal entered an agreement with NovaQuest Capital Management to support these trials in March 2022. NovaQuest is a life science investment firm and will reimburse Grünenthal's investments into the clinical Phase III programme for RTX while sharing the clinical development and approval risks with us. In case of successful development and marketing approval, NovaQuest receives one-time payments or milestones and revenue-based payments over the course of the commercialisation.

In addition, we signed a licensing agreement with the Japanese pharmaceutical company Shionogi in August 2022. Shionogi obtained the exclusive rights

to commercialise RTX for pain associated with OA of the knee in Japan if the Phase III trials are successful. Grünenthal will carry out manufacturing and supply under this partnership's terms.

RTX has the potential to be a transformative asset for Grünenthal and the patients we serve. It strengthens our late-stage pipeline with a global development programme covering Europe, the US and Japan – opening up a significant business opportunity.



## Osteoarthritis

Approximately 528 million people around the world suffer from osteoarthritis.<sup>2</sup> This progressive condition is the most common joint disease in people 65 years of age and older, mainly affecting the knees, hands, hips, neck and lower back. Osteoarthritis causes tissue in the joints to break down over time, and currently, there is no cure for this condition. Patients with inflamed, swollen and painful joints often experience limited mobility and reduced quality of life.<sup>16</sup>

For many patients, the available treatment options are not sufficient. Severe symptoms can sometimes occur, including pain. Osteoarthritis treatment typically involves exercise, maintaining a healthy weight and taking medication such as intra-articular corticosteroids.<sup>17</sup> Many patients eventually require joint replacement surgery.

### **Qutenza™ – Reaching more patients in the US**

The US FDA approval of Qutenza™ for the treatment of pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults marks a major milestone in our efforts to bring this treatment to more patients. Painful DPN is a progressive and debilitating complication of diabetes that affected more than five million Americans in 2020 and is challenging to diagnose, treat and manage effectively.<sup>18</sup>

Qutenza™ is a topical system containing prescription-strength capsaicin. It is a non-opioid treatment that can provide

prolonged pain relief for several months while most frequently reported adverse events were transient, self-limiting, mild to moderate application site reactions.<sup>19</sup>

In Europe, it is approved for the treatment of peripheral neuropathic pain. In the US, it is approved for the treatment of peripheral neuropathic pain associated with post-herpetic neuralgia, and in 2020 it also received approval for the treatment of pain associated with DPN of the feet in adults.<sup>20</sup>

Our life-cycle management efforts focus on making Qutenza™ more widely available by expanding the label particularly in the US. Specifically, our

researchers developed an additional Phase III programme to study the efficacy, safety and tolerability of Qutenza™ in post-surgical neuropathic pain (PSNP). The first patients were enrolled in a pivotal Phase III trial in Q3 2021. We also pursue further exploratory activities with external partners in other indications.



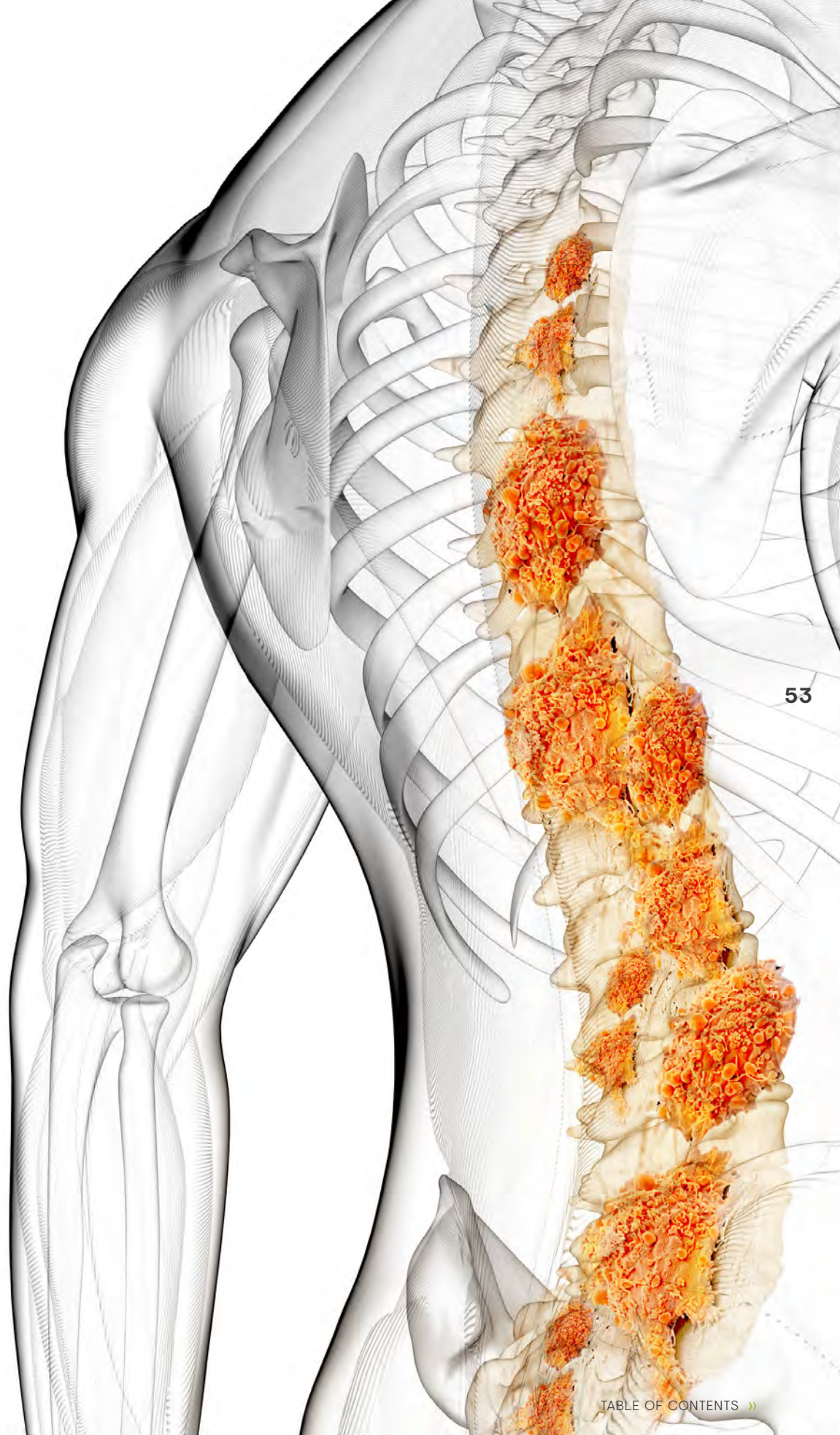


## **MPC-06-ID – Cell therapy for chronic low back pain**

In 2019, we partnered with Mesoblast to develop a highly innovative mesenchymal precursor cell therapy for patients with chronic low back pain associated with degenerative disc disease who have not found effective relief from available treatment options.

Early in 2021, Mesoblast published results from the Phase III trial MSB-DR003 that was carried out in the US and Australia. The trial provided several important findings, including a significant and long-lasting treatment effect on pain relief. However, it did not achieve its primary outcome measure between the treatment groups.

After analysing the data obtained through this trial, Mesoblast anticipated conducting another confirmatory trial in the US and received positive feedback from the FDA regarding a new Phase III programme for MPC-06-ID in patients with chronic low back pain due to degenerative disc disease. The new trial will be conducted with up to 20 percent of the patient population involved being from Europe to support potential product approvals in both the US and Europe.





## NOP – Promising treatment for patients with pain

Our proprietary Nociceptin/Orphanin FQ Peptide receptor (NOP) agonist franchise of molecules reflects the culmination of many years of pioneering research in the field of NOP receptor analgesics. These molecules possess a unique mechanism of action for treating chronic pain and are predicted to provide robust pain relief without the side effects commonly associated with opioids.

Our most advanced NOP agonist was recently tested in a human experimental pain clinical study in healthy participants and produced a significant reduction in both electrical signaling in pain pathways, as well as the subjective perception of pain. Ongoing Phase I trials are further evaluating its safety, tolerability and pharmacokinetics and results from these early clinical studies will inform further testing of the molecule in chronic pain patients.

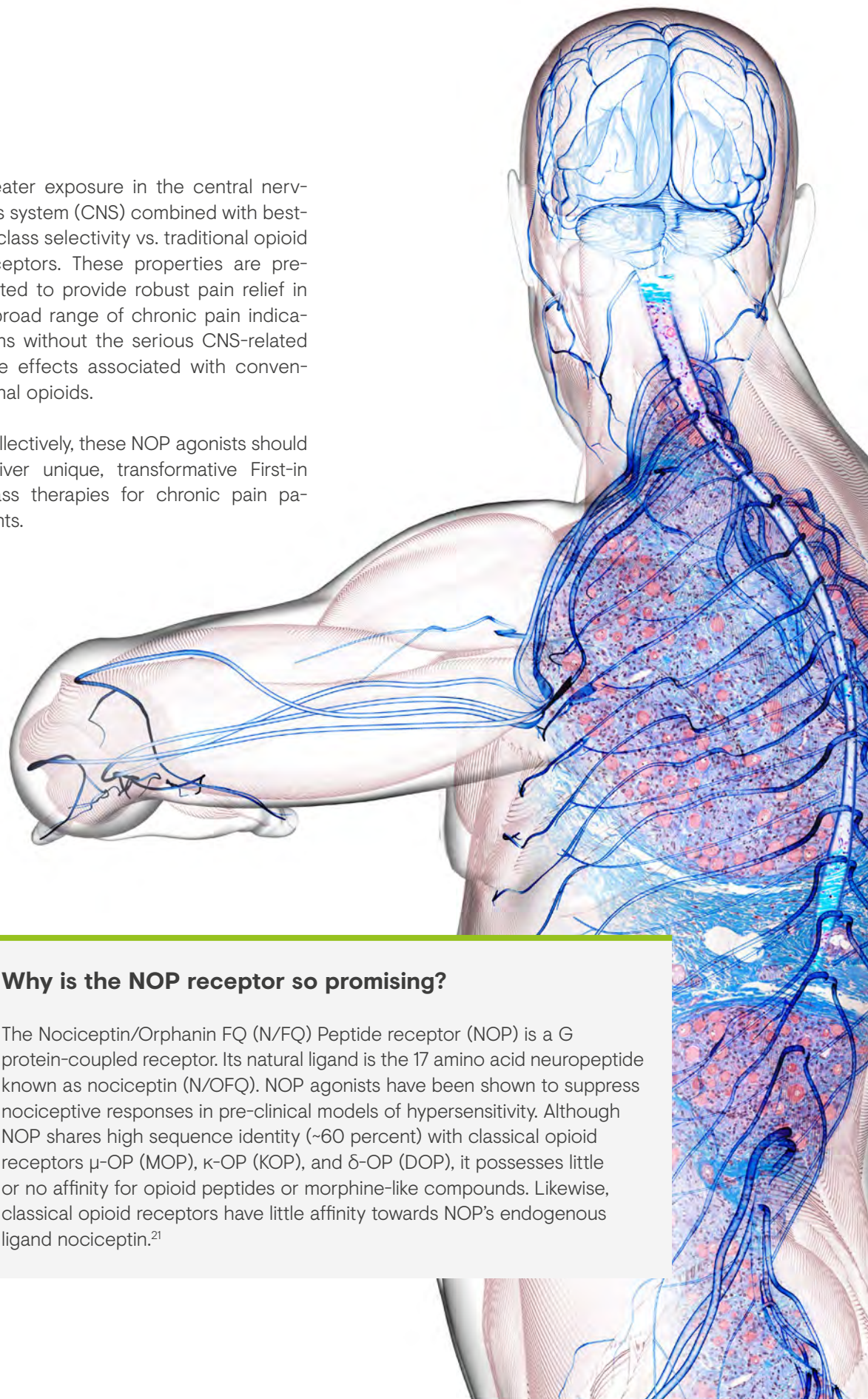
We also have recently selected an additional NOP agonist for clinical investigation. This follow-on NOP agonist has been engineered to have significantly

greater exposure in the central nervous system (CNS) combined with best-in-class selectivity vs. traditional opioid receptors. These properties are predicted to provide robust pain relief in a broad range of chronic pain indications without the serious CNS-related side effects associated with conventional opioids.

Collectively, these NOP agonists should deliver unique, transformative First-in Class therapies for chronic pain patients.

### Why is the NOP receptor so promising?

The Nociceptin/Orphanin FQ (N/FQ) Peptide receptor (NOP) is a G protein-coupled receptor. Its natural ligand is the 17 amino acid neuropeptide known as nociceptin (N/OFQ). NOP agonists have been shown to suppress nociceptive responses in pre-clinical models of hypersensitivity. Although NOP shares high sequence identity (~60 percent) with classical opioid receptors  $\mu$ -OP (MOP),  $\kappa$ -OP (KOP), and  $\delta$ -OP (DOP), it possesses little or no affinity for opioid peptides or morphine-like compounds. Likewise, classical opioid receptors have little affinity towards NOP's endogenous ligand nociceptin.<sup>21</sup>



### **GRM – Potential anti-inflammatory with an improved safety profile**

Our proprietary Glucocorticoid Receptor Modulator (GRM) is an oral investigational medicine developed to bring broad anti-inflammatory efficacy and a safety profile allowing for longer-term treatment addressing unmet medical needs and making a true difference in patients' every-day lives.

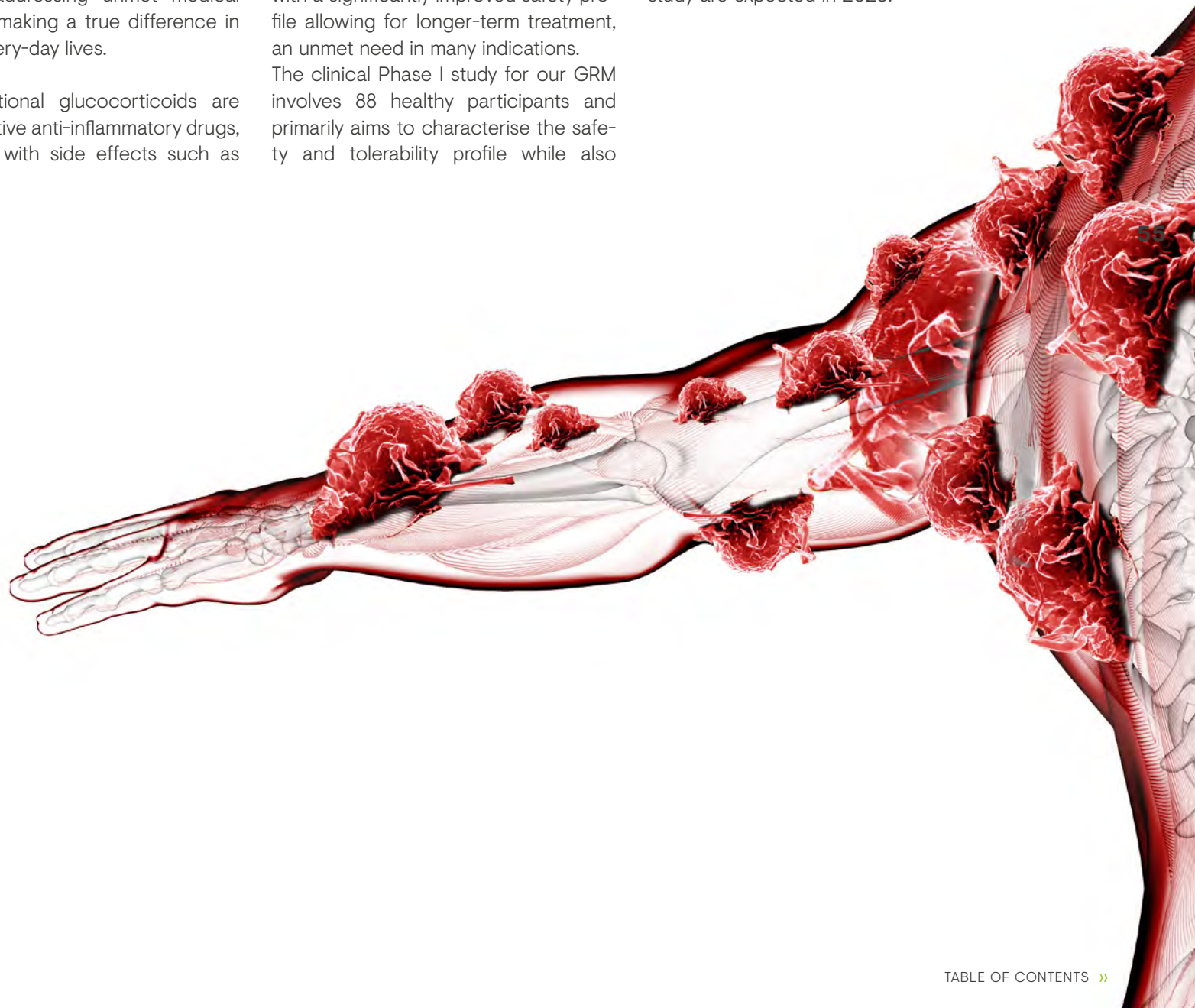
While traditional glucocorticoids are highly effective anti-inflammatory drugs, they come with side effects such as

reduced bone formation that may lead to osteoporosis and increased glucose levels, which raise the risk of diabetes, limiting their use in effective doses to short-term treatment.

