## **Ipsen Investor Day**

*<b>%IPSEN* 

### 2 July 2015

#### **Disclaimer**

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The implementation of the strategy has to be submitted to the relevant staff representation authorities in each country concerned, in compliance with the specific procedures, terms and conditions set forth by each national legislation.



#### **Safe Harbor**

The Group operates in certain geographical regions whose governmental finances, local currencies or inflation rates could be affected by the current crisis, which could in turn erode the local competitiveness of the Group's products relative to competitors operating in local currency, and/or could be detrimental to the Group's margins in those regions where the Group's drugs are billed in local currencies.

In a number of countries, the Group markets its drugs via distributors or agents: some of these partners' financial strength could be impacted by the crisis, potentially subjecting the Group to difficulties in recovering its receivables. Furthermore, in certain countries whose financial equilibrium is threatened by the crisis and where the Group sells its drugs directly to hospitals, the Group could be forced to lengthen its payment terms or could experience difficulties in recovering its receivables in full.

Finally, in those countries in which public or private health cover is provided, the impact of the financial crisis could cause medical insurance agencies to place added pressure on drug prices, increase financial contributions by patients or adopt a more selective approach to reimbursement criteria.

All of the above risks could affect the Group's future ability to achieve its financial targets, which were set assuming reasonable macroeconomic conditions based on the information available today.



## Agenda

### Marc de Garidel Chairman and Chief Executive Officer



### Agenda for the day

14:00-14:25	Introduction	Marc de Garidel, CEO
14:25-15:45	Group strategy	Christel Bories, Deputy CEO
15:45-16:00	Q&A session	
16:00-16:10	Coffee break	
16:10-16:50	R&D strategy	Claude Bertrand, CSO
16:10-16:50 16:50-17:10	R&D strategy Financials	Claude Bertrand, CSO Aymeric le Chatelier, CFO

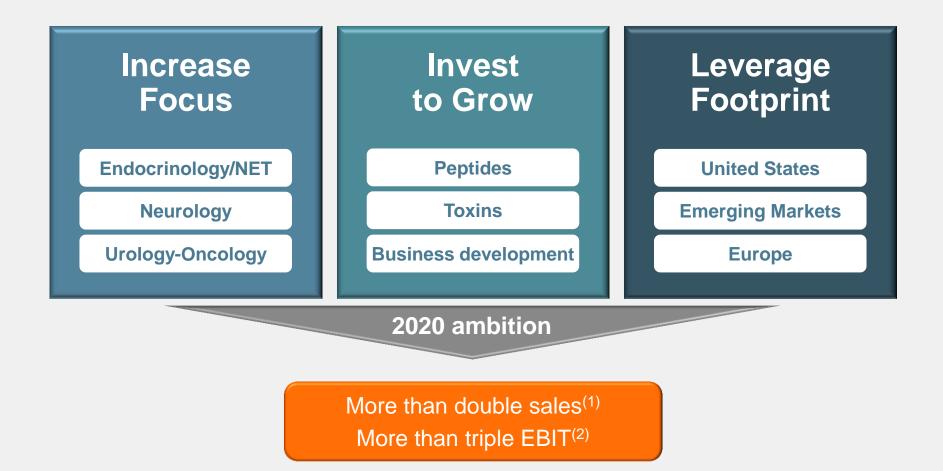


## Introduction

### Marc de Garidel Chairman and Chief Executive Officer



### The 2011 strategy initiated a period of significant progress...

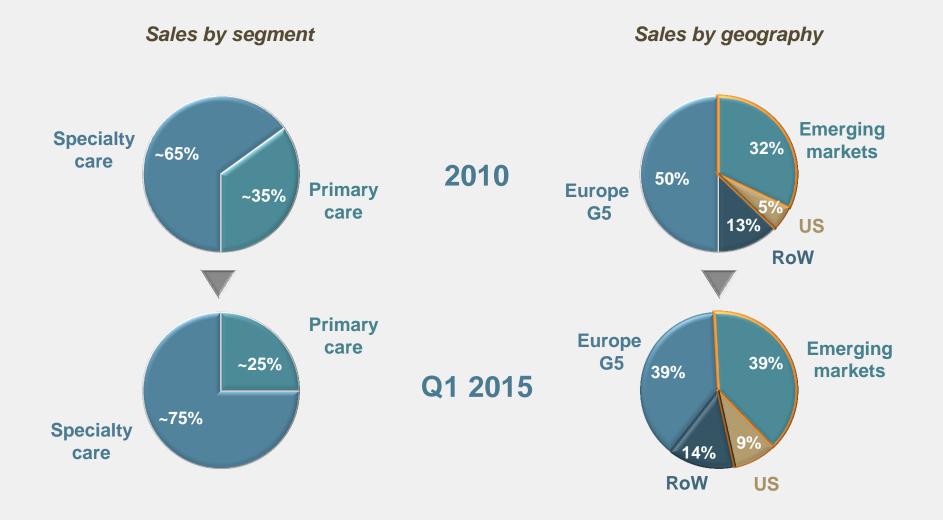




(1) At constant exchange rate vs. 2010 Sales: 2020 sales of €2 billion to €2.5 billion – <sup>(2)</sup> vs. 2010 Core Operating Income: EBIT prior to purchase accounting recordings and non recurring elements: 2020 EBIT of €500 million to €600 million

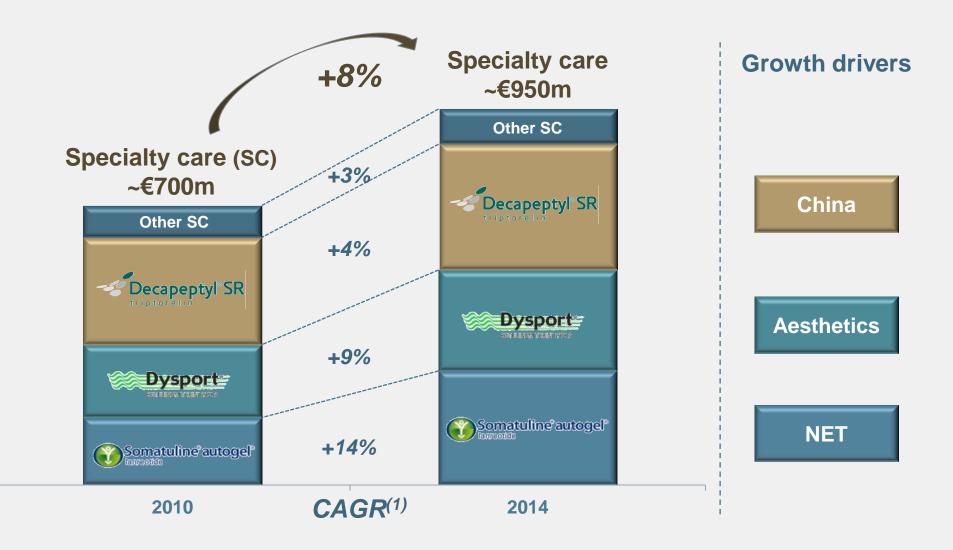


#### ... which led the Group to become a global specialty care company



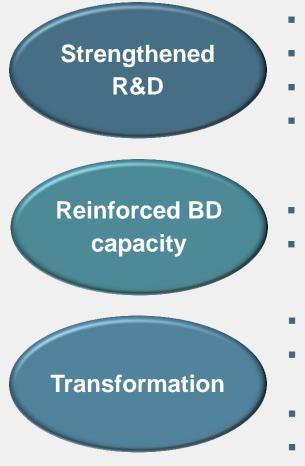


#### Specialty care, the growth engine over 2010-2014





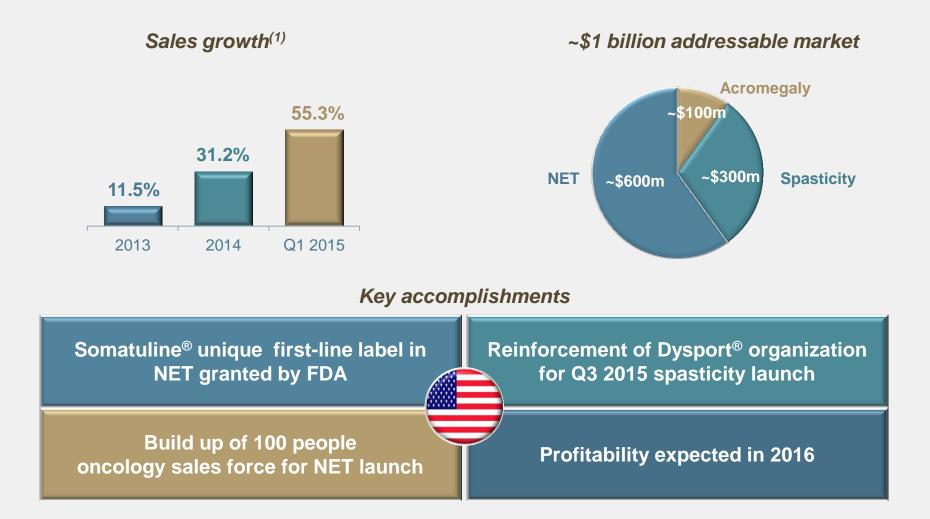
### Key achievements 2010 - 2015



- 8 Phase III programs delivered
- Consolidation in toxin research (Syntaxin/Harvard partnership)
- Boston peptide platform revamped
- FDA approval of Somatuline<sup>®</sup> as first line treatment in NET
- Galderma expanded partnership
- Telotristat etiprate/ Canbex option/ OctreoPharm Sciences
- Inspiration exit with OBI-1 sale to Baxter
- Restructuring of French primary care and Dysport<sup>®</sup> US operations
- Management team reinforced
- Efficiency and cost control efforts

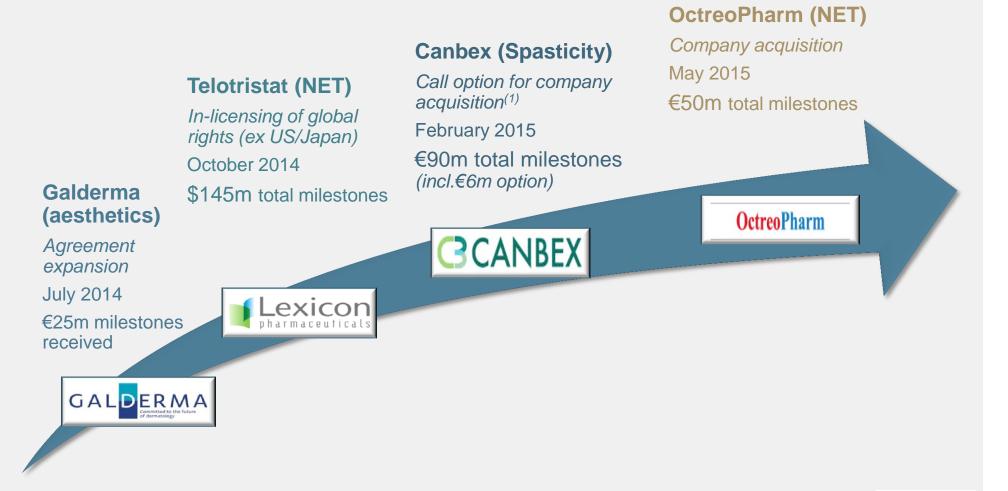


### Turnaround of the US platform, with high potential for growth





## Business development strategy starting to pay off with 4 deals signed in the last 12 months





### 2011-2015 achievements reflected in share price performance





### 2015-2020: A refocused strategy within specialty and primary care



Global leadership in targeted diseases



Focus on GI/OTx



Note: GI:Gastrointestinal, Otx:Dual channel approach (Rx/OTC)



#### **Specialty care strategic focus**

Reach global leadership in niche therapeutic areas...





