



Ronny

Living with neuroendocrine tumors  
Ringwood, UK

## 2018 Annual Report



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# HIGHLIGHTS

2018 was been a remarkable year for Ipsen. We remain focused on executing our internal and external innovation strategy to build a robust pipeline, ensure continued growth and optimize value for patients and shareholders.

## JANUARY 16, 2018

With Exelixis, we announced the CELESTIAL Phase III pivotal trial results of cabozantinib demonstrating significant overall survival benefit in patients with previously treated advanced hepatocellular carcinoma (HCC). Cabozantinib provided a statistically significant and clinically meaningful improvement versus placebo in overall survival for the population of second- and third-line patients enrolled in the study<sup>(1)</sup>.

## MAY 29, 2018

With the University of Texas MD Anderson Cancer Center, we announced a global licensing and joint development agreement for a preclinical oncology drug candidate discovered by researchers at MD Anderson's Institute for Applied Cancer Science (IACS). MD Anderson is leading the Phase I clinical development and Ipsen will be responsible for further global development and marketing.



## FEBRUARY 21, 2018

We signed a strategic agreement with Arrix Bioscience. The objective of this collaboration is to identify opportunities and jointly create new companies focused primarily on the development and marketing of innovative therapies for patients.

## MARCH 28, 2018

We announced that the European Medicines Agency (EMA) validated the filing of a new application for an additional indication for Cabometyx®, for patients with previously treated advanced hepatocellular carcinoma (HCC).



## JULY 4, 2018

*The New England Journal of Medicine (NEJM)* published results from the CELESTIAL Phase III pivotal trial of cabozantinib in patients with previously treated advanced hepatocellular carcinoma (HCC). The data demonstrate that cabozantinib provided a statistically significant and clinically meaningful improvement in overall survival versus placebo<sup>(1)</sup>.

## JULY 19, 2018

We signed an agreement with BioLabs to open a life science co-working facility at our new North America global hub in Kendall Square, Cambridge, Massachusetts. The shared space is a fully equipped office and laboratory facility dedicated to supporting entrepreneurs and startups developing the next generation of therapeutics for patients.

**SEPTEMBER 21, 2018**

We received a positive CHMP (Committee for Medicinal Products for Human Use) opinion for Cabometyx® (cabozantinib) for the second-line treatment of hepatocellular carcinoma (HCC) in adults previously treated with sorafenib.

**OCTOBER 3, 2018**

We joined the Biotechnology Innovation Organization (BIO), the largest association of biotechnology companies, academic institutions and biotech centers around the world, and a leader in biotech innovation for over a quarter of a century.

**NOVEMBER 15, 2018**

The European Commission (EC) approved Cabometyx® (cabozantinib), for the treatment of hepatocellular carcinoma (HCC) in adults previously treated with sorafenib<sup>(1)</sup>.

**NOVEMBER 20, 2018**

Together with 3BP, we announced that the first patient has been dosed in a Phase I/II study for the first-in-class radionuclide <sup>177</sup>Lu-IPNO1087. The compound targets cancer cells in patients with advanced solid tumors which express the Neurotensin Receptor Subtype 1 (NTSR1).

**DECEMBER 31, 2018**

Somatuline® achieved sales of over USD 1 billion, making it Ipsen's first-ever blockbuster.

**JANUARY 11, 2019**

We demonstrated our leadership position in neurotoxin research with a strong presence at TOXINS 2019. Dysport® (abobotulinumtoxinA) and its recombinant botulinum toxins pipeline were the subject of 50 posters.

**FEBRUARY 25, 2019**

We announced that we entered into an agreement to acquire Clementia Pharmaceuticals, including its key late-stage clinical asset palovarotene.

**MARCH 6, 2019**

We simultaneously announced the EU launch of a new pre-filled syringe for Somatuline® Autogel® (lanreotide) for patients with neuroendocrine tumors (NETs), acromegaly or symptoms associated with carcinoid syndrome, and released findings from the human factor studies that underpinned its development as a poster presentation at ENETS 2019.

**APRIL 18, 2019**

We completed the acquisition of Clementia Pharmaceuticals.



# Making patient centricity a reality

An interview with David Meek



David Meek

Chief Executive Officer, Ipsen

## 2018 was another record-breaking year for Ipsen.

### What were some of the highlights?

**David Meek:** 2018 was a remarkable year for Ipsen as a leading global biopharmaceutical company focused on innovation and Specialty Care. We remained passionately committed to and focused on our mission: improving patients' lives through innovative medicines in Oncology, Neuroscience, Rare Diseases and Consumer HealthCare. Few companies have the rare combination of dynamic growth, coupled with outstanding and engaged colleagues with a shared patient-centric mindset.

In 2018, we exceeded the EUR 2 billion revenue mark, something we're very proud of. We also said we'd aspire to launch at least one new drug or meaningful indication every year, and we're delivering on that promise: we received the European Commission's approval for the first-line treatment of kidney cancer and second-line treatment of liver cancer, which makes three indications for Cabometyx®. As we move into 2019, we'll continue to expand its potential for patients.

Somatuline® grew substantially and reached USD 1 billion in revenue worldwide, becoming Ipsen's first blockbuster! This is such a great achievement and one we're all very proud of.

Our Neuroscience franchise continues to experience double-digit growth and sustained strength. In fact, Dysport® had its best-ever year in the US. We're increasingly leveraging Dysport®'s differentiation within the scientific community.

As for Consumer HealthCare, the business delivered a second year of growth, in line with the overall consumer healthcare market. We're on the right track toward the creation of a growing, sustainable and autonomous business, and we will continue our growth momentum in 2019.

Having three global innovation hubs - in the USA, France and the UK - gives us a real advantage in terms of R&D and our ability to reach patients worldwide and allows us to attract top global talent. Being present in thriving healthcare ecosystems is important for our innovation agenda. We are committed to delivering on our growth strategy and further establishing ourselves as a development and commercial powerhouse.

**"Ipsen's purpose is clearer than ever: to deliver new and innovative treatments to patients so they can live the life they deserve."**

**"This focus on patients, on finding new ways to make a difference for them, is the foundation of everything we do. After all, patients can't wait and that means we can't either."**

### How does Ipsen's patient-centric mindset impact your business strategy and the results?

**DM:** Ipsen's purpose is clearer than ever: to deliver new and innovative treatments to patients so they can live the life they deserve. We have a commitment and, I'd argue, an obligation to patients, to innovate, to be bold, agile and find breakthroughs that will improve patients' lives. This focus on patients, on finding new ways to make a difference for them, is the foundation of everything we do. After all, patients can't wait and that means we can't either.

We're continuing to build this patient-centric mindset into every aspect of our business. In Specialty Care in particular, patients often don't have many treatment options. Sometimes our treatments are their only option. So we have a responsibility to continually listen to patients and understand their needs and perspectives so we can improve, go further and offer more.

### What sets Ipsen's company culture apart?

**DM:** The longer I'm in this industry, the more I see that the science and products can only exist because of the people - the patients who use them and the people who work here. Our business is people. And over the last few years, the company's biggest transformation has been its people. At our best, we're a collection of high-performing, patient-focused, innovative people, who inspire and respect each other. Of course, within Ipsen we have multiple, quite distinct cultures. But wherever you look, you see people driven by curiosity. Because only people, in all their creativity, can truly disrupt the status quo. However, we do need to be aligned on our vision and our mission to achieve that. We launched the One Ipsen Way of Being this year. It's a charter built on five pillars that represent our behaviors and serve as both a guide and an inspiration for every single Ipsen employee. Trust, the drive to win, collaboration, integrity and accountability - these shared values unite us and keep us focused on our common goal of improving patients' lives around the world.

...

## What are your ambitions for 2019 and beyond?

**DM:** I'm looking forward to another year of solid industry-leading growth and to creating a sustainable future. In fact, our financial guidance for 2019 calls for revenue growth greater than 13%. Since we're on track to deliver our 2020 financial targets one year earlier than expected, we have provided a new 2022 financial outlook of EUR 3.2 billion in sales, and a margin greater than 32%.

To continue delivering superior value to patients and stakeholders, my first priority in 2019 is to build a sustainable pipeline by executing on our internal and external innovation strategy and bringing strong cornerstone assets in-house. And we're already off to a great start...

We're accelerating the development of several new chemical entities. Though relatively early, some of these programs could advance quickly through clinical development. Through our systemic radiation therapy (SRT) programs in Oncology, we're developing radiolabeled diagnostics and therapeutics for true precision medicine through a theranostic approach. Our SRT programs are currently in Phase I/II development. In early 2019, we also recruited our first patient for a best-in-class oncology drug candidate we're developing with the MD Anderson Cancer Center. Our 2018 growth propelled us to a leadership position as one of the top 14 oncology companies in the world.

As for Neuroscience, in our earlier-stage pipeline we're accelerating our recombinant neurotoxin programs. The fast-acting toxin has completed Phase I, and the two long-acting toxins are currently in preclinical development.

**"Our business is people. And over the last few years, the company's biggest transformation has been its people. At our best, we're a collection of high-performing, patient-focused, innovative people, who inspire and respect each other."**

In Rare Diseases, we completed the acquisition of Clementia Pharmaceuticals. This acquisition enhances Ipsen's ability to treat rare conditions, specifically fibrodysplasia ossificans progressiva (FOP) and multiple osteochondromas (MO) - two rare and disabling bone diseases in which skeletal muscle and connective tissue are gradually replaced by bone. Our new and innovative late-stage clinical asset, palovarotene, has the potential to help manage these diseases. In fact, palovarotene received orphan drug designation for FOP and MO from the FDA (Food and Drug Administration), fast track and breakthrough therapy designations for FOP from the FDA, and orphan status for FOP from the EMA. Palovarotene has also qualified for a Rare Pediatric Priority Review Voucher (PRV). With the Clementia team joining Ipsen, we aim to bring new, life-altering treatments to children and adults who currently have no other therapeutic options.

Moving into 2019 and beyond, we'll continue to increase the value of our key internal R&D programs. Our pipeline is broader and deeper than it has ever been and we will continue to be agile and focus our resources where we have the greatest chances of success for patients. We're looking at digital disruption to revolutionize our industry, starting in Oncology, R&D and business development.

My hope is that every employee, every team member fully embraces our culture: we're people who are different in all sorts of ways, but alike in courage. The courage to take risks, hold each other accountable and disrupt the status quo for better patient outcomes.

To continue delivering on our vision of being a leading global biopharmaceutical company focused on innovation and Specialty Care, we'll need to be bold and not settle for only what we have. We cannot be incremental - only by being bold can we make the breakthroughs that will deliver real value to patients and shareholders alike.



# WE LISTEN

Patients are at the heart of everything we do.  
To serve them, we must understand their needs, gain their insights  
and learn about their hopes for the future. Everything we achieve starts  
with listening to what they have to say.



