# First half 2009: confirming Ipsen's specialist care globalisation

SIPSEN Innovation for politeri care

September 3<sup>rd</sup> – 4<sup>th</sup>, 2009 – London Roadshow



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# Introduction





## Ipsen today: a global, innovation driven, specialty pharma

	SPECIALTY CARE A global business to GROW	PRIMARY CARE OPTIMISE returns of this mostly French business		
27%	ONCOLOGY Decapeptyl®	GI	19%	Atrar
17%	ENDOCRINOLOGY Somatuline®, Nutropin®, Increlex®	Cognitive disorders	13%	transactional
16%	NEUROLOGY Dysport® , Apokyn®	Cardiovascular	8%	nal model
-	HEAMATOLOGY OBI-1			<u> </u>
	A fully-fledged manu	ufacturing capability		
	A unique innovation driven and R&D expense	d differentiated R&D capability ~20% of sales		

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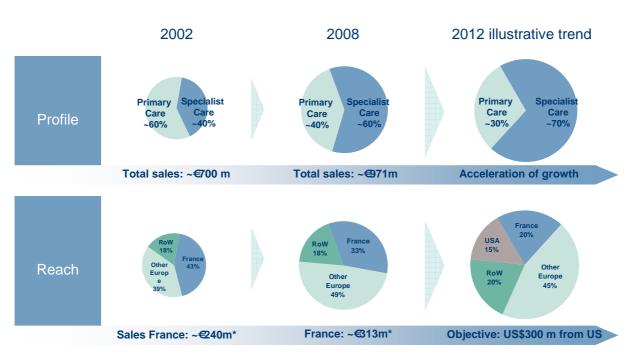


# Ipsen has consistently delivered on its strategic milestones...

LCM	Decapeptyl® - 3 months formulation - Launches in the UK and Germany agreement agreement for 6M filing
	Taspoglutide — Ph I — Roche Opt-in — Ph III →
Pipeline Progress	OBI-1 — Ph I — Octagen Assets — Ph II / III / III — Ph II / III / IIII
	Adenuric® — Ph III — Filing — Approval —
Optimization	Ginkor® Fort divestment  Adrovance® co-marketing  Co-promotion
	Strategic intent  - First step of US entry (endocrinology)  - Somatuline® Depot the US (Endocrinology + Neurology)
US entry	IGF-1 / GH
	Toxin Aesthetics
	Toxin Therapeutic Filing — Approval —

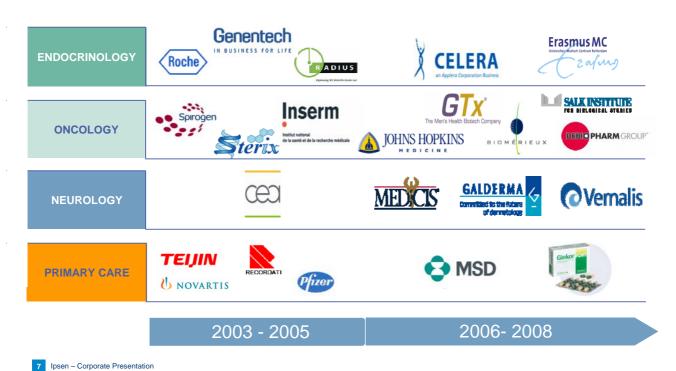


# ... reinforcing the Group's profile and reach





## An increasingly transactional model





## Ipsen today....

- Resilience of business in a difficult macro-economic environment
- A strong and profitable specialty care growth engine
- Substantial growth opportunities through globalization and US entry
- A rich and well balanced R&D pipeline, with potential blockbusters
- A strong cash flow generation and balance sheet

# **Truly Differentiated R&D Capabilities**





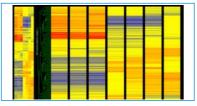
## Defining Ipsen's competitive edge in R&D

Hormones provide well defined templates with matching targets both novel or validated

#### Resident know how based on the integration of basic discovery technologies

## **Technologies**

Target identification, validation and drugability based on clinical observations supported by ...omics technologies



#### **Medicinal chemistry**

Steroids peptides, proteins engineering aiming at enhanced efficacy, potency, selectivity and safety over the endogenous hormone

### **Delivery systems**

Emphasis on improved pharmacological properties, optimization of dosing regimen and improved patients compliance and convenience





# Somatuline® Depot: an improved presentation

	Sandostatin LAR®	Somatuline® Autogel®		
Administration	2.0 ml Intramuscular	0.3 ml – 0.5 ml Subcutaneous		
Presentation	Powder vial + solvent filled syringe + 2 needles	Pre-filled syringe		
Injection technique	10 steps needed to reconstitute	Ready to use Self administration*		



For what reasons would you prescribe Somatuline® Depot to your acromegaly patients?\*\*

