IPSEN
Innovation for patient care

ANNUAL REPORT 2008

IPSEN
ANNUAL REPORT 2008

13.9%
SALES GROWTH
IN SPECIALTY CARE IN 2008

IPSEN, A GLOBAL PHARMACEUTICAL GROUP,
HAS OPTED FOR AN ORIGINAL DEVELOPMENT MODEL TO NURTURE INNOVATION:

- a commitment to actively investing in Research and Development, and particularly in biotechnology (peptides, proteins, steroids, sustained-release formulations);
- a specialisation in four therapeutic areas with strong added value (oncology, endocrinology, neurology, haematology) and historical presence in primary care;
- an active partnership policy with distinguished academic research centres and leading global companies, granting it access to complementary resources and skills, whilst extending its product portfolio.

Ipsen is striving to become a key global player in its targeted therapeutic areas. Ipsen holds a long-term vision to transform its knowledge in life sciences into innovative medicines, providing physicians and patients with the treatment options that fit their needs. ■

MESSAGE FROM THE CHAIRMAN

"THE ACQUISITIONS COMPLETED IN 2008 AND THE ADVANCES MADE IN OUR STRONG PIPELINE OF MOLECULES IN DEVELOPMENT, HAVE REINFORCED IPSEN'S ABILITY TO BRING INNOVATIVE THERAPEUTIC SOLUTIONS TO THE MARKET."

JEAN-LUC BÉLINGARD

2008 marked a turning point in Ipsen's history: with the establishment of a fully-fledged commercial presence on the US market, our company has taken on a new dimension and is now positioned as a global player in public health and life sciences. Its long-term commitment to Research and Development (R&D), its ability to provide international markets with new molecules and its strong sales and financial performance were the landmarks of the past year.

A FULLY-FLEDGED COMMERCIAL PRESENCE IN NORTH AMERICA

In 2008 our penetration of the US market took a major step with the acquisition of all the publicly held shares of the Californian biotech company Tercica, as well as the acquisition of the US subsidiary of Vernalis plc.

Ipsen now markets three drugs in the United States: Apokyn® for treating Parkinson's disease, Increlex® for the treatment of growth failure due to IGF-I deficiency and Somatuline® Depot for the treatment of acromegaly. On 29 April 2009 the FDA granted a marketing authorisation in the US for Dysport™, which means that Ipsen will be able to provide US practitioners and patients with four highly effective products in 2009.

These transactions have given Ipsen access to a strong operational infrastructure in the world's largest pharmaceutical market. Our US platform presents sales potential of more than $300 million by 2012 and close to $1 billion by the end of the next decade.

LONG-TERM COMMITMENT TO RESEARCH AND DEVELOPMENT

In 2008, the Group's R&D expenditure totalled €182.9 million, representing around 19% of sales. The extent of this expenditure epitomizes the Group's scientific impetus, with the number of clinical trials conducted on molecules from its pipeline due to triple in 2009 at over 1,600 sites worldwide.

The originality of Ipsen's research lies in the convergence of its technological platforms (steroid, peptide and protein engineering, advanced drug delivery), which are applied to its specialised therapeutic areas (endocrinology, haematology, oncology, neurology) in order to discover, develop and bring to the market highly differentiated drugs.

In haematology, Ipsen's acquisition of all Octagen's assets related to OBI-1, the porcine recombinant Factor VIII, gave Ipsen complete control over the clinical development of this molecule, for which phase II clinical trial results for the treatment of certain types of haemophilia are very promising.

In oncology, Ipsen has gained specific expertise in the biosynthesis of steroids and is developing BN 83495, a sulphatase enzyme inhibitor with a wide range of potential indications, which is currently in phase I for postmenopausal breast

cancer expressing estrogenic receptors and in metastatic prostate cancer. This molecule is due to enter phase II trials in 2009 for the treatment of endometrial cancer.
In endocrinology, the positive results of phase II trials obtained by Roche and Ipsen with their first human GLP-1 analogue for weekly administration were presented at the American Diabetes Association Congress in June 2008. Based on these promising phase II results, Roche has made the decision to move Taspoglutide into phase III clinical trials, thus demonstrating their confidence in the potential of this very promising anti-diabetic drug. Discovered by Ipsen's research teams, its scientific and technological profile shows great medical benefits and characteristics, thus clearly differentiating it from existing drugs in the same class. In addition, by acquiring Tercica, Ipsen has vastly improved its R&D portfolio in endocrinology.
Ipsen has also synthesised an innovative chimeric compound, BIM 23A760, combining a somatostatin analogue and a dopamine agonist to achieve synergic therapeutic effects in pituitary adenomas such as acromegaly and in neuroendocrine tumours.

RENEWING THE PORTFOLIO OF DRUGS ALREADY AVAILABLE ON THE MARKET

A strong pipeline and development of new alliances will enable the Group to bring new drugs to the market in the near future.
In May 2008, the European Commission granted marketing authorisation for Adenuric® (febuxostat) for the treatment of chronic hyperuricaemia in gout, a severe debilitating disease.
Similarly, in oncology, the filing process of the 6-month sustained-release formulation of Decapeptyl® in Europe for the treatment of locally advanced or metastatic hormone-dependent prostate cancer started in September 2008.

In neurology, on 29 April 2009, the FDA granted marketing authorisation for Dysport™, our botulinum toxin type A for the treatment of cervical dystonia and also for aesthetic medicine.
In February 2009, our botulinum toxin Azzalure® received the collective green light from 15 European countries' Health Authorities for the granting of national marketing authorisations, in aesthetic use for the treatment of frown lines.
National marketing authorisations for Azzalure® have already been granted in the United Kingdom, Denmark, Portugal and France.

SALES AND FINANCIAL PERFORMANCE CONFIRMED

In 2008, for the first time, Ipsen's revenues came out above the symbolic €1 billion mark, up 8.2% on a comparable basis with 2007, which is twice the growth of the global pharmaceutical market.
The operating margin reached 21.6%.
Despite the global economic downturn, Ipsen has confirmed its ability to increase market share and diversify its growth drivers, especially its geographic expansion.
These achievments reflect the daily commitment of the Group's 4,200 employees, to whom I wish to express my gratitude, in addition to the strategic support of the Board of Directors, whose long-term vision is a key asset in building future growth. ■

KEY FIGURES 2008

TOTAL REVENUES* (€ MILLION)

2008: **1,038.1**

2007: **993.8**

2006: **945.3**

In 2008, for the first time ever, Ipsen's revenues came out above the symbolic €1 billion mark.

SALES (€ MILLION)

2008: **971.0**

2007: **920.5**

2006: **861.7**

In 2008, Group sales on a comparable basis (excluding consolidated sales of the North American acquisitions, excluding Ginkor Fort® sales and at constant exchange rates) rose sharply by 8.2% compared with the previous year.

RESEARCH AND DEVELOPMENT EXPENDITURE (€ MILLION)

2008: **182.9**

2007: **184.7**

2006: **178.3**

R&D expenditure totalled €182.9 million in 2008, representing 18.8% of sales, compared with €184.7 million in 2007, i.e. 20.1 % of sales, due to high expenditure incurred in preparing the FDA inspections linked to Dysport™ and Somatuline® Depot being filed for registration in the US Excluding industrial development and foreign exchange impacts, the Group's pharmaceutical R&D expenditure increased 11.1% year-on-year.

CONSOLIDATED NET PROFIT (€ MILLION)

2008: **147.2**

2007: **150.6**

2006: **144.0**

Consolidated net profit (attributable to equity holders of Ipsen SA) remained stable in 2008 compared with 2007.

OPERATING PROFIT (€ MILLION)

2008: **180.1**

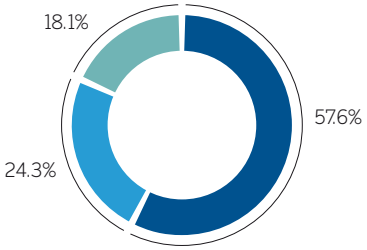
2007: **208.9**

2006: **187.2**

In 2008, operating profit totalled €180.1 million, representing 18.5% of sales. Excluding the impact of the North American acquisitions, the operating margin came out at 21.6% of Group sales.

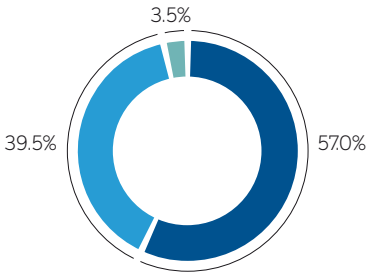
*Total revenues include sales as well as royalties and payments received in conjunction with the Group's partnerships and various other services.

SALES BY GEOGRAPHICAL AREA



- **Major Western European countries 57.6%**
  - France **34.4%**
  - Italy **7.2%**
  - Spain **6%**
  - Germany **5.6%**
  - United Kingdom **4.4%**
- **Other European countries 24.3%**
- **Rest of the world 18.1%**

SALES BY THERAPEUTIC AREA

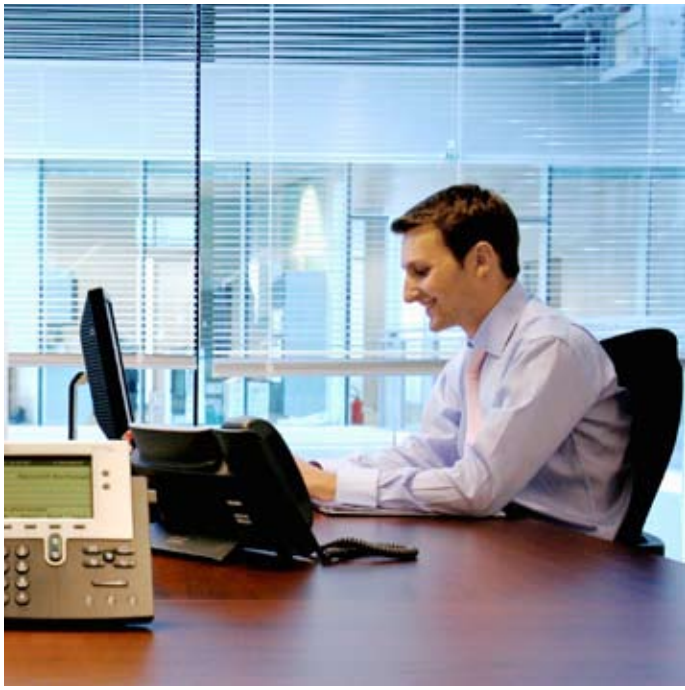


- **Specialty care 57.0%**
  - Oncology **25.6%**
  - Endocrinology **16.5%**
  - Neurology **14.9%**
- **Primary care 39.5%**
  - Gastroenterology **18.8%**
  - Cognitive disorders **11.2%**
  - Cardiovascular **8.0%**
  - Others **1.5%**
- **Drug-related activities 3.5%**
  (active ingredients and raw materials sales)

SALES OF THE GROUP'S LEADING PRODUCTS (€ MILLION)

	2008	2007	change 2008/2007
Decapeptyl®	247.7	235.1	5.4%
Dysport™	142.5	128.7	10.7%
Somatuline®	120.6	103.6	16.4%
Tanakan®	109.2	119.3	-8.5%
Smecta®	93.2	88.9	4.8%
Nisis® and Nisisco®	57.7	53.7	7.5%
Forlax®	53.8	51.8	3.8%
NutropinAq®	32.5	23.7	37.1%

IPSEN SHARES



LISTED ON: Segment A of Eurolist by Euronext™

ISIN CODE: FR 0010259150

MNEMONIC: IPN

FTSE CLASSIFICATION: 486 – Pharmaceuticals

SECTORIAL CLASSIFICATION ICB: 4577 – Pharmaceuticals

NOMINAL VALUE: €1

FIRST TRADING DAY: 7 December 2005

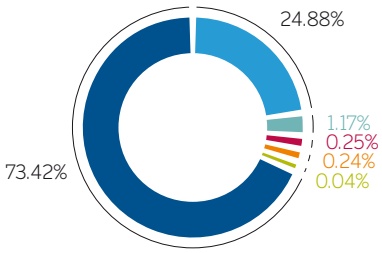
INVESTOR RELATIONS: David Schilansky, Pierre Kemula
investor.relations@ipsen.com

CORPORATE AGENDA 2009[1]

29 January	Full year 2008 sales
2 March	Full year 2008 results
28 April	First quarter 2009 sales
4 June	General Shareholders' Meeting
12 June	Payment of 2008 dividend [2]
28 August	First half 2009 sales and results
29 October	First 9 months 2009 sales

(1) This financial calendar is for indicative purposes only and the Group could change its publication dates should it deem it necessary.
(2) Upon shareholders' approval (General Meeting on 4 June 2009).

SHAREHOLDING STRUCTURE
as of 31 December 2008

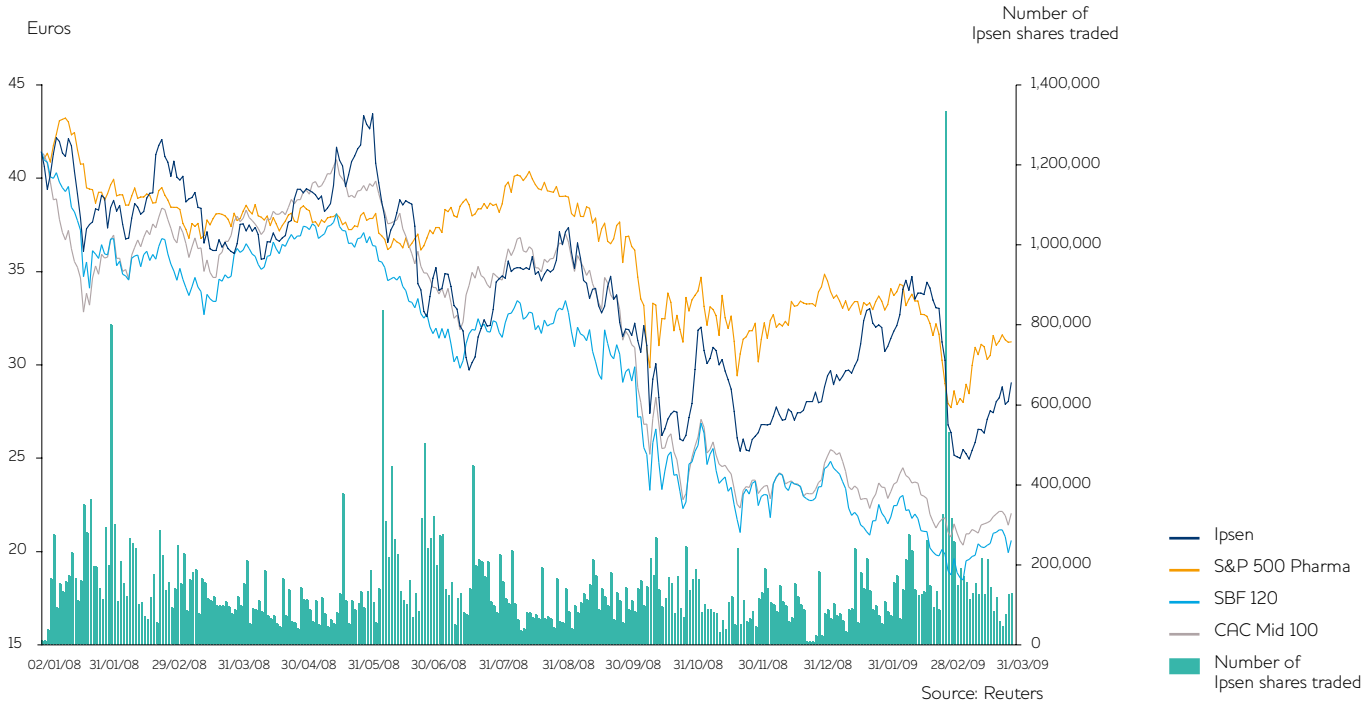


- Mayroy **73.42%**
- Free float **24.88%**
- Treasury shares **1.17%**
- Employees **0.25%**
- Other registered shareholders **0.24%**
- Board members **0.04%**