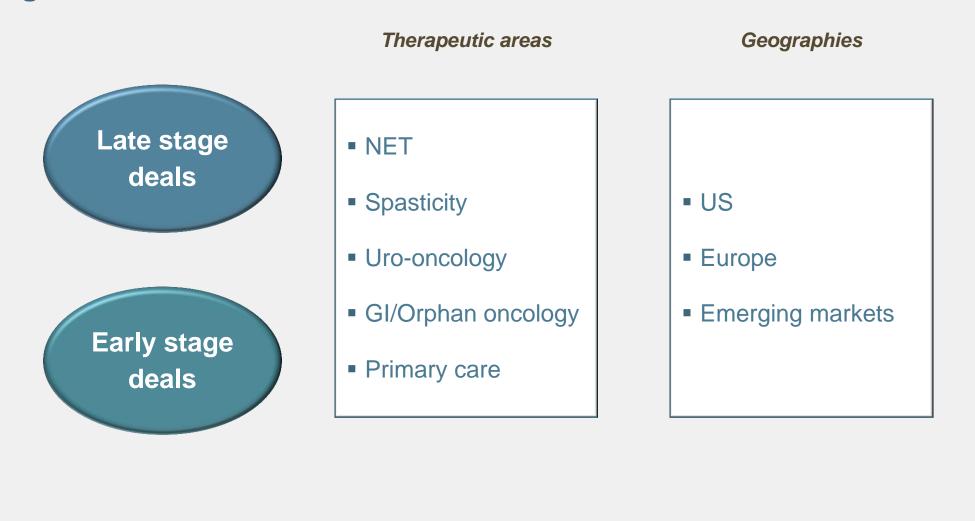
#### **Primary care: focus on GI/OTx**







## Strong Business development focus to complement organic growth





## 2020 outlook showing strong sales growth and profitability momentum

Group organic sales

Core operating income margin<sup>(1)</sup>



Ipsen to outperform industry growth



## **Group strategy**

### Christel Bories Deputy Chief Executive Officer



A refocused strategy within specialty and primary care



Global leadership in targeted diseases





### « Own the disease » business model to achieve leadership

#### « Own the disease » business model

- Focus on few disease areas with high R&D expertise and strong innovation
- Be present at different stages of the treatment pathway
- Offer a range of differentiated products, devices, and services around treatment
- Cover the full value chain from R&D to commercialization

#### Key features of category leaders

Customized solutions combining scientific and marketing perspectives

 Strong relationships with key stakeholders (specialists, KOL, payers...). Partner of choice for new developments

Strong knowledge of disease mechanism resulting in improved clinical PoS

Credible partner for BD and alliances



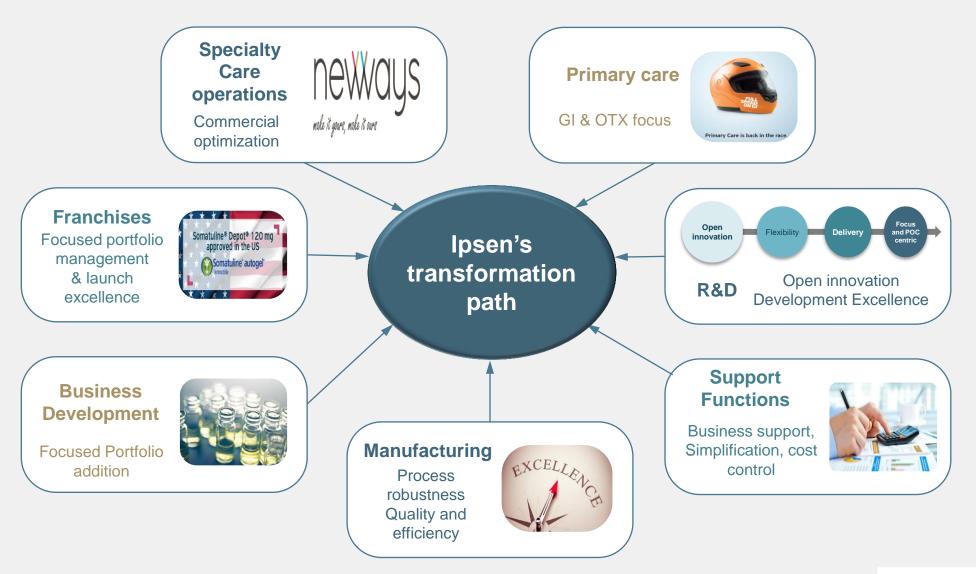
## Ongoing transformation to adapt company profile to fast-changing environment



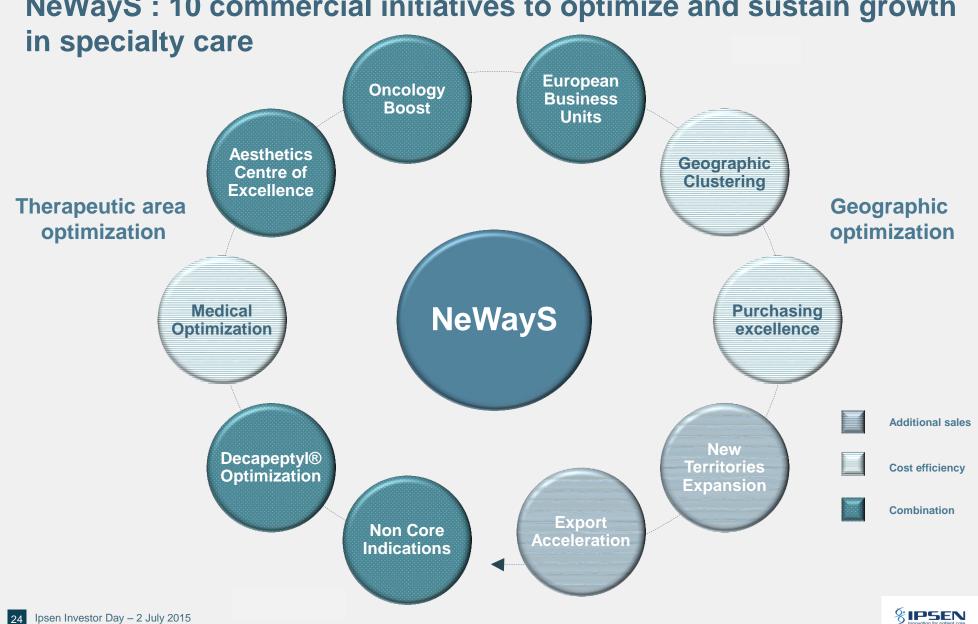
Ipsen to become an agile and flexible entity outperforming industry



#### Deep transformation process involving all parts of the company







### **NeWayS : 10 commercial initiatives to optimize and sustain growth**

## Specialty care

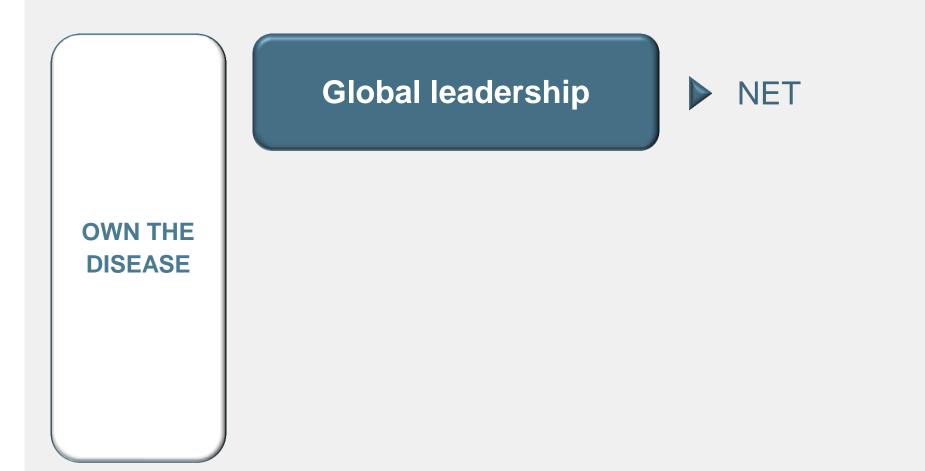


## Reach global leadership in targeted diseases, reinforce position in historical areas, and explore new targets





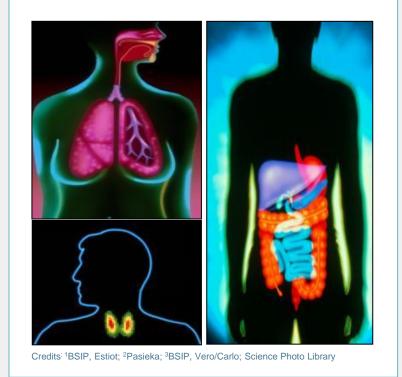
### Focus on Neuroendocrine tumors (NETs)





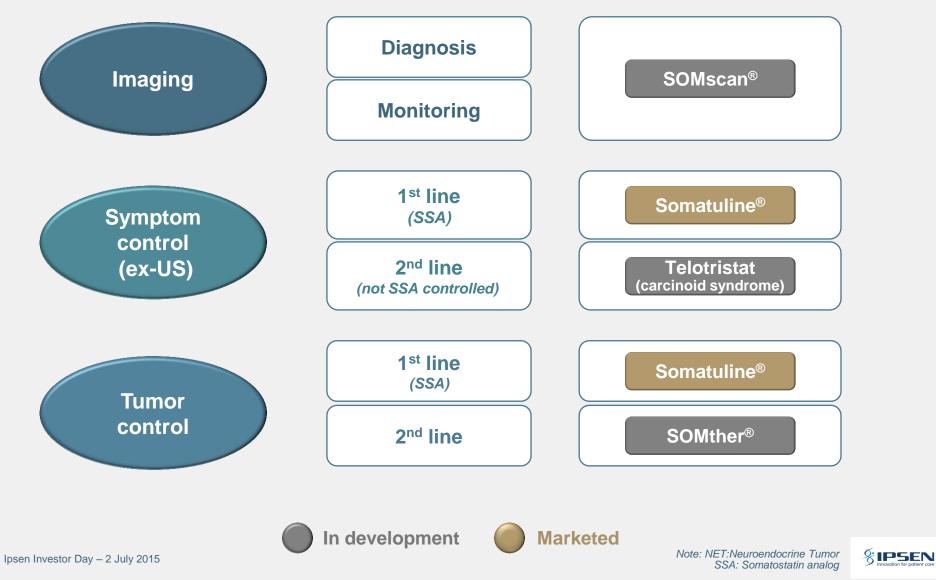
### Neuroendocrine tumors in a nutshell

- Rare, heterogeneous, slow-growing tumors<sup>(1)</sup>
- Arise from cells with neuroendocrine origin<sup>(1)</sup>
- Can arise from most organs, commonly<sup>(1)</sup>:
  - Gastrointestinal tract and pancreas
  - > Endocrine organs
  - > Lung
- US and Europe GEP NET prevalence: ~120 000 patients
- US NET market > \$600m<sup>(2)</sup>, currently underserved
- Europe NET market ~\$400m<sup>(2)</sup>



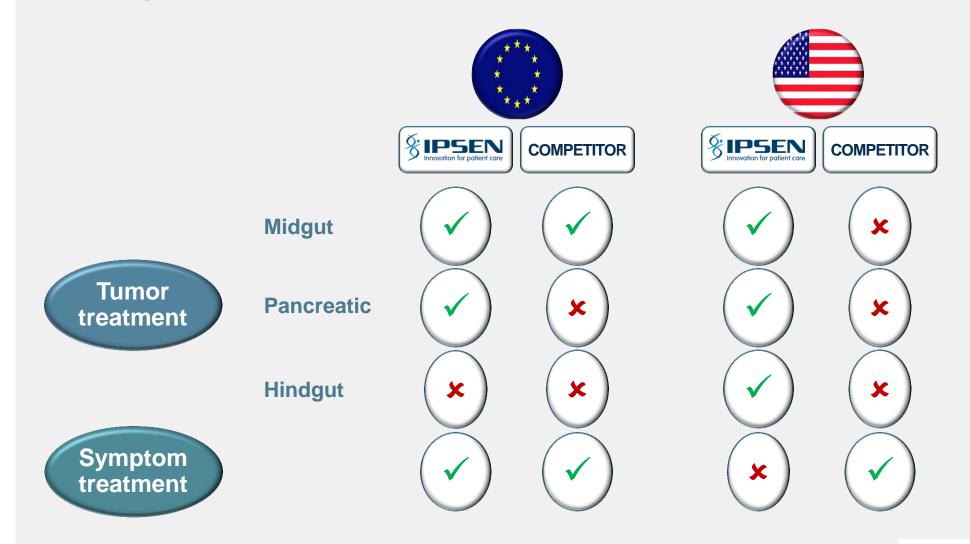


# Beyond Somatuline<sup>®</sup>, Ipsen made two acquisitions to address the whole NET treatment paradigm



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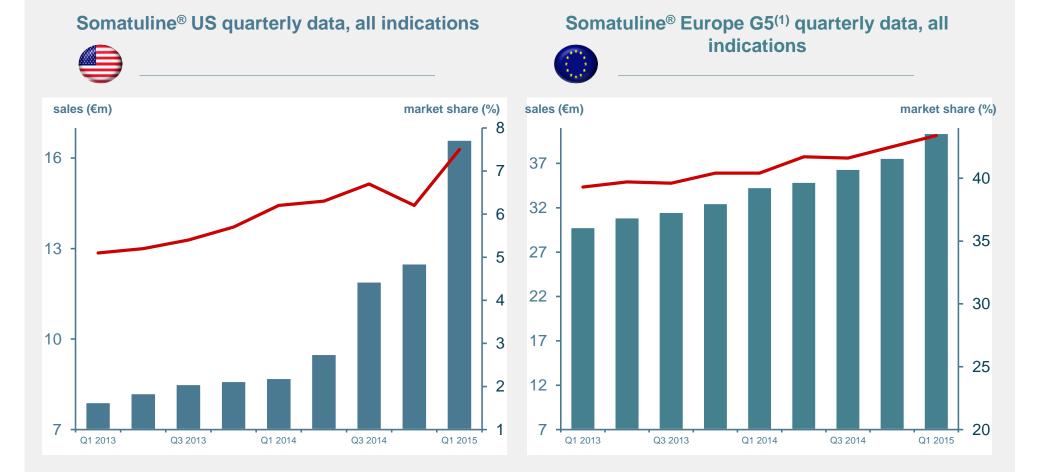
# Somatuline<sup>®</sup>, the first SSA approved for tumor control of GEP-NET in Europe and US