More conve	nient be	cause the	e patient	can self i	nject		83%
Saves staff	time and	resourc	<b>es</b> (self-inje	ction possible	e at home)	65%	

\* In selected countries

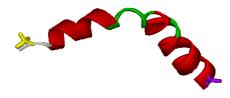
\*\* Study Sample: A total of 50 US endocrinologists completed a 30-minute online questionnaire between April 4 - 17, 2008 25 High Volume Endocrinologists: Endocrinologists who see 11 or more acromegaly patients in a year 25 Low Volume Endocrinologists: Endocrinologists who see between 5-10 acromegaly patients in a year



## An example of this unique technology convergence: taspoglutide

### Once-a-week injection

- Equal / greater potency compared to native compound
- Extended metabolic half-life, 22x more stable in plasma
- Complete retention of incretin properties
- Strong patent positions



### Expected needle gauge

- (LAR) → 23G Quarter inch long
- Taspoglutide Liquid SRF → 29G Insulin type needle for subcutaneous injection

50 to 300 µl of highly concentrated aqueous solution devoid of excipient

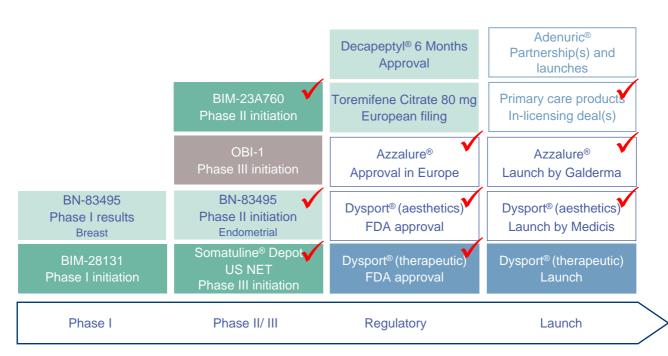
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## First half 2009 achievements





# A rigorous execution of key milestones





# A strong commercial performance in the first half 2009

6.3% Drug sales growth, in line with our full-year objective

A solid 11.5% specialist care sales growth, with endocrinology up 32.7% year-on-year

Stabilisation in Eastern Europe, with Q2 sales up 1.0% year-on-year

Dynamic growth in the US, with Somatuline®, Increlex® and Apokyn® generating \$23 million, up 33% Q2 over Q1

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NOTE: All % sales growth expressed at constant currency



## A strong profitability and cash generation

25.0% operating margin pre-goodwill allocation

A 'clean operating margin'\* of 18.0%, compared with 21.6% a year ago

€147 m generated by operating activities, versus €124 m a year ago

€139 m net cash position as at June 30, 2009, post €203 m net cashed-out on US acquisitions in H2 08

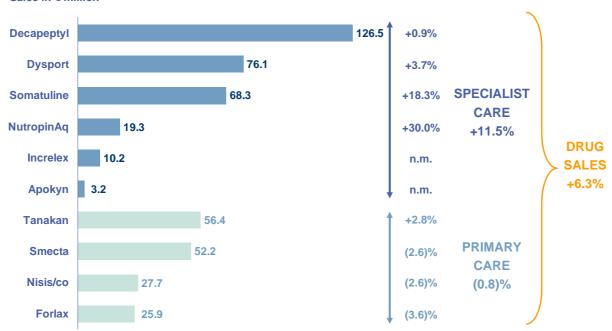
# First half 2009 detailed financial performance





# Main products performances

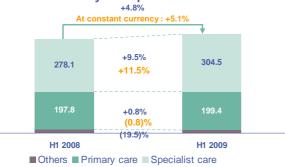




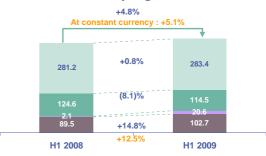


## Top line evolution

# Sales by therapeutic area

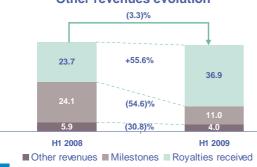


#### Sales by region



■ ROW ■ US ■ Other European Countries ■ European G5

#### Other revenues evolution





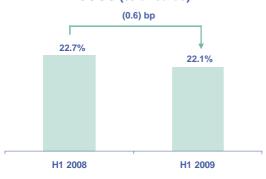


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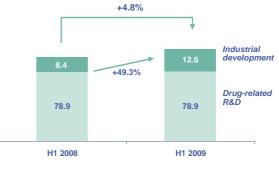


## P&L - above EBIT

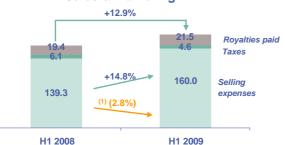
## COGS (% of sales)