€1.75

DILUTED EARNINGS PER SHARE
(BASED ON THE AVERAGE NUMBER
OF OUTSTANDING SHARES)

SHARE PRICE EVOLUTION COMPARED TO MAIN STOCK MARKET INDICES
from 2 January 2008 to 31 March 2009 (rebased on Ipsen share price as of 2 January 2008)



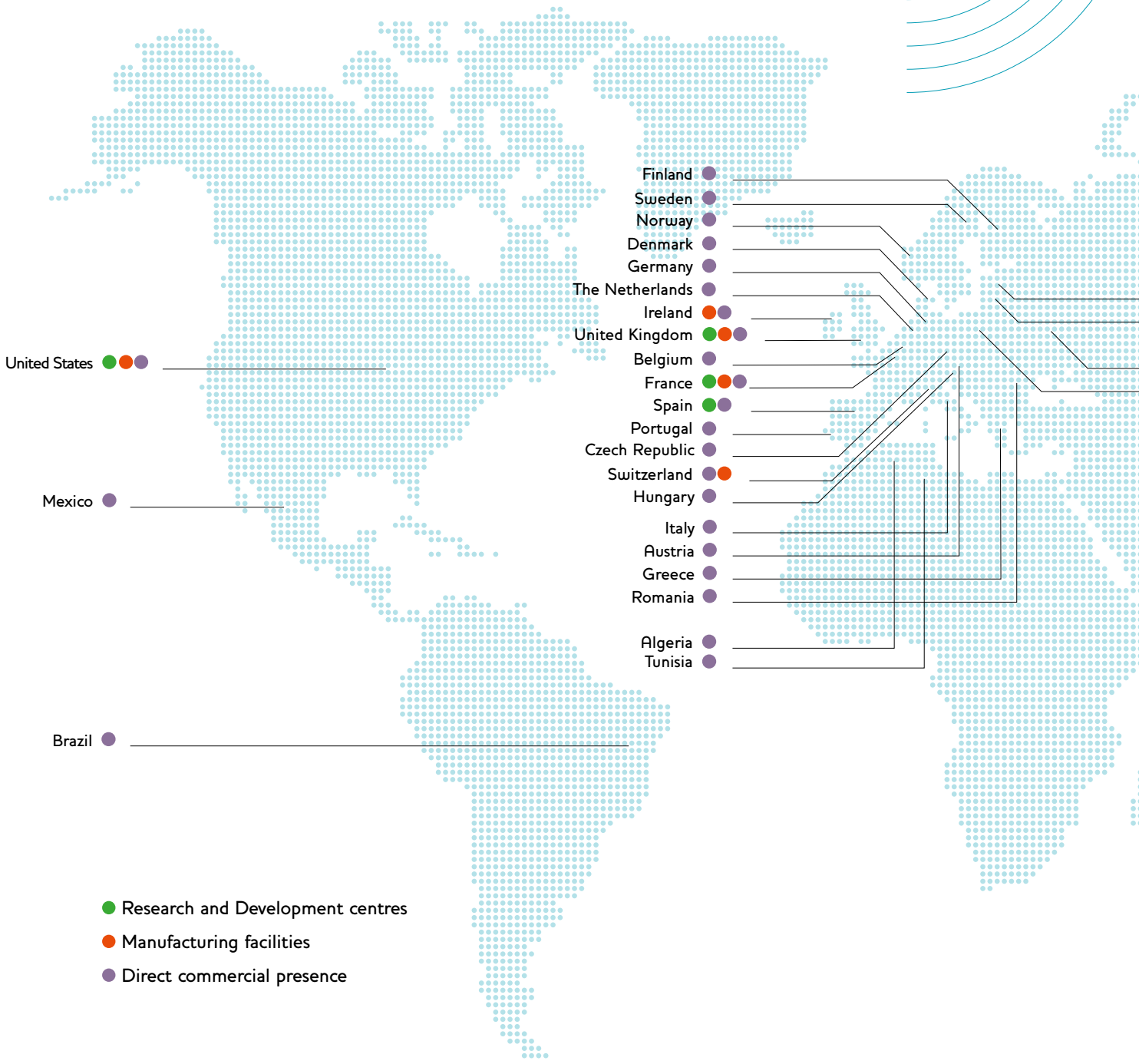
Source: Reuters

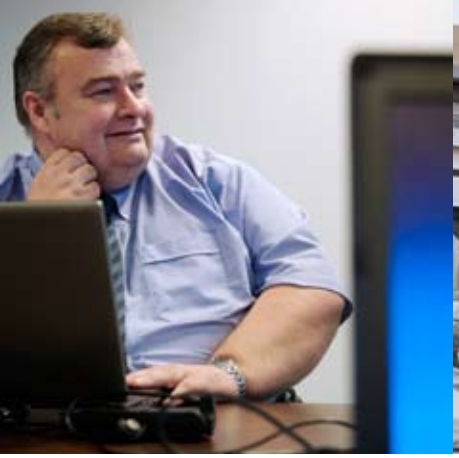
Ipsen shares have been eligible to the *Service de Règlement Différé* (SRD) since 28 March 2007.
On 24 December 2007, Ipsen shares were added to the SBF 120 index.

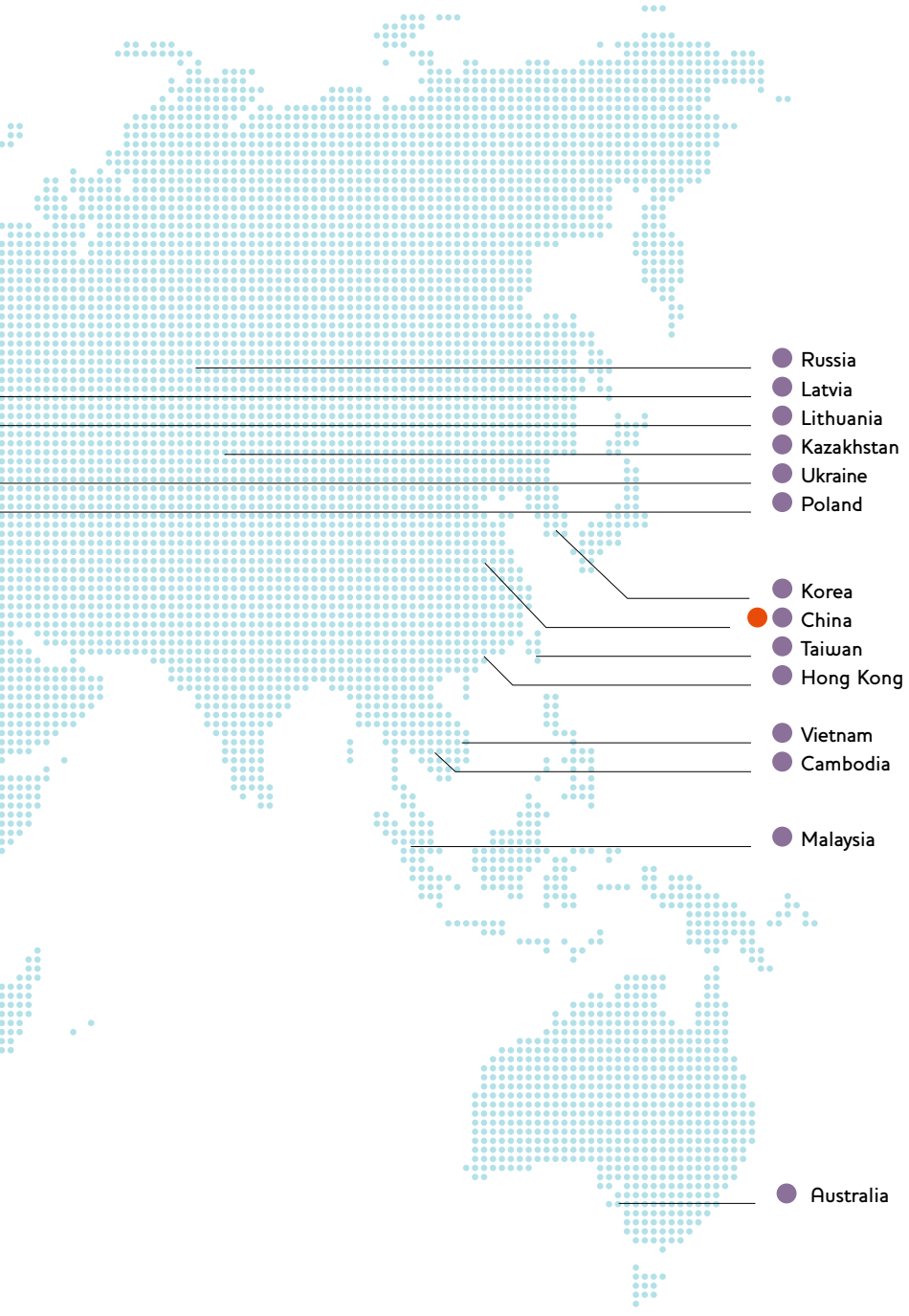
SHARE PRICE EVOLUTION
From 1 January 2008 to 31 March 2009

Average closing price	€33.81
Period high	€43.27
Period low	€24.94
Performance in % (between the period high and the share price on 1 January 2008)	6.9%
Daily average traded volume	141,437

IPSEN WORLDWIDE







PRODUCTION AND SUPPLY CHAIN SERVING EXCELLENCE

Ipsen has manufacturing facilities in France, the United Kingdom, Ireland, Switzerland, China and the United States, and plantations and leaf-drying facilities in France, China and the United States. Each of the Group's manufacturing facilities focuses on a particular technology to maximise its operational efficiency.
For instance, the Dublin site (Ireland) is devoted to the purification of peptides, while the Dreux plant (France) specialises in the manufacturing and packaging of high volumes of oral formulations.
Furthermore, Ipsen promotes continuous improvement in productivity of its manufacturing processes.
Upstream efforts by manufacturing, development and research teams provide mutual enhancement. This integration is a necessary step towards improving product quality, guaranteeing patient safety and developing optimal manufacturing processes within the Group's cost optimisation rationale.

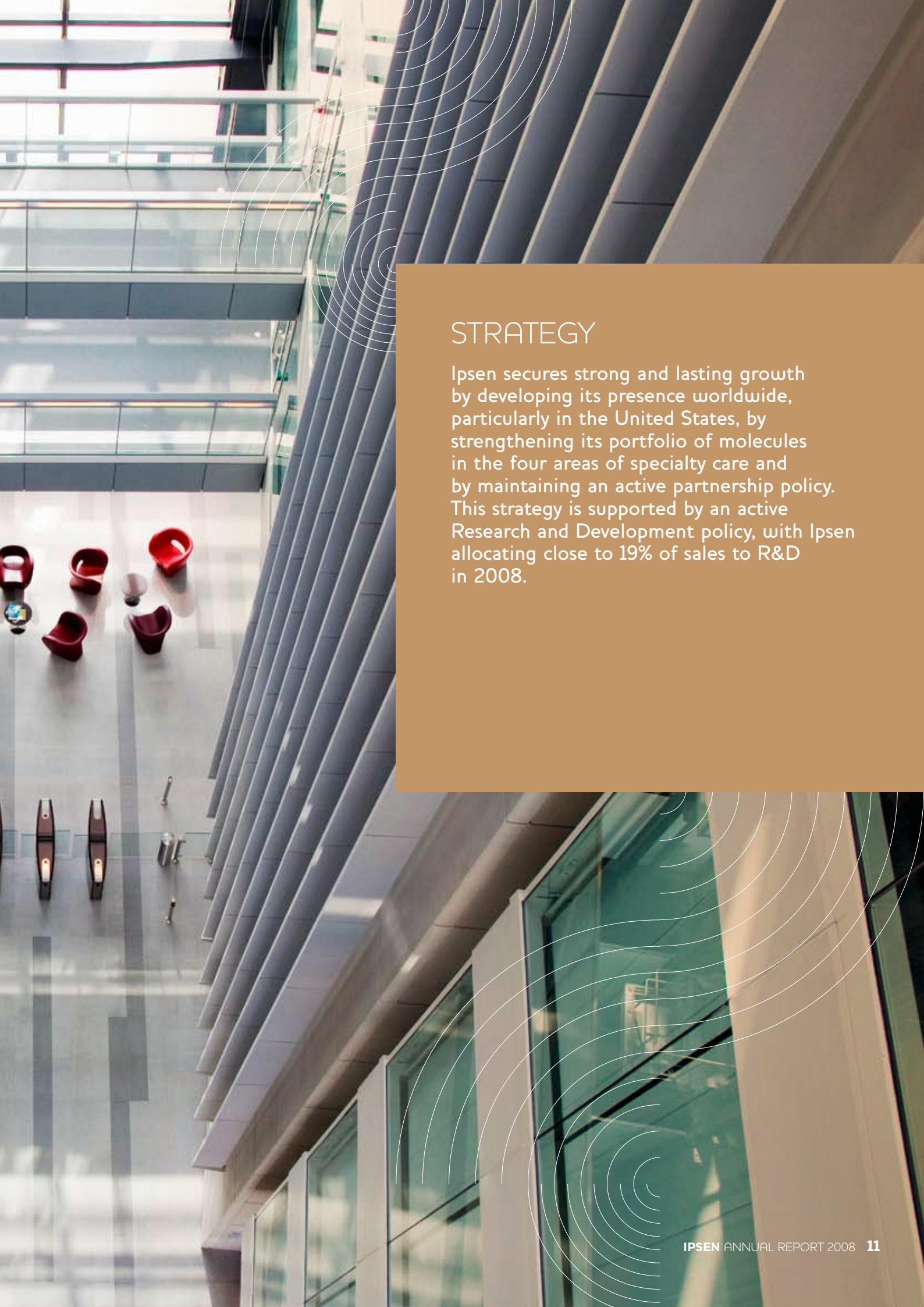
DIRECT COMMERCIAL PRESENCE IN APPROXIMATIVELY

40 countries

DRUGS MARKETED IN OVER

100 countries


CLOSE TO
19%
OF SALES ALLOCATED
TO R&D IN 2008



STRATEGY

Ipsen secures strong and lasting growth by developing its presence worldwide, particularly in the United States, by strengthening its portfolio of molecules in the four areas of specialty care and by maintaining an active partnership policy. This strategy is supported by an active Research and Development policy, with Ipsen allocating close to 19% of sales to R&D in 2008.

Ipsen's threefold strategy aims towards specialty care growth, geographic expansion and optimising the primary care product portfolio.

THREE OBJECTIVES FOR AN AMBITION

Focused on patient care, Ipsen capitalizes on its competitive and coherent portfolio of molecules in its four targeted therapeutic areas: oncology, endocrinology, neurology and haematology. Its original development model is also based on optimising the primary care product portfolio, which finances the Group's R&D activities. Research is indeed at the heart of Ipsen's activities and Group organisation, with around 19% of sales allocated to R&D annually. "Discovery and Innovation" is dedicated to the search for new chemical entities in the area of peptides and proteins. Whether compounds are discovered by internal research teams or via partnerships, "Corporate Development" is responsible for ensuring that a strong and diversified portfolio of molecules is brought to the market and promoted worldwide. To ensure efficiency, this entity is also responsible for preclinical, clinical and pharmaceutical development, business development (agreements and licences) as well as legal and regulatory affairs.

