

**FOCUS.
TOGETHER.
FOR PATIENTS
AND SOCIETY.**



FOCUS. TOGETHER. FOR PATIENTS AND SOCIETY.

**Welcome to Ipsen's 2021
Integrated Annual Report.
Last year, we implemented
our Group strategy.**

**This report is structured
around its four key
elements.**



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create

long-term value
with a patient-centric
approach

FOCUS

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engage

with all our
stakeholders

TOGETHER

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UNITED IN UPHOLDING OUR VALUES

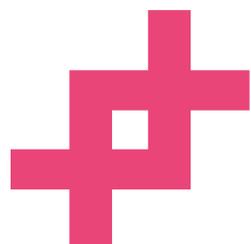
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enable

access to innovative
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FOR SOCIETY

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At Ipsen, we share a strong sense of purpose: to prolong patients' lives, improve health outcomes and create a positive impact for patients and society. "Focus" means carefully choosing our actions and channeling our efforts to create the biggest impact.

Our vision is to lead in the development of transformative medicines for highly specific and under-served diseases in oncology, rare disease and neuroscience.

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€3.5BN

CUMULATIVE REMAINING
FIREPOWER
by 2024 ^{††}

FOCUS. TOGETHER.

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"Together" represents our approach to driving impact. Our highly engaged teams work collaboratively, both internally and with external stakeholders. We know that to improve patient care in

our complex and highly specialized disease areas, we need to work with all stakeholders in healthcare systems. In 2021, we further strengthened our relationships, internally and externally.

^{††} Including the divestment of the CHC business



For more information about Ipsen's strategy, visit [ipsen.com/our-company](https://www.ipsen.com/our-company)



98%

OF EMPLOYEES
have a formalized
development plan

Ipsen's patient-centric approach is at the core of what we do, and our strategy reminds us that we are working "**For Patients.**"

Developing a comprehensive understanding of the patient experience across the value chain means identifying not only what is working, but also potential hurdles to receiving care. When choosing a course of action, we ask ourselves: "How can we make the biggest impact for patients?"



220

PATIENT ORGANIZATIONS
collaborated with Ipsen
in 2021.

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FOR PATIENTS AND SOCIETY.



More than

1,150

EMPLOYEES TOOK PART
in Ipsen in Motion in 2021.

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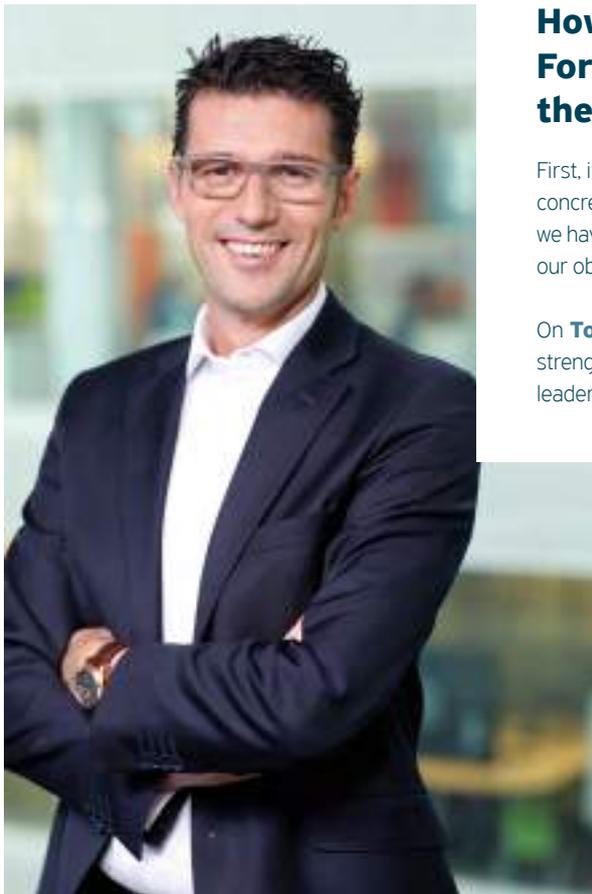
We are also working "**For Society.**" As a global company, we recognize the impact we can have on the local communities in which we operate. We create opportunities for our colleagues to support their communities by volunteering.

In 2021 we set ambitious targets to limit climate change and joined the *Business Ambition for 1.5°C*, a group of companies that have publicly committed to a science-based net-zero and 1.5°C target.

Strategy and progress:

A CONVERSATION WITH DAVID LOEW, CHIEF EXECUTIVE OFFICER

2021 was a time of change and growth for Ipsen. Our strategy, **Focus. Together. For patients & society**, introduced in December 2020, began to positively impact all aspects of our operations. To review the year and the company's major milestones, we sat down with David Loew, Chief Executive Officer.



How has Ipsen's strategy Focus. Together. For patients & society, supported the company's ambitions?

First, it's enabled us to deliberately pinpoint and select what we want to achieve, then take concrete steps towards those goals. This is what we mean by **Focus**. Throughout 2021, we have developed our decision-making approach, which has led to better discussions on our objectives.

On **Together**, we're collaborating more efficiently internally, while, at the same time, strengthening connections with external stakeholders, such as patient groups and opinion leaders. If we want to redefine healthcare, these things go together.

Around **Patients**, among other things, we have redefined patient-centricity, improving our understanding of patient experiences within different healthcare systems around the world. For example, we have gained a clearer understanding of patients' treatment and care needs.

Finally, on **Society**, in 2021 we announced our new objectives for supporting communities and protecting the environment. We have defined more ambitious 2030 targets, as demonstrated by our decision to join the Business Ambition for 1.5°C campaign. We are committed to delivering science-based emissions reduction by working with all our value chain partners.

I've been hugely impressed by the energy and passion Ipsen's people have brought to the journey so far. Their commitment can be felt across every function and business unit.



“Every day, I'm excited by the enthusiasm my colleagues bring to their work, the impact we are making on patients' lives and the efforts our employees make within the communities in which we live and work.”

¹ France, Germany, Italy, Spain and the United Kingdom

² For more information, you can find the press release here: <https://www.ipсен.com/press-releases/health-canada-approves-ipсенs-sohonos-palovarotene-capsules-as-the-first-approved-treatment-for-fibrodysplasia-ossificans-progressiva/>

Can you share some of Ipsen's major achievements from 2021?

We worked together to enact change, be it conducting new research, taking a novel approach to business development, or even commercializing or delivering treatments differently. We can be very proud of all we have delivered in a short amount of time thanks to the agility and adaptability of our teams.

We experienced 12.3% growth, which is extremely strong, especially while everyone is still feeling the effects of the pandemic. We reached €2,868.9 million in sales, and achieved a record core operating margin. Our sales are diversified, with a healthy distribution across North America, the EU5,¹ other European countries, and the rest of the world. Profitability improved, affording us access to more investment and the external opportunities that brings. We have added eight assets to our pipeline, which bodes well for our medium- to long-term future.

In our three key therapeutic areas, we made great progress. In **oncology**, we saw double-digit growth on several medicines, despite the appearance of Somatuline® generics in Europe. Decapeptyl® also continued to grow, driven by more demand in Asia, and increased market share in many countries. Onivyde® grew in the US, and Cabometyx® was approved in combination in first-line renal cell carcinoma (RCC), building upon the current second-line indication in RCC.

On the subject of new treatments, how did Ipsen's approach to business development evolve in 2021?

For the compounds currently in our pipeline, our improved focus has enabled us to put all our efforts into areas where our aim is to make a real difference. We needed to make tough decisions about where to focus our resources. We actually stopped certain trials that we felt didn't have the potential to bring significant value for patients. Instead, we're focusing our efforts on trials that will generate important data for healthcare systems and that bring value to patients.

As for external innovation, we ramped up our activities and made targeted investments. We increased the number of people in both the business development and the external innovation departments. It's about getting more people in the mix, but importantly, the right people with the right skills, and the right processes. We changed how we screen companies and compounds, so we can make decisions faster and focus on the ones we want to push forward. In 2021, we conducted seven deals, for a total of eight assets, across the full spectrum of our pipeline.

In **rare disease**, we continued to focus on innovation, raising awareness, and developing palovarotene, a potential new therapy for patients living with fibrodysplasia ossificans progressiva (FOP), an ultra-rare genetic bone disorder. Currently, people living with FOP have no treatment options at all. Developing treatments for rare diseases is especially complex where there is little precedence for novel therapies, and the path from development to approval is rarely a straight line. In 2021, we withdrew our filing for palovarotene in the US to respond to the FDA's request for additional analysis and are now in the process of resubmitting. And we continue to work closely with other health authorities to make this treatment available to patients. In January 2022, we received approval for Sohonos® (palovarotene) in Canada, which is great news for people living with this devastating disease.² In 2021 we also started the pivotal registration trial of IPN 60130, our second investigational compound to treat FOP.

In **neuroscience**, we saw advances in aesthetics as well as in the treatment of neurological diseases. Treatments such as Dysport® are proving effective against spasticity experienced by patients after stroke.

“We changed how we screen companies and compounds, so we can make decisions faster and focus on the ones we want to push forward.”

Earlier, you mentioned Ipsen's pledge to take ambitious environmental action. What does that mean personally to you, and what progress has Ipsen made toward its 2030 carbon goals?

It's not news that we have to act fast and in a big way to combat climate change. And yes, it is something I'm passionate about. I grew up in Switzerland where, as a child, I could see glaciers in the village of Grindelwald. Now they are no longer visible there, so the work we're doing is close to my heart.

In 2021, Ipsen pledged to take large-scale action to mitigate environmental damage. Joining the *Business Ambition for 1.5°C* exemplified our commitment while we accelerated action across our operations. For example, we now use 100% green electricity for all operations in the UK, Ireland and France. This has increased company-wide use of electricity from renewables to 88% since April 2021. Three of our manufacturing sites in France are certified to ISO 50001 under the international Energy Management System. Also, process efficiency improvements that reduce our environmental impact have seen real results. For instance, volatile organic compound emissions were down 15% against our 2019 base year.

As business travel resumed, we set a goal to limit associated emissions to 30% of 2019 levels. We launched our Fleet for Future project, which aims to make 30% of our vehicle fleet electric by 2025. We'll keep pushing the envelope, and all of these steps combined with our carbon pledge are testament to that.



30%

**OF OUR FLEET
WILL BE ELECTRIC**
by 2025 through the
Fleet for Future project



100%

GREEN ELECTRICITY
for all operations in the UK,
Ireland, and France



88%

**USE OF ELECTRICITY FROM
RENEWABLE ENERGY**
across the company as of
April 2021



15%

**REDUCTION IN VOLATILE
ORGANIC COMPOUND
EMISSIONS**
compared to the 2019 baseline

“We'll keep pushing the envelope, and all of these steps combined with our carbon pledge are testament to that.”

You've used the word "passion" a couple times. What else are you passionate about?

I'm passionate about the entire Ipsen team. Every day, I'm excited by the enthusiasm my colleagues bring to their work, the impact we are making on patients' lives and the efforts our employees make within the communities in which we live and work.

In 2021, we held two Ipsen Community Days, with employees taking part in more than 125 activities. Our sports challenge, Ipsen in Motion, raised on average €10,000 per challenge, resulting in more than €50,000 donated to social causes. Our people around the world uphold the tenets of our CSR policy, and our wider mission to improve and prolong the lives of patients.

And I'm passionate about diversity, where we're making good strides. For example, we're working to ensure women represent 45% of the Global Leadership Team. I'm also passionate about maintaining direct links between employees worldwide. With the Executive Leadership Team members, we are creating a culture of accessibility and openness, and gathering insights that guide our strategic actions. Thanks to our people, our strategy has evolved into a long-term, sustainable and powerful approach to improving the lives of patients and their families, as well as healthcare professionals, around the world.

“In 2021, we conducted seven deals, for a total of eight assets, across the full spectrum of our pipeline.”



Want to hear more from David Loew?
Listen to Ipsen: Behind the Scenes
[here.](#)

Turning strategy into action, every day

Focus. Together. For patients & society.

This strategy sets the overall trajectory at Ipsen.

But it's also essential to ensure our teams are able to put it into practice every day with concrete actions. The four pillars of the strategy guide our decision-making:

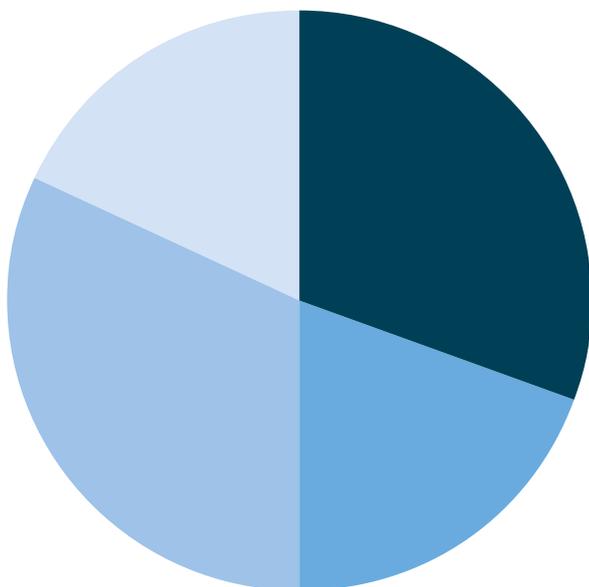
- **Bring the full potential of our innovative medicines to patients**
- **Build a high-value sustainable pipeline**
- **Deliver efficiencies to enable targeted investments and support our growth**
- **Boost a culture of collaboration and excellence**

2021 HIGHLIGHTS AND KEY RESULTS

Strong results across our business

<p>€2,868.9M</p> <p>2021 total sales +12.3% YOY[†]</p>	<p>35.2%</p> <p>Record core operating margin</p>	<p>€2,153.5M</p> <p>2021 Oncology sales +10.8% YOY[†]</p>
<p>€440.7M</p> <p>2021 Neuroscience sales +27.1% YOY[†]</p>	<p>€49.1M</p> <p>2021 Rare Disease sales -10.4% YOY[†]</p>	<p>€225.6M</p> <p>2021 Consumer Healthcare sales +8.1% YOY[†]</p>

[†] At constant exchange rate (CER)



Total sales by region

- **30.8%**
Major Western European countries*
- **31.9%**
North America
- **19.4%**
Other European countries
- **17.9%**
Rest of the world

Executing our external innovation strategy...

Rare Disease

- **GENFIT**
Elafibranor

Oncology

- **Accent Therapeutics**
METTL3
- **BAKX Therapeutics**
BKX-001
- **Queen's University**
FLIP-inhibitor program

Neuroscience

- **IRLAB**
Mesdopetam
- **Exicure**
Spherical Nucleic Acids for Huntington's disease
Spherical Nucleic Acids for Angelman syndrome
- **BCH/UOS****
BoNT/X***



...with €3.5 billion cumulative remaining firepower by 2024^{††}

Pipeline developments

CABOMETYX® (CABOZANTINIB) / OPDIVO® (NIVOLUMAB)

- CheckMate -9ER phase III trial
- Results led to the European Commission approval as a **first-line treatment** for advanced **renal cell carcinoma** (RCC)

DYSPORT® (ABOBOTULINUMTOXINA)

- Phase III trial
- Study reveals that large proportion of **spasticity** patients did not require retreatment for at least **12 weeks**

CABOMETYX® (CABOZANTINIB) / ATEZOLIZUMAB

- COSMIC-311 phase III trial
- Study shows significant improvement in progression-free survival (PFS) in patients with radioactive iodine-refractory differentiated thyroid cancer (DTC)

SOMATULINE® AUTOGEL® / SOMATULINE® DEPOT (LANREOTIDE)

- Phase II CLARINET FORTE study
- Patients with progressive **neuroendocrine tumors** (NETs) received more frequent injections of lanreotide autogel and enjoyed a stable quality of life with no new safety signals



1.5°C

IPSEN JOINED THE BUSINESS AMBITION FOR 1.5°C, pledging to reduce our carbon emissions on the pathway to **net-zero**