Our new GRM compound has the potential to combine the efficacy of traditional glucocorticoids like prednisolone with a significantly improved safety profile allowing for longer-term treatment, an unmet need in many indications. The clinical Phase I study for our GRM involves 88 healthy participants and primarily aims to characterise the safety and tolerability profile while also

confirming the pharmacokinetic characteristics of the compound.

By obtaining biomarker data early in clinical development, our experts aim to confirm whether our GRM has the potential to offer a therapy option that combines high efficacy with a favourable safety profile. The results of the study are expected in 2023.





# TURNING BIG POTENTIAL INTO PATIENT BENEFITS

Since acquiring the promising investigational medicine RTX in 2021, our experts have achieved constant progress to bring this potential life-changer closer to market launch.

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Acquiring innovative investigational medicines is the first step in a complex process. Grünenthal's teams bring together wide-ranging expertise in how to drive investigational medicines through clinical development – and tap into their potential to generate positive outcomes for the patients we serve. Our progress with resiniferatoxin (RTX) is a powerful example of this approach in action. This investigational medicine entered our portfolio in April 2021, when Grünenthal acquired the Swiss biotech company Mestex AG. Since then, we have taken decisive steps to advance this potential treatment on its journey into the lives of patients suffering from pain associated with osteoarthritis (OA) of the knee.

## A promising late-stage asset

RTX is a highly potent Transient Receptor Potential Vanilloid 1 (TRPV1) agonist developed based on research that won the Nobel Prize in Physiology

or Medicine in 2021. The initial data gathered by Mestex AG indicates that this investigational medicine achieved a long-lasting, significant analgesic effect and functional improvements when compared to placebo (saline injection). It also offered a favourable safety profile. This made it an attractive asset for Grünenthal's M&A strategy, mainly because of its potential to provide relief for a large population of pain patients – with approximately 528 million people suffering from osteoarthritis worldwide.<sup>2</sup>

Currently, osteoarthritis cannot be cured. Patients typically receive a range of oral anti-inflammatory medicines, many will also receive intra-articular corticosteroids or even undergo knee replacement surgery to relieve the pain of inflamed and swollen joints. RTX is a non-opioid which has the potential to provide long-lasting pain relief and functional improvement of the joints.

*Latex extraction  
from an euphorbia  
resinifera*







### Entering Phase III

Grünenthal is now investigating the efficacy and safety of intra-articular injections of RTX in adults by conducting three trials across approximately 200 sites in Europe, the US, Latin America, South Africa and Japan. Just one year after the acquisition, the Grünenthal team enrolled the first patients in the global clinical Phase III programme. The trials, which commenced in August 2022, will include more than 1,800 patients with knee osteoarthritis who have exhausted available treatment options and still suffer from moderate to severe pain. The Phase III programme aims to enable marketing approval for RTX in the EU, the US, and Japan if successful.

### Partners for developing RTX

Our partnership with the US-based life science investment firm NovaQuest Capital Management supports these Phase III trials. Grünenthal entered an agreement with NovaQuest in March 2022, and the two companies are now advancing the RTX development process together.

Under the terms of the agreement, NovaQuest will reimburse Grünenthal's investments into the clinical Phase III programme for RTX, and will share the clinical development and approval risks with Grünenthal. If RTX successfully achieves marketing approval, NovaQuest will receive one-time payments or milestones and revenue-based payments throughout the commercialisation. This agreement frees up Grünenthal's resources to make further investments in executing its growth strategy and advancing its promising pipeline into the clinic.

### Reaching patients worldwide

Grünenthal is also engaging in partnerships that aim to maximise the patient population that can benefit from access to RTX if it is approved for market launch. For example, we entered a licensing agreement with Shionogi in August 2022. Shionogi is a leading global research-driven pharmaceutical company based in Japan. With this deal, it obtained exclusive rights to commercialise RTX in Japan for pain associated with knee osteoarthritis for a

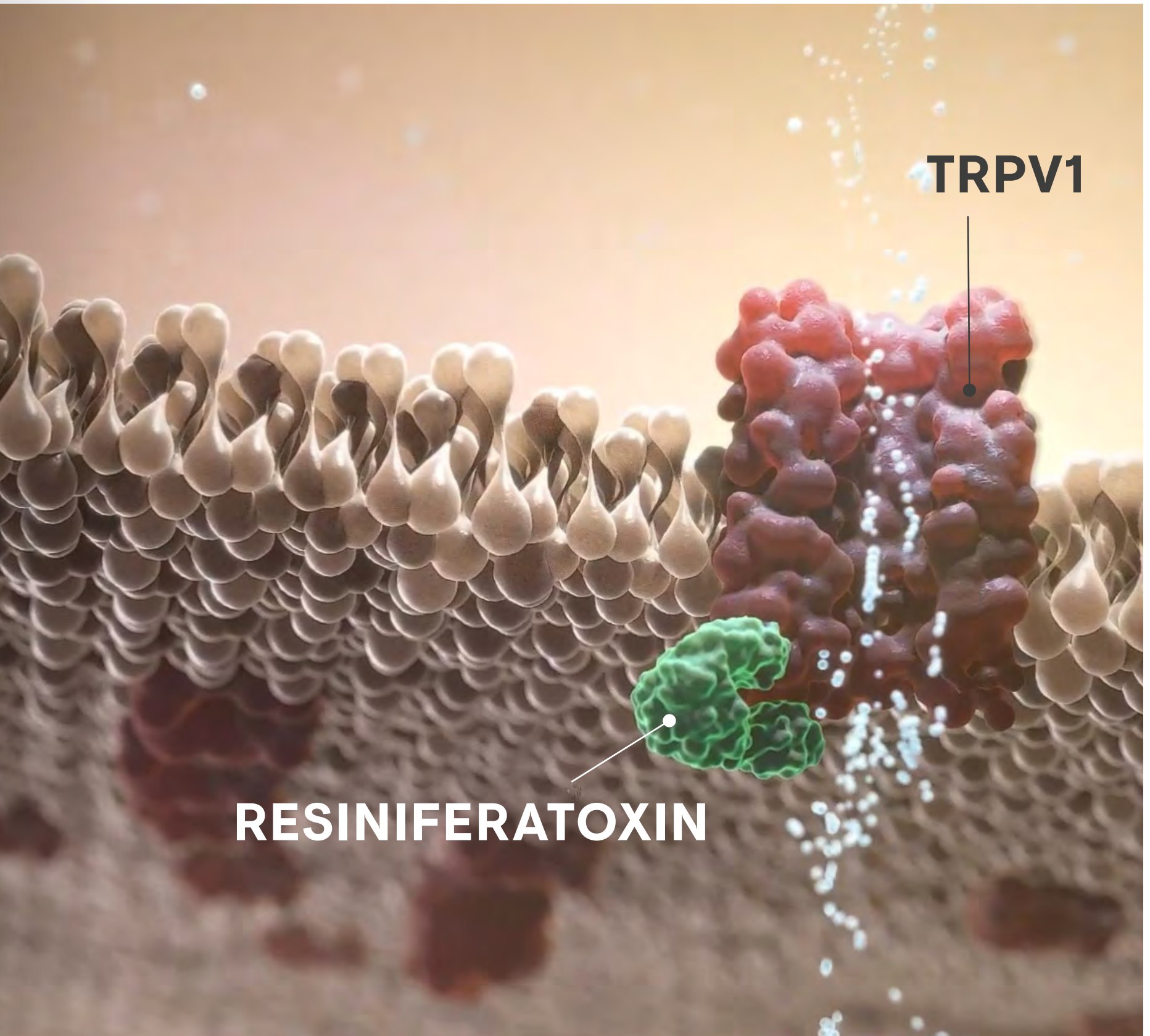
total consideration of up to \$525 million plus additional sales-based payments. The agreement includes competitive investment commitments for launch and commercialisation. Grünenthal will manufacture and supply RTX, and Shionogi will leverage its strong commercial presence in Japan to bring RTX to patients in need.

### The osteoarthritis market

Grünenthal holds the global rights for this treatment – and the global osteoarthritis market is expected to grow approximately \$11.0 billion in 2025<sup>22</sup>. Grünenthal intends to explore the potential of RTX for treating osteoarthritis-related pain in additional joints if the outcome of the Phase III programme is positive.

“ Resiniferatoxin is a promising asset for more than 500 million people worldwide<sup>2</sup> who suffer from osteoarthritis and seek a meaningful non-opioid therapy option.

**Gabriel Baertschi**  
Chief Executive Officer



**TRPV1**

**RESINIFERATOXIN**

# EMPOWERING BETTER PATIENT CARE

We support healthcare professionals in providing improved treatments for patients worldwide.

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We aim to improve the lives of people living with pain by developing and delivering life-changing new treatments. To ensure patients receive the best possible care, we focus on clear and efficient communication with physicians, pharmacists, nurses, hospitals, buying groups, wholesalers and other institutions.

We serve this diverse customer base of approximately 250,000 customers by making our products available in more than 100 countries, directly from our 28 affiliates or indirectly from our strategic partners.

Over the last 50 years, we have built a strong presence in Europe as well as in

Latin America, providing millions of people with access to effective pain treatments. There is a significant unmet need in the Latin American region and a lack of sufficient education about chronic pain for healthcare professionals.

In addition, Grünenthal recently expanded its geographical footprint to the US. We have seen significant growth of our non-opioid cutaneous system Qutenza™ in this important market, and we expect this rapid growth to continue in the coming years.

Engaging with such diverse markets and customer groups in today's world requires new ways of operating. In particular, we are convinced that it is

essential to always focus on our customers' needs. With our omnichannel engagement model, we provide a tailored customer experience through meaningful interactions – wherever and whenever our customers need it.



“ We are focused on understanding and meeting our customers’ needs. With this approach, we provide a tailored customer experience that ensures our products and services match what our customers need most, ultimately helping them better help their patients.

**Janneke van der Kamp**  
Chief Commercial Officer





### **Increasing access to pain relief, improving quality of patient care**

During 2021, the Palexia™ team generated new real-world evidence (RWE) data that supports further differentiation of the brand's value for use in patients with severe chronic pain where a patient's doctor has decided that an opioid is necessary. In 2022, the team utilised this data to help physicians better understand Palexia™'s value for patients with severe chronic pain where a patient's doctor has decided that an opioid is necessary. We have a clear commitment to the responsible use of opioid-based medicines. We always ensure adherence to the highest ethical standards and compliance with our Code of Conduct,<sup>23</sup> Opioid Charter<sup>24</sup> and communication guidelines – in every region and across all relevant communication channels.

For Qutenza™, demand from healthcare professionals rose during 2022 with over 77,000 patients treated globally – 16 percent more than in the previous year. In Europe, we continue to see strong growth and are increasingly focused on key account excellence and the

importance of repeated application in potentially improving patient outcomes. In 2022 the emphasis was on creating inspiring medical education and a patient support programme focused on the best use of Qutenza™ and the latest research in pain. This shows our strong commitment to providing supportive tools that improve quality of patient care.

In the US, we now have a robust team covering the whole country. This allows us to fully address the unmet pain management needs of patients with DPN of the feet. We continue to expand our presence in Europe and have seen strong growth in all countries where Qutenza™ is on the market.

Vimovo™ has become an important part of our portfolio and complements our existing range of treatments. This medicine combines effective pain treatment with gastroprotection and is used to treat osteoarthritis. It continues to grow at a robust rate due to high unmet patient needs in this area.

In 2022, Grünenthal acquired the global rights for Nebido™. The first Marketing Authorization transfers took place in November. Nebido™ is a leading brand for the treatment of symptomatic male

hypogonadism, when testosterone deficiency has been confirmed by clinical features and biochemical tests. Symptomatic male hypogonadism is a condition that affects one in six men over the age of 50. The treatment is an intramuscular injection with a unique depot formulation. It is approved and has been successfully commercialised in over 80 countries.

In Latin America, we have adapted our strategy to focus more on innovation – and particularly on pain, our core competency. This has paid off well, with strong growth across our key brands. We have also transformed our go-to-market model into a digital and/or omnichannel approach. We have substantially increased our share of new ways of detailing (e.g., mail, webinars, e-detailing). We delivered approximately 2.6 million omnichannel interactions with customers worldwide in 2022, approximately 34% of which were digital interactions, thanks to our advanced digital capabilities.

With our customer-centric framework in place, we are further strengthening our ability to reach more patients in need and support healthcare professionals in providing the best possible care.

# ACCELERATING THE GROWTH OF QUTENZA™

Qutenza™ is helping Grünenthal take bold steps to address the unmet needs of patients worldwide.

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Our commercial activities for Qutenza™ focus on the customer experience for healthcare professionals, payers and patients. More than five million people in the US suffer from diabetic peripheral neuropathy (DPN)<sup>18</sup>, which is a debilitating complication of diabetes. Successful pain management could vastly improve quality of life for those people. In this context, the FDA approval of Qutenza™ for the treatment of adults with neuropathic pain associated with DPN of the feet in 2020 was a tremendous milestone. It extended access to Qutenza™ to approximately 1.3 million patients in the US - compared to only 60,000 patients under the previous label for postherpetic neuralgia (PHN).

## Smart investments for growth

We broadened our footprint in the US, growing our key account management,

market access and medical affairs teams and hiring top talent. In 2022 in-market volume increased 270 percent vs 2021. This represents the significant potential to reach even more patients in need.

Aligned with our strategic imperative to match our customers' and patients' preferences, we broadened our distribution network, integrating a partnership with a specialty pharmacy in 2021.

Our significant investments in the speciality care market have identified the 10,000 healthcare professionals who treat over half of all neuropathic pain patients. Our peer-to-peer education programme aims to better communicate the science of Qutenza™. In addition, with a healthcare professional and patient portal, we have a fully functioning omnichannel approach

built for a better customer service experience.

## A patient-centred strategy

Making Qutenza™ affordable for patients is also a crucial part of our strategy. In 2021, we launched the first-ever patient out-of-pocket cost-support programme for eligible patients, to ensure more patients who need it can afford this therapy. A new patient advisory council includes patients living with pain to provide insights into our activities.

Healthcare payers are another link in the chain. We increased our team that focuses on payers, updating and expanding their information on Qutenza™. And we have already broadened access to Qutenza™ for eligible patients by increasing the number of covered lives through health insurance companies to 193



million. Looking ahead, we hope to explore further usage and potential benefits of Qutenza™ with a real-world evidence (RWE) initiative to analyse clinical data.

We also launched our first direct-to-patient TV commercial in 2022, helping to ensure that more patients see the value of Qutenza™ and feel empowered to discuss their treatment options with their HCP.

In 2022, Qutenza™ was included in two important US guideline and compendium

updates. This demonstrates the medical community's confidence in this medicine. The 2022 American Diabetes Association (ADA) Clinical Compendia Series recommended Qutenza™ for DPN, which marked the first time Qutenza™ has been recommended as a topical treatment in a professional compendium. Qutenza™ was also included as a first-line recommended medicine for Painful DPN in the American Association of Clinical Endocrinology (AACE) Guideline. This is one of the major international guidelines that includes

recommendations on the management of painful diabetic neuropathy (pDPN).

Our US expansion reflects our commitment to patients and to widening their access to therapies. It also exemplifies our commercial approach of leading with customer experience – bringing both short-term and long-term value. We do this by scaling up products that will sustain our long-term growth and lay the foundation for our future success.

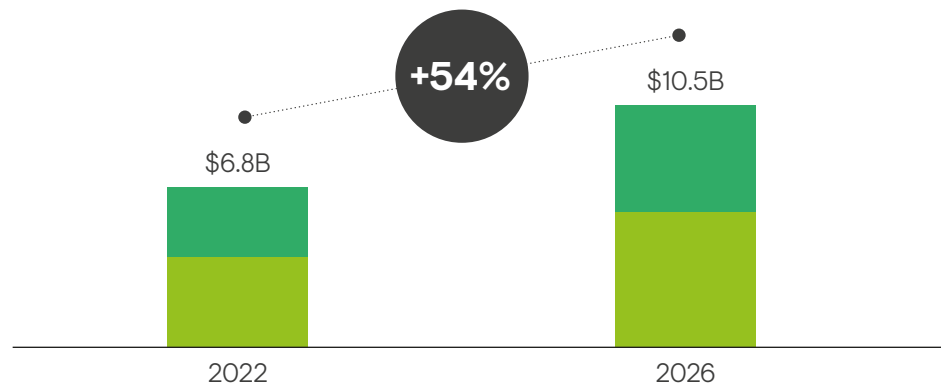




## US business overview

The US represents a 31.6%\* share of the global neuropathic pain market

**Chart: US neuropathic pain market**



**Implication:** As the world's largest neuropathic pain market, the US offers the most favourable unit economics for QUTENZA™, from both a volume and price perspective\*\*.