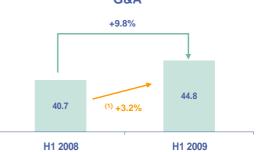
#### **Research & Development**





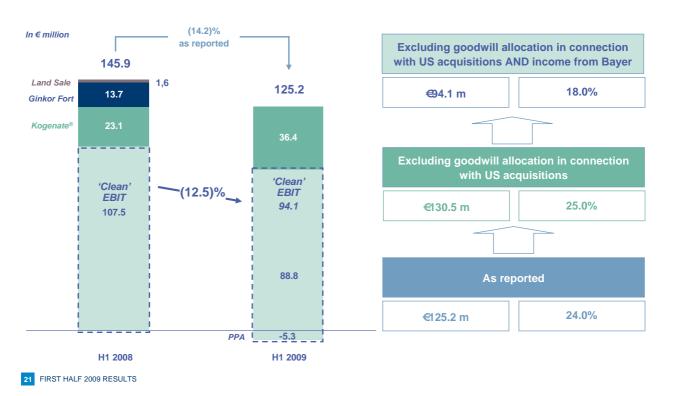


#### G&A



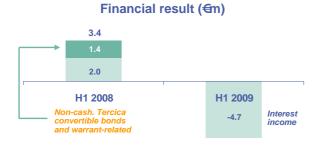


### P&L - EBIT

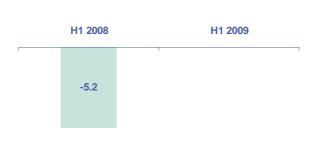




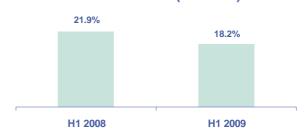
### P&L - below EBIT



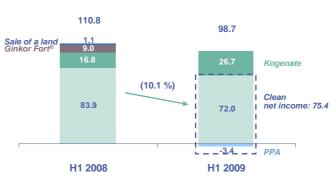
#### Income from Associates (€m)



#### Effective tax rate (% of PBT)



#### Consolidated result (€m - group share)





# **Balance Sheet evolution**

- In million of euros Asset	S		- In million of euros Liabil	ities	
	31 Dec 08	30 Jun 09		31 Dec 08	30 Jun 09
Goodwill	(*) 290.8	290.8	Equity	(*) 885.0	928.4
Property. plans & equipments	237.9	244.7	Minority interests	1.6	1.8
Intangible assets	(*) 232.9	239.3	Total equity	(*) 886.6	930.2
Other non-current assets	(*) 112,9	140.5	Long-term financial debts	160,4	12.7
Total non-current assets	(*) 874.5	915.3	Other non-current liabilities	(*) 196,4	276.3
Total current assets	(*) 688.6	589.7	Short-term debts	8.3	8.0
Incl. cash and cash equivalents	239.6	140.2	Other current liabilities	307.8	275.1
Assets / discontinued operations	1.3	0.7	Liabilities / discontinued operations	4.9	3.5
Total assets	1 564,4	1 505.8	<b>Total Liabilities</b>	1 564,4	1 505.8
Net Cash	66.2	118.9			



(\*) 31 Dec 08 restated after Purchase Price Allocation of Tercica Inc. and Vernalis Inc.



## **Cash flow statement**

	30 Jun 08	30 Jun 09		Comments
- In million of euros				Deferred revenues net increase:
Cash Flow before change in working capital	141.3	121.5	1	€+56.7m (Medicis / Galderma)
- Increase / Decrease in working capital	(17.1)	25.7		,
Net cash flow generated by operating activities	124.1	147.2		Receivables, payables, inventory and others: €-31.0m
Investment in intangible assets and property. plant & equipment	(34.2)	(25.6)	\ \	and others. #31.0111
Others	1.8	(6.8)	1	Tangible assets: €-14.7m
Net cash flow used in investing activities	(32.4)	(32.4)	-	Intangible assets: €-10.9m
Net change in borrowings	(9.8)	(159.4)	\	
Dividends paid	(55.2)	(58.2)		
Others	0.1	-	\-	reimbursement of credit facility:
Net cash flow used in financing activities	(64.9)	(217.6)		€-150m
Discontinued operations	(1.0)	(0.2)	-	Shares buy back: €-6m
Change in cash and cash equivalent	25.8	(103.0)		
Impact of exchange rate fluctuations	(3.0)	4.8		
Closing cash & cash equivalents	263.7	139.1		
Closing Net Cash	239.4	118.9		

# **CEO** update

Jean-Luc Bélingard
Chief Executive Officer





## A productive and unique R&D

Some major projects moving through the pipeline appear to have significant and higher-than-expected market potential

GH+IGF-I combination therapy

BN-83495 in 4 indications

**BIM-23A760** 

OBI-1



An extremely limited attrition:

Over the past 5 years, <u>few major R&D project</u> have been stopped

The Group will ensure the means necessary to develop these new chemical entities match their potential



## **North America: timely acquisitions**

Positive feedbacks received for Dysport®: opportunity in therapeutic use could be larger than anticipated: probable acceleration of launch and intensification of sales & marketing efforts