HOMEOSTASIS: RESTORING PHYSIOLOGICAL BALANCE

Ipsen's research is focused on the fundamental concept of homeostasis: loss or gain of molecular/biological functions can lead to life-threatening diseases, thus the need to restore and sustain physiological balance through the control of chemical messengers such as hormones and neurotransmitters.

Ipsen's approach to diseases consists of restoring physiological levels to their precise and appropriate balance through the enhancement or the suppression of biological functions.

For instance, a number of statural or endometabolic disorders, as well as haemostasis or tissue injury, result from a functional deficiency in growth factors such as growth hormone, IGF-I, gut peptides such as GLP-1 or ghrelin, or haemostatic agents such as Factor VIII. Ipsen's research aims at compensating for these deficiencies with analogs of the natural biological effectors.

On the other hand, other diseases such as hormone dependent cancers, movement disorders (spasticity)

(to be followed p. 14)

Scientific symposium on 19 January 2009 on the major issues of biomedicine. From left to right: J.-L. Bélingard, S. Dehaene, F. Gage, I. Verma, J. Hoffmann, I. Robinson, N. Le Douarin, M. Bishop (Nobel prize), J.-P. Changeux, E. Kandel (Nobel prize) and R. Guillemin (Nobel prize)

IPSEN COMMITTED TO THE SCIENTIFIC COMMUNITY

To mark the occasion of moving its new corporate headquarters in Boulogne-Billancourt, on 19 January 2009, Ipsen organised an international scientific symposium — "Creating the future: New challenges in biology and medicine"

Recent scientific advances have progressed the field of knowledge and revealed the unbelievable complexity of disease mechanisms in cancer and brain diseases, as well as in immune system and endocrine regulation disorders. The understanding of these mechanisms represents a major challenge for the future of medical progress, but they also stand as an ethical duty. As a world-class player in research and innovation, Ipsen is a key contributor to the ongoing biological revolution and is committed to supporting basic research.

This unique event gathered prominent international academics who have contributed to major advances in life sciences over the last decades: Michael Bishop, dean of the University of California San Francisco and laureate of the Nobel Prize for the discovery of oncogenes, who revolutionized cancer research, Jules Hoffmann, former Chairman of the French *Académie des Sciences* who was behind the discovery of innate immunity, Inder Verma, from the Salk Institute, one of the founding fathers of gene therapy, Fred Gage, from the Salk Institute, who discovered neural stem cells in the human brain, Iain Robinson, from the National Institute for Medical Research, who pioneered research on the hormones of the hypothalamus, Eric Kandel, from Columbia University in the City of New York and laureate of the Nobel Prize for his work on memory, as well as Stanislas Dehaene, Professor at the *Collège de France*, whose research has opened new perspectives on the understanding of human conscience.

The meeting was chaired by two of the most prominent personalities in French science: Jean-Pierre Changeux, member of the *Académie des Sciences* who was behind basic research on acetylcholine receptors, and Nicole Le Douarin, pioneer of embryology research and perpetual secretary of the *Académie des Sciences*. Additional scientists who have also been instrumental in the evolution of knowledge, such as Professor Roger Guillemin, Nobel Prize Laureate of Medicine and Director of the Salk Institute, one of Ipsen's key partners, also attended the symposium.

Jean-Luc Bélingard, Chairman & CEO of Ipsen, said: "*We are extremely proud and honoured to welcome these key individuals who have significantly marked the life sciences landscape, to our new headquarters. The calibre of the scientists presenting at this meeting is testament to Ipsen's longstanding commitment, alongside the academic community, to meet today's new biomedical challenges. The drive to develop new drugs to treat the huge unmet medical needs we still see today requires strong collaboration between all stakeholders, including the academic community and the pharmaceutical industry.*"

Ipsen,

COMMITTED TO THE SCIENTIFIC COMMUNITY IN MEETING THE CHALLENGES IN BIOMEDICINE

(continued from p. 12)

and other endometabolic conditions result from an excess of chemical messengers: growth factors (growth hormone, prolactin, insulin), neuropeptides, steroids (estrogens, androgens) or neurotransmitters (acetylcholine). Ipsen's objective is to modulate the level of these substances in order to restore the biological imbalance in the local milieu.

TRANSLATIONAL RESEARCH: AN INTERFACE BETWEEN INNOVATION AND DEVELOPMENT

"Discovery and Innovation" includes a team dedicated to translational research, which forms an interface between innovation and development. The most promising molecules which are discovered by the Group, are subject to stringent tests before progressing to clinical development. The Group employs more than 70 experts in the fields of fundamental biology, pharmacology, toxicology, analytical and chemical methods in translational research. The primary objective is to limit risks of failure of clinical trials, which are the most costly stage of drug development.

The research teams are also responsible for working on molecules which are being developed or are already marketed in order to find new therapeutic indications. This approach enables the Group to identify the areas where investments should be focused, coherently with the range of products already developed, while aiming to respond to therapeutic needs which remain unmet. It takes eight to fifteen years for a molecule to go through all the required tests and clinical trials. Beyond the molecules' ability to alleviate symptoms or cure diseases, they are subject to very strict requirements in terms of toxicity and reducing adverse effects.

Ipsen's R&D portfolio is diversified and homogeneously spread between the different clinical stages, thus ensuring the future development of the Group's targeted therapeutic areas. ■

MAIN RESEARCH AND DEVELOPMENT PROGRAMMES*

Preclinical

Oncology

BIM 46187
Anticancer agent, G-protein signal

CDC25 PHOSPHATASE INHIBITORS
Anticancer agent (cell cycle)

ANGIOMATES (STX 140)
Anticancer agents, anti-tubulin/anti-angiogenic

Endocrinology

MSH AGONISTS FOR THE MC4 RECEPTOR
Metabolic disorders (obesity)

GHRELIN AGONISTS (BIM 28131)
Regulation of food intake and gastrointestinal function and treatment of cachexia

RECOMBINANT HUMAN GROWTH HORMONE
New formulation

11βHSD ENZYME INHIBITORS
Treatment of metabolic syndromes

GIP
Treatment of metabolic disorders and diabetes

*As of 30 April 2009

Phase I

Oncology

BN 83495 (STX 64)
Post-menopausal breast cancer expressing estrogenic receptors

ELOMOTECAN (BN 80927)
Advanced metastatic cancer

Phase II

Oncology

DIFLOMOTECAN (BN 80915)
Advanced metastatic cancer

Endocrinology

COMBINATION OF IGF-I AND RECOMBINANT HUMAN GROWTH HORMONE
Growth failure

COMBINATION OF IGF-I AND RECOMBINANT HUMAN GROWTH HORMONE
Growth hormone deficiency in adults

BIM 23A760
Symptomatic treatment of pituitary and neuroendocrine tumours

Haematology

OBI-1
Haemostasis
(phase II completed)

Phase III

Oncology

DECAPEPTYL®
Combined hormone therapy for premenopausal breast cancer

DECAPEPTYL®
6-month sustained-release formulation (regulatory review)

TOREMIFENE CITRATE
Treatment of side effects from LHRH-a based androgen-deprivation therapy (phase III completed)

Endocrinology

SOMATULINE® AUTOGEL®
Co-administration with pegvisomant

SOMATULINE® AUTOGEL®
Treatment of asymptomatic neuroendocrine tumours

INCRELEX®
Primary IGF-I deficiency in less severe forms

TASPOGLUTIDE (R1583/BIM 51077
Type II diabetes (in partnership with Roche)

Other programme

TANAKAN®
Age-related cognitive impairment

STRATEGY
GROWTH IN TARGETED THERAPEUTIC AREAS

Research and Development of new specialty drugs drives Group growth and is therefore the core of Ipsen's business. Partnerships and agreements offer the Group complementary resources which reinforce its own innovation impetus.

PREPARING THE FUTURE THROUGH TECHNOLOGICAL EXPERTISE

In 2008, specialty care drug sales totalled €553.1 million, up 13.9% excluding foreign exchange impact. This represents 57% of the Group's consolidated sales compared with 53.6% in 2007. In 2012, it should represent 70% of total sales.

The growth strategy is currently characterised by:
– marketing worldwide a competitive and coherent portfolio of new molecules originating both from internal research and from our alliances and partnerships;
– investing in the development of existing drugs to extend their indications, for example for Somatuline® Depot in the US in the symptomatic treatment of neuroendocrine tumours.

2008 was a particularly fruitful year for Ipsen in terms of new developments. In addition to the marketing in Europe of Increlex® and the acquisition of all the assets related to Apokyn® in North America and to OBI-1, significant advances were made in developing the R&D portfolio. The positive results of phase III trials for toremifene citrate in the treatment of prostate cancer should enable the Group to file applications for marketing authorisation in Europe. Taspoglutide (GLP-1 analogue), a molecule used for regulating blood sugar levels which is developed by Roche, is in phase III clinical trials since the second half of 2008. Another promising molecule is BIM 23A760 which could be much more effective than existing molecules in treating acromegaly. Moreover, the Group filed for marketing authorisation of the new 6-month formulation of Decapeptyl® in Europe last September. ■

HAEMOPHILIA HAS BECOME ONE OF IPSEN'S TARGETED THERAPEUTIC AREAS

Ipsen holds longstanding expertise in haemostasis (blood coagulation). The Group's research has enabled it to establish partnerships with Emory University (United States) and Octagen, in order to develop a recombinant version of porcine Factor VIII using its protein engineering platform. OBI-1 is produced at Ipsen's biotechnology unit in Boston. This product is intended for the treatment of congenital hemophilia type A complicated by the presence of antibodies which inhibit Factor VIII – and acquired hemophilia. In 2008, the Group acquired all the assets related to OBI-1 from Octagen. Ipsen now owns the worldwide marketing rights for this very innovative product, which has shown to be very promising in phase II clinical trials.

SPECIALTY CARE REPRESENTED

57%

OF CONSOLIDATED SALES IN 2008

13.9%

SALES GROWTH IN SPECIALTY CARE IN 2008

STRATEGY
GEOGRAPHIC EXPANSION

Head US sales office (Brisbane, California)

With the acquisitions of Tercica, of Vernalis' US subsidiary and of all the assets related to OBI-1 in 2008, Ipsen completed three major transactions in line with its strategy to expand North American operations. The Group thereby increases its commercial presence in the United States, the largest pharmaceutical market in the world.

OUT TO CONQUER THE NORTH AMERICAN MARKET

Conquering the US market has long been part of Ipsen's strategy. The Group has been present in the United States since 1976 when it opened its R&D centre near Boston. The Group has established several partnerships with internationally renowned companies and institutions present in the US. In 2008, its growth strategy received a new boost due to the implementation of projects aiming to market Ipsen's targeted therapeutic products directly in North America, which represents half of the global pharmaceutical market.

GLOBAL POSITIONING

The Group's objective to position itself as a global actor has been achieved through its alliance with Medicis in 2006 for the botulinum toxin in aesthetic medicine in the US, the marketing authorisation for Somatuline® Depot in 2007, the acquisition of Vernalis' US subsidiary in July 2008 and the final acquisition of Tercica last October. Outside the North American market, Ipsen has also developed its activities in several emerging markets: China, Russia and Latin America with the opening of subsidiaries in some countries such as Brazil.

OUTSTANDING US SALES PLATFORM

In the United States, Ipsen markets Increlex® which is used in the treatment of growth failure in children and adolescents with an insulin-like growth factor deficiency, and Somatuline® Depot, aimed at treating acromegaly, a rare disease due to over secretion of the growth hormone. The Group also markets Apokyn®,

STRONG INTERNATIONAL GROWTH:

+13.9%

EXCLUDING FOREIGN EXCHANGE IMPACTS IN 2008

Somatuline®, Increlex® and Dysport™

THREE GLOBAL PRODUCTS

indicated in the treatment of "off" episodes of patients with advanced Parkinson's disease.
Hence the Group has a sound basis in neurology for launching Dysport™ in the US, which was granted market authorisation on 29 April 2009 by the FDA.
Furthermore, to optimise Group organisation and offer clients improved coherence and visibility, Ipsen's sales teams have been grouped together close to San Francisco, California. This North American subsidiary comprises two sales teams, a joint marketing service, a clinical development structure for endocrinology and neurology, a regulatory team and finance, IT, Human Resources, legal and reimbursement departments. ■

STRATEGY
OPTIMISING THE PRIMARY CARE PRODUCT PORTFOLIO

Due to selective clinical research investments and partnerships in targeted territories, Ipsen optimises the development of its primary care product portfolio.

CAPITALISING ON OUR TRACK RECORD

In 2008, primary care sales totalled €383.1 million, down 2.6 % compared with 2007. Primary care represented 39.5% of Group consolidated sales. Excluding sales generated by Ginkor Fort®, which was divested on 1 January 2008, primary care sales rose 3.5% compared with the previous year.

Ipsen has longstanding experience in the field of primary care which is one of the pillars of the Group's strategy. Ipsen notably markets four primary care drugs: Tanakan®, Smecta®, Forlax® and Fortrans®. The strategy of optimising these drugs of established therapeutic value has three objectives: ensure they remain competitive in an ever changing competitive and regulatory environment, constantly create and innovate for them to suit patient needs, and provide therapeutic solutions for major public health issues.

In France, the Group also co-promotes Artotec® and Exforge®, and co-markets Nisis®, Nisisco® and Adrovance®.

MANAGING PRODUCT LIFE-CYCLE

This strategy is supported by the management of the life-cycle of these products. The objective is to develop new dosages and new formulations, and to carry out clinical trials to prove drug efficacy for new applications. The third aim is to reinforce the drugs' technical specifications by promoting their unique composition, which guarantees therapeutic efficiency and safety.

2008, A MAJOR YEAR FOR SMECTA®

2008 brought major developments for Smecta®, indicated for the treatment of chronic and acute diarrhoea in adults and children. Smecta®'s unique technical specifications have been improved and new clinical results were released at international congresses. These changes, together with the launch of the orange vanilla flavour and new packaging, were welcomed by patients and went towards optimising sales growth. Smecta® has expanded internationally, more specifically

GUIDAGE® STUDY

This study assesses the effectiveness of EGb 761®, in the prevention of Alzheimer's disease in patients over 70 presenting a spontaneous memory complaint.
The 2,800 patients were recruited by September 2004 and their treatment is due to continue for five years.

SMECTA SALES UP BY
4.8%
IN 2008

in China, due to an efficient distribution system which covers the entire country and to the development of a scientific activity in respect of the disorders which it treats; China has become Smecta®'s leading market. ■

REINFORCED PARTNERSHIP WITH NOVARTIS

Discussions between Ipsen and Novartis which began in 2008, resulted in the signing of a co-promotion agreement in France in January 2009 with respect to the antihypertensive drug Exforge®. This new deal strengthens the relationships between the two Groups, which have collaborated since 2003 on the co-marketing in France of Nisis® and Nisisco®, indicated in the treatment of hypertension, the leading cause of death worldwide.
The successful collaboration for these two products encouraged the Groups to sign this new agreement, which offers prescribers and patients a value added drug in the field of cardiovascular treatment, which is currently a public health priority.
Ipsen also signed a co-marketing agreement with MSD in France for Adrovance® (for the treatment of post-menopausal osteoporosis), and signed a co-promotion agreement for Artotec® (non steroidal anti-inflammatory drug) with Pfizer.

MORE THAN

€1 billion

IN TOTAL REVENUES IN 2008

ACTIVITIES

The Group is well recognised by the medical world for its expertise in each of its targeted therapeutic areas (oncology, endocrinology, neurology and haematology) and in primary care.

Thanks to internal R&D initiatives supported by strategic alliances and partnerships, Ipsen continued to develop and actively promote its portfolio of molecules throughout 2008.