Ronny  
Living with neuroendocrine tumors  
Ringwood, UK



Ronny's road to being diagnosed with stage IV metastatic neuro-endocrine tumors (NETs) in 2010 began during a routine appointment at an asthma clinic. A lifelong asthmatic, Ronny attended the clinic once a year, and it was during a chat with the clinic nurse that he noticed his sudden weight loss. "I told the nurse, 'I think I'm a bit lighter than I thought I was.' She asked me if I had meant to lose weight -

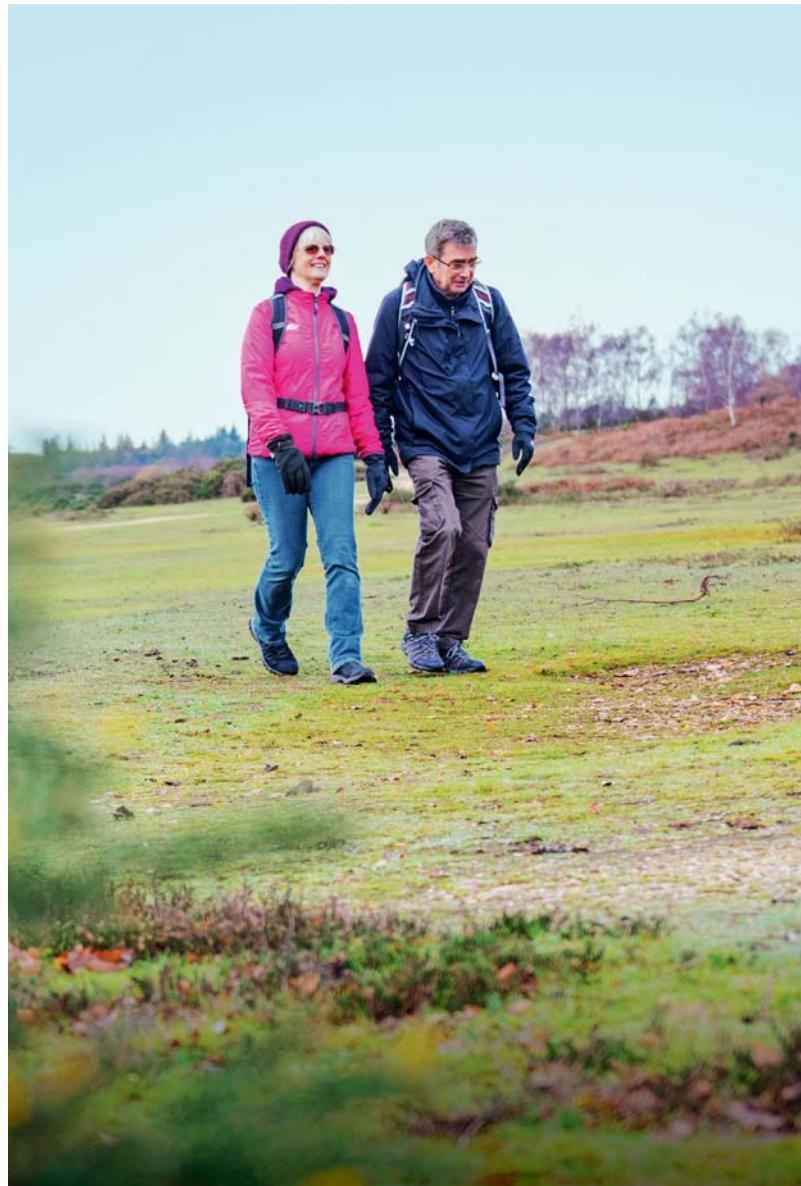
I hadn't, so she ordered some blood tests."

Shortly after, he received the diagnosis. "I suspect I was in complete shock. I think there was a little bit of denial in there that I actually had cancer," he recalls. "At my initial oncologist appointment, I did what people do in the movies. I asked how long I had to live. The doctor said, 'months, years'. I kind of

switched off after that. But what he did say after that was 'With the right treatment, you could live a lot longer.'"

A few months later, Ronny began his treatment. He retired from his job in the army to dedicate himself to his family and focus on his health. He began a blog to raise awareness of this rare and frequently misdiagnosed form of cancer, which has had over 800,000 views to

**“I go on holidays with my wife, Christine, travel to places I never thought I’d see. When I was diagnosed, I had no idea whether I would get to see my grandsons grow up, go to school. Now, I’m sure I’ll get to see the eldest get a job, perhaps even start a family. I didn’t think I had any chance of that.”**

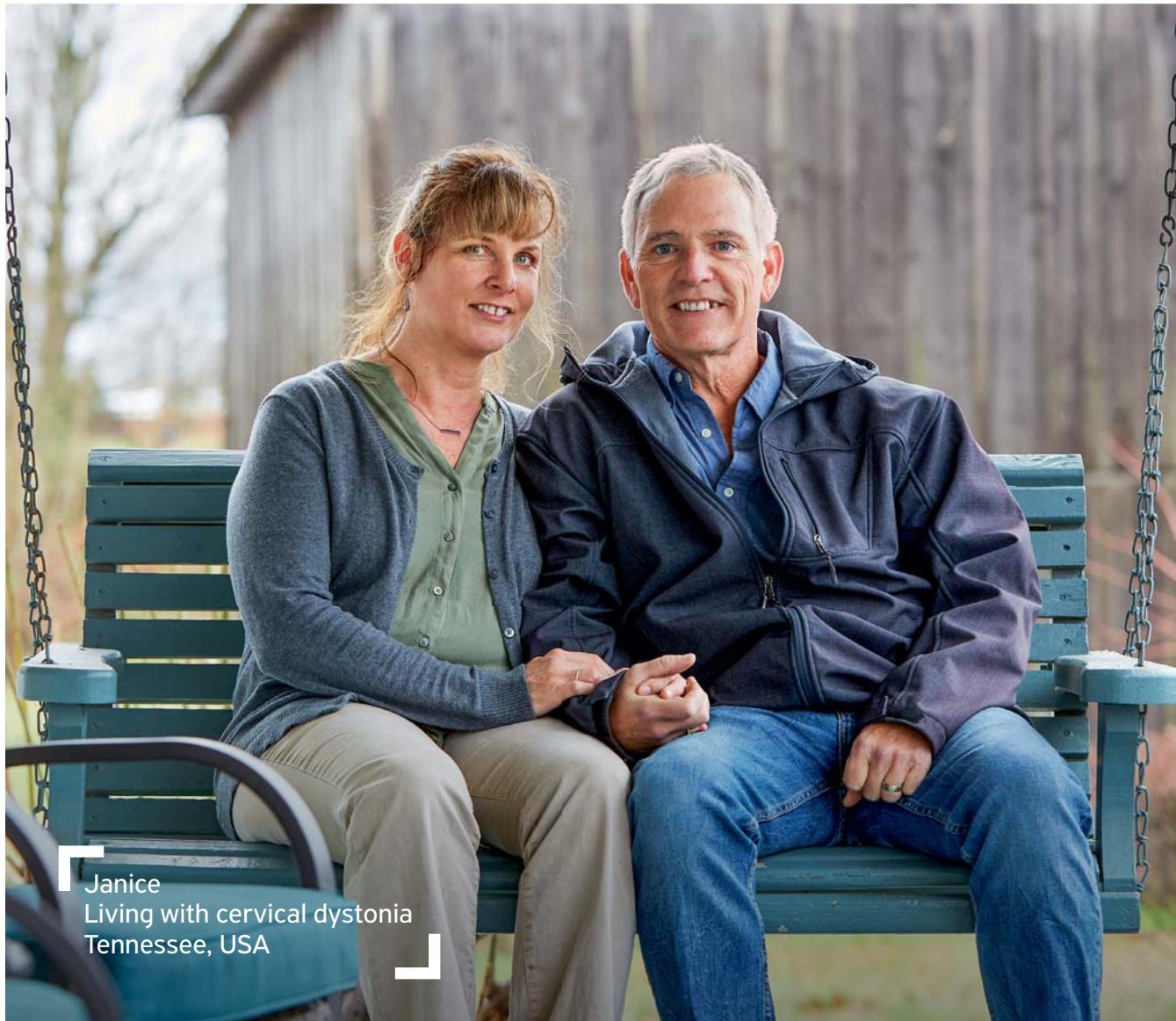


date. Today in Ringwood, Hampshire, England, the 63-year-old grandfather of four enjoys walking, cycling and spending time with his family. “Because I had access to the right treatment at the right time, I’m now living a reasonable quality of life.” But most importantly, Ronny has had the time to do things he wasn’t sure he’d get to do. “I go on holidays with my wife, Christine, travel to places I never thought I’d see. When I

was diagnosed, I had no idea whether I would get to see my grandsons grow up, go to school. Now, I’m sure I’ll get to see the eldest get a job, perhaps even start a family. I didn’t think I had any chance of that.”



Meet Ronny  
on Ipsen.com



**J**anice  
Living with cervical dystonia  
Tennessee, USA

Janice's symptoms first appeared when she was 21 years old. "It started with a slight left-to-right tremor, like I was shaking my head 'no,'" she remembers. Self-conscious about the tremors she couldn't control, Janice took refuge in her home and avoided social situations. "I missed out on graduations, on birthdays, on Christmas Eves," she recalls. "I just totally isolated myself in the comfort of my home."

The tremors made Janice self-conscious and uncomfortable in public. She remarks, "In photos, you'll often see me with my hand up by my face. That little motion would help me keep my head still." It would take more than eight years for Janice to finally be diagnosed with cervical dystonia.

During that time, Janice's symptoms weren't taken seriously by her doctors. The first neurologist she saw chalked her

tremors and neck pains to her pregnancy. But Janice knew it was something else. Her pain and the tremors gradually worsened until Janice had a hard time doing simple daily activities. When she finally found a neurologist who knew what her symptoms meant and diagnosed her, it was a tremendous relief.

"There's no cure for cervical dystonia," she notes. "At first, that scared me. But my doctor had a treatment plan." Today,



**“The treatment has worked well with me; it’s given me a boost of confidence and an opportunity to change my life and make things easier and less stressful.”**

her tremors and pain have diminished and she can once again do the things she loves. She’s also active in a support group for people with cervical dystonia, which has helped her build a community of people who have had similar experiences.

“The treatment has worked well with me,” Janice says. “It’s given me a boost of confidence and an opportunity to change my life and make things easier and less stressful.” After years of isolating herself,

she says the biggest change in her life is that she’s able to be present. “I’m there for my family—I participate in activities and do things I normally would have hidden from. I can live my life, do the things I want to do. And be happy.”



Meet Janice  
[on ipsen.com](http://ipsen.com)



**W**ade, a 38-year-old father of three, lives in Salt Lake City, Utah, USA. In 2015, he began to notice a series of changes in his body: he developed an underbite, his lower teeth were spreading, his feet started to grow, he had pain in his knees and shoulders and he experienced frequent bouts of sleep

apnea. "I was in a lot of pain," he says. "I was in my mid-thirties and I felt like my body was falling apart."

His doctors suggested jaw surgery. "Then my mother, of all people, said 'Hold on! I think you need to get your pituitary checked,'" remembers Wade. He was

skeptical at first. "I said, 'What do you know, you're just my mother!'" But he followed her advice and talked to his doctor. As it turned out, his mother was right. Wade was quickly diagnosed with acromegaly - a tumor on his pituitary gland was causing it to produce an excessive amount of growth hormone, triggering bone growth. He



**Wade**  
Living with acromegaly  
Salt Lake City, USA



**“Now with the treatment, I live the life I want to live: I’m able to play soccer and sports and go skiing and do things with my family that I wanted to do before but wasn’t able to, because I was in a lot of pain.”**

finally had a diagnosis that explained his symptoms, a relief after so much uncertainty.

After undergoing surgery to remove the tumor, Wade began his treatment. “There’s no cure for acromegaly,” Wade notes. “You have to treat it throughout your life. But after my diagnosis, my outlook was very positive. I thought, ‘What do I need to do to get better?’”