- Neuropathic pain market
- Total pain market

\* Persistence Market Research, 2023  
\*\* Averitas Internal Data, 2022

“ We have expanded our US team to address the unmet need of patients suffering from postherpetic neuralgia and painful diabetic peripheral neuropathy of the feet. We strive to provide a seamless customer and patient experience throughout the Qutenza™ journey.

**Jeannie Lloyds**

Senior Vice President Commercial of Grünenthal subsidiary Averitas Pharma



# MAXIMISING OUR PORTFOLIO ACROSS THE BRAND LIFECYCLE

Grünenthal's portfolio includes eleven global brands at different stages of the brand lifecycle.

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In 2022, our growth brands comprised our patent-protected brands Palexia™, Qutenza™ and Vimovo™.

Grünenthal's established brands bring together mature and off-patent products. This includes Zomig™, Nexium™, Crestor™ and Versatis™, and brands we have developed over a longer period of time such as Trama™, Transtec™ and Zaldiar™. These established brands are characterised by high brand awareness, predictable sales and strong profitability.

Combining these product profiles gives our company a well-balanced and resilient overall portfolio.

Vimovo™ was an important part of our portfolio in 2022. Active promotion in several countries helped to achieve significant growth of more than 10 percent. We constantly strive for continuous brand growth because we believe there is still untapped potential to be unlocked from these treatments.

Our Palexia™ team has continued to further differentiate the brand for use in patients with severe chronic pain in cases where a doctor has decided that an opioid is necessary. Following a successful 2022 with intrinsic volume growth, we expect loss of exclusivity in Europe and are well prepared to manage this next phase of Palexia™.

Since acquiring Nebido™ at the end of last year, we have started assessing the best way to promote the brand. This includes an omnichannel approach in some markets, with active field teams promoting the brand. In other markets, we are focusing exclusively on digital promotion.





## Managing established brands

Our established brands are at a later stage of their lifecycle. They already face generic competition or other market pressures that could limit growth in demand.

In 2022, we continued to proactively manage these brands through a customer-centric approach delivered via a range of channels. We maintained our strong focus on these brands, with particular emphasis on Nexium™, Zomig™, Crestor™ and Versatis™. This ensured differentiated strategies that reflected the specific market conditions for each treatment, as well as cross-business transparency to boost synergies. Markets where we operate through partners are now a key growth driver for our business, and we have implemented a new strategy and structure that is optimising our network. At the same time, we have further enhanced our activities to identify opportunities to increase demand and reduce or optimise costs.

The results of these efforts surpassed our expectations, with almost all established brands growing faster than the market and delivering increased year-on-year revenue. Overall, our established brands achieved operational revenue of €1,047 million in 2022, which equates to an increase of 7 percent compared to the previous year.

In Latin American markets, Versatis™ is at a much earlier stage in its lifecycle. In Mexico, for example, this brand is still in the post-launch growth phase. Operational revenue from Versatis™ in Latin America increased by 71 percent in

2022 compared to 2021. Globally, this brand delivered operational revenue of €140.9 million in 2022. This is 3 percent higher than in 2021.

Operational revenue of Nexium™ reached €192.5 million in 2022, which is an increase of 3 percent on the previous year. This was made possible by our omnichannel platform and our close collaboration with strong partners.

For Zomig™, we continued to take over production of nasal sprays. We also launched new formulas and package sizes in some European affiliates. We expanded our geographical distribution by launching the product in Canada, and we are continuing preparation for launching this product in several other partner markets. Globally, Zomig™ delivered operational revenue of €70.2 million in 2022, with impressive growth of 12 percent compared to 2021.

Due to proactive management across geographies, a revitalised way of managing our business partners, and a continued effort to optimise costs, we achieved growth for our mature brands in 2022. Compared to the previous year, Tramal™ grew by 12 percent, Zaldiar™ by 4 percent and Transtec™ by 10 percent.

# 69%

of Grünenthal's operational revenue is from established brands.

# INCREASING ACCESS AND AWARENESS

We want to support people to better manage their pain and help them get back to normality – and we are involved in several initiatives that support this goal.



## Initiatives

**CHANGE PAIN™** is an initiative established by Grünenthal in 2009 and endorsed by the European Pain Federation EFIC and Pain Alliance Europe (PAE). The initiative's mission is to improve patient outcomes by strengthening pain management through adequate research, communication and education.

The CHANGE PAIN™ medical education platform is an international initiative that provides tailored educational content about pain to healthcare professionals and patients. Customers attend the CHANGE PAIN™ educational initiatives like meetings and webinars, and use the tools to help educate their staff and peers while also supporting patients' self-management.

In 2022 we reached more than 50,000 health care professionals through

educational events and approximately 580,000 visitors through our educational websites as part of our efforts to educate the healthcare sector about pain management and improve the patient outcomes from pain treatment by providing practical tools for pain therapy building on communication and education.

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

**SOCIETAL IMPACT OF PAIN (SIP)** is a multi-stakeholder partnership led by the European Pain Federation and Pain Alliance Europe, and Grünenthal is one of the main sponsors. The partnership aims to raise awareness about pain and encourage changes to pain policies by providing opportunities for discussion among healthcare professionals, pain advocacy groups, politicians, healthcare insurance providers, representatives of health authorities, regulators and budget holders.

SIP is endorsed by more than 310 European and national patient and healthcare organisations, and collaborates with organisations from other disease areas to advocate for improved management of pain, for example in cancer and rheumatology.

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





## Grants

### EFIC-GRÜNENTHAL GRANT (E-G-G)

Grünenthal supports this grant with up to €110,000. The scientific framework is under the responsibility of the European Pain Federation EFIC.

These grants support early-career scientists within European Pain Federation EFIC member countries to carry out innovative pain research. Since 2004 the E-G-G has successfully funded 70 innovative research projects, awarding almost €1.8 million to participants in more than 14 countries.

The five recipients of the 2022 E-G-G were recognised at the 12th Congress of the European Pain Federation EFIC in April 2022.

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




**BRAIN, MIND AND PAIN (BMP)** is financially supported by Grünenthal to encourage patient-centred innovation in pain research and care. The BMP grant is the first pan-European grant that selects applications based on their impact from a patient's perspective.



The theme of the third edition of the BMP Grant is prevention and self-management, focusing on “Healthy Sleep For People Living With Brain, Mind And Pain Conditions”. Results from the 2022 projects will be presented in 2023.

[www.bmp-grant.eu](http://www.bmp-grant.eu)

# GLOBAL BRANDS

Providing solutions for patients with high medical needs.

BRAND NAME	ACTIVE INGREDIENT / TECHNOLOGY	INDICATION RANGE*	OPERATIONAL REVENUE** 2022 IN € MILLION
	Capsaicin	<p><b>EU indication:</b> Treatment of peripheral neuropathic pain in adults either alone or in combination with other medicinal products for the treatment of pain.</p> <p><b>US indication:</b> Treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults.</p>	76.0
	Fixed-dose combination of Esomeprazole and Naproxen	In adults for the 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.	66.6
	Lidocaine	<p><b>EU and Peru indication:</b> Symptomatic relief of neuropathic pain associated with previous herpes zoster infection (postherpetic neuralgia, PHN) in adults.</p> <p><b>Latin America indication:</b> Treatment of localized neuropathic pain, including pain associated with a previous herpes zoster infection (postherpetic neuralgia).</p>	140.9
 AscoTop® Nasal	Zolmitriptan	<p><b>Oral formulations:</b> In adults aged 18 years and older for acute treatment of migraine headache with or without aura.</p> <p><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.</p>	70.2

BRAND NAME	ACTIVE INGREDIENT / TECHNOLOGY	INDICATION RANGE*	OPERATIONAL REVENUE** 2022 IN € MILLION
	Testosterone undecanoate	Treatment of male hypogonadism, when testosterone deficiency has been confirmed by clinical features and biochemical tests.	18.1 <sup>#</sup>
	Esomeprazole	<p><b>20 mg; 40 mg gastro-resistant tablets: Indicated in adolescents from the age of 12 years and in adults for:</b></p> <p>Gastroesophageal reflux disease (GERD)</p> <ul style="list-style-type: none"> <li>• treatment of erosive reflux esophagitis</li> <li>• long-term management of patients with healed esophagitis to prevent relapse</li> <li>• symptomatic treatment of GERD</li> </ul> <p><b>Indicated in adults for:</b></p> <p>In combination with appropriate antibacterial therapeutic regimens for the eradication of <i>Helicobacter pylori</i> and:</p> <ul style="list-style-type: none"> <li>• healing of <i>Helicobacter pylori</i> associated duodenal ulcer</li> <li>• prevention of relapse of peptic ulcers in patients with <i>Helicobacter pylori</i>-associated ulcers</li> </ul> <p><b>Patients requiring continued NSAID therapy:</b></p> <ul style="list-style-type: none"> <li>• healing of gastric ulcers associated with NSAID therapy</li> <li>• prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk</li> </ul> <p><b>Prolonged treatment after intravenous-induced prevention of rebleeding of peptic ulcers.</b></p> <p><b>Treatment of Zollinger Ellison Syndrome.</b></p> <p><b>Indicated in adolescents from the age of 12 years:</b></p> <p>In combination with antibiotics in treatment of duodenal ulcer caused by <i>Helicobacter pylori</i>.</p> <p>Nexium™ is also available in other dosage forms with slightly varying indications.###</p>	192.5



\* Status: April 2022. 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)




\*\* without license and milestone income

<sup>#</sup> Comprises operational revenue from sales of Nebido™ in November and December 2022, following initial consolidation of revenue from Nebido™ as of November 1, 2022.

<sup>##</sup> see SmPC for 'Nexium™ 10 mg gastro-resistant granules for oral suspension, sachet' and for 'Nexium™ 40 mg Powder for solution for injection/infusion'



BRAND NAME	ACTIVE INGREDIENT / TECHNOLOGY	INDICATION RANGE*	OPERATIONAL REVENUE** 2022 IN € MILLION
 CRESTOR® rosuvastatin	Rosuvastatin	<p><b>Treatment of hypercholesterolaemia</b></p> <p>Adults, adolescents and children aged 6 years or older with primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate.</p> <p>Adults, adolescents and children aged 6 years or older with homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments ( e.g. LDL apheresis) or if such treatments are not appropriate.</p> <p><b>Prevention of cardiovascular events</b></p> <p>Prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors.</p>	68.5#
PALEXIA	Tapentadol	<p><b>Prolonged-release tablet:</b></p> <p>Management of severe chronic pain in adults which can be adequately managed only with opioid analgesics.</p> <p><b>Film-coated IR tablet:</b></p> <p>Relief of moderate to severe acute pain in adults which can be adequately managed only with opioid analgesics.</p> <p><b>Oral solution:</b></p> <p>Relief of moderate to severe acute pain in children## from 2 years of age and in adults, which can be adequately managed only with opioid analgesics.</p>	Palexia™ 333.7 + Partner sales of Nucynta™ in the US: \$184.5 mn
 Tramadol	Tramadol	<p><b>EU and LATAM indication:</b></p> <p>Treatment of moderate to severe pain.</p>	96.1

BRAND NAME	ACTIVE INGREDIENT / TECHNOLOGY	INDICATION RANGE*	OPERATIONAL REVENUE** 2022 IN € MILLION
 ZALDIAR®	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.	62.6
 Transtec®	Buprenorphine	Transtec™: Treatment of moderate to severe cancer pain and severe pain which does not respond to non-opioid analgesics. Transtec™ is not suitable for the treatment of acute pain.	52.4
 NORSPAN® DAS 7-TAGE-SCHMERZPFLASTER		Norspan™: Management of moderate to severe chronic pain.###	

\* Status: April 2022. 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)

\*\* without license and milestone income

# profit transfer following the acquisition of Crestor™ in February 2021

## in children restricted to hospital use where appropriate equipment to enable respiratory support is available and for a maximum treatment duration of 3 days

### Please note that for Norspan™ Grünenthal is only the Market Authorisation Holder in Latin America

# STATEMENT ON THE RESPONSIBLE USE OF OPIOID-BASED MEDICINES

General considerations for pain management with any medication that contains an opioid mechanism of action.

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## The following general aspects should be considered:

- An individualised, patient-centred approach for diagnosing and treating pain is essential to establish a therapeutic alliance between patient and clinician.
- Consider patient variables that may affect opioid dose for each patient prior to opioid use.<sup>25</sup>
- In patients with acute pain e.g. post-surgery pain, the use of medication should be for the shortest necessary time.<sup>25</sup> All patients should be carefully selected, abuse risk factors evaluated, and regular monitoring and follow-up implemented to ensure that opioids are used appropriately<sup>26-27</sup> and in alignment with treatment goals (pain intensity and functionality), as agreed with the patient.<sup>26-27</sup>
- Patients should be made aware of the potential side effects of opioids and the potential for developing tolerance, dependence and addiction.<sup>26-27</sup>
- It is important to optimally use multimodal, non-opioid approaches in acute and chronic pain before escalating to opioids or in conjunction with opioid therapy.<sup>25</sup>
- Addiction is possible even when opioids are taken as directed. The exact prevalence of abuse in patients treated with opioids for chronic pain is difficult to determine.<sup>28</sup>
- Regular clinical reviews are required for long-term opioid treatment to assess pain control, impact on lifestyle, physical and psychological well-being, side effects and continued need for treatment.<sup>29</sup>
- Any long-term treatment with opioids should be monitored and re-evaluated regularly, incl. tapering down the dose or discontinuing treatment.<sup>26-27</sup>
- Signs of opioid use disorder should be monitored and addressed.<sup>26-27</sup>
- Patients and the general public can benefit from clear educational materials and awareness interventions to support the responsible use of opioids.<sup>30</sup>

Scan here to see  
the Grünenthal  
Statement on the  
Responsible Use of  
Opioids







# CUTTING-EDGE SCIENCE

Our experts engage in pioneering research to find next-generation pain medicines, and develop advanced technologies to bring life-changing treatments to patients in need – wherever they are in the world.









# CREATING INNOVATIVE MEDICINES

Scientists at Grünenthal identify and develop promising potential treatments by identifying the best targets, leveraging our expertise in bioinformatics and systems biology, and combining this with our deep knowledge of pain biology.

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## **Predictive validity**

Scientists in the pain field have learned that pre-clinical behavioural models do not have sufficient predictive validity to serve as the basis for selecting new targets. For example, the expression profile of proteins varies between species and the function of targets may also differ.

Our experts work on human genetic and clinical data and develop pre-clinical models using human tissues and cells to select targets. This should minimise attrition due to a lack of efficacy in clinical development. For example, we investigate human cells such as nociceptive neurones, which carry pain signals from the periphery to the spinal cord. By working on these neurones and

examining how they interact with other cell types, we can understand how they work in health and pain conditions.

Grünenthal's researchers are investigating the role of key targets in processing pain signals and evaluating whether natural variation in a target, such as genetic differences, may have functional consequences. Beyond genetic evidence, we look for existing clinical evidence that modulating the activity or function of a target may impact pain. We consider a target very promising if it is possible to combine an understanding of its function in pain processing with clinical and genetic evidence for a role in pathophysiology. In addition, we consider the safety implications of modulating a target before adopting it into our portfolio.

## **Turning data into knowledge**

We use our bioinformatics and systems biology expertise to screen, analyse and process the large volume of omics data – and to turn that data into knowledge that can inform our research activities. By joining forces with external partners, we build strong collaborative relationships with academic groups and other experts to mine this data and understand how different cells and tissues communicate in painful conditions.





### Omics data

Omics-approaches refer to a group of high-throughput technologies that are used to analyse large sets of biological data, such as genomics, transcriptomics and proteomics. In contrast to genetics, which focuses on single genes, genomics analyses genomes, the entire set of genes of an organism and their inter-relationships. Accordingly, proteomics study all proteins produced by an organism and transcriptomics look into all RNA molecules, including mRNA, rRNA, tRNA, and other non-coding RNAs.



“ At Grünenthal, we bring together diverse international talent, a focused research strategy and an excellent network with organisations that share our passion for scientific progress.

**Gillian Burgess,**  
Head of Research

## Pain research at Grünenthal



### Focused therapeutic area strategy

We focus our R&D efforts on four pain indications characterised by high unmet medical need.



### Comprehensive disease understanding

Deep understanding of the underlying human disease biology enables us to identify well validated, highly promising targets.



### Double down on most promising targets

We pursue targets holistically and leverage a wide range of modalities to minimise compound-specific risks and maximise probability of success.



### Teaming up

We collaborate with leading institutions around the world to tap into the best science and technologies wherever they exist.

