



# GOING FURTHER FOR PATIENTS

**THE GROUP IN 2015**

 **IPSEN**  
Innovation for patient care

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## **GOING FURTHER FOR PATIENTS IS BOTH OUR MISSION AND OUR ENGAGEMENT**

as we pursue our goal to become a leader for treatments in niche therapeutic areas and to expand our expertise in primary care.

## **GOING FURTHER FOR PATIENTS MEANS TAKING THE LEAD IN ALL OUR AREAS OF EXPERTISE**

to find effective therapies for patients' unmet needs and remain their reference throughout their treatment journey.

## **GOING FURTHER FOR PATIENTS MEANS MOVING AHEAD WITH OUR TRANSFORMATION**

and adapting to the challenges of tomorrow so that we can continue to bring value to the community.

**FEBRUARY 24, 2015**

Ipsen was granted an option to acquire **Canbex Therapeutics**, a spin-out of University College London, at the completion of a phase IIa study of Canbex' lead compound, VSN 16R, a potential treatment for spasticity in people with multiple sclerosis.





**APRIL 1, 2015**

Ipsen further expanded its close ties with **Harvard University** with a multi-year agreement that aims to stimulate new research projects in the areas of neuroendocrine tumors, neuromuscular disorders, and platform technologies related to toxins and peptides.



**APRIL 1, 2015**



To mark the inauguration of its new peptide-driven **R&D center in Cambridge** (Massachusetts, USA), Ipsen hosted a scientific symposium called “Connecting with Creativity” which was attended by several Nobel Prize laureates, prominent scientists and researchers.



**APRIL 8, 2015**

Ipsen and **Hannover Medical School** in Germany started a joint research program with the objective to develop new treatments based on recombinant botulinum neurotoxin proteins that would meet the needs of patients with serious neurological, endocrine or oncological diseases.

**MAY 19, 2015**

Ipsen strengthened its oncology expertise with the acquisition of **OctreoPharm Sciences**, a German company developing innovative radiopharmaceutical products for the diagnosis and treatment of neuroendocrine tumors.





**JULY 18, 2015**



The Food and Drug Administration approved botulinum toxin **Dysport®** as a treatment for adult upper-limb spasticity in the US.



**AUGUST 3, 2015**

Ipsen's partner **Lexicon Pharmaceuticals** announced positive results from a late-stage trial that evaluated the efficacy and safety of telotristat etiprate, a treatment being developed for carcinoid syndrome patients with advanced neuroendocrine tumors whose symptoms are inadequately controlled by somatostatin analogs.





**SEPTEMBER 2, 2015**

Ipsen strengthened its primary care portfolio with the launch in France of strawberry-flavored **Smecta®** for the symptomatic treatment of acute diarrhea in children and infants.





**OCTOBER 28, 2015**

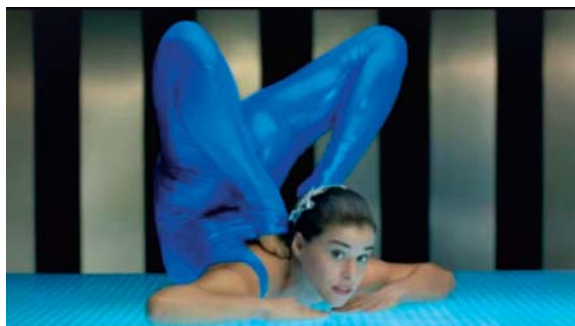
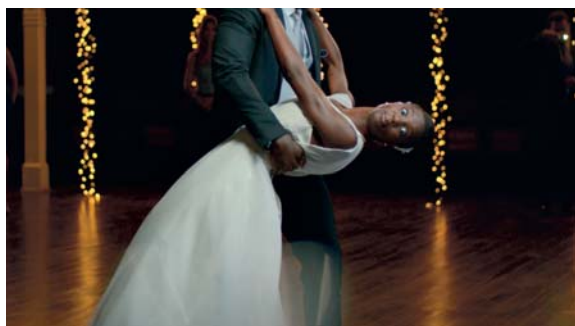
Ipsen bolstered its focus on niche therapeutic areas through a licensing agreement with **Telesta**

**Therapeutics** to develop and commercialize MCNA (mycobacterium phlei cell wall-nucleic acid complex) for the treatment of high-risk non muscle invasive bladder cancer in major markets outside the United States.

**NOVEMBER 19, 2015**

Ipsen and **Interprotein**, a Japanese R&D focused biotechnology company, enter into a research collaboration for novel therapeutic peptides targeting specific receptors with Interprotein's protein-protein interaction (PPI) and helix-loop-helix-peptide (HLHP) technologies intended for serious medical conditions in endocrinology, such as Cushing's disease.



**DECEMBER 7, 2015**

Ipsen further boosted its Primary Care portfolio with the French launch of caramel/cocoa-flavored **Smectalia**<sup>®</sup> stick for adults, an OTC ready-to-use formulation of Smecta<sup>®</sup>.

**smectalia**<sup>®</sup>  
diosmectite 3g



### JANUARY 6, 2016

Ipsen and **Galderma** expanded the geographical scope of their neurotoxin partnership in some key Asia-Pacific territories, and Ipsen acquired the intellectual property for Galderma's liquid toxin.



### JANUARY 8, 2016

Ipsen entered into a partnership with Belgium's **Aepodia** that aims to optimize Ipsen's capacity to perform early development and establish proof of concept for new molecule entities. Aepodia is the first company to integrate the Ipsen's R&D Campus in Paris-Saclay scientific hub.







**FEBRUARY 17, 2016**

Ipsen strengthened its pipeline in niche indication by in-licensing novel radiopharmaceuticals from **3B Pharmaceuticals** targeting a neurotensin receptor for the treatment of pancreatic adenocarcinoma.

**MARCH 1, 2016**

Ipsen bolstered its oncology pipeline by acquiring the rights outside the US, Canada and Japan to **Exelixis' cabozantinib**, a treatment today for medullary thyroid cancer and intended for advanced renal cell carcinoma with survival impact for patients.

**MARCH 8, 2016**

Ipsen announced a research partnership with **Peptimimesis**, a French start-up from a spin-off project of Strasbourg University and INSERM, the French national institute of health and medical research, to develop novel therapeutic peptides targeting a transmembrane receptor, which is overexpressed in a large number of cancers and is implicated in their development.



MARC DE GARIDEL,  
IPSEN CHAIRMAN AND CHIEF EXECUTIVE OFFICER

## **STRATEGY, GROWTH AND TRANSFORMATION AT IPSEN: MARC DE GARIDEL LOOKS AT THE MILESTONES OF 2015 AND THE PROSPECTS FOR 2016 AND BEYOND.**

### **What is your view of the company's performance in 2015?**

We are living through very exciting times at Ipsen. The transformation of the past few years, led by Christel Bories, has been positive. I want to thank all employees at Ipsen, who have demonstrated their strong commitment to patients as we treat more and more debilitating diseases.





**"IN 2015, WE REGISTERED DOUBLE-DIGIT SALES GROWTH FOR THE FIRST TIME IN TEN YEARS AND AT THE SAME TIME WE IMPROVED THE PROFITABILITY OF THE GROUP."**

I also want to recognize the contribution of our partners like Galderma, Debiopharm, and many others that have helped us reach a new level of excellence at Ipsen.

We disclosed in 2015 our refocused strategy on niche indications in Specialty Care and move to OTx commercial model in Primary Care.

For Ipsen, 2015 was a very successful year in many ways. The first accomplishment was our financial performance, as we registered double-digit sales growth for the first time in ten years and at the same time we improved the profitability of the Group.

Beyond the financial performance, the Group continued its transformation with a particular emphasis on the United States, where we became profitable ahead of plan thanks to the excellent launch of Somatuline® in neuroendocrine tumors. We also delivered strong scientific data for Dysport®, which has led to regulatory approvals in a number of markets in Europe and the United States as a treatment for adult upper limb spasticity.

Our pipeline progressed in 2015 through internal efforts and external acquisitions. Ipsen has pursued its goal to become a leader in the field of neuroendocrine tumors thanks to the acquisition of OctreoPharm Sciences as well as the partnership with Lexicon Pharmaceuticals to launch a new treatment for patients with neuroendocrine tumors. In terms of geographical footprint, the contribution from the

United States doubled in 2015: our affiliate now represents 11% of Group sales, compared with 5% a year ago. Emerging markets continue to represent a high share of our geographic footprint with 37% of sales, driven by China, Russia and Brazil. Ipsen has resisted very well in emerging markets, despite the difficult conditions in these countries, where in local currencies we have continued to grow. Europe performed very well, thanks to the launch of Somatuline® in neuroendocrine tumors.

In October 2015, we opened our first affiliate in Canada, the world's tenth largest market.

We ended the year with more than €200 million in cash, which allowed us to recently conclude a very important oncology deal with Exelixis for a drug intended for the treatment of kidney cancer.

### **What were the key achievements in Specialty Care?**

Specialty Care grew 14.4% in 2015 thanks to the growth of Somatuline®, which grew more than 34%, and Dysport®, which rose nearly 10%.

Somatuline® gained market share in Europe to reach more than 44% and in its first year in the market in the United States it has already achieved 12.8%, well above expectations.

The strength of our collaboration with Galderma for Dysport® in aesthetic medicine was another growth driver. Our partner accelerated significantly its market share in the United States to 22% from 14% in just eighteen months. We also signed an extension of our partnership with Galderma in Asia in early 2016.

Dysport® had a good performance in therapeutics, particularly in emerging markets.

Decapeptyl®, our prostate cancer drug, reported a moderate growth of about 1%: it suffered from increased price competition in China, but gained market share in Europe.



&gt;

"IPSEN AIMS TO POSITION ITSELF AS ONE OF THE FASTEST-GROWING PHARMACEUTICAL COMPANIES IN THE WORLD IN THE NEXT FIVE YEARS."

### What about Primary Care?

The historical decline was contained to about – 1%. We outlined an important strategic shift at our investor meeting in July 2015, when we said that we would move our activity increasingly toward promotion at pharmacy level. As a result, we are hiring more than 100 sales representatives in China.

During the fourth quarter of 2015, we launched two new formulations of Smecta® in France: the strawberry flavor, which is specifically designed for children and is the predominant version sold in China, and a convenient ready-to-use formulation called Smectalia®.

Primary Care is undergoing major changes in terms of business model and we are looking forward to a period of growth in the future.

### How important was North America in 2015?

The United States is a strategic market for Ipsen and I am very pleased that we turned around this crucial platform for the future of the Group.

The most remarkable event was the progression of Somatuline®, which grew 112%, compared with 2014 in the United States.

Our affiliate became profitable eighteen months ahead of plan. In April 2015, we strengthened our internal innovation in peptides with the opening of our new R&D center in Cambridge, Massachusetts, where 80 scientists will be based. Located in one of the most important scientific hubs worldwide, this situation is also key to partner with the renowned academic institutions such as Harvard University.



### Clinical innovation is crucial. What were the main advances in R&D during 2015?

Our pipeline advanced on many fronts. First, we received FDA approval for Dysport® in adult upper limb spasticity and in many European countries. We also filed Dysport® as a treatment for pediatric lower limb spasticity; if the FDA approves it in 2016, we would be the first company worldwide to have this unique claim.

We also released positive phase III results for telotristat etiprate in partnership with Lexicon for the treatment of symptomatic neuroendocrine tumors. We aim to file the drug with regulatory agencies in the second quarter of 2016 for a potential launch in 2017.

We also advanced our pipeline in next-generation neurotoxins.

### What are the key success factors that will drive Ipsen's performance in 2016?

In 2016, the focus for Ipsen is to continue the progress of Somatuline® thanks to the expanded label in the United States and Europe.

The second element of growth will come from the expanded label of Dysport® in adult upper limb spasticity, as well as the potential launch of the pediatric lower limb indication.



The newest challenge for us will be the launch of cabozantinib, the drug we have recently licensed from Exelixis as a second line treatment for renal cancer. We expect European regulatory approval in the later part of 2016. We expect a very exciting year for Specialty Care, which should translate into a growth greater than 10% in 2016, compared with 2015.

On the Primary Care front, we hope to benefit from the investment in China and accelerate the growth of Smecta®, a renowned brand internationally. We plan to enlarge our product offering in the future through the licensing of probiotics, which would complement our product range.

Our strategy to lessen our exposure to cost containments should allow Ipsen to register a slight growth in Primary Care for the first time in several years.

### **What is the outlook for 2016?**

We are in a great position to accelerate the growth of the company under a new leadership. We have thus decided to modify the Group's governance to bring it in line with our peers.

The Chairman function will be separated from the responsibilities of the Chief Executive Officer (CEO).

I will become non-executive Chairman upon arrival of the new CEO, someone with a strong pharmaceutical/biotech background, solid international experience, particularly in the United States, and a track record of positive business development.

### **What are your ambitions for Ipsen in the near future?**

We have a very positive outlook for Ipsen in the next five years, as we want to become a leader in key therapeutical areas such as neuroendocrine tumors and spasticity. In financial terms this means an acceleration of our growth to exceed more than €2 billion in sales by 2020 and continue to improve the profitability of the Group to reach more than 26% of sales.

Ipsen aims to position itself as one of the fastest-growing pharmaceutical companies in the world in the next five years. Thanks to a very clean balance sheet without any debt, we will continue our rapid growth, and we look forward to continuing to access external innovation. As our performance across the world improves, we are in an excellent position to attract drugs and partners that will ultimately make a big difference in the lives of patients.



## BOARD OF DIRECTORS & COMMITTEES<sup>(1)</sup>

The Board of Directors determines the Company's business strategy and oversees its implementation.

### BOARD OF DIRECTORS

#### **Chairman and Chief Executive Officer:**

Marc de Garidel

#### **Vice - Chairman:**

Antoine Flochel

#### **Members:**

Hélène Auriol-Potier<sup>(2)</sup>,  
Anne Beaufour,  
Henri Beaufour,  
Hervé Couffin<sup>(2)</sup>,  
Michèle Ollier<sup>(2)</sup>,  
Pierre Martinet<sup>(2)</sup>,  
Mayroy SA (represented  
by Philippe Bonhomme),  
Christophe Vérot and  
Carol Xueref.

ABOUT  
30 MEETINGS  
IN 2015

### STRATEGIC COMMITTEE

#### **Chairman**

Marc de Garidel

#### **Members:**

Henri Beaufour, Anne Beaufour,  
Michèle Ollier<sup>(2)</sup>, Antoine Flochel  
and Carol Xueref.

Its role is to study all significant investment and strategic issues of interest for Ipsen SA and the Group. The Committee also studies, approves and monitors the Group's Strategic plan.

### AUDIT COMMITTEE

#### **Chairman**

Pierre Martinet<sup>(2)</sup>

#### **Members:**

Hervé Couffin<sup>(2)</sup>  
and Christophe Vérot.

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

### APPOINTMENTS AND GOVERNANCE COMMITTEE

#### **Chairperson**

Anne Beaufour

#### **Members:**

Hervé Couffin<sup>(2)</sup>, Christophe Vérot  
and Michèle Ollier<sup>(2)</sup>.

Its role is to review the corporate governance of the Group and make proposals to the Board of Directors concerning re-election, replacement or appointment of new Directors. The Committee gives its opinion on the recruitment or the replacement of the Chief Executive Officer.

### COMPENSATION COMMITTEE

#### **Chairman**

Antoine Flochel

#### **Members:**

Hélène Auriol-Potier<sup>(2)</sup>  
and Pierre Martinet<sup>(2)</sup>.

Its role is to make proposals to the Board of Directors on all components paid to the Group's corporate officers, senior management and senior executives.

It also gives its opinion on Director's fees and makes recommendations notably about compensation policies, employee savings plans and performance shares.

### ETHICS COMMITTEE

#### **Chairperson**

Hélène Auriol-Potier<sup>(2)</sup>

#### **Members:**

Carol Xueref and Mayroy SA  
(represented by  
Philippe Bonhomme).

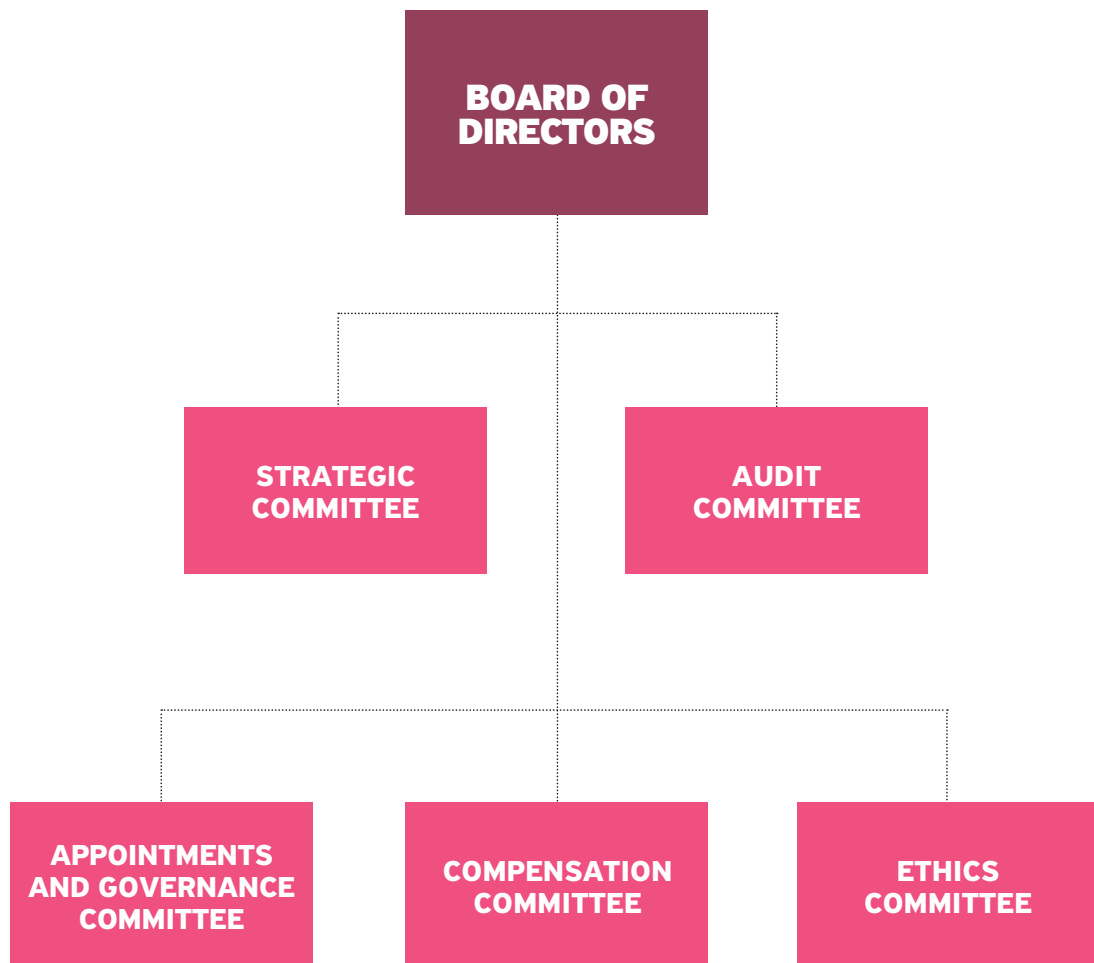
Its role is to review the definition of the Group's fundamental values as well as of its ethics and compliance policies.