ACTIVITIES
KNOW-HOW

Amongst the most innovative pharmaceutical groups, Ipsen allocated close to 19% of sales to R&D in 2008. Its research teams are active in discovering and developing new molecules, and managing the life-cycle of products which are already marketed.

DISCOVERY, INNOVATION, DEVELOPMENT...

TECHNOLOGICAL PLATFORMS SERVING DISCOVERY

PEPTIDE AND PROTEIN ENGINEERING
Active primarily in three areas - synthetic chemistry, pharmacology and biotechnology - Ipsen's research teams, mainly in Boston, selectively modify the structure of naturally occurring proteins and peptides to improve their properties. Replacing certain protein sequences with different ones may reduce antigenicity (detection by existing antibodies), toxicity or immunogenicity (formation of new antibodies) of proteins and peptides; it can also increase the duration of action, specificity or compatibility with sustained-release formulations.

TRANSLATIONAL RESEARCH
Based in Paris, the teams specialised in translational research aim to gain a better understanding of molecular, pharmacological, pharmacodynamic and pharmacokinetic properties of new chemical or biological candidates which may be developed in the fields of oncology, endocrinology and neurology.

STEROID ENGINEERING
In collaboration with Bath University (UK), Ipsen's research teams concentrate on the discovery of enzyme inhibitors involved in the biosynthesis of steroid hormones.

TECHNOLOGICALLY INTEGRATED PLATFORMS SERVING INNOVATION

Ipsen's originality lies within the convergence of:
• medicinal chemistry applied to steroid, peptide and protein engineering, each with its own toolbox such as molecular modelling, but always based on rationale design as opposed to random screening;
• and an expertise in advanced delivery systems, which aims at developing:
– vectorized agents associating an active moiety to an appropriate ligand for the targeted tissue and for intracellular delivery with the objective to increase efficiency and efficacy while sparing or minimizing toxic effects to the non-target tissues;
– controlled delivery systems for enhanced patients' convenience and quality of life.

800 people
DEDICATED TO R&D

CLINICAL TRIALS FOR 2009
TRIPLED AT OVER
1,600 sites
WORLDWIDE

CHIMERIC COMPOUNDS: "ALL IN ONE" MOLECULES

Ipsen has developed advanced expertise in "chimeric compounds". Also known as "hybrid molecules", these compounds are designed to act simultaneously on several molecular targets which are generally linked to the same disease. These compounds are less costly and quicker to develop than drug cocktails which have been used until now for treating complex diseases, and even more importantly, they are potentially much more effective. Ipsen focuses on chimeric compounds which may generate synergies, providing a longer reaching effect than the simple addition of the different properties. Another advantage of these "all in one" molecules is that all the functions of a hybrid molecule act in the same place at the same time, whilst drug cocktails may spread throughout the human body in different directions, with significantly different pharmacokinetic effects.

Ipsen is one of the pioneers in this field. The most advanced project is the BIM 23A760 molecule. This molecule combines the structural elements of somatostatin and dopamine, and could prove to be extremely effective in treating the over secretion of growth hormones, and indeed other tumour disorders. After developing an initial synthesized molecule in 2002, the medicinal chemistry team at Ipsen's Boston research centre has been working since the start of 2008 on a second generation of the molecule BIM 23A760, which is proving to be very promising.

This team is also working on chimeric compounds which have a vectorization function, which enables the molecule to travel to the exact point where it must act.

CORPORATE DEVELOPMENT ORGANISATION AIMED AT ACCELERATING DRUG MARKETING AUTHORISATION

To develop the Group's product portfolio by making the best strategic choices, Ipsen adopts a global and strategic approach for all candidate compounds. Some of the compounds discovered by internal research teams are developed by the Group, whilst others are licensed out to laboratories via strategic partnerships.

Ipsen may also develop and market compounds that do not come from its own research, but which are perfectly in line with its strategy. By optimising the time and resources consumed, Ipsen generates the most added value possible, both in medical and economic terms.

Clinical development teams execute or commission execution of clinical trials, the pharmaceutical development centre produces batches destined for preclinical and clinical research, and the pharmacokinetics department takes part in clinical trials with the advanced drug delivery teams. ■

IPSEN'S EXCELLENCE

In January 2008, Ipsen launched an operational excellence programme in an aim to improve productivity by systemising methods to improve its purchasing and manufacturing processes. This programme is based on the Lean Six Sigma method, and was initiated with an extensive training session with three to four months training for specialists and ten days training for the next level of participants.

A PORTFOLIO MANAGEMENT TEAM BY THERAPEUTIC AREA

This cross-functional organisation, divided into five teams (oncology, endocrinology, neurology, haematology and primary care) which are each headed by a PMT leader, was set up in 2007 and 2008 in order to define the strategy of Ipsen's portfolio in collaboration with the Executive Committee, to coordinate its implementation and to promote a clear and shared vision of this strategy throughout the Group.

ACTIVITIES
PRODUCT LIFE-CYCLE

8 to 10 years | **1 to 3 years**

PRELAUNCH | **AUTHORISATION**

1 RESEARCH

Pharmaceutical companies commit to research in areas based on:

- the progress of basic research conducted in university laboratories, hospitals and companies
- the analysis of the medical needs expressed
- a corporate strategy

At Ipsen, Discovery and Innovation concentrates entirely on discovering new chemical entities, based on its proven expertise in peptide, protein and steroid engineering, and cutting edge advanced drug delivery.

2 PRECLINICAL TRIALS

These combine several approaches in order to select the compounds wich could be studied in humans:

- development of compounds
- setting up databases
- technical feasibility
- animal studies

CLINICAL TRIALS

Clinical trials are governed by strict laws. Three phases:

- evaluation of drug safety on a small number of normal healthy volunteers (not patients)
- evaluation of drug efficacy on a small number of patients, ranging from 100 to 400
- evaluation of the efficacy/safety ratio on several hundred or thousand patients

3

At Ipsen, Corporate Development is responsible for bringing a coherent pipeline of molecules to the market, originating both from its own discovery and innovation, and from the Group's alliances and partnerships. Corporate Development groups together preclinical, clinical and pharmaceutical development, partnerships, and legal and regulatory affairs.

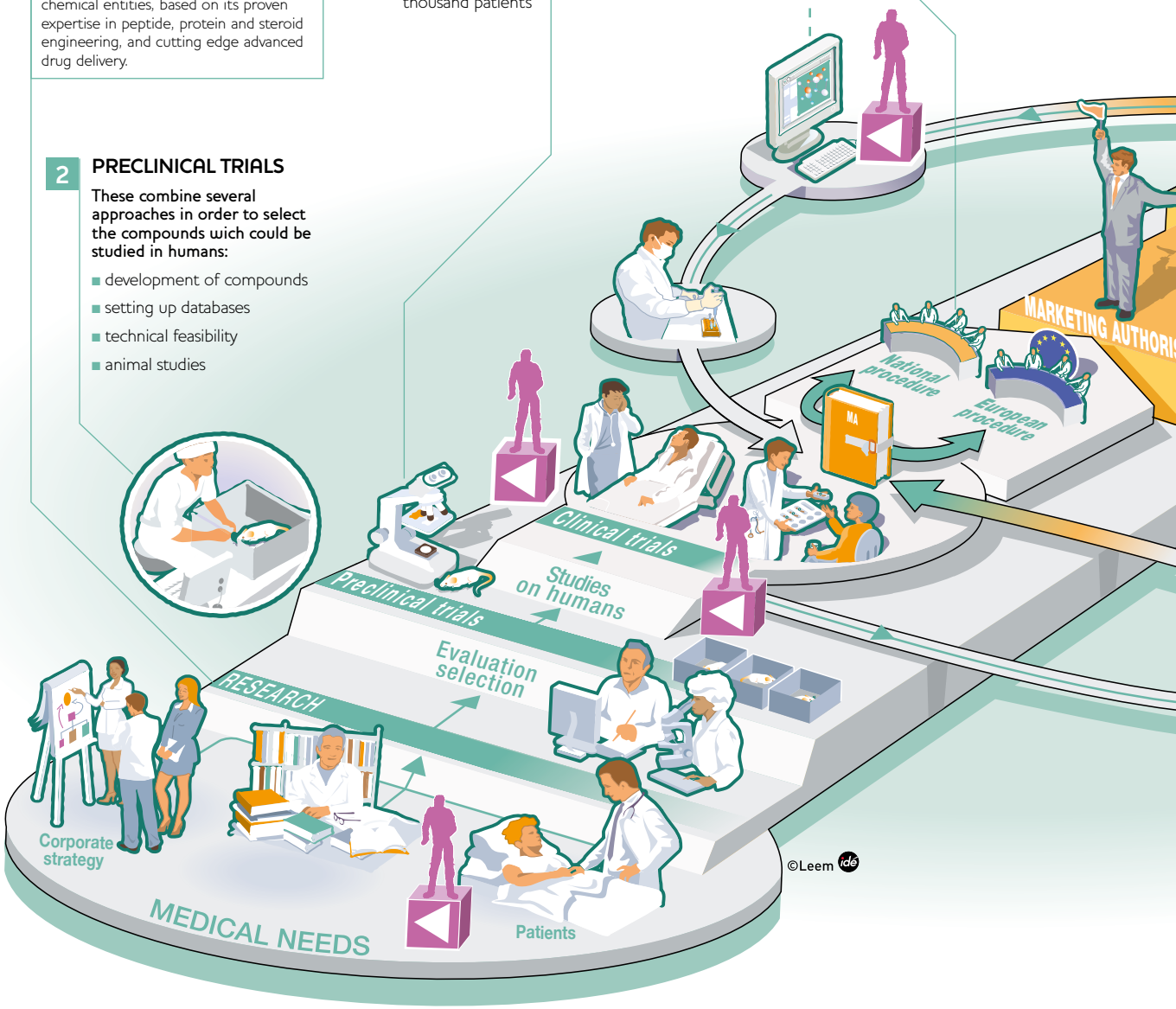
4 MARKETING AUTHORISATION

National procedure

e.g.: Afssaps in France (French Health Products Safety Agency), the FDA (Food and Drug Administration) in the United States, etc.

European procedure

through the EMEA (European Medicines Agency)



20 years

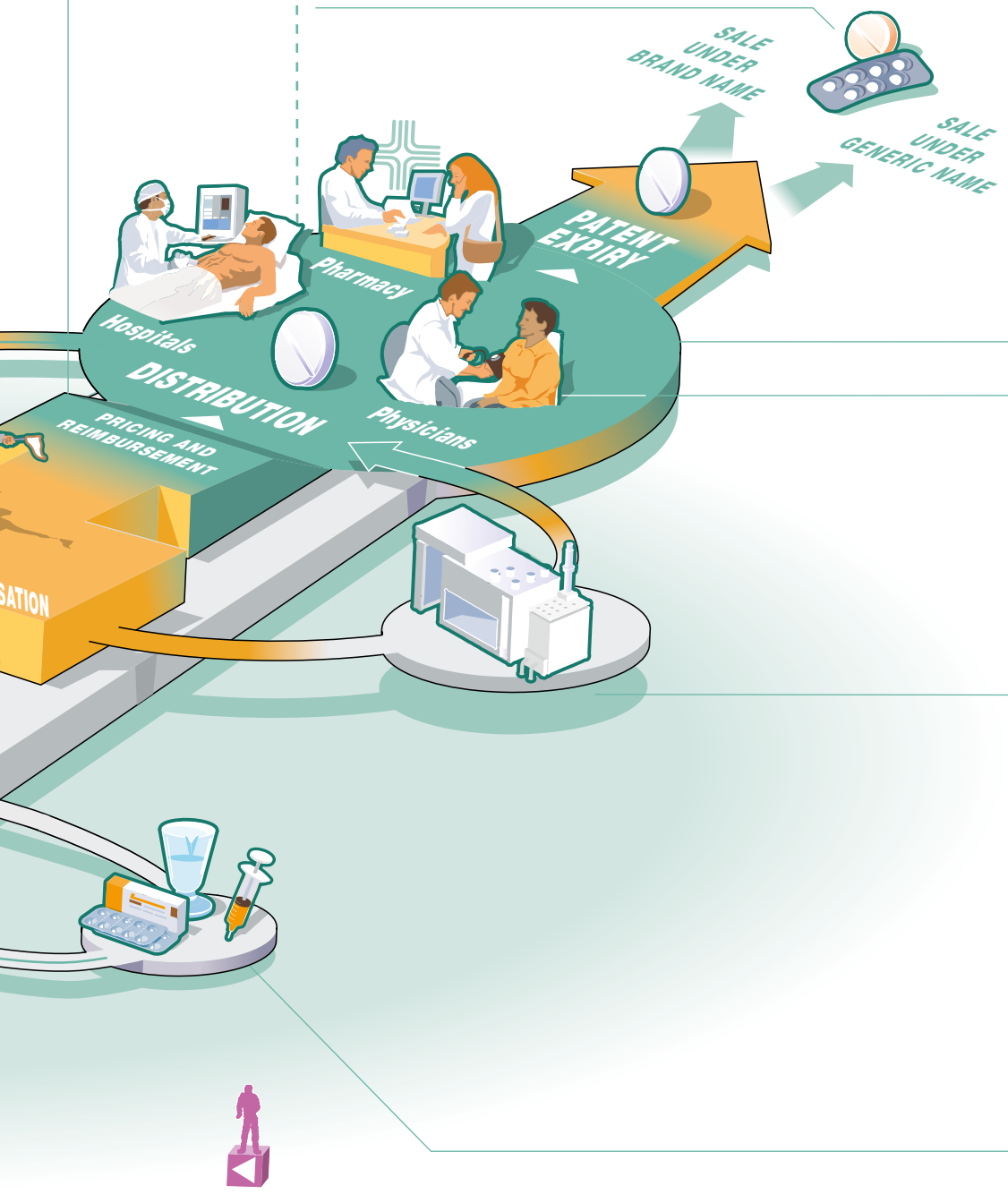
LIFE-CYCLE OF THE PATENTED MEDICINE

5 PRICING AND REIMBURSEMENT

GENERICS

Once the patent has expired, the product life cycle continues under the brand name or under the generic name; new indications may be found for the product, which will be subject to a new marketing authorisation application.

The cycle then starts up again…



7 MONITORING

The product is monitored throughout its life-cycle:

- by recording its effects on patients (case reports from physicians, patient associations)
- by a pharmacovigilance network
- by post-marketing studies

Drug information provided to physicians by medical representatives

6 INDUSTRIAL MANUFACTURE

Ipsen has manufacturing facilities in France, the United Kingdom, Ireland, Switzerland, China and the United States, and plantations and leaf-drying facilities in France, China and the United States.

Industrial and pharmaceutical development

- An industrial development phase takes place while the clinical trials are being conducted. Production of the active substance and the drug delivery system determine the method of administration and packaging of the active substance (syrup, hard capsules, tablets, etc.).
- The marketing authorisation dossier is compiled based on the results of the clinical trials and pharmaceutical and industrial development.

PATIENT ASSOCIATIONS
These are involved at different stages.

ACTIVITIES
ONCOLOGY

Decapeptyl® is the Group's leading product in terms of sales. In 2008, Decapeptyl® sales increased 5.4%, with strong growth in Asia, North Africa and in certain European countries.

Forecasts estimate that the global oncology market will exceed $75 billion. Several new molecules, which have demonstrated their clinical efficacy and obtained approval from health authorities, have been launched over the past months, thus epitomizing the innovative nature of this therapeutic area.

Hormonal agents are a key therapeutic solution for treating cancer, particularly breast and prostate cancer, while biomarkers are used more and more to identify the groups of patients who are likely to respond to a specific treatment. Ipsen has developed cutting edge expertise in these two areas.