## A concise therapeutic area strategy

Substantial in-house research including identification and validation to disease understanding. Projects in all phases from research up to clinical development are potential interest



Peripheral neuropathic pain



Chronic low back pain



Osteoarthritis



Chronic post-surgical pain

Focus on identifying and establishing collaborative partnerships for projects undergoing clinical development.



Peri-surgical pain



Migraine



Fibromyalgia



CRPS



# JOINING FORCES FOR INNOVATION

Grünenthal collaborates with pioneering partners to develop next-generation treatments and research methodologies.

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Despite extensive research, limited progress in bringing forward innovative pain medicines has been made in recent years to address remaining unmet medical needs. One reason is a significant need for better translational models in pain research. Scientists have traditionally used rodent models to investigate the cellular and molecular mechanisms involved in pain. However, the findings frequently failed to translate into the clinical setting due to fundamental differences in molecular, cellular and genetic mechanisms of pain across species. As a result, there is a high interest in establishing pre-clinical models that can more accurately represent the conditions in the human body. Together with their partners around the globe, Grünenthal scientists are taking on this challenge and work on creating humanised pre-clinical models to support the development of the next generation of pain medicines.

## Advancing pain research with partners

Our work with Uniklinik RWTH Aachen and RTWH Aachen University is just one example of this collaborative approach in action. We are joining forces with the shared aim of developing translational research tools and humanised pre-clinical models for target validation, by using human cells and tissue during pre-clinical testing. This will involve creating

a shared local infrastructure to ethically and reliably source human Dorsal Root Ganglia (DRGs) and other tissues of interest. In addition, we are closely examining differences between human and non-human models, and aim to identify the best surrogate species for supporting mechanistic translation into the clinic as efficiently as possible. If successful, this cooperation will enable new methods to be integrated into drug development activities at Grünenthal.

“ We pursue the common goal of creating a distinct translational toolbox for pain R&D and increasing our understanding of the pathological processes causing chronic pain.

**Jan Adams, MD**  
Chief Scientific Officer

## Enhancing human validation

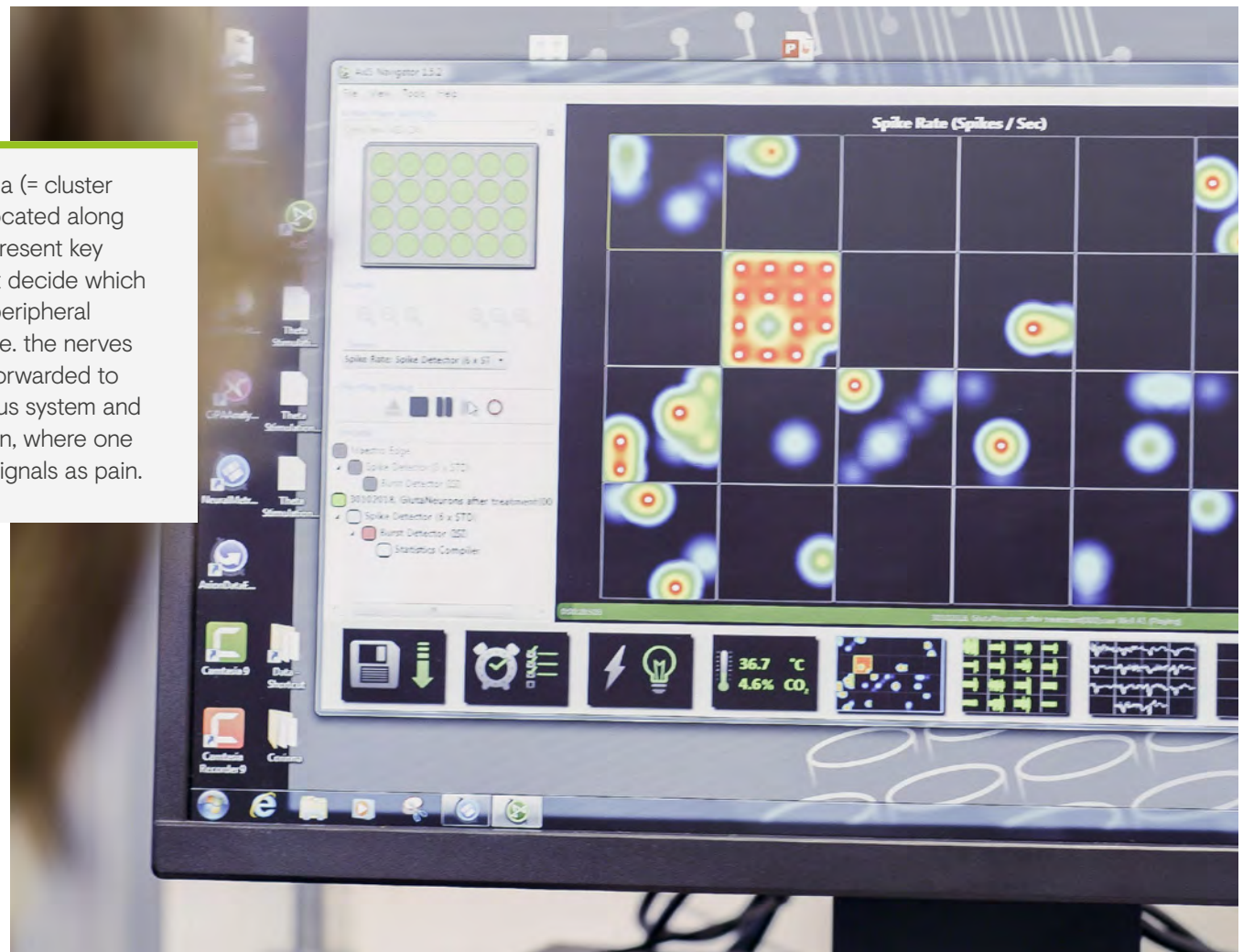
By partnering with McGill University in Montreal, Canada, we are further striving to enhance our access to high-quality human tissue for pain R&D. McGill is a centre of excellence for pain research, with experts conducting pioneering research at the Alan Edwards Centre for Research on Pain. As part of this collaboration, McGill sends human tissue to our strategic partners (Contract Research

Organisations, CROs), which are located in the immediate vicinity of McGill University, to conduct experiments into novel pain treatments.

These tissue samples must be used within experiments fairly quickly because they deteriorate over time. This limits their availability because they cannot be transported over long distances. In turn, this restricts the selection of CROs that we can supply with these samples.

To overcome these limitations, we are currently developing a process to treat samples with Cryofreeze, which would remove restrictions on time and geographies. If successful, this would enable us to enhance the availability of tissue gained through McGill and other partners for our global research network. In addition, the technology might also enable the long-term archiving of the samples which would create a unique bio-bank for Grünenthal and its partners.

Dorsal root ganglia (= cluster of neurons) are located along the spine and represent key gate-keepers that decide which signals from the peripheral nervous system, i.e. the nerves in the limbs, are forwarded to the central nervous system and ultimately the brain, where one perceives these signals as pain.



### **Developing human induced pluripotent stem cell-based microfluidic cultures for pain research**

Together with King's College London, Grünenthal is developing microfluidic culture (MFC) models based on human induced pluripotent stem cells (iPSCs) that are specifically tailored to support pain research. This collaboration aims to establish models with human iPSC-derived neurons that closely mimic the functionality of human nociceptive neurones.

This project offers significant potential to strengthen pre-clinical research because microfluidic cell cultures replicate a cell's natural microenvironment and in-vivo milieu more accurately than traditional

in-vitro models. If successful, this could significantly enhance our understanding of how investigational medicines modulate pain in the human body.

Our ambition with this cooperation is to develop pioneering methodologies that we can then include in our pre-clinical toolbox. In this way, we can improve the accuracy of our early-stage testing – and open up exciting potential to develop novel pain treatments quickly and effectively.

“ As a leading company in pain research, our ambition is to play a crucial role in developing pioneering methodologies.

**Jan Adams, MD**  
Chief Scientific Officer







### **About induced pluripotent stem cells**

Induced pluripotent stem cells (iPSCs) are derived from a somatic cell that has been reprogrammed back into a pluripotent state by either introducing specific genes coding for transcription factors or adding small molecules that regulate cell identity. Those iPSCs can be differentiated into different cell types with unique characters, including peripheral sensory neurons.

### **About microfluidic cultures**

Microfluidic devices are compartmentalised chips consisting of different chambers, sometimes called 'lab on a chip' or 'tissue chips', allowing cell-to-cell contact via a series of connecting channels. Microfluidic cultures are used in this present collaboration to investigate the effects of analgesic compounds on different cellular compartments of the pain-sensing neuronal network, as well as the communication between neurons involved in pathological pain signalling.

# OUR STRONG FOCUS ON PAIN MAKES US A PARTNER OF CHOICE

Interview with Pavithra Sundaresan,  
Head of External Innovation

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Pavithra Sundaresan shares her insights and experiences as Head of External Innovation, leading our efforts to collaborate with innovative companies around the globe to complement our internal R&D in pain. From evaluating new molecules through to supporting development and ensuring successful commercialisation, Grünenthal is an ideal partner for academic institutes, biotech and pharma companies that want to turn bright ideas into life-changing pain treatments.

“ Grünenthal is a uniquely strong and flexible partner for R&D pain projects.

**Pavithra Sundaresan,**  
Head of External Innovation

## What is happening in the pain R&D landscape right now?

The clinical R&D pipeline is still dominated by life-cycle management approaches which are reformulations of existing drugs or are repurposed drugs with an FDA approval in another disease. 2022 saw a number of late-stage clinical failures which underscores the challenges of developing therapeutics for pain. However, breakthroughs related to genomics and being able to investigate biological processes at the level of single cells and moving away from rodent models to better translatable models, the pain landscape is transforming. These methods and others are also enabling identification of novel targets and mechanisms that require further validation in pain.

The flow of funding from industry or venture capital into opportunities in the therapeutic area of pain is very low compared to other disease areas like oncology or immunology, however such investment will be key for innovation to flourish and for novel treatments to reach patients.

With a significant number of big pharma companies having exited pain, innovation is being led by smaller companies and academic institutions who are striving to find these new mechanisms and novel approaches in pain. Numerous smaller biotechs are pursuing applications like gene therapy or cell therapy that carry a higher risk but may have a better patient outcome including a potential for disease modification in the long run. Companies are

also investigating novel modalities that may have better traction for well-known pain targets where small molecules have previously failed.

It is vital for industry to work closely together with academia to tackle this therapeutic area, in order to leverage the key relationships academia has with university hospitals and academic networks to access human tissue, proprietary models, or biomarker research to name a few areas that are important for progressing research in pain. Grünenthal is fortunate to collaborate with thought-leaders from academia who are addressing these topics.

## Why is Grünenthal a strong partner for pain R&D?

Grünenthal is a unique player that is committed to research and development with a leading position in pain. This makes us an attractive partner for small or large companies who are looking for deep pain expertise to progress pain assets, obtain a source of non-dilutive licensing operational revenue through partnering or seeking to divest their pain programmes completely.

We aim to be flexible with our partnering approach depending on the stage of the asset/technology and the aspirations of our partner. This may involve an early research collaboration and access to our capabilities to help compounds advance through early stage R&D, a co-development/co-commercialisation or geography-split type of deal structure for an asset in clinical development, or a straightforward licensing deal or an asset acquisition.

Finally, there are not many companies with our capabilities or leading position in pain. Our company has a long tradition of driving progress for pain management and we are committed to continuing that progress in the future. That makes us a popular partner for innovation.

## What does Grünenthal look for in potential innovation collaborators?

Whilst we remain strongly focused on pain, our scouting approach is broad in that we are looking for pain programmes in any stage of development as well as novel technology platforms with transformative potential for patients.

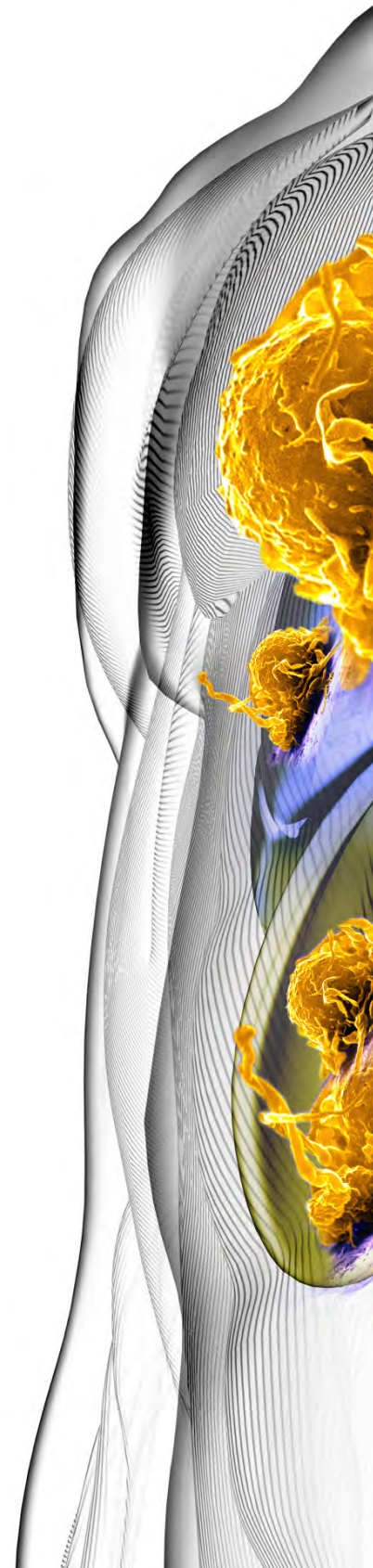
We are seeking selective and potent molecules, of any modality, which address the key pain pathways and where there is strong target validation. As animal models of pain have low translatability to the clinic, I am really interested to speak with companies who are using more “human-relevant” models or cell systems and who are investigating credible biomarkers for pain.

There remains a huge unmet medical need in the many pain indications Grünenthal is pursuing. Ultimately, it is all about connecting with great science and we are super excited about working with fantastic scientists and entrepreneurs who are striving to make a real difference to patients suffering from pain.



# RELIABLE SUPPLY TO PATIENTS

Our Global Operations team brings together 2,000 committed people to supply 95 unique products to patients in over 100 countries.









# MANAGING THE END-TO-END VALUE CHAIN

Our Global Operations team ensures the highest levels of safety, quality and cost-efficiency in all of our activities – and at every stage in our value chain.

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Every day, our Global Operations (GO) team strives to ensure patients have reliable access to medicines across more than 100 countries worldwide. We are proud that we successfully maintained an uninterrupted supply of treatments in 2022, despite several local and global challenges. People in GO share a strong sense of commitment and responsibility. Together, they improve patients' lives and support growth for Grünenthal by ensuring outstanding quality and excellent processes.

Around 2,000 people manage the full end-to-end value chain for our products. We operate five specialised production facilities – in Chile, Ecuador, Germany, Italy and Switzerland. At those sites, we manufacture Grünenthal products and also support external customers. In 2022, third-party manufacturing accounted for 52 percent of our production volume.

**Victor Barbosa, Head Global Operations, shares his opinions about...**



**...GO's contribution to business growth for Grünenthal**

Grünenthal has ambitious growth plans – and GO is a powerful force driving that growth. We are a perfect home for our acquisitions as we have created a powerful manufacturing asset able to drive value post-merger by improving COGS and resilience of the supply chain. We have a proven track record of integrations into our supply chain quickly and effectively to ensure we get the full value out of the investment and maintain continuous quality and patient supply. And we focus heavily on constant improvement of our operations to boost safety, sustainability and efficiency.

**...GO's constant transformation**

In our transformative business environment, staying agile and responding to new challenges is essential. That is a key factor for our work in procurement,



manufacturing, product integration, supply chain management, contract manufacturing and quality assurance. Our GO2025 strategic plan guides our efforts to constantly future-proof Grünenthal's profitability by striving for outstanding levels of cost-efficiency, quality and safety along the entire value chain. Establishing operational excellence in manufacturing operations and implementing digital technologies are significant aspects of this journey. We

invest in our people, our sites and our technologies to improve our operations, ensure high quality and deliver reliable treatments to patients worldwide.

### **...GO's people and culture**

This is a great time to work in GO because there are so many exciting opportunities. Our team is constantly growing, which opens up attractive possibilities for new employees and

fresh pathways for professional growth for our existing colleagues. Employee development, sustainability and safety are of the highest importance in GO. We look for people who want to leave a footprint behind and be part of driving the journey to excellence. That is why our team is a truly cool place to work.



## Investing in the future

We understand that our production sites play an important role in securing safe and reliable supply of medicines to patients. Pursuing excellence is the key to maintaining our strong competitive position. For this reason, we are committed to investing in our manufacturing capabilities worldwide.

Between 2020 and the end of 2023, we will have invested more than €140 million in our sites. The major investments include:

- Approximately €42 million to modernise our site in Santiago, Chile, ensuring world-class infrastructure and robust product quality.
- Approximately €21 million for integrating and insourcing newly acquired products such as Crestor™, Nexium™ and Vimovo™.
- €4 million invested in automation and digitalisation.