Thanks to his monthly injection, his growth hormone rate has returned to normal. Wade now has the tools and support he needs to manage his condition so that he can lead a normal life. “I’m able to play soccer and sports and go skiing and do things with my family that I wanted to do before but wasn’t able to, because I was in a lot of pain,” he says. “Now with the treatment, I live the life I want to live.” What

else has he learned from his experience with acromegaly? “Always listen to your mother, because mothers know best,” Wade says with a smile.



Meet Wade  
on [ipsen.com](http://ipsen.com)

# To the voice of consumers

**F**or our Consumer HealthCare (CHC) division, patients are also consumers. "One specificity of our division is that our products are at the crossroads of patient benefits, backed by clinical evidence, and consumer benefits. They can generate either a doctor's prescription, a pharmacist's recommendation or a direct demand. We must be at that crossroad," says Benoit Hennion, Executive Vice President, Consumer HealthCare. "That's why we're spending more time than ever with consumers." Meeting the needs of consumers and developing innovative products that resonate with them requires a different approach. And that begins with listening.

In 2018, we greatly extended our consumer outreach through new ways of listening, including these two initiatives:

- **Innovation Race Journey:** in April 2018, we kicked off a global digital brainstorming session to identify new products and services for our customers.

We then refined and tested the most promising ideas that were generated internally with more than 1,500 consumers across Europe, Russia and Asia. Based on both quantitative and qualitative interviews and research, this outreach helped further refine and prioritize ideas for the development of new products and services meeting patients' needs.

- **Smecta® Smiles Campaign:** the team also connected in 2018 with more than 1,300 consumers from China, Russia and France who are familiar with the Smecta® brand for their input on the new brand positioning and brand image proposals to gain insight into the market, the competition and how these factors evolve over time.

The goal is clear: to continue demonstrating the clinical benefits of each product, while developing innovations that meet consumers' needs, so that our consumer healthcare products are top-of-mind for physicians, pharmacists and consumers alike.

## INNOVATION RACE JOURNEY

With the Innovation Race Journey, we collected ideas from some of the smartest and most talented people we know: our fellow colleagues! Last year, CHC received more than 4,000 ideas from employees worldwide. From those ideas, four new products have already entered the development phase and more will follow soon.

**≈ 90 million**  
OTC packs sold around the world



# WE INNOVATE

Our ambitious goal is to bring new hope to patients.  
To succeed, we must be bold. That's why we innovate.  
Creative, agile and driven, we seek out new solutions for some  
of the hardest-to-treat conditions, so no patient is left behind.



**Model & Strategy**

# Our strategic approach to deliver sustainable growth



**Dominique Bery**  
EVP, Strategy & Transformation

Over the past few years, Ipsen has experienced a profound transformation across its divisions, functions and geographies. At the same time, we've outpaced the industry in terms of growth rate and we expanded our footprint significantly to better serve patients in need. Our strategic roadmap reflects our ambition to continue delivering sustainable growth in an environment requiring to be ever more agile and innovative. Ipsen's ability to build innovative business models and digital solutions is set to play

an increasingly important role in the execution of our strategy. "The reason why digital is important for us at Ipsen is that it can have a profound impact on patients," says Dominique Bery, Executive Vice President, Strategy & Transformation.

"First, we believe that by developing personalized digital solutions we can improve the quality of life of patients and their clinical outcomes. Second, using digital solutions internally can help to accelerate our time to market and deliver

**"We have established three priorities in our strategic agenda: increase the value of our pipeline through the acceleration of internal programs as well as externally sourced assets, maximize our competitiveness and our differentiation in our three core areas of focus in Specialty Care - Oncology, Neuroscience, and Rare Diseases - and drive productivity gains to reinvest in future growth."**

Dominique Bery  
Executive Vice President,  
Strategy & Transformation

innovative medicines to patients who can't wait.

Imagine if we could reduce the time to diagnosis to a matter of months for a disease like neuroendocrine tumors (NETs), which often goes undiagnosed for years. It would have a tremendous impact on patients. We see this as our responsibility as a leader in NETs treatments, and we are exploring how artificial intelligence (AI) applied to real world data could help diagnose patients earlier."

## Our activities

# Where patients need us

At Ipsen, our aim is to improve the lives of patients by developing new and innovative treatments, particularly in areas with high unmet medical needs. Our ambition is to launch one new product or indication per year.

**“There’s a real sense of urgency: patients’ lives are on the line. If you’re launching a new product or indication one year late, patients who only have months to live won’t be able to benefit from your treatment.”**

Harout Semerjian  
Executive Vice President, Chief Commercial Officer

## ONCOLOGY

Ipsen is proud to offer treatments with significant benefits for cancer patients, including improved patient longevity and quality of life, particularly in areas where there are currently few effective treatments. Our portfolio has treatments for a range of rare and difficult-to-treat cancers: neuroendocrine tumors, renal cell carcinoma, hepatocellular carcinoma, pancreatic cancer, prostate cancer, breast cancer, bladder cancer, carcinoid syndrome and medullary thyroid cancer. Today, Ipsen is among the top 14 oncology companies in the world, with the ambitious goal of launching one new treatment or major indication every year.

## RARE DISEASES

We are committed to becoming a leader in rare diseases to provide innovative therapeutic solutions for small patient populations with high unmet needs. Through the acquisition of Clementia, we are successfully executing our external innovation strategy to identify and acquire innovative medicines. We will continue to strengthen our pipeline and portfolio through targeted business development efforts.



Harout Semerjian  
EVP, Chief Commercial Officer

## NEUROSCIENCE

Our therapeutic treatments are indicated in seven areas including adult and pediatric spasticity and cervical dystonia. Affecting 12 million people around the world, spasticity is one of the most common and disabling conditions associated with neurological diseases in adults, characterized by an abnormal increase in muscle tone or stiffness. With long-lasting benefits between injections, our treatment helps relieve the debilitating and painful symptoms of spasticity in adults and children, offering them improved mobility and quality of life. In 2018, we further advanced our innovative pipeline with rBoNT-E, a novel recombinant fast-acting toxin, and the first to have entered human clinical development in a Phase I clinical trial. rBoNT-E could give clinicians the opportunity to treat conditions that require a significant and early effect.

## CONSUMER HEALTHCARE

We continually reinvent ourselves to find new ways of relieving consumers throughout the world, and improving their well-being. Our portfolio includes 10 key brands related to four therapeutic areas: gastroenterology, cognitive disorders, pain, cough and cold. Through the never-ending effort of listening and observing consumers' needs and behaviors, we are extending these brands into new territories, offering both proven clinical evidence and consumer benefits.

**Focus on**

# Our assets in Oncology

**2**018 was a remarkable year for Oncology at Ipsen. Somatuline® reached blockbuster status, with over USD 1 billion in revenue and 24.4% growth, our first treatment ever to achieve this milestone. Our second consecutive year of growth in Oncology helped consolidate our position as a top Oncology Company. New indications for Cabometyx®, which included approval as a first-line treatment for renal cell carcinoma (RCC) and a second-line treatment for hepatocellular carcinoma (HCC), helped Cabometyx® exceed its sales targets and offered patients new treatment possibilities. Decapeptyl®, which treats prostate cancer, boasted 8% year-on-year growth - an outstanding result for a product that has been on the market for 30 years. All told, our 2018 growth propelled us to a leadership position as one of the top 14 oncology companies in the world.

**A focus on unmet patient needs**

By tackling some of the most difficult-to-treat cancers, we're bringing new treatment options to patients. "Our size and structure are our strengths when it comes to bringing these medicines to the right patients at the right time: we have the capabilities and the agility to innovate in areas with high unmet patient needs. Even a so-called 'small' patient population has the potential to move the

needle for us, which isn't necessarily the case for the biggest pharmaceutical companies," says Bartek Bednarz, Senior Vice President, Global Product & Portfolio Strategy.

**The future looks bright**

Bartek Bednarz is excited and confident about the future for Ipsen in Oncology. "Our pipeline has never been so deep," he says, "which is exciting for patients who need treatment options." One aspect of the secret of this success is a clearly defined pipeline strategy. "Over the course of 2018, we worked as a cross-functional team at enterprise level to clearly articulate our strategy: to be leaders in solid tumors, in areas with significant unmet needs and well-defined patient populations." The strategy is already paying off: by developing new indications, working on new treatments and building strong partnerships, 2018 was one of the best years on record for our Oncology franchise.



**Bartek Bednarz**  
SVP, Global Product  
& Portfolio Strategy

**"Our size and structure are our strengths when it comes to bringing these medicines to the right patients at the right time: we have the capabilities and the agility to innovate in areas with high unmet patient needs."**

Bartek Bednarz  
Senior Vice President,  
Global Product & Portfolio Strategy

**2**

new indications for Cabometyx®

**\$1 billion**

in revenue for Somatuline®

**8%**

year-on-year growth  
for Decapeptyl®

## BOOSTING OUR PORTFOLIO IN ONCOLOGY

Ipsen offers a broad range of high-quality, innovative treatments to help improve the lives of patients with cancer.

### BREAST CANCER

20% of invasive breast cancer in premenopausal patients

#### DECAPEPTYL®

86.6% disease-free survival at five years when added to tamoxifen, 22% risk reduction in distant recurrence when added to exemestane<sup>(2)</sup>.

### HEPATOCELLULAR CARCINOMA

On the global scale, primary liver cancer is a major contributor to both cancer incidence and mortality. It is the sixth most commonly occurring cancer in the world and the second largest cause of cancer mortality.

#### CABOMETYX®

Significant overall survival benefit in patients with previously treated advanced hepatocellular carcinoma (HCC)<sup>(3)</sup>.

### RENAL CELL CARCINOMA

More than 250,000 new cases per year worldwide

#### CABOMETYX®

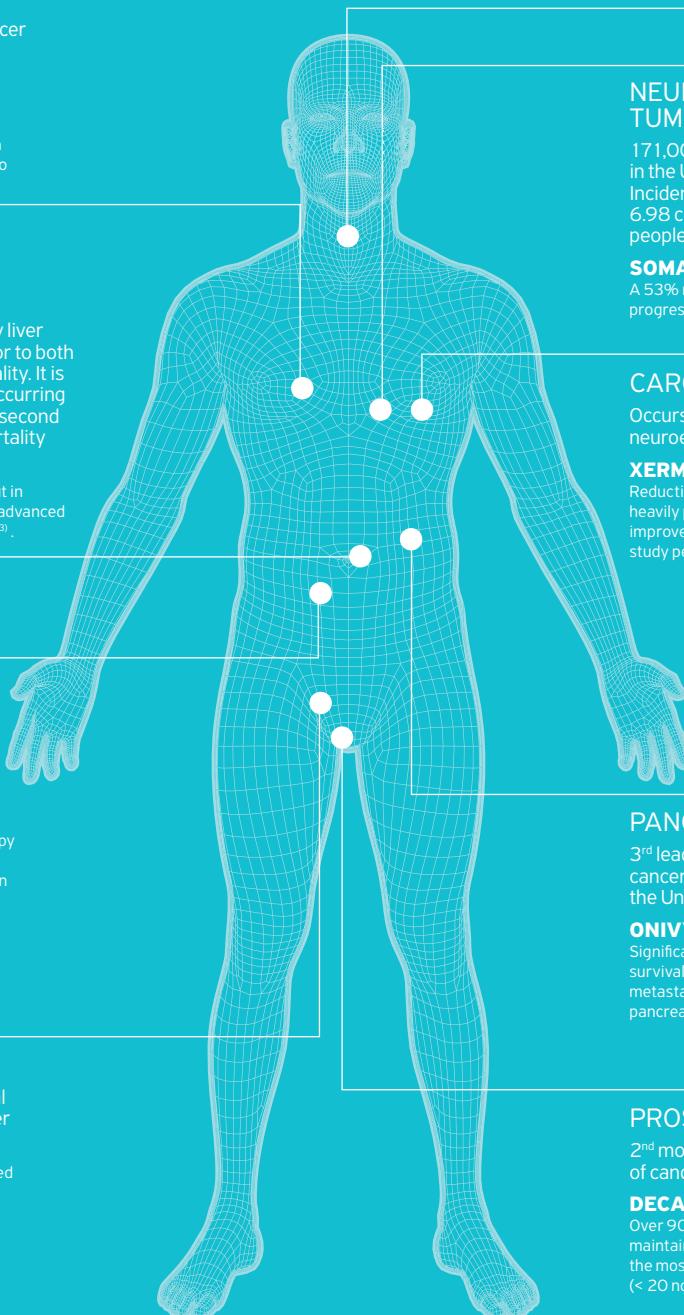
1<sup>st</sup> and only multi-targeted therapy to prolong survival, slow disease progression, and shrink tumors in 1L and 2L RCC<sup>(4)</sup>.

