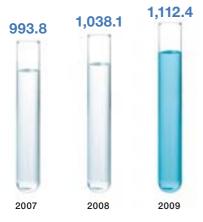


## 2009 Key Figures

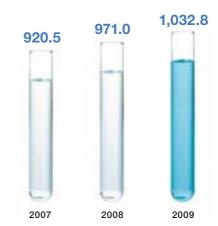
#### Total revenues\* (€ million)



Total revenues rose by 7.2% compared with 2008.

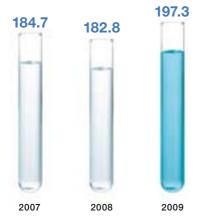
\* Total revenues include sales as well as royalties and payments received in conjunction with the Group's partnerships and various other services.

#### Sales (€ million)



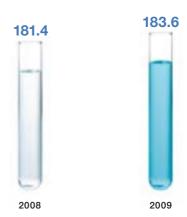
In 2009, consolidated Group sales increased by 6.8% and drug sales rose by 7.6% compared to the previous year (excluding foreign exchange impacts). In 2009, for the first time, drug sales came out above the €1 billion mark.

## Research and Development expenditure (€ million)



In 2009, Research and Development expenditure reached nearly 20% of sales, representing an increase of close to 8%.

## Adjusted operating income (€ million)

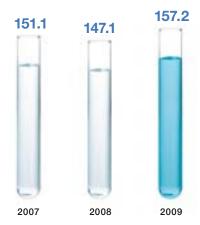


Excluding the purchase price accounting impact related to its acquisitions in North America, the Group's adjusted operating income amounted to €183.6 million in 2009, representing 17.8% of sales.

The information presented above at December 31, 2008 has been restated to account for the purchase price accounting impact related to the Group's transaction with Tercica Inc. and Vernalis Inc.

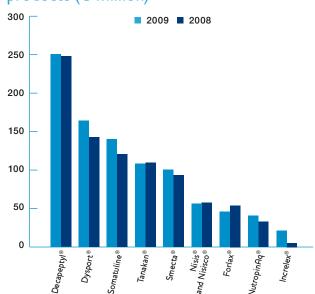


## Consolidated net profit (€ million)

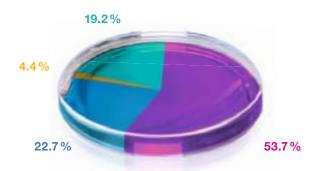


Consolidated net profit (share attributable to shareholders of Ipsen SA) increased by 6.9%. Fully diluted earnings per share (attributable to shareholders of Ipsen SA) amounted to €1.86, a 6.9% increase over 2008.

## Sales of the Group's main products (€ million)



## 2009 sales by geographical area



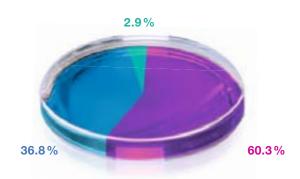
#### Major Western European countries 53.7 %

France 31.3% Spain 5.7% Italy 7.0% Germany 5.5% United Kingdom 4.2%

Rest of Europe 22.7% North America 4.4%

Rest of World 19.2%

### 2009 sales by therapeutic area



#### Specialty care 60.3%

Oncology 24.3% Endocrinology 19.6% Neurology 16.4%

#### Primary care 36.8%

Gastroenterology 17.7% Cognitive disorders 10.5% Cardiovascular 7.1% Other pharmaceutical products 1.5%

**Drug-related activities 2.9%** 

The information presented above at December 31, 2008 has been restated to account for the purchase price accounting impact related to the Group's transaction with Tercica Inc. and Vernalis Inc.

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# Message from the Chairman

With strong financial results, major advances in its R&D portfolio and four new launches in 2009 - including Dysport® in the US – Ipsen strengthened its position as a global biopharmaceutical group throughout the year.

#### STRONG RESULTS

Since 2008, the economic and financial crisis has created a disruption in pharmaceutical markets, characterized by a deterioration of the creditworthiness of healthcare paying agencies and reimbursement systems. Under these conditions, the strong growth rates achieved by Ipsen's drug sales, which reached 7.6% and 13.9% (excluding foreign exchange impacts) for the Group's specialty care products, illustrate both the relevance of the Group's positioning and the recognition of the quality of the therapeutic options it offers the medical profession. The strict financial management policy implemented in 2009 enabled the Group to generate adjusted operating income of €184 million (17.8% of sales), and net cash flow from operating activities of €258 million.

#### **MAJOR ADVANCES** IN THE R&D PORTFOLIO

With an R&D budget of close to €200 million in 2009, representing nearly 20% of sales, the Ipsen group continued to build its future in its targeted specialty care areas: oncology, endocrinology, neurology and now hematology, following the signing of a strategic partnership with Inspiration Biopharmaceuticals in the US in January 2010.

Several significant programs showed remarkable progress in 2009.

In oncology, Ipsen is developing BN 83495, the first oral inhibitor of the steroid sulfatase. In December 2009, highly promising phase I results were published regarding the efficiency of this agent in the treatment of hormone receptor positive breast cancer. The molecule is also in further clinical development for advanced endometrial cancer (phase II clinical study) and for castration-resistant prostate cancer (phase I in North America).

In endocrinology, Ipsen published encouraging interim results of a phase II trial evaluating the co-administration of recombinant human growth hormone and type 1 insulinmimetic recombinant human growth factor as a potential treatment for short stature in children. Ipsen also presented the results of phase I and phase IIa clinical studies for its BIM 23A760 molecule, a chimeric compound combining a somatostatin analog with a dopamine agonist developed for the treatment of acromegaly and neuroendocrine tumors. Lastly, phase III studies evaluating the effectiveness of Somatuline® Depot® in neuroendocrine tumors were initiated in the US.