Clearly focused on innovation, Ipsen is positioned on the hormonal treatment of tumours by targeted agents.
In September 2008, the Group filed for marketing authorisation in Europe for a new 6-month formulation of Decapeptyl® as opposed to the existing 3-month formulation. It should be available on the market in the coming months.

Ipsen is currently running a promising Research and Development programme for the molecule BN 83495. In 2008, an initial clinical trial was carried out for breast cancer. In 2009, research will continue with phase II clinical trials on endometrial cancer; trials on breast, ovarian and prostate cancer will also be launched.

Other important programmes are currently under development at Ipsen in the areas of oncology, namely CDC25 phosphatase inhibitors and G-Protein signal inhibitors, BIM 46187.

> Over the past three years, I have truly appreciated working with Ipsen on uro-oncology on a global scale. Our exchanges as regards the future possibilities of diagnosing and treating prostate cancer have been scientifically commendable.
>
> **PER-ANDERS ABRAHAMSSON**
> Chairman and Professor of the Urology Department
> at Malmö University Hospital (Sweden)

DECAPEPTYL®

Decapeptyl® is a peptide formulation for injection that was initially developed and continues to be used mainly in the treatment of advanced prostate cancer. Additional indications developed subsequently include the treatment of uterine fibroids (a benign tumour of muscle tissues in the uterus), endometriosis (proliferation of endometrial tissue, the mucous membrane that lines the uterine wall outside the reproductive tract) prior to surgery or when surgery is not deemed appropriate, as well as early-onset puberty and female infertility (in vitro fertilisation).

Decapeptyl® is available in monthly or quarterly sustained-release formulations, as well as a daily formulation.

Decapeptyl® was initially launched in France during 1986. At the end of 2008, Decapeptyl® had marketing authorisations in over 60 countries, including 25 in Europe. In 2008, 59% of Decapeptyl® sales were generated in Major Western European countries.

RESEARCH PROGRAMMES

Ipsen's technological platforms in steroid, peptide and protein engineering, allow the Group to explore and develop new approaches to the treatment of cancer under hormonal control, such as:
– key enzyme inhibitors in the biosynthesis of steroids;
– growth factors, notably including prolactins, Growth Hormone Releasing Hormone;
– enzymes regulating cell cycles;
– factors involved in the transduction of the intracellular signal and angiogenesis.
These research programmes are conducted internally with assistance from university and industry specialists.

ANGIOMATES (STX 140)

The angiomates refer to a family of small molecules (steroids) issued from the acquisition of Sterix which are multitargeted anticancer agents, exhibiting both antiproliferative (killing cancer cells) and antiangiogenic properties (inhibiting the blood vessels network supporting the tumour). These cytotoxic molecules will target the treatment of hormone-dependent tumours and probably certain forms of haematological malignancies.

ACTIVITIES
ONCOLOGY

BIM 46187
BIM 46187 is an innovative anti-tumour compound that acts on cellular signals by the receptors attached to G-Protein (the most common form of receptors for neuropeptide hormones and neurotransmitters). BIM 46187 may be used either alone or in combination with other cancer therapies in the treatment of solid tumours, such as lung and prostate cancer, or in treating pain.

CDC25 PHOSPHATASE INHIBITORS
These new molecules target key enzymes, CDC25 phosphatases, which regulate the cell division cycle. It has been demonstrated that these enzymes are abnormally high in a large number of tumours. These inhibitors are currently under advanced preclinical evaluation.

DEVELOPMENT PROGRAMMES

BN 83495 (STX 64)
BN 83495 and similar molecules issued from the acquisition of Sterix, are selective inhibitors of the sulphatase enzyme involved in a key stage of the biosynthesis of estrogens, one of the principal factors contributing to breast cancer in post-menopausal women. A first phase I clinical trial in patients with breast cancer has been completed and the results demonstrated the inhibition of the sulphatase enzyme at the dosages tested in tumour biopsies. An additional phase I clinical trial is currently being conducted and aims to determine the optimal dose of BN 83495 for postmenopausal patients with advanced breast cancer expressing hormonal receptors. In 2007, Ipsen and bioMérieux signed an agreement by which bioMérieux will develop a companion test for BN 83495; bioMérieux will devise a companion test to determine those patients who are best suited to benefit from this new treatment.

DECAPEPTYL®
Ipsen is participating in two phase III studies conducted under the auspices of the International Breast Cancer Study Group in the treatment of breast cancer in premenopausal women, comparing the conventional treatment methods with hormone therapy combining Decapeptyl® with estrogen suppressant agents, such as Aromasin®, marketed by Pfizer. These trials are due to take place until 2015. The results could lead to the review of therapeutic recommendations for breast cancer in premenopausal women expressing hormonal receptors.

Ipsen exclusively in-licensed from Debiopharm the know-how and new patent applications for the commercialisation rights of Decapeptyl® (triptorelin pamoate) in the world excluding North America, and certain other countries (Sweden, Israel, Iran and Japan). It further enables Ipsen to access future sustained-release formulations of Decapeptyl® developed by Debiopharm, among which a 6-month sustained-release formulation which was filed for marketing authorisation in Europe in 2008.

TOREMIFENE CITRATE
The Group has acquired the rights in the European Union, Switzerland, Norway, Iceland, Lichtenstein and the Commonwealth of Independent States from the US biotech company GTx Inc., specialised in men's health, for the development and marketing of toremifene citrate for all indications except breast cancer. Phase III (two indications) clinical trials for toremifene citrate, Selective Estrogen Receptor Modulator (SERM), developed in line with a new strategy of estrogen receptor modulation have been completed. The first indication involves the treatment of side effects from LHRH-a based androgen-deprivation therapy in the treatment of advanced prostate cancer (80 mg). The second indication involves preventing prostate cancer in men with

a high grade prostatic intraepithelial neoplasia (20 mg). The Group retains the marketing rights for the first indication and an option for the second one.

The Group is looking for a partner with which to continue the development of a patented class of cytotoxic agents:

• **diflomotecan (BN 80915)** is a cytotoxic agent (cell killer) that inhibits the topoisomerase 1 enzyme. The agents inhibiting this enzyme are used in the treatment of metastatic colorectal and ovarian cancer. Nonetheless, they can cause very serious side effects which are difficult to control. Compared with other existing agents, diflomotecan was designed to improve the benefit/risk ratio. It has been tested in phase I clinical trials and an oral dosing regimen has been established in phase II. With this dosing regimen, diflomotecan showed high oral bioavailability and low gastrointestinal toxicity. Investigations into other indications are due to be carried out.

• **elomotecan (BN 80927)** is a cytotoxic (cell killer) inhibitor of topoisomerase 1 and topoisomerase 2 enzymes, intended for the treatment of certain types of advanced metastatic cancer (colon, breast and prostate). Elomotecan is currently undergoing phase I clinical trials.

• **BN 2629 (SJG-136)**
BN 2629, a product originating from Spirogen, is a synthetic molecule that has demonstrated during preclinical studies its ability to block the anarchic cellular proliferation process characteristic of cancerous diseases. This product is being studied in three phase I studies of different administration regimens in patients with metastatic tumours resistant to certain types of chemotherapy conducted by two renowned institutions, namely Cancer Research in the United Kingdom and the National Cancer Institute in the United States. ■

Decapeptyl® 6-month formulation

FILED FOR REGISTRATION IN EUROPE IN 2008

ACTIVITIES
ENDOCRINOLOGY

In endocrinology, Ipsen focuses on diseases affecting relatively small groups of patients whose treatment requires specialists.

Leveraging its capacity to integrate "peripheral tools"—genetics, molecular markers, diagnosis methods, etc.—, the Group has developed cutting edge expertise in acromegaly, in growth failure in children and in neuroendocrine diseases.
The know-how acquired by Ipsen in endocrinology research and particularly in peptides, has led the Group to explore other diseases. Ipsen may develop and market certain products itself or may decide to transfer the development of others to partners.

In acromegaly which is the first indication of Somatuline®, Ipsen outperformed its competitors in 2008. This specialty maintained its positions in the countries in which it has been marketed for several years; namely in France, the United Kingdom, Italy and Spain. From this solid base, the Group expanded the geographic reach of Somatuline® to countries such as the US, Germany or Poland, thus generating an outstanding growth which was also enhanced by the extension of the indications of the drug to neuroendocrine tumours.

In disorders linked to growth failure in children, Ipsen's sales in 2008 for the growth hormone NutropinAq® also outperformed the market: NutropinAq® sales rose by 20%, whilst the market benchmark saw 5 to 8% growth. In 2008, Ipsen introduced Increlex® in Europe which rounds off its range of treatments for growth failure disorders. Launched in January 2006 in the United States by Tercica, a Californian biotech company which is now owned by Ipsen, this drug fulfills particular needs where the use of growth hormone itself has proved ineffective.

Thanks to the strong synergies provided by this new drug, it has also played a part in the improved performance of NutropinAq® by positioning Ipsen as the sole company capable of offering paediatric endocrinologists with several solutions for treating growth failure disorders.

The launches of Somatuline® in the United States and of Increlex® in Europe position Ipsen as a truly global player.

63.3%
OF SOMATULINE® AND SOMATULINE® AUTOGEL® SALES WERE GENERATED IN WESTERN EUROPE IN 2008

SOMATULINE®

Somatuline® and Somatuline® Autogel® (Somatuline® Depot in the US) are sustained-release formulations for injection containing lanreotide, a somatostatin analogue (a hormone that inhibits the release of growth hormone at the pituitary gland). Somatuline® was initially developed and continues to be used mainly in the treatment of acromegaly, a disorder caused by the over-production of growth hormone or prolactin due to a benign tumour of the anterior pituitary gland. This product subsequently underwent further development in the treatment of symptoms associated with neuroendocrine tumours (particularly of a carcinoid type).

Ipsen believes that the Somatuline® Autogel® formulation, to which it holds the patent, represents a major technological advance. As far as the Group is aware, this represents the first semi-solid formulation for injection without any excipient, since the active substance itself controls the sustained-release. Somatuline® Autogel® releases the active substance with no excipient other than water over a period of at least 28 days, thus requiring just one injection per month compared with the two or three injections previously necessary, which makes it much easier to use.

Somatuline® was initially launched in France in 1995. At 31 December 2008, Somatuline® and Somatuline® Autogel® were registered in almost 60 countries and were marketed in more than 45 countries (including 26 in Europe) for the treatment of acromegaly and neuroendocrine tumours and in 45 countries for the treatment of acromegaly alone. Furthermore, on 30 August 2007 the FDA approved Somatuline® Depot Injection 60, 90 and 120 mg in the United States for the treatment of acromegaly. In 2008, 63.3% of Somatuline® and Somatuline® Autogel® sales were generated in the Major Western European countries.

“I work with Ipsen in the field of endocrinology, especially on treatment of pituitary tumours. Ipsen’s R&D team has developed a very promising follow up around taking advantage of major breakthroughs on basic research in the field. Hybrid molecules able to simultaneously activate somatostatin and dopamine receptors have been synthesized. This new compound is probably an important step forward in the treatment of different types of pituitary tumours.

The reason why I like the company and it’s R&D team is their broad and interesting fields of interests where new compounds are discussed against the background of progress and science. I anticipate a number of these compounds will be translated into successful drugs.

Another attractive aspect of Ipsen, for me, is the way an original French company has so quickly adapted to the international world of drug companies, while it’s successful to keep its cohesive and cultural background intact.”

STEVEN LAMBERTS, Rector of Rotterdam Hospital, worldwide specialist in endocrinology in adults, researcher and clinical practitioner working with Ipsen on acromegaly and neuroendocrine tumours

NUTROPINAQ®

NutropinAq® is a liquid formulation of a recombinant human growth hormone administered using the NutropinAq® Pen. The growth hormone is involved in several physiological processes including growth in stature and bone development in children. NutropinAq® is prescribed for:

– the long-term treatment of children with growth failure due to inadequate endogenous growth hormone secretion;

ACTIVITIES
ENDOCRINOLOGY

– the long-term treatment of growth failure associated with Turner's syndrome;
– the treatment of prepubertal children with growth failure associated with chronic renal insufficiency ahead of kidney transplantation;
– the treatment of adults with growth hormone deficiency of either childhood or adult-onset.

In September 2002, Genentech, a US company specialised in biotechnology, granted the Group exclusive marketing rights for NutropinAq® worldwide outside North America, Mexico, Canada and Japan.

At 31 December 2008, the Group had marketing authorisations for NutropinAq® in 33 countries. This drug has been launched in 25 European countries since 2004.

INCRELEX®

In October 2006, Tercica Inc. (now an Ipsen Group subsidiary) granted Ipsen the exclusive licence to develop and market Increlex® worldwide except for the United States, Japan, Canada, the Middle East and Taiwan.

The main active substance of Increlex® is recombinant human Insulin-like Growth Factor-I (IGF-I). IGF-I is the principal hormonal mediator of statural growth and must be present for normal growth of bones and cartilage in children. In severe primary IGF deficiency, children's' serum IGF-I levels are low, despite the presence of normal or elevated growth hormone level. If the IGF-I is not present in sufficient quantities, the child will not reach his/her normal stature. In patients with this disorder, low IGF-I levels are due to growth hormone resistance associated with mutations in growth hormone receptors, post-GH receptor signalling pathways, or to defects in IGF-I gene expression. Hence, these children cannot be expected to respond adequately to exogenous growth hormone treatment. Some individuals may also have a range of metabolic disorders, including lipid abnormalities, decreased bone density, obesity and insulin resistance that can lead to diabetes.

Increlex® has been marketed in the United States since the beginning of 2006. Increlex® was granted marketing authorisation in Europe on 9 August 2007 and is now marketed in the majority of European countries.

RESEARCH PROGRAMMES

In pituitary disorders, the Group is involved in several programmes, chiefly in pituitary adenomas, such as acromegaly and in neuroendocrine tumours.

The Group is also exploring the role of certain peptide hormones (ghrelin, MSH/MC4) in regulating food intake and the gastrointestinal function with the priority objective of treating obesity and cachexia, which are often the causes of functional disorders in the elderly, cancer patients and patients with chronic illnesses.
The Group is continuing to pursue the programmes it initiated in 11βHSD enzyme inhibitors with a view to developing a therapy for the related metabolic syndromes associated with obese patients, that lead to greater cardiovascular risks.

Regarding the life-cycle management of NutropinAq®, the Group is pursuing its preclinical investigations to identify the sustained-release formulations which could improve the daily injections of growth hormone in children and adults. The Group signed a research collaboration agreement with Celera in 2007, to develop biomarker and pharmacogenomic tests for growth failure patients.

NUTROPINAQ® HAS MARKETING AUTHORISATIONS IN MORE THAN

30 COUNTRIES

DEVELOPMENT PROGRAMMES

SOMATULINE® AUTOGEL®

With regard to managing the life-cycle of Somatuline® Autogel®, the Group is pursuing the following developments:

– a phase III clinical trial of Somatuline® Autogel® is being conducted in Europe in the treatment of asymptomatic neuroendocrine tumours and a phase III trial is currently under way with Somatuline® Depot in the United States in the treatment of symptomatic neuroendocrine tumours;

– a phase III clinical trial of Somatuline® Autogel® in co-administration with pegvisomant in the treatment of acromegaly is being finalized in Europe;

– in Japan, the Group's partner Teijin is currently finalising a phase II clinical trial of Somatuline® Autogel® for the treatment of acromegaly;

– the Group envisages securing additional marketing authorisations for Somatuline® Autogel® shortly, in Russia and Brazil for the treatment of acromegaly and neuroendocrine tumours.