### BLADDER CANCER

2<sup>nd</sup> most frequent urological cancer, after prostate cancer

#### HEVIX®

Improved treatment and improved detection and resection of non-invasive bladder cancer<sup>(5)</sup>.



### MEDULLARY THYROID CANCER

5% of thyroid cancers

#### COMETRIQ®

Significant difference in the duration of progression-free survival with cabozantinib (11.2 months) versus placebo (4 months)<sup>(1)</sup>.

### NEUROENDOCRINE TUMORS

171,000 people living with NETs in the United States. Incidence rate of approximately 6.98 cases per 100,000 people<sup>(6a)</sup>

#### SOMATULINE®

A 53% relative risk reduction of disease progression or death<sup>(6b)</sup>.

### CARCINOID SYNDROME

Occurs in about 20% of all neuroendocrine tumors<sup>(7a)</sup>

#### XERMELO®

Reduction in bowel movements in heavily pretreated patients; 30% improvement for more than 50% of the study period in durable responders<sup>(7b)</sup>.

### PANCREATIC CANCER

3<sup>rd</sup> leading cause of cancer-related death in the United States

#### ONIVYDE®

Significant improvement of overall survival in adult patients with metastatic adenocarcinoma of the pancreas<sup>(8)</sup>.

### PROSTATE CANCER

2<sup>nd</sup> most common type of cancer in men

#### DECAPEPTYL®

Over 90% of patients achieve and maintain medical castration below the most stringent threshold levels (< 20 ng/dl)<sup>(9)</sup>.

**Focus on**

# Our assets in Neuroscience

**2**018 was a turning point for Dysport® (abobotulinumtoxinA), our spasticity and cervical dystonia treatment in the neuroscience area. Dysport® recorded 12.6% growth in 2018, fueled by strong performance in the US. "To see that growth coming now is extremely encouraging," says Guillermo Castillo, Head of Neuroscience Franchise. "Dysport® offers many patients control of symptoms for the full three-month period between injections, demonstrating its value for patients for whom symptom control is essential to quality of life," he says. Meanwhile, in the esthetic area, Dysport® continued its strong performance in Europe and the US, and in some countries like Australia and Brazil, thanks to the leadership of our partner Galderma.

## Breaking new ground with Dysport®

In a change of strategy for Dysport®, Neuroscience is now also focusing on identifying and developing new indications in therapeutics. Since 2018, two Phase II clinical trials are studying how Dysport® could be used to treat vulvodynia<sup>(1)</sup> and hallux valgus<sup>(2)</sup>, common conditions for which the unmet medical need is high. "This is groundbreaking work," says Castillo.

## A promising pipeline

rBoNT-E is the first of these exciting developments in our neuroscience pipeline. In 2018, data from the first in-human study of a new recombinant botulinum toxin E were presented. The now published Phase I study<sup>(3)</sup> demonstrated a significantly faster onset of action than the currently available BoNT-A. "rBoNT-E has the potential to offer patients a more tailored treatment, as a complement to BoNT-A, as well as

the potential to treat a different range of diseases," says Castillo. And our 'research group' has advanced toxins technology even further by incorporating both toxin and non-toxin domains in a new class of proteins: Targeted Secretion Inhibitors (TSIs). We believe that these proteins will target both neurons and other types of cells in the body, potentially leading to different clinical applications such as pain, endocrine disorders and inflammatory conditions.

## Working with patients for a better future

When it comes to developing new indications, Castillo is clear about the important role our patients must play in the process. "We'll need to be extremely patient-focused to understand the value we can bring to patients and to develop endpoints, and the entire Neuroscience team will be working closely to do just that," he says.



**Guillermo Castillo**  
VP, Head of Neuroscience Franchise

**"We'll need to be extremely patient-focused to understand the value we can bring to patients and to develop endpoints, and the entire Neuroscience team will be working closely to do just that."**

Guillermo Castillo  
Vice President,  
Head of Neuroscience Franchise

**12.6%**

growth in the US for Dysport®

**50**

posters presented at the  
TOXINS 2019 Conference  
(January 2019)

# BOOSTING OUR THERAPEUTIC PORTFOLIO IN NEUROSCIENCE

With botulinum toxin type A Dysport®, Ipsen is able to offer a single product<sup>(1)</sup> to treat a range of therapeutic indications.

## 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 estimated at 57 cases per million in the EU<sup>(1)</sup> and at 89 cases per million in the USA<sup>(2)</sup>. Sustained symptom control and a significant reduction of disease associated pain with reduction of symptoms for up to 15-17 weeks<sup>(3)</sup>.

## AXILLARY HYPERHIDROSIS

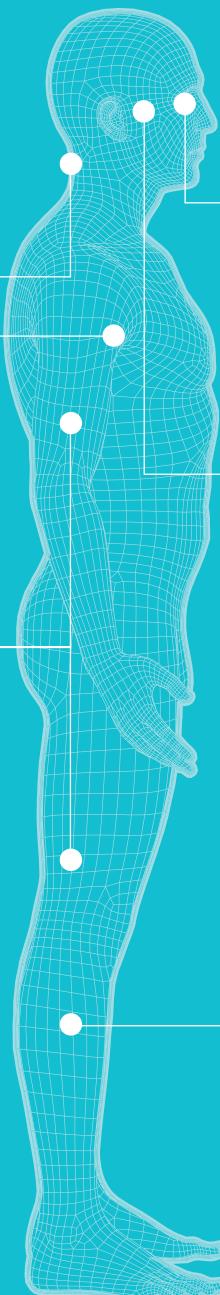
Axillary hyperhidrosis (HH) is excessive sweating due to overactivity of the sweat glands. It affects about 1%-3% of the population<sup>(12)</sup>

The median duration of efficacy ranges from 5 to 9 months<sup>(13)</sup>.

## 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 between 17% and 42.6%<sup>(8)</sup>. Significant and sustained improvement of muscle tone and passive function after repeated injections in adult upper limb spasticity, as well as significant and sustained reduction of tone associated with improvement of walking in adult lower limb spasticity.



## BLEPHAROSPASM

Blepharospasm is an abnormal contraction of the eyelid that can be chronic and persistent

Prevalence from 16 to 133 cases per million<sup>(4a)(db)</sup>. Significant reduction of the frequency and intensity of facial spasms as well as sustained improvement in the reduction of functional disability up to 16 weeks<sup>(5)</sup>.

## 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<sup>(6)</sup>. Significant reduction in functional disability and improvement of quality of life<sup>(7)</sup>.

## PEDIATRIC LOWER LIMB SPASTICITY

Cerebral palsy is the most common cause of spasticity and physical disability in children

Prevalence of 1.5 to 3 cases per 1,000 live births<sup>(9)(10)</sup>. 90 percent of patients with CP will present spastic hypertonia<sup>(11)</sup>. Sustained clinical improvements in muscle tone, spasticity, overall clinical benefit and goal attainment across treatment cycles, for children aged 2 and above.

**Focus on**

# Our assets in Rare Diseases

**G**iven our long-standing focus on addressing unmet medical needs, the Rare Diseases field is a natural fit. So called because they affect a very small proportion of the patient population, ranging from several hundreds to many thousands of people worldwide, rare diseases vary greatly in their severity, symptoms and outcomes.

But they usually have two significant things in common: it's a field with extremely high unmet medical needs, and the patients diagnosed with rare diseases tend to be deeply involved and engaged patients. "They have to be," Monia Vial, Senior Director Rare Diseases, Commercial Head, says. "There's often so little knowledge about their condition that patients have to join forces with others like them to advocate for themselves with the medical community and health authorities."

These vibrant patient communities represent an opportunity for us to involve patients in every aspect of clinical development.

## Transformation for and with patients

2018 was a year of transformation for our Rare Diseases division. The goal is to acquire an anchor asset for the franchise; one that would offer the potential to develop several indications and fulfil our promise to invest in rare diseases. In April 2019, we acquired Clementia Pharmaceuticals and its late-stage clinical asset palovarotene, which has been fast-tracked for approval by the FDA for fibrodysplasia ossificans progressiva (FOP). "This is an ultra-rare condition with high unmet medical needs," says Monia Vial.



**Monia Vial**  
Senior Director Rare Diseases,  
Commercial Head

**"This acquisition represents a true transformation for Ipsen, one built on our legacy and our capabilities in rare diseases. It's a natural evolution, from being experts in highly specialized medicine, to taking it a step further in our ability to treat rare conditions."**

Monia Vial  
Senior Director Rare Diseases,  
Commercial Head

"There's absolutely no treatment out there and we were really struck by the tremendous suffering of the patients. Becoming the first company with the potential to provide treatment was profoundly inspiring."

This acquisition gives us a cornerstone drug candidate with rare pediatric disease and breakthrough therapy designations, potential US approval in 2020 and additional indications to follow, as well as new scientific expertise.

## THREE KEY IMPERATIVES FOR 2019

- Deliver on Ipsen's commitment to rare diseases
- Ensure a best-in-class launch of palovarotene
- Continue to build an innovative portfolio and pipeline for rare diseases

## BOOSTING OUR PORTFOLIO IN RARE DISEASES

Ipsen offers a broad range of high-quality, innovative treatments to help improve the lives of patients with rare diseases.

### SOMATULINE®

is used for the long-term treatment of acromegaly in patients who cannot be treated with surgery or radiation.

Acromegaly is a rare disease caused by excessive growth hormone production resulting from a tumor in the pituitary gland. Between 2.8 to 13.7 people in 100,000 are affected by this disease<sup>(1)(2)</sup>.