The Committee ensures the dissemination throughout the Group of the Code of Ethics and general ethics policies defined by the Group and their updates.

(1) See chapter 4 of the 2015 Registration Document for further information.

(2) Independent Director.

The Board of Directors has established five permanent specialized Committees to assist in fulfilling its control and monitoring responsibilities. They issue proposals and recommendations and report their work to the Board.



## EXECUTIVE COMMITTEE

The executive management team leads the Group business, in the areas of scientific, legal, financial, commercial and strategic matters. It is responsible for assisting the Chairman of the Board of Directors in implementing the Board's decisions.



### MARC DE GARIDEL

Chairman and Chief Executive Officer

Marc de Garidel is responsible for defining the corporate strategy and the development of Ipsen SA in the long term, in particular projects for acquisition and partnerships. He also leads the transformation of the organization and the operations. He chairs the Board of Directors and the Executive Committee.



### JONATHAN BARNSELEY

Executive Vice President, Technical Operations

Jonathan Barnsley is responsible for the Specialty Care manufacturing sites and CMC (Chemistry, Manufacturing, Controls) development activities, and the Global Support Functions of Purchasing, Quality, EHS, Technical Services and Supply Chain; he collaborates closely on a functional level with the Primary Care manufacturing sites.



### CLAUDE BERTRAND

Executive Vice President, R&D, Chief Scientific Officer

Claude Bertrand is accountable for the discovery, development, and approval of new molecules. He oversees product lifecycle management for Ipsen's commercial portfolio.



### CHRISTOPHE JEAN

Executive Vice President, Strategy and Business Development

Christophe Jean leads the Strategy, Business Development and strategic alliances with the responsibility for ensuring a rich product portfolio through licensing and acquisitions, and for the dynamic management of the Group's key and strategic alliances.



### AYMERIC LE CHATELIER

Executive Vice President, Finance

Aymeric Le Chatelier is in charge of the Finance of the Group, including the financial performance management, the responsibility of the liquidity and financing of the Group, and the supervision of investors relations.



### PHILIPPE ROBERT-GORSSE

Executive Vice President, Specialty Care Franchises

Philippe Robert-Gorsse defines and manages, in close liaison with R&D and Business Development, the Specialty Care portfolio strategy (Oncology, Endocrinology and Neurosciences franchises). He defines and manages, in cooperation with Commercial Operations, brand strategies and new drug launches.




**STÉPHANE BESSETTE**

Executive Vice President,  
Human Resources

Stéphane Bessette supports and accompanies Ipsen's dynamics and strategy, notably its transformation. He is also responsible for individual and team performance, the development and acquisition of new skill sets and support for change management.


**PIERRE BOULUD**

Executive Vice President,  
Specialty Care Commercial  
Operations

Pierre Boulud heads up global Commercial Operations for Specialty Care. He defines and implements commercial policies and strategies for Specialty Care medicines.


**JEAN FABRE**

Executive Vice President,  
Primary Care Business Unit

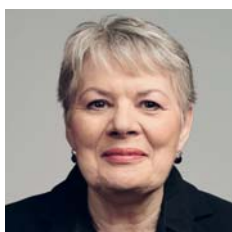
Jean Fabre defines and leads the strategy and business model for the Primary Care Business Unit across the value chain (medical, industrial, marketing, sales operations, strategy and business development).


**FRANÇOIS GARNIER**

Executive Vice President,  
General Counsel

François Garnier is in charge of the Legal Department which provides legal support to the operations, manages Corporate Governance, Litigation, Intellectual Property, Enterprise Risk Management and Insurance.

## ➤ OTHER KEY FUNCTIONS


**DOMINIQUE LAYMAND**

Senior Vice President,  
Chief Ethics and  
Compliance Officer

Dominique Laymand is in charge of leading the strategy, maintenance and monitoring of the Global Compliance & Ethics program, based on an integrated risk mitigation approach and on strong business integrity standards.


**MALIKA MIR**

Chief Digital Officer and  
Senior Vice President IT

Malika Mir leads the strategy to implement a global digital strategy, and to identify the opportunities for differentiating digital capabilities and solutions, including emerging digital business models and technologies. In IT, she leads the information system to constantly modernize it in order to proactively respond to new business challenges.


**DIDIER VÉRON**

Senior Vice President,  
Public Affairs and Corporate  
Communication

Didier Véron defines the global communication strategy to enhance the Group's visibility, image and reputation. He also supports Ipsen's transformation by developing internal communication actions. He is responsible for securing the best possible environment for the Group's operations by managing relationships with public institutions and key external stakeholders.


**HEATHER WHITE**

Vice President, Global  
Internal Audit

Heather White is primarily focused on providing objective, independent risk-based assurance to executive management and Board of Directors that key business risks are being identified and managed appropriately, and that the risk management and internal control frameworks are operating effectively and in strict respect of our values and commitment to transparency.

## AS OUR INDUSTRY UNDERGOES DEEP STRATEGIC CHANGES, WE CONTINUE OUR TRANSFORMATION TO PREPARE THE GROUP FOR TOMORROW'S CHALLENGES.

At Ipsen, we are convinced that our strategic focus will allow us to better serve our patients' needs and to become one of the best-performing companies in our industry.

**Ipsen is consistently improving its efficiency across all company operations with the objective of delivering profitable growth.**

It supports a sharper focus on high-growth specialty care therapeutic areas that offer the best opportunities for development, in addition to the optimization of established products. Ipsen's goal is to become a global leader in targeted indications in specialty care and to focus on gastro-intestinal pathologies with an OTx model in primary care.

### THREE GROWTH PILLARS FOR SPECIALTY CARE

Ipsen has based its specialty care strategy around therapeutic areas where the Group has the potential to become a leader. These areas comprise neuroendocrine tumors, spasticity, and the aesthetic indication of botulinum toxin Dysport® in partnership with Galderma. The reinforcement of the Group's presence in its historical therapeutic areas of oncology and endocrinology remains an important strategic priority for Ipsen, along with the exploration of complementary therapeutic areas that could bring new treatments for gastrointestinal and orphan cancers.

### A STRENGTHENED PRIMARY CARE BUSINESS

Ipsen has refocused its Primary Care business with the aim to bolster Smecta®, the flagship gastrointestinal brand, by strengthening its over-the-counter presence in pharmacies



and drawing on the Group's strong heritage in this field. The expansion of the business will be further supported by the portfolio diversification into complementary gastrointestinal pathologies, which could include new products like probiotics, in addition to a wider geographical footprint in Europe and in emerging countries through acquisitions and partnerships.

### R&D FOCUS ON INNOVATIVE PLATFORMS

In order to bring new specialty care products to the market in the Group's targeted therapeutic areas, Ipsen's R&D operations will continue to focus on two differentiated technological platforms: peptides and toxins. In line with Ipsen's strategy of exploring complementary therapeutic areas, R&D will also deploy resources for the development of molecules that could further boost the portfolio of existing treatments for gastrointestinal and orphan cancers. Partnerships and acquisitions will remain an important option to help complement the internal pipeline.

### A STRONGER OUTLOOK FOR 2020

On March 1, 2016 Ipsen improved its outlook for 2020 sales, which are now expected to be in excess of €2 billion, driven by the contribution of new products and by the addition of new indications for drugs already on the market. The Group also expects to post a core operating margin above 26% in 2020.



## VOICE OF AN EXPERT

INTERVIEW WITH **ROBERT CHU**,  
SENIOR VICE PRESIDENT, TECHNOLOGY  
SOLUTIONS, IMS HEALTH

### **What are the prospects for the global pharmaceutical industry by 2020?**

Industry is expected to grow by 29% to 32% from 2015 to reach a size of \$1.4 trillion by 2020. Innovation and new drug launches will be the key growth drivers with specialty care medicines to increase their share versus overall drugs. In particular, the field of oncology is expected to be valued in a range of \$100-120 billion in 2020. However a slowdown in emerging markets is anticipated with single digit growth compared to double digit growth in the previous years.

### **How can the pharmaceutical industry anticipate these important changes?**

The challenge for patients is to get access to innovative drugs as soon as possible to drive the best health outcomes. For the pharmaceutical industry, the challenge is to have its drugs reimbursed at "acceptable" rates and levels to reward innovation at a time when R&D expenses have dramatically increased.

### **Could the next five to ten years be disruptive in terms of patient access and disease management?**

Wearable devices, which can monitor vital signs such as sugar levels, will change the way the industry can manage patients. We also see the emergence of big data as a predictive and analytical tool. As the issues of affordability and access become more acute in the next five years, the industry will have to be more sophisticated when it comes to proving the clinical and economic value of their products to payers and authorities within real world settings. Moreover, payers will also require stricter treatment pathways and target patient population definitions to avoid unnecessary spending.

### **Should patients be considered as part of the industry ecosystem?**

Patients will increasingly take an active role in disease management and we expect a very active dialog between patients, life sciences companies, payers and healthcare professionals. While the United States is the most advanced country for patient communications, we see progress in Europe where there's interest from regulatory agencies to have pharmaceutical companies proactively monitor social media to advance adverse-event reporting in the interest of public health. We believe this is an important first step and predict, that over time, patients and patient engagement with pharmaceutical companies will play a larger role in advancing public health overall.



#### **BIOGRAPHY**

Robert Chu joined IMS Health in 2007, leading development, product management and commercial oversight of the company's end-user technology solutions.

He has been President, Asia Pacific and China, responsible for IMS Health operations in 17 countries, from July 2013 to April 2015.

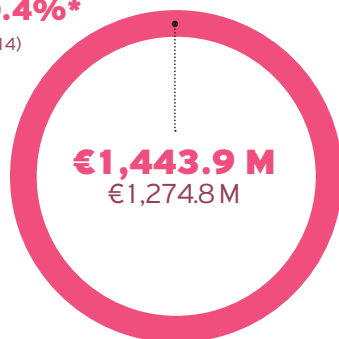
In charge of management positions during a fifteen-year career at IBM Corporation, in Europe and the US.



## 2015 GROUP SALES

▲ **+10.4%\***

(2015 VS 2014)

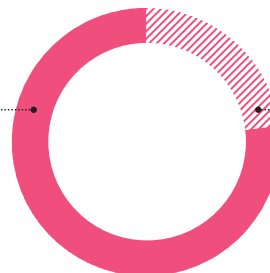


In 2015, Group sales reached €1,443.9 million, up 10.4% year-on-year at constant currency exchange rates.

## SALES BY SEGMENT

SPECIALTY  
CARE  
**€1,114.2 M**  
~77%

PRIMARY  
CARE  
**€329.7 M**  
~23%



The contribution from Specialty Care to total sales continued to increase to reach 77.2% in 2015. Primary care sales totaled €329.7 million, down 1.1%, contributing to 22.8% of Group sales.

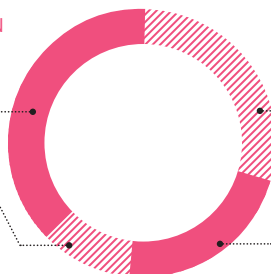
## SALES BY GEOGRAPHIC AREA

**~38%**  
MAJOR WESTERN EUROPEAN  
COUNTRIES  
**€543.8 M**  
+5.3%\*

**~29%**  
REST OF THE WORLD  
**€420.8 M**  
+6.9%\*

**~11%**  
NORTH AMERICA  
**€157.9 M**  
+67.1%\*

**~22%**  
OTHER EUROPEAN  
COUNTRIES  
**€321.4 M**  
+6.0%\*



In 2015, major European countries sales accounted for 37.7% of total sales compared with 39.9% in 2014, while sales in other European countries represented 22.3%, down from 25.4% the previous year. Sales in North America represented 10.9% of consolidated Group sales, up from 6.2% a year before, while the rest of the world contributed 29.1%, up from 28.4% in 2014.

— **2015 figures**  
— 2014 figures

\* At constant exchange rates.

NB: Reporting of Ipsen sales per therapeutic area differs from the breakdown per pathology as presented in the "More results" section of the annual report.



## CONSOLIDATED NET PROFIT

➤ **+23.8%**

(2015 VS 2014)

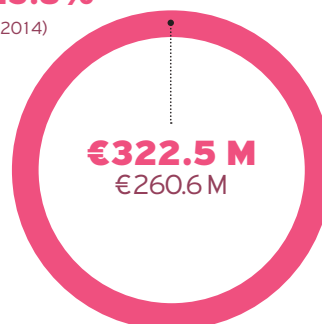


Consolidated net profit increased by 23.8% to €190.7 million (€189.9 million attributable to Ipsen SA shareholders) compared with consolidated net profit of €154.0 million in 2014 (€153.5 million attributable to Ipsen SA shareholders).

## CORE OPERATING INCOME

➤ **+23.8%**

(2015 VS 2014)



Core Operating income totaled €322.5 million in 2015, up 23.8%, representing a core operating margin of 22.3%, up 1.9 point (compared to 2014), mainly driven by the acceleration of the development in the United States, the good performance in Europe, and appropriate cost control.

## DIVIDEND PER SHARE IN 2015



The Board of Directors, which met on February 29, 2016, has decided to propose at Ipsen's annual shareholders' meeting to be held on May 31, 2016 the payment of a dividend of €0.85 per share, stable year-on-year.

## R&D EXPENSES

➤ **13.3%  
OF SALES**



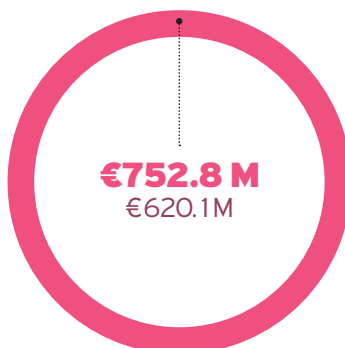
In 2015, research and development expenses totaled €192.6 million, representing 13.3% of sales, compared with €186.9 million, representing 14.7% of sales a year earlier. The decline in research and development costs ratio is notably related to the decision to discontinue the clinical trials of tasquinimod in prostate cancer.



## SALES SPECIALTY CARE

### ONCOLOGY

➤ +17.3%\*



SALES  
BY PRODUCT



### NEUROSCIENCES

➤ +10.0%\*



SALES  
BY PRODUCT

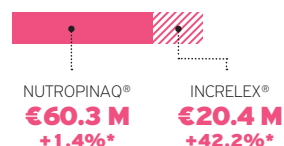


### ENDOCRINOLOGY

➤ +9.6%\*

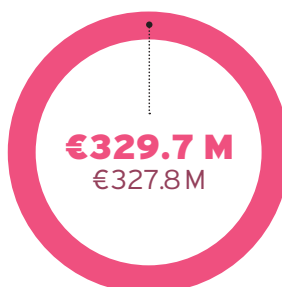


SALES  
BY PRODUCT

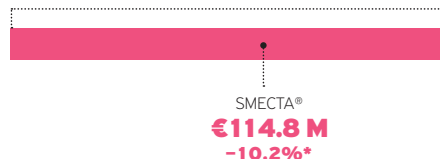


## SALES PRIMARY CARE

➤ -1.1%\*



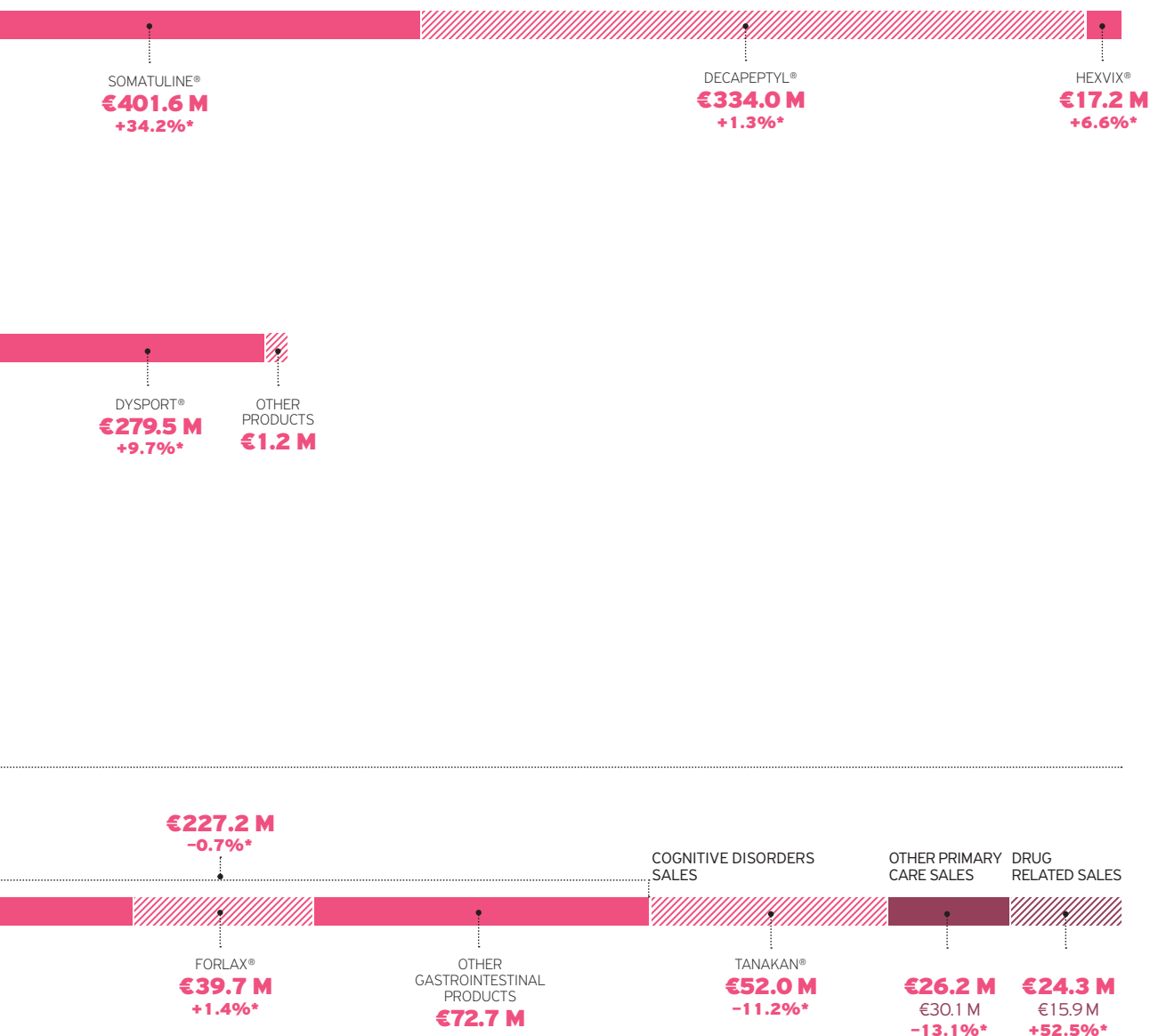
GASTROENTEROLOGY SALES



— 2015 figures  
— 2014 figures

\* At constant exchange rates.