Concurrently to its efforts to optimize the Group's presence in primary care, Ipsen grew its specialty care franchise with the addition of a fourth pillar: hematology. The transaction with Inspiration Biopharmaceuticals enables the Group to create a world-class franchise in this field. With the acquisition of the exclusive license for OBI-1 – the recombinant porcine factor VIII developed by Ipsen - Inspiration now has, along with its own recombinant factor IX, IB1001, two recombinant proteins ready to enter phase III in 2010, and two compounds in earlier stages of development for the treatment of coagulation disorders. Under the terms of the agreement, Ipsen acquired an initial 29% stake in Inspiration's capital (on a diluted basis), with the possibility of gradually raising its stake up to 47%.

In June 2010, Roche will present a review of the phase III clinical studies conducted on a GLP-1 analog, taspoglutide - a very promising anti-diabetic which stems from Ipsen's research. The development of taspoglutide, which is endowed with specific structural characteristics that provide it with intrinsic sustained-release properties, illustrates Ipsen's expertise in developing innovative formulations applied to therapeutic peptides and proteins.

#### FOUR DRUG LAUNCHES

The Group's therapeutic offer was further strengthened by the launch of four drugs by Ipsen and its partners in 2009.

In April 2009, the FDA granted Dysport®, Ipsen's type A botulinum toxin, a marketing authorization for the US



Jean-Luc Bélingard Chairman and CEO

Our competitive edge and our reliability allow us to look forward to steady and balanced growth, thanks to an original development strategy based on international partnerships. 9 9

for its indications in neurology and esthetic medicine. Dysport® is marketed by Medicis for esthetic use. The drug was launched in the US for both indications in 2009.

In Europe, under the name Azzalure®, the same toxin obtained its first marketing approvals for use in the esthetic treatment of frown lines. Galderma, Ipsen's partner in Europe for the marketing of this product, has already launched Azzalure® in several countries.

In addition, in October 2009, Ipsen and its partner Debiopharm announced the completion of the European decentralized procedure for Decapeptyl® 6-month for the treatment of locally advanced or metastatic prostate cancer. The first product launches took place in February 2010.

Finally, in October 2009 Ipsen granted Menarini the rights for the development and marketing of Adenuric® in Europe for the treatment of chronic hyperuricemia in gout patients. The first product launches in Europe took place in March 2010.

Thanks to its recent launches (Somatuline® Depot® in North America in 2008 and Increlex® in Europe in 2008), Ipsen's global drug portfolio is expanding across all of its targeted therapeutic areas.

#### A GLOBAL **BIOPHARMACEUTICAL GROUP**

In a world where scientific and medical knowledge is undergoing rapid change, Ipsen aims to strengthen its ability to discover, develop, register and market innovative treatments that provide true added value to physicians and patients. The permanent improvement of our R&D organization combined with the constant enhancement of our technological platforms in the engineering of peptides, proteins and steroids provide Ipsen with a strong competitive advantage in offering a coherent portfolio of specialty care products. The vitality of our alliances and partnerships is testimony to the international recognition of our expertise in the most advanced biological technologies.

As a result, in 2009, the strong growth of our biopharmaceutical operations allowed Ipsen to further expand the Group's global footprint. I would like to take this opportunity to thank each and every Ipsen employee, without whom this performance would not have been possible, as well as the Board of Directors, whose trust and strategic vision are key to the Group's long-term development.

## Corporate Governance

#### **BOARD OF DIRECTORS**

The Board of Directors sets the strategic guidelines for Ipsen's activities and oversees their implementation. Subject to the powers expressly attributed to shareholders' meetings, the Board considers all matters regarding the operation of the company and, through its deliberations, settles all matters concerning it.

The Board of Directors ensures that the company's shareholders and the general public are provided with accurate information. It ensures that the company has reliable procedures for identifying, measuring and monitoring its commitments and risks, as well as adequate financial and operational internal controls. The Board of Directors met ten times in 2009.

#### MEMBERS OF THE BOARD OF DIRECTORS

Chairman: Jean-Luc Bélingard

Directors: Anne Beaufour, Henri Beaufour, Alain Béguin, Hervé Couffin, Antoine Flochel (Vice Chairman), Gérard Hauser, Pierre Martinet, René Merkt, Yves Rambaud and Klaus-Peter Schwabe.

#### COMMITTEES OF THE BOARD OF DIRECTORS

The Board of Directors has set up four permanent committees and has defined both the composition and the powers of these committees.

Each committee submits proposals and recommendations as appropriate regarding those areas for which it is responsible. The authorizations granted to the committees may not engender a delegation of the powers conferred by law or by the company's by-laws to the Board of Directors.

#### STRATEGIC COMMITTEE

The role of the Strategic Committee is to:

- review all strategic issues and evaluate all significant proposed investments, divestments, restructurings, alliances and partnerships;
- submit reports, proposals and recommendations on all matters falling within its scope of responsibility.

The Strategic Committee is chaired by the Chairman of the Board of Directors, and comprises no less than three and not more than six other Directors. It meets at least four times a year. The committee met five times in 2009.

Chairman: Jean-Luc Bélingard

Members: Anne Beaufour, Henri Beaufour, Hervé Couffin

and Antoine Flochel.