### INCRELEX®

is a recombinant insulin-like growth factor (IGF-1) that treats Severe Primary IGF1 Deficiency (SPIGFD), an extremely rare growth disorder. It has obtained orphan drug status based on the low incidence of the disease, which affects fewer than 2 people per 10,000<sup>(1)</sup>. In 2017, a new European Ipsen manufacturing site was approved by both the European Medicines Agency and the Food and Drug Administration to produce Increlex®. It is the only drug available in Europe and US for children living with severe primary insulin-like growth factor deficiency.<sup>(2)</sup>

### NUTROPINAQ®

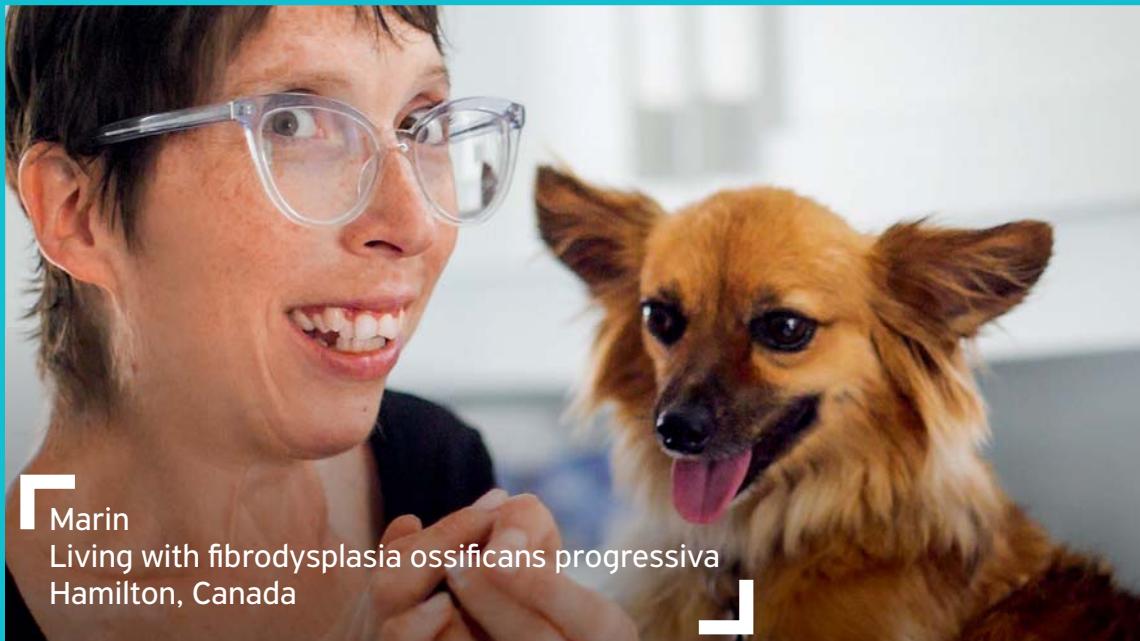
is a liquid formulation of recombinant human growth hormone administered with the NutropinAq® Pen<sup>(1)</sup>. Available in more than 20 countries, notably in Europe and Australia, it is indicated in children and adults for the treatment of growth failure stemming from various origins.

### DECAPEPTYL®

is approved for the treatment of central precocious puberty (CPP)<sup>(1)</sup>. There is potential opportunity for greater use of this treatment in the European Union, China and Russia.

### PALOVAROTENE : A LATE-STAGE ASSET IN CLINICAL DEVELOPMENT

- A potential treatment for patients living with fibrodysplasia ossificans progressiva (FOP) is expected to be submitted to the US Food and Drug Administration (FDA) in the second half of 2019
- A potential treatment for patients living with multiple osteochondromas (MO), also known as hereditary multiple exostoses (HMO)



**Focus on**

# Our assets in Consumer HealthCare

**O**ver the past two years, our Consumer HealthCare (CHC) division has been focused on transformation, with a three-fold ambition: establishing a true consumer healthcare business, returning the division to growth and making it sustainable. "Which is why it's so satisfying to us," says Benoit Hennion, Executive Vice President, Consumer HealthCare, "to have driven the second year of growth in 2018, up 2.7% from 2017. Driven in large part by the Smecta® brand and its recent extensions (+5% in 2018), this growth is the direct result of our new strategy. CHC has also undergone a business structure transformation, with the creation of a separate legal entity in France which aims to facilitate the integration of future acquisitions and partnerships and reinforces the division's sustainability."

**Building consumer healthcare skills**

"We can now say that we're a true consumer healthcare business, which means we speak not only to physicians but also to pharmacists and consumers," he says. "That's the particularity of consumer healthcare. We offer products that have a proven clinical benefit, but they must also demonstrate true consumer benefits to gain pharmacist recommendations and ensure consumers turn to us directly," he explains. By offering consumers a proven

medical benefit, plus a consumer benefit, such as liquid sticks or new flavors, we're continuing to innovate to meet consumers' needs and, in turn, driving growth.

**Listening to consumers and colleagues**

In true One Ipsen fashion, finding and developing ideas to extend brands and offer consumers innovative benefits was a collaborative effort. In April 2018, CHC launched the CHC Innovation Race, a massive global brainstorming session within the company. After gathering, sorting and processing more than 4,000 ideas from employees, four new brand extensions are already in development, with more sure to follow in the coming years. "I'm very optimistic about the future," Hennion says. "We're going to continue growing in Europe, Russia and Asia, fine-tune our consumer healthcare skills and reinforce our portfolio to better meet consumers' needs."

**€300 million**

sales in 2018

**More than 1,500**

employees across the globe



**Benoit Hennion**  
EVP, Consumer HealthCare

**"We can now say that we're a true consumer healthcare business, which means we speak not only to physicians but also to pharmacists and consumers."**

Benoit Hennion  
Executive Vice President,  
Consumer HealthCare

## 2018 KEY FACTS

- Creation of a new, separate legal entity in France
- Launch of a joint venture in Algeria
- Acquisition of a platform in Italy
- Opening of a Liquid Stick production line in Dreux
- Opening of a development plan in L'Isle-sur-la-Sorgue dedicated to clay-based products

# BOOSTING OUR PORTFOLIO IN CONSUMER HEALTHCARE

The Ipsen Consumer HealthCare product portfolio continues to grow, improving existing treatments and providing new solutions for patients and consumers.



## Gastrointestinal conditions



### SMECTA®<sup>(1)</sup>

Stops and treats diarrhea, removes the toxins and germs at the heart of the problem, helps repair intestinal damage with its natural coating properties and relieves abdominal pain.



### SMECTAGO®<sup>(2)</sup>

This ready-to-use liquid stick is used in the short-term treatment of acute diarrhea, in addition to use for dietary measures.



### SMECTAGAS®<sup>(2)</sup>

An exclusive dual action against gas and bloating that favors fast gas elimination and restores a healthy gut microbiota.



### SMEBIOCTA®<sup>(3)</sup>

Scientifically proven multiaction probiotic that interacts with the multiple mechanisms of functional GI disorders.



### FORLAX®<sup>(1)</sup>

Reactivates the bowel's natural efficacy and restores the regular frequency of stools within 24 to 48 hours to respect the natural rhythm. It operates by reeducating the bowel without irritating the bowel or making it dependent.



### FORLAXGO®<sup>(2)</sup>

Ready-to-use liquid stick, Forlaxgo® is a laxative treatment of occasional constipation in adults and children from 8 years old.



### EZICLEN® / IZINOVA®<sup>(1)</sup>

New generation of bowel cleansing preparation. Reduces considerably the quantity of liquid to be ingested by the patient, improves the cleansing quality, and increases the efficacy of colonoscopies.



### FORTTRANS®<sup>(1)</sup>

Colon-cleansing solution to use before an endoscopy procedure (colonoscopy), surgery, or radiology. The active substance is Macrogol 4000, a linear polymer of polyethylene glycol (PEG) of high molecular weight with added electrolytes.



### ETIASA®<sup>(1)</sup>

Treats Inflammatory Bowel Diseases (ulcerative colitis and Crohn's disease) during acute phase and to maintain remission.



### BUSCOPAN®<sup>(1)</sup>

An antispasmodic used to relieve smooth muscle spasms (cramps) in the stomach and intestines and in the bladder and urethra.

## Other conditions



### ADENURIC®<sup>(1)</sup>

First major treatment of gout for more than 40 years and best in class for the treatment of symptomatic gout.



### TANAKAN®<sup>(1)</sup>

Standardized, patented ginkgo biloba extract (EGb 761®) for the symptomatic treatment of such cognitive disorders as memory deficit and concentration disturbances in the elderly, and for vertigo and tinnitus.



### PAXELADINE®<sup>(1)</sup>

Used for irritative cough, allergic cough, cough in patients with heart disease, tracheitis, bronchitis and other conditions.



### PRONTALGINE®<sup>(1)</sup>

An analgesic for the treatment of moderate to severe pain, combining paracetamol, caffeine and codeine.

## Our R&D

# To deliver on our promise and be a partner-of-choice

**W**hat powers our R&D? First of all, a sense of urgency. "Patients can't wait," says Alexandre Lebeaut, Executive Vice President of R&D & Chief Scientific Officer. "Our products have the potential to provide meaningful clinical benefits and we've made a commitment to innovate for improved outcomes including extending lives, function and quality of life. This is what drives us every day," he continues. Delivering on that commitment is an immense task and requires our skills, expertise, lean governance and empowered project teams who can prioritize projects with the greatest potential for success. "R&D isn't for the faint-hearted," Lebeaut says. "We know that, statistically, a certain number of projects won't move forward. We call this the 'win or fail quickly' principle: you have to know when to pull the plug so you can allocate resources to the projects with the highest probability of delivering for patients." To fulfill our promise to bring at least one new asset or major indication to the market each year, our teams work tirelessly to identify and develop the most promising assets in an ever-evolving scientific environment.

### A pipeline built around patients

In this driven and intense field, what role do patients play? "Patients are pushing the industry to find new treatments," says Lebeaut. "Patients are inspiring us. Their insights and experience are at the forefront when we design our clinical trials. We listen to patients to understand what matters to them. And we're connecting with them in new ways. Our digital transformation and artificial intelligence (AI) tools are helping us define patient profiles and thanks to in silico clinical trial strategies we can better approximate the right sample size of patients to test our hypotheses and answer our questions in clinical trials, exposing only the necessary and sufficient number of patients".



**Alexandre Lebeaut**  
EVP, R&D, Chief Scientific Officer

**"Our first commitment to patients is to bring both quality products and information to the table. Our second commitment to patients is time. We're at a moment of great transformation: we can offer much better outcomes for cancer patients, and we take pride in that. This is where we hope to make a difference in our lifetime."**

Alexandre Lebeaut  
Executive Vice President  
R&D, Chief Scientific Officer

### Ipsen as a talent incubator

Building a robust pipeline requires highly-skilled employees. "We operate in extremely specialized fields of medicine, which means we're truly a talent incubator in oncology and neurotoxins. A lot of our talent comes from large pharma companies because we offer them something unique: a great opportunity to make a real impact on strategies, and to experience development from A to Z. When you work here, you're very close to the science, very close to patients," comments Lebeaut.