WOMEN MAKE UP

42.3%

of the Global Leadership Team



19

COUNTRIES RECOGNIZING Ipsen as a top workplace

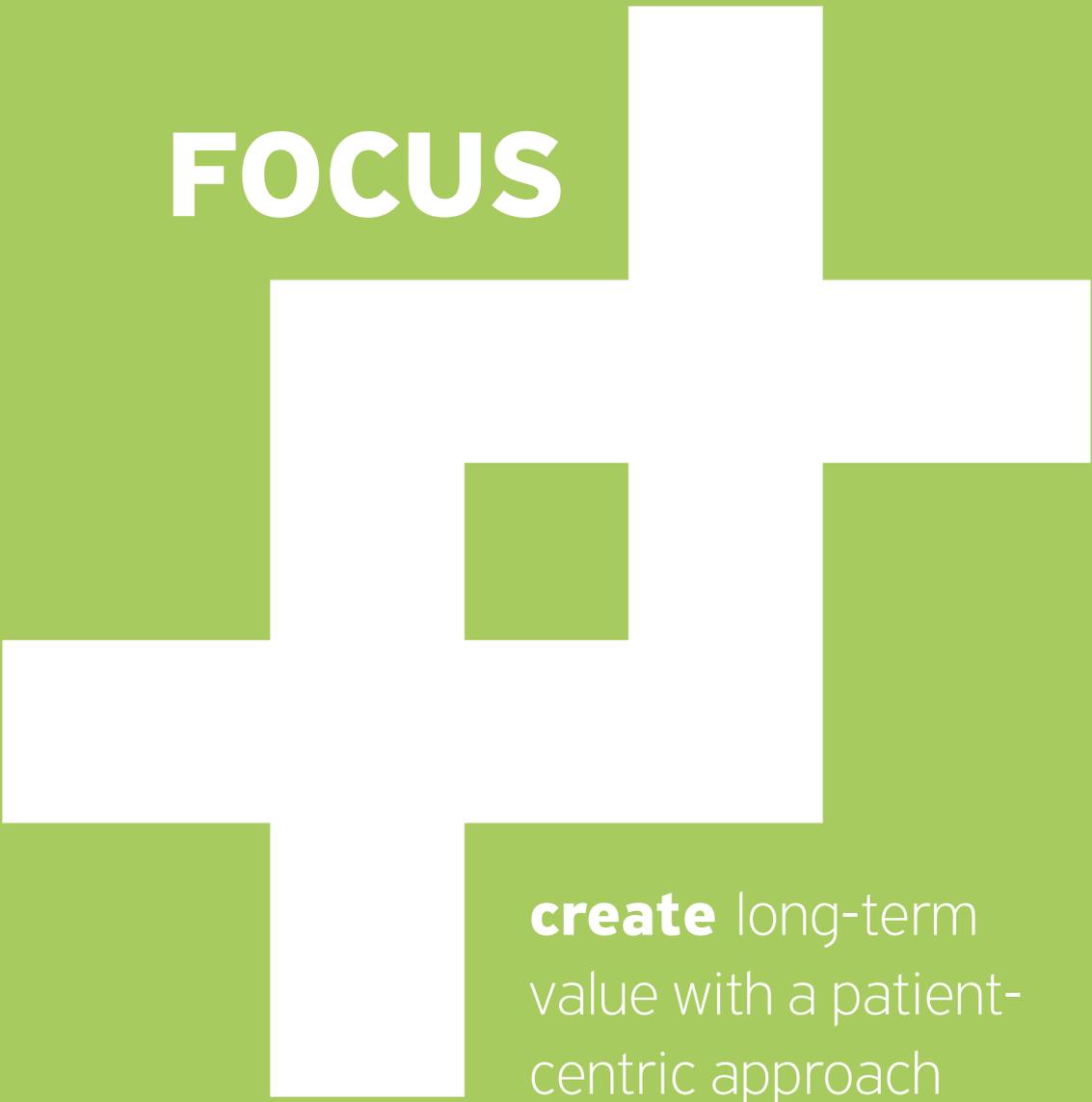
^{††} Including CHC divestment

*France, Germany, Italy, Spain and the United Kingdom

**Boston Children's Hospital / University of Stockholm

***A novel botulinum toxin serotype

FOCUS



create long-term
value with a patient-
centric approach



FOCUS means carefully choosing our actions and channeling our efforts to create the biggest impact. We leverage our portfolio and pipeline to achieve sustainable growth. And we are always searching for the best ways to ensure our assets and our actions to create the highest value for patients and all stakeholders.



€3.5BN

FIREPOWER
for external innovation
by 2024^{††}

Ipsen sales

<p>2019 €2,576.2M</p>	<p>2020 €2,591.6M</p>	<p>2021 €2,868.9M</p>
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We **define success** by the impact we have on patients' lives and society as a whole.

We are guided by our mission to **prolong and improve patients' lives and health outcomes.**

Listen to Ipsen: Behind the Scenes [here.](#)



CREATING VALUE FOR PATIENTS, SOCIETY AND ALL STAKEHOLDERS

We define success by the impact we have on patients' lives and society as a whole. To create the most value for patients and society, our business model leverages our assets and resources to create tangible results. Our mission – to prolong and improve patients' lives and health outcomes – guides us.



Our mission

■ We are guided by our mission to prolong and improve patients' lives and health outcomes, aiming to be our stakeholders' partner of choice.

Our innovations and our R&D pipeline

■ We develop medicines to address conditions with high unmet medical needs and continuously invest in innovation to deliver outcomes that genuinely improve patients' lives.



Our capitals

Financial

- €2.9 billion in total sales
- Net debt to EBITDA of 0.1x
- A publicly traded business under family control

Manufacturing

- 7 manufacturing sites
- External CMO* partners
- 85 million units produced
- €47.3 million manufacturing investment

Intellectual

- 710+ employees in R&D
- 4 global R&D hubs in Cambridge (USA), Oxford (UK), Paris (France) & Shanghai (China)
- 14.9% of sales invested in R&D

Natural

- 88% of our global electricity use is from renewable sources
- 33% reduction in total water used**
- 37% reduction in waste**

Human

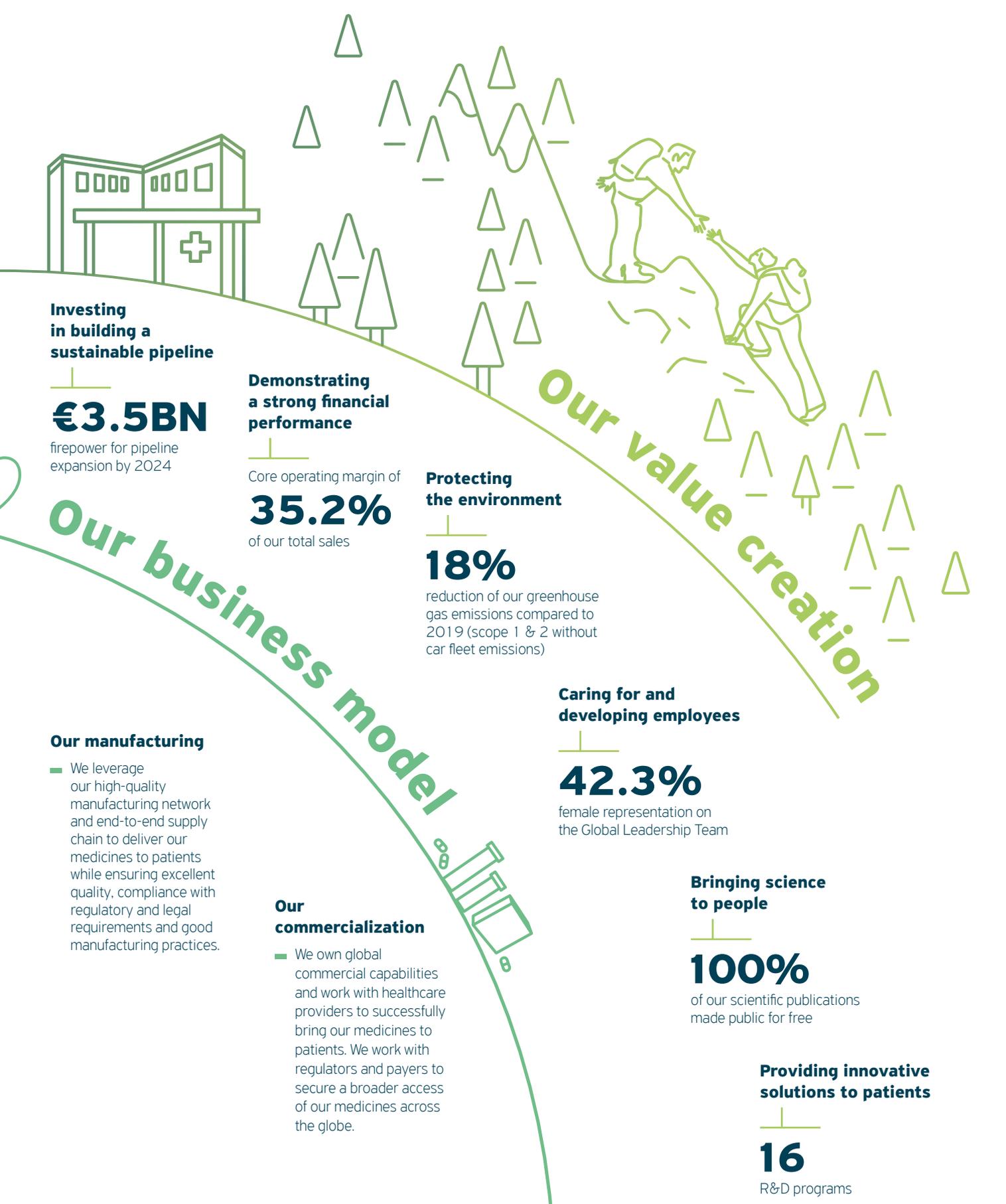
- 5,700+ employees in more than 30 countries
- 19 HR certifications
- Medicalized accident frequency rate of 0.40

Social and relationship

- Collaboration with healthcare professionals and patient associations to improve impact for patients
- Partnerships with external organizations to accelerate innovation and expand access to medicines

*Contract manufacturing organization

**Compared to 2019



Investing in building a sustainable pipeline

€3.5BN

firepower for pipeline expansion by 2024

Demonstrating a strong financial performance

Core operating margin of

35.2%

of our total sales

Protecting the environment

18%

reduction of our greenhouse gas emissions compared to 2019 (scope 1 & 2 without car fleet emissions)

Our value creation

Our business model

Our manufacturing

■ We leverage our high-quality manufacturing network and end-to-end supply chain to deliver our medicines to patients while ensuring excellent quality, compliance with regulatory and legal requirements and good manufacturing practices.

Our commercialization

■ We own global commercial capabilities and work with healthcare providers to successfully bring our medicines to patients. We work with regulators and payers to secure a broader access of our medicines across the globe.

Caring for and developing employees

42.3%

female representation on the Global Leadership Team

Bringing science to people

100%

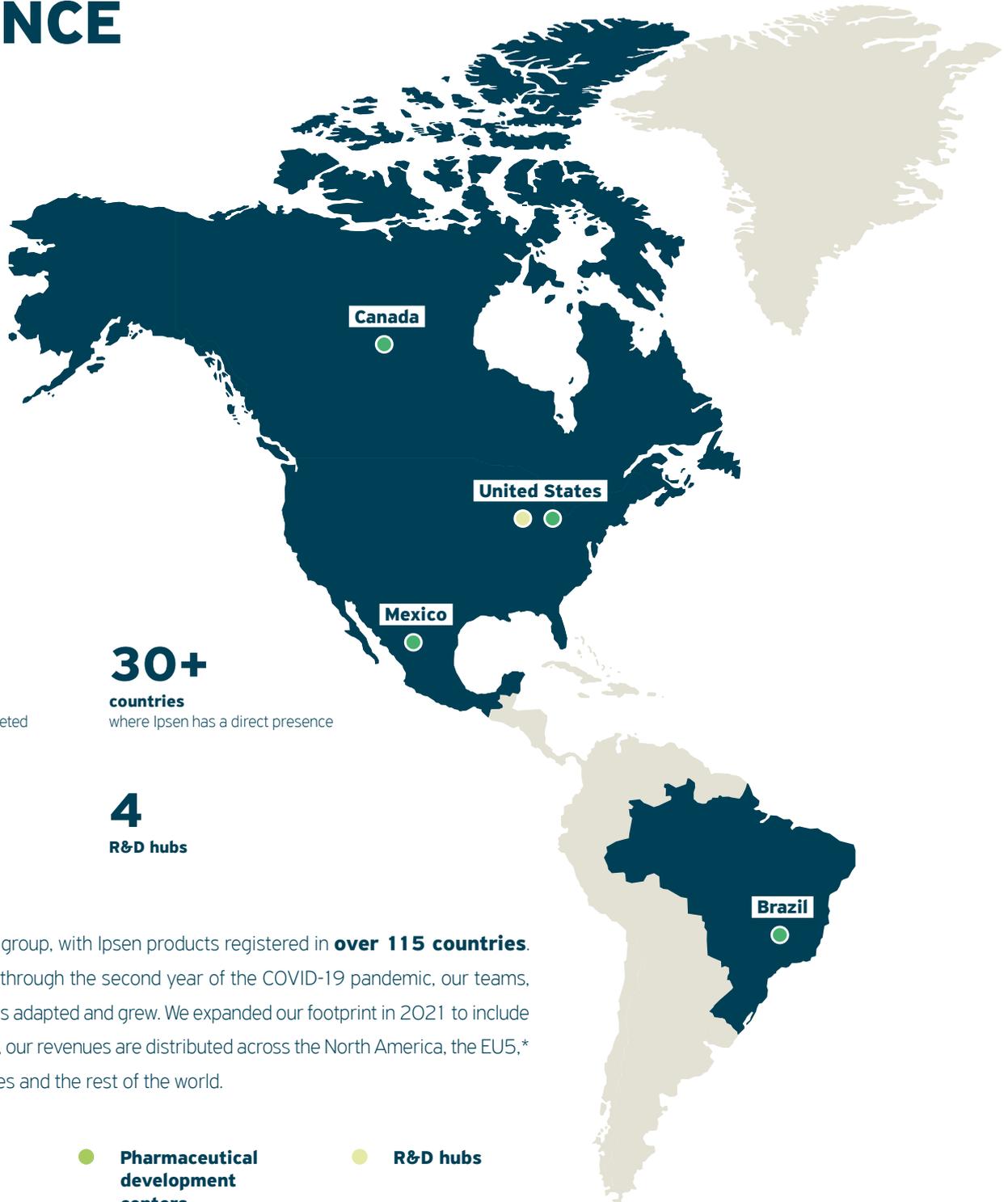
of our scientific publications made public for free

Providing innovative solutions to patients

16

R&D programs

OUR GLOBAL PRESENCE



100+
countries
where Ipsen products are marketed

30+
countries
where Ipsen has a direct presence

5,700+
employees
around the world

4
R&D hubs

We are an international group, with Ipsen products registered in **over 115 countries**. As the world advanced through the second year of the COVID-19 pandemic, our teams, partners and subsidiaries adapted and grew. We expanded our footprint in 2021 to include Japan and Dubai. Today, our revenues are distributed across the North America, the EU5,* other European countries and the rest of the world.

- **Countries where Ipsen operates**
- **Pharmaceutical development centers**
- **R&D hubs**

* France, Germany, Italy, Spain and the United Kingdom



OUR PRODUCTION AND R&D SITES

Ipsen scientists and innovators around the world are developing life-changing treatments. Through our global network and collective expertise, we are changing patients' lives for the better.

France

Paris-Saclay – R&D Power Base

The site's core mission is to accelerate clinical development and deepen our understanding of new molecules in oncology, rare disease and neuroscience.

Dreux – Manufacturing and R&D

Dreux develops the groundbreaking Novel Formulation Technologies drug delivery system. Dreux also supports the global distribution of products and hosts clinical supply chain activities for our clinical programs.

In addition, Dreux manufactures medicines for the Consumer HealthCare (CHC) business, notably Smecta®, Bedelix®, Forlax®, Fortrans®, Tanakan® and Eziclen®.

Signes – Manufacturing

This site specializes in the aseptic manufacturing of sustained release injectable products. Signes also performs testing, packaging and distribution of Ipsen specialty products, notably Somatuline®, Decapeptyl® and Onivyde®, which are distributed globally to over 70 countries.

L'Isle-sur-la-Sorgue – Manufacturing

This is Ipsen's only site for processing clays, used in Smecta®, Bedelix®, Actapulgit® and Gelox®.

United Kingdom

Oxford – R&D Power Base

Welcoming around 100 employees – including neuroscience researchers – our Milton Park site was designed to encourage innovation and collaboration. It also hosts our technological platform for botulinum toxins.

A seamless transition between Ipsen sites

In 2021, Ipsen completed the hand-off of Onivyde® production from its site in Cambridge, US to its site in Signes, France. The multi-step production process requires a specialized, sterile environment and technical training. In the face of pandemic travel restrictions, the teams on both sides of the Atlantic got creative. Signes built a one-to-one scale model of the lab in Cambridge, equipped with large screens that could project the US-based

instructor at life-size. Employees at Signes could therefore follow the exact motions and steps of their colleagues, as if they were in the same lab. Consolidating Onivyde® production at Signes ensures patient safety, a shorter supply chain and compliance with all EU regulations. For the US market, bulk production will continue at the Cambridge site until a bio-equivalence study is performed.



Wrexham – Manufacturing and R&D

This world-class biologic campus is specialized in the manufacturing of biological neurotoxins. The site has full end-to-end capabilities from development, active ingredient and aseptic manufacturing, to testing, packaging and distribution. The site is also a strategic R&D center for the development of recombinant neurotoxins. Wrexham produces and distributes Dysport®, Azzalure® and Alluzience® worldwide to more than 85 countries.

Investing in Wrexham

Ipsen has invested in a new £24.5 million Flexible Drug Product Filling (FDPF) facility in Wrexham, UK. This new building and filling line increase the site's production capacity. The rapid scale-up project was launched to ensure we will meet our growth ambitions in the coming years.

North America

Cambridge, US – Manufacturing and R&D Power Base

Placing Ipsen at the center of the biotech revolution in Cambridge, our Bioscience R&D center primarily focuses on oncology and rare disease. The site specializes in the manufacture of Onivyde® bulk, a liposomal formulation. Onivyde® is manufactured under aseptic conditions, then tested and distributed for the US market only.

Montreal, Canada and Newton, US – R&D Centers

These R&D centers focus on developing palovarotene as a potential treatment of fibrodysplasia ossificans progressiva (FOP) and other diseases.



85 M

UNITS PRODUCED
in 2021



7

MANUFACTURING SITES
around the world



4

POWER BASES
driving our innovation
in Specialty Care

China

Tianjin – Manufacturing

The local production facility for Smecta®, Tianjin also packages and distributes the rest of Ipsen's portfolio and other medical products in China.