# Somatuline<sup>®</sup> sales and market share accelerating in US and Europe





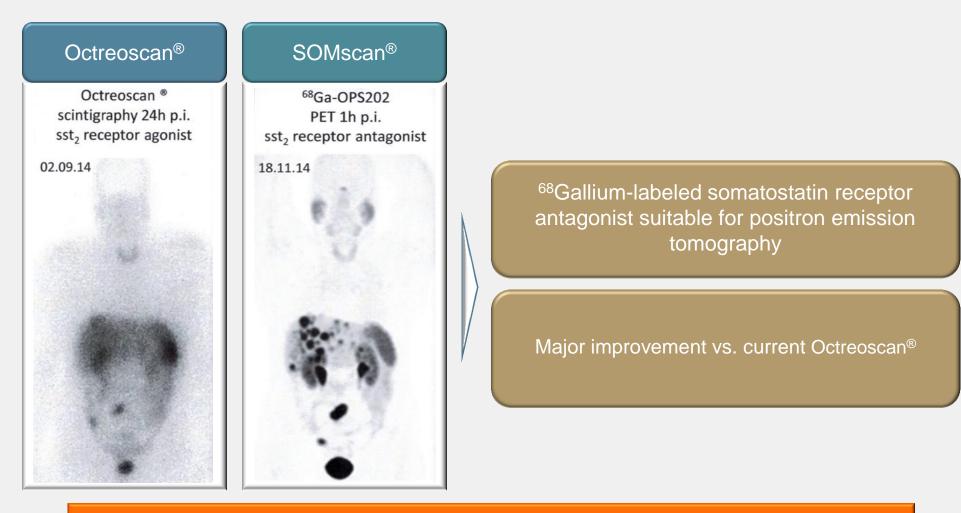
# Xermelo<sup>®</sup> (telotristat etiprate): a novel oral treatment for NET symptom<sup>(1)</sup> control currently in Phase 3



- SSA add-on therapy for symptomatic patients
- Strong Phase 2 data with >40% reduction in bowel movements<sup>(2)</sup>
- Phase 3 results expected in Q3 2015
- Expected launch in 2017 in Europe
- ➢ Estimated peak sales > €50m



### SOMscan<sup>®</sup>: a new generation imaging agent for NET

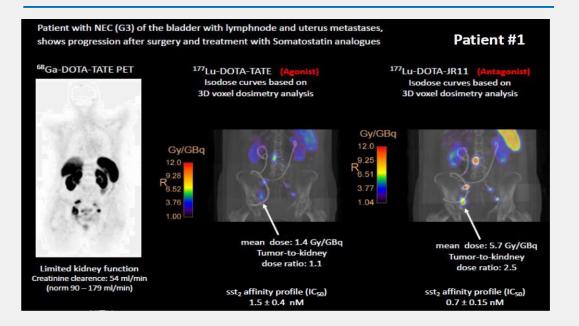


Potential to change patient diagnostic and management



# **SOMther®:** potentially best in class PRRT with a wider therapeutic window for NET patients progressing under SSA

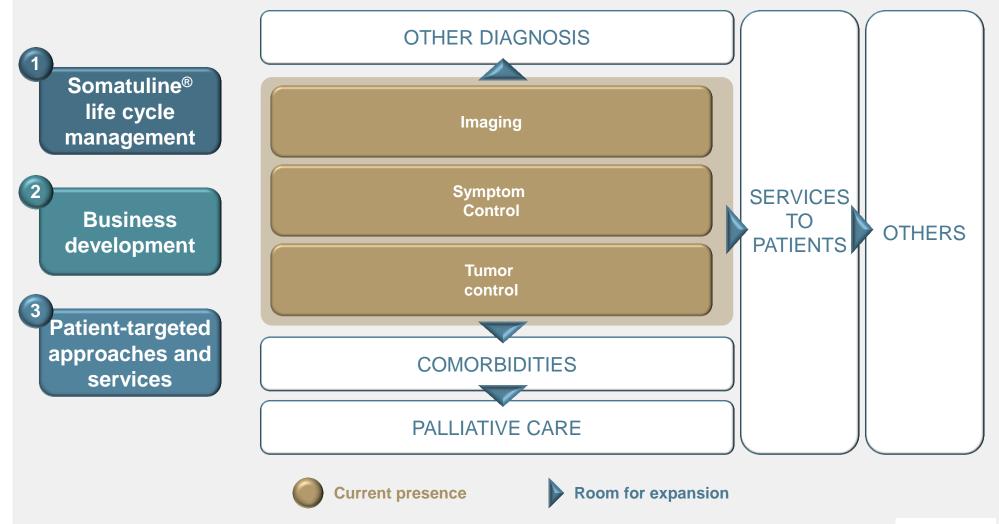
Dosimetry comparison <sup>177</sup>Lu-DOTA-JR11 vs. <sup>177</sup>Lu-DOTATATE



- Lutetium combined with SSTR2 antagonists for 2<sup>nd</sup> line treatment of NET patients progressing under SSA
- > To be manufactured and distributed inclusive of peptide and radionuclide
- Currently in preclinical development, launch expected beyond 2020

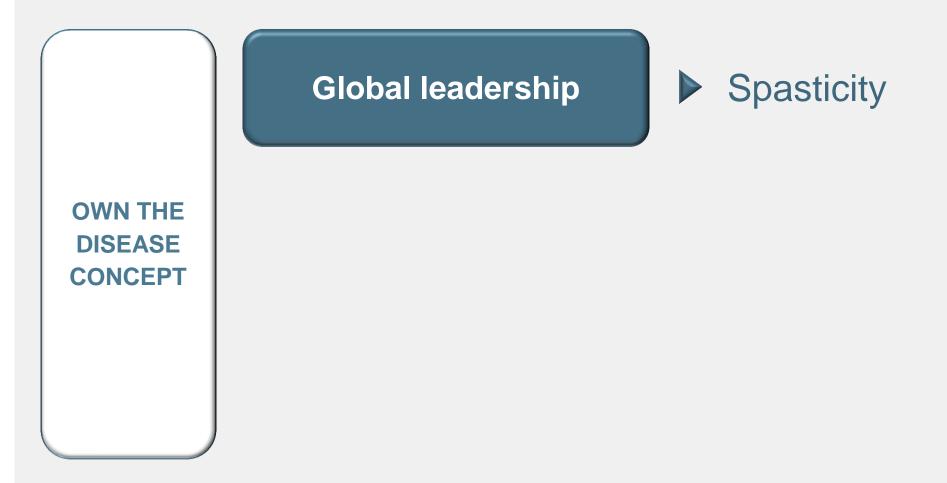


### NET treatment paradigm still offers room for expansion









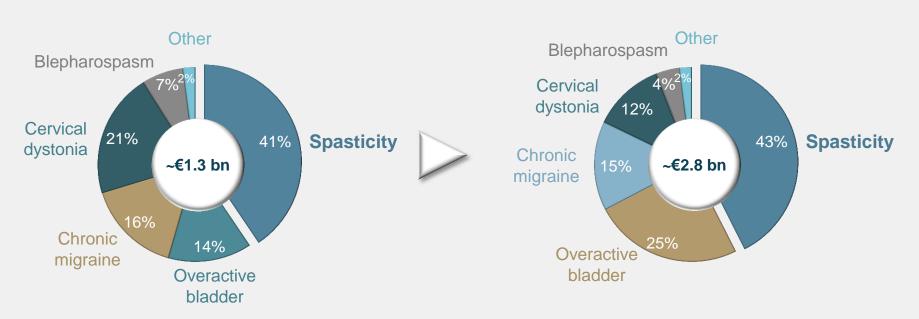


# Spasticity to remain the largest segment of the fast-growing therapeutic toxin market

Toxin therapeutic market by indication

2014

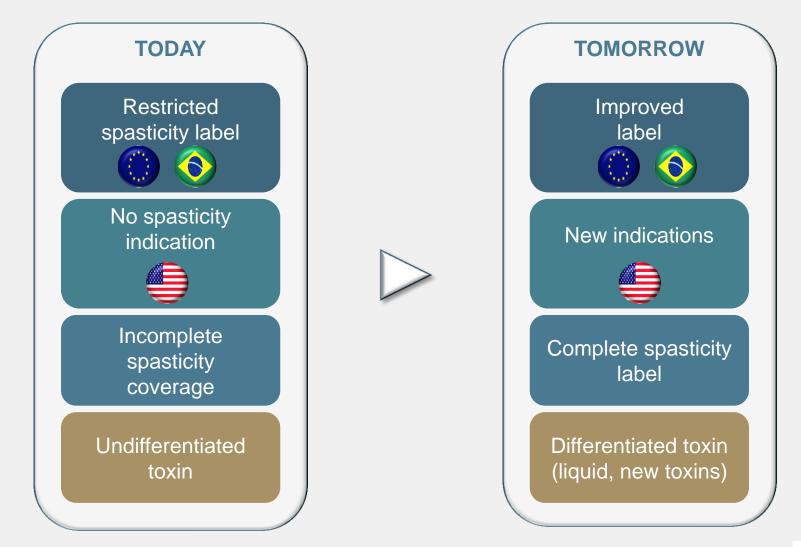
2022



### Therapeutic market CAGR 2014-2022: +11%



# Dysport<sup>®</sup> to become a global differentiated toxin with full spasticity reach





Note: US spasticity indications are subject to approval by regulatory authorities AUL: Adult Upper Limb, PLL: Pediatric Lower Limb, ALL: Adult Lower Limb

## Ipsen, a leading player in spasticity, catching up in the US

### 2014 Dysport<sup>®</sup> market share in spasticity (ex US)



Ipsen boasts high market shares in its spasticity markets

Ipsen currently absent in the US, spasticity launch planned in Q4 2015



## Dysport<sup>®</sup>, a great potential of differentiation in spasticity

### Greater duration of patient relief:

- Earlier onset of action
- Longer duration of action

### Only toxin to improve voluntary movements in entire limb<sup>(1)</sup>

Key to help patients gain autonomy

### First toxin to show efficacy on Tardieu scale<sup>(2)</sup>

Recognized as the best efficacy measure, specifically in spasticity

<sup>(1)</sup> Dy : study 145 (AROM); Bx : NA; X : NA <sup>(2)</sup> Dy : study 145; Bx : NA; X : NA



### Ipsen on track to succeed with US spasticity launch

### Best toxin to treat AUL spastic patients

Only toxin to demonstrate improvement of voluntary movements Long relief period thanks to fast onset and long duration of action



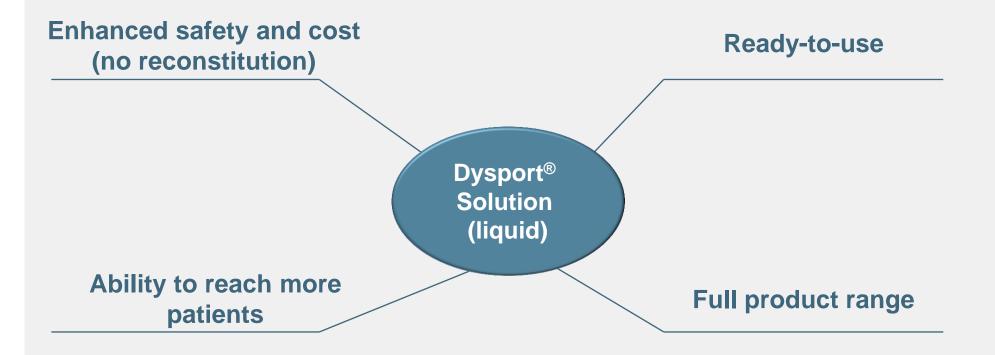
"First Mover" advantage in PLL Filing expected by end 2015 Potential full adult spasticity coverage with ALL

Significant increase of US addressable market

Spasticity sales force of ~20 reps to support launch



Dysport<sup>®</sup> Solution, potentially the first liquid toxin on the market (ex-US)