## GO2025 – Our way forward

Our Global Operations team is driving progress towards Grünenthal's vision of a World Free of Pain. Alongside our mission to deliver a safe, effective and reliable supply of medicines to patients, we have a clear strategic plan called GO2025. This plan guides our efforts to boost Grünenthal's profitability by

making sure we achieve optimal quality, safety and cost-efficiency levels throughout the full value chain.

Digital technologies are a significant part of this journey. We take advantage of smart innovations inspired by Industry 4.0 to maximise productivity, improve our reactions to market changes and make our manufacturing processes more resilient. These technologies include data capture, advanced analytics and assembly line robotics. We are also creating a Global Operations Business System (GOBS) across our main end-to-end processes to further strengthen our operational excellence.

## Digitalisation – Our facilitator

Digital technologies are opening up exciting opportunities for our Global Operations team. We are determined to explore every possible way of creating value through digital solutions – from embracing automation to unleashing the power of data. Our core focus is on strengthening our fundamentals by creating more efficient processes and enabling smoother end-to-end operations.

Here are just a few examples:

- We have introduced cobots in the packaging centres at our site in Aachen, Germany. Cobots are used

for highly repetitive activities like carton handling. This boosts efficiency and gives our people more freedom to focus on other tasks.

- We are introducing robots in the biopharma business at our site in Italy. We also use Autonomous Guided Vehicles (AGVs) in the warehouse to increase efficiency, reduce errors and improve safety.
- We now use an automated and standardised digital performance system across all sites. It provides ongoing global data transparency while also improving the efficiency of our packaging and bulk operations.
- Our data collection systems have now been extended to reach from our manufacturing lines to the bulk manufacturing areas of our sites. This enables us to even better understand the manufacturing process and improve its performance.
- We have applied innovative advanced analytics algorithms to increase the yield of our Active Pharmaceutical Ingredient (API) site.
- Our eProcurement platform for tendering, offer comparison and Supplier Relationship Management (SRM) is helping to increase efficiency in our procurement activities.
- We have implemented the E2Open platform to connect to our Enterprise Resource Planning (ERP) systems. This platform takes our digitalisation to the next level, increases transparency and improves our process management. The system also allows automatic exchange of supply chain data, such as information about orders, updates, inventory levels and deliveries.

# €140 mn

invested in our sites between 2020 and the end of 2023







# SUSTAINABLE RESULTS IN LINE WITH THE HIGHEST QUALITY STANDARDS

Driving operational excellence to create long-term value.

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Jorge Sosa, Head of Global Operations Business System, leads Grünenthal's approach to achieving operational excellence by optimising the company's processes and culture. He speaks about how the Global Operations Business System (GOBS) prepares the business for the future and ensures a safe, reliable and efficient supply of products for patients worldwide.





### How does Grünenthal define operational excellence?

When we talk about operations, we describe all areas of our business that convert inputs into outputs. That includes procurement, manufacturing, quality, safety, sustainability, and even other areas of the business. Excellence is about making the best use of resources and ensuring a culture of continual improvement, where we are able to adapt to evolving business requirements – while pursuing superior performance and meeting patients' needs. Operational excellence brings the two parts together. Essentially, it is about empowering everyone at Grünenthal to be excellent at everything they do, every day.

### What is GOBS and how is it creating value?

Every facet of a business – on the shop floor, production, warehouse or office – can be improved by applying correct principles. A GOBS defines the elements needed to drive excellence. It is a set of standards, processes, practices, principles, tools and templates to deliver superior performance and results in all areas of an organisation. It also requires embedding a supportive, strong culture and mindset that focuses on creating sustainable improvement.

We are implementing our GOBS across Grünenthal's main end-to-end processes to strengthen operational excellence. It will allow us to attain consistent, measurable results, to grow faster

– and above all, to meet the promises to our patients: ensuring a safe, reliable and efficient supply of products.

### What are your ambitions for the future with GOBS?

GOBS is putting Grünenthal in a strong position for whatever the future brings. It reflects our commitment to delivering sustainable results in line with the highest quality standards. People are the key factor in this ambition because our success will depend on the mindset and culture within our team. With GOBS, we are empowering our people to take actions and make decisions that create real-world value for our company and the patients we serve. That is my ambition for the future – and it is already shaping our work today.





## Building growth capabilities

Acquisitions are a key factor in our company's growth strategy – and successful acquisitions depend on integrating new brands into our supply chain quickly and effectively. Our GO team has a strong track record of helping to unleash the full growth potential of Grünenthal's acquired products and technologies. Our dedicated team for integrating acquisitions ensures that we get maximum value for our investments, and we are often able to achieve substantial cost reductions in production. The successful acquisitions of the European rights for Nexium™ and the global rights for Vimovo™ (excluding the US and Japan) are both strong examples of this approach in action. Since acquiring these two brands in 2018, we have invested €11.8 million in state-of-the-art packaging equipment at our Aachen site. Following the takeover of packaging activities from AstraZeneca in 2022, we already realised cost savings of approximately €10.2 million per annum. Zomig™, acquired from AstraZeneca in 2017, is another integration success story. We expect synergies from acquiring Zomig™ of up to approximately €3.7 million annually through our in-house bulk and packaging capabilities.

From 2023 onwards, Grünenthal's Italian site will take over production of the nasal spray formulation and supply it to Europe, Canada and the USA. After investing around €10 million in a new 10,000 m<sup>2</sup> facility and the related equipment, we can now ensure patients have access to this valuable treatment beyond AstraZeneca's original supply agreement ending in 2022.

For the integration of Crestor™, we expect to take over production and packaging activities in all relevant markets in 2025. We anticipate substantial synergies worth up to approximately €15 million per annum through in-house bulk and packaging.

## Grünenthal PRO – Serving our customers

Our Contract Manufacturing Business, called Grünenthal PRO, is always ready to embrace fresh opportunities to support new partners worldwide. Grünenthal PRO offers high-quality products and services for customers around the globe – and we are recognised as a trusted partner in our industry worldwide. We constantly optimise our capabilities and capacities to expand the range of support we provide

from our five production sites. Together with partners at every stage in our supply chain, we ensure our customers are satisfied.

We provide a strong service portfolio that includes controlled drugs handling, regulatory services, production process design, special technologies such as hormones, hot melt extrusion and biopharma packaging.

In 2022, Grünenthal PRO achieved revenue of €66 million. Our teams supplied 34 million packs and 94 tons of API to 55 customers and welcomed two new customers. Biopharma assembly and packaging was the main driver of growth for our Contract Manufacturing Business, with a 32 percent compound annual growth rate (CAGR). Looking ahead, we expect this positive trend to continue.

Our site in Italy is now able to provide assembly and packaging for nasal spray products, thanks to a state-of-the-art new 10,000m<sup>2</sup> facility. And in addition to this investment, we are also increasing our capacities to provide assembly and packaging for pre-filled-pen and syringes for our biopharma customers.

# 52%

of our overall production volume is for external customers.

For more information: [www.grunenthal-pro.com](http://www.grunenthal-pro.com)

## Production volume 2022



**3.2 billion tablets**



**145 million packs**



**300 tons API**

## Strong results and high expectations

Our Global Operations team expects an overall production volume increase of 13 percent in 2023 compared to 2022. This growth is being driven by the successes of our brands and our global Partner Business expansion – and reaches across all of our global sites.

- Amongst others, as a result of Grünenthal taking over packaging activities for Nexium™ and Vimovo™ from Astra-Zeneca, the production volume at our site in Aachen, Germany, increased by 27 percent in 2022 compared to 2021, and we expect a further increase of 21 percent in 2023. Due to this rapid expansion, we aim to make this site a Centre of Excellence for Packaging in Europe.
- The excellent performance of our Contract Manufacturing Business has earned trust from customers – and is opening up new possibilities. In particular, biopharma customers are

awarding Grünenthal opportunities to enter new markets because of the outstanding service levels at our site near Milan, Italy. We expect the production volume at this site to increase further driven by being a trusted partner for biopharma products and integrating acquisitions. The bulk production volume is expected to grow by 21 percent in 2023 compared to the previous year.

- Our Contract Manufacturing Business is also growing in Latin America. The modern Grünenthal manufacturing site in Quito, Ecuador, already meets European standards. We have started exporting from Ecuador to Brazil, and will begin exporting to Europe soon.
- Our production site that makes Active Pharmaceutical Ingredients (API) in Mitlödi, Switzerland is another strong example of our achievements. According to McKinsey's proprietary Pharma Operations Benchmarking service (POBOS), it is one of the most competitive API sites in the entire pharmaceutical industry. We have been manufacturing the API Tramadol in Mitlödi for over 30 years, and cover about one-third of the world's demand for this prescription pain medication from this facility.

We will continue to move forward with the strategy for our Contract Manufacturing Business, and will structure our activities and target our investments in line with this approach. In this context, our site in Ecuador became a regional manufacturing and distribution centre for liquids and semi-solids. The production of all liquids and semi-solids is being transferred from our site in Chile to our site in Ecuador. This transfer will be

finalised at the end of 2023, resulting in a 32 percent increase in volume for the site in Quito.

## Safety first

One element of our company's approach to manufacturing will never change: We always put safety first. Every accident is one accident too many. In this spirit, we continuously develop preventative measures and provide education and training activities to improve the level of occupational safety at Grünenthal. Every step, however small, brings us closer to achieving our goal of zero accidents. This requires safe framework conditions and safe behaviour. To promote these two components of workplace safety, we actively search for unsafe situations and behaviour – and then make sure they are corrected. We also analyse every accident at one of our locations and then share key learnings with our other sites around the world.

Here are some examples of our success with boosting safety:

- Over 95 percent of our GO staff have taken part in the Behaviour Safety Observation programme. This simple and effective approach supports employees in identifying potential hazards and taking corrective actions.
- Lost Working Day Accidents have decreased by 52 percent across our manufacturing sites in the last three years.
- Two of our five manufacturing sites were accident-free for one year during 2023, and one of those sites has now completed more than two years without an accident.

## Quality always

Grünenthal is absolutely committed to providing patients with medicines they can trust. We operate in line with strict regulatory standards, and our robust Quality Management System (QMS) ensures compliance and quality at every stage in our global value chain. Our Pharmaceutical Quality System (PQS) is monitored by a comprehensive set of Quality Key Performance Indicators (QKPIs). These QKPIs allow us to track progress and monitor success in meeting our ambitious quality targets. Digitalisation is a key component of our

approach to quality. Our QMS is now transforming the culture of quality at Grünenthal by reshaping and streamlining our processes, while also creating an efficient, digital and global way of working. Based on the results of internal and external audits, inspections and certifications, we are certain that we are on the right track.

In 2022, we maintained and extended our certifications. Our manufacturing facility for Active Pharmaceutical Ingredients (APIs) in Germany passed an inspection by the U.S. Food and Drug Administration (FDA) last year. On top of this, our plant in Chile was re-certified

by the Peruvian health authorities and various countries re-certified our sites in Ecuador, Germany and Switzerland. During 17 inspections in 2022, inspectorates confirmed the appropriateness and maturity of our PQS at our headquarters, our manufacturing sites and our sales affiliates.

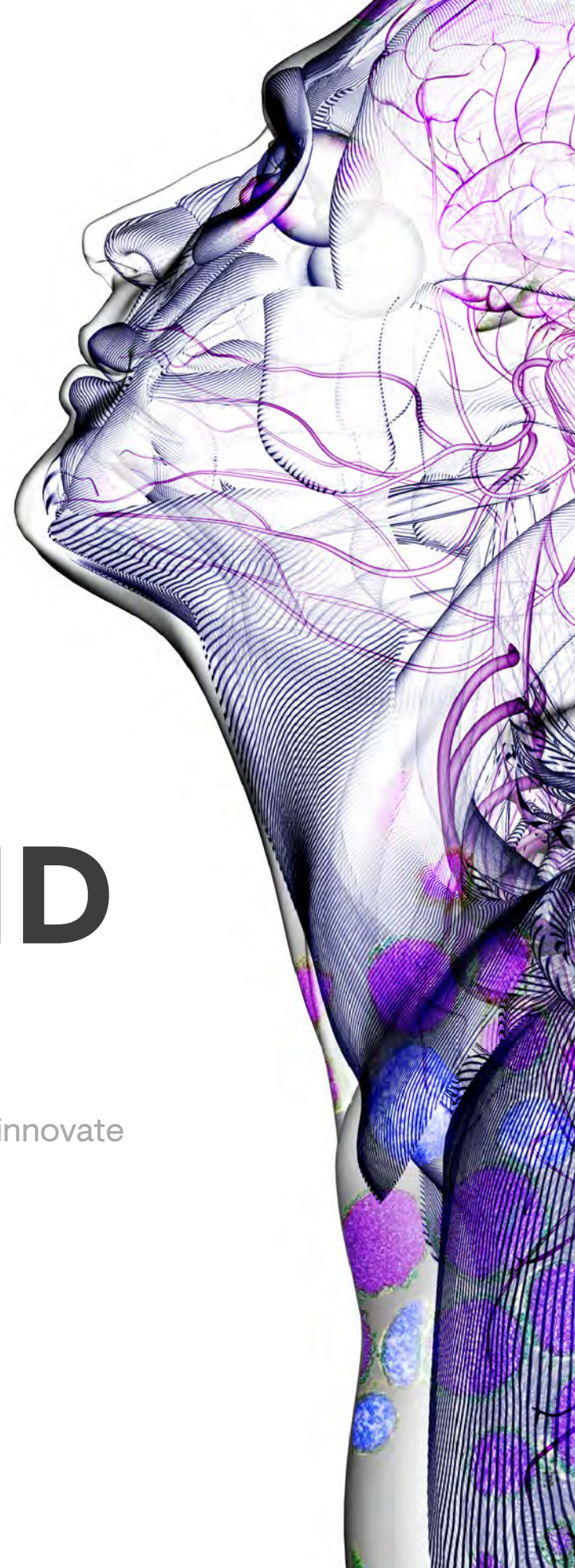
In addition, our manufacturing sites successfully passed 31 client audits. To effectively oversee our supplier and vendor network, we performed 484 audits in total last year. This included on-site audits, remote audits and documentation assessments to check the adequacy of our partners' operations.

“ At Grünenthal, when we talk about quality excellence, it stands for operational excellence. It is all about business activities that need to be excellent from an operational perspective, which means ensuring outstanding quality by doing the right things effectively, consistently and in a timely manner – to meet our patients' needs and expectations.

**Johan Vandaele,**  
Head Global Quality Excellence



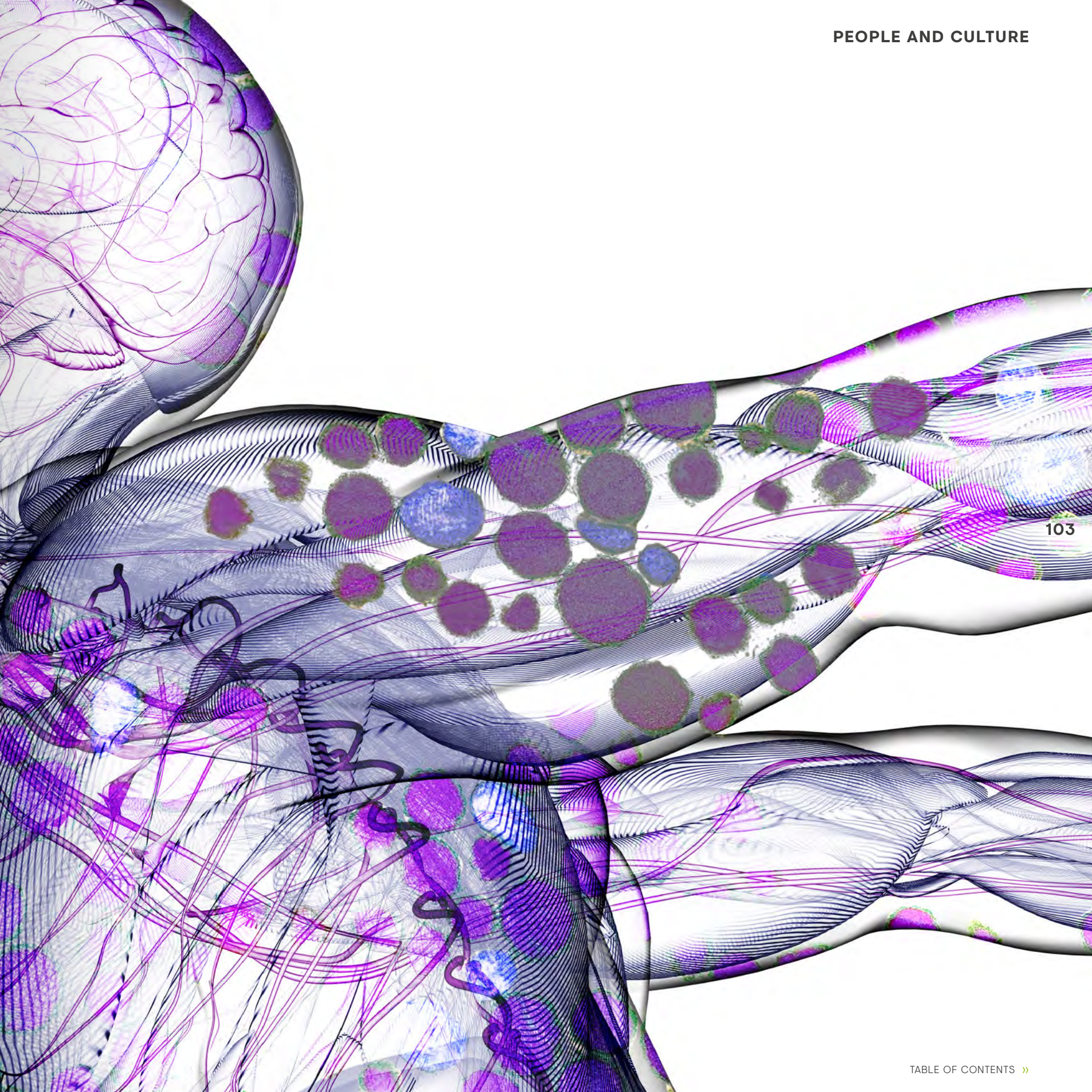




# PEOPLE AND CULTURE

At Grünenthal, we join forces, make an impact and innovate for a World Free of Pain.