Beijing – R&D

Established in 2012, the Asia Group Drug Development team oversees clinical trial coordination in Asia.

Shanghai – Manufacturing and R&D

The Ipsen Innovation Hub opened in 2019 develops strategies to register new indications and compounds in China. It also works with Global External Innovation and Partnering to pursue more development opportunities.

Ireland

Cork – Manufacturing

This site produces extract of ginkgo biloba – EGb 761®, which is used in the production of Tanakan® and Ginkor®.

Dublin – Manufacturing and R&D

This site manufactures bulk peptide active pharmaceutical ingredients (APIs) for Somatuline® and Decapeptyl®. Dublin is also a center for R&D product development for peptides and small molecules, as well as being the release testing center for Dysport® for the EU market.

BUILDING A ROBUST PIPELINE WITH EXTERNAL INNOVATION

External innovation plays a crucial role in our growth strategy. We are focused on **creating a robust and balanced pipeline** with indications in all stages of development (early-, mid- and late-stage), across our three core therapeutic areas, and with an appropriate balance between first-in-class and best-in-class potential. Our teams dedicated to partnering and external R&D innovation are working closely and tirelessly to deliver on this goal.

Together with our external partners, we are developing transformative medicines that positively impact the lives of patients with highly specific and underserved diseases. To support this vision, each year we make targeted investments in new, cutting-edge treatments and fields of research.

Ipsen has a solid global footprint to support a variety of programs worldwide, and our capabilities ensure we will see them through all the way to approvals and licensing. We are the right size to be agile, while investing meaningfully in our partners. Instead of employing a one-size-fits-all approach, we tailor each partnership and structure deals to match the specific needs of each program. We seek to understand the story behind each partner program, and each asset that we partner on becomes a priority in our pipeline or portfolio. Our commitment to patients ensures that **we will choose our investments with care.**

In 2021, we accelerated our drive to **build a high-value sustainable pipeline with seven deals** for a total of eight assets. Our goal is always to direct our resources to the precise points in the patient journey where they can have the greatest impact, especially in highly specific and underserved areas of Oncology, Rare Disease and Neuroscience. We aim to add 20 new treatments to our pipeline by 2025, primarily through external innovation.



€3.5BN

SET ASIDE FOR EXTERNAL innovation by 2024**



8

NEW ASSETS added to our portfolio through

7

EXTERNAL PARTNERSHIPS





Partnering to pioneer new treatments

GENFIT

Ipsen entered into a long-term strategic partnership with GENFIT, a biopharmaceutical company developing therapeutic and diagnostic solutions in metabolic and liver-related diseases.

We are advancing research for a late-stage, first-in-class PPAR alpha and delta agonist, elafibranor. This treatment will help patients living with Primary Biliary Cholangitis (PBC), a chronic disease that destroys bile ducts in the liver. Elafibranor is being evaluated in a global Phase III trial, with topline data expected in 2023.

IRLAB

We entered an exclusive worldwide licensing agreement with IRLAB, a Swedish company developing innovative treatments for Parkinson's disease.

Ipsen is interested in IRLAB's data and promising indication for mesdopetam, a dopamine antagonist under assessment as a treatment for people living with Parkinson's disease who experience levodopa-induced dyskinesia. Phase IIb data will be published in 2022, after which Ipsen and IRLAB will move to Phase III trials together, aiming to eventually bring the product to market.

BAKX Therapeutics Inc.

Ipsen began an exclusive worldwide collaboration with BAKX Therapeutics, a US-based company developing therapeutics that use mitochondrial apoptosis (cell death) pathways.

The deal strengthens our pre-clinical oncology pipeline. Ipsen and BAKX will collaborate on the research, development, manufacture and commercialization of novel therapeutics (BKX-001) that target the BCL-2 associated protein (BAX). This could lead to an innovative treatment option for patients living with leukemia, lymphoma and solid tumors.

Queen's University Belfast

With this world-class research institution, Ipsen will further explore cancer therapies based on innovative research into apoptosis. Through this partnership, Ipsen has been granted rights to a pre-clinical stage, first-in-class FLIP inhibitor program. FLIP inhibitors block tumor cells from evading cell death and prevent tumor growth and therapy resistance.

Exicure

We entered an exclusive agreement with American biotech firm Exicure to research, develop and commercialize Spherical Nucleic Acids (SNAs). Currently, two programs are under discovery evaluation, one for Huntington's disease and another for Angelman syndrome. Both programs reinforce our commitment to serving patients living with rare neurodegenerative disorders.

Accent Therapeutics

Ipsen signed an exclusive worldwide collaboration agreement with Accent Therapeutics to research, develop, manufacture and commercialize Accent's METTL3-inhibitor.

This deal strengthens Ipsen's expansion into hematological malignancies by targeting the RNA modifying protein (RMP) METTL3 that is being investigated in acute myeloid leukemia (AML).

Boston Children's Hospital

Ipsen is also strengthening our innovation efforts through academic partnerships like our collaboration with Boston Children's Hospital (BCH). Together, Ipsen and BCH are investigating BoNT/X, an innovative neurotoxin that can treat a range of conditions including spasticity.⁽¹⁾



We aim to add 20 new treatments to our pipeline by 2025, primarily through external innovation.

TOGETHER



engage
with all our
stakeholders



TOGETHER is a core value at Ipsen. From our teams to our partners to our stakeholders, we believe we can achieve more together. We believe in empowering every member of our global team, so each can contribute with passion and care to address patients' challenges. Our team members work with all stakeholders in the healthcare ecosystem to deliver innovations to people living with hard-to-treat conditions.



19

CERTIFICATIONS

recognizing Ipsen as a Top® Employer / Great Place to Work®



98%

OF EMPLOYEES

have a formalized development plan



Our approach is science-led and patient-driven, with the patient experience at the heart of everything we do.

“2021 was a year of implementation: we rolled out new programs, launched new initiatives and changed our ways of working. We embraced the needs of our employees, adhering to the hybrid work model and putting more support systems in place.”

Régis Mulot

Executive Vice President & Chief HR Officer

Listen to Ipsen: Behind the Scenes [here.](#)



UNITED IN UPHOLDING OUR VALUES

At Ipsen, our employees create a culture of excellence. Their dedication to healthcare providers and patients all over the world enables us to grow and keep developing life-changing treatments. We aim to foster an inclusive and agile work environment that strengthens our employee value proposition, so we can attract, develop and retain the best talent.

Our distinctive culture empowers employees by bringing together people from diverse backgrounds into thriving, collaborative teams. This is key to our goal to provide a workplace where everyone feels a connection to Ipsen's values and is recognized for, and understands first-hand, the impact each of them makes.

As a global, mid-sized company, we are a nimble force within the industry. If we see an opportunity for change and improvement, we seize it quickly. In 2021, we continued to evolve our Ipsen Way of Being to match our new and more ambitious vision.

Reconnecting around the globe

We understand the value of in-person connections, as they build lasting relationships between patients, customers and colleagues. As COVID-19 restrictions eased around the globe, team members began to return to the office. Ipsen operates on a 60-40 model, working three days in the office and two days from home. Starting in September 2021, teams all over the world hosted #Reconnect events, inviting employees to mark the return to the office with festivals, food, photo booths, and more!

Committed to our clear purpose

At Ipsen we are guided by a clear, shared purpose: to promote patients' lives, improve health outcomes and create a positive impact for patients and society. To fulfill this purpose with confidence and determination, we have four pillars underpinning our strategy:

- **Bring the full potential of our innovative medicines to patients**
- **Build a high-value, sustainable pipeline**
- **Deliver efficiencies to enable targeted investments and support our growth**
- **Boost a culture of collaboration and excellence**





We Lead with purpose

Our inclusive and diverse teams openly engage with our communities. Our decisions are ethical, and our actions compliant. We are dedicated to caring for Ipsen employees and the environment.

We Own the outcome

We consistently promote single-point accountability. We understand the importance of celebrating success and are committed to unleashing our full potential and excellence in execution.

We Learn & Share every day

Driven by data, science and deep insights into the health-care system, we leverage our collective intelligence toward testing, experimenting and piloting initiatives. We focus externally to fully understand and interact with our health systems and its actors.

Ipsen Way of Being

Our Ipsen Way of Being is organized into five pillars. Each is a key ingredient to cultivating a culture of collaboration and excellence among our teams, and also advancing the Ipsen strategy.



We Trust each other

Together we build trust through respect, listening, an openness to feedback and taking responsibility for our words and actions. As active communicators, we are ready to speak up to advance progress.

We Drive for success

Determined to be the partner of choice for all of our stakeholders, we are agile, decisive and committed to proactive collaboration. We innovate to address patients' most difficult challenges, and channel our optimism into an entrepreneurial spirit.

OUR TEAMS



Ipsen's teams are composed of a wide range of different roles. From scientists conducting clinical trials at our world-class research hubs to HR professionals organizing community-building initiatives for employees, each person's daily actions are visible and lead directly to our strong performance. As a mid-sized company, we are agile enough to move fast and large enough to make a real impact for patients. Together, we will continue to grow to become an industry leader in our core therapeutic areas.

Ipsen is recognized in 19 countries as a top workplace. We are proud of our distinctive, creative and passionate teammates who enliven our company culture and engender a partnership mindset. In line with our goal of creating this culture of collaboration and excellence, we continue to develop and build our capabilities. Our approach is science-led and patient-driven, with **the patient experience at the heart of everything we do.**

Eighty-eight percent of our employees responded to our latest engagement survey, which revealed that **77% of our employees are highly engaged working at Ipsen.** This indicates that Ipsen's employees are connected to our mission and share our vision for the future of our company. Many are inspired by a personal connection to the mission; they have seen firsthand the impact that an innovative new treatment can have on someone living with a difficult-to-treat condition. Everyone at Ipsen shares a sense of responsibility – we know that our work has the potential to make real, life-altering impacts and improve the lives of patients and their families.



19
HR CERTIFICATIONS
 recognizing Ipsen as
 a top workplace



61%
OF SENIOR LEADERSHIP ROLES
 filled through internal promotion



77%
OVERALL ENGAGEMENT SCORE



Encouraging, promoting, supporting

Ipsen helps employees evolve within their roles, and grow through them. We encourage internal mobility, with a goal of filling 65% of senior leadership roles by internal promotion by 2025. Through initiatives like the Ipsen Leadership Pathway, we help young leaders develop their talents and springboard into the next stage of their career with Ipsen.

We also promote Diversity and Inclusion through an array of local and global initiatives. Platforms such as the **World Café forum**, as well as fair and transparent hiring practices, all encourage open and healthy discussion.

Ipsen also supports its employees, putting their best interests front and center in conversations about health and safety, remote working and mental wellbeing. Through another year of modified working practices, a variety of initiatives and safe events helped highlight the need for community and mutual support.



Sharing in our company success

In 2021, Ipsen offered a new **Employee Shareholding Plan**, its third such move in the past five years. This involves employees even more closely with the company's operations by giving them the opportunity to own a stake in the company.



“2021 was a year of implementation: we rolled out new programs, launched new initiatives and changed our ways of working. We embraced the needs of our employees, adhering to the hybrid work model and putting more support systems in place.”

Régis Mulot
Executive Vice President & Chief HR Officer

PARTNERSHIPS: AN INTEGRAL PART OF OUR SUCCESS STORY

Prolonging and improving patients' lives and health outcomes is our core mission – to this end, we develop partnerships with all of our stakeholders and act to provide concrete responses to their needs and expectations.

We maintain transparency and open dialogue with employees, health-care professionals and patients, investors and the financial community, suppliers and partners, regulatory authorities and agencies, local communities and the media. Through our work with patient organizations, we support a patient's wider network, including their family and caregivers.

Our suppliers, R&D collaborators, centers of excellence and partners in academia are also stakeholders. They contribute to help **create value** for the business and for patients and communities. Our stakeholders encompass our local and global communities, our investors and the general public.

Partnerships built on trust

Our close relationships with all stakeholders enable our operational excellence, as we provide differentiated and innovative solutions for patients. We ensure that three things underpin every partnership:

- **We build relationships based on mutual goals.** We view every partnership opportunity as a unique process, customized to our partner's aims and ambitions.
- **We work together with our stakeholders.** We match stakeholders with an Ipsen specialist with expertise in their area of focus. They adopt a collaborative mindset, to ensure a mutually beneficial relationship.

- **We believe in collaboration and transparency.**

Our stakeholders have dedicated contact persons within Ipsen who are transparent and stay fully engaged with them throughout our partnership.

We approach stakeholder relationships with great care and respect. Concern for patients remains at the center of everything we do, as we strive to become best in class.

Connections are the key

Working with our broad network of stakeholders is the most important way we identify unmet needs in the communities we serve. This helps us increase access to our life-improving treatments.

As the COVID-19 pandemic revealed, there are serious gaps in the global availability of medical care. To tackle this issue in our complex and highly specialized disease areas, we need to work with all stakeholders in the healthcare system to change the paradigm.

A partner for patient organizations

In consultation with patient organizations, Ipsen commissioned a survey of 103 such groups across the globe, representing oncology, neuroscience and rare disease across a range of organization types (national, global, regional and umbrella). In 2021, Ipsen's patient engagement performance scored a mean average of **8.4** out of 10.

OUR PARTNERS



THIRD-PARTY STAKEHOLDERS

CIVIL SOCIETY
COMMUNITIES
PATIENT ADVOCACY GROUPS
INVESTORS AND ANALYSTS
MEDIA



PARTNER STAKEHOLDERS

R&D PARTNERS
COMMERCIAL PARTNERS
EMPLOYEES
SUPPLIERS



INSTITUTIONAL STAKEHOLDERS

REGULATORY AUTHORITIES
POLICY MAKERS
HEALTHCARE PROFESSIONALS
HEALTHCARE ORGANIZATIONS
PAYERS



PATIENTS

PATIENTS



enable

access to innovative
treatments



PATIENTS are at the heart of our strategy. By better understanding when, where and how patients access treatments, we can create and deliver innovations that make a real impact. This data- and insights-driven patient-centricity is what empowers us. At Ipsen, our shared purpose is to prolong patients' lives and improve health outcomes. We channel our efforts into three therapeutic areas: Oncology, Rare Disease and Neuroscience.



5

CLINICAL STUDIES
in Phase III of development



220

PATIENT ORGANIZATIONS
collaborated with
Ipsen in 2021



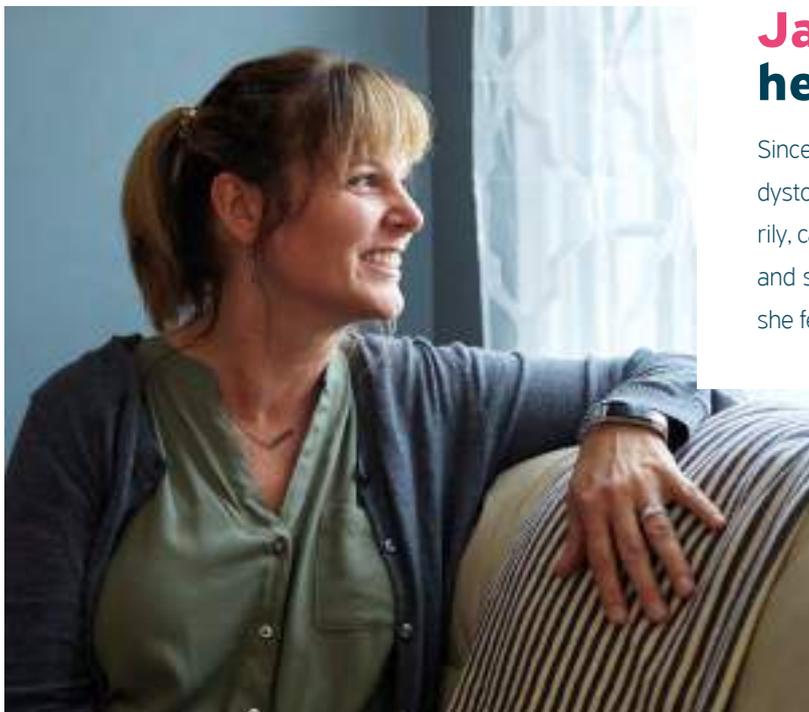
We maintain a culture of innovation at Ipsen, targeting differentiated treatments in our three core areas: Oncology, Rare Disease and Neuroscience.

“I’ve just been able to be present in the lives of my family and participate in activities, and things that I normally would have hidden from. I can live my life and do the things I want to do, and be happy.”

Janice

Living with cervical dystonia
Tennessee, USA

PARTNERING WITH PATIENTS TO IMPROVE OUTCOMES



Janice: Recovering her confidence

Since the age of 21, Janice has been living with symptoms of cervical dystonia, a painful condition in which neck muscles contract involuntarily, causing one's head to twist or turn to one side. It's a rare condition, and she wasn't properly diagnosed until she was 30. By that time, she felt withdrawn and isolated, often avoiding social situations.



“I would try to stay in the background. I missed out on birthday parties. I would try to hide.”

“I would try to stay in the background,” she says. “I missed out on graduations; I missed out on birthday parties. I would try to hide.”

When Janice found a neurologist who really understood the condition, it was a hugely positive step forward. Together, they came up with a treatment plan that helped Janice manage her cervical dystonia and recover some of her confidence. With the correct diagnosis, the right treatment, and the support of her healthcare provider and her family, Janice is now able to engage fully with life once again.