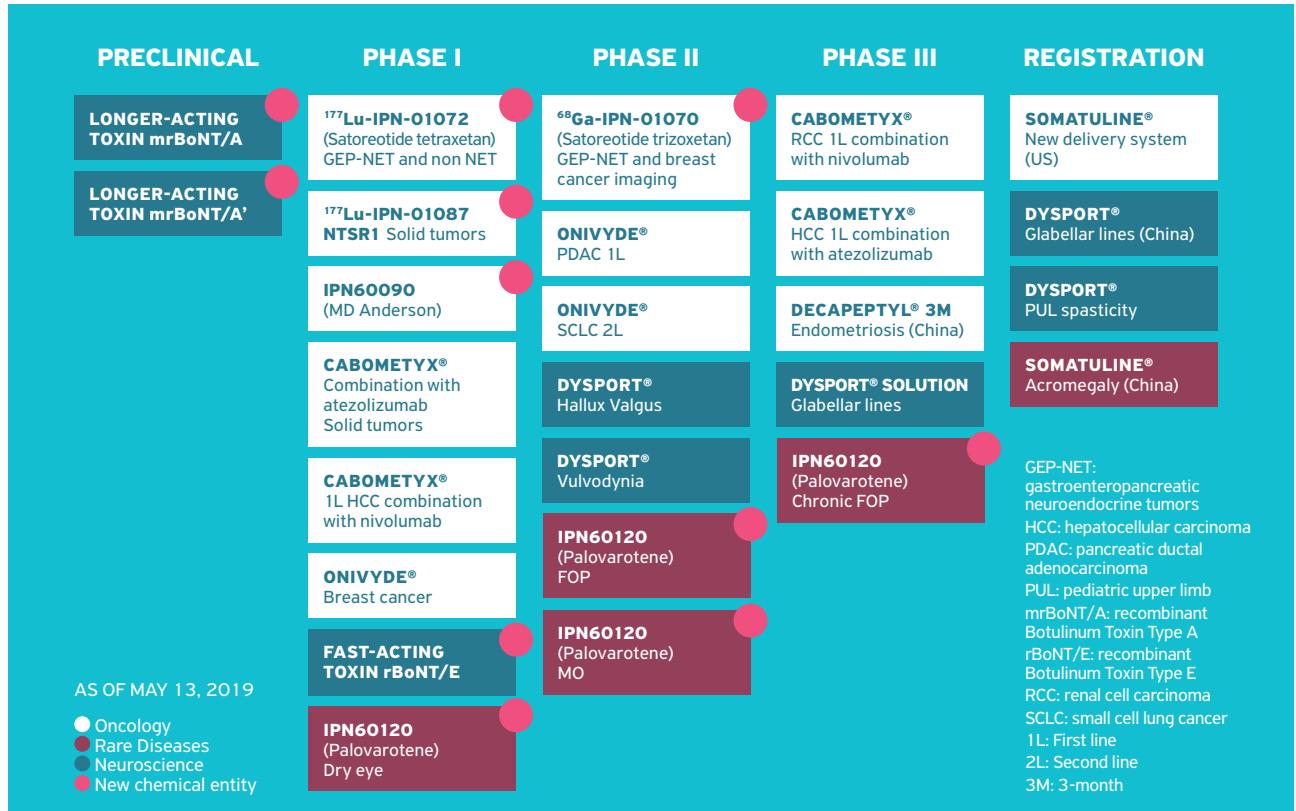
### 2019 VISION

- Continue to transform, innovate and deliver to grow a valuable and sustainable pipeline
- Accelerate all priority projects that have the potential to change the treatment paradigm as the main output of our development powerhouse

## Our R&D

# Pipeline

We are growing our pipeline with new drugs and new indications in Oncology, Neuroscience and Rare Diseases to serve patients worldwide.



**"We've created a partner-of-choice approach, which means that in everything we do, we aim to bring value to our partners. We offer transparency in our processes and seek to ensure alignment from the very beginning. Above all, we share the same passion and sense of urgency as our partners: to realize the potential of their innovation and improve patients' lives."**

Ivana Magovčević-Liebisch  
Executive Vice President, Chief Business Officer



# Our manufacturing and R&D sites

At Ipsen, we draw on our manufacturing and R&D expertise to propose life-changing molecules across the globe.



**Aidan Murphy**  
EVP, Technical Operations

**“Our sites and our people are our best assets to provide patients and people with quality products and innovative services. Every day we can make a difference in the lives of patients and their families.”**

Aidan Murphy  
Executive Vice President,  
Technical Operations

## UNITED KINGDOM

### MANUFACTURING AND R&D Wrexham

The site is the company's sole biological R&D and fully integrated manufacturing facility. This center of expertise is specialized in active ingredients, clinical drug and commercial manufacturing and distribution. Some teams focus on the development of novel products in Neuroscience supported by bioprocess, formulation and analytical functions, while others work in lifecycle management and new recombinant toxin manufacturing projects.



**R&D**  
**Oxford**

Designed to foster innovation and collaboration in Neuroscience, this pioneering R&D center hosts Ipsen's technological platform for botulinum toxins and has unique experience in recombinant botulinum toxins technology. The site also hosts other R&D activities such as regulatory affairs, pharmacovigilance, publications, and clinical development.

## GERMANY

**R&D**  
**Berlin**

The Berlin site specializes in the radiopharmaceutical development of peptides and small molecules. These activities focus on radiolabeling process development and validation.

## IRELAND

### MANUFACTURING Cork

This site joined Ipsen as a result of a joint venture with Schwabe. The extract of ginkgo biloba - EGB 761® - is produced there and used for Tanakan® and Ginkor®.

### MANUFACTURING AND R&D Dublin

As Ipsen's center for the production and development of peptide active pharmaceutical ingredients (APIs), the site produces the APIs for both Somatuline® and Decapeptyl®. It also handles chemical process and analytical method activities for peptide and small molecule APIs.

## UNITED STATES

### MANUFACTURING AND R&D Cambridge

The R&D site is dedicated to enhancing the pipeline with clinical assets, with a focus on Oncology and Rare Diseases. It also hosts teams dedicated to coordinating and conducting worldwide clinical research and North America regulatory activities. The manufacturing site produces the bulk drug product for Onivyde® patients worldwide.

## FRANCE



### MANUFACTURING AND R&D Dreux

The manufacturing site, specialized in the production of oral formulations, also handles global distribution of products. R&D activities focus on the pharmaceutical development of new products for Specialty Care (Oncology and Rare Diseases) and Consumer HealthCare. The site also hosts the clinical supply chain activities for clinical studies.

### MANUFACTURING Signes

This facility specializes in the manufacturing and packaging of injectable formulations, particularly sustained release formulations of peptides (Decapeptyl®/Pamorelin®, Somatuline® and NutropinAq®). The site exports to over 70 countries worldwide.

### MANUFACTURING L'Isle-sur-la-Sorgue

L'Isle-sur-la-Sorgue is Ipsen's only site for processing clays, notably used in Smecta®, Bedelix®, Actapulgite® and Gelox®. Approximately two-thirds of the production is for Europe and China.

### R&D Paris-Saclay

The site's core mission is to accelerate clinical development, translational and fundamental research to deepen the understanding of the molecular, pharmacologic, pharmacodynamic and pharmacokinetic properties of new molecules in Oncology, Neuroscience and Rare Diseases.

## CHINA



### MANUFACTURING Tianjin

Present in Tianjin since 1992, Ipsen created a local production facility for Smecta® in 2000. The site packages this product for the Chinese market and is also the distribution platform for Ipsen's portfolio and other medical products in China.

### R&D Beijing

Created in Beijing in 2012, the Asia group Drug Development team is the platform in charge of clinical trial coordination in Asia.

# Our global presence

Ipsen operates in 115 countries. Our most important sites in R&D and manufacturing are located in China, France, Ireland, the United Kingdom and the United States.

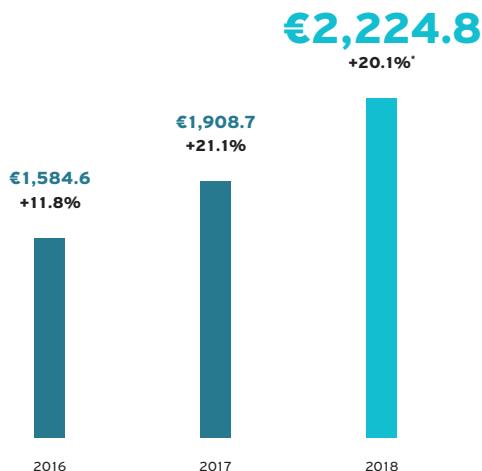




# Our key indicators

## Sales and operating income growth

2018 IPSEN SALES  
(in millions of euros)



CORE OPERATING INCOME  
**€659.9m**

CORE OPERATING MARGIN  
**29.7%**

\* Change at constant currency.  
Year-on-year growth excluding foreign exchange impact established by recalculating net sales for the relevant period at the rate used for the previous period.

## 2022 financial outlook

COMPANY  
SALES  
**≈€3.2bn**

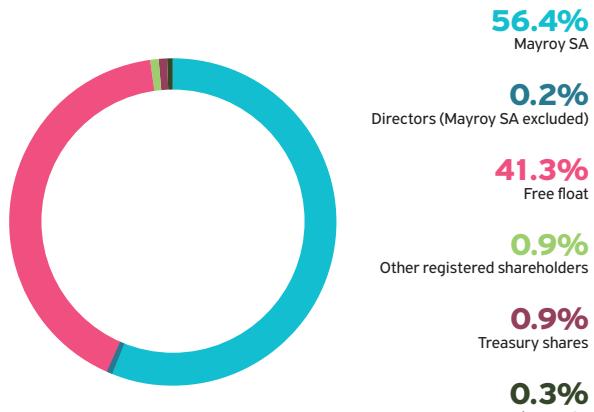
CORE OPERATING  
MARGIN  
**>32%**  
of net sales

## Ipsen's dividend per share evolution



\* Proposed by Ipsen S.A. Board of Directors, which met on 13 February 2019.

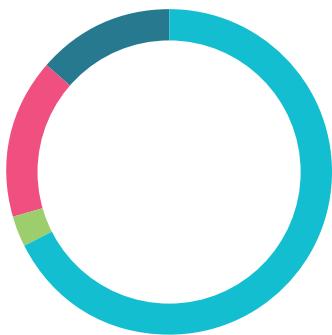
## Ownership of Ipsen's share capital as of December 31, 2018



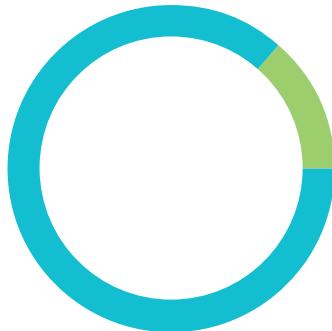
**“For the second year in a row we have generated more than 20% growth and for the first time in our history we can claim a blockbuster with Somatuline®. Our 2020 objectives will be achieved as early as 2019, one year earlier than expected.”**

Aymeric Le Chatelier  
Executive Vice President, Chief Financial Officer

## Sales by therapeutic area



**68%**  
Oncology  
**16%**  
Neuroscience  
**13%**  
Consumer HealthCare  
**3%**  
Rare Diseases



**87%**  
Specialty Care  
Sales growth  
+24.7%  
**13%**  
Consumer HealthCare  
Sales growth  
+2.7%\*

\* Year-on-year re-stated from Etiasa new contractual set-up.

## Sales by geographic area

**34%**  
Major Western European Countries'  
Sales growth  
+17.1%

**28%**  
North America  
Sales growth  
+37.9%



**20%**  
Other European Countries  
Sales growth  
+16.9%

**18%**  
Rest of the world  
Sales growth  
+7.3%

\* France, Germany, Italy, United Kingdom and Spain.