#### **AUDIT COMMITTEE**

The role of the Audit Committee is to:

- evaluate the accounting policies used to prepare both the parent company and consolidated financial statements, review and assess the consolidation scope and the relevance of the accounting methods applied to the Group;
- examine interim and annual financial statements, together with budgets and forecasts;
- control the quality of and compliance with procedures, and evaluate information received from management, internal committees and internal and external auditors;
- monitor the effectiveness of internal control and risk management systems;
- supervise the selection and reappointment of the statutory auditors, to satisfy itself of their independence.

The Audit Committee comprises three members. Two of its members, including its Chairman, are independent. It meets at least four times a year. The committee met six times in 2009.

Chairman: Yves Rambaud

Members: Alain Béguin and Pierre Martinet.

#### **APPOINTMENTS** AND GOVERNANCE COMMITTEE

The role of the Appointments and Governance Committee is to:

- make any proposals to the Board concerning the reelection, replacement or appointment of new Directors;
- provide an opinion on the appointment or replacement of the Chief Executive Officer and Deputy Chief Executive Officers if required;
- prepare the annual executive session of the Board of Directors regarding its method of operation;
- give an opinion on independent members of the Board of Directors.

The Appointments and Governance Committee comprises three members, none of whom may be the Chairman of the Board of Directors. It meets at least twice a year. The committee met four times in 2009.

Chairman: Anne Beaufour

Members: Alain Béguin and Hervé Couffin.

#### COMPENSATION COMMITTEE

The role of the Compensation Committee is to:

- make proposals to the Board of Directors on all components of the compensation paid to the Group's officers, members of executive management and senior
- give an opinion on the amount and distribution of Directors' fees;
- make recommendations to the Board of Directors on the Group's compensation policies and employee savings plans, employee share ownership, stock options and bonus shares or any other similar compensation.

The Compensation Committee comprises three members, two of whom are independent. It meets at least twice a year. The committee met seven times in 2009.

Chairman: Antoine Flochel

Members: Gérard Hauser and Yves Rambaud.

#### **EXECUTIVE COMMITTEE**

The Executive Committee is responsible for managing the Group's day-to-day operations and for coordinating the Group's various scientific, legal, financial, commercial and strategic actions. The Executive Committee is also responsible for assisting the Chairman in implementing the Board's decisions.

#### MEMBERS OF THE EXECUTIVE COMMITTEE



#### From left to right:

#### Stéphane Thiroloix

Executive Vice President, Corporate Development

#### Claude Bertrand

Executive Vice President, Chief Scientific Officer

#### Claire Giraut

Executive Vice President, Chief Financial Officer

#### Jean-Luc Bélingard

Chairman and Chief **Executive Officer** 

#### Éric Drapé

Executive Vice President, Manufacturing and Supply Organization

#### Christophe Jean

Executive Vice President, Chief Operating Officer

#### Frédéric Babin

Executive Vice President, Human Resources

# Principal Research and Development Programs\*

The Ipsen group's Research and Development activities are focused on the discovery and development of new molecules and on programs for the life cycle management of products already marketed by the Group (new formulations, extensions of indications and registration of products in new geographical areas). In 2009, Ipsen's R&D expenditure totaled close to €200 million, representing nearly 20% of sales.



## PHASE II **Endocrinology** CO-ADMINISTRATION OF HUMAN GROWTH HORMONE + IGF-1 BIM 23A760 Treatment of pituitary and neuroendocrine symptomatic tumors Oncology BN 83495 Advanced endometrial cancer DIFLOMOTECAN (BN 80915) Advanced metastatic cancer Hematology OBI-1 (licensed to Inspiration Biopharmaceuticals) Hemostasis (phase II completed)

#### PHASE III

#### **Endocrinology**

TASPOGLUTIDE (BIM 51077) Type 2 diabetes (partnership with Roche)

#### SOMATULINE® AUTOGEL®

- neuroendocrine tumors
  Symptomatic
  neuroendocrine tumors (US)

#### Oncology

#### TOREMIFENE

- Treatment of side effects related to androgen deprivation therapy (second phase III to be initiated in 2010)
  Prevention of prostate cancer
- among men with high grade intraepithelial neoplasia

#### **DECAPEPTYL®**

Combined hormone therapy for premenopausal breast cancer

#### Neurology

#### DYSPORT®

Muscle spasticity of upper and lower limbs in children and adults (US) (phase III required by the FDA for the approval of Dysport®)

#### Other programs

#### TANAKAN®

Age-related cognitive impairment (GuidAge study)

## A Global Presence

Ipsen has adapted its organization and operating methods to a changing health market and is expanding extensively outside France. The Group currently markets more than 20 drugs in some 100 countries, and has a direct commercial presence in close to 40 countries.



#### A GROWING PRESENCE OUTSIDE FRANCE

- In 2009, for the first time, Ipsen's drug sales exceeded €1 billion, more than two thirds of which are now generated outside France, thus reinforcing the Group's global footprint.
- Ipsen received several important regulatory approvals in 2009, including Azzalure® in Europe, Dysport® in the US in two indications and Decapeptyl® 6-month in Europe.
- In October 2009, Dysport® was launched in the US for the treatment of cervical dystonia. Dysport® is the fourth drug marketed directly by Ipsen in the US, after Apokyn® (management of Parkinson's disease), Increlex® (treatment of growth deficiency in children), and Somatuline® Depot® (treatment of acromegaly). In 2009, sales in North America grew by over 60% (on a comparable basis) compared to the previous year.
- The Group continued its expansion strategy in highgrowth territories, in particular in Russia, China and Latin

- America. Two of the Group's leading products were launched in Russia in 2009: Somatuline® Autogel® and Decapeptyl® 3-month. Several primary care products posted strong sales, in particular Smecta® and Tanakan® in Russia
- A strong presence in Asia: sales on the Asian continent increased by almost 20% in 2009, and several products, such as Decapeptyl®, Smecta® and Tanakan®, posted significant market share growth in China.
- Ipsen has been present in South America since December 2009 via its Brazilian subsidiary. Its goal is to rapidly launch Group products in Brazil, especially in the fields of neurology and endocrinology. Ipsen has already developed a number of clinical trials in partnership with major research centers in Brazil.