Differentiated and competitive products addressing significant markets driven by strong and committed local teams

After a transition phase in the context of intense launch activities, Ipsen remains confident on the success of its products in North America in the long term





## **Primary care: toward opportunities**

#### Forlax®:

Mitigation strategy currently in force

#### Smecta®:

Capitalising on the strength of the brand

**Ipsen's primary care products:** Strong brands, strong recognition, significant market potential

Strong sales networks, with significant presence in emerging markets, notably China and Russia

Ipsen is regularly evaluating the business opportunities presented by the evolution of the primary care environment



Ipsen is moving up toward a reinforced profile, with enhanced growth potential

A unique R&D

A strong potential in the US

Primary care opportunities

A strong financial situation

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Outlook and progress on the remaining milestones





# A rigorous execution of key milestones

IGF-I+GH combo

Decapeptyl® 6 Months **Approval** 

Adenuric<sup>®</sup> Partnership(s) and launches

Toremifene Citrate 80 mg European filing

OBI-1

BN-83495 Phase I results Breast / Prostate

BIM-28131

Phase I

Phase II/ III

Regulatory

Launch

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## Delivering on our key objectives...

#### IGF-I + GH combo

Phase II pediatric results LWPES/ESPE

## Decapeptyl® 6 Months

First approvals expected before year-end

#### **Adenuric**®

In final negotiation stage Partnership expected before year-end

### OBI-1

#### BN-83495

Phase I results at San **Antonio Breast Cancer** Symposium on December 9-13, 2009

Phase I

Phase II/ III

Regulatory

Launch



### **Outlook**

2009 financial objectives confirmed

Drug sales growth of 7.0 to 9.0%

Operating margin pre-Kogenate royalty and before goodwill allocation of around 14.0%

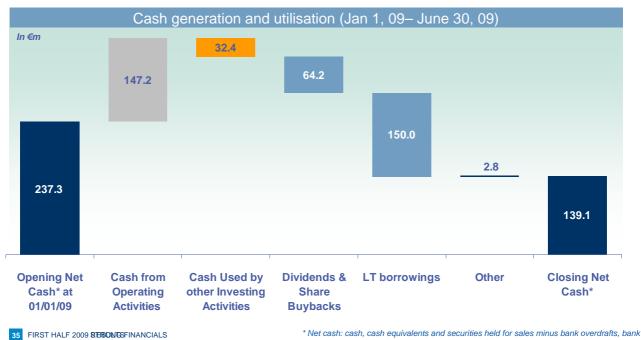
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# **Financial appendices**





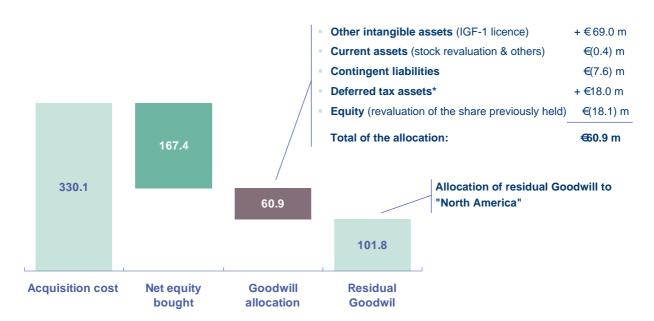
## **Cash flow generation**



borrowings and other financial liabilities plus or minus derivative financial instruments



# Allocation of the Tercica purchase price accounting





# Milestones Cashed in but not yet Recognised as Revenues

- In million of euros	30 Jun 08	30 Jun 09
Payments recognised as revenues in year N+1	11.2	12.1
Payments recognised as revenues in years N+2 and beyond	205.7	195.2
Total Milestones cashed in but not yet recognised as revenues	216.9	207.3



Decrease linked to global consolidation of Tercica and elimination of deferred revenues on Somatuline US

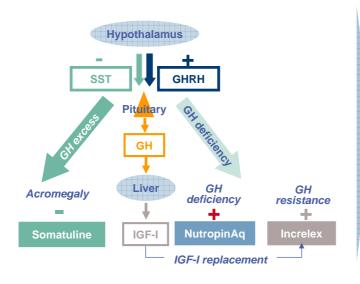


# An endocrinology franchise outgrowing competition





## A unique focus on pituitary disorders and hormone dependent diseases



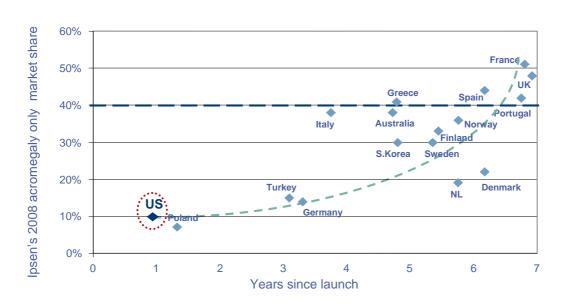
#### A strong franchise

- A range of products addressing today Short Stature, Acromegaly and NET
  - High morbi-mortality
  - Debilitating pathologies
  - High unmet medical needs
- Somatuline®, NutropinAq® and Increlex® contributed to ~16 % of 2008 Group sales, ie. ~ €158 million.
- A fast growing franchise: sales doubled in the past 3 years