## A strong commitment to R&D

**€302.1m**  
INVESTED IN R&D  
13.6% OF 2018  
SALES

EMPLOYEES  
WORKING IN R&D  
**680+**

MAJOR R&D  
CENTERS  
**3**

CLINICAL STUDIES  
IN PHASE III  
**5**

# WE DELIVER

We promise our patients innovative treatments,  
a bold vision for the future and new hope. Our outstanding results  
speak for themselves: we deliver on our promises every day  
because patients can't wait.



Ana  
Medical and Regulatory Affairs  
Barcelona, Spain



# Our Executive Leadership Team

and Extended Management

**François Garnier**  
Executive Vice President,  
General Counsel

**Christian Marcoux**  
Senior Vice President,  
Global Communications

**Aymeric Le Chatelier**  
Executive Vice President,  
Chief Financial Officer

**David Meek**  
Chief Executive Officer

*Extended*



**James Levine**, MD-PhD.  
President, Fondation Ipsen

**Harout Semerjian**  
Executive Vice President,  
Chief Commercial Officer

**Ivana Magovčević-Liebisch**  
Executive Vice President,  
Chief Business Officer

**Richard Paulson**  
Executive Vice President  
& CEO, Ipsen North America

**Benoit Hennion**  
Executive Vice President,  
Consumer HealthCare

**Alexandre Lebeaut**  
Executive Vice President,  
R&D & Chief Scientific  
Officer

**Aidan Murphy**  
Executive Vice  
President, Technical  
Operations

**Christopher Masterson**  
Senior Vice President,  
Global Quality  
—  
*Extended*



**Dominique Laymand**  
Executive Vice President,  
Ethics & Social Responsibility  
Chief Officer

**Dominique Bery**  
Executive Vice President,  
Strategy & Transformation

**Régis Mulot**  
Executive Vice President,  
Chief Human Resources Officer

# OUR BOARD OF DIRECTORS & COMMITTEES

The Board of Directors<sup>(1)</sup> determines the company's business strategy and oversees its implementation. It has established six permanent specialized committees to assist in fulfilling its oversight and monitoring responsibilities. The composition and role of the Board of Directors and its Committees as of December 31, 2018 are described below.

BOARD OF DIRECTORS
<b>Chairman:</b> Marc de Garidel
<b>Vice-Chairman:</b> Antoine Flochel
<b>Members:</b> Anne Beaufour Henri Beaufour Philippe Bonhomme Margaret Liu <sup>(2, 3)</sup> David Meek <sup>(3, 4)</sup> Michèle Ollier <sup>(3)</sup> Jean-Marc Parant <sup>(5)</sup> Paul Sekhri <sup>(2, 3)</sup> Carol Stuckley <sup>(2, 3)</sup> Piet Wigerinck <sup>(2, 3)</sup> Carol Xueref <sup>(3)</sup>
The Board of Directors determines the broad lines of the company's business activities and ensures their implementation. The Board of Directors deals with all matters relating to the conduct of the company's business and rules on all pertinent issues through its deliberations. More generally, the Board exercises the functions assigned to it by the law to act at all times in the company's corporate interest, and takes particular care to prevent any conflicts of interest and to take all interests into account.

## NOMINATION COMMITTEE

**Chairperson:** Carol Xueref<sup>(3)</sup>

**Members:** Philippe Bonhomme and Paul Sekhri<sup>(2, 3)</sup>

Its main role is, particularly, to make proposals to the Board of Directors concerning the re-election, replacement or appointment of new Directors, and gives its opinion on the appointment of the Chief Executive Officer and Executive Leadership Team members.

## COMPENSATION COMMITTEE

**Chairman:** Antoine Flochel

**Members:** Carol Xueref<sup>(3)</sup>, Carol Stuckley<sup>(2, 3)</sup> and Piet Wigerinck<sup>(2, 3)</sup>

Its main role is, particularly, to make proposals to the Board of Directors on all components of the compensation paid to the company's Corporate Officers, senior management and senior executives. It also gives its opinion on Directors' fees and makes recommendations notably on compensation policies, employee savings plans and performance shares.

## ETHICS AND GOVERNANCE COMMITTEE

**Chairperson:** Margaret Liu<sup>(2, 3)</sup>

**Members:** Philippe Bonhomme and Carol Xueref<sup>(3)</sup>

Its main role is, particularly, to review the corporate governance of the company and the definition of the company's fundamental values as well as of its ethics and compliance policies. The Committee ensures the dissemination throughout the Company of the Code of Ethics and general ethics policies defined by the Company and their updates. It also monitors the application of the rules of corporate governance defined by the Board of Directors.

## AUDIT COMMITTEE

**Chairperson:** Carol Stuckley<sup>(2, 3)</sup>

**Members:** Philippe Bonhomme and Paul Sekhri<sup>(2, 3)</sup>

Its main role is, particularly, to review the financial statements as well as to ensure the relevance and permanence of the accounting policies, and to examine the press releases on financial results and guidance. The Committee also monitors the effectiveness of internal control and risk management systems.

## INNOVATION AND DEVELOPMENT COMMITTEE - CONSUMER HEALTHCARE

**Chairman:** Marc de Garidel

**Members:** Philippe Bonhomme and Carol Xueref<sup>(3)</sup>

**Guests:** Anne Beaufour, Henri Beaufour and David Meek<sup>(3, 4)</sup>  
Its role is to review the proposals presented by the Management on Business Development and Mergers & Acquisitions relating to Consumer HealthCare. The Committee follows the update of the Consumer HealthCare portfolio. It also reviews Consumer HealthCare divestiture programs, if any, to be endorsed later by the Board.

## INNOVATION AND DEVELOPMENT COMMITTEE - SPECIALTY CARE

**Chairman:** Marc de Garidel

**Members:** Antoine Flochel, Margaret Liu<sup>(2, 3)</sup>, Michèle Ollier<sup>(3)</sup>,  
Paul Sekhri<sup>(2, 3)</sup> and Piet Wigerinck<sup>(2, 3)</sup>

**Guests:** Anne Beaufour, Henri Beaufour and David Meek<sup>(3, 4)</sup>

Its role is to review the proposals presented by the Management on internal Research & Development programs, Business Development and Mergers & Acquisitions. The Committee follows the update of the Business Development portfolio by therapeutic areas. It also reviews divestiture programs, if any, to be endorsed later by the Board.

(1) See chapter 5 of the 2018 Registration Document for further information.

(2) Independent Director.

(3) Director of non-French nationality, including binational.

(4) David Meek is Chief Executive Officer of Ipsen SA.

(5) Director representing the employees.

# Our people make us who we are

**P**eople make all the difference," begins Régis Mulot, Executive Vice President, Chief Human Resources Officer. In recent years, Ipsen has experienced rapid transformation driven by a strong desire to move away from a traditional pharmaceutical model and to a more agile one: a biopharma company. "I can honestly say that fully embracing patient centricity and acting like a biotech isn't always easy, but through the unwavering commitment of our people, it has become a reality at Ipsen." One of our key achievements over the past few years has been to articulate our ways of being to bring the biotech mindset to life. "In 2018, we finalized and launched five guiding principles, our One Ipsen Way of Being - behaviors that drive our daily decision-making. The aim is to foster an environment that encourages employees to innovate and improve patients' lives around the world."

## A clear employer value proposition

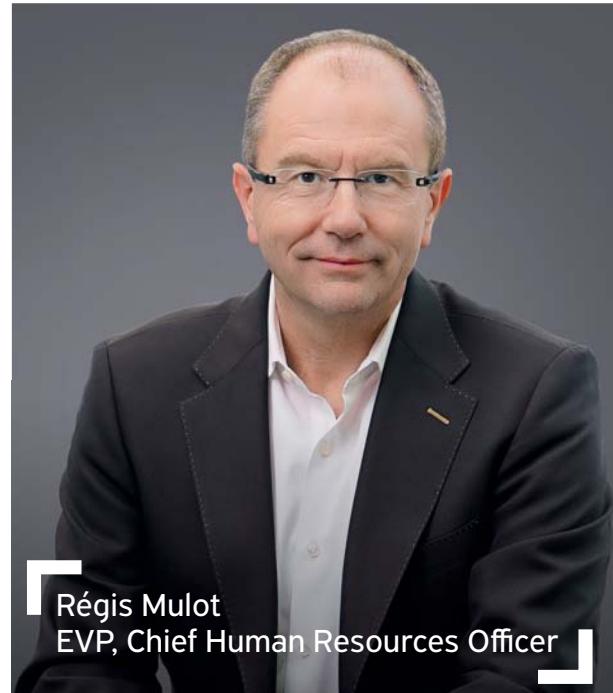
Being recognized as a top pharma player isn't necessarily our main goal, but it would highlight our strong commitment to patients and increase our attractiveness among top pharma/biotech and non-pharma talent. With that in mind, "We began working on our employer value proposition in 2017 and launched it in 2018," remarks Mulot. "Defining what we offer employees - the opportunity to make a real impact in an innovative, patient-centric company - helped increase our visibility with candidates worldwide. As such, we were able to recruit 100+ people at our Cambridge, Massachusetts headquarters, despite being a new arrival in an extremely competitive biotech job market."

## Sharing success and rewarding what matters

Another major project in 2018 was working to share our success with employees. "We see it as rewarding what matters - both individual or team results and the results of the company. We're very close to having 100% of our employees receive pay based on results and shared successes," says Mulot. "Beyond that, we want employees to be truly invested in our outcomes. Worldwide, 52% of our people have participated in the 2018 employee share ownership plan. This year, to celebrate our outstanding results, we're giving five shares to all employees worldwide. Our Board and the Executive Leadership Team felt strongly that it was the right thing to do: after all, our achievements are built on the incredible efforts of our people," he says.

## 2019 focus

Talent development is our focus for 2019. Without our people, we can't deliver on our strategy, and that means attracting and retaining top global talent, taking the time to mentor and invest in our people so they can realize their full potential.



Régis Mulot  
EVP, Chief Human Resources Officer

**In 2018, we made 300 net hires, representing over 5% of new talent. This is an impressive figure, which shows our growth and dynamism."**

Régis Mulot  
Executive Vice President,  
Chief Human Resources Officer

## ONE IPSEN WAY OF BEING

We trust each other

We share and learn everyday

We own our outcomes

We honor our word

We drive to win together

# Our patient-centric culture



Richard Paulson  
EVP & CEO,  
Ipsen North America



Ana  
Medical and Regulatory Affairs  
Barcelona, Spain

“I’m extremely proud of all that we’ve accomplished here at Ipsen and the tremendous growth our company is experiencing. But what excites me most is the thoughtfulness, dedication and commitment our employees bring to work every day. We all have our own personal connection to why the work we do is important, and it’s our shared passion for helping those suffering from difficult-to-treat diseases that drives us each and every day.”

Richard Paulson  
Executive Vice President & CEO,  
Ipsen North America

Ana  
Medical and Regulatory Affairs  
Barcelona, Spain

“I’m an oncologist. These days, I’m not in direct contact with patients, but everything I’m working on concerns improving their lives. My work has a real impact on them, such as our research on new molecules that might bring results to those with no therapeutic alternatives.”

**Jason**

**Marketing, Consumer HealthCare  
Shanghai, China**

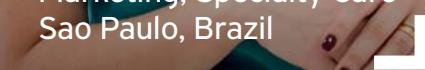
"It's a big responsibility to make sure patients have access to the medicine which best meets their needs. Our leadership puts a lot of trust in me and we're given lots of opportunities to try new approaches. Everything we do, we do for patients."