“I’ve just been able to be present in the lives of my family and participate in activities, and things that I normally would have hidden from,” she says. “I can live my life and do the things I want to do, and be happy.”





Nadine: Living with and researching FOP

At the age of 13, Nadine developed a limp and was diagnosed with fibrodysplasia ossificans progressiva (FOP), a disorder in which muscle and connective tissue such as tendons and ligaments are gradually replaced by bone.

By the time she was 22, Nadine's condition had spread to her shoulder and then to her jaw. "I really went into my shell when my jaw became paralyzed," she says. "Whenever I had to go out in public, I didn't dare to eat, and I felt so bad."



“Whenever I had to go out in public, I didn’t dare to eat, and I felt so bad.”

But with the unconditional support and encouragement of her family, Nadine has continued to do the things she loves. Now 28, she sings regularly with a choir, plays the flute, and also works in a lab, researching FOP. Her goal is to help others living with this condition and to raise awareness about its impact.

“Working on your own illness is a double motivation,” she says. “You’re not just doing it for yourself. You know there are other patients, and that the results we want might produce something that others will benefit from, along with yourself.”

Ronny: Engaging fully with family

In 2010, Ronny was diagnosed with stage IV metastatic neuroendocrine tumors, a rare cancer that affects nerve cells and hormone production in areas throughout the body. Ronny learned that with the right treatment he could potentially extend his life, so he set up a blog to help gather information and raise awareness of this complex, little-discussed disease.

Thankfully, Ronny was able to access the right treatment for his condition, at the right time. With suitable medical care and treatment, he has been able to live a more active and full life. He can now enjoy bike rides and walks, and travel with his wife.

“‘You look so well!’ You just wouldn’t guess that I had stage four cancer.”

“Had I not had treatment, I wouldn’t be here today,” he says. “When people first meet me, they always say: ‘You look so well!’ You just wouldn’t guess that I had stage four cancer.”

Ronny has four grandsons. When he was first diagnosed, he says he had no idea whether he would even see them grow up. “Now, I’ve been watching them go to school. I’m sure that I will see my oldest grandson getting his first job and perhaps even starting a family.”





R&D: THE BEDROCK OF OUR COMMITMENT TO PATIENTS

Research and development are core to our mission of helping prolong patients' lives and improve their health outcomes. We seek to develop differentiated treatments in our three core therapeutic areas: Oncology, Rare Disease and Neuroscience. To support innovation and expand our pipeline, we have **€3.5 billion** firepower dedicated to support new partnerships by **2024**. Our main R&D centers are located in world-class scientific hubs, including Paris-Saclay in France; Oxford in the UK; Cambridge in the US; Shanghai in China.

Enriching a diversified portfolio

In 2021, we pursued our R&D strategy on both internal and external innovations. Our teams researched and commercialized new indications, while we also invested in external partnerships with entities developing promising potential treatments for hard-to-treat conditions in each of our three therapeutic areas.

Our approach to pipeline development prioritizes **best-in-class collaborations** for new, for new medicines in areas where we have proven experience, global capabilities and a strong partner network. Ipsen's ambition is to continue to build a robust, valuable, and sustainable portfolio of medicines to meet the needs of patients and their healthcare teams.

Milestones and new assets in 2021

Oncology: milestones

- The European Commission granted approval to Ipsen's innovative first-line treatment for advanced renal cell carcinoma (aRCC): the Cabometyx® (*cabozantinib*) and Opdivo® (*nivolumab*) combination. Read the press release on [ipсен.com](#).

- Several Phase III oncology studies have life cycle management (LCM) potential for Ipsen. These studies are evaluating Cabometyx® in combination with *atezolizumab*, as well as Onivyde® for a variety of difficult-to-treat cancers.
- Data, including quality-of-life data, were presented from the CLARINET FORTE Phase II study of Somatuline® Autogel® / Somatuline® Depot (*lanréotide*). Read the press release on [ipсен.com](#).

Oncology: new to the pipeline

- Opt-in decision with Exelixis added a new Phase III asset to the pipeline. Read the press release on [ipсен.com](#).
- Exclusive worldwide partnership with BAKX Therapeutics added a new pre-clinical asset to the pipeline. Read the press release on [ipсен.com](#).
- Exclusive worldwide partnership with Accent Therapeutics added a new pre-clinical asset to the pipeline. Read the press release on [ipсен.com](#).

Rare disease: milestones

- Sohonos™ (*palovarotene* capsules) approved by Health Canada for the treatment of fibrodysplasia ossificans progressiva (FOP). Read the press release on [ipсен.com](#).
- IPN60130, a potential further treatment for FOP, entered clinical trials and is now in Phase II.

Rare disease: new to the pipeline

- A partnership with GENFIT added ELATIVE™, a Phase III clinical trial of elafibranor for the treatment of Primary Biliary Cholangitis (PBC), to Ipsen's pipeline. Read the press release on [ipсен.com](#).
- An exclusive partnership with Exicure Inc. added two different research and development programs for Spherical Nucleic Acids (SNAs™) in the treatment of Angelman syndrome and Huntington's disease. Read the press release on [ipсен.com](#).



Neuroscience: milestones

- Results from Phase III clinical trials of Dysport® (botulinum toxin type A) showed positive indications in a range of neurological conditions. Read the press release on ipsen.com.

Neuroscience: new to the pipeline

- An exclusive worldwide deal with IRLAB Therapeutics added a Phase IIb clinical trial for mesdopetam, a potential therapy for reducing treatment-induced side effects of Parkinson's disease, to the pipeline. Read the press release on ipsen.com.
- Two Phase I trials assessing IPN10200 Ax and IPN10200 Tx – long-acting neurotoxins (LANTs) to treat spasticity – began recruiting participants.



€428.4 M
INVESTED IN R&D
in 2021



5
CLINICAL STUDIES
in Phase III of development



550+
EMPLOYEES
dedicated to R&D worldwide

A DIVERSE AND BALANCED PIPELINE

Pipeline as of end of Q1 2022



Ax: aesthetics, Tx: therapeutics, FOP: fibrodysplasia ossificans progressive, PD-LID: Parkinson's disease-levodopa-induced dyskinesia, HCC: hepatocellular carcinoma, RR DTC: radio-refractory differentiated thyroid cancer, NSCLC: non-small cell lung cancer, mCRPC: metastatic castrate-resistant prostate cancer, SCLC: small cell lung cancer, PBC: primary biliary cholangitis, PDAC: pancreatic ductal adenocarcinoma, NDO: neurogenic detrusor overactivity, 1L: first line, 2L: second line

Information shown as at the end of Q1 2022

⁽¹⁾ Data readout anticipated in H2 2022

⁽²⁾ Data readout anticipated in 2023

⁽³⁾ Regulatory Decision (EU) anticipated in Q2 2022



ONCOLOGY: A STRONG PORTFOLIO AND PATIENT FOCUS

Oncology is the largest of Ipsen's portfolios, accounting for 75% of sales in 2021.* We have continued to invest in this core area of our business, harnessing our expertise and long-standing heritage in oncology to deliver outcomes that matter most to patients.

75%

OF IPSEN'S SALES
are from the Oncology portfolio

€2,153.5M

IN TOTAL ONCOLOGY
sales

In 2021, we made progress in new indications for Cabometyx® (cabozantinib) and maintained growth for our blockbuster treatment Somatuline® Autogel/Somatuline® Depot (lanreotide), as well as Decapeptyl® (triptorelin) and Onivyde® (irinotecan liposome injection).

The European Commission (EC) confirmed its approval of the **Cabometyx® and nivolumab combination** in March 2021. This first-line treatment doubled median progression-free survival versus the comparator sunitinib in people living with advanced renal cell carcinoma (RCC).⁽¹⁾ We have seen further approvals and successful launches worldwide (outside of the US and Japan).

Cabometyx®, an important treatment option in both RCC and hepatocellular carcinoma, is now approved in 60 countries across our licensed indications. In May, we sought to expand these indications further by working with Exelixis to develop Cabometyx® as a second-line treatment for radioactive iodine-refractory differentiated thyroid cancer (RAI-R DTC). Promisingly, the COSMIC-311 trial demonstrated that Cabometyx® reduced the risk of disease progression or death by 78% versus the placebo.⁽²⁾

Somatuline® is an important long-term asset for Ipsen, and we are evolving its value proposition. Our delivery system remains unrivaled as we continue our long-term commitment to serving people living with gastroenteropancreatic neuroendocrine tumors and acromegaly.

2021 saw launches of generic and competitor lanreotide in Europe and the US. However, Somatuline® continues to experience market growth and expanded market share, demonstrating gradual sales erosion. We are a brand of choice thanks to our redesigned delivery system, patient offerings and long-standing heritage.

Decapeptyl® continues to be an important growth driver for Ipsen and will build upon our strong position in many markets. This treatment has one-month, three-month and twice-yearly dosing formulations in prostate cancer and central precocious puberty (CPP) allowing for treatment customization based on patient and healthcare professional needs. We remain committed to people living with prostate cancer and CPP, investing to expand access in these therapy areas while Phase III trials are ongoing in China.

* For more financial results, see https://www.ipсен.com/websites/ipсен_Online/wp-content/uploads/2022/02/10225600/FY-2021---Results-announcement.pdf

THE IPSEN ONCOLOGY PORTFOLIO: TACKLING SOME OF THE MOST DIFFICULT-TO-TREAT CANCERS

MEDULLARY THYROID CANCER

5% of thyroid cancers.^(3a)

COMETRIQ®

- Clinically meaningful difference in progression-free survival with cabozantinib (11.2 months) versus placebo (4 months).^(3b)

NEUROENDOCRINE TUMORS (NETs)

171,000 people living with NETs in the US. Incidence rate of approximately 6.98 cases per 100,000 people.^(4a)

SOMATULINE®

- 53% relative risk reduction of disease progression or death.^(4b)
- Unique ready-to-use delivery system and availability of independent injection (by oneself or from a partner) where approved.

RENAL CELL CARCINOMA (RCC)

There are over 400,000 new cases of kidney cancer diagnosed worldwide each year.^(5a) RCC is the most common type, accounting for approximately 90% of cases.^(5b)

CABOMETYX®

- Multi-targeted tyrosine kinase inhibitor therapy, which prolongs survival, slows disease progression and shrinks tumors in first-line and second-line RCC as a monotherapy and as a first-line combination with nivolumab.
- Ipsen is funding several trials to explore combining cabozantinib with immunotherapy in solid tumors.^(5c)

PANCREATIC CANCER

Third-leading cause of cancer-related death in the US.^(6a)

ONIVYDE®

- Significant improvement of overall survival in adult patients with metastatic adenocarcinoma of the pancreas when used as second-line therapy.
- Numerous investigator-sponsored studies are ongoing to explore Onivyde® in combination with other treatments for different types of cancer.^(6b)

BREAST CANCER

The most common cancer in the world and the first most frequent in women^(7a); 65% to 75% of all breast cancers are hormone receptor positive^(7b)

DECAPEPTYL®

- The 8-year overall survival was 85.1% together with tamoxifen, and 87.2% together with exemestane.^(7c)

HEPATOCELLULAR CARCINOMA (HCC)

More than 900,000 new cases of liver cancer, 90% of which are HCC, are diagnosed worldwide each year.^{(8a)(8b)} HCC is expected to cause 1 million global deaths annually by 2030.^(8c)

CABOMETYX®

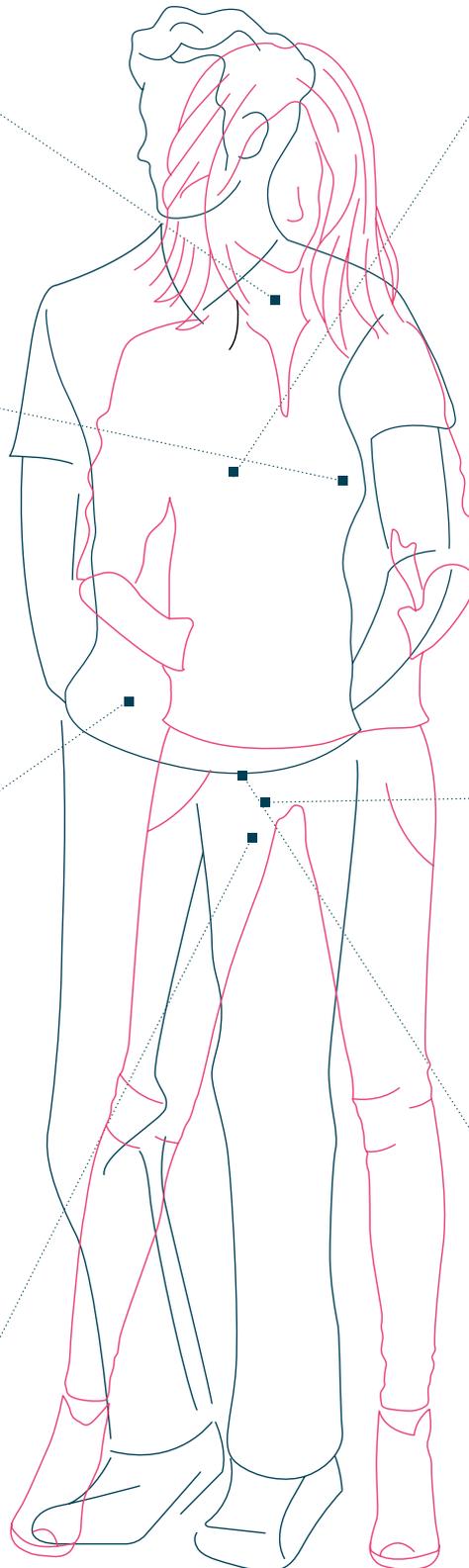
- Significant overall survival benefit in people living with previously treated advanced HCC.^(8d)

PROSTATE CANCER

In 2020, over 1.4 million new cases of prostate cancer were diagnosed worldwide, making it the fourth most commonly occurring cancer globally and the second in male population.^(9a)

DECAPEPTYL®

- Castration is the main treatment objective, with over 90% of patients achieving and maintaining medical castration below the most stringent threshold levels (<20 ng/dl).^(9b)



Listen to Oncology: Behind the Scenes 
here.

BUILDING A PORTFOLIO OF TREATMENTS FOR RARE AND ULTRA-RARE DISEASES

Ipsen is committed to developing treatments to help improve the lives of people living with rare and ultra-rare diseases. Placing patients at the center of what they do, our Rare Disease teams research and trial new approaches to treating conditions.

94%

OF RARE DISEASES
lack approved treatments

~7,000

RARE DISEASES AFFECT AN ESTIMATED
350-400 million people worldwide

An estimated 350 million to 400 million people worldwide are impacted by one of ~7,000 rare diseases. Ninety-four percent of rare diseases still have no treatment. This makes the work of our Rare Disease teams even more crucial. They focus on four main areas of expertise: extremely rare bone disorders, growth disorders, rare cancers and rare neurogenetic disorders.

Innovating for the rare disease community

The pathway for launching treatments for rare diseases is rarely straightforward. In 2021, we continued our push to develop potential treatments for fibrodysplasia ossificans progressiva (FOP), an ultra-rare genetic disorder characterized by new bone formation outside of the normal skeletal system. Healthcare professionals may not have seen a case of FOP before and initial misdiagnosis is common.

We progressed two potential treatments: palovarotene and IPN 60130, despite the complexities inherent in the development of treatments for ultra-rare diseases. We also pursued a robust external innovation strategy, with three partnerships focused on rare and ultra-rare diseases.

Partnering for progress

In 2021, we entered into a long-term strategic partnership with GENFIT. This gave us global rights to develop and commercialize elafibrinor, currently being evaluated in a global Phase III trial, as a treatment for Primary Biliary Cholangitis (PBC), a rare, chronic autoimmune liver disease. PBC is difficult to treat, and patients have previously faced limited treatment options. Elafibrinor may unlock a higher quality of life for patients and lead to significantly reduced levels of disease activity.

Studying SNAs™

Ipsen also entered an exclusive collaboration with US biotech firm Exicure, which develops therapeutics for neurology, immuno-oncology, inflammatory diseases, and other genetic disorders. The collaboration focuses on novel Spherical Nucleic Acids (SNAs™) as potential investigational treatments for two conditions. These are Huntington's disease, a progressive, fatal neurodegenerative disorder, and Angelman syndrome, a rare condition that causes delayed development, problems with speech and balance, intellectual disability and possibly seizures.

WHAT LIFE-CHANGING LOOKS LIKE

We offer a range of innovative treatments to help those with high unmet medical need. Here is a look at these therapies:

GROWTH FAILURE IN CHILDREN

NUTROPINAQ® (somatropin)⁽¹⁾

treats girls of two years and older with Turner syndrome, and prepubertal children with growth failure associated with chronic renal insufficiency.

CENTRAL PRECOCIOUS PUBERTY

CPP is a rare disorder, characterized by premature puberty onset and significant impairment of final adult height. ^{(2a) (2b)}

DECAPEPTYL® (TRIPTORELIN PAMOATE)^(2c)

Efficacious in suppressing the pituitary release of luteinising hormone and follicle-stimulating hormone, and consequently secretion of estradiol in girls and testosterone in boys to pre-pubertal levels. ^(2d)

GROWTH FAILURE IN CHILDREN AND ADOLESCENTS WITH CONFIRMED SEVERE PRIMARY INSULIN-LIKE GROWTH FACTOR-1 DEFICIENCY (IGFD)

INCRELEX® (mecasermin)⁽⁴⁾

is the only treatment available for patients in the US, the European Union and Australia living with primary IGFD, an ultra-rare disease affecting normal bone and tissue growth and development, which can result in growth failure.