### Strategy

## Combining performance and **innovation**

By combining an active development strategy in its four specialty care areas (oncology, endocrinology, neurology and hematology) with the optimization of its primary care franchise, Ipsen has established a solid foundation for sustainable growth. As a result of a dynamic alliance and partnership policy and a strong commitment to Research and Development, Ipsen has the resources to achieve global and balanced growth.

# Three Objectives, One Ambition

The Ipsen group's growth strategy is driven by its products in its targeted specialty care areas. This development strategy is combined with an active policy of international partnerships and alliances in both Research and Development and marketing.

### GROW

A growth strategy focused on its targeted therapeutic areas (oncology, endocrinology, neurology and hematology), in which Ipsen aims to become a major player by providing innovative treatments that satisfy unmet medical needs.



## **GLOBALIZE**

A strategy of geographical expansion in highgrowth markets, with an active registration program for its leading products in its targeted therapeutic areas, including the US where Somatuline® and Dysport® have been approved by the Food and Drug Administration (FDA).



### **OPTIMIZE**

An optimization strategy of the Group's primary care franchise (gastroenterology, cardiology and cognitive disorders) through selective life cycle management investments in its products or via partnerships, as required.





lpsen has established a profitable growth strategy targeting specialty care areas, whose needs remain largely unmet and which present growth opportunities.

In this context, the Group leverages its technological and sales expertise, as well as its financial strength, to implement its strategy.

A growth strategy focused on its targeted therapeutic areas (oncology, endocrinology, neurology and hematology), in which Ipsen aims to become a major player by providing innovative treatments that satisfy unmet medical needs.

A strategy of geographical expansion in high-growth markets, including the US where Somatuline® and Dysport® were granted marketing authorizations by the FDA in 2007 and 2009, respectively.

An optimization strategy for its primary care franchise (gastroenterology, cardiology and cognitive disorders) through selective life cycle management investments in its products or via partnerships, as required.

These ambitions are based on two fundamentals.

A partnership and alliance strategy across Ipsen's therapeutic areas, enabling Ipsen to:

- obtain resources for programs that the Group does not want to finance alone, or to enrich its expertise through agreements with partners possessing complementary capabilities or technologies;
- optimize the profitability of its distribution network by obtaining marketing rights for products belonging to third parties in countries, in particular in France, where the Group has a commercial presence;
- maximize commercial benefits from products originating from Ipsen's research which do not fall within the Group's targeted therapeutic areas, by granting licences to partners to develop and market them in specific territories.

In 2009 and 2010, the Ipsen group entered into agreements with a number of significant players. These partnerships include:

- an agreement with Spirogen on a DNA minor groove ligand. SJG-136 is expected to be studied in phase II multicentric clinical trials sponsored by the National Cancer Institute in patients with ovarian cancer and hematologic malignancies;
- a partnership with Menarini in Europe, whereby Ipsen grants Menarini the exclusive license for Adenuric®, its treatment for chronic hyperuricemia in gout patients;
- an agreement with Inspiration Biopharmaceuticals for the creation of a franchise in the field of hemophilia;
- a licensing agreement with Rhythm Pharmaceuticals for the research, development and marketing of therapeutic peptides, to which Ipsen holds intellectual property rights, targeting obesity, metabolic and gastrointestinal disorders;
- an extension of the partnership with GTx for the development and marketing of toremifene for the prevention of prostate cancer in patients with precancerous lesions;
- an exclusive research partnership with Dicerna Pharmaceuticals to combine the respective expertise of Ipsen and Dicerna to research Dicer substrate siRNA molecules (DsiRNA) and peptide engineering.

A dynamic and insightful strategy in other therapeutic areas in which the Group develops and markets its products, based on its expertise (in Research and Development as well as marketing) and opportunities which might arise.

## A Global Biopharmaceutical Group

As a result of a focused strategy, which places innovation at the heart of the Group's development, Ipsen shows steady growth.

Ipsen's ambition is to be a global reference in its targeted therapeutic areas: endocrinology, oncology, neurology and hematology. The Group's growth is driven by its original, innovation-driven business model. This model, which is adapted to both health needs and the transformations the life sciences industry is undergoing. is based on three fundamentals.

A specialization in a small number of high added-value therapeutic areas in which medical needs are not sufficiently met and in which Ipsen can make a difference: oncology, endocrinology, neurology and hematology. These four therapeutic areas were selected because they correspond to the Group's know-how and expertise, and because Ipsen benefits from a competitive edge. Ipsen has implemented this strategy continuously and rigorously.

A commitment to a policy of sustained investment in therapeutic innovation, especially in biotechnology.

Ipsen invests approximately 20% of its sales each year in Research and Development in its targeted therapeutic areas, by deploying technology platforms covering the engineering of peptides, proteins and steroids.