NB: Reporting of Ipsen sales per therapeutic area differs from the breakdown per pathology as presented in the "More results" section of the annual report.



## **MORE RESULTS**

**IPSEN OBJECTIVE IS TO PROVIDE DRUGS  
IN TARGETED THERAPEUTIC AREAS,  
NOTABLY THE TREATMENT OF  
GASTROINTESTINAL AND ORPHAN  
CANCERS. IN PRIMARY CARE, FOCUS  
IS ON GASTROINTESTINAL PATHOLOGIES  
IN THE OTx MODEL.**





## VOICE OF AN EXPERT



INTERVIEW WITH **JEAN-PIERRE BIZZARI, M.D.**, FORMER EVP, CLINICAL RESEARCH ONCOLOGY, CELGENE CORPORATION, AND FORMER VP, CLINICAL DEVELOPMENT ONCOLOGY, SANOFI – SANOFI/AVENTIS

### **How do you define niche indications? How can they better be addressed?**

Niche indications should be seen in the light of biology as tumors are heterogeneous.

There is not only one disease, but specific patients and specific diseases. The next five years will be key because there will be tremendous progress linked to a better understanding of biology and a better analysis of the data we get. The better we understand the biology of cancer, the better we understand how to treat a patient, the best strategy we define to treat a particular patient. Pharmaceutical companies will have to narrow down the diseases they want to treat, to become more and more specialized to be the best in their field.

### **As patients and patient groups are now totally involved in the “health ecosystem”, how can the pharmaceutical industry optimize the relationship with them?**

Advocacy patient groups play a major educational role in the way diseases are perceived. Education is key for patients but also for society. I believe that strong interactions between biologists, researchers, academia, patient advocacy groups and pharmaceutical industry will be critical for the future development of anticancer drugs. Advocacy groups can also play a huge role in convincing people to take part in clinical trials, crucial to follow patients and compare drug results. Selection of patients and enrichment of the patient population will be the main drivers for the clinical benefit in terms of overall survival and in terms of reimbursement.

### **Breakthroughs in niche or orphan indications have led to discoveries for larger populations. Do you think it could be an argument for funding this type of research?**

If you understand the biology of a rare disease you might have applications for a more widespread one. This is why research should focus on the biology of the disease and not only on the disease. In that context, you have multiple niche indications within a broader disease, with a transformation shift from acute to chronic management. Patients should remain at the center of a drugmaker's mission.

### **How can we ensure that breakthroughs will be reimbursed by payers and be accessible to patients?**

In my opinion, sooner or later, there will be a link between the benefit and the effect a drug has and its likelihood of reimbursement. And therefore it seems to me that patient selection and enrichment of target population will be one of the key drivers in future clinical development.

#### **BIOGRAPHY**

Dr. Bizzari has been involved in the development of numerous oncology compounds such as docetaxel, oxaliplatin, lenalidomide, irinotecan or liposomal paclitaxel formulation, as well as anti-angiogenics (VEGF-trap), gene therapy, vaccines and bio-reductive agents. He published more than 70 articles in peer review journals and more than 160 abstracts in scientific congresses. Dr. Bizzari's research interests include the methodology of clinical trials, and pk/pd analysis.

# ONCOLOGY

Ipsen has a strong heritage in oncology. Through our current products, pipeline breakthroughs and partnerships, we remain committed to developing effective and innovative therapeutic solutions to improve treatment outcomes for patients and to support healthcare professionals in their daily practice.

## NEUROENDOCRINE TUMORS

NEUROENDOCRINE TUMORS (NETs) ARE RARE CANCERS, SLOWGROWING TUMORS THAT CAN ARISE ANYWHERE IN THE BODY. NETs ARE OFTEN DIAGNOSED AT A LATE STAGE BECAUSE THE SYMPTOMS, IF ANY, LACK OF SPECIFICITY. GASTROENTEROPANCREATIC NETs (GEP-NETs) REPRESENT 60% OF ALL NETs.

**112,000**

PEOPLE LIVING WITH NETs IN THE US

**178,000**

PEOPLE LIVING WITH NETs IN EUROPE

## BLADDER CANCER

BLADDER CANCER BEGINS MOST OFTEN IN THE CELLS THAT LINE THE INSIDE OF THE BLADDER AND TYPICALLY AFFECTS OLDER ADULTS, ALTHOUGH IT CAN OCCUR AT ANY AGE.

## PROSTATE CANCER

PROSTATE CANCER BEGINS WHEN CELLS IN THE PROSTATE GLAND START TO GROW ABNORMALLY AND MAY SPREAD TO OTHER PARTS OF THE BODY. IT MAY INITIALLY CAUSE NO SYMPTOMS, BUT IN LATER STAGES IT CAN LEAD TO DIFFICULTY URINATING, PAIN OR BLOOD IN THE URINE

## NEUROENDOCRINE TUMORS

**5 TO 7**

YEARS BETWEEN  
THE ONSET  
OF SYMPTOM AND  
THE DIAGNOSIS

**5 PER  
100,000**

PEOPLE  
CURRENT INCIDENCE  
OF NETs

**35  
OVER 100,000**

PEOPLE  
CURRENT  
PREVALENCE  
OF NETs

## BLADDER CANCER

**2<sup>ND</sup>**

MOST FREQUENT  
UROLOGICAL CANCER  
AFTER PROSTATE  
CANCER

**165,000**

DEATHS  
EVERY YEAR  
WORLDWIDE

**1<sup>ST</sup>**

MOST COMMON  
MALIGNANCY  
OF THE URINARY  
TRACT

## PROSTATE CANCER

**5<sup>TH</sup>**

LEADING  
CAUSE OF DEATH  
BY CANCER IN MEN

**307,000**

DEATHS  
EVERY YEAR  
WORLDWIDE

**2<sup>ND</sup>**

MOST COMMON  
TYPE OF CANCER  
IN MEN

**Ipsen's commitment to oncology is highlighted by its growing portfolio of key therapies that improve the care of patients with prostate cancer, bladder cancer, neuroendocrine tumors, or other niche oncology diseases.**

Focusing on these selected oncology diseases, Ipsen aims to provide fully integrated patient care, contribute to improved diagnosis and provide treatment options tailored to patient needs along with targeted support services. In particular, Ipsen aims to become a leader in the treatment of neuroendocrine tumors and to improve patient outcomes at each stage of the disease. A major step toward this goal was the launch of Somatuline® in 2015 as a treatment for gastroenteropancreatic tumors in the United States and in 2016 in Europe. These approvals were based on the landmark CLARINET® study demonstrating the antitumor effect of Somatuline® to reduce the risk of disease progression or death by 53% in patients with gastroenteropancreatic neuroendocrine tumors. In addition to Somatuline®, Ipsen's leadership in NETs

will be further reinforced with the anticipated launches of telotristat etiprate (ex. US) in the next years as a treatment for symptom control in combination with somatostatin analog for patients with carcinoid syndrome, in partnership with Lexicon Pharmaceuticals.

Moreover, in October 2015, Ipsen acquired OctreoPharm Sciences to gain access to new resources to advance diagnosis and treatment of neuroendocrine tumors using radiopharmaceuticals. This new therapeutic expertise has been further reinforced by the licensing agreement from 3B Pharmaceuticals in early 2016 to develop novel radiopharmaceuticals in oncology. This product portfolio will allow the coverage of the full spectrum of neuroendocrine tumor management while providing theranostic solutions to patients.

## BECOMING A LEADER IN THE TREATMENT OF NEUROENDOCRINE TUMORS

In early 2016, Ipsen bolstered its oncology pipeline with a very important oncology deal with the US company Exelixis. Ipsen acquired (ex-North America and Japan) a potential best in class oral drug with solid scientific data. Cabozantinib has the potential to become a key drug in various oncology indications. Its commercial launch is expected in 2017 in Europe for the second line treatment of kidney cancer as the drug is the first therapy to demonstrate in the METEOR® phase III trial, robust and meaningful improvements in all three key efficacy parameters: overall survival, progression-free survival and objective response rate.





### **BUILDING LONG-LASTING PARTNERSHIPS AND RAISE AWARENESS**

Ipsen has built its strength in oncology through strong, long-lasting partnerships with research hubs, such as Harvard University or Curie Institute. This long-standing approach resulted in several new key partnerships, such as with Telesta, 3B Pharmaceuticals, Exelixis or Peptimimesis between May 2015 and March 2016.

Ipsen is a key partner of the most important medical societies, in Europe and the United States in urology (EAU, ESOU), in endocrinology (ENETS, ENDO) and in oncology (ESMO, ASCO). In many countries, the Group cooperates closely with patient groups to raise awareness of its targeted disabling conditions and make progress towards earlier diagnosis. Ipsen also supports initiatives (e.g. Acromegaly Day, World NET Cancer Day) or programs (e.g. IPSEN CARES™ in the United States) to support access of patient to treatment and raise awareness on these diseases. In addition, Ipsen is actively involved in creating networks of experts to promote international dialog between specialists with world experts in the field.

Ipsen supports a personalized approach to patient management and launched the 3i Pathways program (identify, individualize, improve) to facilitate decision-making by healthcare professionals and to improve communication among specialized physicians and with patients. It aims at increasing patients' involvement in the management of their disease.

### **A STRONG PORTFOLIO**

**Ipsen current portfolio** is built around three current commercialized standard of care therapeutic solutions (Decapeptyl®, Somatuline®, Hexvix®).

#### **SOMATULINE®, A KEY STEP FORWARD FOR NEUROENDOCRINE TUMORS**

**Somatuline® is an injectable treatment** that is particularly effective in inhibiting the secretion of growth



hormone as well as certain hormones secreted in the digestive system, which are respectively involved in two rare conditions: acromegaly and neuroendocrine tumors. Somatuline® is the only somatostatin analogue indicated in EU and US for the treatment of pancreatic and gastrointestinal neuroendocrine tumors. The approval in this indication represents a significant step forward in the treatment of this type of tumors, which are rare and difficult to diagnose.

#### **DECAPEPTYL®, A MAJOR PLAYER IN PROSTATE CANCER**

**Decapeptyl® is a synthetic hormone made of triptorelin, decapeptide analog of GnRH** (gonadotrophin releasing hormone), an hormone secreted by the hypothalamus. Decapeptyl® is primarily indicated for the hormonal treatment of locally advanced metastatic prostate cancer and is also approved for the treatment of endometriosis, uterine fibroma, precocious puberty and female infertility. This treatment offers now a subcutaneous route of injection, allowing more patients to benefit from Decapeptyl®.





#### **HEXVIX®, A BREAKTHROUGH TECHNOLOGY AGAINST BLADDER CANCER**

**Hexvix®** is a photosensitizing agent used in the **detection and treatment** of bladder cancer. It produces specific fluorescence in the tumor cells in the bladder during a procedure called "cystoscopy", which involves the examination of the bladder via the urethra. As a result, it improves detection and resection of non-invasive bladder cancer and considerably reduces the risks of incomplete resection of missing a tumor that may not be seen through examination under white light. This technology represents a significant improvement for urologists and their patients.

## **CLINICAL TRIALS**

### **PROSTATE CANCER**

**10 PHASE IV STUDIES** IN PROSTATE CANCER PATIENTS INVOLVING UP TO **4,400 PATIENTS**

**1 PHASE IV STUDY** IN CHINA AND RUSSIA INCLUDING MORE THAN **200 PATIENTS** IN HIGH RISK PROSTATE CANCER

### **NEUROENDOCRINE TUMORS**

IPSEN HAS JUST STARTED **2 LARGE PROSPECTIVE CLINICAL TRIALS** ASSESSING THE ANTIPROLIFERATIVE EFFECTS OF SOMATULINE® IN PATIENTS WITH **LUNG NEUROENDOCRINE TUMORS** (SPINET®) BUT ALSO IN PROGRESSIVE MIDGUT AND PANCREATIC NEUROENDOCRINE TUMORS (CLARINET® FORTE).

### **RENAL CELL CARCINOMA (RCC)**

**9 OUT OF 10** CASES OF KIDNEY CANCERS ARE RCC

**1 IN 63 PEOPLE** WILL DEVELOP KIDNEY CANCER IN HIS OR HER LIFETIME

**20,000 NEW PATIENTS** PER YEAR IN IPSEN'S TERRITORIES

## NEUROSCIENCES

Ipsen has a long-standing commitment to treat mobility impairment in adult and pediatric patients. The Group has made a commitment to support and improve the quality of life of patients who are affected by conditions that restrict mobility. Interdependent treatment approaches must be used to deliver optimal benefits to patients seeking recovery. The Group's preliminary contribution supporting a multi-modal approach in managing patient care was initiated with the introduction of its botulinum neurotoxins, twenty-five years ago.

### DYSPORT® INDICATIONS\*

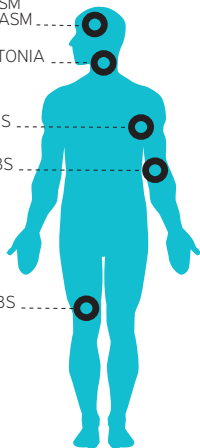
GLABELLAR LINES  
BLEPHAROSPASM  
HEMIFACIAL SPASM

CERVICAL DYSTONIA

HYPERHIDROSIS

SPASTICITY  
OF UPPER LIMBS

SPASTICITY  
OF LOWER LIMBS



\* Indications may vary according to country.

### CLINICAL TRIALS

#### AESTHETIC MEDICINE

##### 3 PHASE III

TRIALS (IN COLLABORATION  
WITH GALDERMA)  
ARE IN PROGRESS

##### 2 TRIALS

WITH DYSPORT®  
SOLUTION (CLINICAL  
CENTERS MAINLY  
IN EUROPE)

##### 1 TRIAL

WITH THE EXISTING  
FORMULATION  
OF DYSPORT®  
IN CHINA

#### THERAPEUTICS

##### 1,000

ADULT AND CHILDREN  
PATIENTS WITH SPASTICITY  
IN PHASE III CLINICAL  
TRIALS PERFORMED IN  
150 CLINICAL CENTERS  
WORLDWIDE

##### 800

PATIENTS TARGETED FOR  
RECRUITMENT  
IN 200 SITES WORLDWIDE  
IN THE NEUROGENIC  
DETRUSOR OVERACTIVITY  
PHASE III  
PROGRAM INITIATED  
IN MARCH 2016

**S**ince 1990 Ipsen has dedicated its focus on pioneering research in neurotoxins and recombinant neurotoxin engineering.

Dysport® is a drug treatment based on the type-A botulinum toxin, which inhibits the transmission of nerve impulses to the muscle. Botulinum toxin injections cause contracted muscles to relax, relieving patients' symptoms and contributing to improvements in the quality of their daily lives.

The recent approval of Dysport® for the treatment of upper limb spasticity in adults in the United States will complement the Groups' focus over the next five years. Clinical trials are underway to generate additional data in support of the therapeutic uses of Dysport®. In areas where national labels are currently in place, the Group will submit evidence in support of improved Dysport® labelling for spasticity in adults and pediatrics. Ipsen aims to further explore and develop additional Dysport® indications in neurology (hypersalivation) and urology (neurogenic detrusor overactivity) conditions often associated with

spasticity patients. Research is also underway on a liquid formulation of Dysport®. The Group has advanced the consolidation of its innovative toxin platform and has actively focused on developing the next generation of neurotoxins.

## OUR ENGAGEMENTS FOR PATIENTS

Ipsen has built a strong, long-term partnership with Dystonia Europe, an organization dedicated to representing dystonia patients across the continent, as well as with the American Dystonia Society. The Group also continues to support initiatives for physicians who seek further research in cervical dystonia, disease awareness campaigns for patients and the creation of patient networks in Europe. Fully committed to improving spasticity management for patients, Ipsen launched I-CAN, an innovative spasticity management program that engages patients in their treatment to improve outcomes. To support this innovative approach, the Group recently launched a digital application called "i-GSC" to assist patients performing guided self-rehabilitation, in complement of their traditional physiotherapy.