GROWTH HORMONE DEFICIENCY IN ADULTS

NUTROPINAQ® (somatropin)

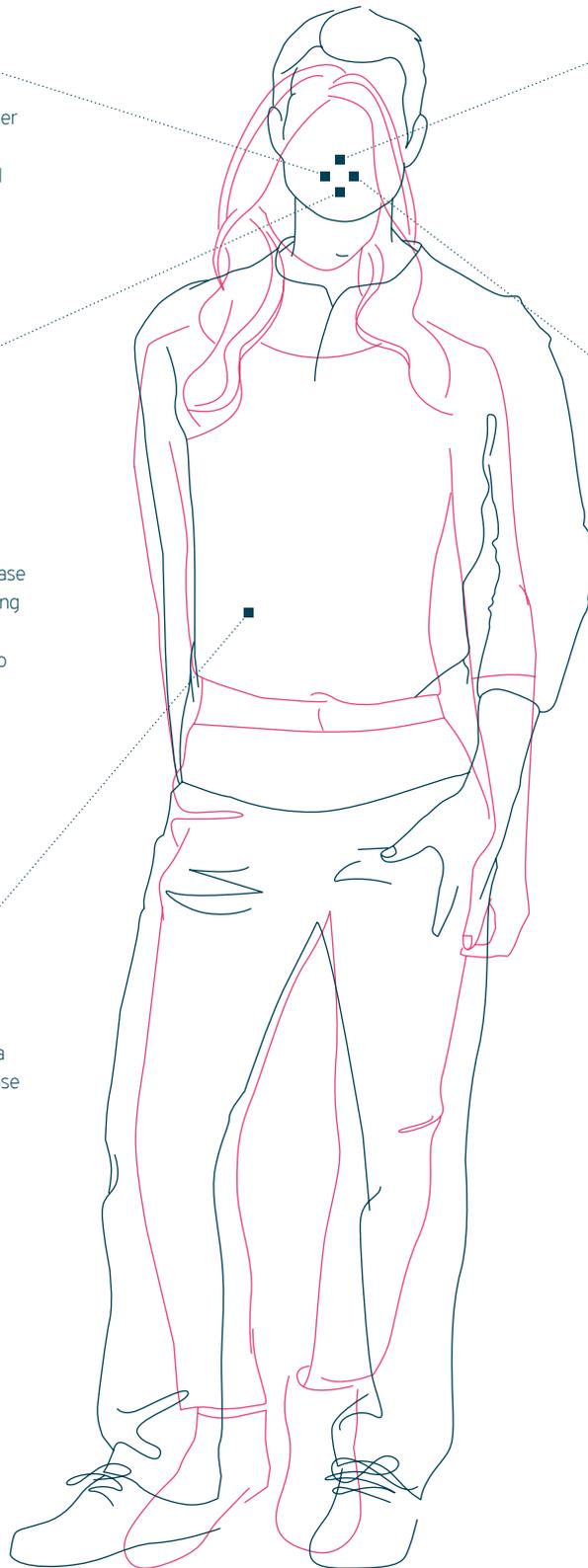
serves adults living with growth hormone deficiency, acting as a replacement of endogenous growth hormone.

ACROMEGALY

SOMATULINE® (lanreotide)⁽³⁾

is used in the long-term treatment of acromegaly when the circulating levels of growth hormone (GH) and/or insulin like growth factor (IGF-1) remain abnormal after surgery and/or radiotherapy or for whom surgery and/or radiotherapy is not an option. It is also used to relieve the symptoms associated with acromegaly.

Also offered in the Somatuline® Autogel® self-administering syringe.





DRIVING A REVOLUTION IN NEUROSCIENCE

Neuroscience is a key strategic driver for our business. More than 30 years of expertise in toxins and neuroscience research provides the foundation for Ipsen's exciting next chapter: creating longer-acting neurotoxins (LANTs). Having laid the groundwork, we are ready to help shape the future of this industry.

Ipsen has

**over
30 years**

of experience in neurotoxins

€434.6M

IN TOTAL SALES
from Dysport® in 2021

Ipsen scientists continuously research potential new indications at Ipsen Bioinnovation – Ipsen's technological platform for toxins in Milton Park, UK – and in other R&D centers worldwide. In 2021, not only did we identify potential new indications for our existing treatments, we also expanded our portfolio with new assets targeting difficult-to-treat conditions.

Promising results in neuroscience

In January 2021, Ipsen announced new analyses from Phase III clinical trials of Dysport® (*abobotulinumtoxinA*). The treatment shows potential for an array of neurological conditions such as cervical dystonia, adult lower-limb and upper-limb spasticity, and pediatric lower-limb and upper-limb spasticity. The DIRECTION study, another Ipsen-supported trial, was launched in June 2021, comparing the efficacy and safety of Dysport® in the treatment of adult upper limb spasticity. This Phase IV trial is now enrolling participants in the US, Canada and France to compare and collect insights into quality of life, duration of response and more. Finally, throughout the year Ipsen adapted its aesthetics activities to the current health situation. We offered online training for those administering Alluzience® (the liquid form of Dysport®). Our expertise was made widely and safely accessible for healthcare professionals all over the world.

Developing the next generation of treatments

During the year, we saw progress in our pipeline, both thanks to internal research and external partnerships:

- We advanced as a result of our unique toxin expertise. Ipsen became the first company to advance modified, recombinant toxins into the clinical stage, launching three integrated Phase I/II trials with two longer-acting neurotoxin assets in aesthetic and therapeutic indications. These studies, the first in human participants, continue to progress well in 2022.
- Ipsen secured exclusive worldwide development and commercial rights to Sweden-based IRLAB's treatment, mesdopetam, a novel dopamine D3-reception antagonist. It is being assessed in a Phase IIb clinical trial as a potential treatment option for people living with Parkinson's disease who are experiencing levodopa-induced dyskinesia (LID). Mesdopetam is also in the early stages of development for Parkinson's Disease Psychosis.
- Ipsen signed an exclusive collaboration agreement with Excire Inc. to research, develop and commercialize novel Spherical Nucleic Acids (SNAs™) as potential investigational treatments for Huntington's disease and Angelman syndrome.

ONE PRODUCT, MULTIPLE INDICATIONS

Dysport® (botulinum toxin type A) ⁽¹⁾ has been a game changer for patients living with debilitating neurological conditions. Worldwide, it has helped relieve pain, restore motor function and bring ease to people's lives.

CERVICAL DYSTONIA

Cervical dystonia is a rare neurological disorder characterized by involuntary muscle contractions in the neck that cause abnormal movements and posture of the neck and head. Prevalence is estimated at 57 cases per million in the EU ^(2a) and at 89 cases per million in the US. ^(2b)

HEMIFACIAL SPASM

Hemifacial spasm is a neuromuscular disease characterized by irregular, involuntary muscle contractions on one side of the face. Estimated prevalence of 14.5/100,000 in women and 7.4/100,000 in men. ⁽⁴⁾

PEDIATRIC LOWER AND UPPER LIMB SPASTICITY

Cerebral palsy is the most common cause of spasticity and physical disability. Prevalence of 1.5 to 3 cases per 1,000 live births. ^(6a) ^(6b) 90% of patients with CP will present spastic hypertonia. ^(6c)

BLEPHAROSPASM

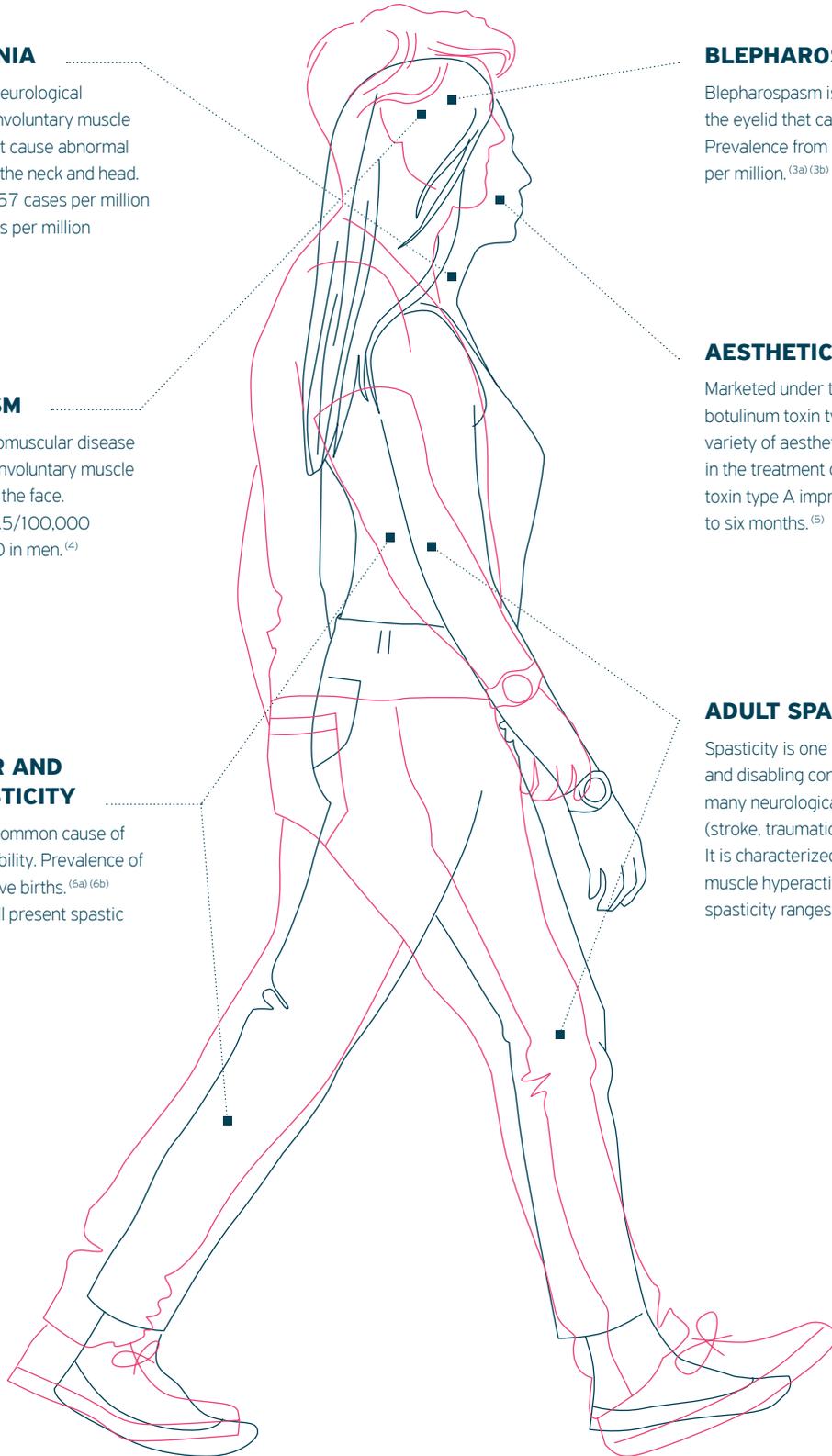
Blepharospasm is an abnormal contraction of the eyelid that can be chronic and persistent. Prevalence from 16 to 133 cases per million. ^(3a) ^(3b)

AESTHETICS

Marketed under the name Alluzience®, botulinum toxin type A is also used for a variety of aesthetic treatments. When used in the treatment of glabellar lines, botulinum toxin type A improves their appearance for up to six months. ⁽⁵⁾

ADULT SPASTICITY

Spasticity is one of the most common and disabling conditions associated with many neurological diseases in adults (stroke, traumatic brain injury, etc.). It is characterized by velocity-dependent muscle hyperactivity. Incidence of post-stroke spasticity ranges between 17% and 42.6%. ⁽⁷⁾



Listen to Neuroscience: Behind the Scenes [here.](#)



GROWTH IN A RECOVERING CONSUMER HEALTHCARE MARKET

For more than 90 years, Ipsen has built a solid Consumer HealthCare (CHC) business with a large portfolio of prescription and over-the-counter (OTx) treatments.

€225.6M

IN TOTAL SALES
for CHC

46

YEARS OF EXPERTISE
in functional gastrointestinal
disorders

+8.1%

FROM 2020 SALES
at CER

Through the challenges of the past two years, the CHC team has continued to take steps to grow its business and create a sustainable future. Already, by transforming from a prescription-based model to a combination of prescription and OTC treatments, the CHC team has improved access to its products. It helps people all over the world manage a range of symptoms and conditions.

As more countries emerge from lockdowns, demand has risen for gastrointestinal treatments and bowel cleansers. CHC sales have grown, largely driven by strong performance in China and Eastern Europe.



Total CHC sales grew to €225.6 million in 2021, an increase of 8.1% at Constant Exchange Rate (CER). CHC sales constitute 14.1% of total sales for Ipsen. CHC's core operating income more than doubled in 2021 to €31.7 million.

CHC's strong growth, even in a difficult sales environment, is due both to COVID-19 recovery and to strong cost management by the CHC team. Several key products were drivers of this growth:

- 10.1% growth in sales of **Smecta® (diosmectite)**, CHC's best-selling product. Smecta® sales amounted to €88.8 million, or 3.1% of Ipsen's sales. 2021 also marked 46 years since the launch of Smecta®, which has been trusted by consumers and healthcare providers alike for decades.
- 29.1% growth in sales of colon and bowel cleansing solutions **Fortrans®** (macrogol 4000 and salts combination) and **Eziclen®**.
- 5.7% growth in sales of **Tanakan®** (EGb761®), a supplement that treats symptoms of memory and attention disorders. This increase was also largely driven by increased performance in Vietnam.



For more information about Consumer HealthCare, please visit our website: [here](#).

PROFILES OF KEY CONSUMER HEALTHCARE PRODUCTS

GASTROINTESTINAL CONDITIONS

— **SMECTA®** (1)
(DIOSMECTITE)

— **SMECTAGO®** (2)

— **SMECTAGAS®** (2)

— **SMEBIOCTA COMFORT®**
(LACTOBACILLUS
PLANTARUM 299V)

— **SMEBIOCTA PROTECT®**
(SACCHAROMYCES BOULARDII,
LACTOBACILLUS RHAMNOSUS
GG AND VITAMIN C)

— **FORLAX®**
(MACROGOL 4000)

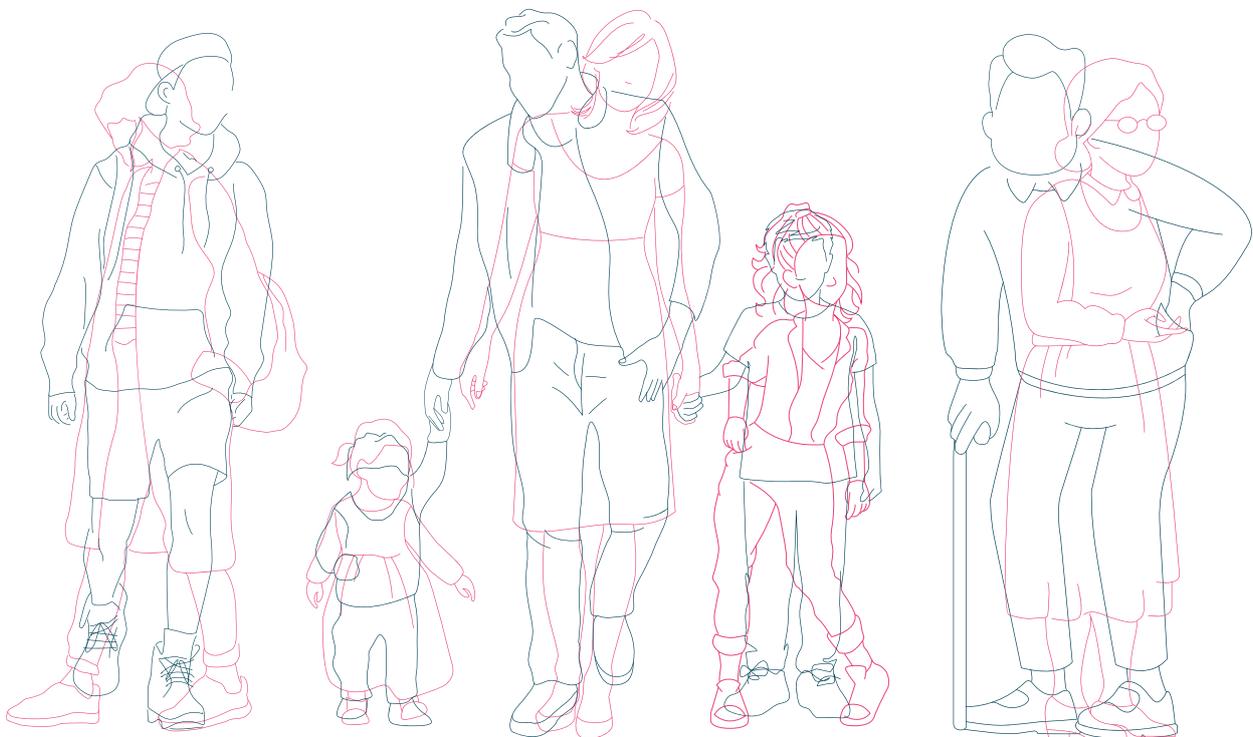
— **FORLAXGO®** (2)

— **FORTTRANS®** (1)
(MACROGOL 4000 AND
SALTS COMBINATIONS)

— **EZICLEN®/IZINOVA®** (1)
(BLI-800)

— **ETIASA®** (1)
(MESALAZINE)

— **BUSCOPAN®** (1)
(HYOSCINE BUTYLBROMIDE)



OTHER CONDITIONS

— **TANAKAN®** (1)
(EGB761®)

— **PAXELADINE®** (1)
(OXELADIN HYDROGEN
CITRATE)

— **PRONTALGINE®** (1)
(CODEINE, CAFFEINE,
PARACETAMOL)

— **SUPPOSITORIA
GLYCERINI**
(GLYCEROL)

— **PRONTADOL®**
(PARACETAMOL AND 50 MG
OF CAFFEINE)

SOCIETY



contribute
to a sustainable
future



Working to improve **SOCIETY** is everyone's responsibility. We are committed to supporting our communities, employees and the environment, and creating positive change today that will still be felt by future generations. Recognizing the important impact we can have on the communities we serve worldwide, we've joined the *Business Ambition for 1.5°C* to decrease carbon emissions. We continue to think big as we strive to benefit all society.