**Jason**  
**Marketing, Consumer HealthCare  
Shanghai, China**



**Janaine**  
**Marketing, Specialty Care  
Sao Paulo, Brazil**

**Janaine**

**Marketing, Specialty Care  
Sao Paulo, Brazil**

"What motivates me is my commitment to bring the best possible treatment to improve patients' lives. Our work allows them to take a child in their arms, catch a ball, lead a normal life. And that brings stars to my eyes!"

# Our strong Environment, Health & Safety culture

Our Environment, Health and Safety (EHS) department is leading us forward with an ambitious goal in mind: to become the best in EHS, both in the pharmaceutical industry and beyond. For the past three years, the team has been busy laying the foundation of a strong EHS culture, meeting and surpassing the goals they set for themselves. "Now we're looking for strategic opportunities to give us a competitive advantage and become a partner-of-choice," says Mike Whaley, Vice President, Environment, Health & Safety.

"A strong EHS program and culture that puts us ahead of the competition is a great performance indicator across the board," says Whaley, "and gives us a competitive advantage. If you have a really effective EHS program, you're probably running the business as effectively, if not more effectively. It's a good indicator that the company is looking seriously at every aspect of business and is committed to doing all of them very well. From a reputational point of view, a strong EHS performance is a differentiator and communicates our values as a company, helping us to achieve partner-of-choice status."

In 2018, EHS delivered a long list of achievements, many well ahead of schedule. How? By listening. "We've built a philosophy and a culture of involvement, of speaking up, of listening to employees and ensuring they're part of the solution, which is an integral component of our Ipsen culture globally. Employees are the experts on EHS issues because they're the ones facing them every day. If employees don't support our initiatives and programs, they



**Angelina,**  
Production Operator, Tech Ops  
Dreux, France

won't use them. Then we won't have the performance results we're expecting," says Whaley.

But don't expect Whaley and the EHS department to rest on their laurels. In 2019, the team will launch a 10-year plan to take us through 2030. Based on the UN Sustainable Development Goals, the plan will tackle the 17 goals, from carbon emissions and clean water to justice, peace, poverty and inequality. "It's helpful to have an international set of goals that are broad and ambitious," says Whaley. But his ultimate goal is even bigger: to build EHS into every aspect of the business. "My vision is that one day Ipsen won't have an EHS department, but we'll still be leading the way in EHS. Then we can focus all our efforts on what we do best—finding new treatments and offering new hope to patients."

## 2018 ACHIEVEMENTS

- Achieved Ipsen carbon reduction goal - due in 2020; two years ahead of schedule
- Achieved EHS top 10 with biotech peers - going for the best next
- Company ISO Certification achieved
- Achieved Ipsen FR2 accident goal - due in 2020; two years ahead of schedule
- Lowest number of accidents ever at Ipsen
- CSR awards received at Signes (two regional awards) - first department to receive one at Ipsen



# Fondation Ipsen

**F**ondation Ipsen is building on its 30-year legacy. Fondation Ipsen has been transformed to champion Science for People. "We work to improve the lives of millions of people around the world through science," says James Levine, MD-PhD, President of Fondation Ipsen. How? By rethinking scientific communication, with an approach that combines traditional media, such as world-class scientific conferences, with innovation; for example, using theater or producing books for children. The stakes are high. "Modern science is depicted as inconsistent, untrustworthy, unreliable, disorganized and unethical," says Levine. "There's a moral prerogative to change that."

Over the course of 2018, the team initiated a 28-component program to deploy a new approach to scientific communication. Events included:

- High-level conferences hosted in Singapore, Hong Kong and the United States, in collaboration with the prestigious scientific journals *Science*, *Nature* and *Cell*.
- An event on child abuse, co-hosted with the Mayo Clinic that was live-tweeted to an international audience: the combined audience was over 7,000 people.



James Levine, MD-PhD,  
President of Fondation Ipsen

**"Science is for  
people. All people.  
In a dark world,  
science brings light."**

James Levine, MD-PhD,  
President of the Fondation Ipsen

**160,843**

people interacted with us  
on social media

**35,000**

attendees to our webinar  
on gender parity in science

• Co-creation of public-library science programs, where scientists teach children from disadvantaged backgrounds about scientific discovery.

- A play about caregivers of people with Alzheimer's disease, staged in Paris.
- A multimedia program co-created with the journal *Science*, on the issue of gender parity in science.
- In July 2018, Fondation Ipsen announced the launch of its publishing house and the publication of eight titles - three for children in collaboration with Institut Curie.

Major partners now collaborate with Fondation Ipsen:

- UNESCO: A three-year agreement over 140 countries.
- National Press Foundation: The Paris Accord on Science. This four-day conference brings together 25 top science journalists to meet and interact with leading scientists.
- The journal *Science* and the American Association for the Advancement of Science: a series of monthly international live filmed open-access webinars.
- Institut Curie: a children's bookwriting program.
- Institut Pasteur: an international web-based diploma in Public Health to train health workers around the world without fee.



Shirley Malcolm, Ph.D. (Science/AAAS, Washington, USA) - Kathryn Clancy, Ph.D. (University of Illinois, Urbana, USA) - Anna Han, Ph.D. (NIH, Bethesda, USA) - Isabelle Collet, Ph.D. (University of Geneva, Switzerland)

# Ethics & Social Responsibility

## Building a culture of Ethics

When asked what defines Ipsen's approach to ethics, Dominique Laymand, Executive Vice President, Ethics and Social Responsibility Chief Officer, doesn't hesitate. "A focus on patients, our One Ipsen Way of Being and Social Responsibility are at the core of our approach," she says. "We start with patients: this is what gives us our sense of purpose. When you think about patient benefits and the patient perspective, naturally you must act in an ethical manner. We have clear responsibilities and accountability when it comes to providing solutions to patients. Whether you're the

CEO, whether you work in R&D, in the medical organization or any aspect of our business, this is a shared value; it creates a shared language," she explains.

## The role of the One Ipsen Way of Being

This ethics-driven patient focus is embodied in the One Ipsen Way of Being, the charter for all employees. "It is composed of five equally important pillars," Laymand explains. "It's a balanced mix of values and behaviors. When companies rely too heavily on listing values to create a charter, they quickly become empty inspira-

tional phrases. When they rely too heavily on behaviors without explaining why the behaviors are important, they become like a mechanical role-play," she says. "The One Ipsen Way of Being, combined with our social responsibility strategy, builds a solid foundation for an excellent culture that allows us to conduct the business in an ethical and compliant manner".

## Ethics & Social Responsibility: a natural fit

As for social responsibility, Laymand says, "We have a real vision and strategy built around three pillars: employees, patients



Dominique Laymand  
EVP, Ethics & Social Responsibility  
Chief Officer

**"A focus on patients, our One Ipsen Way of Being and Social Responsibility are at the core of our approach."**

Dominique Laymand  
Executive Vice President,  
Ethics & Social Responsibility  
Chief Officer

and society, and the environment. This year, social responsibility was integrated into the Ethics & Compliance department, because we see a deep connection between our social responsibility efforts and our ethical culture; it is essential that we act in a responsible manner for society at large." We haven't waited for directives on social responsibility from the French government, choosing instead to embed the concept into our company culture. "Our CEO David Meek was already convinced of the importance of social responsibility; it was already on the table in 2017. So it came quite naturally in our vision and strategy," says Laymand.

#### **How a strong ethical culture drives value creation**

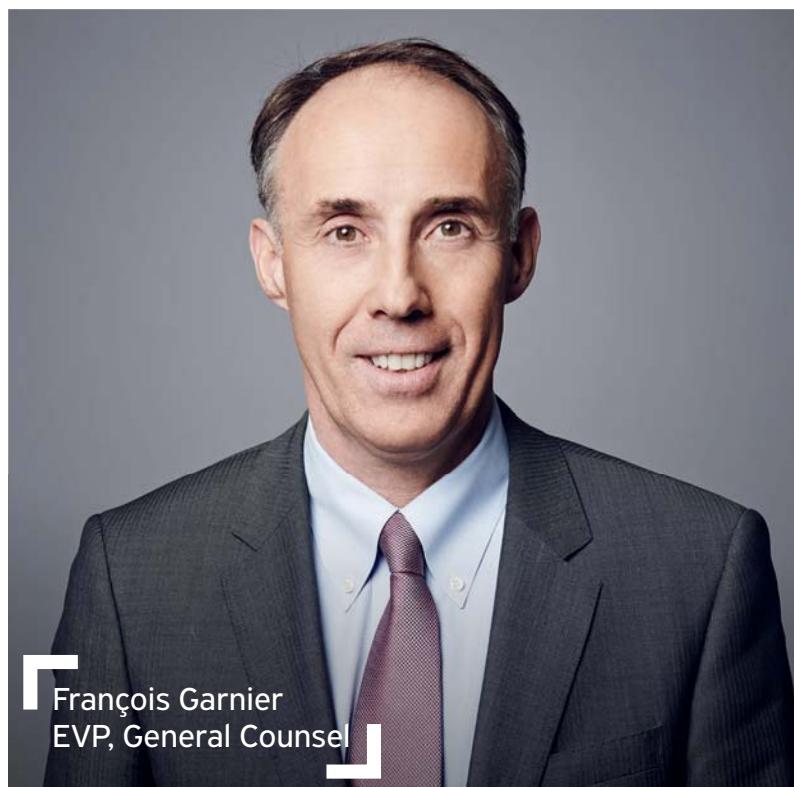
As Laymand sees it, a strong culture of ethics is a driver of value creation. "If you look at an organization that is exclusively compliance-driven and rule-based, it leads to a lot of bureaucracy, and no one likes that. The impact of driving engagement through conviction and a shared

vision is two-fold. First of all, it allows you to create a true strategic vision. If you're stuck in a 'tick-the-box' mentality, you cannot be strategic. Secondly, it makes it easier to follow the necessary rules, because you understand why they are important. If you find the right balance between inspiration and behavior, your behavior drives your work, rather than having procedures drive the way you work. That way, when you have a procedure to follow, you will follow it, because it is meaningful in the framework of what you have to achieve. But you must first understand why you have to do something before you think about how to do it," she says.

#### **Ethics & Social Responsibility in 2018**

Aside from integrating social responsibility into the Ethics & Compliance department to become the Ethics & Social Responsibility department, the team developed the new Code of Conduct, which will be launched in 2019. The team also reviewed

its anti-corruption risk approach and has revised the compliance program to develop a more global, simple, effective and user-friendly approach. Laymand is pleased to see the development of a more global approach to Business Ethics: "Having a global Business Ethics program helps us avoid situations where there is a different set of rules in each country. The more common ground we can have, the better, while being sensitive to cultural differences. Sometimes it's better to be a little stricter globally, because otherwise you have a variety of procedures and it becomes extremely difficult for employees to navigate. It's also a good support for employees' international development. If you're working in one country and move to another, the compliance structure is easy to understand because you're starting from a common ground. Then you can familiarize yourself with local differences, but you don't have to digest a completely different set of standards which would render development in other countries quite difficult," she notes.



**François Garnier**  
EVP, General Counsel

**"At Ipsen, we are committed to conducting our business in a sustainable way, supported by accountability and fairness, and driven by the highest ethical standards in the best interest of patients."**

François Garnier  
Executive Vice President,  
General Counsel

## DISCLAIMER AND REFERENCES

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(2) Product Intended Use Document

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