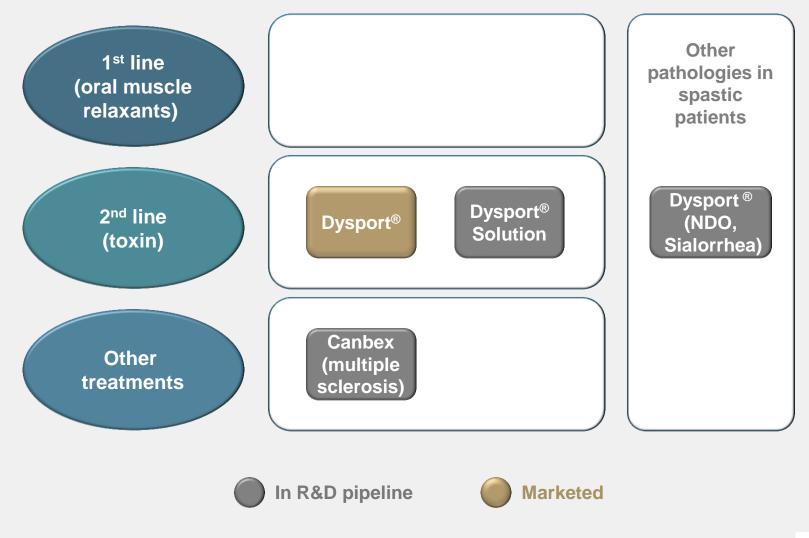


Dysport<sup>®</sup> Solution to be filed in Cervical Dystonia in Europe and Brazil in H1 2016





## Through LCM and Canbex acquisition, Ipsen well-positioned on the spasticity treatment paradigm

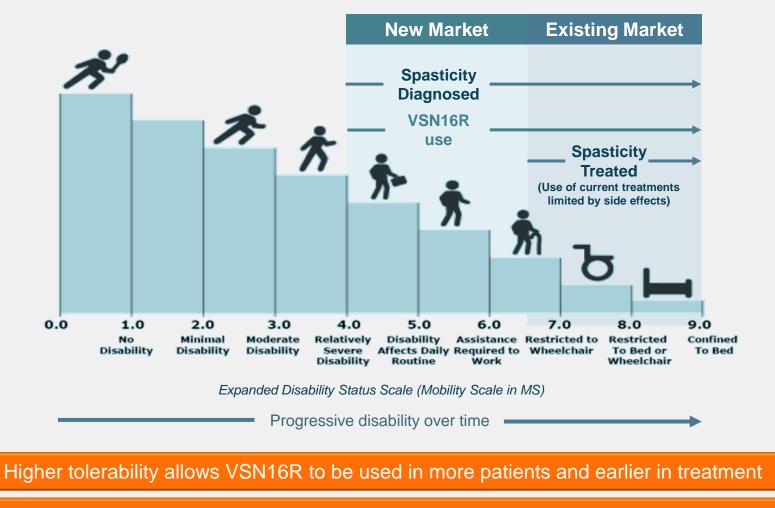




Note: LCM: Life Cycle Management , NDO: Neurogenic Detrusor Overactivity



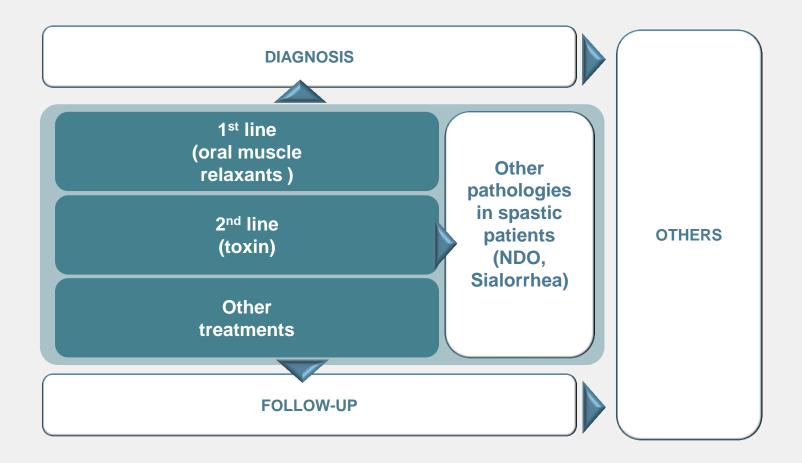
## Canbex's deal option, a promising opportunity



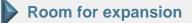
80% of the ~2 million MS patients worldwide suffer from some degree of spasticity



## Spasticity treatment paradigm still offers room for expansion









## Spasticity strategy key takeaways

### Short / Mid term

#### **Focus**

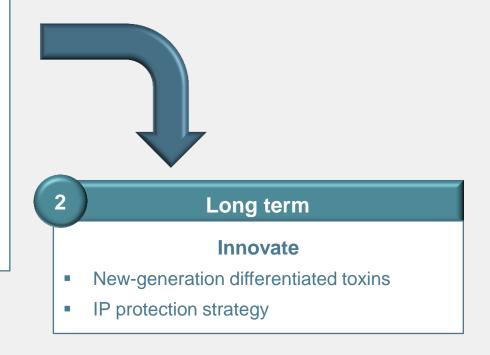
- Gain full spasticity reach (adult and pediatric)
- Launch in the US
- Leverage Dysport<sup>®</sup> differentiation

#### Differentiate

 First company to potentially launch liquid form in Europe and Brazil with Dysport<sup>®</sup> Solution

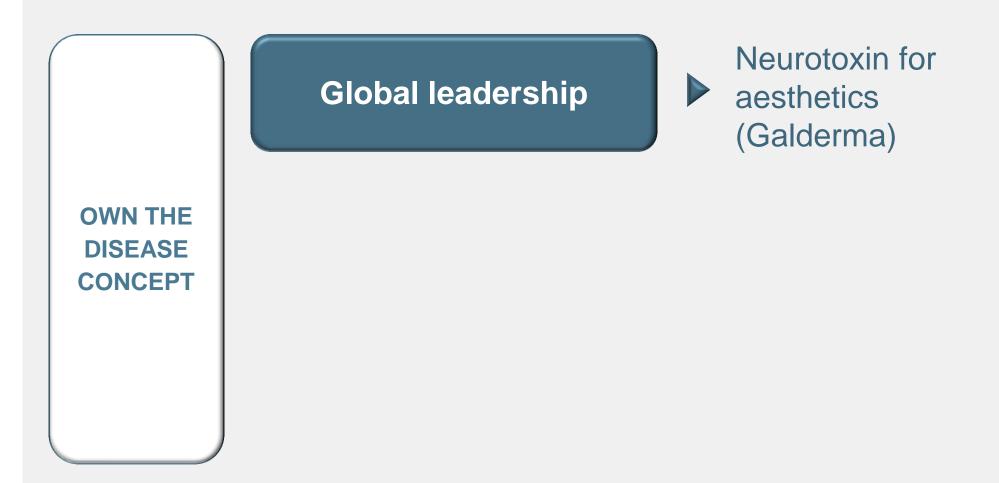
#### Invest

- Expand to new indications/ areas:
  - R&D
  - Business development





## **Neurotoxin for aesthetics through Galderma alliance**



47 Ipsen Investor Day – 2 July 2015



## Aesthetics, a fast-growing market generating half of Dysport<sup>®</sup> sales

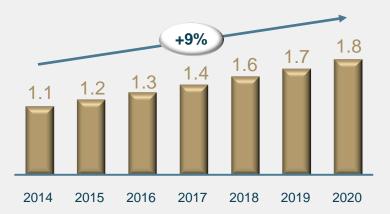
## Dysport<sup>®</sup> 2014 revenues<sup>(1)</sup> split (%)



#### Ipsen markets Dysport<sup>®</sup> in Aesthetics:

- Directly in Russia and some Eastern European countries
- Via Galderma in Europe, USA, Brazil, Australia, Argentina, and Mexico
- Via other third parties in South America, Middle East, etc.

### Aesthetics BonT market<sup>(2)</sup> (€ billion)



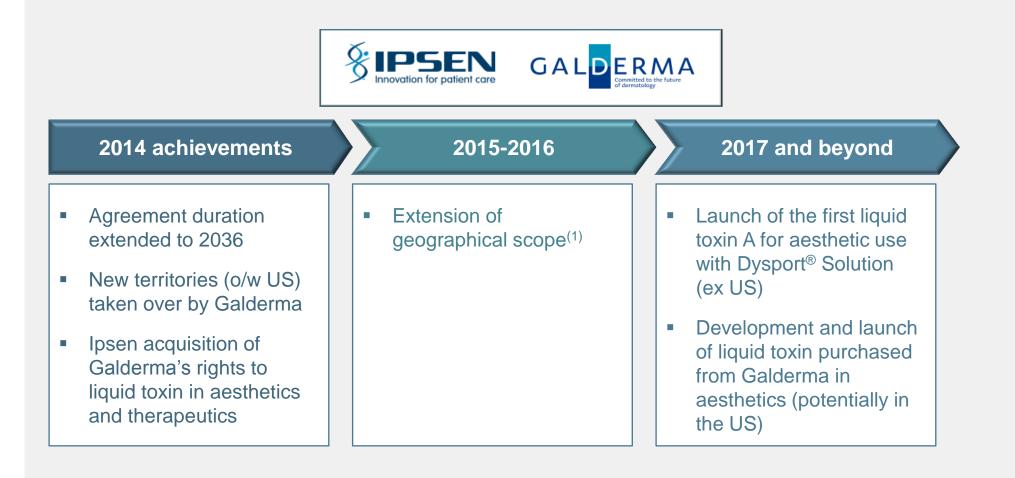
#### Strong volume growth driven by:

- Emerging countries
- Favorable demographics
- Growing acceptance, in particular in men

#### Price pressures due to:

- Emergence of lower priced Asian toxins
- Limited innovation

## The scope of Ipsen and Galderma alliance to keep expanding





### Areas to reinforce and new targets





# Ipsen to leverage infrastructure and expertise in urology-oncology through late-stage deals

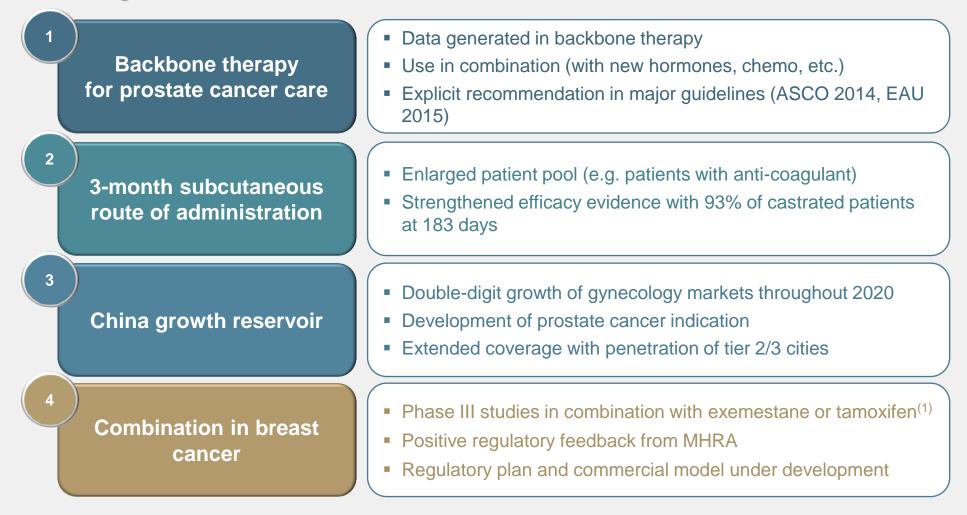


Strong expertise acquired through Decapeptyl<sup>®</sup>, Hexvix<sup>®</sup> and tasquinimod