## OUR COMMITMENT FOR HEALTH CARE PROFESSIONALS

Ipsen provides ongoing training and medical education at local and regional levels for physicians who want to improve treatment outcomes using Dysport®. For years, Ipsen has delivered an elite-level medical training program, "Ixcelle Network", which supports specialists who wish to expand their





practical expertise and improve outcomes in support of better patient management. In aesthetics, educational masterclasses are critical to elevate clinical and practical expertise and improve outcomes for customers and their clients.

### OUR MILESTONES

- > **February 2015:** Option agreement to acquire Canbex Therapeutics Ltd upon completion of the phase IIa study of Canbex's VSN 16R lead candidate for the treatment of spasticity in patients with multiple sclerosis (MS).
- > **April 2015:** Joint collaboration agreement with Hannover Medical School to test recombinant botulinum neurotoxin proteins to affect intracellular molecular pathways with targeted secretion inhibitors (TSIs).
- > **July 2015:** The US Food and Drug Administration approved Dysport® for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors, wrist flexors and finger flexors. This differentiated label is a testimony to the quality of the clinical research. In most European countries, the Dysport® adult spasticity label was strengthened to incorporate these data.
- > **August 2015:** *The Lancet Neurology*\* published results from the Ipsen-sponsored phase III study demonstrating the efficacy and safety of Dysport® in post-stroke and traumatic brain injury patients with upper limb spasticity.
- > **January 2016:** Scientific journal *Pediatrics*\*\* published detailed results of a phase III study that confirm the efficacy and safety profile of Dysport® in the treatment of lower limb spasticity in children with cerebral palsy and demonstrate improvement in functional benefit after a single injection of Dysport®. Also known as pediatric lower limb spasticity, this debilitating condition is the most common cause of chronic motor disability in childhood.
- > **January 2016:** Ipsen and Galderma expanded the geographical scope of their neurotoxin partnership, whereby Galderma acquired the exclusive rights to develop, promote and distribute Dysport® in the aesthetic indications in some key Asia-Pacific markets, including China, India, South Korea and Indonesia.

### OUR PARTNERSHIP WITH GALDERMA

Ipsen has granted the rights to distribute Dysport® as an aesthetic treatment in several countries to strategic partner Galderma Pharma SA, a specialty pharmaceutical company focused on dermatology. Ipsen markets therapeutic indications for Dysport® while under the terms of the collaboration, Galderma distributes aesthetic treatment under the brand names of Dysport® and Azzalure® depending on the country of registration. Ipsen and Galderma continue to collaborate on the future development and commercialization of new neurotoxin therapies. The partnership with Galderma now covers over 75% of the world's aesthetics market including the United States, Canada, Europe, Brazil and Australia.

### OUR SOLUTIONS

#### DYSPORT®, ONE PRODUCT FOR A RANGE OF INDICATIONS

**Dysport® is a type-A botulinum neurotoxin complex.** It inhibits the transmission of nerve impulses responsible for muscle contraction and allows the muscle to relax temporarily, without affecting normal function. Dysport® was first registered for the treatment of blepharospasm in the United Kingdom in 1990 and has been marketed since 1991. Today, Dysport® is primarily used for patients with spasticity, cervical dystonia, hemifacial spasm, blepharospasm, and hyperhidrosis. In aesthetic medicine, Dysport® is indicated for the reduction of glabellar lines depending on the territory. Dysport® is authorized in more than 80 countries for 7 therapeutic and aesthetic indications.

#### NEXT-GENERATION NEUROTOXINS

**Botulinum toxins** have the potential for very broad applications across multiple therapeutic areas, such as urology, oncology, endocrinology, and regenerative medicine.

\* Online at <http://www.thelancet.com/neurology>

\*\* Online at <http://pediatrics.aappublications.org/content/early/2016/01/24/peds.2015-2830>





Ipsen Bioinnovation is focused on the discovery of new recombinant botulinum toxins, mainly for therapeutic indications, in addition to the promising area of targeted secretion inhibition.

The acquired technology platform has led to opportunities for collaborative research with renowned university research centers. Ipsen is currently in collaboration with Harvard University to identify new ways to deliver further neurotoxin innovations to meet patients' needs.

### **COMMITMENT TO SPASTICITY IN MULTIPLE SCLEROSIS**

#### **The Group and British company GW**

**Pharmaceuticals** have signed an agreement under which Ipsen gained promotion and distribution rights in Latin America for Sativex®, a cannabis extract spray indicated as an add-on treatment for symptom improvement in patients with moderate to severe spasticity due to multiple sclerosis. GW Pharmaceuticals and Ipsen are conducting regulatory filings in selected countries in Latin America for this indication.

## **“I-CAN” PROGRAM**



### **“I-CAN” IS A SPASTICITY MANAGEMENT PROGRAM**

THAT ENGAGES PATIENTS IN THEIR TREATMENT TO INCREASE THEIR MOTIVATION AND IMPROVE TREATMENT OUTCOMES.

IT COMBINES DYSPORT® WITH NEW STANDARDS OF CARE IN SPASTICITY MANAGEMENT:

- THE AGREEMENT ON INDIVIDUALIZED TREATMENT GOALS BASED ON OPTIMAL PATIENT ASSESSMENT;
- THE EFFICIENT USE OF DYSPORT® IN THE RIGHT MUSCLES WITH THE RIGHT DOSE AT A PATIENT-TAILORED FREQUENCY;
- THE PARTNERSHIP BETWEEN THE MULTIDISCIPLINARY TEAM AND THE PATIENTS FOR THEIR GUIDED SELF-REHABILITATION PROGRAM, IN SYNERGY WITH PHYSICAL AND OCCUPATIONAL THERAPY.

THE “I-CAN” PROGRAM IS SUPPORTED BY THE DEVELOPMENT OF A DIGITAL APPLICATION CALLED “I-GSC” WHICH HELPS PATIENTS PERFORM GUIDED SELF-REHABILITATION IN COMPLEMENT OF THE TRADITIONAL PHYSIOTHERAPY. IT WILL BE AVAILABLE IN GERMAN, FRENCH, SPANISH, ENGLISH, RUSSIAN AND PORTUGUESE.

# ENDOCRINOLOGY

Ipsen has helped improve the lives of people affected by rare endocrine disorders and continues to develop high-quality innovative treatments that address the unmet needs of these patients. With a portfolio of therapies to treat endocrine disorders, or other endocrine diseases, our goal is to support patients with products, services and solutions across the entire continuum of care for these disabling conditions, from diagnosis to treatment follow-up.

## ACROMEGALY

ACROMEGALY IS A HORMONAL DISORDER CHARACTERIZED BY DEFORMATIONS AND EXAGGERATED GROWTH IN THE FACE AND EXTREMITIES.

**4-10 YEARS:** AVERAGE TIME BETWEEN THE ONSET OF THE DISEASE AND THE DIAGNOSIS.

## GROWTH DISORDERS

GROWTH DISORDERS ARE PROBLEMS THAT PREVENT CHILDREN AND TEENAGERS FROM ACHIEVING NORMAL HEIGHT AND WEIGHT. THEY ARE CAUSED WHEN THE BODY DOES NOT PRODUCE ENOUGH GROWTH HORMONE OR, IN RARE CASES, INSULIN-LIKE GROWTH FACTOR.

## PRECOCIOUS PUBERTY

CENTRAL PRECOCIOUS PUBERTY (CPP) IS CHARACTERIZED BY THE SAME BIOCHEMICAL AND PHYSICAL FEATURES AS NORMALLY TIMED PUBERTY BUT OCCURS AT AN ABNORMALLY EARLY AGE. UNTREATED, CPP HAS THE POTENTIAL TO RESULT IN EARLY EPIPHYSEAL FUSION AND A SIGNIFICANT COMPROMISE IN ADULT HEIGHT. THUS, THE MAIN GOAL OF THERAPY IS PRESERVATION OF HEIGHT POTENTIAL.

## ACROMEGALY

**69,000**

PATIENTS  
WORLDWIDE

**3-4**

NEW CASES  
PER 1 MILLION PEOPLE  
EVERY YEAR

**40-50**

YEARS OLD:  
AVERAGE AGE  
AT DIAGNOSIS

## GROWTH DISORDERS

**34,500**

CHILDREN WITH  
GROWTH HORMONE  
DEFICIENCY  
IN WESTERN EUROPE

**42,500**

ADULTS WITH  
GROWTH  
HORMONE DEFICIENCY  
IN WESTERN EUROPE

**2-3 YEARS**

AVERAGE TREATMENT  
DURATION FOR ADULT  
WITH GROWTH  
HORMONE DEFICIENCY

## PRECOCIOUS PUBERTY

**1/5,000  
1/10,000**

CHILDREN  
INCIDENCE OF CENTRAL  
PRECOCIOUS PUBERTY

**OVER 50%**

MOST CASES  
OF CPP ARE SEEN  
IN GIRLS

### **Ip**sen is committed to endocrine disorders

with therapies to treat pituitary diseases (acromegaly), growth disorders (growth hormone and IGF-1 deficiencies) or other endocrine diseases (such as precocious puberty). Ipsen's innovative medicines address the unmet medical needs of patients. Our ambition is to become a recognized and unique partner in patient program management and provide innovative resources. Acromegaly is a rare disease caused by excess growth hormone production as a result of a tumor in the pituitary gland. Acromegaly can cause a wide range of symptoms that tend to develop slowly over time, but common signs include a thickening and widening of the hands and feet as well as an alteration of facial features. Patients with acromegaly often experience a long journey of multiple doctors' visits and debilitating symptoms that can last for years before the correct diagnosis is made. Many patients experience substantial pain and discomfort, which affects sleep, family life, and their ability to work, causing

depression and anxiety. Early diagnosis, effective treatment and frequent monitoring are critical for improving clinical symptoms and outcomes of the disease. Ipsen continues to work on solutions that will improve the quality of life of patients living with acromegaly. The Group is currently developing extended-release formulations of Somatuline® that would enable patients to have fewer injections.

Ipsen's long-term commitment to treat adult and pediatric endocrine disorders is supported by its portfolio of growth disorder products. Our therapies for short stature, NutropinAq® and Increlex®, have the potential to treat the continuum of this disabling condition from growth-hormone deficiency to growth-hormone resistance.

### **PARTNERSHIPS FOR PATIENTS**

As part of its mission to be a global advocate for patients affected by rare endocrine disorders, Ipsen is engaged with patient groups, key scientific leaders, medical societies and institutions to develop educational projects and initiatives that help physicians manage the treatment of these conditions worldwide. The Group is also involved in supporting the development of networks of experts to promote international dialog between specialists, including several initiatives with the European Society of Endocrinology.

Ipsen actively supports the development of SAGIT (Signs and symptoms, Associated comorbidities; Growth hormone levels; Insulin-like growth factor-1 levels;



&gt;

and Tumor Size), a tool that has been designed to assist endocrinologists in managing acromegaly in everyday practice. Although still in development, SAGIT is a promising instrument offering the potential to assess the status and evolution of disease in patients with acromegaly and to guide physicians in decision making. In the United States, Ipsen supports IPSEN CARES™ (Coverage, Access, Reimbursement and Education Support), a program that assists patients in overcoming obstacles to start or continue treatment with Somatuline® for gastroenteropancreatic neuroendocrine tumors and acromegaly, Increlex® and Dysport®, including coverage access, distribution and financial concerns. In Europe, the Group has set up INKEP (Ipsen Network of Knowledge Exchange Program), an exchange program for small groups of physicians focusing on pediatric endocrinology which combines scientific presentations, case discussions and interactive sit-in clinic visits. Other initiatives in pediatric endocrinology include APPRI in France, a personalized training program for patients that helps increase their autonomy at home during treatment with the recombinant growth hormone NutropinAq® and the NutropinAq® injection pen, improving compliance with the treatment. Two years after its launch, more than 1 00 prescribers are using this service in France.

## OUR SOLUTIONS

### SOMATULINE®, ONE PRODUCT FOR TWO RARE DISEASES

**Somatuline® injection is used for the long-term treatment of acromegaly** in patients who cannot be treated with surgery or radiation. Somatuline® works by reducing the amount of growth hormone that the body produces. Somatuline® is also used to treat neuroendocrine tumors from the gastrointestinal tract or the pancreas (GEP-NET) that has spread or cannot be removed by surgery. Somatuline® has been proven to deliver sustained control of acromegaly, with more than 80% of patients experiencing more than 50% decline in growth hormone levels from baseline and nearly 60% of patients demonstrating normalized insulin-like growth factor (IGF-1) levels. Somatuline® is a semi-solid



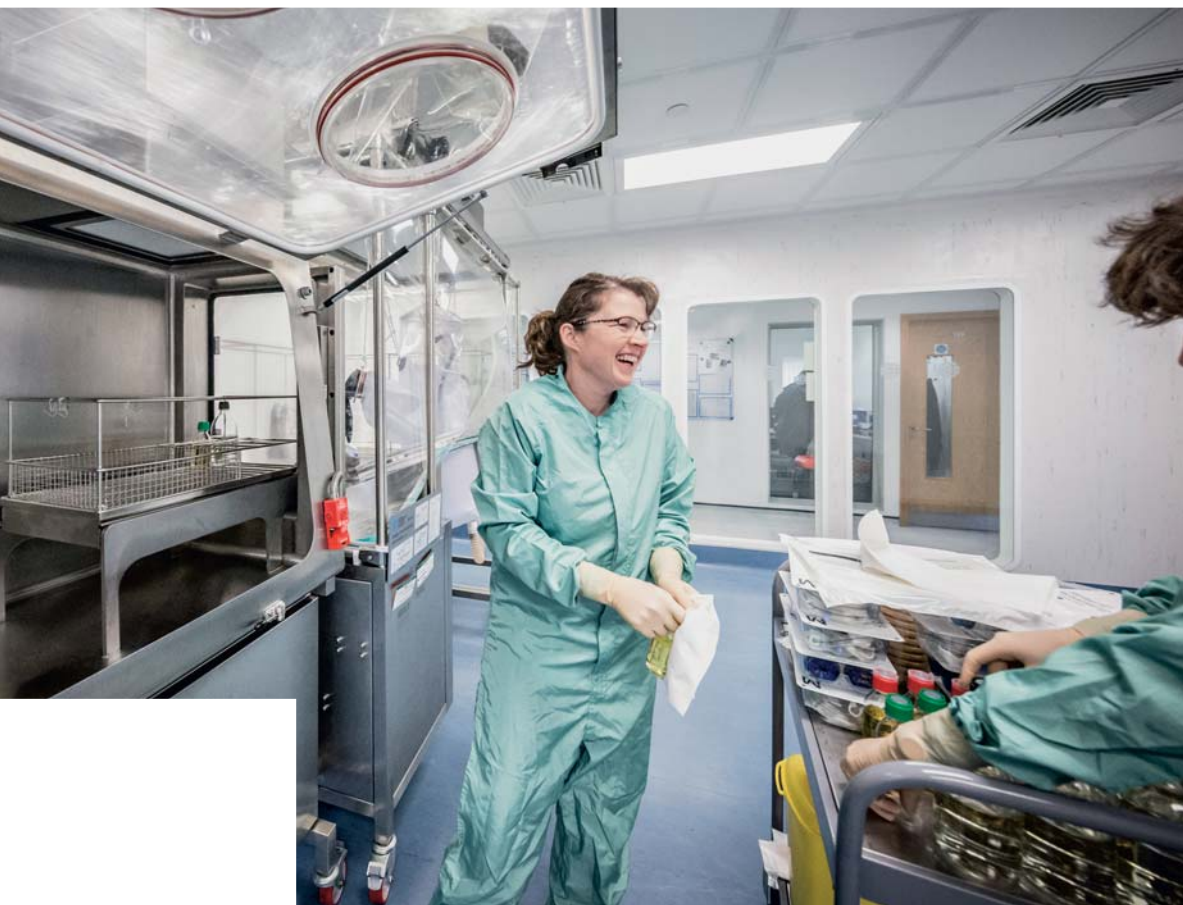
### IPSEN'S INNOVATIVE MEDICINES ADDRESS THE UNMET MEDICAL NEEDS OF PATIENTS.

formulation for injection with the active substance controlling the sustained release of the treatment. The new device with a retractable needle enables the full dose of the medicine to be safely administered. The device allows self-injection for certain indications in many countries. Somatuline® is marketed in over 55 countries, including 27 in Europe, for the treatment of acromegaly and neuroendocrine tumors.

### INCRELEX®, AN ORPHAN DRUG FOR A RARE GROWTH DISORDER

**Increlex® is a recombinant insulin-like growth factor (IGF-1)** of human origin that treats growth delay in children who lack it in their bodies. If IGF-1 is not present in sufficient quantities, the patient will not reach normal stature, despite having normal or high growth-hormone levels. As a result, these children do not respond adequately to growth hormone treatment. Increlex® has obtained orphan drug status based on the low incidence of the disease, which affects fewer than 5 people per 10,000.





### **NUTROPIN AQ®, HELPING PATIENTS WITH GROWTH HORMONE DEFICIENCY**

**Nutropin Aq® is a liquid formulation** of recombinant human growth hormone administered using the Nutropin Aq® Pen. Nutropin Aq® was available in more than 20 countries at the end of 2015, notably in Europe and Australia. It is indicated for the treatment of growth failure from various origins.

### **DECAPEPTYL®, A MULTI-USE THERAPY FOR REPRODUCTIVE SYSTEM CONDITIONS**

**Decapeptyl® is an injectable hormone therapy drug** with several indications. Because it stimulates the release of hormones produced by the pituitary gland, which in turn controls hormonal secretions by the testicles and ovaries, it is marketed in many countries as a treatment for precocious puberty in boys and girls. Additional gynecological indications have also been approved, including uterine fibroids, endometriosis and in-vitro fertilization.