BIM 23A760

The Group has synthesised a new chimeric compound combining a somatostatin analogue and a dopamine agonist to achieve synergic therapeutic effects in disorders such as acromegaly and neuroendocrine tumours. The Group is currently studying this molecule whose spectrum of activity is wider than that of existing drugs. It also hopes that it will not only improve the symptomatic treatment of acromegaly and neuroendocrine tumours but will also reduce the size of tumours, thereby eliminating certain limits in treatments currently available.

TASPOGLUTIDE (R1583/BIM 51077)

Taspoglutide is an analogue of peptide hormone GLP-1 (Glucagon Like Peptide-1), which is covered by a partnership agreement with Roche. This molecule will offer a new treatment for diabetes with great medical benefits and characteristics which differentiate it clearly from existing drugs in the same class. In Japan, Teijin is carrying out a phase I trial with sustained-release formulation of this peptide. ■

ACTIVITIES
NEUROLOGY

In neurology, Ipsen has developed specialised expertise in the treatment of neuromuscular disorders. The Group currently markets two products corresponding to two distinct markets.

Dysport™, the Group's botulinum toxin type A, has been marketed in more than 70 countries since 1991 and is primarily used by neurologists and physical therapy specialists in the symptomatic treatment of three illnesses: spasticity, cervical dystonia and blepharospasm. Ipsen ranks second worldwide in this specialty and will launch Dysport™ for cervical dystonia in the United States during 2009 as the FDA granted marketing authorisation on 29 April 2009.

In aesthetic medicine, the Group has transferred the marketing of its botulinum toxin to two partners: Medicis for North America and Japan, and Galderma for Europe and the rest of the world.

Furthermore, in the United States, Ipsen markets Apokyn®, an injectable solution which stops the "off" motor episodes which cause sudden freezes in patients with advanced Parkinson's disease. The drug can be injected by the patient using an injector pen similar to the insulin injection pen. It has been available for prescription by neurologists in the US since the end of 2008. Apokyn® and Dysport™ are prescribed by the same specialists, which facilitates and improves exchanges with the medical world. In July 2008, Ipsen acquired the US subsidiary of Vernalis, the UK company which marketed Apokyn®. This drug must be initially prescribed by a highly specialised practitioner, which provides a solid contact base with the medical world for the launch of Dysport™. Through this transaction, Ipsen also acquired a neurology sales force in the United States.

In 2008, Ipsen started to build its range of products and promote its expertise in neurology and functional rehabilitation, focusing its strategy on developing activities in two directions. The first aim is external with the Group acquiring a drug aimed at the same prescribers, but designed to treat a different disease, such as Parkinson's disease. Whilst the Group's second aim is to focus on internal development using its outstanding technical expertise, illustrated by the Wrexham facility (United Kingdom), which has been approved by the FDA. Worldwide, only few companies compete with Ipsen's technological excellence in the area of toxins.

DYSPORT™

GRANTED MARKETING AUTHORISATION
IN THE US BY THE FDA ON 29 APRIL 2009

Botulinum toxin manufacturing facility in Wrexham (Wales)

DYSPORT™

Dysport™, which blocks the release of acetylcholine, hence reducing muscular spasm, was initially developed for the treatment of motor disorders and various forms of muscular spasticity, including cervical dystonia (a chronic condition in which the neck is twisted or deviated), spasticity of the lower limbs (heal) in children with cerebral palsy, blepharospasm (involuntary eye closure) and hemifacial spasm. Dysport™ was later developed for the treatment of other neuromuscular disorders, such as the spasticity of limbs, and in aesthetic medicine.

Dysport™ was initially launched in the United Kingdom in 1991. At 31 December 2008, it had marketing authorisations in 75 countries. In 2008, 40.4% of Dysport™ sales were generated in the Major Western European countries.

APOKYN®

Apokyn® (apomorphine hydrochloride injection) is the only therapy available for treating advanced Parkinson's disease patients in the US who experience the severe "on/off" motor fluctuations (re-emergence of Parkinson's disease symptoms). Treatment using Apokyn® is used as an adjunct to other conventional Parkinson's disease therapies and is administered, as needed, by means of an injector pen to treat periods of poor mobility in people with advanced disease. In April 2004, Apokyn® was granted orphan drug status by the FDA for treating patients in the US, who experience the severe "on/off" motor fluctuations that are unresponsive to other oral Parkinson's disease therapies.

Parkinson's disease is a condition that results from selective degeneration of an area of the brain called the substantia nigra, which is located towards the base of the brain in the basal ganglia. Normally these nerve cells release dopamine—a chemical that transmits signals between nerve cells. This central signalling pathway is essential for the fine control of movement and posture, and breakdown results in the symptoms of Parkinson's disease, namely tremor, rigidity, slow movements and postural instability. Muscle rigidity can become so severe as to result in "freezing" also referred to as "off" episodes, when patients are rendered immobile. Patients also suffer from problems related to a fall in blood pressure (postural hypotension) and intestinal motility, which can compromise the absorption of food and drink. This disease is gradual and the signs and symptoms generally worsen over time.

Apokyn® generated sales of €2.4 million in the US in 2008.

ACTIVITIES
NEUROLOGY

RESEARCH PROGRAMMES

The Group's research programmes in neurology mainly focus on the development of new botulinum toxin formulations.

In neurodegenerative conditions, Ipsen has synthesised several original classes of chimeric compounds, i.e. compounds capable of performing several pharmacological activities simultaneously and used to protect mitochondria (intracellular organelles responsible for the production of energy) in connection with neurodegenerative conditions, such as Parkinson's and Huntington's disease or amyotrophic lateral sclerosis.

DEVELOPMENT PROGRAMMES

BOTULINUM TOXIN TYPE A

On 29 April 2009, the FDA granted marketing authorisation for Dysport™ for the therapeutic indication (cervical dystonia) and in aesthetic medicine (glabellar lines). Ipsen will market Dysport™ for the therapeutic indication and its partner Medicis will be responsible for the distribution of the drug for use in aesthetic medicine.

In February 2007, Ipsen granted Galderma the right to develop, promote and distribute the Group's botulinum toxin type A product for aesthetic indications in Europe and certain other territories. Galderma will market this product under its own brand name Azzalure®. On 2 February 2009, Azzalure® received the collective green light from 15 European countries' Health Authorities for the granting of national marketing authorisations. This assessment was based on clinical trials involving more than 2,600 patients, which confirmed the safety and efficacy of Azzalure®. The first marketing authorisations have been granted in the United Kingdom, Portugal, Denmark and France. ■

OBI-1,

A VERY INNOVATIVE MOLECULE OFFERING HIGH ADDED VALUE

Commercially, Ipsen is not yet present on the haematology market. Leveraging its expertise in protein engineering, the Group has launched a major research programme in haemostasis (blood coagulation).

OBI-1 is the first recombinant therapeutic protein, designed by Ipsen's biotechnology platform in Boston.

The Group has entered into partnerships with Emory University in the United States and with Octagen in order to develop a recombinant version of the porcine Factor VIII to treat congenital haemophilia type A complicated by the presence of antibodies which inhibit Factor VIII — and acquired haemophilia. Following the very encouraging results in phase II, Ipsen has started to consult with the regulatory authorities on the protocol for phase III clinical trials.

In 2008, the Group acquired from Octagen all the assets related to OBI-1. Ipsen now owns the worldwide marketing rights for this very innovative product, which provides high added value in the treatment of serious diseases, in line with the Group's strategy.

ACTIVITIES
HAEMATOLOGY

"I AM EAGERLY AWAITING OBI-1 SINCE, AS A RECOMBINANT PFVIII PRODUCT, IT SHOULD PROVIDE A SIMILARLY BENEFIT TO STOP BLEEDING."

DR. ARTHUR THOMPSON,
Director of the Haemophilia Treatment Center, Puget Sound Blood Center, Seattle, Washington

Hemophilia A is characterized by a deficiency in the blood of a clotting protein known as Factor VIII. As an X-linked condition, it occurs almost exclusively in males, with an incidence of 1 in 5,000 male births. While treatment with human Factor VIII allows these patients to live a relatively normal life, up to 1/3 of severe hemophiliacs develop antibodies, or inhibitors, to Factor VIII which render this therapy ineffective, placing the patient at risk for life-threatening hemorrhage. For example at least a dozen such inhibitor patients in Washington State are being followed by our center at any time. Although rare, effective therapies for patients with an inhibitor represent the biggest unmet need in hemophilia care today. This includes both how to treat bleeding when it occurs, and also how to prevent inhibitors from occurring with less immunogenic FVIII products. There is active research on the latter as well that includes recombinant hybrid Factor VIII proteins that have portions of both the human and porcine sequences.

Acquired hemophilia, in which non-hemophilia patients develop a neutralizing autoantibody which inhibits their own Factor VIII, is pretty rare, as we see maybe 4 or 5 per year in our area. On the other hand, it oftens results in severe bleeding, as most experts that care for patients with bleeding disorders state that the worst bleeding they have ever encountered over the course of their careers is seen in acquired hemophilia patients. In fact, in a number of these patients the diagnosis is made only after bleeding cannot be stopped following a surgical procedure.

I am eagerly awaiting OBI-1 since, as a recombinant pFVIII product, it should provide a similarly benefit to stop bleeding. For a significant number of these patients pFVIII still represents by far the most effective therapy for stopping life-threatening hemorrhage. I expect OBI-1 to become the first-line treatment for these desperate patients when it becomes available."

ACTIVITIES
PRIMARY CARE

In primary care, Ipsen markets essentially four products: Tanakan®, Smecta®, Forlax® and Fortrans®. In France, it is also responsible for the co-promotion of Exforge® and Artotec® and the co-marketing of Nisis®, Nisisco® and Adrovance®.

On the neurosensorial and cognitive disorders treatment market, Tanakan® sales dropped in 2008. Whilst 2008 was a difficult year in France, due to the overall market underperforming and to the arrival of a new competitor, the rest of Europe posted strong growth and offers a promising outlook. The Group's strategy is supported by development programmes which give priority to life-cycle management.

In gastroenterology, sales generated by Smecta®, Forlax® and Fortrans® improved overall in 2008. Smecta® saw growth of 4.8%. Whilst domestic sales remained stable, international sales grew strongly, also in China, the drug's leading market. Growth perspectives are excellent, especially in certain European countries, despite ever increasing competition. In 2008, Ipsen completed the regulatory dossier of Smecta® and implemented product life-cycle management. A new flavour was launched at the beginning of 2008, and research for new formulations is currently underway. The Group also launched Smecta® in Latin America, and strengthened its European marketing platform.

ACTIVITIES
PRIMARY CARE

TANAKAN®

Tanakan® is an oral formulation of EGb 761®, extracted from the leaves of the Ginkgo biloba tree using a standardised and patented process that ensures a consistent composition of the various pharmacologically active substances. It was initially developed in the treatment of various neurological disorders, mainly the treatment of age-related cognitive impairment, neurosensorial disorders such as vertigo, tinnitus, acute or chronic hearing difficulties and retinal disorders.

At the end of 2008, Tanakan® had marketing authorisations in more than 60 countries, mainly in Europe and in Asia. Since 2004, it has been indicated and reimbursed in Belgium in the symptomatic treatment of mild to moderate forms of Alzheimer's-type dementia associated with memory and cognitive disorders. In 2008, 57.8% of Tanakan® sales were generated in France.

The Group also promotes three studies in Europe:
– The GuidAge® study assesses the effectiveness of EGb 761® in the prevention of Alzheimer's disease in patients over 70 presenting a spontaneous memory complaint. The 2,800 patients were recruited by September 2004 and their treatment is due to continue for five years. The results of this study are likely to be available at the end of 2010;
– a study evaluating the effect of EGb 761® on cerebral glucose metabolism, evaluated by FDG-PET scan (in conjunction with the French Atomic Energy Commission), in patients suffering from memory loss and patients with Alzheimer's disease;
– a study evaluating the effect of EGb 761® on the mitochondrial metabolic functions in children suffering from Friedreich's ataxia, a rare genetic disorder.

SMECTA®

Smecta® is an oral formulation of pharmaceutical clay devised and developed by Ipsen. It is used in the treatment of both chronic and acute diarrhoea in adults and children and in the symptomatic treatment of pain associated with oesophageal, gastric, duodenal or colonic disorders. At 31 December 2008, Smecta® had marketing authorisations in more than 70 countries. In 2008, around two thirds of Smecta® sales were generated in equal proportions in France and China, the product's main markets. A new flavour was launched in 2008 and research on new formulations is underway.

FORLAX®

Forlax® is a macrogol of high molecular weight, an oral laxative devised and developed by Ipsen. It is used in the treatment of constipation for both adults and children. At 31 December 2008, Forlax® had marketing authorisations in more than 60 countries. In 2008, more than 75% of Forlax® sales were generated in France.

NISIS® AND NISISCO®

In 2003, the Group added Nisis® and Nisisco®, two anti-hypertensive products, to its portfolio by signing an agreement with the Swiss group Novartis, to market the products in France, Andorra and Monaco. Nisis® and Nisisco® are oral formulations. Nisis® contains valsartan, while Nisisco® contains valsartan and hydrochlorothiazide. These products are used in the treatment of arterial hypertension. The active substance of Nisis® and Nisisco® is valsartan, a synthetic angiotensin II antagonist compound.

ADROVANCE®

On 30 January 2007, MSD granted Ipsen the marketing rights in France for Adrovance®, for the treatment of postmenopausal osteoporosis in patients at risk of vitamin D deficiency. Osteoporosis is a diffuse disease of the skeleton,

IN 2008, ALMOST **70%** OF SMECTA® SALES WERE GENERATED OUTSIDE FRANCE

whose main characteristic is low bone mass and deterioration of bone tissue. Resulting bone fragility increases susceptibility to fractures.

ADENURIC® (FEBUXOSTAT)

Within the framework of the partnership established in July 2003 with the Japanese group Teijin, Ipsen signed a specific agreement to develop febuxostat, a drug intended for the treatment of symptomatic hyperuricaemia, in Europe. Febuxostat is a new chemical entity, a nonpurine selective inhibitor of xanthine oxidase which degrades puric and pyrimidine bases in uric acid. In October 2006, the Group filed Adenuric for registration with the EMEA, and the Committee for Medicinal Products for Human Use delivered a positive opinion on 21 February 2008 for Adenuric® (febuxostat) in 80 mg and 120 mg tablet form for the treatment of chronic hyperuricaemia in gout patients and recommended it for marketing authorisation. ■

“Longer life expectancy which is a major fact of the 21st century, points towards an ever more critical issue for society: dependency. Ipsen has long been involved in this area. This company carries out extremely interesting studies on Alzheimer’s disease, which alone is responsible for 70% of dependency cases. *La Fondation Ipsen* is renowned in our community of specialists, who consider its conferences and publications authoritative. Furthermore, Ipsen provides precious and active support to the Foundation for scientific cooperation on Alzheimer’s disease. In our field, I do not know any one researcher who has not been able to count on Ipsen’s support when needed.”

FRANÇOISE FORETTE
Professor of internal medicine and geriatrics at Paris-V University, Chairperson of the Supervisory Board of Broca hospital, Director of the *Fondation nationale de gérontologie* and member of the Board of Directors of the Foundation for scientific cooperation on Alzheimer’s disease.

MORE THAN

4,200

EMPLOYEES WORLDWIDE

SOCIAL AND ENVIRONMENTAL RESPONSIBILITY

Ipsen's commitment to social responsibility is carried out on a daily basis in the initiatives aimed at promoting a code of ethical conduct ensuring equal opportunities for all employees and implementing best practices across its teams. The Group is also committed to protecting the environment, and its involvement in sponsorship programmes and solidarity projects demonstrates the humane approach adopted by employees.