Note: BD: business development

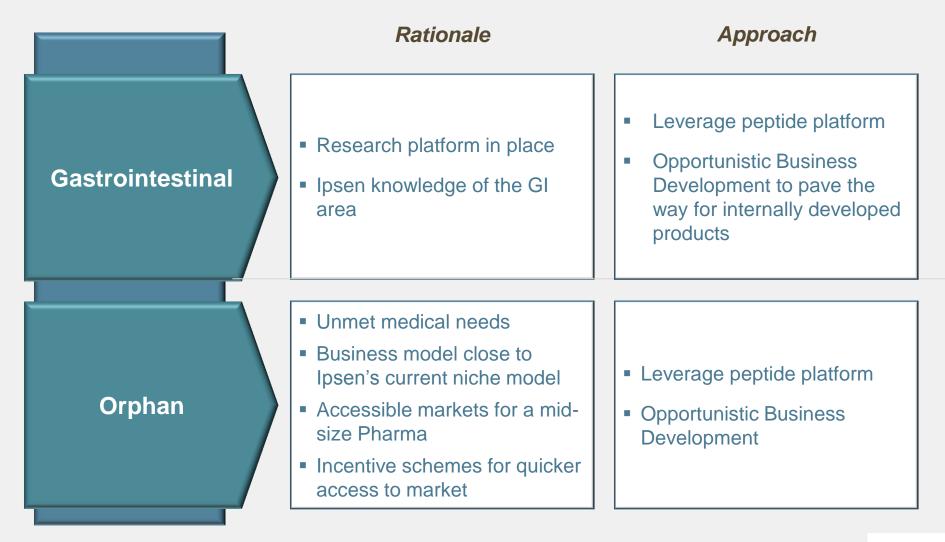


# Decapeptyl<sup>®</sup> to benefit from life-cycle management and emerging market growth





# GI and Orphan oncology offer the best rationale for opportunistic expansion

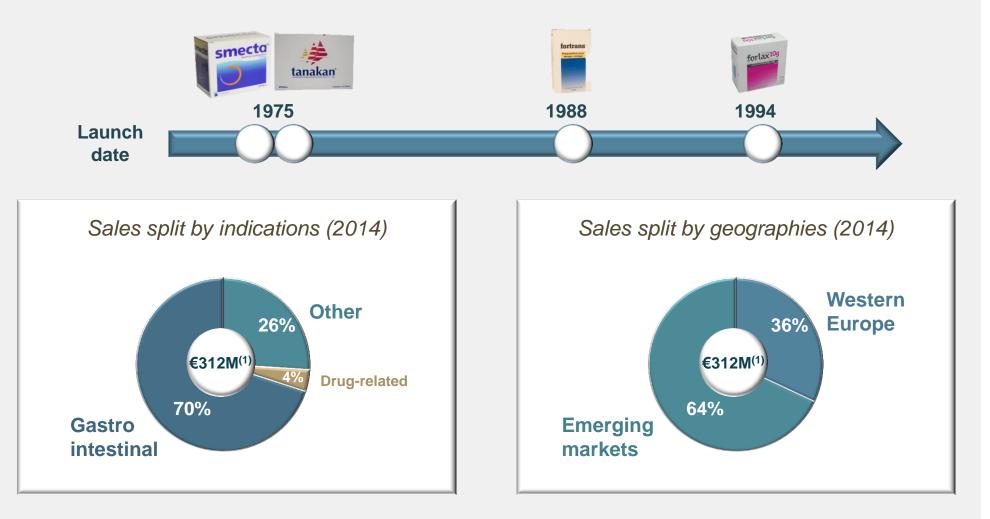




## **Primary Care**



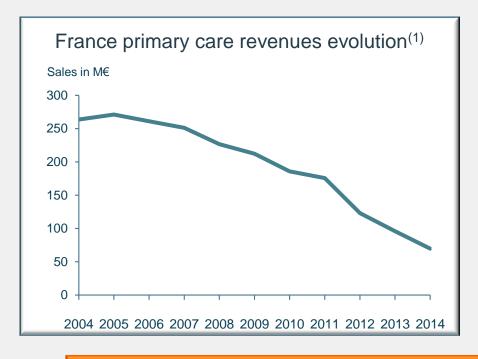
# Ipsen primary care legacy composed of strong brand equity, GI franchise, and emerging market footprint



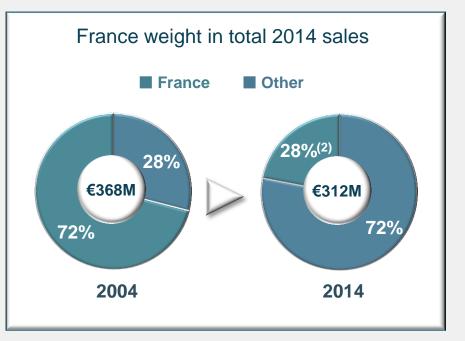


## Primary care decline in France to reach a floor

### After 10 years of decline ...



## ... France now accounts for 28% of total primary care



Primary care France remains profitable thanks to significant restructuring

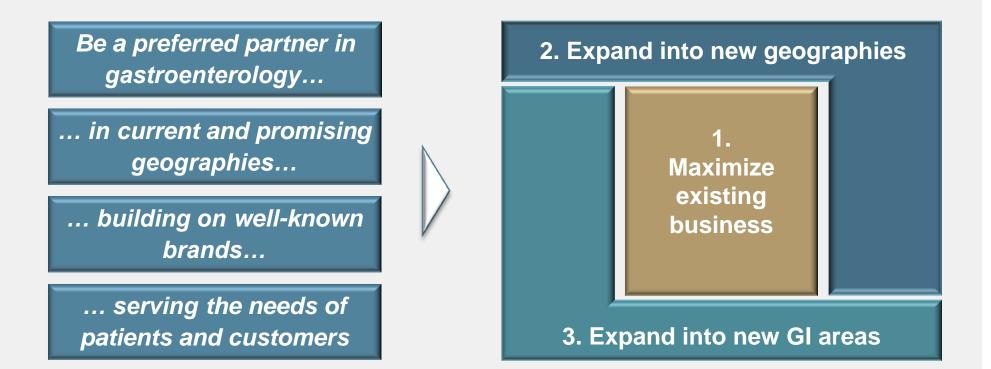
Emerging market growth limiting French decline



### A new strategic vision for Primary Care

A vision...

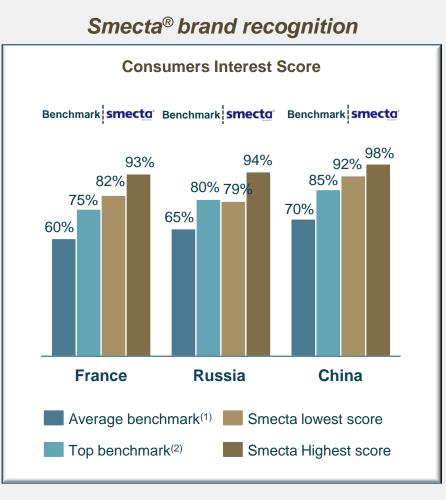
... Leaning on three pillars



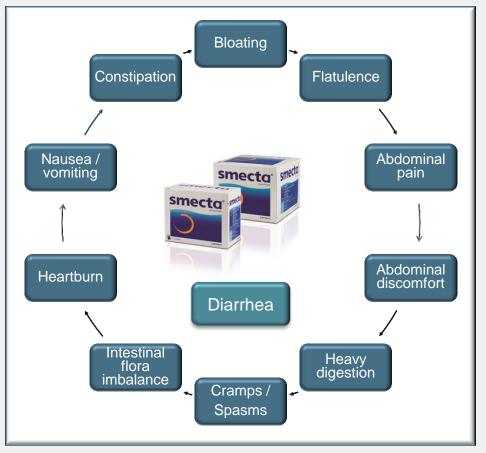
Ipsen to build OTx capabilities to serve new strategy



## Smecta<sup>®</sup>, a powerful brand value with untapped potential

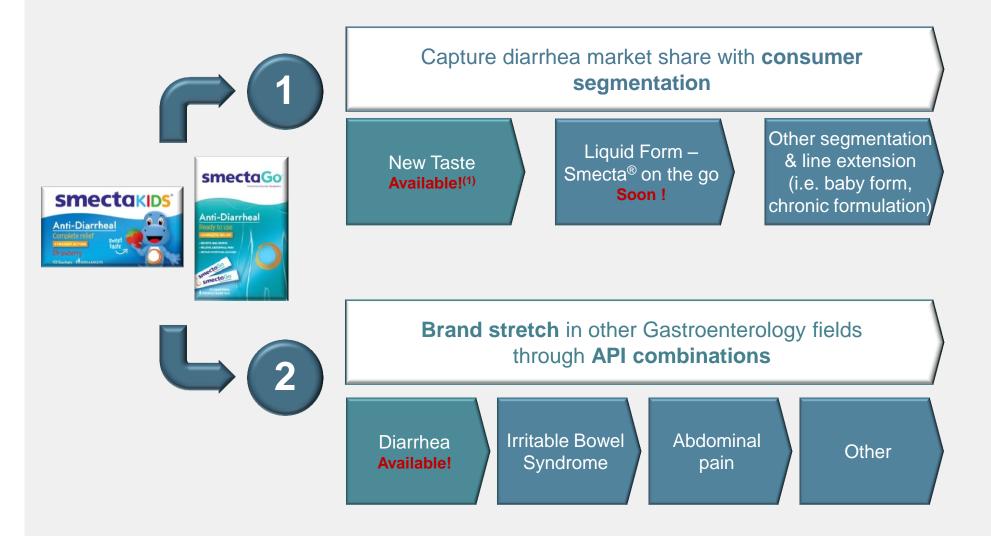


### High potential in other GI fields





## 1 - Maximize existing business through LCM and BD

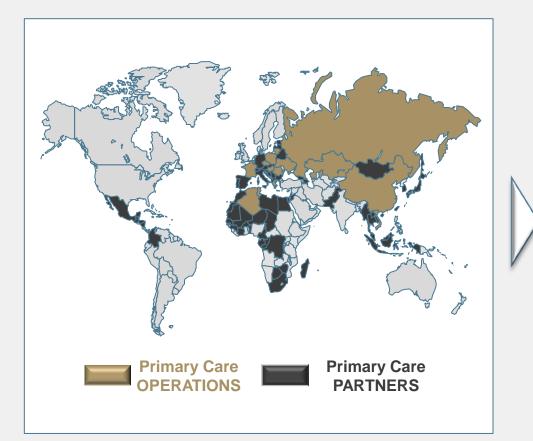


<sup>(1)</sup> Smecta<sup>®</sup> strawberry flavor available in China, soon in France Note: GI: Gastrointestinal, LCM=Life Cycle Management, BD=Business Development, API=Active Principle



## 2 - Expand into new geographies

*Ipsen primary care current footprint* 



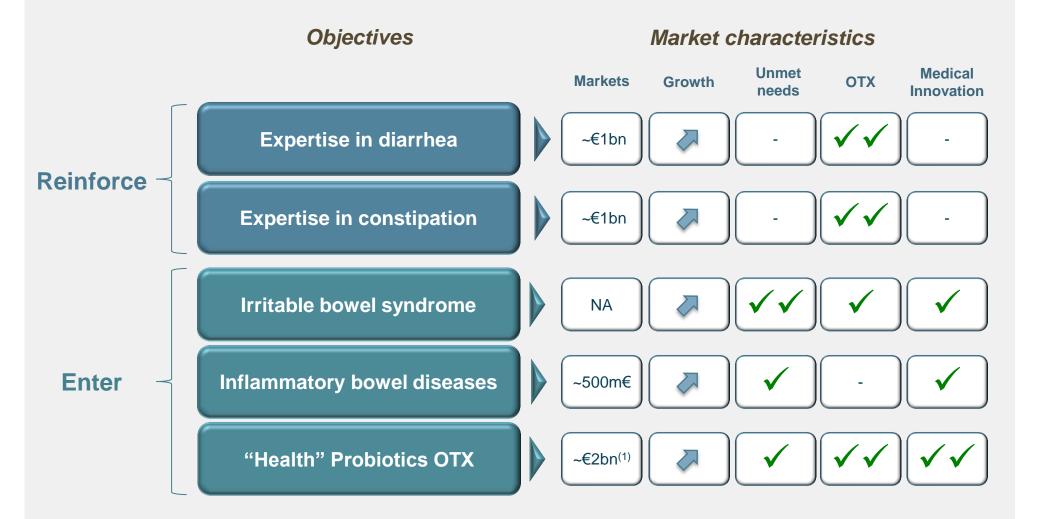
### Targets for geographical expansion







## 3 - Expand into new GI areas, notably in probiotics





## Ipsen's strong primary care assets validate the move to OTx model

	OTx model	Ipsen's assets
Portfolio	Brand power Reimbursed if prescribed	<ul> <li>Strong brand recognition</li> <li>Portfolio originally in Rx</li> <li>Available in self-medication in many countries</li> </ul>
Innovation	Strong innovation to constantly adapt to consumer needs	<ul> <li>Innovation &amp; LCM (Smecta<sup>®</sup> RTU, Smecta<sup>®</sup> Strawberry)</li> <li>Industrial legacy</li> <li>BD capacity</li> </ul>
Geographical presence	Countries with history of patient co-pay	<ul> <li>Strong presence in France &amp; emerging markets (China, Russia, Algeria)</li> <li>Absence from Americas and Western Europe</li> </ul>
Sales force capabilities	Mixed model from GPs to Pharmacies	<ul> <li>Mixed model in France, Russia and evolving towards pharmacies in China</li> </ul>



### Key strategy takeaways

### **Specialty care**

- 3 niche therapeutic areas with potential to become leader (NET, spasticity, and Dysport<sup>®</sup> aesthetics through Galderma partnership)
- > 2 historical therapeutic areas to reinforce (urology-oncology and adult endocrinology)
- Adjacent therapeutic areas to explore (GI and orphan cancers)

### Primary care

- Building of GI/OTx franchise on strong existing brands
- Reinforcement of geographical coverage