## PRIMARY CARE

Ipsen has a long history in the primary care marketplace, since the origin of the company. With its industrial investment, Ipsen manages the entire value chain, from active principles to finished product to the patient. Its expertise covers gastrointestinal disorders, neurodegenerative pathologies and rheumatology. Today the Group continues to develop new formulations and secure new partnerships to better serve the needs of patients around the world.

### COLON CLEANSING / COLONOSCOPY

#### BOWEL PREPARATION

IS THE PROCESS OF EMPTYING AND CLEANSING THE BOWEL BY REMOVING ALL FECAL MATTER AND LIQUID.

#### THE ULTIMATE GOAL OF BOWEL PREPARATION

IS TO OBTAIN AN EMPTY AND CLEAN BOWEL TO ALLOW PHYSICIANS TO VISUALISE IT ENTIRELY.

#### BESIDE ITS DIAGNOSTIC ROLE, COLONOSCOPY

CAN BE THERAPEUTIC NOTABLY FOR POLYPECTOMIES.

**MORE IMPORTANTLY, COLONOSCOPY** IS ONE OF THE BEST TOOLS AVAILABLE FOR THE DETECTION OF INTESTINAL ABNORMALITIES, BUT PARTICULARLY FOR COLORECTAL CANCER (CRC) OR PRE-CANCEROUS LESIONS.

**AN EFFECTIVE VISUALIZATION** AND REMOVAL OF PRECANCEROUS LESIONS AND POLYPS DURING COLONOSCOPY IS DEPENDENT ON SUCCESSFUL BOWEL PREPARATIONS.

### DIARRHEA

**2,195**

CHILDREN DIE FROM DIARRHEA WORLDWIDE EVERY DAY, MORE THAN AIDS, MALARIA, AND MEASLES COMBINED

**1 IN 9**

CHILD DEATHS WORLDWIDE, MAKING DIARRHEA THE SECOND LEADING CAUSE OF DEATH AMONG CHILDREN UNDER THE AGE OF 5

**ONE**

OF THE MOST COMMON DIAGNOSES IN GENERAL PRACTICE IS ACUTE DIARRHEA IN ADULTS

### CONSTIPATION

**7% TO 27%**

OF THE ADULT POPULATION CAN SUFFER FROM CHRONIC CONSTIPATION

**5%**

OF THE PEDIATRIC POPULATION SUFFER FROM CHRONIC CONSTIPATION

**MOST OF**

THE PATIENTS USE PRESCRIBED OR OVER-THE-COUNTER MEDICATION TO IMPROVE THEIR CONDITION

**I**n 2015, the Primary Care Business Unit has launched a refocused strategy to optimize the gastrointestinal (GI) portfolio, diversify on adjacent GI pathologies and reinforce its geographical coverage. It is supported by an OTx (dual channel approach of prescription and over-the-counter) commercial model to benefit from its strong brand recognition and to maximize its commercial reach. The Group considers equally patients, nurses, physicians and pharmacists. Ipsen has developed the know-how and has designed drugs to address the needs of the millions of patients suffering from gastrointestinal disorders worldwide. They could be patients being treated for cancer who need to address the gastrointestinal side effects of their therapies. They could be the men and women who live with the debilitating symptoms of irritable

bowel syndrome, a condition for which there is no current treatment. Or they could be the thousands of young children that every day are at risk of dying of diarrhea. Patients need to have simple, effective and accessible solutions to treat their symptoms.

## CHOOSING THE RIGHT PARTNERS

The Primary Care Business Unit works with an international network of more than 55 partners for the manufacturing, marketing and distribution of medicines to better serve patients' needs in the countries where Ipsen operates. In July 2015 the Group entered into a manufacturing partnership with Rosta Group, one of the largest medicine distributors in Russia and the owner of one of the country's main pharmacy chains. The first step of the joint project with Rosta involves the manufacturing of Tanakan® with a planned annual output of approximately 120 million tablets. Their common interest is to develop a successful over-the-counter strategy in Russia and its neighboring countries.

## ANTICIPATING PATIENTS' NEEDS

Looking ahead, Ipsen aims to stay at the forefront of medical innovation and develop its primary care business to better address the concerns of its patients. Key achievements in 2015 are exemplified by the launch in France of a new strawberry aroma for Smecta® and a ready-to-use formulation of Smectalia®.





Ipsen will be expanding treatment portfolio into the probiotics field. Probiotics have become a major focus of attention in the world due to recent advances that have helped understanding their functionality and mode of action. There is now sufficient clinical evidence that probiotic treatments could be effective in various types of gastrointestinal conditions and as such would fit in with Ipsen's expertise in this field.

### A SOLID PORTFOLIO

Ipsen's Primary Care treatments extend across several therapeutic areas with a strong focus on gastroenterology, but also through a range of solutions that address cognitive impairment and rheumatology.

#### GASTROENTEROLOGY

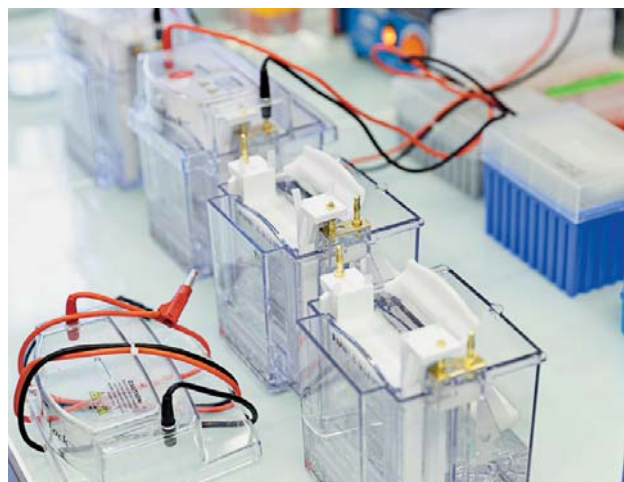
**Smecta® is based on naturally extracted purified clay** and is primarily indicated for the symptomatic treatment of acute diarrhea in children and adults, and for chronic diarrhea and functional bowel pain in adults. Smecta® is one of Ipsen's key products, particularly in China, where the Group has a production facility serving the local market.

**Smectalia® is the OTC formulation** reserved for adult use for the treatment of short term acute diarrhea.

**Forlax® is an osmotic laxative.** Its ingredient is macrogol 4,000, a polymer that causes the intestines to hold more water within and create an osmotic effect that stimulates a bowel movement. It is indicated for the symptomatic treatment of constipation in adults and children.

**Fortrans® is a colon cleansing solution** indicated for patients in preparation for endoscopic and radiological examinations as well as colonic surgery.

**Eziclen®/Izinova® is a second generation of bowel preparations** that increases visualization in all segments of the colon, including the right side, hence



PROBIOTICS HAVE BECOME  
A MAJOR FOCUS OF  
ATTENTION IN THE WORLD  
DUE TO RECENT  
RESEARCH ADVANCES.

enabling better polyps detection and removal during colonoscopy. It is indicated for cleansing prior to endoscopic examinations and treatments or colonic surgery, and may also be used with video capsule techniques. It is a valuable addition to the range in support of Fortrans®, which remains the leading colon cleansing product for Ipsen. Eziclen®/Izinova® considerably reduces the quantity of liquid to be ingested by the patient, while improving the cleansing quality, especially in the right colon, and increasing the efficacy of colonoscopies, notably for the detection of colorectal cancers. It has been launched in 12 countries since 2013, including 5 new countries in 2015 by Ipsen or its partners (France, Italy, Spain, Romania and the UK).

#### NEURODEGENERATIVE DISEASES

**Tanakan® is a standardized and patented ginkgo biloba extract** (EGb 761®) indicated for the symptomatic



treatment of cognitive disorders such as memory deficit and concentration disturbances in the elderly, as well as vertigo and tinnitus.

#### **RHEUMATOLOGY (GOUT)**

**Adenuric® is a therapy in the management of gout**, an inflammatory form of arthritis caused by elevated levels of uric acid in the blood which triggers periodic pain attack, stiffness and swelling in a joint, usually a big toe. It inhibits the metabolism of certain substances (purines) that convert to uric acid in the body.

## **CLINICAL TRIALS**

**850 PATIENTS IN**  
90 CENTERS ACROSS 6 COUNTRIES  
FOR PHASE IV TRIAL OF SMECTA®

**ABOUT 300 PATIENTS IN**  
3 CENTERS IN RUSSIA FOR PHASE III  
TRIAL OF EZICLEN®

**1,200 PATIENTS IN**  
17 CENTERS ACROSS 4 COUNTRIES  
FOR PHASE IV TRIAL OF EZICLEN®

## **KEY PARTNERSHIPS**

**55 ALLIANCES**  
AT GLOBAL LEVEL FOR THE PRODUCTION  
OF ACTIVE PRINCIPLES AND RAW MATERIALS,  
THE MANUFACTURING OF DRUGS FOR THIRD  
PARTIES OR THE IN- OR OUT-LICENSE OF DRUGS  
INCLUDING DISTRIBUTION AND MARKETING  
OF FINISHED PRODUCTS.

**LEADING INDUSTRIAL PARTNERS**  
IN CHINA, FRANCE, GERMANY, RUSSIA.



● LEADING INDUSTRIAL PARTNERS



# **MORE INNOVATION**

**INNOVATION IS THE FOUNDATION  
OF IPSEN. IT DEFINES WHO WE ARE  
AS A COMPANY AND IS THE KEY  
TO HOW WE WILL CONTINUE STRIVING  
TO SATISFY THE UNMET NEEDS  
OF PATIENTS AND HEALTHCARE  
PROFESSIONALS WORLDWIDE.**

## VOICE OF AN EXPERT

INTERVIEW WITH **RON EVANS**, ADJUNCT PROFESSOR, THE SALK INSTITUTE AND INVESTIGATOR, HOWARD HUGHES MEDICAL INSTITUTE PH.D., UNIVERSITY OF CALIFORNIA, LOS ANGELES



### Is there a change in the way academia operates?

Understanding a disease is one thing, curing disease is something else. The power of technology (e.g. DNA sequencing) will be developed in institutions where each advance will be pushed to the very edge of the state of the art. In addition to basic science, in the academic setting, funding of programs from Pharma partners will add a big therapeutic component. Moreover, more personalized medicine will encourage high-level and top labs to begin to incorporate a physiologic and medical perspective in their research and to begin to use clinical models that have predictive outcomes for human health or a disease.

### What are the therapeutic and research fields where you anticipate the most important breakthroughs in the years to come?

Drug combinations based on a patient's DNA sequence are going to bring major advances in cancer treatment, as well as in other therapeutic areas. Epigenetic-based therapies that target genes and reprogram cellular networks will bring new innovation in reversing chronic inflammation and restoring tissue health. The tumor microenvironment is the fuel supply line of a tumor. It is a rich source of discovery that will lead to new drugs that modify the tumor ecosystem and make cancer more vulnerable to standard care. Mitochondria ("the powerhouse of the cell") will be also a key target of research, notably in Parkinson disease, as it generates the energy (the ATP), that is needed to keep cells alive. Drugs targeting mitochondria will have profound effects on tissue regeneration and healthy aging. Finally, it will be important to better understand chronic inflammation, at the origin of many diseases and newer treatments that focus on the cause of disease rather than on the symptoms.

### What is your view on the potential of multidisciplinary approaches to drive changes in medicine?

It's very important to understand how to bring major players, such as patient groups and payers, together. While the pharmaceutical industry and academia understand each other, the academic centers do not understand patient groups and payers very well. One of the challenges of medicine is that it is practiced in silos. Very little of it is multidisciplinary as each symptom is treated individually (e.g. high blood pressure and high lipids are treated by cardiologists, while high sugar levels are managed by diabetologists). However, because cells and organs communicate and send signals from one tissue to another, we have to better understand this "vital circuit". The next generation of scientists needs to be skilled in integrated medicine and physiology to better understand how diseases develop in the body as a whole. Creation of networks of communication will promote closer relationships between researchers (the one who finds) with clinicians (the one who treats) with the aim of building innovative solutions for patients to tackle unmet medical needs.

### BIOGRAPHY

Ron Evans is known for his work on nuclear receptors and the mechanism of hormone signaling. His cloning of the genes encoding the receptors for steroid retinoid and thyroid hormones, revealed the evolutionary conservation of all nuclear hormone receptors.

Ron Evans' initial isolation of steroid receptors led to the surprising discovery of a class of related proteins termed "orphan receptors" whose characterization revealed the existence of previously unknown signaling pathways for cholesterol, bile acids and fatty acids, fundamentally changing our views of both physiology and the treatment of disease.

## AT IPSEN, THE PATIENT IS THE DRIVING FORCE BEHIND OUR RESEARCHERS

Ipsen's R&D is recognized for its unique expertise and leadership in peptide and toxin discovery and development, all guided by the principle of service to patients to deliver therapeutic solutions for unmet medical needs.

Ipsen has decided to concentrate its R&D efforts on selected specialty care therapeutic areas in niche oncology indications and rare diseases where the medical need is greatest to bring new therapies to patients.

### **D**are, share, care drive Ipsen's R&D.

Dare, because our vision is based on scientific curiosity and risk-taking as we continue to innovate and push the frontiers of knowledge. To discover new targets, create innovative therapeutic treatments, and explore emerging fields, Ipsen has teamed up in unique partnerships at the very early stages of research tackling the major scientific challenges of the future. To develop new therapeutic solutions with significant clinical and patient benefits we need to explore new scientific ground and take calculated risks at each step along the way. Share, because creativity feeds on multiple collaborations with both academic research and innovative companies. This tradition of collaborative efforts and partnerships is in Ipsen's R&D DNA. The Group deploys a "win-win" approach with partners and internal teams to respond as quickly as possible to scientific and medical challenges. Care, because the patient always comes first and is central to the company's primary aims to provide patients with therapeutic solutions and define molecules with the

desired efficacy and safety. Translational medicine is integrated into all R&D phases to lead the emergence of therapeutic concepts and guide the clinical research during the drug development process. The aim of precision medicine approach is to accurately identify the patient group most likely to benefit from the proposed treatment and to optimize the use of new molecules.

### **A LONG TRADITION OF SUCCESSFUL PARTNERSHIPS AND ALLIANCES**

Since its inception, Ipsen has consistently implemented an open Research and Development strategy to nurture its own innovation capacities. These networks are built around Ipsen's areas of expertise in endocrinology, neurology and oncology. The goals of these partnerships are to strengthen Ipsen's R&D innovation capacity, notably by giving access to new and promising technologies and support the exploration of new research fields.

### **ACTIVE CLINICAL RESEARCH**

Ipsen pioneered sustained-release formulations and could be the first company in the world to offer a botulinum toxin in a ready-to-use liquid formulation. More than 20 studies were in progress or completed in 2015 and early 2016, from preclinical to phase III clinical phases. Four phase III clinical studies will start recruiting patients in 2016 to evaluate the safety and efficacy of new drugs or existing drugs in new indications. Based on the positive results from some of these trials, the Group has discovered and developed new molecules or for drugs which are already marketed, new formulations, indications, or registrations in new geographical zones.

### **PATIENT-DRIVEN RESEARCH AND DEVELOPMENT**

Ipsen aims to limit the number of patients it recruits in early-stage studies. For each molecule, we design the best possible clinical development plan, thanks to the use of various tools such as modelling and simulation and integrated biological markers.

We want to provide effective and safe therapeutic solutions for our patients who suffer from disabling diseases.



**“YVES CHRISTEN, OF THE FONDATION IPSEN, AND MATHIAS JUCKER, OF THE TÜBINGEN UNIVERSITY, ORGANIZED A MEETING ON A REMARKABLE SET OF BREAKTHROUGHS, WHAT I LIKE TO CALL: THE THIRD JUDGEMENT OF PARIS. THIS CONFERENCE WAS TO PROVE UNIQUE.”**

---

**STANLEY PRUSINER**, LAUREATE FOR THE NOBEL PRIZE IN PHYSIOLOGY AND MEDICINE IN 1997, WROTE IN HIS AUTOBIOGRAPHY





# 50

> MORE INNOVATION

## INNOVATION CAMPUSES

Ipsen has decided to locate its R&D centers at the heart of three internationally renowned science hubs: Paris-Saclay (France), Oxford (United Kingdom) and Cambridge (United States). Each site is strategically located in close proximity to major academic research institutes, leading hospitals and biotechnology companies. They open access for Ipsen to the most innovative new technologies to facilitate and accelerate the discovery of new drug candidates.

### CAMBRIDGE UNITED STATES

Ipsen's peptide platform is located at its US-based R&D center in Cambridge (Massachusetts), a leading biotechnology and life science hub. This advanced technological platform is at the forefront of research in peptides, and the center has a well-established expertise in the discovery, delivery and development of bioactive peptides that is being leveraged to create highly differentiated drugs for targets that are not readily addressed by small molecules or antibodies in the areas of adult endocrinology and oncology.

### PARIS-SACLAY FRANCE

The R&D center at Les Ulis is located in the Paris-Saclay hub, which is home to several thousand life sciences researchers. Ipsen's largest R&D center has a focus on clinical development. Drug discovery in oncology and neurology is also located at Les Ulis, where the pharmacological, pharmacokinetic, pharmacodynamic and safety properties of new molecules are designed and explored. In early 2016, Aepodia, a company specialized in early clinical development up to proof of concept, was the first company to inaugurate the "R&D campus initiative", which is changing the way Ipsen does R&D.

### ABINGDON/OXFORD UNITED KINGDOM

Ipsen, with its leading experts in recombinant toxin engineering, is competitively positioned to accelerate discovery of new therapeutic solutions in neurology. One toxin candidate is expected to enter clinical trials in 2016, with several to follow, a portfolio that firmly places Ipsen at the forefront of innovation in this field.