WOMEN MAKE UP

42.3%

of the Global Leadership Team

**88%**of our **GLOBAL ELECTRICITY USE**
comes from **RENEWABLE SOURCES**

Our efforts are focused on achieving real results and slashing our carbon emissions to meet the 2030 targets. Given the scale of the climate challenge, we believe everyone has a role to play.

Our commitment to CSR is integrated into our strategy, and impacts every aspect of our business.

Listen to Ipsen: Behind the Scenes [here.](#)



MAKING A BROADER IMPACT

Guided by our CSR strategy, we pursued multiple initiatives in 2021 to create real impact where results are needed most.

Embracing our communities

Organizing Community Day is one of Ipsen's key initiatives to encourage engagement with our local communities, all over the world. Through this initiative, Ipsen partners with associations to connect employees with volunteer activities several times throughout the year. Employees select their activity and spend either a half or full day working with the association.

Our **2021 Community Day** was a return to form after the complexities of 2020. More than 1,800 people took part across 38 countries, representing a participation rate of 32% – exceeding our expectations and reaching **our highest-ever engagement**.

Ipsen staff and local affiliates organized events to support patients, healthcare communities, caregivers and environmental associations. Working together, Ipsen employees took part in **more than 125 activities supporting over 100 associations**.

Some of the actions taken by Ipsen employees include:

- Making 1,000 hygiene kits for students in extremely precarious situations
- Hosting an online presentation raising awareness of cerebral palsy in children, to support patients and their families
- Raising funds for medical care for children living in poverty



These represent just a selection of the activities our teams took part in. Staff also volunteered at food banks, hospitals, and schools, and helped with tree-planting, litter-picking, and creating Christmas decorations. We are proud that our teams could make such an impact.

Supporting those affected by the crisis in Ukraine

Our company has a responsibility to employees and patients impacted firsthand by the conflict in Ukraine. In February 2022, Ipsen created a crisis committee dedicated to guarding the safety and health of these two groups. More broadly, Ipsen has sought to support humanitarian efforts that are bringing aid to civilians through a **donation of €1.5 million**. These funds were sent to the Red Cross in France and to Tulipe, an organization that collects donations from healthcare companies and distributes them in areas affected by conflict or disasters.



Joining the GoodPlanet Foundation

Part of the funds raised by our Ipsen in Motion program were donated to the GoodPlanet Foundation, which raises awareness of environmental issues and protection. We supported the Foundation's Women and Shells project in Senegal, which empowers women in the wetlands of the Saloum Delta to protect the environment and create a sustainable economy through shellfish harvesting.

Exercising our collective powers

Ipsen in Motion is an internal program we have run since 2018 to promote the health of all employees while raising money for worthwhile causes. It consists of a series of five sports challenges: one that runs throughout the year, plus four local, month-long events.

2021 was a banner year for Ipsen in Motion. We easily surpassed our target of one in five employees taking part, with 1,150 participants in total. **More than €50,000 were raised**, with funds donated to five causes close to our mission and values.

Well-being at work

With work-from-home orders ongoing in many countries throughout 2021, we launched initiatives aimed at protecting employee health and well-being. **CSR ambassadors** around the world worked with HR teams to ensure employees had the support they needed to maintain their well-being during highly challenging times.

Our HR team also launched two new diversity and inclusion (D&I) initiatives. The **Global D&I Council** was established, with a core team of business leaders tasked with driving Ipsen's D&I efforts globally. Local Inclusion Groups were also set up to expand D&I efforts in France, the US, the UK, and the DACH region.

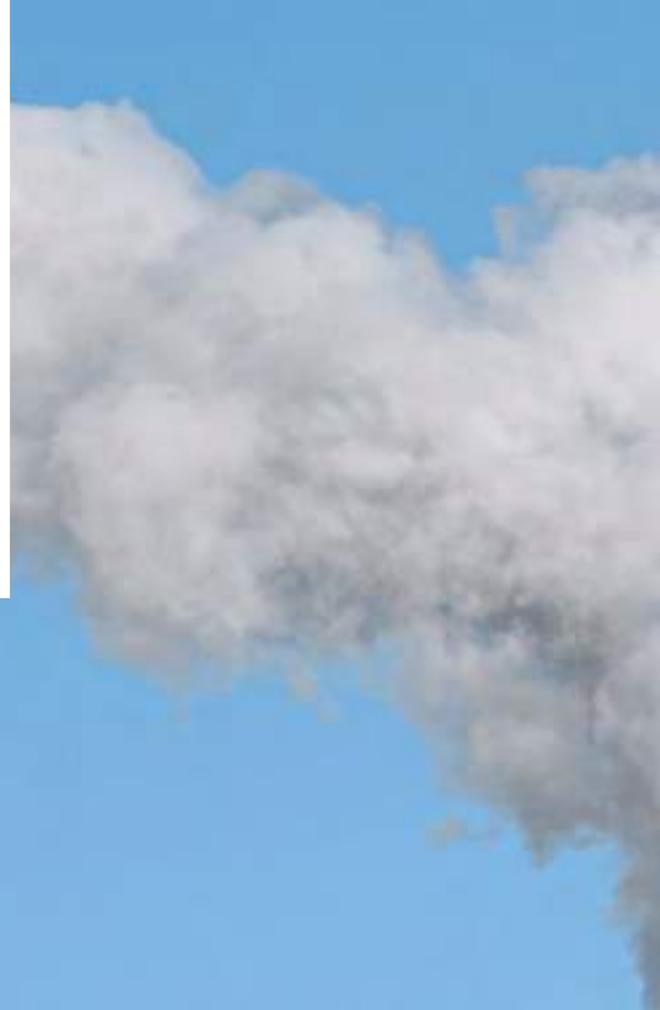
As a testament to the change these groups are making, **women now represent 42.3% of Ipsen's Global Leadership Team (GLT)**. We aim to increase this percentage even further in years to come.

Sustainable by design

Environmental protection is one of the three pillars underpinning our CSR strategy, and we've chosen to protect the environment in any and all ways we can. Notably, we have begun holding virtual conferences and have cut back on business travel where possible, and our fleet is going electric thanks to the Fleet for Future project. Furthermore, under our Green IT initiative, we are continuously evaluating our digital presence and finding new opportunities for emissions reductions. For example, this Integrated Annual Report was created using an eco-design approach. This methodology prioritizes design choices, such as user experience (UX), picture size and color choice, that use less energy, both in the digital and physical space.

A BOLD – AND NECESSARY – COMMITMENT

As a global company with staff and operations around the world, we take our commitment to the environment very seriously. Man-made climate change is a reality that threatens the future security and welfare of the entire planet. This is why we made a public commitment in 2021 to take ambitious action to reduce our carbon emissions, in line with strategies to limit **the rise in global temperature to 1.5°C above pre-industrial levels.**



United with other business leaders

In October 2021, we joined the **Business Ambition for 1.5°C campaign**, committing to setting science-based targets and reducing our emissions to net zero by no later than 2050. While we will keep this end date in mind, we aim to achieve our objectives as soon as possible.

Ipsen pledged to cut in half the absolute greenhouse gas emissions from our direct activities, such as Ipsen's facilities and fleet, by 2030.* In addition, **we will deliver a science-based reduction in emissions across the rest of the value chain** by working with upstream and downstream partners. With this pledge, we join a group of 1,244

other companies who are shaping the future of responsible business.

The business benefits of science-based climate action are clear, and we firmly believe businesses will not be successful in the future unless they adopt sustainable practices. Our efforts are focused on achieving real results and slashing our carbon emissions to meet the 2030* targets. Given the scale of the climate challenge, we believe everyone has a role to play. Together with the company's value-chain partners, and our peers within the *Business Ambition for 1.5°C* campaign, we will achieve the positive change needed for future generations.



The change has already begun

Ipsen has been working to reduce emissions and environmental impact for some years. Over **88% of our global electricity** already comes from renewable sources. We continue to make our facilities more energy efficient, investing in innovative heat-recovery technology and transforming our fleet to a greener energy mix.

From 2030, we will also take part in climate-compensation measures to offset any emissions not yet removed from our value chain. Carbon offsetting will never be a substitute for real emissions reductions, but we feel they still have an important role in preserving or enhancing existing carbon stocks as we make the transition towards a net-zero world. Our climate change strategy and all our environmental efforts are founded on science-based targets in line with the UN's Paris Agreement.



100%

GREEN ELECTRICITY

powers our operations in the UK, Ireland and France



30%

OF OUR FLEET

will use electric vehicles by 2025



IPSEN WILL HALVE

carbon emissions

BY 2030*

*All targets based on 2019 base year

A CSR STRATEGY BUILT ON ETHICS AND TRANSPARENCY

Our company social responsibility (CSR) strategy is underpinned by three pillars: Employees, Communities and Environment. Each pillar is fundamental to our activity, and informs the way we make decisions, interact with stakeholders, and further develop our environmental and social governance.

Empowering our employees

Ipsen's employees are the real source of the value we bring to patients, society and the environment. We are committed to empowering them with a culture of excellence and by providing a great place to work. In 2021, we received 19 external and independent recognition awards, and we're on track to meet our goal of 30 awards in this category by 2025.

Key to this is our culture of safety and ethics, which is built into our Code of Conduct. For example, Ipsen maintains a management system to identify, control and mitigate the risk of bribery and corruption. In 2021, Ipsen achieved ISO 37001 certification in recognition of this system and the Group-wide engagement that upholds it. We are one of the first companies in the pharmaceutical industry to receive this certification.

Supporting our communities

Every year, the Ipsen Community Day program encourages all employees to donate time and resources to those in need. Our teams also frequently step up to provide aid when communities are struggling. In 2021, our corporate HQ teams in Boulogne, France provided 500 meals per month to students during the pandemic. Meanwhile in China, local teams provided water purification equipment to three schools.

Responsibility at every level of Ipsen

Our commitment to CSR is integrated into our strategy, and impacts every aspect of our business.

In this effort, we are in touch with the entire healthcare ecosystem: payers, regulators, investors, employees and of course, patients.

By listening and responding to external and internal CSR needs, we are able to build stronger initiatives and, in the long-run, create a bigger impact.

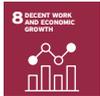
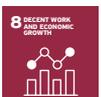
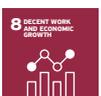
Safeguarding our environment

Our ecological commitments start with managing risks around our sites to protect the surrounding environment. Our waste, water and air emissions management program focuses on eliminating or reducing adverse emissions. Biological oxygen demand and suspended solids in wastewater are down 35% and 43% since 2019. We are also dedicated to reducing the energy intensity of our fleet by 2025 notably by transitioning 30% of the fleet to electric vehicles.

Ipsen has also developed a Group-wide Biodiversity Strategy to increase the variety of plant and animal life at Ipsen-owned sites. Surveys have been conducted at our Wrexham and Dublin sites, and this data is stored and monitored in a dedicated new database.

BUILDING VALUE – ADDRESSING RISK

Integrating UN Sustainable Development Goals, our materiality analysis identifies 13 main CSR risks classified into four categories.

CATEGORY	SDG'S CONTRIBUTION	NAME OF THE RISK/ OPPORTUNITY	DESCRIPTION OF RISK AND LINKS TO IPSEN'S ACTIVITIES	CHAPTER REFERENCES
Improving people's life by offering innovative and safe medicines	 	<ul style="list-style-type: none"> Product quality 	Protecting patients against the risks inherent to the biologic action of medicinal products and ensuring that benefit/risk for all products is positive.	2.1.5.4 and 4.2.1
		<ul style="list-style-type: none"> Product and Patient Safety 	Non compliance with security requirements that could jeopardize patients' health.	2.1.5.4 and 4.2.2
		<ul style="list-style-type: none"> Animal welfare 	Ensuring the respect of the highest standards of animal welfare while guaranteeing the safety of Ipsen.	4.2.3
		<ul style="list-style-type: none"> Committed to ensure supply continuity 	Risk of Ipsen medicines supply shortage.	4.2.4 and 2.1.3.1
		<ul style="list-style-type: none"> Counterfeit products 	Counterfeit products of low quality and not complying with Ipsen's health standards, which may endanger patients' health and generate loss in sales revenues.	2.1.5.3 and 4.2.5
		<ul style="list-style-type: none"> Responsible product promotion 	Improper marketing claims resulting in legal proceedings and mistrust of patients and Healthcare professionals, which could damage Ipsen.	2.1.2.9 and 4.2.6
		<ul style="list-style-type: none"> Access to health 	The implementation of initiatives and actions to improve healthcare in countries where access to medicines is difficult and diseases are difficult to treat.	4.2.7
Enhancing integrity to maintain a trusted relationship with our stakeholders	   	<ul style="list-style-type: none"> Data privacy 	Inability to ensure integrity and confidentiality of data, resulting in disclosure or theft of patient's information and breach of data privacy.	2.1.5.2 and 4.3.1
		<ul style="list-style-type: none"> Anti-Corruption 	Corruption and conflicts of interest situations which could lead to major fines and penalties and damage to Ipsen's image.	2.1.2.9 and 4.3.2
		<ul style="list-style-type: none"> Human Rights 	Respect of human rights in Ipsen's operations and in its supply chain.	4.3.3
Driving our employees' excellence and engagement	  	<ul style="list-style-type: none"> Talent attraction 	Loss and/or lack of key skills leading 4.4.1 to delay of key programs and research projects launch, which could jeopardize Ipsen's ability to improve patients' health.	4.4.1
		<ul style="list-style-type: none"> Employee engagement 	Negative impacts on employee motivation or on the quality of social relations that could jeopardize the achievement of some objectives and lead to a corresponding impact on the Group's results or financial position.	4.4.2
		<ul style="list-style-type: none"> Health and safety 	Compliance or risk control failure which could result in several incidents causing injury or impacting employees' health.	2.1.3.2 and 4.4.3
Minimizing our environmental impact	     	<ul style="list-style-type: none"> Climate and energy 	The climate risk related to business and supply chain disruption. Failure to take action on climate change which could have an impact on investor confidence and talent retention.	2.1.3.2
		<ul style="list-style-type: none"> Management of water, waste and air emissions 	Failure of compliance or risk control which could result in water, waste and/or air pollution harming the environment and/or human health.	2.1.3.2

FONDATION IPSEN: RAISING AWARENESS FOR RARE DISEASE DETECTION

Since its creation in 1983 under the aegis of the *Fondation de France*, *Fondation Ipsen* has been dedicated to increasing scientific knowledge and patient research. It is focused on helping improve the lives of patients with rare diseases. The *Fondation* has contributed to numerous major advances in biological and medical research, organized scientific conferences, and produced literature and content to help patients and the wider community understand rare diseases. In 2021, through its relationships with patient organizations, its publishing enterprise, and international scientific collaborators, the *Fondation* interacted directly with more than 22 million people in 100 countries.

Rare But Not Alone

Fondation Ipsen is a major presence in medical advocacy, helping to advance science and treatments. The *Fondation's* latest strategic focus, "Rare But Not Alone," was launched in 2020. It reoriented efforts toward rare disease awareness and early detection, with the goal of improving detection and diagnosis.

This is an underserved area. There are an estimated 5,000 to 8,000 rare diseases in the world. They affect around **400 million people worldwide. 75% of those affected are children.** Furthermore, it is estimated that **50% of all patients** suffering from a rare disease **do not yet have an accurate diagnosis.** Finally, one in four patients will wait four years to get the correct one.

But those are just numbers. And patients are not numbers. This is why we see family outreach as so important. It's a key channel to help share information and improve early detection. *Fondation Ipsen* is uniquely equipped to raise awareness and address these problems, and its work is reinforced by Ipsen's overall mission to prolong all patients' lives, while improving their quality of life.

Our multi-faceted approach

In 2021, *Fondation Ipsen* worked directly with 146 organizations to assess the needs of patients with rare diseases. The work produced an outcome-based, research-grade, publishable needs assessment that identified gaps and opportunities to accelerate rare disease detection and diagnosis. To successfully raise awareness with a hugely diverse variety of communities and patients, *Fondation Ipsen* has taken a multi-media approach to communications.

Along with producing magazines, children's books, pamphlets, manga and podcasts, the *Fondation* hosts free online courses on rare diseases, improving patients' and families' access to clear, essential information. These international training sessions also support healthcare providers from underserved countries.