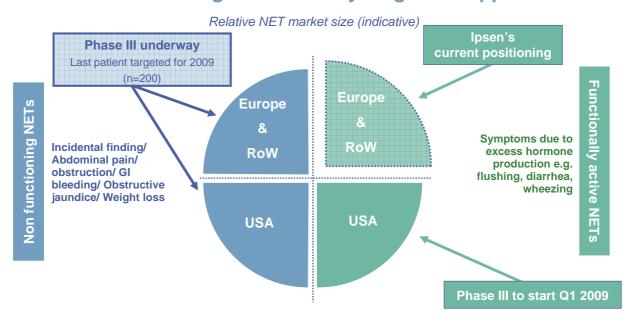
## Somatuline® Depot is poised to grow and gain market share



Somatuline® market share is directly correlated to its time on market



# Somatuline® offers significant life cycle growth opportunities



Significant scope for expansion

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## Increlex® in the US: steady performance with continued growth expectations

Physician demand

- Target audience : ~1,000 US paediatric endocrinologists
- Up to 20% of Rx come from new prescribers each month
- 2/3 of pediatric endocrinologists have prescribed Increlex®; 78% continued prescription

Reimbursement

- ~ 90% of private and public covered lives have formulary access
- 75% Increlex patients approved upon final decision (similar to GH)

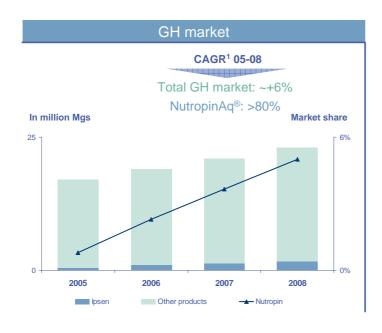
Patient experience

- Sharp increase in patients on Increlex® initially GH-naïve to 60% in '08 from
- Dose increasing to appropriate targets, to 100 mcg/kg BID in '08 from 70 mcg/kg BID in '07
- Younger patients initiated with Increlex®, to average age at start of 10.0 years old in '08 from 11.5 years in '07





# NutropinAq® in Ipsen territories is steadily gaining market share



#### NutropinAq® attributes

- 1st liquid formulation launched WW
- A simple and user friendly pen
- An experienced post marketing surveillance database
- A dedicated experienced and professional team

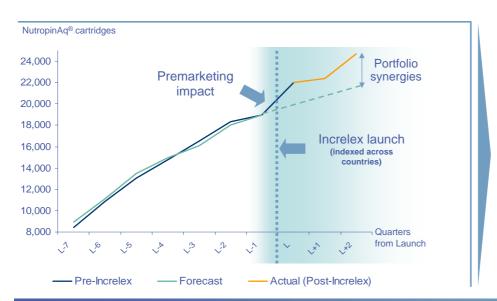
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Source: Strategix





# NutropinAq® + Increlex®: evidence of portfolio synergy



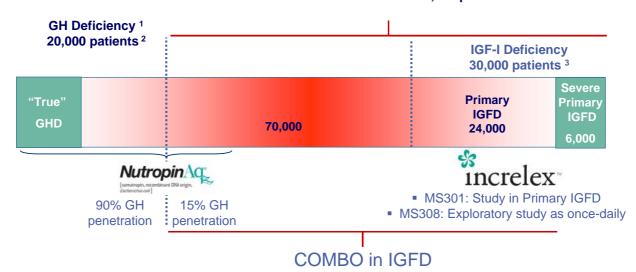
**Up to 10%** favorable impact

"Ipsen is the only company that can legitimately claim to treat all forms of growth failures through the spectrum of GH deficiency to GH resistance' Pr. Martin Savage, St Bartholomew's Hospital, London



# **Ipsen** is redefining the treatment of short stature

#### Non-GH Deficient Short Stature: 100,000 patients in the US



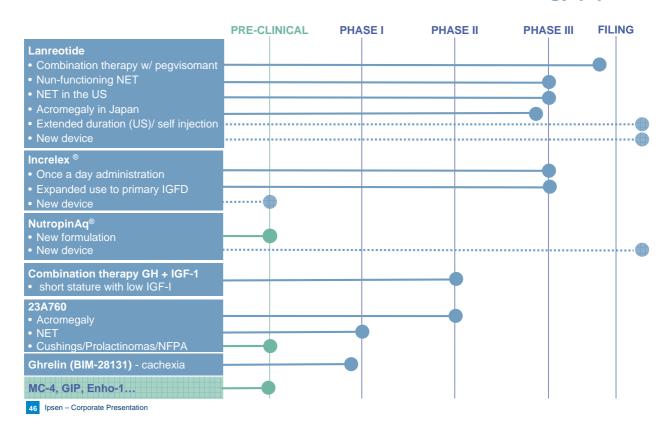
- MS316: Ph.II dose titration studyrecruitment to be completed by Q2 '09
  - Ph.II study in GH Deficient children to start by end '09