**“IPSEN REALLY LIVES IPSEN –  
INNOVATION FOR PATIENT CARE.”**

**KATHARINA MELLAR**, CHAIR OF  
NET E.V. PATIENT ASSOCIATION, GERMANY



## THE PARTNER OF CHOICE FOR TOMORROW'S THERAPIES

Successful drug development doesn't happen in a void. That's why Ipsen actively seeks collaborations with experts and stakeholders to stay abreast of scientific breakthroughs that will benefit human health. Thanks to its extensive scientific network and collaborations with renowned research institutions, Ipsen is the partner of choice for successful alliances that will develop the treatments of tomorrow.

### HARVARD UNIVERSITY UNITED STATES

Ipsen and Harvard University announced in April 2015 a multi-year research alliance agreement designed to stimulate new research projects. The alliance enables researchers at Ipsen and Harvard to identify and develop collaborative programs in the areas of Ipsen's expertise, such as neuroendocrine tumors, neuromuscular disorders, and platform technologies related to toxins and peptides. The agreement provides the template for the kind of partnerships Ipsen aims to foster through open innovation to jump-start drug discovery. The new partnership with Harvard builds upon the success of an existing three-year program initiated in July 2013 with the goal of engineering novel recombinant botulinum toxin molecules for the treatment of serious neurological conditions. Ipsen will have exclusive worldwide rights on any candidates stemming from the collaboration and will be responsible for the development and marketing of the new products.

### AEPODIA BELGIUM

Aepodia and Ipsen signed a partnership in early 2016 for early-stage development programs in R&D to maximize Ipsen capacity to develop early clinical phase programs and proof-of-concept (POC) studies while expanding its R&D portfolio. Aepodia is the first company to have integrated into Ipsen's R&D campus in Paris-Saclay biotechnology hub. This "campus initiative" will lead and catalyze early stage research and clinical studies programs. This partnership paves the way to build new relationships and agreements with other leading innovators in the life sciences and leverage the cutting edge competencies of both companies in the effective development of innovative new therapies.

### PEPTIMIMESIS FRANCE

Ipsen and Peptimimesis announced in early 2016 a research partnership for novel therapeutic peptides targeting a transmembrane receptor overexpressed in a large number of cancers and implicated in their development (including angiogenesis, immune tolerance and proliferation) in oncology. Ipsen was granted the option to acquire the exclusive rights to develop and market the novel drug candidates. This project extends Ipsen's expertise in peptides.





## 4 PILLARS TO ACHIEVE 2020 AMBITION:

- 1 **DATA-DRIVEN DECISION MAKING**
- 2 NEW R&D MODEL BASED ON **OPEN INNOVATION**
- 3 EXTERNAL FLEXIBILITY AND INTERNAL FOCUS ON **DIFFERENTIATION**
- 4 FOCUS ON DELIVERING **PROOF OF CONCEPT**



## TWO TECHNOLOGICAL PLATFORMS WITH LEADING EXPERTISE

Research at Ipsen is focused on toxins and peptides, the areas in which the Group has the most expertise, know-how, recognition and potential for the development of highly differentiated and competitive products. For each platform, the focus is on sharing and lessons learned across the projects.

**C**linical proof of concept is the cornerstone of the drug discovery process, the principle used by all involved that determines the entire life cycle of the molecule in R&D as early as possible. This mindset means that key questions are being asked in order to rapidly determine the unique properties of the molecule and its potential clinical differentiation and benefit to patients at each stage of the process.

### PEPTIDES: LONG-STANDING EXPERTISE

The Group has considerable expertise in projects relating to natural peptide analogs. The peptide platform at Ipsen Bioscience builds on this knowledge in innovative ways, with a view to the high proportion of molecular targets which are difficult to exploit by classical drug therapy, such as small molecules and antibodies. The acquisition of Octreopharm in 2015 has added another innovative technology, peptide receptor radionuclide therapy (PRRT), to the Ipsen peptide platform.

### PRECLINICAL

**IN PROGRESS  
IN 2015  
G PROTEIN-  
COUPLED  
RECEPTORS**

**IN PROGRESS  
IN 2015  
CABOZANTINIB  
(PARTNERSHIP  
WITH EXELIXIS)  
RENAL CELL CARCINOMA  
(FIRST LINE)**

**IN PROGRESS  
IN 2015  
VSN 16R (STUDY  
PERFORMED BY  
CANBEX UNDER AN  
OPTION TO ACQUIRE)  
SPASTICITY IN MULTIPLE  
SCLEROSIS**

**IN PROGRESS  
IN 2015  
BN82451B  
HUNTINGTON  
DISEASE**

**IN PROGRESS  
IN 2015  
SOMATULINE®  
PROLONGED RELEASE  
FORMULATION  
ACROMEGALY**

**COMPLETED IN  
2015/EARLY 2016  
486A-OPS202  
DIAGNOSTIC  
AGENT FOR NET**

### PHASE 3

**IN PROGRESS  
IN 2015  
DYSPORT®  
ADULT LOWER  
LIMB SPASTICITY**

**IN PROGRESS  
IN 2015  
DYSPORT®  
PEDIATRIC UPPER  
LIMB SPASTICITY**

PRRT uses the ability of peptides to target specific receptors to deliver a radionuclide directly to a tumor. This targeted approach provides an exciting “theranostic” opportunity that offers the promise of use for both detection and treatment of the disease. This research field is also at the heart of the partnership signed in early 2016 with the German company 3B Pharmaceuticals. Novel peptide radiotherapy programs for neuroendocrine and other tumor types are also being designed at Ipsen. To achieve its goal of developing highly differentiated peptide drugs for unmet medical needs in endocrinology and oncology, the peptide platform works in close collaboration with other Ipsen R&D centers of excellence, including Ipsen Bioinnovation in Oxford, Ipsen Innovation in Paris-Saclay, and our manufacturing facility in Dreux (France).

## TOXINS: FOCUS ON BOTULINUM TOXIN

The toxins platform, located at Ipsen Bioinnovation, is leading engineering activities for recombinant toxins, that

are developed by modifying the sequence of a toxin to introduce new properties “on demand” and to produce the resulting toxin in a well-characterized bacterial strain. This R&D center has complementary expertise and technologies which will allow us to consolidate the toxins platform and ensure we stay a step ahead of the competition, in particular by combining peptides and toxins to obtain targeted secretion inhibitors (TSIs). TSIs enable the toxin to be directed towards different types of cells depending on the peptides used. This technology has notably been the object of the partnership concluded in April 2015 with Hannover Medical School. Ipsen is one of very few entities to master the manufacture and development of TSIs, together with the technologies required to explore new applications and to develop new toxin-based products.

### As of 03/31/2016

- ONCOLOGY
- ENDOCRINOLOGY
- NEUROSCIENCES

IN PROGRESS  
IN 2015  
NOVEL  
BOTULINUM  
TOXIN

IN PROGRESS  
IN 2015  
LRRK2  
(PARTNERSHIP  
WITH ONCODESIGN)

IN PROGRESS  
IN 2015  
INTRACELLULAR  
ONCOLOGY TARGET

IN PROGRESS  
IN 2015  
TRANSMEMBRANE  
ONCOLOGY TARGET

IN PROGRESS  
IN 2015  
PEPTIDE RECEPTOR  
RADIONUCLIDE  
THERAPY  
<sup>177</sup>LU-OPS201

IN PROGRESS  
IN 2015  
NOVEL  
RADIOPHARMA-  
CEUTICALS  
(LICENSED FROM  
3B PHARMA)

## PHASE 2

COMPLETED IN  
2015/EARLY 2016  
BIM238065  
CUSHING DISEASE

## PHASE 1

IN PROGRESS  
IN 2015  
DYSPORT® NEXT  
GENERATION  
GLABELLAR LINES

IN PROGRESS  
IN 2015  
DYSPORT®  
GLABELLAR LINES

COMPLETED IN  
2015/EARLY 2016  
TELOTTRISTAT  
ETIPRATE  
(PARTNERSHIP  
WITH LEXICON)  
CARCINOID SYNDROME

COMPLETED IN  
2015/EARLY 2016  
CABOZANTINIB  
(PARTNERSHIP  
WITH EXELIXIS)  
RENAL CELL CARCINOMA  
(SECOND LINE)

IN PROGRESS  
IN 2015  
CABOZANTINIB  
(PARTNERSHIP  
WITH EXELIXIS)  
HEPATOCELLULAR  
CARCINOMA  
(SECOND LINE)

COMPLETED IN  
2015/EARLY 2016  
DYSPORT®  
PEDIATRIC LOWER  
LIMB SPASTICITY



## THE FONDATION IPSEN: A UNIQUE CATALYST OF KNOWLEDGE

Created in 1983 under the aegis of the Fondation de France, the Fondation Ipsen is a unique, independent organization that aims to identify emerging scientific thinking, foster interaction among top researchers and kick-start ideas for research fields and new treatment options for patients.

**T**he ambition of the Fondation Ipsen is to identify emerging knowledge and paradigm and to foster interconnections between different scientific domains. By paying attention to the cross-roads of knowledge, the Fondation Ipsen seeks to facilitate the process of interdisciplinary fertilization and draw out its meaning. About the last three decades, Fondation Ipsen has organized over 250 top-level international meetings and produced several hundreds publications. About 250 scientists have been awarded prizes for their pioneering work in an emerging research field. Every meeting brings together renowned international specialists and researchers from various fields. Its meetings have been recognized at worldwide level, with speakers including top scientists who have made or are making milestone achievements in the field of Alzheimer's disease, longevity, neurosciences, endocrinology, the vascular system and cancer sciences.

In 2015 the Fondation Ipsen organized 7 meetings that gathered almost 1,000 international participants focused on cutting-edge subjects such as stem cells in neuroendocrinology, heterogeneity and microenvironment in cancer, neurotechnology, neurodegeneration and brain dynamics. The annual meeting in the cancer series is a major event for the research in cancer. Fondation Ipsen's reputation has been closely linked to the development of new insights into Alzheimer's disease. Fondation Ipsen's meetings and newsletter *Alzheimer Actualités* have since become a major reference point for the medical and scientific communities.

When the Fondation Ipsen organized its first Alzheimer's meeting, in September 1987, this condition was little known to the medical community and was often considered as the normal process of cognitive aging. Almost three decades on, none of these statements remains valid thanks to the advances driven by the activities of the Fondation Ipsen.

In many fields of biology and medicine, the Fondation Ipsen organized the very first meeting on topics which became of major importance: gene therapy and stem cells in the nervous system, retrotransposition in the brain, neurophilosophy, neurobiology of human values, protective genes, hormonal control of cell cycle or tumor metabolism.

The Fondation Ipsen has also established long-lasting partnerships with major international institutions and organizations. Joint meetings with the most renowned scientific journals – *Science*, *Nature* and *Cell* – are organized. With the Salk Institute, focus is made on biological complexity and with the Karolinska Institute it is molecular medicine. Other leading partnerships were also established with the World Health Organization, The Fondation Nationale de Gérontologie, Harvard University, or the Massachusetts General Hospital.

Primarily focused on basic science, all of these meetings put together scientists and clinicians in a translational research approach, keeping in mind the unmet needs of the patient.



Photo 1

11<sup>th</sup> annual Colloque  
Médecine et Recherche en  
Cancer Science : "Tumor  
heterogeneity and  
microenvironment"  
(Mysore, India, February 28  
– March 4, 2015).



## **"THE FONDATION IPSEN HAS BUILT UNIQUE EVENTS WHICH PROVIDE YOU TIME AND OPPORTUNITY TO NETWORK WITH THE MOST PROMINENT INTERNATIONAL SCIENTISTS."**

**HUGUES DE THÉ**, MEMBER OF THE ACADEMIE DES  
SCIENCES, PROFESSOR AT THE COLLÈGE DE FRANCE

**7 MEETINGS** ORGANIZED IN 2015

**927 PARTICIPANTS** AT THESE MEETINGS

**31 YEARS** OF ACTIVITY

**FIRST ALZHEIMER'S** DISEASE MEETING IN 1987

ABOUT **250 MEETINGS** ORGANIZED SINCE 1983

MORE THAN **100 BOOKS** PUBLISHED

**35 NOBEL LAUREATES** INVOLVED IN THE  
ACTIVITIES OF THE FONDATION IPSEN

ABOUT **250 PRIZES** AND GRANTS AWARDED



Photo 2

2<sup>nd</sup> meeting in the Bridging  
Biomedical Worlds series  
"From neural circuitry to  
neurotechnology" (Tokyo,  
Japan, May 11–12, 2015);  
Yves Christen (President of the  
Fondation Ipsen), Thierry Dana  
(Ambassador of France in  
Japan) and Susumu Tonegawa  
(Nobel Prize for Physiology or  
Medicine).

Photo 3

Award lecture of the  
Endocrine Regulations Prize  
(May 9, 2015); Philippe  
Bouchard (President of  
the European Society of  
Endocrinology), Yves Christen  
(President of the Fondation  
Ipsen), C. Ronald Kahn  
(laureate of the 2015  
Fondation Ipsen Endocrine  
regulations Prize, Harvard  
University, Boston, USA) and  
Iain Robinson (President of the  
jury of the Fondation Ipsen  
Endocrine Regulations Prize).

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## **MORE PROXIMITY**

**OUR GEOGRAPHICAL FOOTPRINT  
DEPENDS NOT ONLY ON OUR  
RESOURCES OR THE MARKET:  
IT IS DEFINED BY THE NEEDS  
OF PATIENTS.**





## VOICE OF AN EXPERT

INTERVIEW WITH **GÉRARD DE POUVOURVILLE**,  
PROFESSOR, ECONOMICS DEPARTMENT,  
HEALTH ECONOMICS CHAIR, ESSEC  
BUSINESS SCHOOL

### **What are the trends for rewarding innovation? What is the impact on drug prices?**

We need to differentiate pharma in emerging markets and developed countries. In emerging countries there is no reward for innovation because governments are trying to build universal coverage and prioritize drugs for main conditions with the lowest possible impact on budget. On the other hand, there are developed countries, with universal coverage but also budget pressures, where innovation is recognized. Payers appreciate the value of new drugs because these products address unmet needs, but they have to be cautious about how much they pay for them. In the next three to four years there will be strong pressure on prices in developed countries.

### **Will health economics be mandatory to deliver innovative drugs to patients everywhere?**

Budget impact is mandatory everywhere, while cost-effectiveness analysis is mandatory only in some countries in Europe, and the way it's used is specific to each country. Other countries look at cost effectiveness and benchmark cost-effectiveness ratios in comparable disease areas and will negotiate the price. Finally, some countries will not pay if the price is higher than that of another country. The US is a very atypical market compared with Europe, because each insurance company makes its own decisions with the patient's "willingness to pay" component.

### **How to determine a price that takes into account the added value of innovative medicines for patients and the potential savings they bring to healthcare systems?**

Actually setting a price is a power balance. A "fair" price is the result of a negotiation: companies make tradeoffs between long price negotiations and rapid access to market, payers balance the budget impact with the potential loss of chance to patients if access is delayed. With the public and politicians becoming more and more sensitive to prices, and with price pressure, pharmaceutical companies need to develop a clever pricing strategy, where there is no loss of opportunity for the patient to get rapidly access to innovative therapies and where payers will not only set a price, but will negotiate a "full package deal", including prescription restrictions, target populations and coverage with real life evidence.

#### **BIOGRAPHY**

Gérard de Pouvourville, PhD, is presently chair professor for health economics at ESSEC business school. Formerly, he has led a career as a researcher in the field of health care economics and management, at École polytechnique, at the French national school of public health and at the INSERM. His main contributions have dealt with hospital funding and management, physician payment scheme, health technology assessment and pharmaco-economics, and health policy.



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&gt; MORE PROXIMITY

## IPSEN WORLDWIDE, OUR MAIN SITES

The Ipsen group 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.