350-400M

PEOPLE WORLDWIDE
are estimated to live with a rare disease



75%

OF PATIENTS WITH RARE DISEASE
are children



50%

OF PATIENTS WITH A RARE DISEASE
do not have an accurate diagnosis



IN 2021,

36M

PEOPLE
received information
from the *Fondation* and

22M

PEOPLE
interacted with us
directly



INITIATIVE 1: SUPPORTING PATIENTS AND FAMILIES IN UKRAINE

By leveraging its connections in the rare disease and scientific communities, the Fondation was able to respond to the needs of Ukrainian patients and families with rare disease and handicaps. The following are some of the groups supported by the Fondation:

- **Healthcare Education Foundation in Poland**
- **The Romanian National Alliance for Rare Diseases**
- **Handicap International's Vulnerability Laboratory and its emergency team in Ukraine**
- **France terre d'asile**

Furthermore, **Booklab, the publishing arm** of the Fondation, has published three children's books about rare disease in Ukrainian.

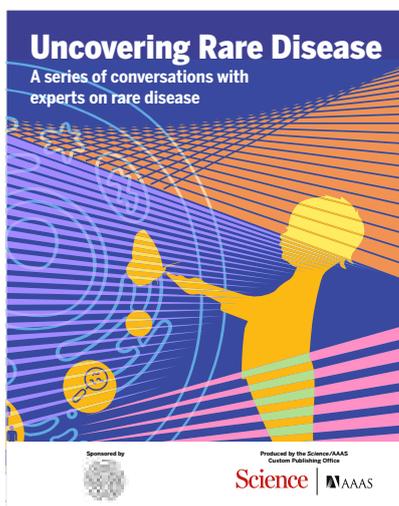
Visit our online annual report for more details about the actions the Fondation has taken.



INITIATIVE 2: PARTNERING WITH SCIENCE MAGAZINE

In 2021, Fondation Ipsen and *Science Magazine* organized nine webinars with the world's leading specialists in rare diseases, as well as policymakers from all over the world. Through social media channels, each webinar was distributed to 800,000 people.

The webinars addressed a variety of essential topics for patients living with rare diseases and their families. The webinars received such a strong response that *Science Magazine* and the Fondation now co-publish an international magazine for the rare disease community: the *Rare Disease Gazette*.



INITIATIVE 3: UNITED WE STAND

The Fondation's strategic focus, "Rare But Not Alone," is an ambitious program, but it must be realized in order to end unnecessary suffering for patients around the world. The Fondation's strategic goals are:

1. **Amplify the voices** of patients with rare diseases, and those of their caregivers
2. **Develop new rare disease communication strategies** for children
3. **Engage leading science journals and journalists** to report on rare disease detection
4. **Reach underserved communities** to promote awareness of rare diseases
5. **Develop international open-access communications and training** in rare disease detection
6. **Fight discrimination and stigma faced** by patients living with rare diseases or handicaps

The Board of Directors determines Ipsen's business strategy and oversees its implementation. The Board provides accurate information about Ipsen's operations to company shareholders and the general public. It ensures the company has reliable procedures for identifying, measuring and monitoring its commitments and risks, as well as adequate financial and operational internal controls.

The Board also appoints six permanent committees to assist in its oversight and monitoring responsibilities. The current composition and individual roles of the Board of Directors and its Committees as of 15 May 2022 are as follows:

42%

GENDER BALANCE
within the Board of Directors

12

ELT MEETINGS
30 Committee meetings
13 Board meetings
in 2021

THE BOARD OF DIRECTORS

The Board of Directors

Chairperson: Marc de Garidel

Vice-Chairperson: Antoine Flochel

Members:

Highrock SARL (represented by Anne Beaufour), Henri Beaufour, Beech Tree SA (represented by Philippe Bonhomme), Laetitia Ducroquet, Margaret Liu, David Loew, Michèle Ollier, Jean-Marc Parant, Paul Sekhri, Piet Wigerinck, Karen Witts, Carol Xueref

Six Board Committees¹

Nomination Committee

Chairperson:

Carol Xueref

Members:

Beech Tree SA³
Paul Sekhri²

Ethics and Governance Committee

Chairperson:

Margaret Liu²

Members:

Beech Tree SA³
Jean-Marc Parant⁴
Carol Xueref

Compensation Committee

Chairperson:

Antoine Flochel

Members:

Laetitia Ducroquet⁴
Piet Wigerinck²
Karen Witts²
Carol Xueref

Audit Committee

Chairperson:

Karen Witts²

Members:

Beech Tree SA³
Paul Sekhri²

Innovation and Development Committee – Specialty Care

Chairperson:

Marc de Garidel

Members:

Antoine Flochel
Margaret Liu²
Michèle Ollier
Paul Sekhri²
Piet Wigerinck²

Permanent guests:

Highrock SARL⁵
Henri Beaufour
David Loew

Innovation and Development Committee – Consumer Healthcare

Chairperson:

Marc de Garidel

Members:

Beech Tree SA³
Margaret Liu²
Carol Xueref

Permanent guests:

Highrock SARL⁵
Henri Beaufour
David Loew

(1) For more information on the activities of each committee, see:

<https://www.ipsen.com/our-company/>

(2) Independent member

(3) Company governed by Luxembourg law, represented by Philippe Bonhomme

(4) Director representing the employees

(5) Company governed by Luxembourg law, represented by Anne Beaufour

THE EXECUTIVE LEADERSHIP TEAM

The ELT is composed of the Chief Executive Officer and 13 executive members. The current composition of the ELT as of 15 May 2022 is as follows:



David Loew
Chief Executive Officer



Catherine Abi-Habib
Executive Vice President,
Strategy, Transformation &
Digital



Bartosz (Bartek) Bednarz
Executive Vice President,
Head of Global Product
and Portfolio Strategy



Stewart Campbell
Executive Vice President,
President of North America



François Garnier
Executive Vice President,
General Counsel and Chief
Business Ethics Officer



Benoît Hennion
Executive Vice President,
Consumer Healthcare



**Steven Hildemann,
M.D., Ph.D.**
Executive Vice President,
Chief Medical Officer, Head of
Global Medical Affairs, Patients
Safety and Patients Affairs



Aymeric Le Chatelier
Executive Vice President,
Group Chief Financial Officer



Philippe Lopes-Fernandes
Executive Vice President,
Chief Business Officer



Howard Mayer, M.D.
Executive Vice President,
Head of Research and
Development



Régis Mulot
Executive Vice President,
Chief Human Resources Officer



Aidan Murphy, Ph.D.
Executive Vice President,
Technical Operations



Mari Scheiffele
Executive Vice President,
Specialty Care International



Gwenan White
Executive Vice President,
Communications and
Public Affairs

ASSESSING AND ADDRESSING OUR RISKS

Ipsen's Risk Management Team and Committee are dedicated to performing our global risk assessment. Their work enables us to identify and monitor sources of potential challenges, anticipating and mitigating risks according to our strategy and risk appetite.

Below, we highlight some of the major risks identified in 2021, and explore how we work to address them.



Business risks

The business risks facing Ipsen include dependence on products, cyberattacks and systemic events that could disrupt supply.

Much of Ipsen's risk arises from **market competition and dependence on products**. For example, in late 2021, a pharmaceutical alternative to Somatuline® (lanreotide) was registered in the United States. Thanks to risk monitoring, Ipsen anticipated this particular change and was able to expand the market leadership of Somatuline® in Europe.

Ipsen's activities also depend on information systems, which face the risk of **cyberattacks**. They can lead to disruption of activities and potential loss, alteration, theft or corruption of data. The Group has implemented a cyber security plan across all Ipsen entities, which is overseen by a dedicated team and governance system.

Ipsen must also prepare for the eventuality of facing a **systemic risk**, an event that could have a major impact on the system of operations. Ipsen defines and continuously updates its business continuity measures to be able to adapt and continue to operate in all environments. Recently, Ipsen avoided supply shortage in the face of two systemic events: the COVID-19 pandemic and the conflict between Russia and Ukraine.



For a complete list of identified risks, please see chapter 2 of our 2021 Universal Registration Document, available for download at [here](#).



Industrial and environmental risks

Industrial risks range from supply chain shortages and disruptions to environmental and safety risks.

Supply chain issues impact patients by reducing access to Ipsen's treatments. They may be the result of regulatory problems, technical difficulties, natural disasters or, most recently, the COVID-19 pandemic. Ipsen prepares for such problems through, for example, risk identification, continuously improving manufacturing and maintaining security stocks. Thanks to great preparation and management by our Technical Operations teams, Ipsen has faced no stock-outs during the pandemic.

Environmental risks can come from stricter legislation and enforcement in different countries where Ipsen operates. Ipsen also uses dangerous or potentially pollutant substances in our operations, which could generate considerable liabilities and costs. Handling, storing and using such substances also generates **safety risks like contamination or disease**.

Ipsen's dedicated Environment Health and Safety (EHS) governance bodies operate at all levels of the company, with the aim of protecting Ipsen's employees. They also seek further opportunities to reduce our energy consumption and environmental impact (for more information on Ipsen's sustainability measures, see page 48).



Financial Risks

Some of Ipsen's financial risks arise from exchange rates and share price fluctuation.

Owing to our international business scope, Ipsen is exposed to **exchange rate risks**. Ipsen implements a foreign exchange rate hedging policy that reduces the risk of currency fluctuations to net profits.

A range of events could cause Ipsen's **share price** to fluctuate, including R&D failures, competitor announcements, or changes to the executive team. Ipsen is aware of this and other financial risks, and relies on financial controlling and the Investor Relations team to ensure the timeliness and accuracy of announcements.



Regulatory and legal risks

Regulatory and legal risks pertain to intellectual property, information disclosure and product liability, among others.

Ipsen holds patents to protect the Group's **intellectual property (IP)**, but unauthorized parties could claim rights to Ipsen's IP. The Group must equally prepare for the risk of **undesired disclosure of critical information**. Ipsen cannot eliminate the possibility that private data or strategic information could be disclosed in a way that adversely affects our financial position, competitive situation or share value. To anticipate both of these risks, Ipsen has defined procedures that control the dissemination of sensitive information, particularly intellectual property or competitive positions. All privileged information is shared with investors in a way that complies with existing legislation.

As Ipsen expands into new markets, it's necessary to anticipate the possibility of **product liability** risks. Pharmacovigilance, Quality and Technical Operations controls all further protect Ipsen by working to prevent any such issues from arising. Ipsen maintains sufficient insurance coverage in case the Group is faced with any damages, claims or complaints.

IPSEN'S 2021 KPIs

2021 was a year of strong growth for Ipsen. Our key performance indicators (KPIs) are testament to the power of our strategy. By focusing our expertise in oncology, rare disease and neuroscience, we are advancing medicine and improving patients' lives.

Sales and operating income growth

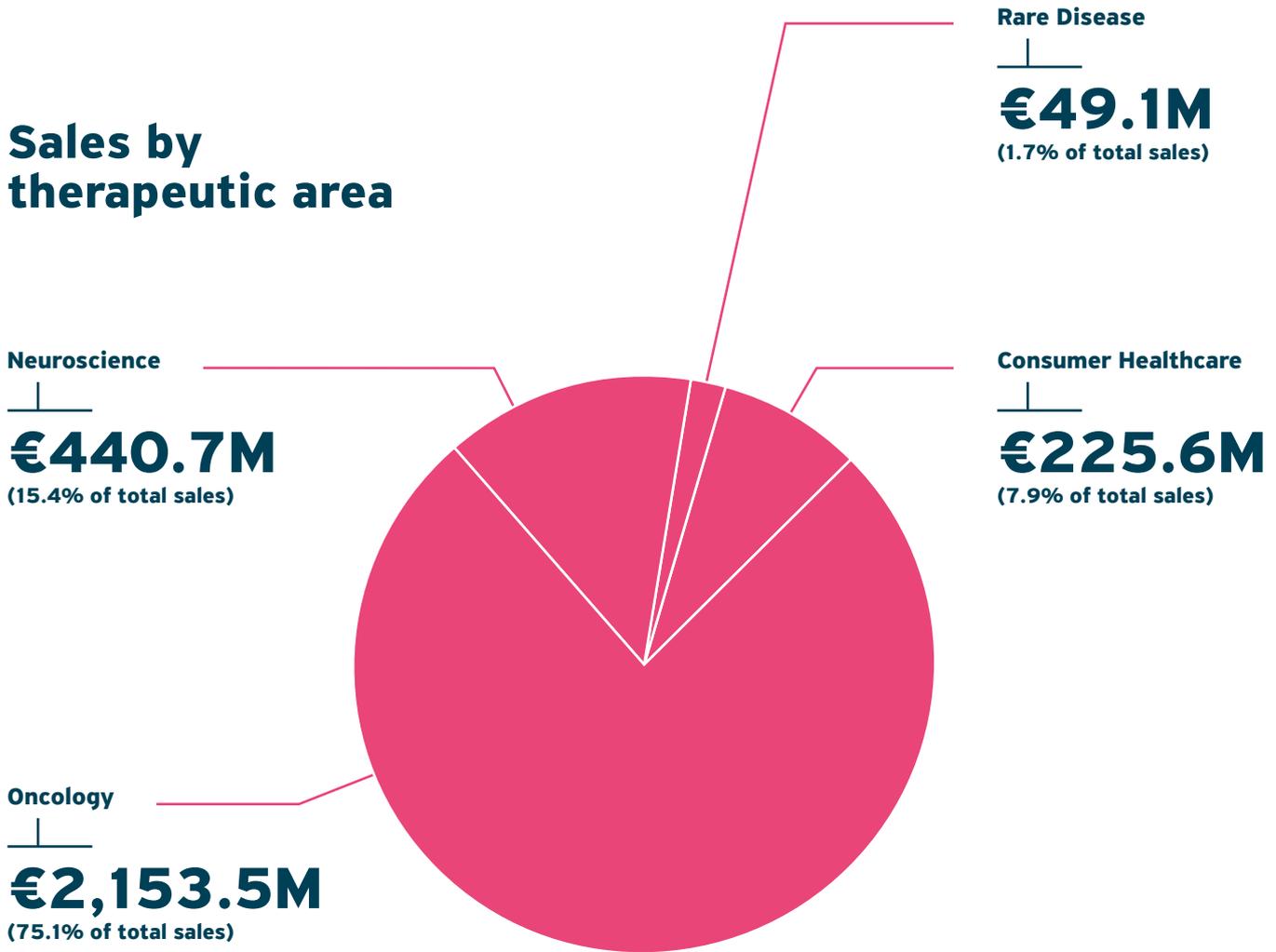
Ipsen sales

2019 €2,576.2M	2020 €2,591.6M	2021 €2,868.9M
---------------------------------	---------------------------------	---------------------------------

Core operating income

2019 €782.6M	2020 €829.3M	2021 €1,011.3M
-------------------------------	-------------------------------	---------------------------------