Continued transformation to improve efficiency

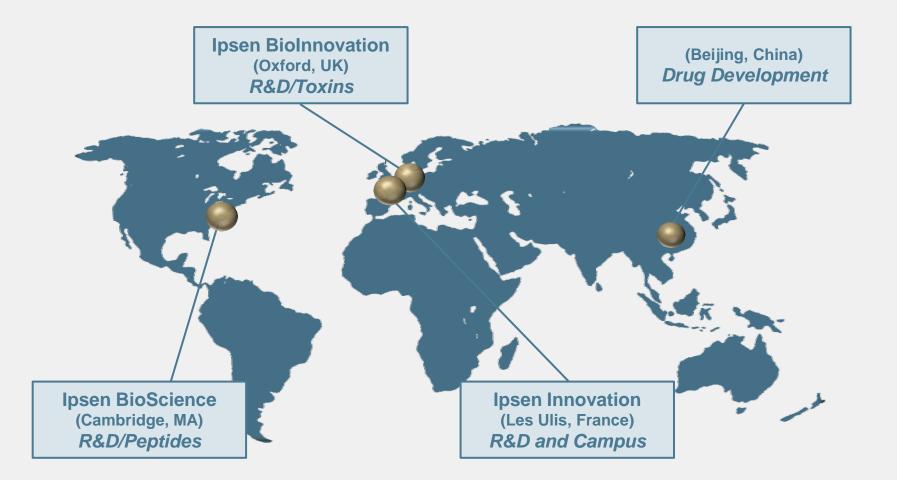


## **R&D** update

## Claude P. Bertrand Chief Scientific Officer



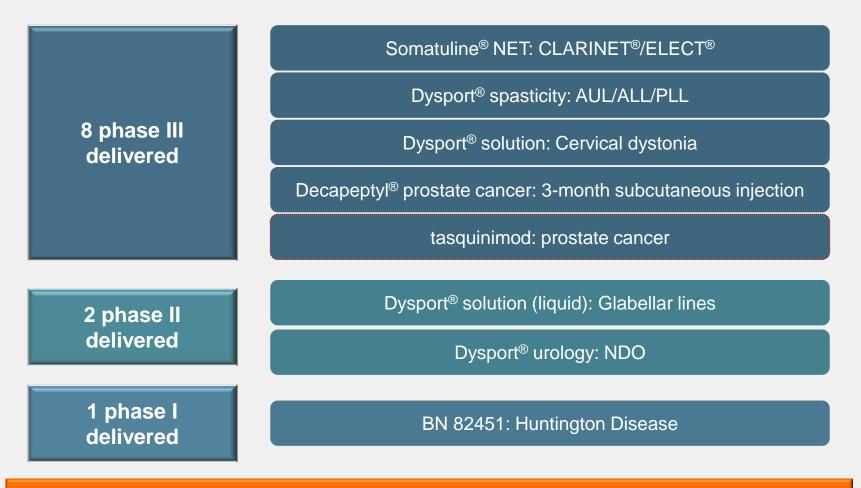
### **Global Core R&D footprint: 350 employees in four main sites**



€187 million (~15% of sales) invested in R&D in 2014



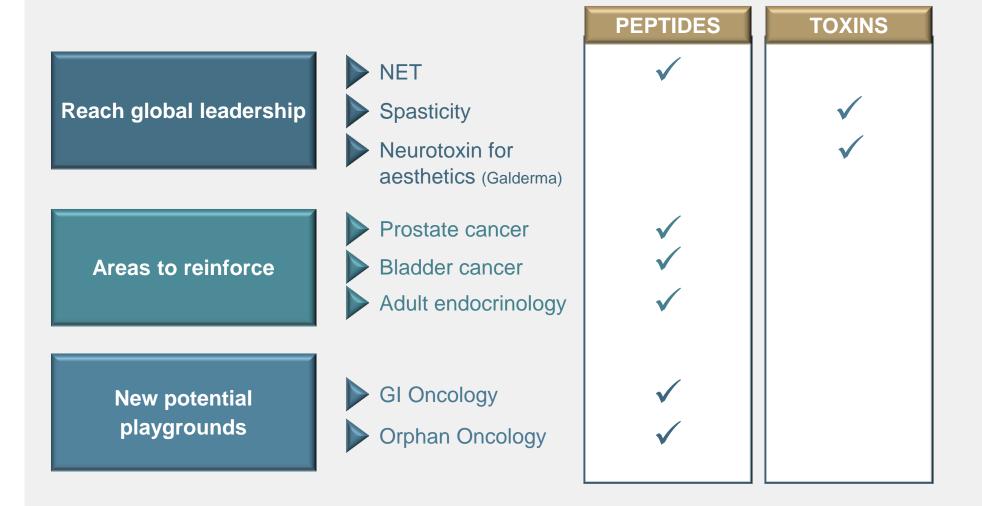
## Key R&D achievements over the 2010-2015 period



Consistent R&D execution allowing on-time deliveries



# R&D fully aligned with Group strategy with two core platforms serving niche therapeutic areas





## Peptides Oncology / Endocrinology



# A new state-of-the-art facility for peptides research recently inaugurated in Cambridge, USA



World-class office and laboratory space within #1 Biopharma cluster in the US

Good position to fully exploit the Cambridge ecosystem

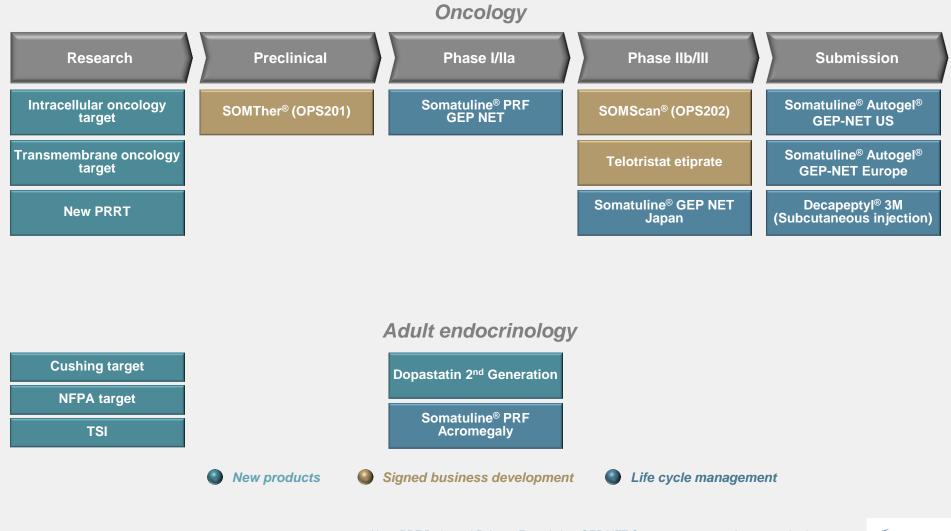
Project completed on time (July 2014) and on budget

At the heart of the global scientific and technological hub

Ipsen Bioscience well positioned to develop entrepreneurial spirit of a start-up company



## A rich oncology/endocrinology pipeline



Note: PRF:Prolonged Release Formulation, GEP NET:Gastroenteropancreatic neuroendocrine tumors PRRT: Peptide Receptor Radionuclide Therapy, NFPA: Non-Functioning Pituitary Adenoma, TSI: Targeted Secretion Inhibitors



# SOMscan<sup>®</sup> and SOMther<sup>®</sup>, PRRT with high NET potential A theranostic approach

Description

Peptide-Guided Radioisotope for PRRT

Peptide Analog Radioisotope Chelator Peptide Receptor on Chelator Cell Tumor Cell Step 1 Step 2 Step 3

Scientific rationale

Improved receptor binding through antagonist properties



- Targets: pancreatic, ileal and bronchial NETs
- Combination potential: kinase inhibitors, chemotherapy...
- Expansion potential using different GPCR ligands

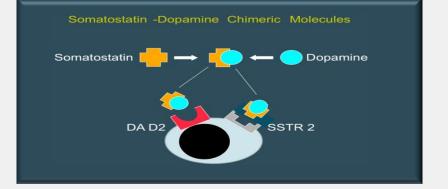
### SOMscan<sup>®</sup> to enter Phase III and SOMther<sup>®</sup> to enter Phase I in 2016



## **Dopastatin 2<sup>nd</sup> generation**



- Enhanced suppression of growth hormone
- Combination of Somatostatin and Dopamin analogs



*∲***IPSEN** 

Scientific rationale

 Improved potency and efficacy in growth hormone suppression vs, Dopastatin 1<sup>st</sup> generation

Medical rationale

- Prime target: acromegaly
- Additional applications: Cushing's Disease, aggressive Adenomas, NETs, non-Functioning Pituitary Adenoma



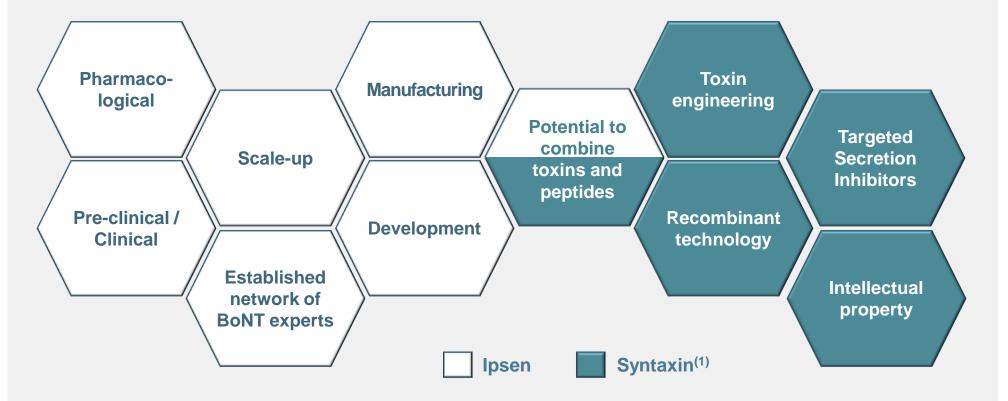
## **Toxins Movement disorders**



# Syntaxin acquisition has significantly reinforced Ipsen's R&D toxin platform

From natural BoNT expertise...

... to full recombinant potential



Ipsen now at the forefront of botulinum technology



# Ipsen BioInnovation, state-of-the-art R&D toxin facility in Abingdon, UK



Full and effective integration of Syntaxin Ltd, acquired in 2013

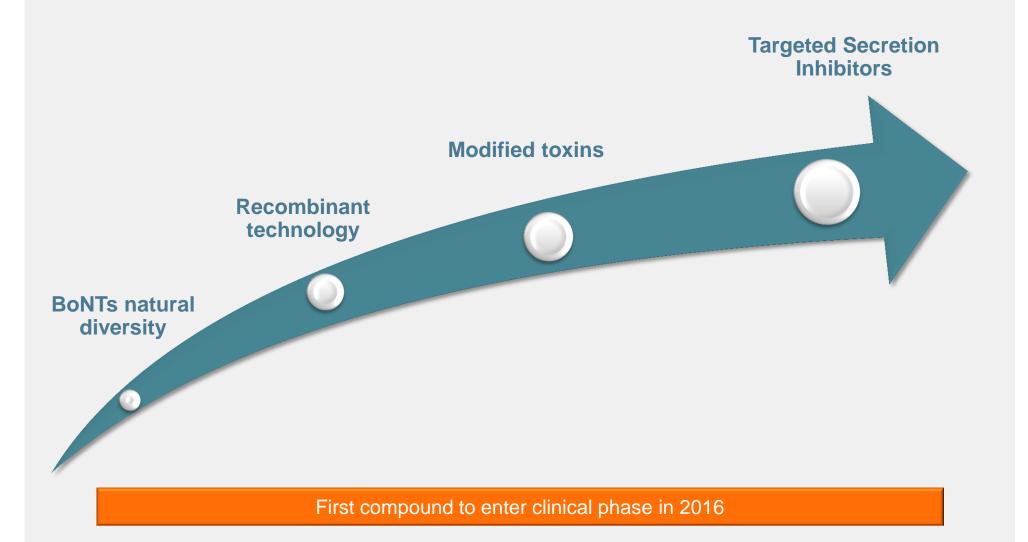
Fully equipped platform for design, manufacturing, and testing of novel toxin-derived proteins

All aspects covered from early research to first-in-man studies

Syntaxin Ltd renamed Ipsen Bioinnovation Ltd in March 2015

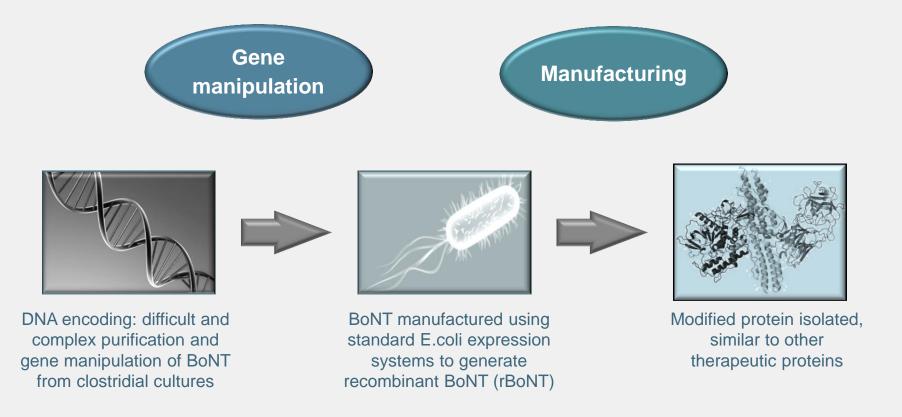


### Ipsen's new-generation toxin programs





### **Recombinant expression of botulinum toxins**

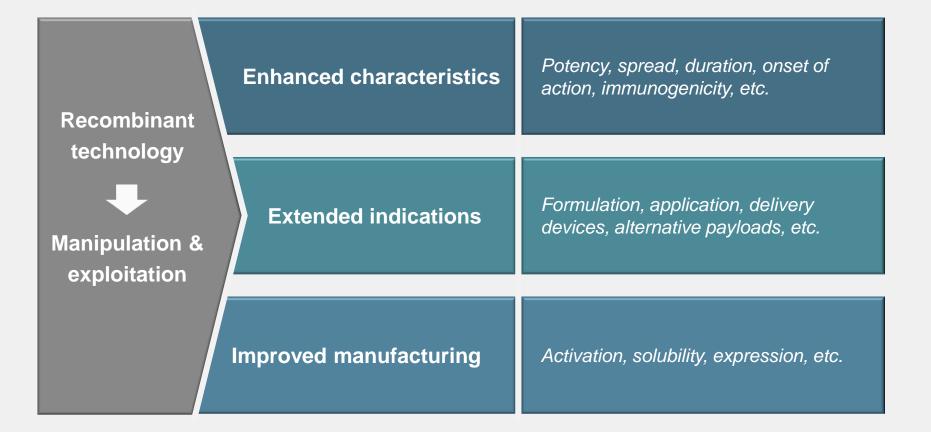


Recombinant expression enables specific modifications to be incorporated into neurotoxin