- |                    |                     |
|--------------------|---------------------|
| 1 — ALGERIA        | 23 — ROMANIA        |
| 2 — AUSTRALIA      | 24 — RUSSIA         |
| 3 — BELGIUM        | 25 — SINGAPOUR      |
| 4 — BRAZIL         | 26 — SOUTH KOREA    |
| 5 — CANADA         | 27 — SPAIN          |
| 6 — CHINA          | 28 — SWEDEN         |
| 7 — CZECH REPUBLIC | 29 — TAIWAN         |
| 8 — GERMANY        | 30 — TUNISIA        |
| 9 — FRANCE         | 31 — UNITED STATES  |
| 10 — GREECE        | 32 — UNITED KINGDOM |
| 11 — HONG KONG     | 33 — UKRAINE        |
| 12 — HUNGARY       | 34 — VIETNAM        |
| 13 — IRELAND       |                     |
| 14 — ITALY         |                     |
| 15 — KAZAKHSTAN    |                     |
| 16 — LATVIA        |                     |
| 17 — LEBANON       |                     |
| 18 — LITHUANIA     |                     |
| 19 — MEXICO        |                     |
| 20 — NETHERLANDS   |                     |
| 21 — POLAND        |                     |
| 22 — PORTUGAL      |                     |



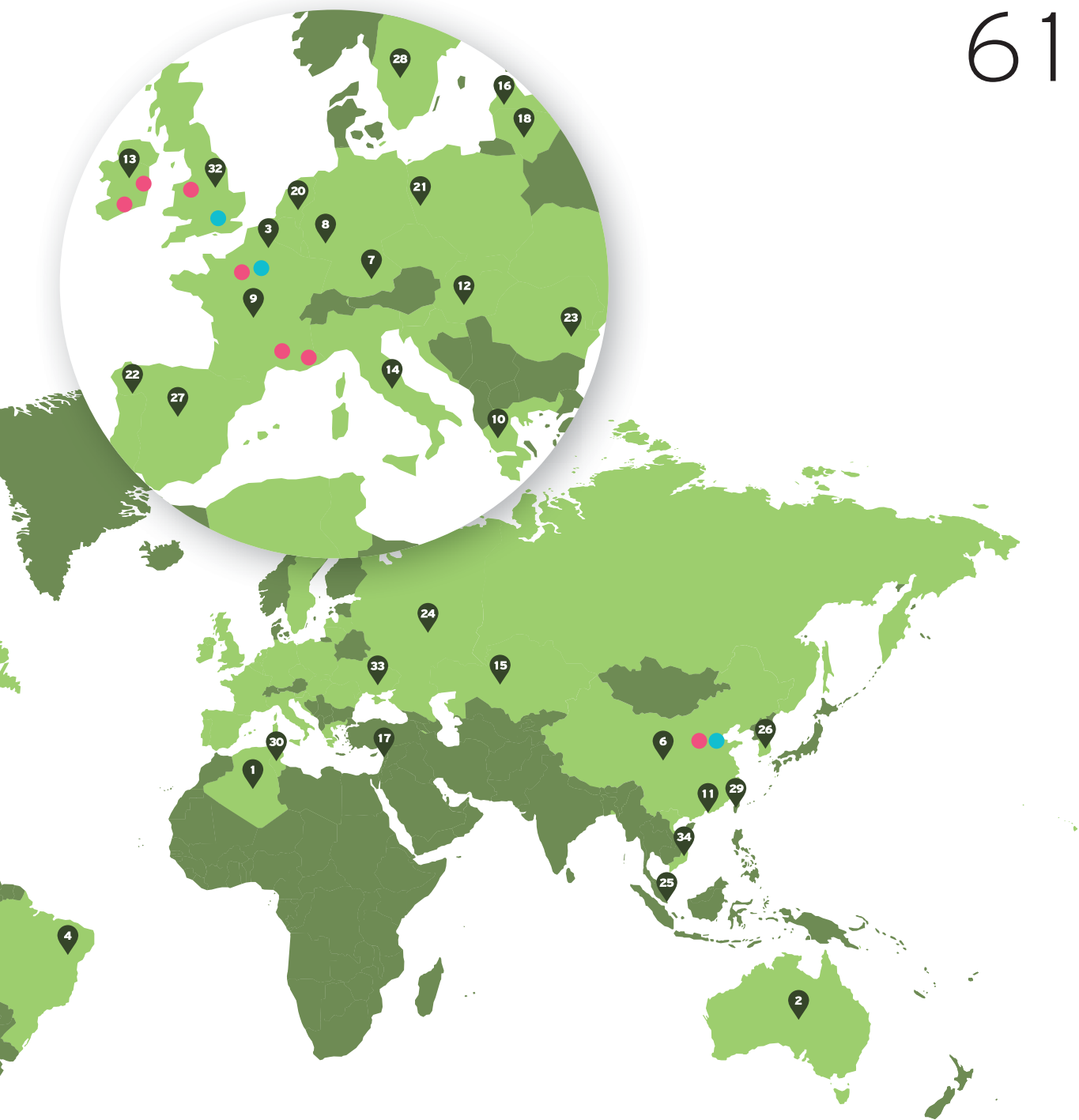
**115**  
COUNTRIES

**7**  
INDUSTRIAL  
SITES

**3**  
MAJOR R&D  
CENTERS

- DIRECT PRESENCE
- MANUFACTURING
- RESEARCH & DEVELOPMENT





# IPSEN WORLDWIDE, OUR MANUFACTURING AND R&D SITES

Our extensive and diverse geographical footprint is organized into 10 major sites.

## IRELAND

### DUBLIN DEVELOPMENT AND MANUFACTURING

The Dublin site, opened in 1989, is the Group's center for the production and development of peptide active pharmaceutical ingredients (APIs). The site currently produces the APIs for both Somatuline® and Decapeptyl®. As well as peptide API production and development, Ipsen in Dublin also has responsibility for the development of small molecule APIs and analytical development.

### CORK MANUFACTURING

The industrial site in Cork is the result of a joint venture with Schwabe dating back to 1969. The extract of ginkgo biloba – EGb 761® – produced there is used for Tanakan® and Ginkor® drugs. In 2015, 90 tons of EGb 761® were produced from 3,000 tons of ginkgo biloba leaves.

## UNITED KINGDOM

### WREXHAM BIOLOGICAL DEVELOPMENT AND MANUFACTURING

Ipsen Biopharm Ltd is the Group's sole biological manufacturing and development facility. The site is a fully integrated neurotoxin manufacturing and development center of expertise including active ingredients, drug manufacturing and distribution capability. The site also has development teams involved in lifecycle management projects and new recombinant toxin projects.

## SLOUGH/ OXFORD R&D

In Slough, the site has a concentration of important R&D activities (project management, regulatory affairs, pharmacovigilance, publications, clinical trial registries and scientific affairs). Ipsen's site in Abingdon, close to Oxford, hosts the Group's toxins engineering platform, whose goal is to discover and develop new therapies in neurosciences.

## FRANCE

### DREUX DEVELOPMENT AND MANUFACTURING

This center of expertise is specialized in both pharmaceutical development and industrial manufacturing. Pharmaceutical development is focused on both small chemical entities and peptides, including formulations, delivery systems and devices, analytical and manufacturing control methods, as well as manufacturing processes. This facility also hosts the clinical supply chain activities for all Ipsen clinical studies around the world, i.e. 31 clinical studies in 27 countries in 2015. The manufacturing site, created in 1961, is specialized in the production of oral formulation (sachets, tablets, capsules, liquid forms). The site also handles global distribution of Ipsen products. In 2015, the site manufactured almost 1.1 billion sachets, 370 million tablets, 200 million capsules and 3.7 million bottles. The CMC Development activity for both Specialty Care and Primary Care products is also hosted at this site.

## L'ISLE-SUR- LA-SORGUE MANUFACTURING

L'Isle-sur-la-Sorgue has been Ipsen's only site for processing clays since 1963. It is dedicated to the production of clays used in Smecta®, Bedelix®, Actapulgit® and Gelox®. In 2015, the facility produced 3,522 tons of finished products. Approximately two-thirds of the production is for Europe and China.

### SIGNES MANUFACTURING

The Signes facility was created in 1990 for the manufacturing and packaging of products intended for export. It specializes in the manufacturing and packaging of injectable formulations, particularly sustained-release formulations of peptides (Decapeptyl®/Pamorelin®, Somatuline® and NutropinAq®). The site manufactures almost 50% of the Group's drug sales (approximately 3 million boxes per year) and exports to over 70 countries worldwide.

## LES ULIS R&D

The R&D center was created in 1969. One of the site's missions is to advance knowledge of the molecular, pharmacological, pharmacodynamics, and pharmacokinetic and safety properties of new chemical or biological entities as candidates for development in the fields of oncology and neurology. The center also houses significant clinical development activity and scientific affairs.

## CHINA

### TIANJIN MANUFACTURING

Ipsen opened its first office in China in 1992 and subsequently, in 2000, created a local production facility in Tianjin for Smecta®, a product manufactured with the clay supplied by L'Isle-sur-la-Sorgue. The maximum production capacity in 2015 is 25.3 million boxes. The site packages this product for the Chinese market and is also the distribution platform for Ipsen portfolio and other medical products in China.

### BEIJING DEVELOPMENT

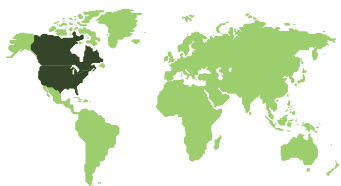
Ipsen opened its first clinical and scientific affairs development center dedicated to Asia in Beijing in 2012.

## UNITED STATES

### CAMBRIDGE R&D

In 2014, Ipsen opened its R&D center in Cambridge (Massachusetts) in the USA, and inaugurated it on April 1, 2015, at the heart of a global hub for research and innovation in the fields of life sciences and biotechnologies. The site supports an active policy of developing partnerships with the scientific affairs team. This center is specialized in the synthesis of complex peptides designed to address innovative targets for oncological and endocrinological indications.

## NORTH AMERICA



## IPSEN TOOK SEVERAL MAJOR STEPS FORWARD IN NORTH AMERICA DURING 2015

The Group launched Somatuline® Depot for neuroendocrine tumors in Canada and the United States as well as Dysport® in adult upper limb spasticity. These milestones allowed Ipsen Biopharmaceuticals to achieve profitability eighteen months ahead of plan.

2015 also marked the inauguration of the new Ipsen Bioscience R&D facility in Cambridge, Massachusetts, a top biopharma hub where Ipsen researchers work on the discovery and development of highly differentiated therapeutic peptides that address unmet medical needs in endocrinology and oncology. Clinical candidate BIM23B065, discovered by the Cambridge R&D team, successfully completed phase I clinical tests in 2015.

## 6,355

**NUMBER OF PATIENTS ENROLLED IN 7 IPSEN-SPONSORED CLINICAL TRIALS ACROSS OVER 110 CENTERS.**

### ABOUT US

Ipsen's presence in North America dates back to 1976, when the company opened a research and development center in Milford, MA.

The Group now employs more than 300 people in the United States and Canada.

Ipsen is engaged in strategic partnerships with leading research institutions including the Salk Institute and Harvard University. Ipsen works closely with key medical associations such as the North American NeuroEndocrine Tumor Society (NANETS) and supports patients through several initiatives such as the IpsenCares™ access program and the KnowYourNets.com website.

**Sales in 2015 reached almost €158 million, representing a year-on-year growth of more than 65%.**

### KEY DATES

#### JANUARY 2015

The United States become the first country to launch Somatuline® Depot in gastroenteropancreatic neuroendocrine tumors

#### APRIL 2015

Grand opening of the Ipsen Bioscience R&D center in Cambridge, Massachusetts

#### APRIL 2015

Partnership with Harvard University

#### JULY 2015

Approval of Dysport® in adult upper limb spasticity

#### OCTOBER 2015

Grand opening of Canada affiliate. Approval of Somatuline® Depot in neuroendocrine tumors in Canada

### PRODUCTS

#### NEUROSCIENCES:

Dysport® (adult upper limb spasticity, cervical dystonia) – US only

#### ONCOLOGY:

Somatuline® Depot (gastroenteropancreatic neuroendocrine tumors)

#### ENDOCRINOLOGY:

Somatuline® Depot (acromegaly)

Increlex® (recombinant insulin-like growth factor)

**FIND OUT MORE:** [www.ipsenus.com](http://www.ipsenus.com)  
[www.ipsen.ca](http://www.ipsen.ca)  
[www.knowyournets.com](http://www.knowyournets.com)

## SPAIN



## IPSEN PHARMA HAS ESTABLISHED AN EXCELLENT REPUTATION AND HIGH-VALUE RELATIONSHIPS

Despite a challenging environment, Ipsen posted double-digit sales growth in Spain thanks to Somatuline®, which became a market leader in 2015, and a stronger market share for Decapeptyl®, driven by a robust promotional effort by the sales team. In January 2015, Ipsen Pharma set up the “Iberia cluster” formed of Spain and Portugal to maximize synergies, efficiency and team collaboration. Since its creation in 1988, Ipsen Pharma has established an excellent reputation and high-value relationships in Spain during the last years based on a combination of patient focus, best-in class products and strong scientific approach.

## +9.5% GROWTH

### €66.5 MILLION OF SALES IN 2015.

#### ABOUT US

Ipsen Pharma started its activities in Spain in 1988 with the acquisition of Laboratorios Lasa. Since then, the company expanded its commercial operations and in 2015, Spain accounted for 4.5% of total Group sales with a team of almost 90 people. Ipsen staff are recognized volunteers to support patient initiatives. Ipsen's goal is to become the leading reference for neuroendocrine tumors and one of the top five reference companies in oncology in the region, as well as the leader of the analogs market for prostate cancer. As part of its strategy, Ipsen Pharma has a very high involvement in R&D with almost 900 patients participating in clinical studies. Ipsen Pharma is very active in collaboration agreements with educational institutions like the International University of Catalonia, ISE in Madrid and in Barcelona to offer high level training to healthcare professionals and developing studies to address patient needs with neuroendocrine tumors and other debilitating diseases.

Within the Social Responsibility program, the Spanish Ipsen Foundation has developed a series of activities focused on patients, some of them with a long and sustainable history like the “Urology Brigades”, where more than 1,000 patients from Central America have benefited from urology surgeries within the program “Health with love” and the fifth edition of the race for Cerebral Paralysis involving 5,000 participants, and raising more than €150,000 donations.

#### KEY DATES

##### JANUARY 2015

Ipsen Pharma set up the “Iberia cluster” formed of Spain and Portugal to maximize synergies, efficiency and team collaboration

##### FEBRUARY 2016

Guillermo Castillo is appointed as Vice President Commercial Operations of the region of Iberia, acting also as General Manager for Spain and Portugal

#### PRODUCTS

##### NEUROSCIENCES:

Dysport® (spasticity, cervical dystonia)

##### ONCOLOGY:

Decapeptyl® (prostate cancer)

Somatuline® (gastroenteropancreatic neuroendocrine tumors)

##### ENDOCRINOLOGY:

Increlex® (recombinant insulin-like growth factor)

NutropinAq® (growth hormone therapy)

Somatuline® (acromegaly)

##### UROLOGY:

Decapeptyl® (female infertility, endometriosis, precocious

puberty) Hexvix® (bladder cancer diagnostics)

**FIND OUT MORE:** [www.ipsen.es](http://www.ipsen.es)

## AUSTRALIA



## IPSEN'S STRENGTH IN AUSTRALIA AND ALSO NEW ZEALAND IS A COMBINATION OF DEDICATED STAFF AND VISION

Ipsen has been present in Australia since 2001 and currently employs more than 50 people. The Group achieved a significant milestone in 2015 with the GEP-NET launch of Somatuline®, which is now the market leader in three Australian states and has achieved a total market share of 39.5% in the country. Ipsen's strength in Australia (and also New Zealand) is a combination of dedicated staff and vision. The passion of its dedicated staff is to improve the lives of patients with the aim of becoming a leader in oncology.

## 30%

**SALES GROWTH IN 2015  
IN AUSTRALIA AND NEW ZEALAND.**

### ABOUT US

The affiliate is fully dedicated to specialty care and aims to reach national market leadership of Somatuline® in Australia (notably it is already the market leader in South Australia, Western Australia and Tasmania).

To boost its activities in oncology it has recently increased staff numbers for product promotion and physician education. Ipsen has a large number of partnerships with hospitals and medical societies such as the Australasian Gastro-Intestinal Trials Group (AGITG) and the Urological Society of Australia and New Zealand (USANZ), to support funding, research and educational initiatives. It also works with patient groups through a collaboration with the Unicorn Foundation, the only Australian not-for-profit medical charity that focuses on raising awareness about neuroendocrine tumors.

The affiliate is committed to research with participation in three international studies in the treatment of cervical dystonia, upper limb spasticity and glabellar lines with Dysport® in 2015. Further participation in international studies for the treatment of neuroendocrine tumors is planned for 2016.

### KEY DATES

#### JULY 2015

Approval of Somatuline® for the treatment of gastroenteropancreatic neuroendocrine tumors

#### SEPTEMBER 2015

Support of the Australian Gastro-Intestinal Trials Group annual scientific meeting

#### NOVEMBER 2015

Support of the Clinical Oncology Society of Australia annual scientific meeting

### PRODUCTS

#### NEUROSCIENCES:

Dysport® (spasticity, cervical dystonia)

#### ONCOLOGY:

Diphereline® (prostate cancer)

Somatuline® (gastroenteropancreatic neuroendocrine tumors, symptoms of carcinoid syndrome)

#### ENDOCRINOLOGY:

NutropinAq® (growth hormone therapy)

Somatuline® (acromegaly)

**FIND OUT MORE:** [www.ipсен.com.au](http://www.ipсен.com.au)



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# **MORE ENGAGEMENT**

**AT IPSEN, WE ARE  
COMMITTED TO SUPPORTING  
OUR PATIENTS, PARTNERS  
AND EMPLOYEES.**



## VOICE OF AN EXPERT

INTERVIEW WITH **YANN LE CAM**,  
CHIEF EXECUTIVE OFFICER, EURORDIS  
(RARE DISEASES EUROPE)



### **What were the factors behind the more active role that patients now have in the management of their disease?**

The most important element is the constant drive toward greater patient empowerment, which has led patients to join forces into organized advocacy groups to ensure that their challenges and needs are better understood, and that their voice is better heard by policymakers, regulators and society at large. It is particularly critical for rare diseases, which had only very limited recognition until EURORDIS was founded, in 1997. Since then, our work in the political, scientific or therapeutic fields – to name but a few – has made a real difference and encouraged more patients to become active advocates too.

### **Do you foresee varying patient behavior trends emerge in different parts of the world?**

We can see different levels of maturity and approach between regions. But, while the United States and many European countries tend to be very advanced overall, we notice that several countries in Asia or Latin America are today increasingly active. There are also striking similarities among persons living with rare diseases and the challenges they are facing, regardless of where they live. So, the picture I see emerging is one of diversity but also unity. The rare disease community is today seeking common answers across regions and more resolute action at the global level. Initiatives like Rare Diseases International or International Rare Diseases Research Consortium (IRDiRC) are ample proof of that.

### **What do you foresee for 2020?**

I believe that rare diseases will achieve greater prominence in the international health policy agenda. The years to come are also going to be pivotal in the debate on the affordability of, and access to, innovative medicines for rare diseases. We will also see a number of profound changes in the research and development model – with new statistical methods, more patient-relevant outcomes, broader use of biomarkers. Early dialog between regulators, HTA and payers for earlier approvals will become a more common practice. And companies' commercialization models will increasingly rely on a combination of value, volume (of patients treated) and continuous post-approval evidence generation in the real world to help reduce the high uncertainty associated with the new orphan drugs that enter the market.

#### **BIOGRAPHY**

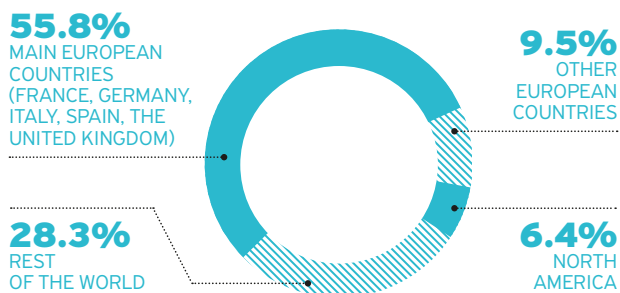
Yann Le Cam was elected chairman of the therapies scientific committee of the International Rare Diseases Research Consortium (IRDiRC).