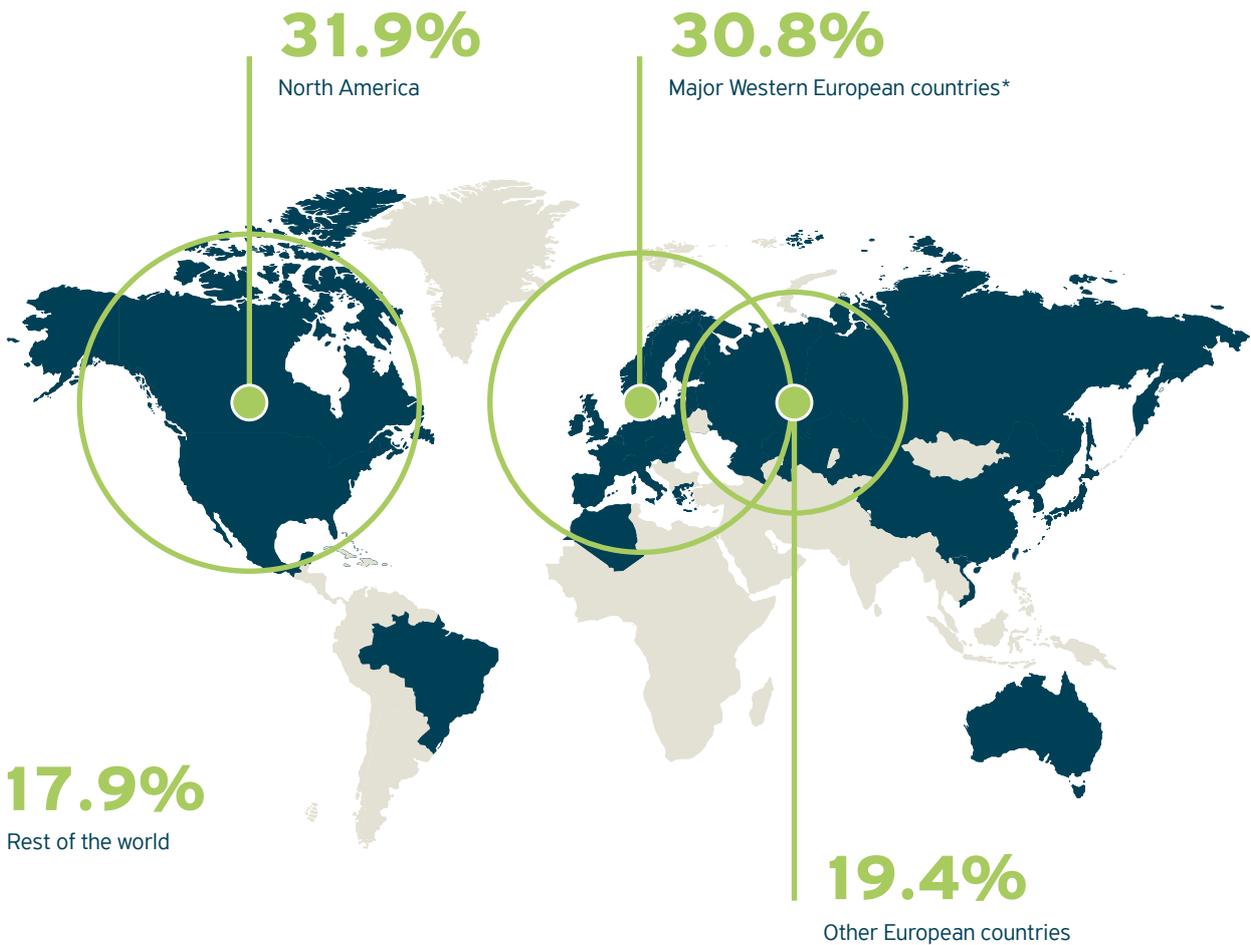
Sales by therapeutic area



R&D investment

2019	2020	2021
€388.8M	€405.6M	€428.4M

Sales by geographic area



2024 financial outlook

Total sales CAGR

**between +4%
and +6%**

from 2021 to 2024

€3.5BN

cumulative remaining firepower
for investment by 2024^{††}

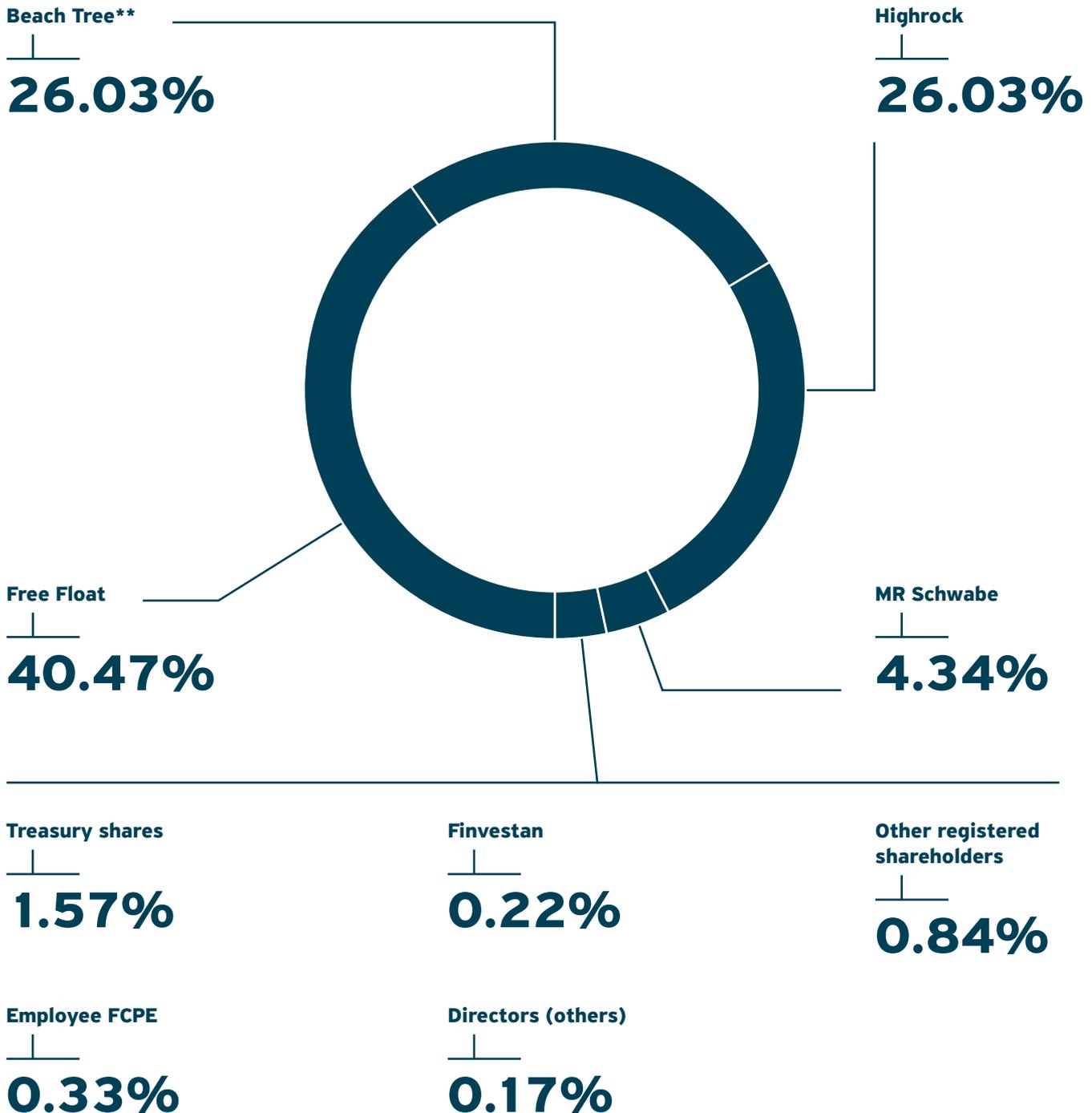
* France, Germany, Italy, Spain and
the United Kingdom

†† Including the divestment of
the CHC business

** Directly and indirectly through its
subsidiary MR BMH

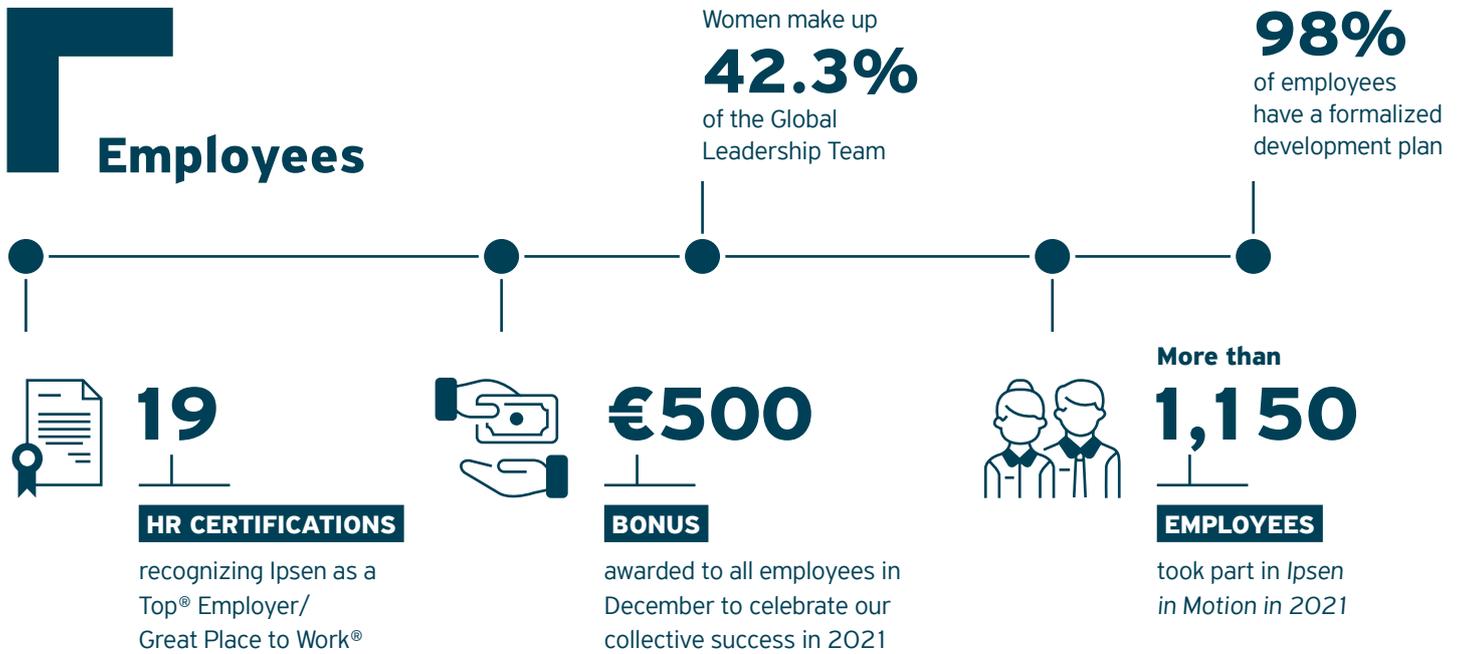
Ownership of Ipsen's share capital (% of total capital)

As of December 31, 2021:



CSR BY THE NUMBERS

To see the full picture of Ipsen's value creation, we must also consider non-financial KPIs. All three pillars of our CSR strategy create positive results, a selection of which is presented here.





Communities

Over **1,800** employees participated in more than _____

125



ACTIVITIES

across 38 countries for Ipsen Community Day.



220



81,233

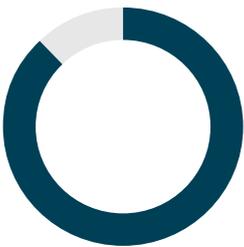
PATIENT ORGANIZATIONS

collaborated with Ipsen in 2021

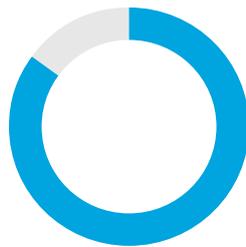
DOWNLOADS

from Fondation Ipsen's 3 podcast channels as of November 8, 2021

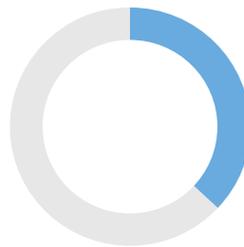
Environment



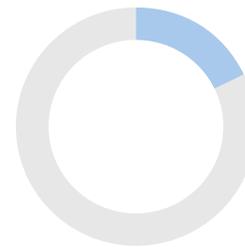
88% of our global electricity use comes from renewable sources



85% of Ipsen's water comes from low water risk basins



37% decrease in waste production compared to 2019



18% reduction in facilities' carbon intensity compared to 2019



7% decrease in facility energy intensity compared to 2019

REFERENCES AND CREDITS

pp. 20-21: Building a robust pipeline with external innovation

⁽¹⁾ Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7077807/> and Ipsen's end of year results, available on [ipsen.com](https://www.ipsen.com)

pp. 36-37: Oncology: a strong portfolio and patient focus

⁽¹⁾ Choueiri, et al., DOI: <https://doi.org/10.1016/j.annonc.2020.08.2257>

⁽²⁾ Brose, et al., DOI: [https://doi.org/10.1016/S1470-2045\(21\)00332-6](https://doi.org/10.1016/S1470-2045(21)00332-6)

Medullary thyroid cancer

^(3a) <https://www.macmillan.org.uk/cancer-information-and-support/thyroid-cancer/medullary>

^(3b) Cometriq® SmPC: https://www.ema.europa.eu/en/documents/product-information/cometriq-epar-product-information_en.pdf

Neuroendocrine tumors (NETs)

^(4a) Dasari, et al., 2017. <https://jamanetwork.com/journals/jamaoncology/fullarticle/2621997>.

^(4b) <https://www.livingwithnets.com/en-us/how-common-are-neuroendocrine-tumors-nets/>

Renal cell carcinoma

^(5a) Kidney Cancer Factsheet. GLOBOCAN 2020. Last accessed: September 2021. Available: <https://gco.iarc.fr/today/data/factsheets/cancers/29-Kidney-fact-sheet.pdf>.

^(5b) Kidney Cancer. Mayo Clinic. Last accessed: September 2021. Available: <https://www.mayoclinic.org/diseases-conditions/kidney-cancer/symptoms-causes/syc-20352664>

^(5c) Cabometyx® SmPC: https://www.ema.europa.eu/en/documents/product-information/cabometyx-epar-product-information_en.pdf

Pancreatic cancer

^(6a) <https://pancreatic.org/pancreatic-cancer/pancreatic-cancer-facts/#:~:text=Pancreatic%20cancer%20has%20the%20highest,States%20after%20lung%20and%20colon.>

^(6b) Onivyde® SmPC:

<https://www.medicines.org.uk/emc/product/9200/smpc#gref>

Breast cancer

^(7a) <https://www.wcrf.org/cancer-trends/worldwide-cancer-data/>

^(7b) Allison, et al., <https://pubmed.ncbi.nlm.nih.gov/31928404/> ASCO/CAP Guideline. J Clin Oncol 38:1346-1366; 2020

^(7c) Francis, et al., NEJM 2018

Hepatocellular carcinoma

^(8a) International Agency for Research on Cancer. GLOBOCAN 2020. Liver Fact Sheet. Available at:

<http://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf>

^(8b) Llovet, et al., <https://doi.org/10.1038/s41572-020-00240-3>.

^(8c) Kim, Viatour. <https://doi.org/10.1038/s12276-020-00527-1>.

^(8d) Abou-Alfa, et al., 2018. DOI: 10.1056/NEJMoa1717002

Prostate cancer

^(9a) Prostate Cancer Fact Sheet. GLOBOCAN 2020. Last accessed: September 2021. Available at:

<https://gco.iarc.fr/today/data/factsheets/cancers/27-Prostate-fact-sheet.pdf>

^(9b) Decapeptyl® SmPC:

<https://www.medicines.org.uk/emc/product/780/smpc#gref>

pp. 38-39: Building a portfolio of treatments for rare disease

NutropinAq®

⁽¹⁾ NutropinAq® SmPC: https://www.ema.europa.eu/en/documents/product-information/nutropinaq-epar-product-information_en.pdf

Decapeptyl®

^(2a) Cantas-Orsdemir, et al., Expert Rev Endocrinol Metab. 2019;14:123-130

^(2b) Carel, et al., Hum Reprod Update. 2004;10:135-47

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^(2d) Klein. Pediatr Endocrinol Metab 2016

Somatuline®

⁽³⁾ Somatuline® SmPC: <https://base-donnees-publique.medicaments.gouv.fr/affichageDoc.php?specid=63871159&typedoc=R>

Increlex®

⁽⁴⁾ Increlex® SmPC: https://www.ema.europa.eu/en/documents/product-information/increlex-epar-product-information_en.pdf

pp. 40-41:**Driving a revolution in neuroscience**Dysport®

⁽¹⁾ Dysport® SmPC: <https://www.medicines.org.uk/emc/product/7261/smpc>

Cervical dystonia

^(2a) Neurol. <https://pubmed.ncbi.nlm.nih.gov/11127535/>

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Blepharospasm

^(3a) Defazio, Hallett, Jinnah, Conte, Berardelli. <https://pubmed.ncbi.nlm.nih.gov/28186662/>

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⁽⁴⁾ Tan NC, Chan, Tan EK. <https://pubmed.ncbi.nlm.nih.gov/12145388/>

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^(6c) Lance. Symposium synopsis. In: Feldman RG, Young RR, Koeller C. Spasticity: disordered motor control. Chicago: Year Book Medical, 1980;485-494

Adult spasticity

⁽⁷⁾ Milnis, Young. <https://pubmed.ncbi.nlm.nih.gov/26713898/>

pp. 42-43: Driving growth in a recovering Consumer HealthCare market

⁽¹⁾ Product CCDS (Company Core Data Sheet)

⁽²⁾ Product Intended Use Document

Credits

Thank you to all the Ipsen colleagues who appear in this report. Special thanks to everyone who contributed to its creation: reading, writing, reviewing and more.

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Bug Agency

Edited by:



HOLLIS & BEAN

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Forward-looking statements

The forward-looking statements, objectives and targets contained herein are based on Ipsen's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. All of the above risks could affect Ipsen's future ability to achieve its financial targets, which were set assuming reasonable macroeconomic conditions based on the information available today. Use of the words 'believes', 'anticipates' and 'expects' and similar expressions are intended to identify forward-looking statements, including Ipsen's expectations regarding future events, including regulatory filings and determinations. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by Ipsen. These targets depend on conditions or facts likely to happen in the future, and not exclusively on historical data. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties, notably the fact that a promising medicine in early development phase or clinical trial may end up never being launched on the market or reaching its commercial targets, notably for regulatory or competition reasons. Ipsen must face or might face competition from generic medicine that might translate into a loss of market share. Furthermore, the research and development process involves several stages each of which involves the substantial risk that Ipsen may fail to achieve its objectives and be forced to abandon its efforts with regards to a medicine in which it has invested significant sums. Therefore, Ipsen cannot be certain that favorable results obtained during preclinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the medicine concerned. There can be no guarantees a medicine will receive the necessary regulatory approvals or that the medicine will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Other risks and uncertainties include but are not limited to, general industry conditions

and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and healthcare legislation; global trends toward healthcare cost containment; technological advances, new medicine and patents attained by competitors; challenges inherent in new-medicine development, including obtaining regulatory approval; Ipsen's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of Ipsen's patents and other protections for innovative medicines; and the exposure to litigation, including patent litigation, and/or regulatory actions. Ipsen also depends on third parties to develop and market some of its medicines which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to Ipsen's activities and financial results. Ipsen cannot be certain that its partners will fulfil their obligations. It might be unable to obtain any benefit from those agreements. A default by any of Ipsen's partners could generate lower revenues than expected. Such situations could have a negative impact on Ipsen's business, financial position or performance. Ipsen expressly disclaims any obligation or undertaking to update or revise any forward-looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. Ipsen's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers. The risks and uncertainties set out are not exhaustive and the reader is advised to refer to Ipsen's 2021 Universal Registration Document, available on [ipсен.com](https://www.ipсен.com).

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