"Engineered proteins" then created through modified neurotoxins



### Recombinant technology opens up new therapeutic opportunities

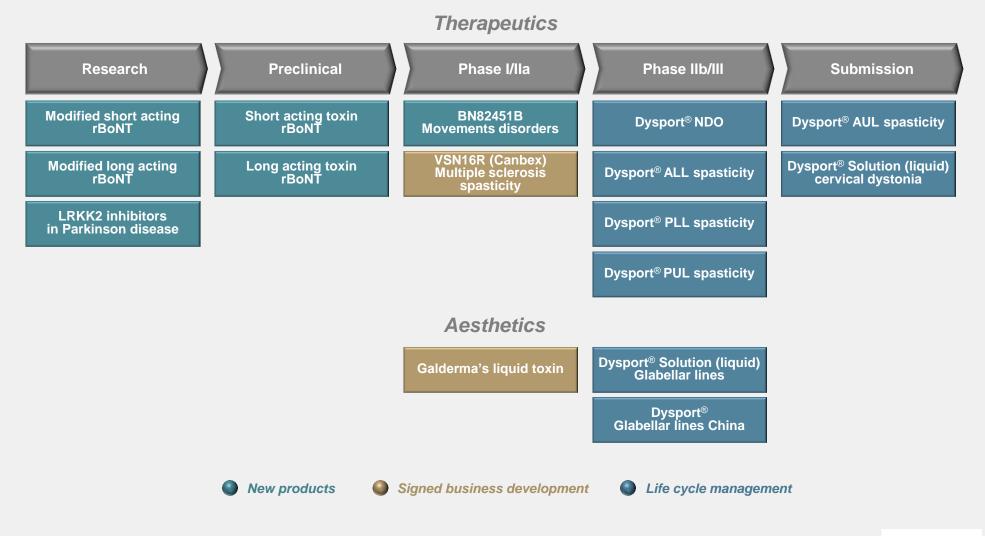


Modified rBoNTs used to design variants across all subtypes of natural BoNTs

New candidates can potentially be used in all therapeutic areas



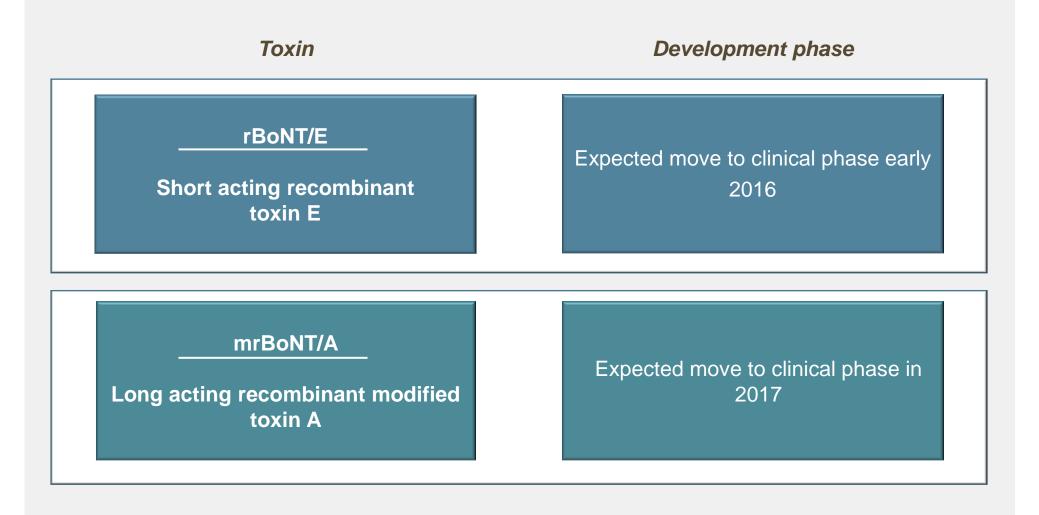
### A rich and balanced neurology/toxin pipeline



Note: AUL:Adult Upper Limb, ALL:Adult Lower Limb, PLL:Pediatric Lower Limb, PUL:Pediatric Upper Limb, NDO:Neurogenic Detrusor Overactivity, rBoNT: recombinant Botulinum neurotoxin

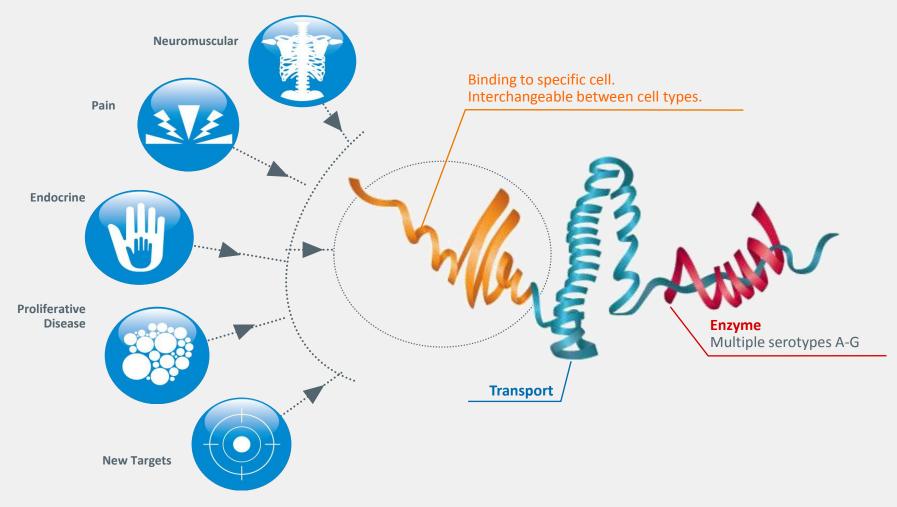


### New generation short and long acting toxins





### **Targeted Secretion Inhibitors (TSI)**



Ability to change the binding site to broaden therapeutic potential



## An R&D model under transformation



### Initiatives to improve R&D productivity



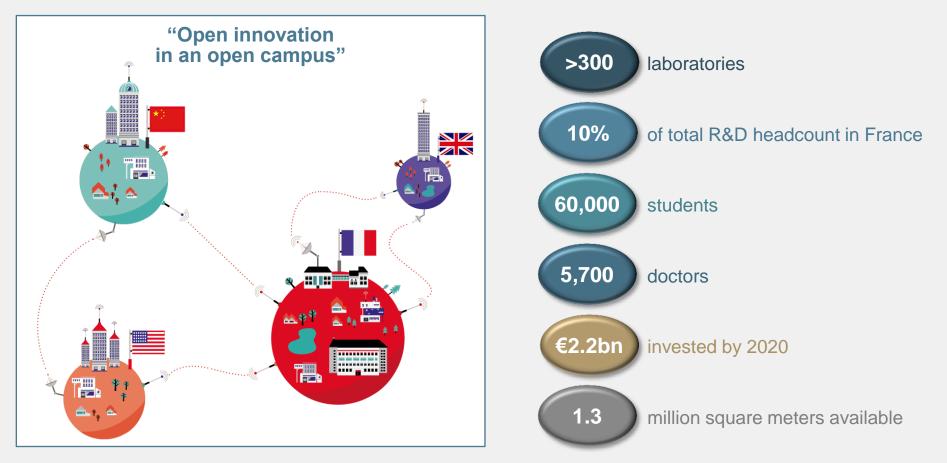
- Biotechs
- Academic clinical centers of excellence
- Strategic sourcing

- In-house resource focused on core activities
- Efficient use of CROs for non-core activities
- Lean organization

- One NME<sup>(1)</sup> every 4 years
- Value-added products: precision medicine and targeted therapies
- 2 technology platforms
- 3 therapeutic areas
- Strengthening early drug development/ POC<sup>(2)</sup> know-how and capabilities