# THRIVING WITH ENGAGED AND DIVERSE TEAMS

Our employees bring great ideas to the table and develop their full potential as contributors to the success of Grünenthal and the communities we serve.

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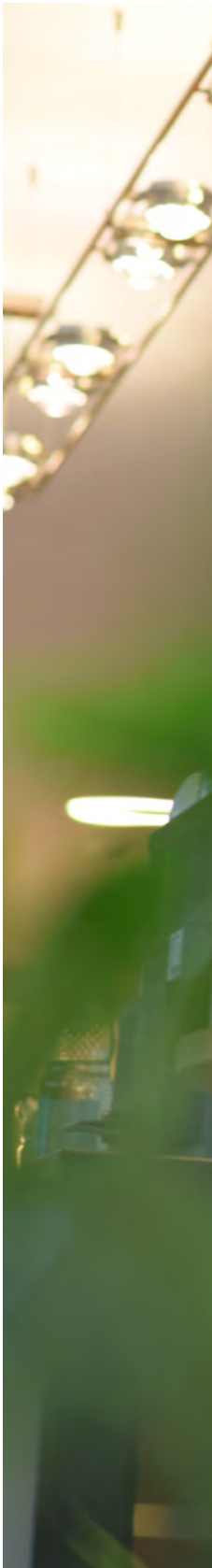
Our employees are highly engaged and empowered, making us a certified Great Place to Work® in most of our countries. We continue to build new capabilities internally, as well as by bringing in diverse talent from outside the company to help us achieve our strategic priorities today and in the future.

Driving a high-performance culture is key to our success. To achieve this

and keep our employees engaged in the pursuit of our shared priorities, we take action to make sure everybody at our company understands and fully supports Grünenthal's strategy. Together, we strive to bring our Values & Behaviours to life – every day, everywhere, every one of us.

“ Diversity and inclusion are important. We strive to create an environment where all employees feel valued, respected and involved, and can bring their full selves to work – where they are empowered to give their best.

**Leen Hofkens,**  
Head Global Human Resources

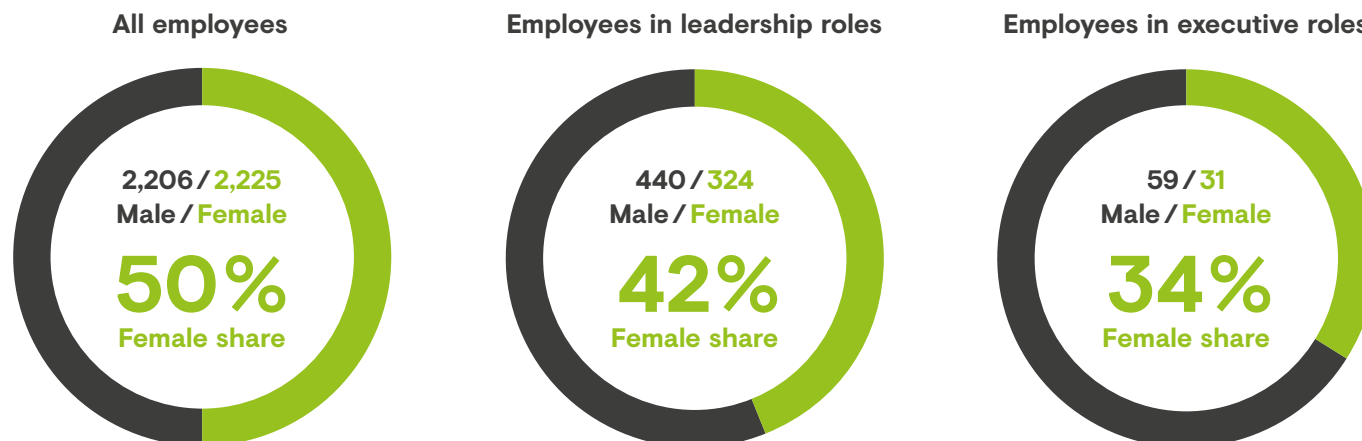




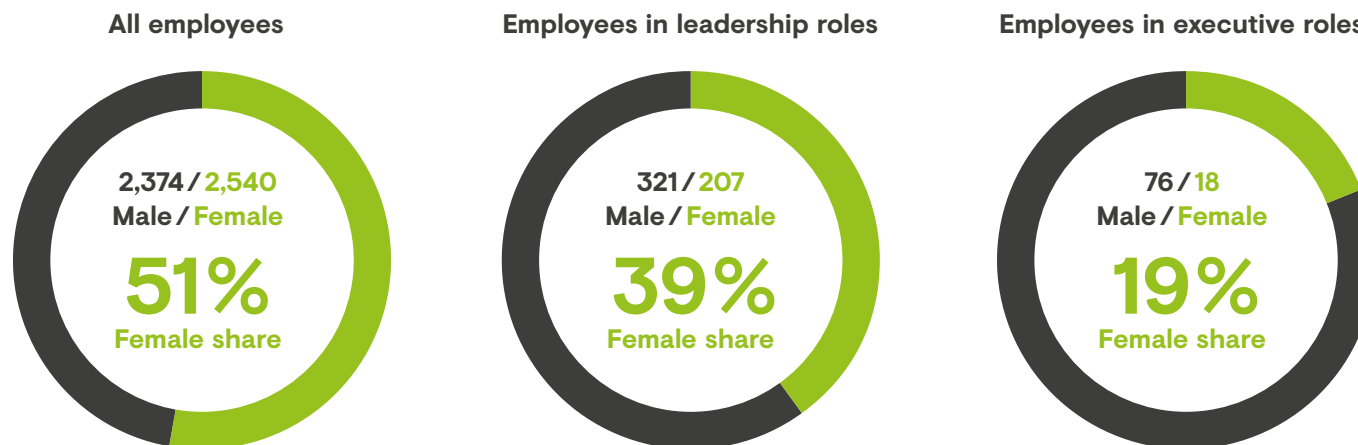


**Gender balance 2022 vs 2018**  
in headcount and percent male / female

2022



2018



In 2023, we are committed to continuing our journey and making further progress to enhance our diversity mix and build an inclusive work environment.

### Teams joining forces around the world

We welcomed over 600 new colleagues worldwide in 2022, including 240 people in our Global Operations team. We also continued strengthening our footprint in the US.

- 674 new hires in total
- US sales organisation nearly doubled:
  - December 2021: 110 employees
  - December 2022: 185 employees

Employees by function	December 2022
R&D	297
Global Commercial	1,631
Corporate Functions	616
Global Operations	1,887
Total	4,431

# 28

Countries

# 63

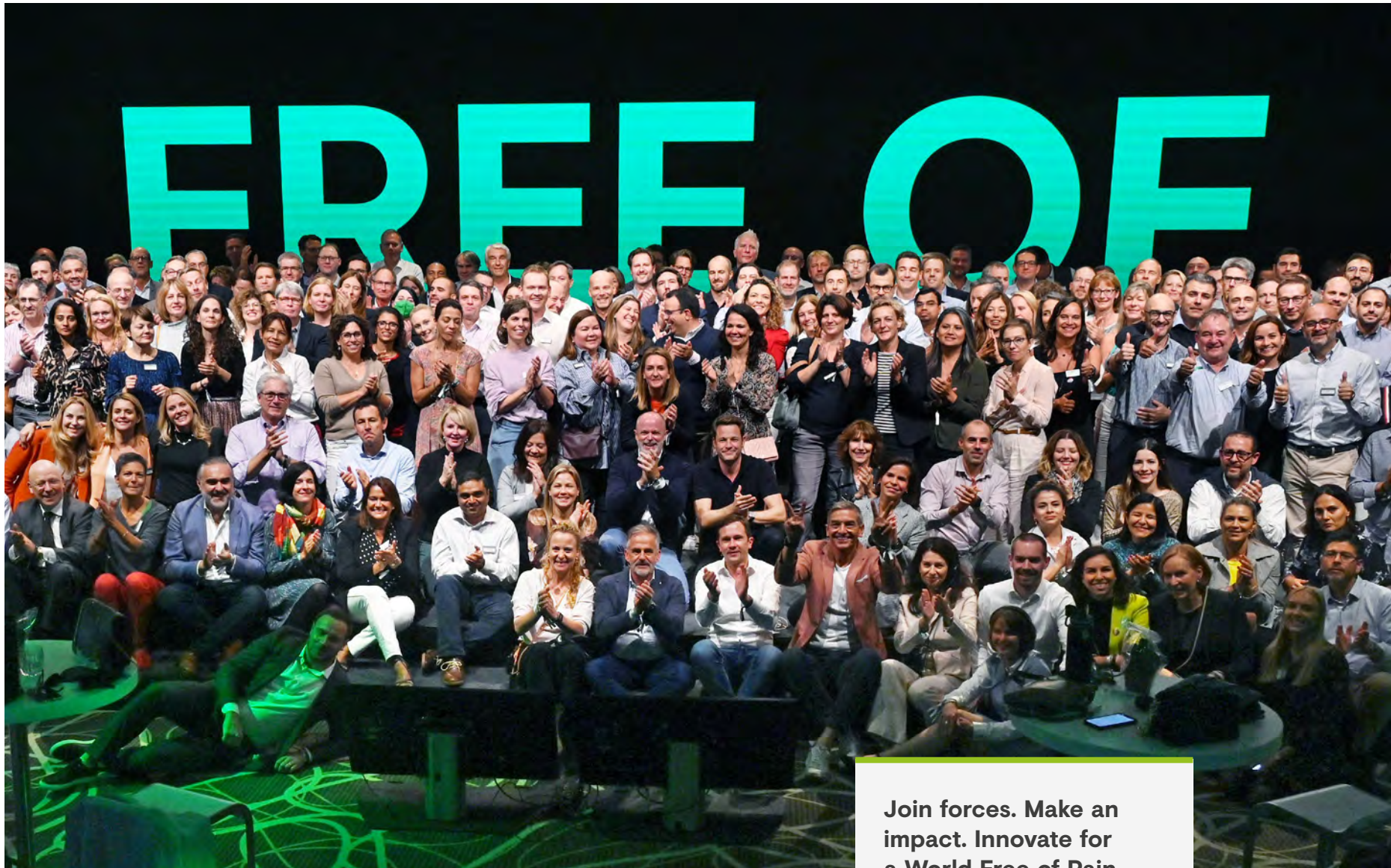
Nationalities

# >600

New colleagues worldwide







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*Global leaders at  
Grünenthal Group  
Conference*

**Join forces. Make an impact. Innovate for a World Free of Pain.**

Our strengthened Employer Brand helps us attract, develop and retain talented and diverse colleagues. Follow us on LinkedIn for regular updates, or check out open positions on our careers website.



[careers.grunenthal.com](https://careers.grunenthal.com)

## Empowering diversity and engagement

In 2022, we launched our Diversity & Engagement strategy. It brings together existing local and global events and initiatives, ranging from our Pride talks through to local Diwali celebrations and graduate recruitment. By focusing on three pillars, the strategy provides a clear

plan with global commitments to truly empower, inspire, support and engage all of our people, partners and communities. Everyone is encouraged to support the initiatives personally – wherever they are based in our organisation and hierarchy. As part of this approach in 2022, we founded an LGBT+ community and increased support for mental health and colleagues experiencing menopause.

## Three pillars

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### Enhancing our diversity

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Enhancing our talent pool through attraction, retention and enablement of diverse talent

### Driving conscious inclusion

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Creating psychological safety and belonging through our people processes and leadership

### Positively impacting our local communities

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Inspiring younger generations, partnering with diverse suppliers and supporting through volunteering

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**Our Diversity & Engagement vision:  
All employees feel valued, respected,  
included and empowered to do their  
best, bring great ideas to the table and  
develop their full potential as a contributor  
to the success of Grünenthal and the  
communities we serve.**



When nobody gets left behind,  
**everybody moves forward**

# A GREAT PLACE TO START

Young graduates play a big role at Grünenthal by fuelling our future talent pipeline, diversifying our workforce and bringing fresh ideas into the company.

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We offer graduate and trainee programmes that provide a smooth and varied start to professional life. In this way, we empower graduates to develop skills and gather experiences that will enable them to make a real positive impact in our teams.

## Global Graduate Programme

Our Global Graduate Programme is designed to provide highly talented graduates and PhD students with a personalised career journey.

Over 24 months, graduates gain a well-rounded view of our organisation through rotations across roles, global affiliates and sites. Exciting projects and a chance to develop a strong professional network await the young talents participating in this programme.

Working in close collaboration with a senior leader who acts as a mentor, our graduates are supported in

identifying strengths and development areas, getting the most out of their potential, and growing continuously. At the end of this programme, graduates are ready to take the next step in their career at Grünenthal.

We recently evolved our Graduate Programme to offer a more international experience. Since making that change, 17 talented young people from 10 countries have started their journey at Grünenthal. They completed over 30 rotations in our different business areas, including

international assignments. With the Global Graduate Programme, we fuel our pipeline of future leaders and experts within Grünenthal worldwide. By 2022, 10 alumni from the programme had taken on roles within our organisation.

“ I am committed to increasing the hiring and development of the younger generation, together with our leaders and managers.

**Leen Hofkens,**  
Head Global Human Resources





### Javier Martin

*Head Global Strategy & Development  
Operations, Global Graduate Mentor*

I am motivated to give something back to our company by providing guidance, influence and support to graduates during the critical early stages of their careers – just like my first manager did for me. It is an honour and pleasure to watch them succeed.

When working with the graduates, there are two stand-out rewarding moments. First, when they land their first “real job”, I am always impressed by their capacity

to adapt to new roles, and I find their passion truly energising. Second, I enjoy seeing graduates grow and reach senior positions with lots of responsibility. Together, we can look back at where they started and how much they have developed.

I always try to remember what it was like starting out. At that point, we often feel less “important” than other employees and might even feel a little bit vulnerable too. As a mentor, it is important for me to make them feel valued and create a sense of belonging.

### Noemi Lewald

*Graduate Global Operations*

At Grünenthal, I have had the opportunity to grow by taking the lead in projects at an early stage. While I was given the confidence to jump into the cold water sometimes, I always had a support network I could also rely on. The programme is unique because it allows you to develop in your chosen direction without any predefined job rotations. You become the captain of your own journey. My mentor supported me in selecting the right road and provided high visibility for my work throughout the organisation. I truly feel empowered in my current role.



# A GREAT PLACE TO DEVELOP YOUR CAREER

Retaining and developing talent is essential for the success of our business.

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We are building capabilities that help us achieve our strategic priorities at the functional and leadership levels – today and in the future. To strengthen our succession pipeline for critical roles at Grünenthal, we aim to maintain a balance between attracting external candidates and developing internal employees.

For our internal talent, we provide a range of growth opportunities. This includes activities and initiatives within their existing role and advancing into new positions or taking lateral moves across functions to gain additional perspectives. Our senior leaders and managers are expected to regularly support

their employees' growth based on individual development plans, and by providing frequent feedback and coaching.

We focus on on-the-job learning combined with training and learning from others. In 2022, we invested in additional online learning platforms like LinkedIn Learning and Coursera. In this way, we allow employees to flexibly design and enhance their learning journey by accessing relevant content that is fully focused on their individual needs – at any time and from anywhere. 42 percent of our senior leadership vacancies were filled by internal talents and successors.