Ipsen's technological platforms for the engineering of peptides, proteins and steroids allow the Group to explore and develop new approaches in the treatment of hormone-dependent tumors such as (i) inhibitors of key enzymes in the biosynthesis of steroids (ii) agonists and antagonists of hormone receptors including notably prolactins, somatostatins, and dopamines, (iii) cell cycle regulatory enzymes (notably phosphatases) and (iv) factors involved in intracellular signal transduction and angiogenesis. These research programs are conducted in-house, with the support of international academic or industrial cooperations.









Through the division of the Research and Development structure into two separate entities - "Research" and "Corporate Development" - Ipsen has created optimal conditions to enhance the creativity and productivity of in-house research, and to accelerate the transformation of its molecules into registered and marketed drugs. The Corporate Development department brings together the usual components of the development function (preclinical and clinical development, drug development and regulatory affairs) with the business development activity (partnerships, acquisitions) and legal affairs.

The Group's research pipeline is promising, diverse and well-balanced, with products evenly distributed across the different clinical phases.

A collaborative approach aimed at expanding and maximizing the value of the Group's product portfolio through an alliance strategy with leading research centers, innovative biotechnology companies and some of the world's largest pharmaceutical companies.

The Ipsen group markets its drugs either directly, through its own network, or through third parties to whom it entrusts the responsibility for the marketing of its products. In some cases, the Group has entered into agreements with third parties for the manufacturing of products or raw materials.

The Ipsen group complements the activities of its in-house Research and Development program by collaborating with university teams and pharmaceutical and biotechnology companies. Thanks to its Research and Development centers, the Group sustains contacts with leading academic centers and attracts high quality staff.

These collaborations allow the Group to have access to advanced technologies in complex areas of expertise and to finance the development of its products while enhancing its existing line. The Group explores high quality, complementary and sustainable collaborations for the marketing of its products and for Research and Development.

One example of this policy: in March 2010, Ipsen and Dicerna Pharmaceuticals entered into a proprietary research partnership agreement to combine their expertise in research on Dicer substrate siRNA molecules (DsiRNA) and peptide engineering.

Through this agreement, Ipsen and Dicerna Pharmaceuticals will develop new compounds using Dicerna's DsiRNA molecules and Ipsen's peptide vectors for applications in oncology and endocrinology. RNAi is a key cellular mechanism that regulates gene expression in normal and pathological processes. By targeting the gene sequence rather than the protein structure, RNAi-based therapies have the potential to use small molecules of synthetic RNA to inactivate genes responsible for disease, which may allow the development of novel treatments for many acute and chronic diseases. The inactivation of the target gene obtained reduces gene expression in a highly selective and specific manner.

Ipsen enjoys worldwide recognition as a key partner by industry leaders (Roche, Novartis, Teijin, Celera, bioMérieux, etc.) and academic institutions (Salk Institute and MIT in the US, Inserm and CEA in France, Erine Institute in the Netherlands, etc.).

#### **SALK INSTITUTE**

Since 2008, Ipsen has been collaborating with the Salk Institute for Biological Studies, an American non-profit research institution dedicated to fundamental research in life sciences and the training of future generations of researchers. Ipsen was the first company to sign a research agreement with the Salk Institute.

The Salk Institute consistently ranks among the leading research institutions in the world for its faculty contributions and the impact of their findings. The Institute has trained more than 2,000 scientists, including five Nobel Prize winners.

The agreement created the "Ipsen Life Sciences Program" within the Salk Institute, granting the Group access to significant technologies and expertise in the field of inflammatory, proliferative and degenerative diseases.

The Ipsen Life Sciences Program sponsors three categories:

- a grant devoted to jointly defined exploratory studies, that combine the Salk Institute's and Ipsen's expertise in molecular biology and medical chemistry. One example of this research is transgenic models and the role of nuclear receptors in metabolic diseases;
- a grant that allows Ipsen to benefit from the Institute's scientific advances and their potential therapeutic applications. These programs encompass a range of research projects such as metabolic disorders, neurodegenerative diseases, regenerative medicine, inflammatory diseases, autoimmune diseases and cancer;
- a grant under which i) Ipsen finances the works of young researchers, and ii) Ipsen and the French Foundation for Scientific Cooperation for Alzheimer's and Related Diseases sponsor the postdoctoral fellowship of a French researcher at the Salk Institute for two years.

This partnership with the Salk Institute allows Ipsen to further strengthen its collaboration with the scientific and academic world, to remain at the forefront of major advances in understanding the basic mechanisms of metabolic, neurodegenerative and proliferative diseases, and to improve its scientific excellence.



Salk Institute La Jolla (USA).



#### **Activities**

## Breaking new ground, finding innovative therapeutic solutions

Ipsen's Research and Development activities are devoted to the discovery and development of innovative molecules and to the life cycle management of products that are already on the market. Ipsen holds leading positions in its targeted therapeutic areas.



## A Strong Commitment to Research and Development

Close to 900 employees of the Ipsen group play a part in the discovery and development of innovative drugs for patient care. In 2009, R&D expenditure totaled close to €200 million, representing nearly 20% of consolidated sales.

Ipsen's R&D endeavors primarily target the Group's key therapeutic areas:

- discovery and development of new products, in particular in the fields of oncology and endocrinology;
- management of the life cycle of products which are already marketed, including the development of new formulations (alone or in combination with other molecules), the extension of their indications or their registration in new territories.