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1) Includes TS, SGA, CRI, PWS 2) Approximate number seen by Ped Endos; Finkelstein et. Al. 3) NCGS Analysis



## A rich endocrinology pipeline

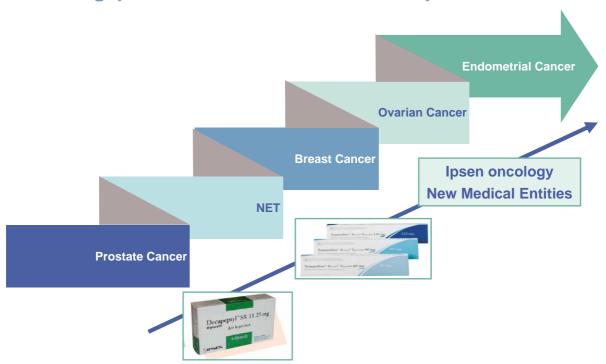


# Confirming Ipsen as a leader in the field of hormone dependent cancers





# **Confirming Ipsen as a leader in Hormone Dependent Cancers**





## Decapeptyl® 3 months formulation: a competitive product profile

# Formulation and efficacy

- Marketed 1 month (1M) and 3 month (3M) formulations
- Maintenance of castrate testosterone levels at 3M in 98% of patients<sup>1</sup>
- At 3M, 91% decrease of PSA levels, showing tumor control

#### Local tolerance/ convenience

- IM route of administration, good local tolerance
- Injection not visible for the patient

# Storage and reconstitution

- Stored at room temperature
- 5 steps reconstitution
- Safety needle system

#### Competitor 1

#### itor 1 Competitor 2

#### Competitor 3

# Formulation and efficacy

- Various formulations across territories:
   1M formulation = 3,75mg or 7,5mg and 3M formulation = 11,25mg or 22,5mg
- Increased survival rate at 9 months in triptorelin group vs competitor 1<sup>2</sup>
- Conservation between 2 4° = needs to be warmed up before reconstitution
- Manual reconstitution to obtain SR
- Risk of nodules, abscess
- Ready to use implant
- Very large needle : need of local anesthesia

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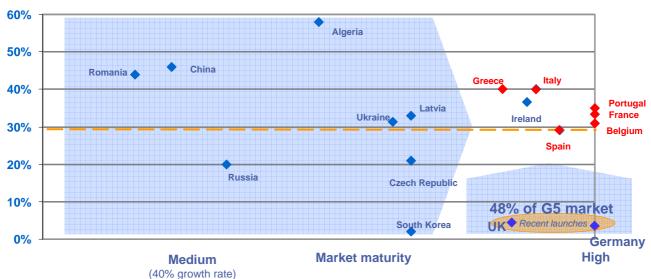
SOURCE: French SmPC

REFERENCE . 1: Teillac, Horm Res,2004, 252-58 2: Heyns, BJU Int, 2003, 226-231



## Decapeptyl®: strong positions, and poised to grow

#### **Current market share**



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# Decapeptyl® 6 month formulation: a more differentiated product profile

Efficacy

- Comparable efficacy to 1 and 3 months formulation
  - Castration levels (testosterone)
  - Disease control (PSA)

Local Tolerance

Limited local side effects (6.7% of patients )

Storage and

- Storage at room temperature (no need to heat up before reconstitution)
- 5 Steps to reconstitute, change needle, and inject IM route

#### 6 month competitor 1

# Formulation/

- 80% of patients castrated after 6M<sup>2</sup>
- Testosterone to be tested every 6M\* 1
- Formation of Nodules or abscess <sup>1</sup>

#### 6 month competitor 2

- Slow release formulation dependent on manual 60 mixture¹ step
- Storage at 2-4°: need to heat up for reconstitution ¹

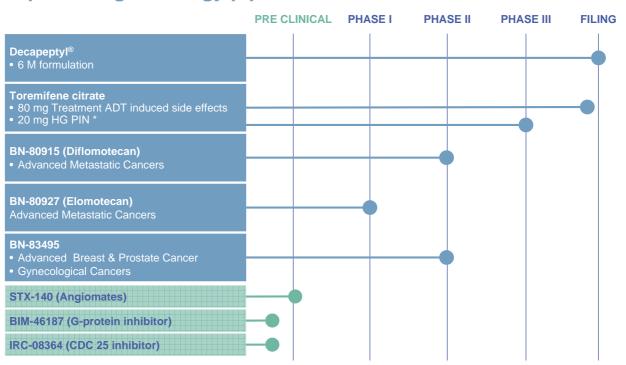
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Reference 1: French SmPC