MEMBERS OF THE EXECUTIVE COMMITTEE

- **Jean-Luc BÉLINGARD,** Chairman and Chief Executive Offficer
- **Frédéric BABIN,** Executive Vice-President, Human Resources
- **Éric DRAPÉ,** Executive Vice-President, Manufacturing and Supply Organisation
- **Claire GIRAUT,** Executive Vice-President, Chief Financial Officer
- **Christophe JEAN,** Executive Vice-President, Chief Operating Officer
- **Jacques-Pierre MOREAU,** Executive Vice-President, Chief Scientific Officer
- **Stéphane THIROLOIX,** Executive Vice-President, Corporate Development

EXECUTIVE COMMITTEE

It ensures complete co-ordination of the Group's scientific, legal, financial, commercial and strategic actions, for which it guarantees consistent management policies. It also assists the Chairman of the Board of Directors in implementing the decisions of the Board.

BOARD OF DIRECTORS

The Board of Directors carries out its functions in accordance with the provisions of law, the Company's Articles of Incorporation and standard corporate governance practice for listed companies. The Board is assisted by four permanent committees which are responsible for making proposals, recommendations and opinions for the approval of the Board. To this end, the committees may conduct or commission external reports which may assist the Board in its decision making role. These committees report to the Board on their work at every Board meeting and assist it in reviewing the strategic guidelines and investment projects, in validating the quality and accuracy of financial statements, and in assessing the compensation and appointments policy. The Board of Directors ensures clear communication with shareholders and the general public. It ensures that the Company has reliable procedures for identifying, assessing and monitoring its liabilities and risks, together with an appropriate internal control system at both operational and financial level. In 2008, the Board of Directors convened ten times.

MEMBERS OF THE BOARD OF DIRECTORS

Chairman and Chief Executive Officer
Jean-Luc BÉLINGARD

Directors
Anne BEAUFOUR
Henri BEAUFOUR
Alain BÉGUIN
Hervé COUFFIN
Antoine FLOCHEL (Vice-Chairman)
Gérard HAUSER
Pierre MARTINET
René MERKT
Yves RAMBAUD
Klaus-Peter SCHWABE

BOARD COMMITTEES

STRATEGIC COMMITTEE

Its principal role is to review all strategic issues affecting the Group with regard to R&D, industrial, commercial and financial matters, and alliances and partnerships. The Committee convened fours times during 2008. These meetings concerned mainly the Group's external growth strategy and the development of the R&D portfolio.

Chairman
Jean-Luc BÉLINGARD

Members
Anne BEAUFOUR
Henri BEAUFOUR
Hervé COUFFIN
Antoine FLOCHEL

AUDIT COMMITTEE

Its principal role is to examine the individual and consolidated financial statements, together with budgets and forecasts, prior to their presentation to the Board, and to control the quality of and compliance with internal control and risk management procedures, and assess information received from management, internal committees and internal and external auditors. The Committee convened eight times during 2008. The agenda for these meetings mainly dealt with the review of the annual and interim financial statements and budget.

Chairman
Yves RAMBAUD

Members
Alain BÉGUIN
Pierre MARTINET

APPOINTMENTS AND GOVERNANCE COMMITTEE

Its principal role is to make proposals to the Board of Directors on the re-election, replacement or appointment of new Directors, to prepare the annual assessment of the Board of Directors, and to issue an opinion on the list of independent Directors. The Committee convened twice in 2008. The agenda mainly dealt with analysis of and recommendations regarding the assessment of the Board and re-election of the Chairman and Vice-Chairman

Chairman
Anne BEAUFOUR

Members
Alain BÉGUIN
Hervé COUFFIN

COMPENSATION COMMITTEE

Its principal role is to make proposals to the Board of Directors on all components of the compensation paid to the Group's company officers, members of its executive management and senior executives. The Committee convened four times in 2008. The agenda related mainly to stock option plans and the allocation of bonus shares, examination of the compensation of the Chairman and Chief Executive Officer and of the members of the Executive Committee, and review of the AFEP/MEDEF recommendations.

Chairman
Antoine FLOCHEL

Members
Gérard HAUSER
Yves RAMBAUD

Ipsen places the development of individual and collective skills at the heart of its Human Resources policy.

ACCOMPANYING GROUP STRATEGY

Headcount by division at the Group's headquarters in 2008

Corporate Services: 16%

Manufacturing and Supply: 2%

Research & Development: 6%

Operations: 76%

Each employee is assessed as regards 4 behavioural skills

- **Accountability**
- **Teamwork**
- **Continuous improvement**
- **Acting responsibly**

Human Resources are committed to supporting and accompanying the Group's strategy. Hence, in 2008, once Ipsen acquired Tercica and the US subsidiary of Vernalis, its teams implemented an action plan to ease the integration of these new employees. During 2008, the Group's rapid growth and its global development led Ipsen to group together its 500 Paris-based employees at the same site in Boulogne-Billancourt, in South West Paris. This new headquarters rationalises travel between sites, encourages cross divisional exchanges and communication, whilst building adherence to a shared strategy. The transparent and fluid architecture of the building is a reflection of the company's image, values and daily operations.

Through their initiatives, Human Resources are also committed to improving individual and collective performance, which has led to the review of the Individual Performance Approval Process (IPAP).

This annual individual performance assessment is a key process as it serves to recall and clarify the Group's strategy and helps to transform Group objectives into individual objectives. In 2008, the assessment process was modified, adding two new levels of targets, both short-term and long-term. In addition behavioural skills criteria have also been introduced: accountability, teamwork, continuous improvement, and acting responsibly. The next step will enable each employee to determine a personal and professional development plan with his/her manager aimed at accompanying the employee in order to respond to his/her needs in terms of long-term career advancement.

Over recent years, the Group has focused actively on acquisitions, building partnerships and developing innovative products. It was supported throughout by teams of employees, highly qualified each in their own field. To support and boost its commercial achievements, Ipsen will now strive to develop managerial excellence. Human Resources will design a managerial development programme aiming to professionalise Group managers in terms of their skills in team, project, and change management.

IPSEN IS DIRECTLY
PRESENT IN APPROXIMATIVELY

40 COUNTRIES

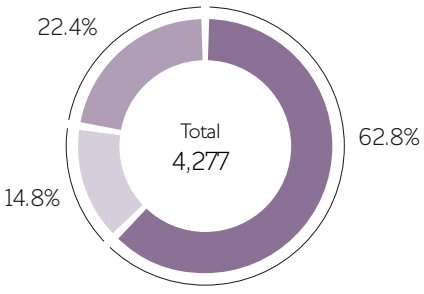
A BONUS SHARE PLAN FOR ALL GROUP EMPLOYEES

The Board of Directors at its meeting on 22 January 2009 decided to allocate 30 bonus shares to all Group employees. This decision reflects Ipsen's confidence in the future despite the current troubled economic environment. These bonus shares are granted to all Group employees subject to at least three months service in the Group on the grant date. These shares will become transferable after a vesting period of four years. The employees were not required to take any specific steps in order to benefit from this initiative which is a reflection of Ipsen's intention to reward employee loyalty. This programme, named Ipsen Global Equity, concerns more than 4,000 employees in over 30 countries.

DIVERSITY: AN AGREEMENT IS SIGNED

"Our diversity and mutual respect amongst employees strengthen our performance." This is one of Ipsen's corporate values which has resulted in management and social partners in France deciding to initiate a global diversity policy. The first stage of this policy was the signature, in June 2008, of the PHARE project (plan to help the recruitment and employment of disabled workers). This plan includes proactive steps to recruit disabled workers and creates specific training sessions for Ipsen managers or its purchasers of sub-contracting services. Communication campaigns are also planned to increase awareness among employees of disability in the workplace: photographic exhibitions, a theatre play, etc. Equal opportunities between men and women is a strategic issue both for individual and corporate development and is due to form the second stage of this global diversity policy. ■

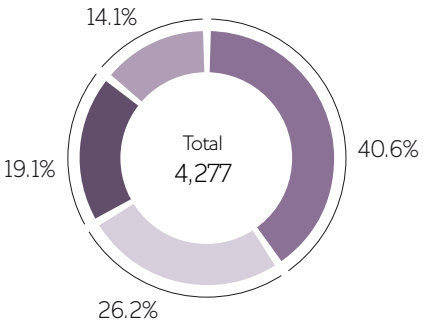
Headcount by geographical area in 2008



- Major Western European countries (1)
- Other European Countries
- Rest of the world (2)

(1) Germany, Spain, France, Italy and United Kingdom
(2) Including North America and Asia.

Headcount by activity in 2008



- Operations
- Manufacturing and Supply
- Research and Development
- Administration and others

Ipsen has been historically involved in solidarity projects where it is committed in various fields. Ipsen's initiatives are in keeping with the Group's humanist approach, involving its employees on a daily basis for innovation and improved patient care.

SOLIDARITY AND SPONSORSHIP: A DAILY COMMITMENT

SHORT AND MID-TERM SOCIAL AND HUMANITARIAN ACTIONS

Ipsen's major recurring humanitarian action, which is totally consistent with its activity, is the donation of drugs to disaster stricken populations throughout the world. But the Group's ambition goes beyond this, and more specifically strives towards improved patient care, which also includes donating equipment to targeted causes. Ipsen recently financed work required to rehabilitate buildings destined to accommodate parents of children suffering from cancer in Algeria. In Dreux (France) Ipsen supports the *Fondation de la 2e Chance* whose Director is Michel Giraud, a former cabinet minister. The aim of this foundation is to provide individuals who are in unstable social and financial conditions with humane and financial support.

AIMING TOWARDS MULTIDISCIPLINARY SCIENTIFIC COOPERATION

The Foundation for the scientific cooperation on Alzheimer's disease created in June 2008, (Alzheimer's Foundation) is responsible in France for implementing the research stages of the Alzheimer's plan (2008-2012) launched by the French President. More specifically the Foundation is to lay the basis for multidisciplinary scientific co-operation, by federating both public and private Alzheimer's research teams. Ipsen is one of the four international pharmaceutical laboratories who are members of the Foundation.

RESEARCH AND INNOVATION AT THE FOREFRONT

Supporting research is clearly a natural and legitimate vocation for Ipsen, with innovation being its core business. *La Fondation Ipsen* is a pioneer, first in its field to launch international seminars on topics which with hindsight have clearly become key biological and medical issues: gene therapy in the central nervous system, brain stem cells, the role of apolipoprotein E in Alzheimer's disease, etc. Education and training are key aspects in public health, where collaboration may last for many years. The Group has awarded grants or prizes to support researchers and fund study programmes in various countries, participates in training sessions (about

From left to right: Jean-Luc Bélingard, Christine Albanel, Minister of Culture and Communication, Henry Loyrette, Chairman and Director of the Louvre museum

A PAPYRUS FOR THE FUTURE

In June 2007, an Egyptian medical papyrus was acquired by the French State thanks to sponsorship from Ipsen, and given to the Louvre museum. This 7 metre long papyrus which dates back to the 2nd millenium BC is a medical manual presenting several practical case studies, examples of diagnosis and indications in detail. The papyrus was exhibited for three months and is now being restored and analysed by the Egyptian Antiquities department of the Louvre museum. Ipsen's sponsorship initiative marked its adherence to the Louvre museum Corporate Programme, which brings together a group of companies which contribute towards preserving and expanding the collections of this renowned museum.

thirty such sessions in the United Kingdom) and supports projects or academic research centres, etc. Ipsen is also involved in major public health programmes, such as Paquid, in France, which focuses on analysing the ageing brain and related disorders, namely Alzheimer's senile dementia and assessing the degree of dependency of the elderly.

ASSOCIATIONS, FOUNDATIONS AND UNIVERSITIES: A VAST SPECTRUM OF PARTNERSHIPS

Ipsen is also the privileged partner of learned societies, medical and health institutions and patient associations. The Group is closer than ever to its vocation of improving the quality of life and information of patient's and their families. It collaborates with associations supporting cancer patients in Italy and associations accompanying patients suffering from acromegaly in Korea. In the United Kingdom, the Ipsen Fund focuses on sick children. The Group also supports the Australian Pituitary Foundation, which since 2006, publishes reviews to inform and educate patients. The Group also works together with learned and health institutions, to support research programmes and training for health personnel. The Group is involved in several initiatives worldwide with university or academic groups, medical centres and associations. Pursuant to a partnership with the Healthcare Chair of the Paris Institute of Political Sciences *(Sciences Po)*, the Group focuses on diversifying university courses, developing professional training and stimulating research in life sciences. ■

FIGHTING CEREBRAL PALSY WITH THE CANDY ASSOCIATION

Ipsen supports the Mexican foundation Candy, which fights against cerebral palsy and motor disorders, the largest cause of disabled children in Mexico due to the conditions of monitoring pregnancies and births. Candy aims to help these sick young children gain access to the recommended treatment. Due to Ipsen's funding, Candy will manage a network of doctors and physical therapists to set up a suitable healthcare protocol and reduce treatment costs for this disease, which is three times as prevalent in Mexico than in Europe, with more than 500,000 children affected by this disease.

SOCIAL AND ENVIRONMENTAL RESPONSIBILITY
LA FONDATION IPSEN

Created in 1983 under the patronage of *La Fondation de France*, *La Fondation Ipsen* aims to contribute to the development and dissemination of scientific knowledge. The long-standing action of *La Fondation Ipsen* is aimed at furthering the interaction between researchers and clinical practitioners, which is crucial given that these professions are extremely specialised.

INITIATING A REFLECTION ON THE MAJOR SCIENTIFIC ISSUES OF THE FORTHCOMING YEARS

La Fondation Ipsen seeks the involvement of its international partners from university and scientific spheres to independently present the major issues it has chosen and to review current knowledge.

INTERNATIONAL SEMINARS

La Fondation Ipsen brings together distinguished scientific experts who meet every year at the Medicine and Research Seminars dealing with emerging themes in medicine and biology:

• **Alzheimer's disease**. Since 1987, 23 conferences have been held on this theme. The last conference in this series which was held in Paris on 28 April 2008, covered intracellular traffic and neurodegenerative disorders.

• **Neurosciences.** Launched in 1990, this set of conferences focuses on the major issues emerging in this field, concerning molecular biology or cognitive sciences. The 16th conference in this series, "Neurobiology of the *Umwelt*: how living beings perceive the world", was held in Paris on 18 February 2008.

• **Endocrinology**. This topic, launched in 2002, focuses on the interactions of the endocrine system, and their involvement in the body's functioning. The 8th conference in this series was held on 1 December 2008, and discussed "IGF : local repair and survival factors".

• **Vascular tree.** This series, initiated in 2004, aims to explore the different steps leading to the development of the vascular system, its growth in harmony with the other organs, its physiology, its degeneration, death and potential for regeneration. The last conference in this series, dedicated to the relationships between oxygen metabolism and the vessels, was held on 27 October 2008.

• **Cancer.** In 2008, the 4th conference in the series was dedicated to the relationships between metabolism and cancer. The top specialists in the world, including several Nobel Prize laureates, gathered together in Costa Rica, from 8 to 12 March 2008.

La Fondation Ipsen has established a number of partnerships with international institutions or organisations, bringing together experts from

IPSEN, COMMITTED TO THE SCIENTIFIC COMMUNITY

YVES CHRISTEN, Chairman of *La Fondation Ipsen*

"Ipsen has long been committed to the scientific community in dealing with the issues of biomedicine and fighting for therapeutic innovation together with all stakeholders. This commitment to science is clearly illustrated by the initiatives of *La Fondation Ipsen*, created in 1983 under the patronage of *La Fondation de France*. *La Fondation* has entered into partnerships with international organisations such as WHO, the *Fondation Nationale de Gérontologie* and Harvard University. The collaboration with the Salk Institute and Nature journal gave rise to a symposium in 2008 on the relationship between genes, neural circuits and behaviour.