He is a patient advocate who has dedicated twenty five years of professional and personal commitment to health and medical research non-governmental organizations in France, Europe and the United States in the fields of cancer, HIV/AIDS and rare diseases.

## ATTRACTING, RETAINING AND ENGAGING TALENT

Hiring and retaining talented individuals are key to Ipsen's success. We focus on helping our employees achieve their best by investing in training, development and support as part of an inclusive workplace where people from all backgrounds and cultures can thrive. We support talent development and encourage the emergence of leaders.

### BREAKDOWN OF OUR TALENTS BY GEOGRAPHIES



**O**ur culture is critical to retaining our best teams. Ipsen regularly monitors its pulse through employee surveys that get excellent response rates from our workforce. In 2015 the response rate was 83%, which is remarkable. When large numbers of employees take part in surveys it shows they feel the

questions are relevant and that their views will be heard and acted upon. In addition, Ipsen's engagement index was higher than the set benchmark (75 against 56), demonstrating that teams are familiar with the company's strategy, optimistic for the future of Ipsen, enthusiastic and that they have strong confidence in management.

#### > The way we develop our teams is essential.

As part of our management processes, a personal development meeting is organized during which each manager spends time to help the employee develop. Moreover, Ipsen has implemented a Management Academy with a complete set of learning paths.

> **The Group's internal mobility** policy fosters career progression by encouraging teams to move from one country to another. Whether functional or geographical, mobility is essential for individual development and sustaining the Group's momentum. As of December 31, 2015, there were 60 employees on permanent international assignments. Ipsen actively discourages any type of discrimination. As a result, gender diversity is strong, with female employees accounting for 59% of our workforce of 4,600.

> **To support the execution** of the Group's strategy, we have set four action principles that provide each and every employee with a frame of reference for their daily work:

- accountability;
- team spirit;
- result orientation;
- agility.

> **For our teams**, these principles translate into an empowerment to make decisions, come up with solutions to problems and see the impact of their decisions on others, whether colleagues or patients. They also mean there is little internal competition, a much stronger emphasis on tracking success and achieving objectives, as well as a leaner company structure that fosters quick decisions.

> **These principles** are the foundation of our culture, which is essential to achieve our plans for 2020.





## WHY JOIN IPSEN?

IPSEN IS A GLOBAL COMPANY THAT DIRECTLY OPERATES IN MORE THAN 30 COUNTRIES AND AS SUCH IT CAN LEVERAGE ON ITS WIDE GEOGRAPHICAL FOOTPRINT TO CONNECT WITH TALENTED INDIVIDUALS. WE HAVE DEVELOPED A COMPENSATION AND BENEFIT POLICY THAT IS COMPETITIVE, EQUITABLE AND THAT REWARDS PERFORMANCE. THIS INCLUDES PROFIT SHARING PLANS TOGETHER WITH LONG-TERM INCENTIVES AND COMPELLING BENEFIT PROGRAMS.

MORE THAN **4,600 EMPLOYEES** WORLDWIDE IN 2015.

**485 PERMANENT CONTRACTS** OFFERED IN 2015.



## EHS: ANALYZE THE RISKS TO BETTER AVOID THEM

Ipsen's activities require a high level of safety and a development strategy that respects the environment. Ipsen has formalized its commitment through its Environment, Health and Safety (EHS) policy, based on ISO 14001 (environment) and OHSAS 18001 (health and safety) standards. This approach is part of a continuous improvement policy that places accountability at all levels of the organization.

**Ipsen is committed to find effective therapeutic solutions to cure diseases,** relieve suffering and bring value to the community. Sustainability is the balance between the competing priorities of economic, social and environmental responsibilities. Ipsen has and will continue to commit resources and measure performance to ensuring that the highest ethical standards are applied within the whole organization, notably by applying the environment and safety principles into all aspects of its activities, from research and development through supply chain and manufacturing and its relationships with its stakeholders.

> **Certifications.** Ipsen is committed to a voluntary policy of ISO 14001 and OHSAS 18001 certifications and has decided to lead a certification project for its 10 manufacturing and Research & Development sites. The aim is that they achieve both certifications by 2017. The Ipsen sites located in Dreux (France) and Cork (Ireland) are already certified to these two international

standards. The Ipsen sites located in Signes (France), Tianjin (China) and L'Isle-sur-la-Sorgue (France) are certified under the ISO 14001 standard. The Ipsen facility located in Wrexham (UK) obtained BS 8555 certification, attesting to the implementation of its environmental management system. The site also received the Corporate Health Standard certification from local authorities in recognition of its efforts to promote workplace health as well as the Gold Award from the Royal Society for the Prevention of Accidents.

> **Trained and accountable.** As the cornerstones of the prevention program, awareness campaigns and training on environment, health and safety were continued in 2015. Each site has defined its training program as a function of its own risks and impacts. As such, all employees are trained to recognize the inherent risks associated with their workplace and the environmental impact of their activities.

## OUR FIGHT AGAINST CLIMATE CHANGE AND FOR REDUCING CO<sub>2</sub> EMISSIONS

Ipsen is committed to monitoring its direct and indirect greenhouse gas emissions (carbon) to measure the environmental impact of its activities and implement measures to reduce them. In 2015, the improvement action plan allowed the Group to decrease its CO<sub>2</sub> emissions. Furthermore, Ipsen has rolled out a number of initiatives over the past several years to reduce its carbon footprint, focusing on energy consumption. Initiatives were launched to conduct energy audits at industrial or Research and Development sites, replace old equipment with more energy efficient installations, use videoconferencing and Web conferencing rather than travels, gradually replace the corporate fleet with low carbon emitting vehicles, and organize carpooling and shuttles to reduce the use of private cars.

Regarding article 75 of the French environmental law, Grenelle II, Ipsen published its carbon reports and demonstrated its commitment to countering global warming.





### **THE EHS CODE OF CONDUCT 3S: OUR THREE COMMITMENTS**

## **STEP UP**

GET PERSONALLY INVOLVED IN YOUR OWN SAFETY AND THAT OF YOUR COLLEAGUES AS WELL AS IN THE PRESERVATION OF THE ENVIRONMENT. BE PROUD OF CHOOSING THE SAFEST WAY.

## **SPEAK OUT**

SHARE YOUR IDEAS AND CONCERNS REGARDING ENVIRONMENT, HEALTH AND SAFETY AND EXPECT TO BE LISTENED TO AND SUPPORTED. HAVE THE COURAGE TO DISCUSS RISK SITUATIONS OPENLY WITH OTHERS, EVEN WHEN THEY ARE BEYOND YOUR SCOPE OF RESPONSIBILITY.

## **STAY SAFE**

LOOK FOR WAYS TO CONTINUOUSLY IMPROVE OUR EHS PERFORMANCE SO WE CAN PREVENT FUTURE INJURY OR ENVIRONMENTAL DAMAGE.



## STRENGTHENING OUR ETHICAL APPROACH

The commitment of our employees and partners to our ethical values is the foundation on which we build the development, manufacturing and marketing of our products.

**I**psen's commitment to improve patients' health and quality of life demands the highest ethical standards in all our activities, from research and development to marketing, for which the Code for Ethical Conduct and the Compliance program are key.

We ensure we act in an ethical way with patients, healthcare professionals and organizations, public institutions, competitors, partners, shareholders and our employees.

Our global anti-corruption policy has been communicated to all countries and entities. A specific Code of Conduct and a Due Diligence system are being deployed for our contractual relationships with third parties, to reinforce mitigating controls in order to prevent corruption risk. We have achieved important milestones at global and country levels to strengthen employee awareness through educational and training programs focused on the key values of our Code for Ethical Conduct.

As a pharmaceutical company, we comply with the principles, rules and codes that regulate relationships with healthcare professionals and other stakeholders to ensure transparency. We are also an active member of professional associations such as the European Federation of Pharmaceutical Industries and Associations (EFPIA).

### OUR CODE OF ETHICAL CONDUCT IS BASED ON SIX AREAS OF ETHICS:

#### EQUITY

Equity of employees is the cornerstone of our success: ensuring that employees and applicants are treated in a fair way. The success of our company can only be achieved by upholding labor and human rights.

#### TRANSPARENCY

Transparency is key to ensure the safety of our patients, and reinforces the trust of our stakeholders.

#### HEALTH DEDICATED

Improving the lives of our patients is what drives us. The search for innovative solutions to disabling conditions is at the heart of everything we do. Increased life expectancy is making the pursuit of our inspiring vocation more vital than ever: finding safe and effective therapeutic solutions to cure diseases, relieve suffering and bring value to the community.

In addition, we strive to protect the health of our employees and the general environment.

#### INTEGRITY

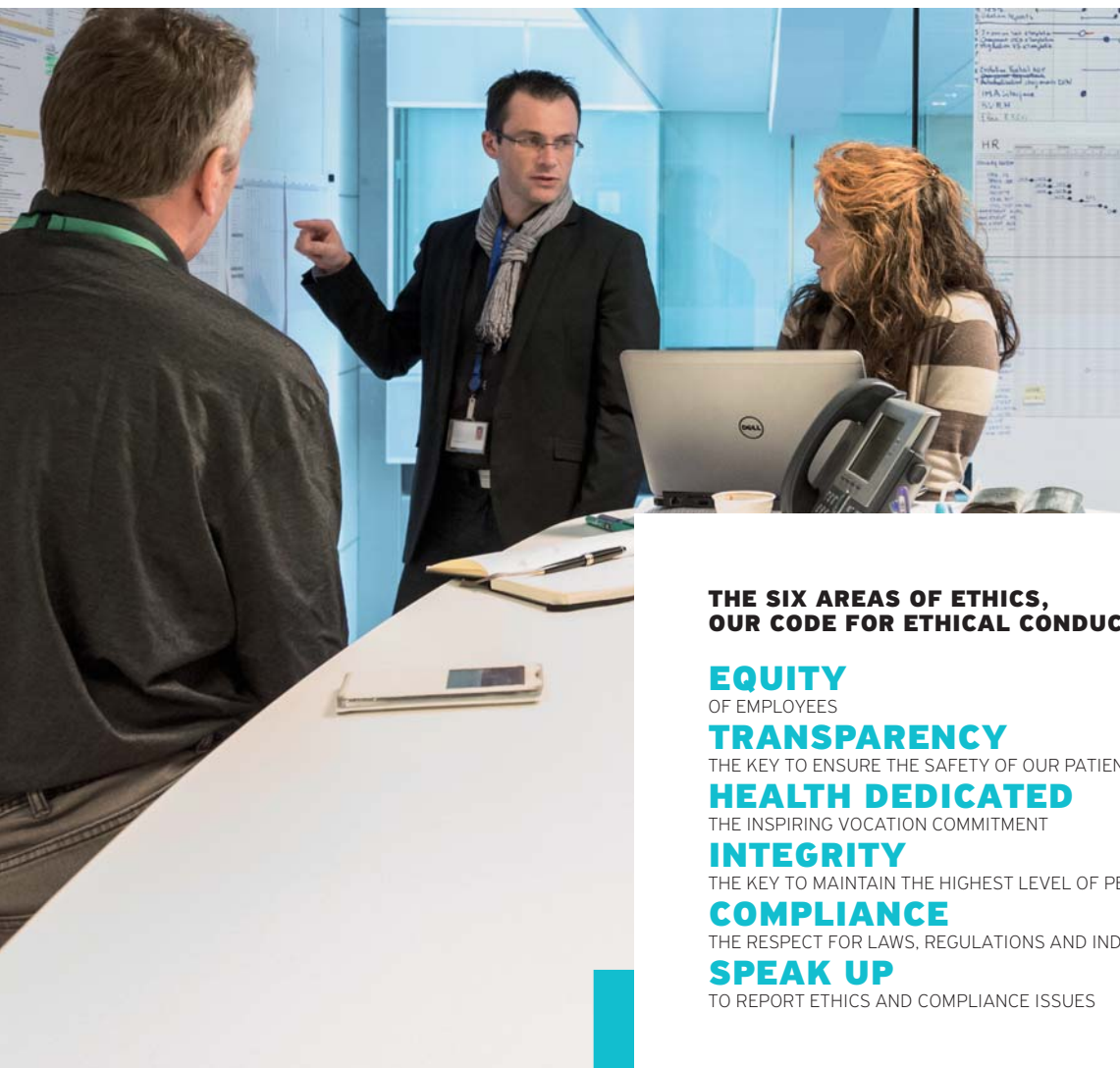
Business integrity is key to maintain the highest level of performance, and the trust of our stakeholders.

#### COMPLIANCE

Ipsen complies with all laws, regulations and industry codes applicable to its activities. The employees also comply with Ipsen policies and procedures that apply to their business and their role.

#### SPEAK UP

There are many channels to address ethics and compliance inquiries or issues. Every employee can contact his/her manager, the Human Resources department, the Ethics and Compliance department or Ipsen Ethics helpline.



## THE SIX AREAS OF ETHICS, OUR CODE FOR ETHICAL CONDUCT

### EQUITY

OF EMPLOYEES

### TRANSPARENCY

THE KEY TO ENSURE THE SAFETY OF OUR PATIENTS

### HEALTH DEDICATED

THE INSPIRING VOCATION COMMITMENT

### INTEGRITY

THE KEY TO MAINTAIN THE HIGHEST LEVEL OF PERFORMANCE

### COMPLIANCE

THE RESPECT FOR LAWS, REGULATIONS AND INDUSTRY CODES

### SPEAK UP

TO REPORT ETHICS AND COMPLIANCE ISSUES



## OUR FOCUS ON PATIENT NEEDS

Ipsen invests in the community, focusing its efforts on patient associations and charitable work. Our commitment reflects the Group's corporate social responsibility policy, and Ipsen's employees are our leading ambassadors. Examples include:

### ALGERIA



**Run against prostate cancer:** In partnership with a patient association and the Algerian association of urologists, Ipsen sponsored a run/walk to enhance public awareness on prostate cancer. More than 300 participants attended this event in order to exchange and to fight against this taboo: cancer. This event also aimed to encourage early diagnosis for the benefits of Algerian patients.

### AUSTRALIA

#### Ipsen staff under the banner of Ipsen Stripes Challenge

competed in the "Run Melbourne" on July 27, 2015 and raised funds for the Unicorn Foundation. The Unicorn Foundation is Australia and New Zealand's only not-for-profit medical charity directed towards neuroendocrine cancers. Its mission is to assist and support patients and carers; lobby for access to new and appropriate investigations and treatments; raise awareness and knowledge of neuroendocrine cancers within the medical community and general public and to encourage and support Australian and New Zealand research in the area of neuroendocrine cancers.



### CHINA



To improve awareness and public understanding of endometriosis, Ipsen China supported the global NGO **Worldwide EndoMarch** and the China Association of Health Promotion and Health Education (CAHPHE) to join hands and launch the Yellow Ribbon Movement in China. CAHPHE organized free lectures and clinical consultations in Beijing, Shanghai, Guangzhou, Chengdu that gathered gynecologists and more than 400 patients.

### FRANCE

To enhance awareness on **neuroendocrine tumors**, 20 employees of Ipsen in France took part to the fourth edition of the "heroes race" (on June 21, 2015) and raised a total of €15,000 to support the activities of patient association APTED.





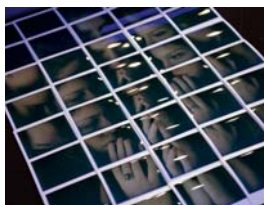
## GERMANY



Since 2014, Ipsen's employees in Germany have committed to the project **"Ipsen tut Gutes" (Ipsen for the better)**. In 2015, around 80 people worked together with professional craftsmen to renovate community facilities such as a kindergarten or a home for refugees. They also raised €5,000 to be handed over to the NET e.V. patients association.

## ITALY

To celebrate the 25<sup>th</sup> anniversary of Ipsen's presence in Italy, a conference was organized on November 26, 2015 with URI (Urological Research Institute) of IRCCS San Raffaele Hospital under the auspices of **Europa Uomo Italia Onlus association**. Patients and public audience had the opportunity to understand how prostate cancer is diagnosed, the treatments available and the consequences of the disease in daily life. A photography competition was organized with renowned photographer Maurizio Galimberti as president of the jury.



## RUSSIA

Every year Ipsen Russia participates in charitable activities across the country. With the help of Ipsen employees, well-known artists entertain **disabled children**, help clean the territory, plant lawn flowers and paint benches. In 2015, other employees of the Russian affiliate joined a new initiative to help children with severe diseases and raise funds for the charity foundation that sponsors high-tech surgeries for children with heart disease.



## SPAIN

Ipsen Pharma sponsored the Convives association, that created **"I Escuela de Afrontamiento Activo para personas que conviven con la espasticidad"** (the School for Active Coping for people living with spasticity) to help young people between 18 and 35 years old with spasticity (and their families) to get independency and personal autonomy. The first pilot program was developed in the teaching building of the University Hospital Mútua de Terrassa (in Barcelona).



## UNITED KINGDOM

Ipsen UK provided a grant of £40,000 to the NET Patient Foundation to support the analysis of **quality of life** (QoL) data for patients with a pancreatic neuroendocrine tumor (pNET). As part of this program the quality of life data from phase IV clinical trials in patients with pNETs is being undertaken as well as an online survey specifically about pNETs and subsets of Insulinoma, Gastrinoma and VIPoma.



## USA

The Ipsen US Oncology Educational Grants Committee approved funding of \$55,000 to support the **Caring for Carcinoid Foundation's** 2015 Patient and Caregiver Educational Conferences. Ipsen's support went to the direct costs associated with conducting the conferences. This enabled the association to focus on content to ensure the most informative conferences possible.



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65, quai Georges-Gorse  
92100 Boulogne-Billancourt  
France

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