The Group's R&D programs are based on three technologically integrated platforms:

- Peptide engineering focuses on the synthetic modification of derivatives of naturally occurring neuropeptide hormones. It is coupled with advanced drug delivery technologies, dosage form innovation and development, which targets the design and development of innovative formulations for new and existing products in order to maximize the effectiveness of active ingredients while improving the quality of life of patients and facilitating the use of these products by health care practitioners;

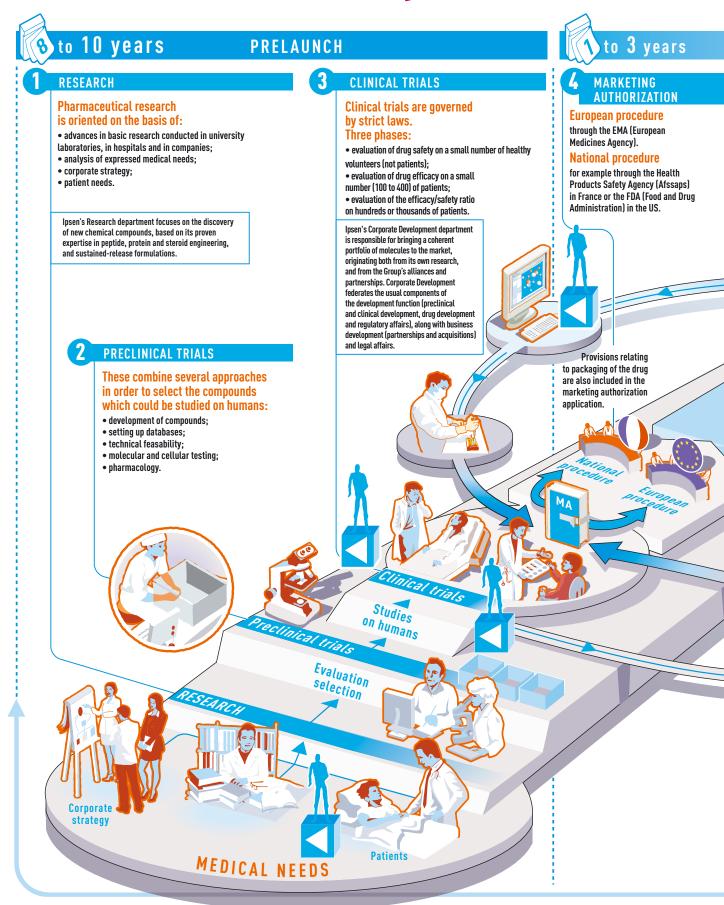
2009 R&D expenditure close to

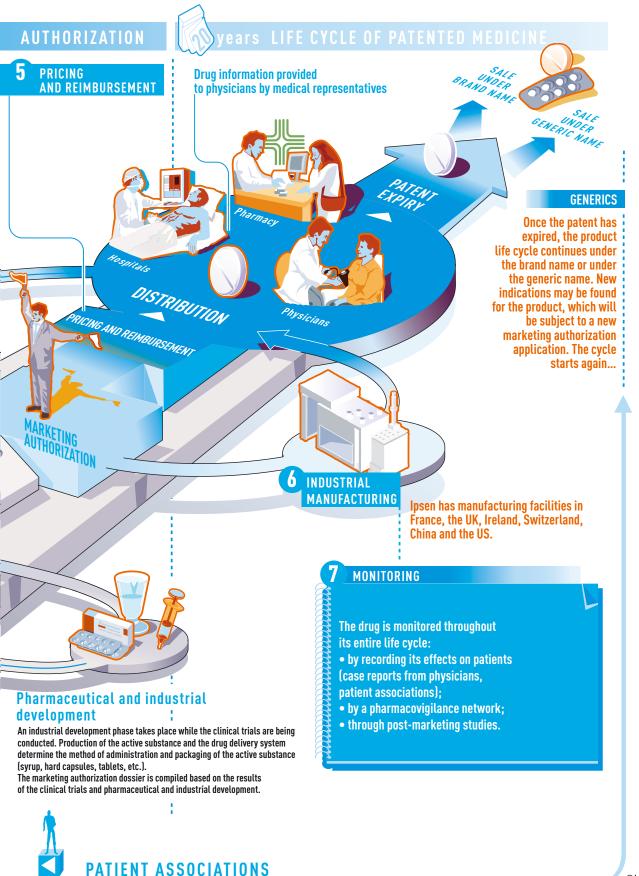


representing nearly 20% of consolidated sales

- Protein engineering to improve the therapeutic properties of naturally occurring proteins, through the selective modification of amino-acid sequences. These studies are conducted in collaboration with academic research centers;
- Steroid engineering aimed at discovering inhibitors of enzymes involved in the biosynthesis of steroid hormones. These studies are conducted in collaboration with academic research centers.

## Product Life Cycle







## Oncology: a Field of Excellence

Cancer is a major cause of death throughout the world. The World Health Organization estimates that the number of deaths by cancer is likely to continue to rise between now and 2030, reaching over 12 million people.

In the field of oncology, Ipsen has forged expertise that is well recognized by the medical profession. Thanks to its ambitious R&D policy, the Group is actively developing and enhancing its portfolio of molecules.

Ever since cancer treatments have existed. therapies have been evolving towards ever more precise targeting and the alignment of treatments to patient profiles. In the future, scientists will continue to develop increasingly targeted molecules. Ipsen's strategy is fully aligned with this process.

A significant proportion of Ipsen's R&D effort is focused on developing treatments for hormone-dependent cancers such as breast and prostate cancer, which respectively represent almost one in three cases of cancer among women and more than one in five cases among men.