### The Campus concept in les ULIS begins to emerge



#### Paris Saclay: a worldwide cluster at the heart of open innovation

84 Ipsen Investor Day – 2 July 2015



### In-house R&D complemented with an active partnership policy

#### **Early-stage and academic**

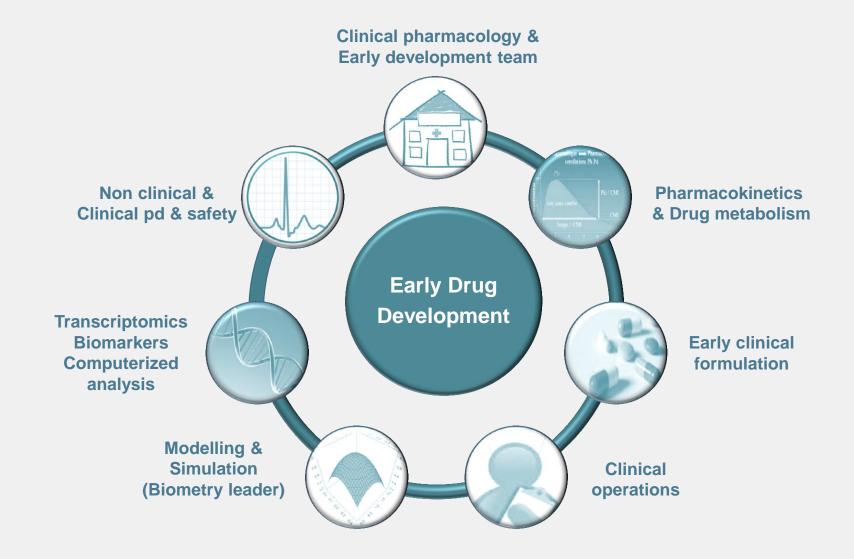
#### Late-stage development & marketing



Open culture at the heart of Ipsen's R&D model

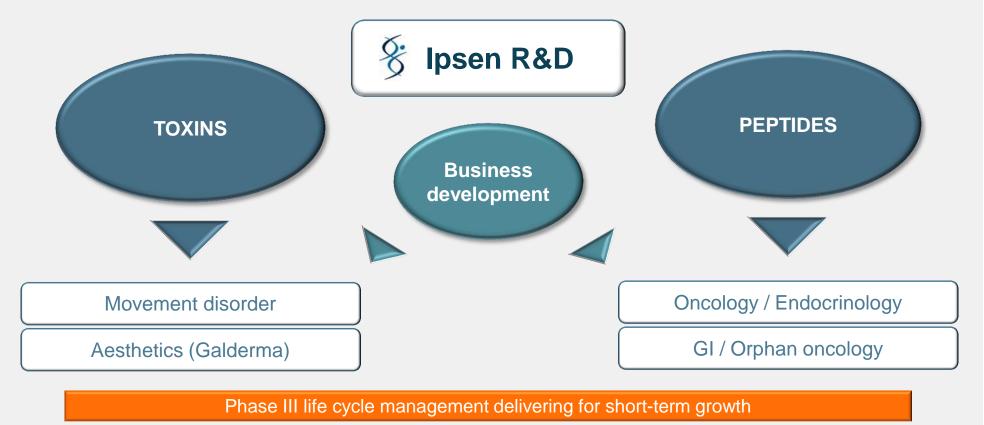


### Early drug development based on integrated expertise





### Key R&D takeaways: a model under transformation fully aligned with Group strategy



A replenished research portfolio to enter clinical phase in the next 5 years

A clinical pipeline to be reinforced with BD and partnerships

Ongoing transformation to improve flexibility and accelerate deliveries

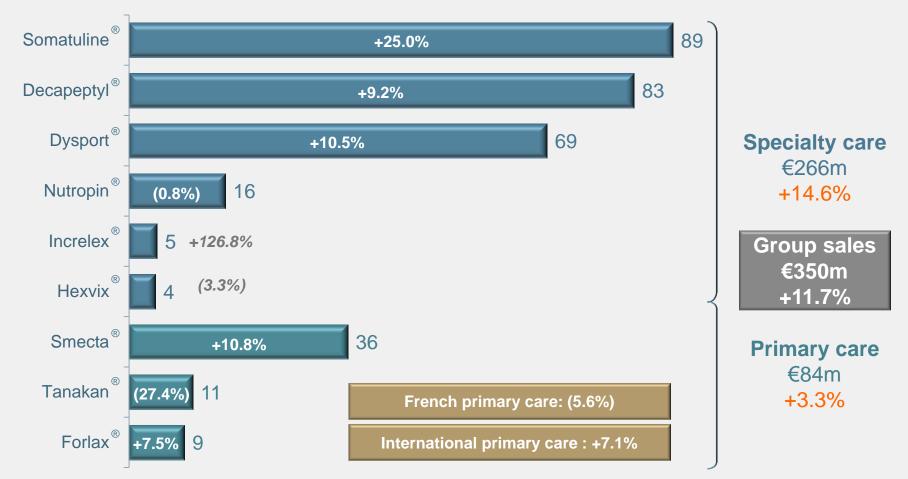


## **Financials**

### Aymeric Le Chatelier Chief Financial Officer



### First quarter 2015 sales driven by strong specialty care

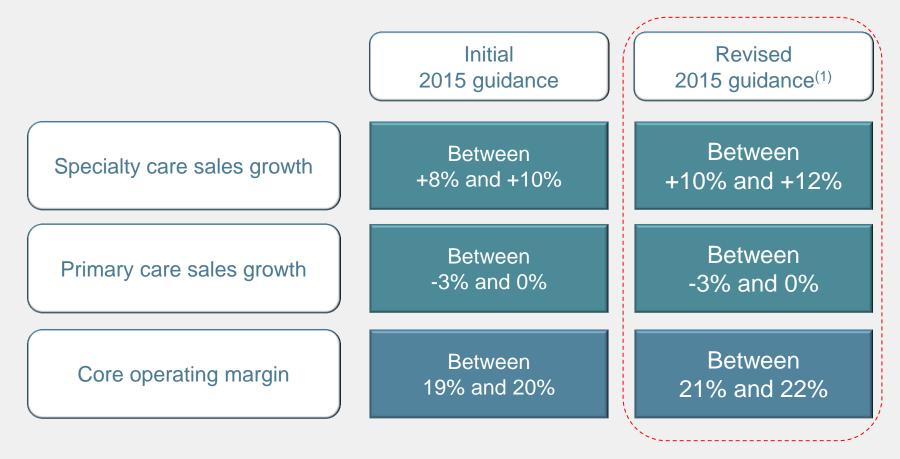


Sales – Q1 2015 (in million euros) – % excluding foreign exchange impact





# 2015 guidance revised upwards to reflect strong specialty care and tasquinimod savings



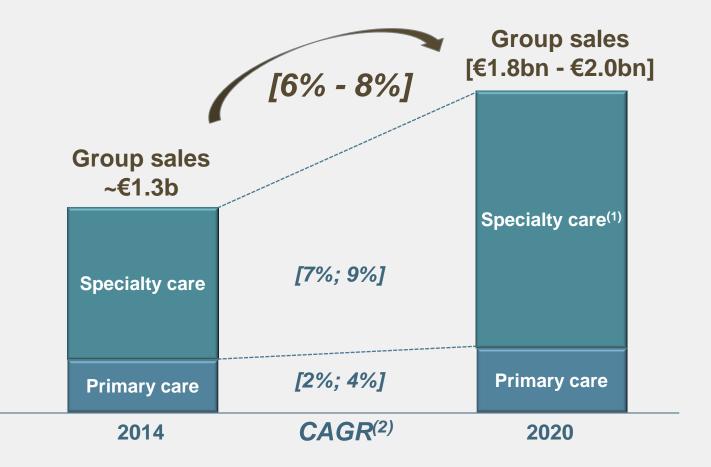
Sales objectives are set at constant currency







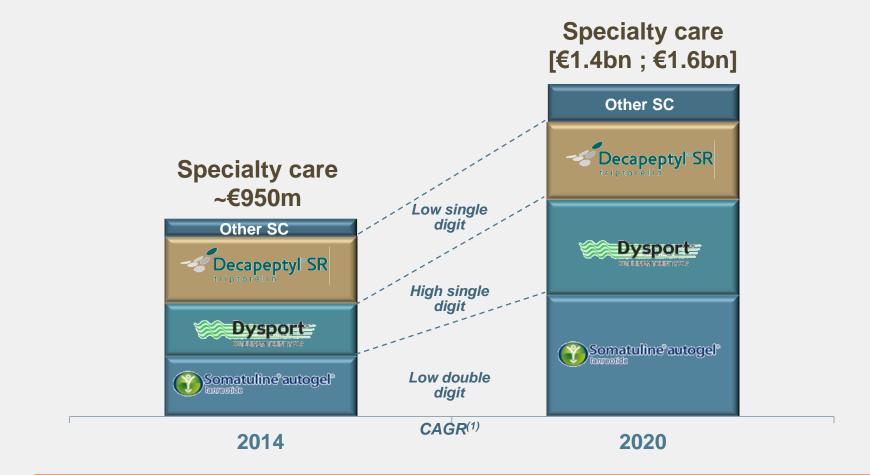
#### 2020 organic sales outlook



Potential Business Development to complement €1.8bn to €2.0bn organic sales target



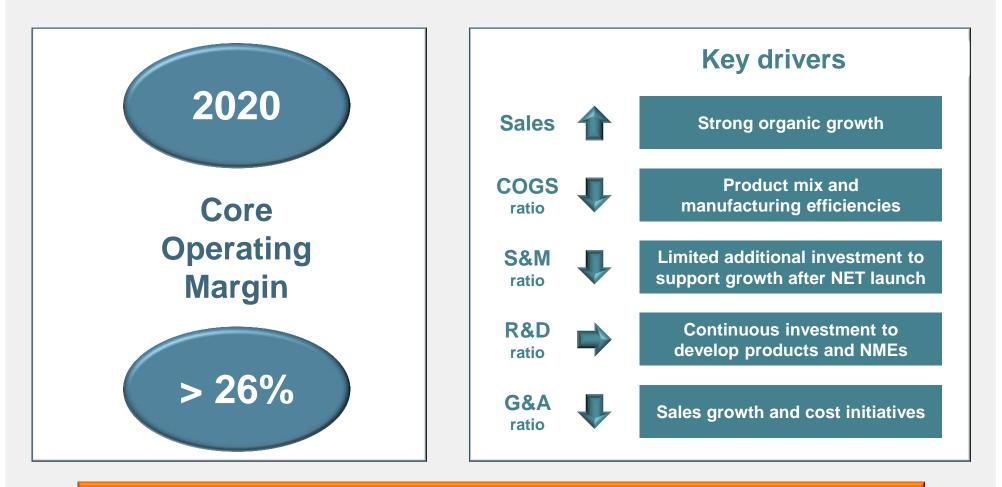
### 2020 specialty care organic sales growth outlook



Somatuline<sup>®</sup> and Dysport<sup>®</sup>, the Group's main growth drivers throughout 2020



### 2020 profitability outlook and drivers



Margin expansion to be mainly driven by sales growth and US profitability



Note: COGS: Cost of Goods Sold, S&M: Sales and Marketing, R&D: Research and Development, G&A: General and Administrative NMEs: New Molecular Entities



### Illustrations of SMM and G&A optimization initiatives

European	<ul> <li>Creation of 3 European business units: Dysport<sup>®</sup> Therapeutics,</li></ul>
Business Units	Hexvix <sup>®</sup> and pediatric endocrinology to: <li>Support growth and optimize resource allocation in Europe</li> <li>Focus on key European accounts</li>

Geographic clustering	Creation of <b>clusters</b> in Spain/Portugal, UK/Ireland, Nordics/Baltics and Eastern European countries:
	<ul> <li>Resource pooling (medical, regulatory, marketing and sales, finance)</li> </ul>

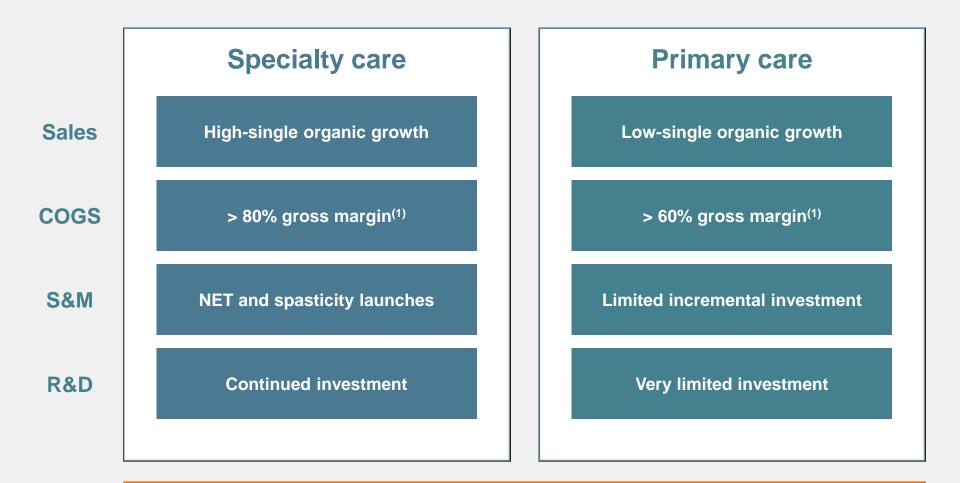
Support functions Streamlining, back-office consolidation, shared services, outsourcing across all support functions: Finance, Human resources, IT...



Note: S&M: Sales and Marketing, G&A: General and Administrative



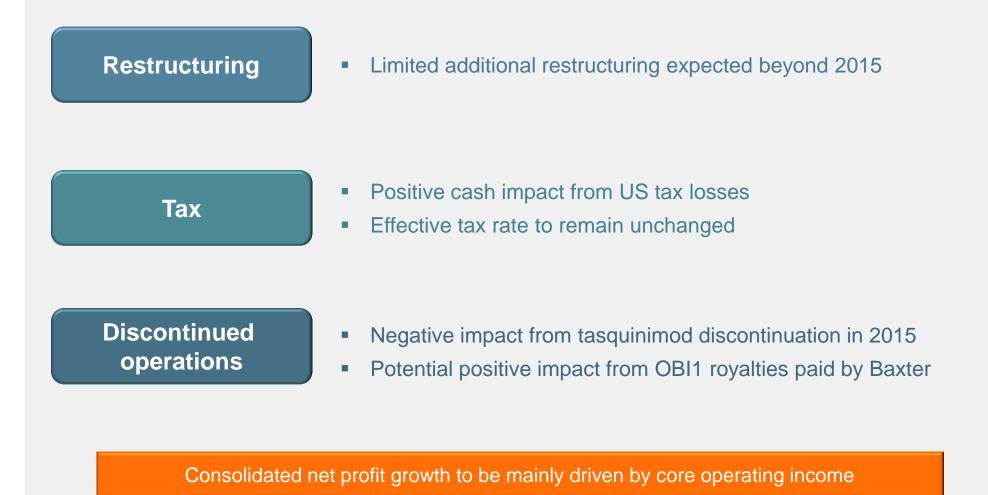
### 2020 profitability drivers per business unit



Specialty care to drive 2020 Group margin improvement



## Evolution of P&L items below Core Operating Income over 2015-2020







### Ipsen to derive potentially significant value from non core outlicensed assets



- Lead compound abaloparatide for treatment of osteoporosis successfully completed Ph3
- Market capitalization > \$2bn
- Ipsen to receive regulatory milestones and royalties on future global sales (ex Japan)



- FDA approval of OBI-1 in
   acquired hemophilia A
- Acquired OBI-1 (factor 8 from porcine origin) from Inspiration Inc bankruptcy
- Ipsen and other sellers to receive royalties based on sales level (started end of 2014)



- 2 lead programs: Relamorelin (Ph2 completed for diabetic gastroparesis) and MC4 (Ph2 ongoing for obesity)
- Ipsen owns 6.11% of equity shares on a fully diluted basis
- Ipsen to receive development and regulatory milestones and royalties on both programs





### **Evolution of cash flow over 2015-2020**



Solid cash generation to finance operations, external growth and return to shareholders

Note: BD:Business development



# Strong balance sheet and financial discipline to support business development ambition



- €600m envelope for acquisitions
- Strong operating cash-flow generation
- €500m revolving credit facility and €180m<sup>(1)</sup> in cash at disposal
- Unleveraged balance sheet/access to attractive financing



- DCF value-based assessment
- Risk-return balance
- Expected synergies
- Specific assessment for early-stage projects

#### Strategic fit and financial discipline drive decision-making





Strong base business growth and financial discipline to increase cash generation...





## Conclusion

### Marc de Garidel Chairman and Chief Executive Officer



#### Key takeaways



Ipsen committed to deliver superior shareholder value



## Thank you