# 42%

senior leadership  
vacancies filled internally

## Supporting individual development



### Corinne Pala

*Regional Head Regulatory Affairs EU*

I have a PhD in chemistry, and I started working at Grünenthal in October 2002 as the very first graduate in R&D. My focus was on project management and project leadership. Over the years, I progressed through 6 different roles. My journey began in Clinical Outsourcing, and I am now Head of Regulatory Affairs for Europe. Along the way, I held positions as Head of Relationship Management, Head of Project Management Office, and International Project Lead for Palexia, Versatis and Zalviso. This growth was made possible by the

guidance and support of my managers and mentors, who encouraged me to take on more responsibilities. The recognition I received for my achievements also motivated me to keep going the extra mile. I kept asking for more responsibilities and learned from every new role and the people around me. Each year, I had the opportunity to take on new challenges that enriched my roles – and kept my daily work fresh and inspiring. The Grünenthal learning model, which states that the biggest part of learning – 70% – actually happens on-the-job, perfectly summarises my own development here.

### Wladimir Sviercovich

*Finance Director CAMEX*

I have had the privilege to work for Grünenthal at the country level in Ecuador, at the regional level at the Latin America Head Office, and at the global level at our Corporate Hub in Lisbon. This was possible thanks to the support and mentorship of amazing leaders and professionals who have challenged and supported me every step of the way. I have benefited from the mentorship programmes provided by Human Resources, which are a great tool for getting advice from

experienced professionals who can offer an outside-in view. This type of perspective works wonders for problem-solving and creative solutions. Development opportunities are always a two-way street: I am a firm believer in volunteering for challenging projects, stepping outside of your comfort zone and taking on tasks that are outside your area of expertise. I have thoroughly enjoyed working on different projects, especially when I get to work with colleagues from other business areas, cultures or geographic locations.





# A GREAT PLACE TO WORK AND GROW

We actively engage our employees on our cultural journey by creating an environment of trust, transparency, respect, fairness, learning and collaboration.

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In 2022, we were certified as a Great Place to Work® in 24 entities spread across 19 countries, including our headquarters and all of our production sites. This reflects our employees' positive feedback about our workplace culture and leadership approach, and reveals the significant progress we have made together. Grünenthal has conducted the Great Place to Work® survey regularly since 2009. We are proud that we have maintained the positive results achieved in this survey in recent years.

## Maintaining employee engagement

Regular employee surveys help us gain a clear picture of our progress in evolving our culture. The consistently high participation rates strongly indicate our employees' commitment to shaping our culture. And we are proud of how these results indicate positive progress on our cultural journey.

The 2022 results of the Great Place to Work® survey confirmed the positive

trends seen in previous surveys. More than 3,500 of our employees shared their feedback last year, a participation rate of 83 percent.



*More Grünenthal entities are now certified than ever before*



Chilean colleagues celebrating Great Place to Work® certification

- 81% of participants stated that Grünenthal is a great place to work.
- We achieved a Trust Index of 76%, maintaining high scores across all key dimensions, with especially high scores for pride (81%).
- We have a strong foundation for further enhancing Diversity & Engagement across our company, with scores above 90% for fair treatment irrespective of gender, race or sexual orientation. 84% of respondents agreed that diversity is seen as a strength at Grünenthal, and 88% agreed that our people are accepted and respected for all aspects of their identity.
- Those participating in our hybrid working model stated that they feel equally connected to the company and their team when working remotely (91%), and that collaboration with their team works well (92%).
- The results in the Great Place to Work® survey also prove that we really bring our Employer Brand to life: Join forces. Make an impact. Innovate for a World Free of Pain. 82% say they feel they make a difference at Grünenthal; for 81%, their job has special meaning – it's "not just a job". 88% feel a sense of pride when they look at our accomplishments, and 80% say that people here are willing to give extra to get the job done.

**Our employees' feedback will help us to continue taking the right steps forward on our cultural journey.**

# WE ARE GRÜNENTHAL: OUR VALUES & BEHAVIOURS

Our people and our decisions are guided by Grünenthal's Values & Behaviours.

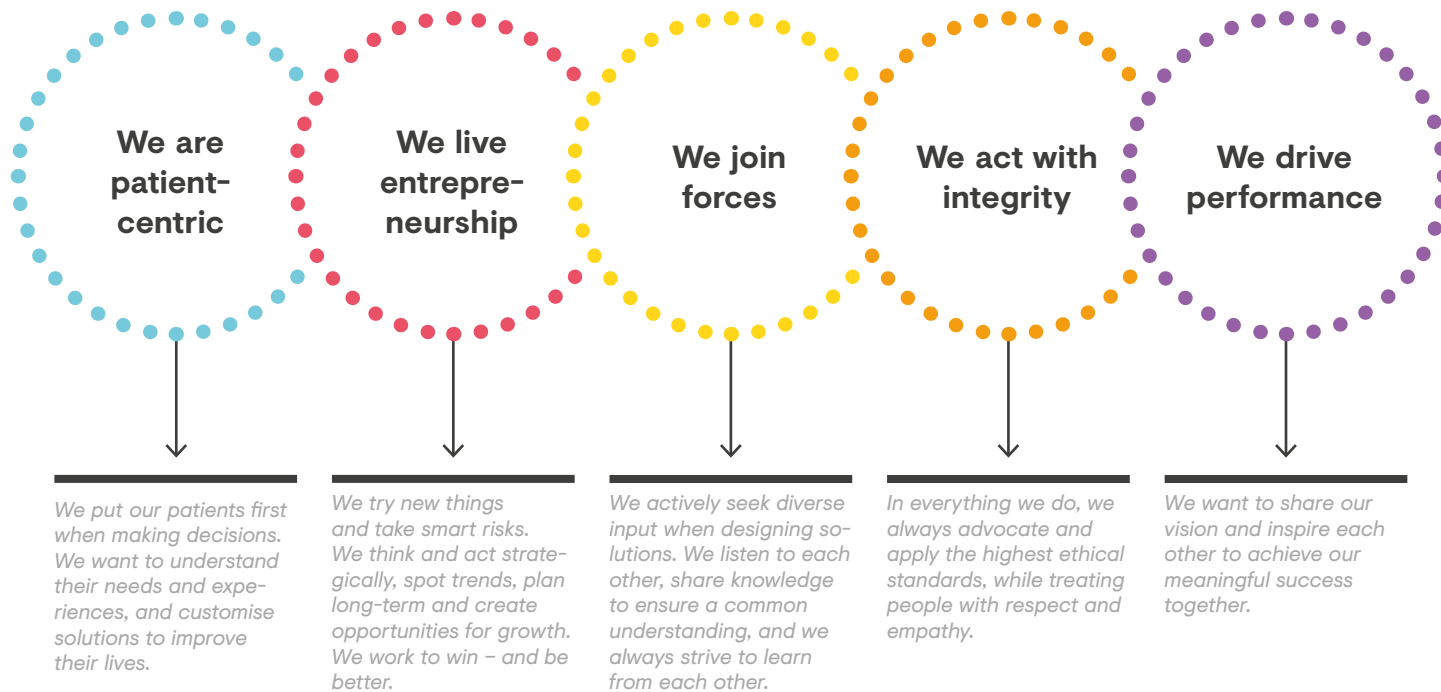
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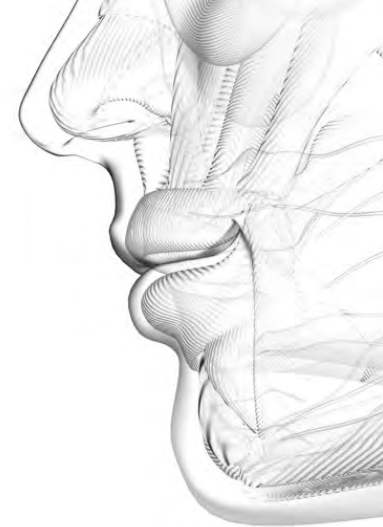
We work hard and challenge each other to take our collective performance to the next level. At the same time, we support each other, work closely together and demonstrate integrity in everything we do. We make sure outstanding results are recognised and rewarded, while always considering how achievements have been made possible.

Great leadership at Grünenthal means exemplifying our Values & Behaviours. In 2022, we conducted broad research and involved many of our senior leaders in identifying the essential personal attributes and skills that enable our leaders to live up to that expectation. In this way, we provide consistent and targeted development guidance for all current and aspiring leaders across the company.









# RESPONSIBLE BUSINESS

Grünenthal aspires to create a positive impact on society – in our core business and beyond. Our firm commitment to integrity, transparency, and the highest ethical standards always guides us.









# POSITIVE IMPACT

As a global leader in pain management, we constantly seek to achieve positive outcomes for patients and their families. In addition, Grünenthal aims to maximise its beneficial effect on employees, partners and society – while reducing the environmental footprint of our business activities. These ambitions drive our approach to Corporate Responsibility.

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To bring this approach to life, we launched a holistic Corporate Responsibility Programme in 2021. Our global team took decisive steps to implement this programme in 2022. We will continue to build on this solid foundation in the coming years. Our Corporate Responsibility Programme focuses on four modules: Fields of Action, Ethical Framework, ESG Risk Management, and Corporate Governance.

## Fields of Action

In 2021, we conducted a materiality analysis to identify the topics that matter most to our stakeholders. Based on these insights, we clustered the material topics into four dedicated Fields of Action: Compliance, Ethics and Transparency, Patients, People and Planet. We then set ambitious targets and defined KPIs for measuring progress. In the 2022 reporting period, we re-assessed all important strategic and operational topics within our company and

its environment. This involved analysing both their impact on Grünenthal's business activities ('financial materiality') and the impact of Grünenthal's business activities on sustainability topics ('impact materiality'), known collectively as the double materiality concept.

To gain a holistic view, we analysed the identified topics regarding their relevance in our value chain. You can find more details in our Responsibility Report.

## Ethical Framework

It is our fundamental responsibility to maintain the highest ethical standards in everything we do. We aim to build trust and give confidence to patients, employees, partners and communities. Our strict ethical framework – including our bioethics and data ethics frameworks – provides guidance in areas that lack clear legal regulations.

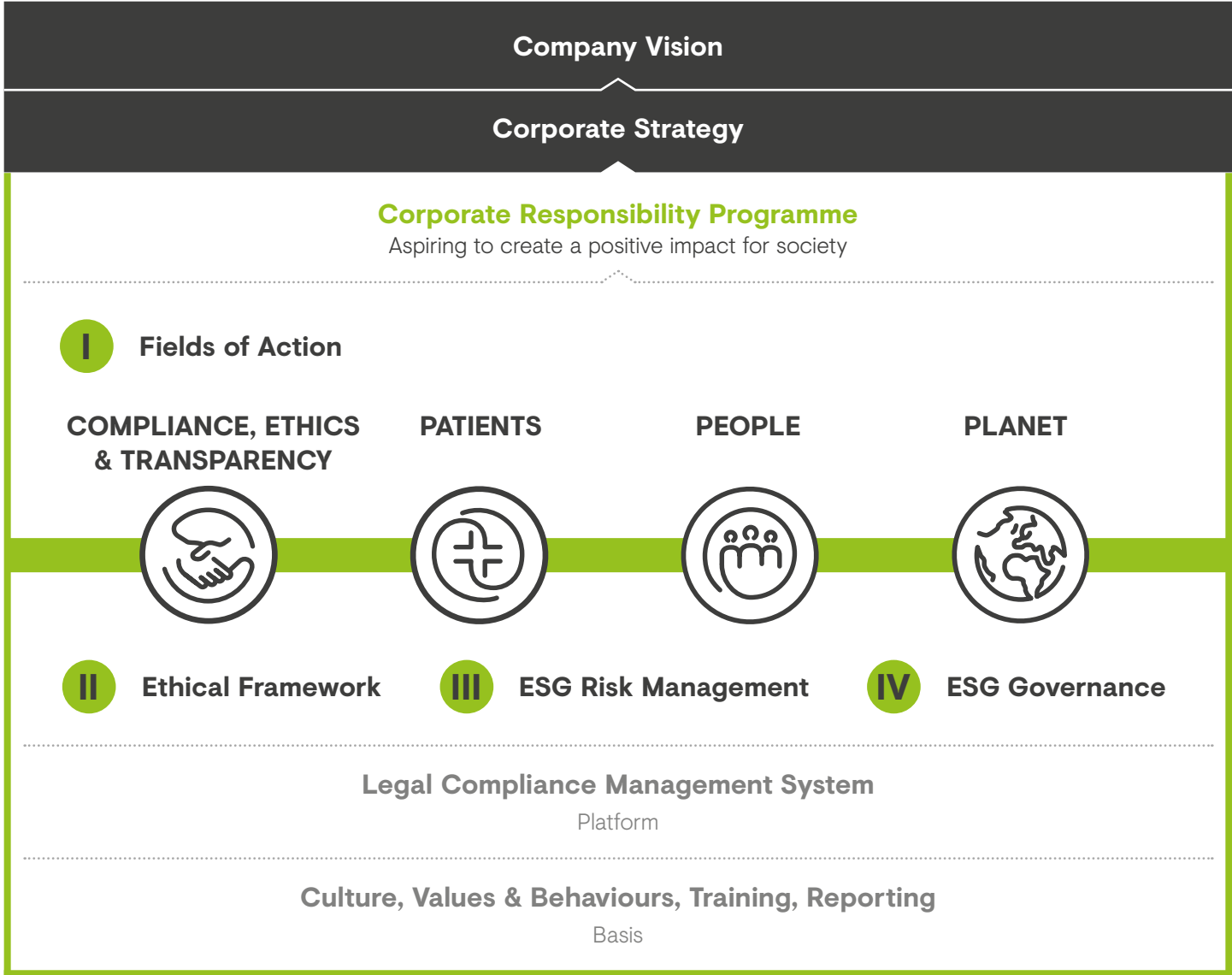
## ESG Risk Management

Managing risks is an essential aspect of Corporate Responsibility. Potential risks in this area can be clustered into Environmental, Social and Governance (ESG) categories. An independent agency regularly monitors and assesses our ESG risks and our approach to managing them.

## Corporate Governance

Our corporate governance system ensures that we always act in line with our belief in decent entrepreneurship. We further strengthened our governance approach by introducing the Grünenthal Responsibility Board in 2021. It drives the implementation and development of our Corporate Responsibility Programme.

Our Corporate Responsibility Programme is embedded in our strategy



# OUR IMPACT INITIATIVES

We have created dedicated impact initiatives for our Fields of Action for Patients, People and Planet. These initiatives are designed to boost our positive impact around the world.

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## Patient

### Educating Patients and Healthcare Professionals

– To better support patients on their journey to achieving optimal pain management, we have established an initiative to educate healthcare professionals on the responsible use of pain medication. With regard to opioids, our Charter on the Responsible Use of Opioids sets out our commitment to exploring and endorsing measures that minimise the risk of inappropriate and illegitimate use of prescription opioids – while striving to ensure that individual patients with a clear need for opioid-based pain relief are not denied access.

### Data-driven Human Disease Understanding

– To enhance our ability to create truly novel medicines for patients in need, we are expanding our understanding of human disease based on concrete data.

**Awareness and Accessibility** – The mission of the Awareness and Accessibility Initiative is to positively impact patients' lives by improving access to adequate pain management and raising awareness about chronic pain and palliative care.

Further insights into how we develop innovative medicines are available in the chapter a World Free of Pain of this report.

## People

**Circle of Trust** – To foster a culture of trust among employees, partners and the community, we have established a Diversity & Engagement Council. It raises awareness, identifies needs, governs initiatives and monitors impact. We have launched our first Diversity & Engagement strategy to guide our work on building an inclusive and diverse workplace with engaged colleagues.

You can read more about how we create a positive impact for the people we work with in the chapter People & Culture of this report.

## Planet

### Driving Environmental Sustainability

– To reduce the environmental impact of our business, we have established a number of initiatives to ensure we use resources more sustainably, avoid waste in our operations wherever possible, and switch to low-carbon or renewable energy sources at our sites.

In order to create a meaningful impact and achieve our environmental goals, we have established three major areas of action:

- Sustainable Operations: This targets net zero emissions from our sites, as well as a reduction of waste and improved wastewater treatment.



- Sustainable Procurement: This focuses on working with key suppliers to reduce carbon emissions, and aligning with waste and wastewater standards.
- Sustainable Products: This targets a reduced environmental impact associated with our product packaging, while also embedding green design principles into the development and manufacture of our products.

Alongside improving the environmental impact of our own operations, we launched our #TreesForOurPlanet initiative to support reforestation in 2021. It marked our 75-year anniversary by planting 7,500 trees worldwide in 2021, and our teams beat this target by planting more than 10,000 trees. We continued this project in 2022 and planted over 11,000 trees across the globe.



Our Responsibility Report provides regular and transparent information about our progress, and is published alongside this report. It shares insights into how we conduct our business responsibly, as well as details about our impact on society and the environment – and how we reflect external factors in our daily work. The report also offers updates on the goals and KPIs that measure our progress along the value chain. We report in line with the Global Reporting Initiative (GRI) standards and subject our reporting to external auditing.