In this field, Ipsen favors two complementary approaches: hormone therapies and targeted molecular therapies. Hormonal treatments, which use molecules that are able to act directly on the production and effects of hormones responsible for the growth of tumors, have proven their efficacy in fighting many prostate cancers and other hormone-dependent tumors.

> increase in Decapeptyl® sales (including one-month and daily formulations) in China in 2009

In this area, managing the life cycle of Decapeptyl® and developing new molecules such as BN 83495 are major strategic priorities for Ipsen.

#### Decapeptyl®

The active substance in Decapeptyl® is triptorelin, a decapeptide analog of GnRH, a hormone secreted by the hypothalamus, which stimulates the release of pituitary gonadotrophins (hormones produced by the pituitary gland) that control hormonal secretions by the testes and ovaries. Decapeptyl® contains a formulation that was initially developed and continues to be used primarily in the treatment of advanced metastatic prostate cancer.

Subsequently, additional indications have included the treatment of uterine fibroma, endometriosis either prior to surgery or when surgery does not appear sufficient, and the treatment of precocious puberty and female infertility (in vitro fertilization). Decapeptyl® is available in monthly or quarterly sustained-release formulations, as well as a daily formulation. Ipsen and its partner Debiopharm submitted a marketing authorization application for 6-month triptorelin 22.5mg in Europe in September 2008. European regulatory authorities gave the green light through a decentralized procedure in October 2009 for the treatment of locally advanced and metastatic prostate cancer. Decapeptyl® 6-month was launched in France in February 2010. At end 2009, Decapeptyl® was registered in over 60 countries.

#### RESEARCH PROGRAMS

#### Angiomates (STX 140)

Angiomates are multitargeted anticancer agents exhibiting both antiproliferative (which kill cancer cells) and antiangiogenic (which inhibit the network of blood vessels supporting the tumor) properties. These molecules could be used in treating hormone-dependent tumors and certain types of hematologic malignancy.

#### **BIM 46187**

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

"To date, four of the patients who received BN 83495 had tumors that remained stable for at least 6 months. One of these had cutaneous metastases that improved after one month of treatment. This is very encouraging, as these women are patients who are reaching the end of their hormonal treatment options. Importantly, BN 83495 was well tolerated at the selected dose. I am confident that BN 83495 will become a new hormonal option in the treatment of postmenopausal women with estrogen receptor positive metastatic breast cancer."

Professor R. Charles Coombes, Clinical Professor, Division of Surgery, Oncology, Reproductive Biology and Anaesthetics, Imperial College (London, UK)

#### Inhibitors of the enzyme 17B-hydroxysteroid dehydrogenase (1 and 3)

These molecules are enzyme inhibitors involved in the biosynthesis of steroid hormones. They will be targeted at treating hormone-dependent tumors (breast and prostate).

#### Cytotoxic peptide conjugates

These molecules are designed to target tumors which exhibit a specific receptor to a peptide hormone in order to selectively deliver an antiproliferative agent. The targeted tumors are neuroendocrine tumors which exhibit high levels of receptors for peptide hormones.

#### **DEVELOPMENT PROGRAMS**

#### Decapeptyl®

Ipsen is participating in two phase III studies, conducted under the auspices of the International Breast Cancer Study Group (IBCSG), for the adjuvant treatment of premenopausal breast cancer. These studies compare conventional treatment methods with hormone therapy combining Decapeptyl® with estrogen suppressor agents, such as Aromasin® marketed by Pfizer. They are scheduled to continue through to 2015. Their findings could lead to a revision of adjuvant treatment guidelines for breast cancer in premenopausal women expressing hormonal receptors. The Group has obtained an exclusive license covering expertise and new patent applications relating to the worldwide marketing rights for Decapeptyl® (excluding North America and certain other countries). Under the terms of the agreement, Ipsen has access to future sustainedrelease formulations of Decapeptyl® developed by Debiopharm.





#### **Toremifene**

The Group has acquired an exclusive European license to develop and market toremifene, a Selective Estrogen Receptor Modulator (SERM), from US biotech company GTx Inc. One of the two phase III studies of toremifene conducted by GTx in the US is now complete. It relates to the treatment of side-effects linked to anti-androgen hormone therapy in advanced prostate cancer. After submission of the supplemental New Drug Application (sNDA), the FDA requested a second phase III clinical study for this indication. This second phase III study will begin in 2010. In addition, a phase III study is in progress in connection with the prevention of prostate cancer among men with precancerous lesions (high grade intraepithelial neoplasia).

#### BN 83495

BN 83495 and the related molecules are selective inhibitors of the enzyme sulfatase involved in a key stage of the biosynthesis of estrogen, a major contributor to breast cancer among postmenopausal women. An initial phase I clinical trial among patients has been completed and the results demonstrate that the enzyme sulfatase is inhibited in tumor biopsies at the tested doses. A second phase I study has determined the optimal dose of BN 83495 in postmenopausal patients with advanced breast cancer expressing hormone receptors. During this second phase I trial, close to complete inhibition (95%) of the target enzyme in peripheral blood mononuclear cells was obtained at a dose of 40mg.

A pilot program in advanced prostate cancer is currently underway, together with a phase II study in advanced endometrial cancer.



# Endocrinology: a Leading Expertise

Endocrinology, or the study of the endocrinal glands, is a key medical specialty within Ipsen's portfolio. The endocrinal glands secrete hormones whose role is to control the functioning of specific tissues within the body. In 2009, the company's endocrinology franchise experienced growth of nearly 30%.