<sup>2</sup>Avis de la commission de transparence



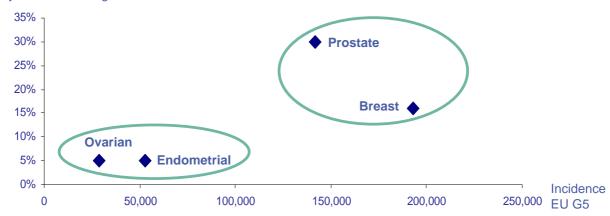
## A promising Oncology pipeline





## Moving up to higher prevalence diseases and higher unmet medical needs

5 year survival stage IV disease



Ipsen New Medical Entities: multi targeted agents aiming at large markets as well as niche indications with large unmet medical needs BN-83495 is potentially a company transforming product

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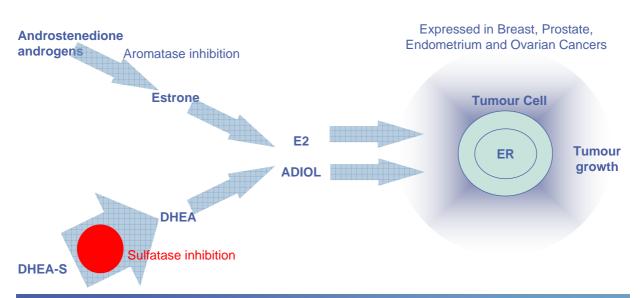
SOURCE: deVita (2008), Datamonitor

BN-83495



## Rationale for Sulfatase inhibitor development

Inhibition of Androstenediol synthesis from DHEA-S



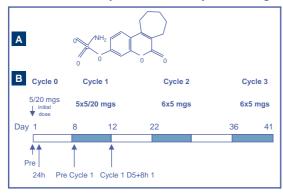
Adiol can bind to oestrogen receptor and stimulate tumour growth (90% Adiol derived from DHEA-S in post-menopausal women)

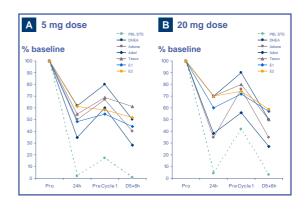


## First clinical study in Breast Cancer patients

STS inhibition leads to significant reduction in circulating steroids and induces clinical benefit\*\*

First clinical study CR UK \* - Daily x 5 dosing





Next step: confirmation of the results in Metastatic Breast Cancer and exploration of the full range of hormonal dependent tumours

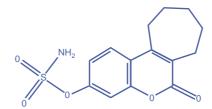
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\* SOURCE: Stanway, S. J. et al. Clin Cancer Res 2006;12:1585-1592 \*\* 3 patients with stable disease >6M

BN-83495



## BN-83495 in a nutshell: a new mechanism of action and potential therapeutic breakthrough



Tricyclic coumarin sulfamate

#### Irreversible Oral steroid sulfatase (STS) inhibitor

Preclinical data supporting correlation between STS inhibition and tumour suppression in **Endocrine Cancers** 

Early clinical POC in metastatic Breast Cancer

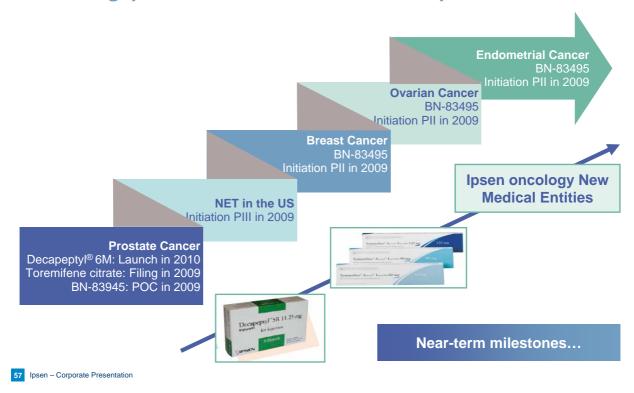
POC trial in HR Prostate Cancer commenced Jan. 2009