# VALUES AND ETHICAL FRAMEWORK

Everything we do is guided by our deep commitment to strong values and ethical behaviour.

We want our patients, customers, employees, partners, suppliers, investors and all the communities we serve to have the confidence to trust and do business with us. This is key to our long-term success.

We have a shared set of Values & Behaviours that make clear how we work together to achieve successful outcomes for our company and our patients. These Values & Behaviours guide our decision-making and give a clear indication of how we behave – as individuals and as an organisation.

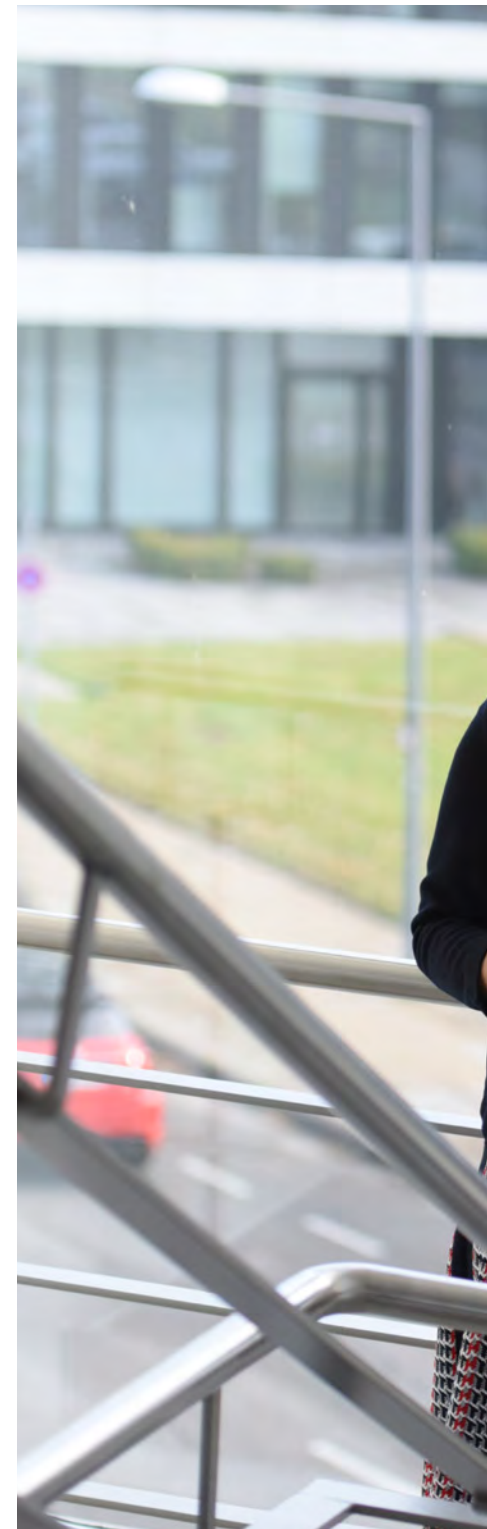
## **Business ethics**

Our Code of Conduct provides a framework for our actions and decisions. Everyone in our organisation has the responsibility to live up to these standards in their daily work. All employees are requested to sign the Code of Conduct when joining the company. We bring it to life through face-to-face and online

training. We also offer a confidential 24-hour Ethics Helpline for anyone with questions, concerns or doubts. Every complaint or concern is investigated by our Compliance organisation, which is fully integrated within the business.

Our Compliance Officers sit on decision making bodies across the company and report to the Chief Responsibility Officer, who regularly reports to the Executive Board and the Supervisory Board.

In addition, we insist that our business partners act lawfully and with integrity in line with this framework. To ensure this, we have established our Code of Conduct for Business Partners, which clearly sets out our expectations related to compliance and ethics for all business partners before entering into a working relationship.







### Bio ethics

We are committed to conducting our research activities within a strict bioethical framework. We adhere to clear rules on animal trials, human biological sampling and emerging technologies. In addition, we share clinical information that is necessary for conducting legitimate research, serving patients' safety and improving public health.

### Data and digital ethics

We handle all personal data responsibly and conduct all of our data processing activities in line with applicable legal standards. In addition, we live the principles set out in our Digital Ethics Charter:

- Human beings keep oversight and accountability of our digital activities.
- Safety and security are embedded into all of our digital activities as cornerstones to protect our values.
- We can explain all of our digital activities.
- Our digital activities do not cause bias and discrimination.
- Digital ethics are engrained in our decision-making processes.
- All digital activities must be conducted in line with this charter.



# OUR ENVIRONMENTAL, SOCIAL AND GOVERNANCE RATING

Independent, external evaluations have ranked Grünenthal as a leader in managing risks related to Environmental, Social and Governance (ESG) criteria.

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One part of our Corporate Responsibility Programme is to manage non-financial risks effectively. Possible risks for our business can be clustered into three main categories: Environmental, Social and Governance (ESG). Examples include pollution, discrimination or corruption. Each year, our performance against ESG criteria is recognised by an external rating. Sustainalytics' ESG Risk Rating's framework focuses on exposure and management of a company's material ESG issues.

## “Exposure”

This dimension reflects the degree to which a company's enterprise value is exposed to material ESG issues including:

- Ethical marketing.
- Clinical trial transparency.
- Corruption and bribery.
- Human capital.

## “Management”

This criterion measures a company's preparedness and track record in managing its exposure to material ESG issues through its:

- Policies.
- Programmes.
- Training.
- Management systems.

## ESG Risks

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**Environment**  
(e.g. pollution)



**Social**  
(e.g. discrimination)



**Governance**  
(e.g. corruption)

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### A proud position

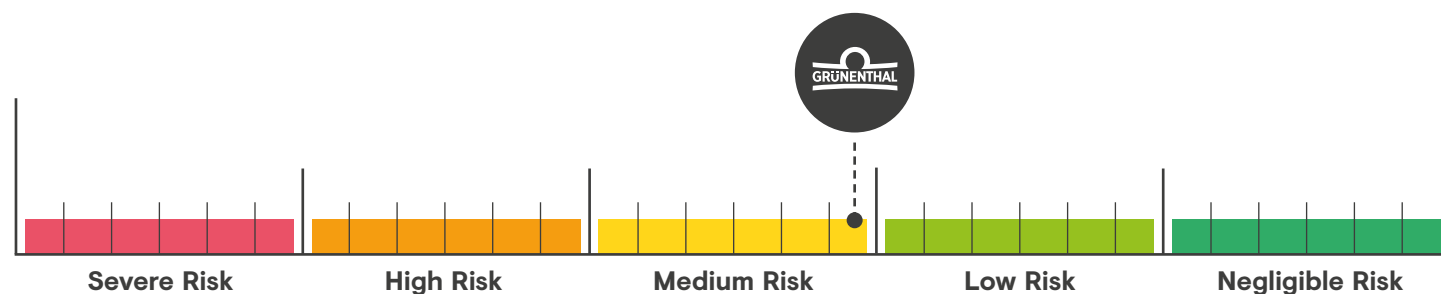
In 2022, Grünenthal was placed in the top three percent of the global pharmaceuticals subindustry. This puts our company just outside the low-risk category and ahead of our key peers. The rating agency Sustainalytics assessed Grünenthal as having a medium ESG risk overall and managing our ESG risks in a strong way.

“ We aim to continuously improve and optimise our ESG performance. To achieve this, we have set ambitious targets for each responsibility topic.

**Sebastian Köhler,**  
General Counsel

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### ESG Rating



# TURNING WORDS INTO ACTIONS

Our authentic and practical approach to implementing Corporate Responsibility at Grünenthal.

## What does Corporate Responsibility really mean at Grünenthal?

Corporate Responsibility means conducting our business legally, ethically, respectfully and sustainably. This covers everything we do – from selecting suppliers through to how we treat employees, the conditions in our production facilities and the way we market products. Our Corporate Responsibility Programme is not just a collection of buzzwords. It is a clear and specific plan for how we engage with the world in a positive way.

## How does it fit together with the company's overall strategy?

Corporate Responsibility is deeply embedded in our business strategy, and is a high-priority topic at Grünenthal. All business areas are required to contribute to our ambitious goals and initiatives. Corporate Responsibility is one of the four strategic dimensions of our yearly Corporate Scorecard. Adhering to our Scorecard is part of our incentive system for employees, so it is built into our approach to measuring the performance of all individuals and teams.







### Why is it important to take action now?

Today, every company is operating in a rapidly transforming world – with climate change, rising digitalisation, political power shifts, a global pandemic, inflation and war. The roles and responsibilities of stakeholders worldwide are also changing. Governments cannot respond to modern challenges like water and energy scarcity by acting alone. Other players like civil society, non-governmental organisations, international institutions, industries and businesses need to play a central role by stepping up and making a contribution.

Society is right to expect companies to take increased responsibility for their actions and to conduct business sustainably. Corporate Responsibility involves going beyond minimum legal requirements to manage the economic, environmental and societal impact of a business' operations.

Governance systems ensure that organisations live up to these responsibilities. And because investors, customers, employees and suppliers are becoming increasingly selective when choosing business partners, it is incredibly important for companies to meet these requirements and report on them transparently.

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“ We have an authentic Corporate Responsibility policy, meaning it is not just a “tick the box” exercise but a way for us to invest in and engage with the world around us in a positive way.

**Prof. Dr. Cordula Meckenstock,**  
Chief Responsibility Officer

# SUPPORT FOR THALIDOMIDE-AFFECTED PEOPLE

The Grünenthal Foundation for the Support of Thalidomide-affected People provides help where it is most needed.

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Thalidomide is a pharmaceutically active ingredient developed by Grünenthal in 1954 and brought to market in Germany in 1957 and globally from 1958 on. Grünenthal marketed it in Germany as a sleep aid and sedative under the brand Contergan, and it was marketed globally either by Grünenthal or by licensees under various trademarks. In 1961 Grünenthal withdrew its products containing Thalidomide and urged its licensees to do the same following what came to be known as the Thalidomide Tragedy. It was discovered that the drug caused severe deformities in newborns if taken between the 34th and 50th day of pregnancy. An estimated 10,000 people worldwide were affected by the tragedy. Today, around 5,000 affected people are still alive and have to deal with the challenges of their limitations.

Back in 2011, a Thalidomide-affected person asked Grünenthal for a second wheelchair because he needed one for the house and a separate one for

outside. This request led to the creation of a hardship initiative – and one year later the Grünenthal Foundation for the Support of Thalidomide-affected People was established to provide a framework for handling requests like this. Since then, the Foundation has supported almost 3,500 cases, giving Thalidomide-affected people increased autonomy and mobility.

The relationship between Thalidomide-affected people and Grünenthal has seen significant changes in the last 10 years. The Foundation's team serves as the first point of contact, as well as advisors to Thalidomide-affected people. "For me, working at the Grünenthal Foundation is meaningful and has taught me a lot of humility," said Tom Hermes, a representative of the Foundation. "It is enriching to accompany those affected, sometimes over many years, and to develop projects with them. I look forward to seeing what we achieve together in the future."

## How does the Foundation provide support?

The Thalidomide Tragedy will always be a part of our history. We will never forget what happened, and we deeply regret the terrible consequences for those affected and their families. We see it as a responsibility to contribute to improvements in the living situations of Thalidomide-affected people. Thalidomide-affected people live with disabilities, such as shortened limbs, that make day-to-day activities extremely challenging. The Foundation supports them by co-financing home and vehicle modifications to enable affected people to drive their own vehicle and spend time outside their home working or socialising. Our work has enabled almost 500 changes to cars based on individual needs, and over 350 bathrooms and 360 kitchens are now more accessible. The use of a keyboard can also be an obstacle to applying for support, so we co-finance speech recognition

software for personal computers. More than 350 Thalidomide-affected people have learned how to use this technology, which helps them carry out professional duties. Through ongoing dialogue with those affected and their representatives, members of the Foundation identify individual needs and find customised solutions. This mainly deals with challenges related to increasing age and a deteriorating health situation.

“ We always encourage and empower others to share their knowledge of Thalidomide and its effects, and we will continue this work with the same dedication in the future.

**Fabia Kehren**  
Grünenthal Foundation

## Grünenthal Foundation – 10 years of support

To learn more about the Grünenthal Foundation, please visit: <https://www.grunenthal-foundation.com>

Since it was established 10 years ago, the Grünenthal Foundation has been helping Thalidomide-affected people to maximise their independence, self-determination and quality of life.



So far, the Foundation has supported Thalidomide-affected people with almost

**3,500**

activities such as renovation measures for barrier-free homes.

When co-financing housing renovations, the Foundation focuses on adapting living spaces to the unique needs of each individual.



The Foundation promotes digital technologies that enable affected people to access helpful information.

Since it was established, the Foundation has supported adjustments to almost

**500**

cars to meet the specific needs of Thalidomide survivors.



Technological innovations have enabled the Foundation to provide even better support for the daily lives of Thalidomide-affected people.

The Foundation has co-financed the remodelling of more than 350 bathrooms and

**360**

kitchens since it was established in 2012.



The Foundation supports affected people by arranging companions for vacations and other activities outside the home.



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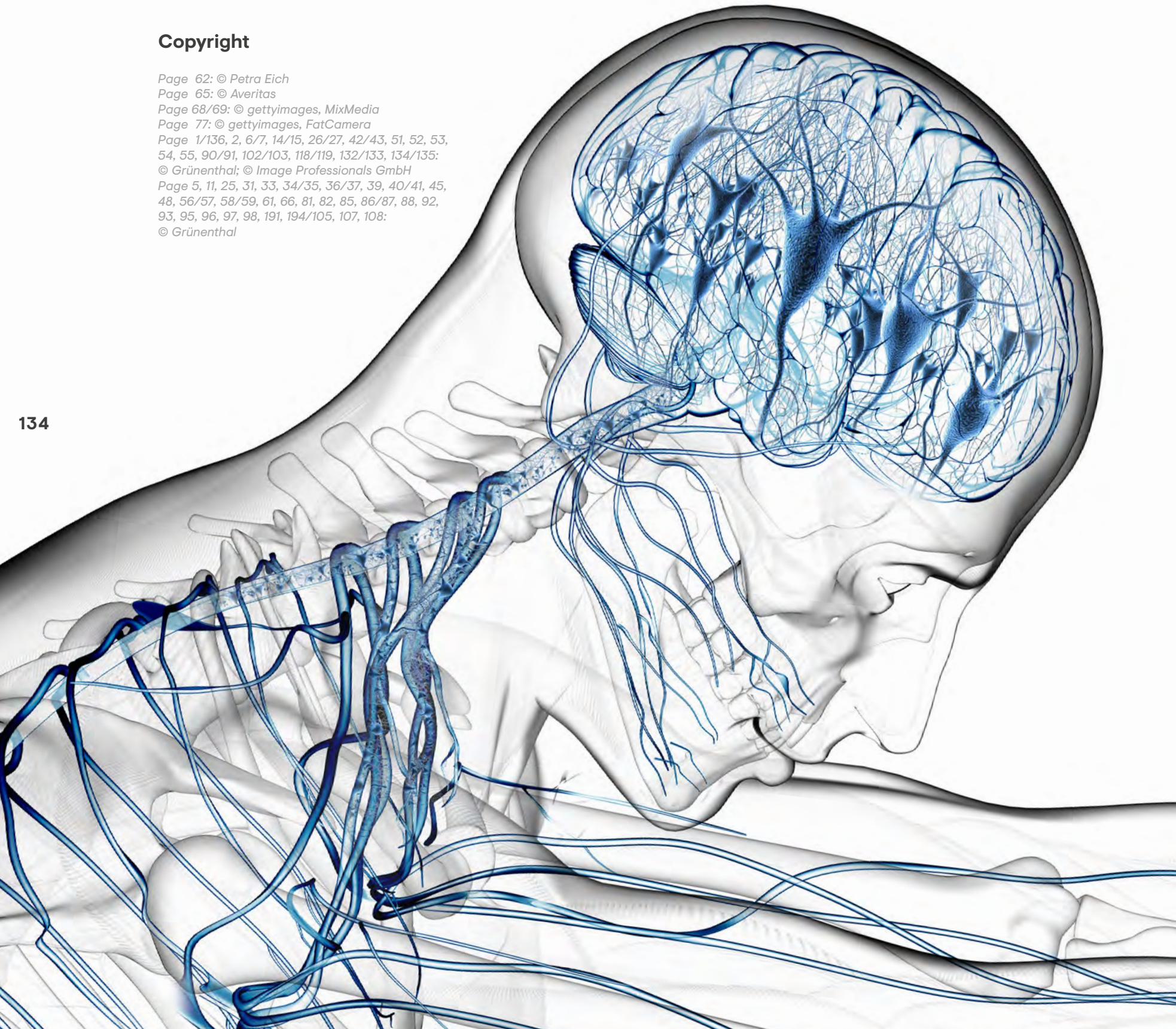
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