In 2008, together with Cell Press and Massachusetts General Hospital, Ipsen launched scientific exchanges in the fields of biology and cognition. In partnership with Nature journal, four conferences on "Emergence and convergence" were organised in 2008 in the United States and in France. *La Fondation Ipsen* publishes reference works after the conferences, and encourages research by awarding prizes for pioneering research."

various disciplines, including the World Health Organization (WHO), the *Fondation Nationale de Gérontologie* and Harvard University.

Three new partnerships were launched in 2007 with:
• **the Salk Institute** (La Jolla) and **Nature** journal. This partnership consists of a series of annual meetings dedicated to biological complexity.
In January 2008, this focused on the relationships between genes, neural circuits and behaviour.
• **Cell Press** and **Massachusetts General Hospital**. This series is called "Exciting Biologies". The second meeting in this series was held in Chantilly (France), from 16 to 18 September 2008, and focused on the biology of the mind.
• **Nature** journal. In 2008, four meetings based on the theme "Emergence and Convergence" took place in the United States in Houston (31 March), Chicago (29 September), Durham (8 December), and in France in Paris (6 June).

INTERNATIONAL PUBLICATIONS

La Fondation Ipsen publishes reference works after the conferences, distributed by international publishers as part of different collections:
– Research and Perspectives in Alzheimer's disease;
– Research and Perspectives in Neuroscience;
– Research and Perspectives in Longevity;
– Research and Perspectives in Endocrinology;
– WHO/Fondation Ipsen Collection;
– Mind and Brain Collection.
Three publications were released in 2008.

Furthermore, since 1986, *La Fondation Ipsen* has published a periodical dedicated to Alzheimer's disease, *Alzheimer Actualités* (202 issues released to date). It also publishes reports from the Medicine and Research seminars focusing on decrypting the vascular tree and cancer.

AWARDS TO ENCOURAGE RESEARCH

La Fondation Ipsen rewards pioneers in research in the following four fields:
• **Neurosciences.** In 2008, an international jury chaired by Prof. Wolf Singer (Max Planck Institute, Frankfurt) awarded the 19th Neuronal Plasticity Prize to Prof. Jean-Pierre Changeux (Institut Pasteur, Paris), Prof. Peter Kalivas (University of South Carolina, Charleston), and Prof. Eric Nestler (University of Texas, Dallas) for their work on the molecular bases of addiction.
• **Longevity.** In 2008, this prize was awarded to Prof. Gerald McLearn (Pennsylvania State University, University Park) for his work on the role of genetic factors in cognitive ageing.
• **Neuropsychology**. The Jean-Louis Signoret Prize was awarded to Elizabeth Warrington (National Hospital for Neurology & Neurosurgery, London) in 2008, for her work on semantic memory.
• **Endocrinology.** In 2008, the international jury chaired by Iain Robinson (National Institute for Medical Research, London) selected Prof. Ronald Evans (Salk Institute, La Jolla) for his pioneering work on the mechanisms of expression for genes involved in endocrine regulation. ■

SOCIAL AND ENVIRONMENTAL RESPONSIBILITY

ENVIRONMENT, HEALTH AND SAFETY

Preserving human health is at the heart of Ipsen's vocation. Its activities have naturally led the Group to provide its employees with the optimal level of safety in carrying out their duties and to build a development strategy which respects the environment. Ipsen's commitment has been formalised in the Group's Environment, Health and Safety measures (EHS).

A GLOBAL AND SUSTAINABLE COMMITMENT

Ipsen is constantly focused on protecting the environment and its employees' health, with a proactive prevention policy, aimed at ever improved quality, based on an internal benchmark and best practices which may reach beyond the regulatory requirements in the countries where Ipsen operates. The Group also aims to strengthen its image with its internal and external partners: the neighbourhood, local councillors, associations, etc.

In 2008 volumes sold by Ipsen increased 8%, however, its energy consumption grew by only 5.8% (electricity, gas, fuel). Another reflection of the Group's environmental commitment: 83.5% of the Group's waste was recycled in 2008.

2008-2012 STRATEGIC PLAN

The first stage in the Group's 5-year EHS plan was launched in 2008 at all Group sites, when a management system was set up to identify and class the potential chemical risks for all products arising from Ipsen's R&D. The PDCA process (Plan Do Check Act) of this strategy has four phases: plan the EHS policy by aligning governance policies at all sites; check the results and take corrective measures where necessary; lastly, act in line with management reviews. These four phases strive together to improve the results of the EHS policy and prepare the second stage which will be launched in 2010. At that date, all of Ipsen's manufacturing facilities will be valid candidates for ISO certification, and the EHS policy will be an integral part of all areas of business, including operations and head offices in the countries where Ipsen is based. After the audit in 2008, the ISO certification initially granted to the Isle-sur-la-Sorgue facility in 2004, was renewed. In the United Kingdom, the Wrexham plant secured Green Dragon Level 3 certification once again from the local environmental authorities, demonstrating the steps taken to preserve ecosystems. The third stage will be launched in 2012 with three major priorities:

- reducing dependency on individual protection equipment, favouring collective protection;
- significantly reducing its environmental footprint;
- setting up visible EHS initiatives, generating added value.

The design of Ipsen's new headquarters in Boulogne-Billancourt, which complies with the highest environmental quality standards is fully in line with the Group's strategy.
Furthermore, in France on 25 March 2009, The French Pharmaceutical Companies Association (Leem), a professional body of which Ipsen is a member, signed an agreement on progress in the pharmaceutical industry pursuant to the commitment undertaken at the Environment Round Table meetings on sustainable development for 2009-2011, with the Ministry of Ecology and Sustainable Development and the Ministry of Health and Sport .
The Leem committed on five targeted areas resulting from the Environment Round Table initiative:
• reduce greenhouse gas emissions and improve the energy efficiency of the pharmaceutical industry (fleets of vehicles eligible for the ecological bonus, vehicle pooling, Carbon Balance®, etc.);
• involve employees on environmental issues via training, information, and increasing awareness;
• continue to develop a lasting relationship with stakeholders (patient associations, environmental protection associations, experts, etc.) on sustainable development and health issues;
• commit in favour of a responsible communication policy limiting the impact on the environment;
• strengthen the partnership between public and private sectors on sustainable development and health issues (unused drugs, healthcare waste with risk of infection, protecting biodiversity, etc.). ■

83.5%
OF WASTE RECYCLED IN 2008

TRAINING AND INCREASING AWARENESS

In 2008, the Group continued its training programme on EHS risks and impacts at all sites. Upbeat training sessions were organised for newcomers to the company. Sessions specific to the activity of certain sites were also organised: information on risks linked to carcinogenic, mutagenic, or reprotoxic products at the Dreux site, increasing awareness about legionnella and biological handling in laboratories at the Wrexham site, information on the management system at the Barcelona site, risk assessment sessions at the Dublin site. All these initiatives work towards a clearer understanding of risks and sustainable development.

CONSOLIDATED FINANCIAL STATEMENTS

With revenues breaking above the one billion euros mark for the first time, sales growth of 8.2% on a comparable basis year-on-year and a standalone operating margin of 21.6%, the Group's performance during 2008 was highly satisfactory and in line with the financial objectives set a year ago, in spite of the downturn in the economic environment.

Today, the Group is stronger and its positioning has improved significantly thanks to its move into the North American market, which has diversified its growth engines.

SALES UP
8.2%
IN 2008

CONSOLIDATED INCOME STATEMENTS

(in thousand euros)	31 December 2008	31 December 2007	31 December 2006
Sales of goods	971,022	920,475	861,676
Other revenues	67,090	73,282	83,581
Revenue	**1,038,112**	**993,757**	**945,257**
Cost of goods sold	(219,928)	(199,025)	(181,377)
Research and development expenses	(182,921)	(184,739)	(178,348)
Selling expenses	(358,400)	(321,052)	(307,795)
General and administrative expenses	(85,899)	(80,429)	(75,220)
Other operating income and expenses	(8,257)	368	(8,223)
Restructuring costs	(2,620)	8	190
Impairment losses	-	-	(7,265)
Operating income	**180,087**	**208,888**	**187,219**
Investment income	21,425	11,541	7,974
Cost of financing	(4,348)	(1,950)	(2,142)
Net finance cost	**17,077**	**9,591**	**5,832**
Other financial income and expense	(5,156)	(2,855)	(5,707)
Income taxes	(33,320)	(54,478)	(40,891)
Share of loss/profit from associated companies	(10,847)	(8,764)	(1,666)
Net profit from continuing operations	**147,841**	**152,382**	**144,787**
Net loss from discontinued operations	(172)	(1,313)	(290)
Consolidated net profit	**147,669**	**151,069**	**144,497**
- Attributable to shareholders of Ipsen	147,164	150,611	144,006
- Minority interests	505	458	491
Basic earnings per share, continuing operations (in € per share)	1.76	1.81	1.72
Diluted earnings per share, continuing operations (in € per share)	1.75	1.81	1.72
Basic earnings per share, discontinued operations (in € per share)	(0.00)	(0.02)	(0.00)
Diluted earnings per share, discontinued operations (in € per share)	(0.00)	(0.02)	(0.00)
Basic earnings per share (in € per share)	1.75	1.80	1.71
Diluted earnings per share (in € per share)	1.75	1.79	1.71

CONSOLIDATED BALANCE SHEETS BEFORE ALLOCATION OF NET PROFIT

(in thousand euros)	31 December 2008	31 December 2007	31 December 2006
ASSETS			
Goodwill	351,736	189,013	188,836
Other intangible assets	163,911	89,169	68,203
Property, plant & equipment	237,860	221,891	198,186
Equity investments	2,650	1,457	1,825
Investment in associated companies	-	40,948	50,832
Non-current financial assets	3,810	25,883	12,583
Other non-current assets	8,039	55,632	18,018
Deferred tax assets	111,439	61,393	64,025
Total non-current assets	**879,445**	**685,386**	**602,508**
Inventories	115,944	87,111	78,947
Trade receivables	217,845	216,214	191,702
Current tax assets	49,509	26,569	2,665
Other current assets	63,652	53,753	43,700
Current financial assets	2,528	96	901
Securities held for sale	-	6,000	-
Cash and cash equivalents	239,584	247,068	285,459
Total current assets	**689,062**	**636,811**	**603,374**
Assets of discontinued operations	1,333	725	8,391
TOTAL ASSETS	**1,569,840**	**1,322,922**	**1,214,273**
EQUITY & LIABILITIES			
Share capital	84,060	84,044	84,025
Additional paid-in capital and consolidated reserves	680,216	582,557	506,244
Net profit for the period	147,164	150,611	144,006
Foreign exchange differences	(44,535)	(17,350)	(7,789)
Equity – attributable to shareholders of Ipsen	**866,905**	**799,862**	**726,486**
Minority interests	1,580	1,247	1,419
Total shareholders' equity	**868,485**	**801,109**	**727,905**
Retirement benefit obligation	11,530	10,038	9,299
Long-term provisions	27,181	14,981	11,421
Bank loans	148,941	4,379	6,286
Other financial liabilities	13,803	16,449	15,313
Deferred tax liabilities	36,404	3,932	2,371
Other non-current liabilities	142,560	192,043	172,270
Total non-current liabilities	**380,419**	**241,822**	**216,960**
Short-term provisions	8,952	6,598	5,323
Bank loans	4,000	5,375	6,973
Financial liabilities	4,346	3,831	2,251
Trade payables	103,835	104,181	100,269
Current tax liabilities	36,315	12,327	27,215
Other current liabilities	156,345	136,234	114,824
Bank overdrafts	2,259	6,161	1,716
Total current liabilities	**316,052**	**274,707**	**258,571**
Liabilities of discontinued operations	4,884	5,284	10,837
TOTAL EQUITY AND LIABILITIES	**1,569,840**	**1,322,922**	**1,214,273**

CONSOLIDATED STATEMENT OF CASH FLOWS

(in thousand euros)	31 December 2008	31 December 2007	31 December 2006
Consolidated net profit	**147,669**	**151,069**	**144,497**
Net profit from discontinued operations	172	1,313	290
Share of loss/profit from associated companies	10,847	8,764	1,666
Net profit from continuing operations before share from associated companies	**158,688**	**161,146**	**146,453**
Non-cash and non-operating items			
- Depreciation, amortisation, provisions and impairment losses	50,649	41,226	49,940
- Change in fair value of derivative financial instruments	2,474	(1,929)	1,562
- Net gains or losses on disposal of non-current assets	(24,744)	(252)	(877)
- Share of government grant released to profit and loss	(94)	(97)	(112)
- Exchange differences	(1,432)	3,905	694
- Change in deferred taxes	948	394	(34,227)
- Share-based payment expense	6,585	7,562	3,282
- Gain or loss on disposals of treasury shares	(724)	545	221
- Other non-cash items	4,165	1,754	690
Cash flow from operating activities before changes in working capital	***196,515***	***214,254***	***167,626***
- (Increase)/decrease in inventories	(12,576)	(9,026)	(4,644)
- (Increase)/decrease in trade receivables	(4,294)	(25,395)	(27,419)
- (Decrease)/increase in trade payables	1,176	5,087	(7,121)
- Net change in income tax liability	(1,261)	(38,456)	33,051
- Net change in other operating assets and liabilities	23,849	29,506	166,142
Change in working capital related to operating activities	***6,894***	***(38,284)***	***160,009***
NET CASH PROVIDED BY OPERATING ACTIVITIES	**203,409**	**175,970**	**327,635**
Acquisitions of property, plant & equipment	(61,447)	(58,672)	(40,630)
Acquisitions of intangible assets	(33,762)	(26,483)	(41,217)
Proceeds from disposal of intangible assets and property, plant & equipment	27,272	1,160	3,044
Acquisition of investments in non-consolidated companies	(3,224)	(698)	(15)
Acquisitions of investments in associated companies	-	(2,129)	(63,082)
Convertible note subscriptions	-	(44,386)	(20,966)
Proceeds from disposal of investment securities	1,410	-	-
Payments to post-employment benefit plans	(1,904)	(5,026)	(4,226)
Impact of changes in the scope of consolidation	(214,669)	8	-
Change in cash securities held for sale	6,000	(6,000)	-
Cash flows related to investing activities	1,265	(944)	(1,028)
Deposits paid	(1,012)	(4,601)	-
Change in working capital related to investing activities	(5,145)	7,493	5,796
NET CASH USED BY INVESTING ACTIVITIES	**(285,216)**	**(140,278)**	**(162,324)**
Additional long-term borrowings	148,941	1,900	-
Repayment of long-term borrowings	(6,521)	(2,170)	(31,824)
Net change in short-term borrowings	(1,375)	(1,584)	(89)
Treasury shares	(9,284)	(24,758)	(1,294)
Dividends paid by Ipsen	(55,027)	(50,389)	(50,407)
Dividends paid by subsidiaries to minority interests	(215)	(631)	(358)
Deposits received	174	-	-
Change in working capital related to financing activities	2,264	814	464
NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES	**78,957**	**(76,818)**	**(83,508)**
Impact of operations due to be sold or discontinued	732	1,285	647
CHANGE IN CASH AND CASH EQUIVALENTS	**(2,118)**	**(39,841)**	**82,450**
Opening cash and cash equivalents	**240,907**	**283,743**	**200,564**
Impact of exchange rate fluctuations	(1,464)	(2,995)	729
Closing cash and cash equivalents	**237,325**	**240,907**	**283,743**

Thank you to all Ipsen members of staff who appear in this publication.

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