POC trials in Gynecological Cancers to commence in 2009

Strong patent platform position & available back-up



# **Confirming Ipsen as a leader in Hormone Dependent Cancers**

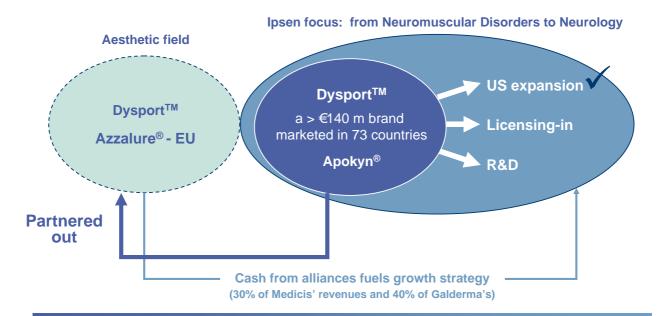


# From a Regional Neuromuscular Specialty to a Global Neurology Franchise





## A specific therapeutic focus

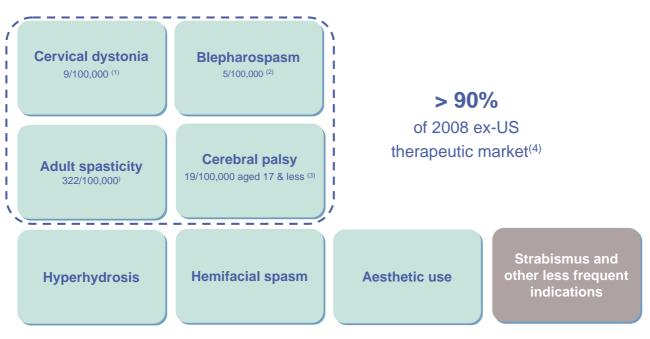


Dysport<sup>™</sup>: the cornerstone of a Neurology franchise

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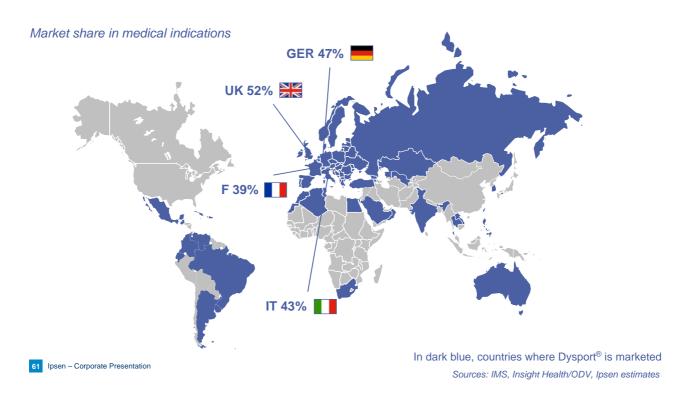


# Dysport<sup>™</sup>: approved ex-US in most key indications





# Dysport<sup>TM</sup>: launched in 1991, approved in 73 countries





# A good track record at catching-up market shares...





# Dysport<sup>™</sup> in the US: a step further toward a global neurology franchise

- 1. Dysport<sup>TM</sup>: a proven track record and field proven product
- 2. A true global product
- 3. A unique focus on medical use
- 4. Focus on US opportunity strong positioning with well prepared launch
  - Sound value proposition: the medical treatment alternative
  - Targeted and appropriate sales force
  - Managed care experience
- 5. Building up a neurology franchise leveraging the business development capability
- 6. Intense efforts in the discovery area



# A focused haematology presence





## An agent targeting both acquired and congenital hemophilia

### Congenital hemophilia A

with inhibitors to human FVIII

- Affects 1:4000 male births
- The development of neutralizing antibodies (inhibitors) to hFVIII following replacement therapy is a major complication
- Inhibitors develop in about 28% of severe patients and in between 3% to 13% of mild and moderate hemophilia A patients
- Patients no longer respond to hFVIII therapy

#### Acquired hemophilia

Acquired factor VIII inhibitor

- Affects 1 to 2 individuals in 1,000,000. predominantly in older individuals
- A small proportion of younger patients may develop the disease, predominantly postpartum women
- Clinical manifestation is more severe and anatomically diverse than in congenital hemophilia A
- A mortality rate approaching 20%. Bleeding is often spontaneous or in response to minimal trauma

pFVIII is a promising treatment to stop bleeds in patients with inhibitors to hFVIII



65 Ipsen – Corporate Presentation



## Now preparing for phase 3...

2 prospective clinical trials, in liaison with Medical Community & Regulatory Agencies

Study in patients with acquired factor VIII inhibitor (acquired hemophilia)

Treatment of all acute bleeding episodes

Study in patients with congenital hemophilia A and inhibitors to hFVIII

Treatment of life or limb threatening bleeding episodes

Both will be of similar design Open label, non comparative prospective studies, with about 40 patients in each study

Standards setting: first ever prospective trial in acquired hemophilia

Protocols finalization and pre-phase 3 CMC consultations with regulatory agencies to be completed in H1 2009



# A highly specialized hospital product addressing unmet need

First biologics to conclude Phase 2 resulting from strategic biotechnology platform

Patent protection until 2023 in Europe and US

World-wide commercialization rights

Lean commercial infrastructure

A commercial potential in excess of US\$200 million

Fourth specialty therapeutic focus in Haematology