Ipsen concentrates its efforts on pituitary diseases affecting relatively small populations and requiring specialist treatment: in children, pathologies leading to growth failure and short stature, and in adults, acromegaly (a pathology characterized by exaggerated growth in certain bones and soft tissues) and neuroendocrine diseases.

The Group has developed a particularly high level of expertise in this area. Nonetheless, Ipsen's know-how in the field of endocrinology also drives it to take an interest in other pathologies. Depending on each specific case, the Group may develop products through to the marketing stage, or may delegate their development to partners.

With NutropinAq® and Increlex®, Ipsen is currently the only pharmaceutical company to offer more than one solution for pathologies related to short stature. Clinical research work to evaluate the effects of treatment combining the hormone growth NutropinAq® with Increlex® is in progress, and has delivered very promising results.

2009 sales of over in endocrinology (+26% excluding foreign exchange impacts)

Somatuline®, which is mainly indicated for acromegaly, is marketed in over 45 countries. Two studies aimed at evaluating the effectiveness of this drug in treating symptomatic neuroendocrine tumors (which secrete peptides), as well as in treating asymptomatic neuroendocrine tumors, have recently entered phase III.

#### Somatuline®

The active substance in Somatuline® and Somatuline® Autogel® (Somatuline® Depot® in the US) is lanreotide, a somatostatin analog that inhibits the secretion of several endocrine, autocrine and paracrine functions. It is highly effective in inhibiting the secretion of growth hormones and certain hormones secreted by the digestive system. The Somatuline® Autogel® formulation represents a major technological advance. As far as the Group is aware, this is 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 only one injection per month, and in some cases one injection per six to eight week period, compared with the two or three injections previously required. This product is presented in a pre-filled syringe for easier administration. Somatuline® was developed and is used for the treatment of acromegaly, and was subsequently developed for the treatment of certain symptoms associated with neuroendocrine tumors (carcinoid syndrome). At end 2009, Somatuline® and Somatuline® Autogel® were marketed in over 45 countries.

#### NutropinAq®

NutropinAq® is a liquid formulation of recombinant human growth hormone administered using the NutropinAq® Pen. Growth hormone is involved in physiological processes such as growth in stature and bone development in children.

NutropinAq® is indicated for the following:

- long-term treatment of growth failure in children due to inadequate endogenous growth hormone secretion;
- long-term treatment of growth failure associated with Turner syndrome;
- treatment of growth failure in prepubescent children associated with chronic renal failure prior to kidney transplantation:
- treatment of adults with either childhood or adult onset growth hormone deficiency.

At end 2009, NutropinAq® benefited from marketing authorizations in over 30 countries.

#### Increlex®

The active substance in Increlex® is a recombinant insulin-like growth factor of human origin (IGF-1). IGF-1 is the direct hormonal mediator of growth, and must be present for normal growth of bones and cartilage in children. In severe primary IGF-1 deficiency, serum IGF-1 levels are low in spite of normal

"Neuroendocrine tumors are a spectrum of tumor diseases presenting, behaving and responding differently to treatment compared to other tumors/cancers. Thanks to increased awareness - and not because there are more cases - a doubling in the incidence of cases has been reported in each of the past three decades. As awareness develops, the condition will be even more frequently diagnosed. Because it is such a slow grower usually, the original concept that these tumors are practically benign has been perpetuated - that is a mistake. While awareness is essential, dissemination of knowledge about therapies available and customization for the particular needs of each tumor is equally necessary. Progress is being made in research which better defines the molecular mechanisms involved in neuroendocrine tumors and genomic studies are beginning to come to the forefront for diagnosis and development of molecularly specific drugs. The key trend in the near future in treating patients is to combine treatments acting simultaneously on various pathways. This could be the way to significant progress in disease management and improved life expectancy.

#### Professor Richard R P Warner,

Professor of Medicine, Mount Sinai School of Medicine, New York, NY (USA) Medical Director of the Carcinoid Cancer Foundation

Neuroendocrine tumors include gastrointestinal carcinoid tumors and pancreatic islet cell tumors. This group as a whole is commonly known as gastroenteropancreatic neuroendocrine tumors (GEP NETs).

or high growth hormone levels. If IGF-1 is not present in sufficient quantities, the child will not reach normal stature. These low IGF-1 levels are usually due to growth hormone resistance associated with mutations affecting the GH receptors and the post-GH receptor signaling pathways, or defects in IGF-1 gene expression. This explains why these children cannot respond adequately to exogenous growth hormone treatment. At end 2009, Increlex® was marketed in the US and the vast majority of European countries.

#### RESEARCH PROGRAMS

In the field of pituitary disorders, Ipsen is conducting several research programs, mainly in pituitary adenomas. Work initiated by the Group in the field of enzyme 11BHSD inhibitors is continuing in order to develop a therapeutic treatment of metabolic syndromes associated with high cardiovascular risk among obese patients. Ipsen is continuing to pursue preclinical research to develop sustained release formulations of growth hormone antagonists to replace daily injections of growth hormone in both children and adults.

GIP is a peptide which enhances the secretion of insulin only when glucose levels are high. GIP can also restore the function of pancreatic beta cells in diabetes and could be used in the treatment of the final prediabetic condition.

#### PRECLINICAL DEVELOPMENT PROGRAMS LICENSED TO PARTNERS

#### MSH/MC4 and ghrelin

In March 2010, Ipsen granted Rhythm Pharmaceuticals exclusive worldwide rights to the research, development and marketing of its drug candidates, MC4 and ghrelin agonists, targeting obesity, metabolic disorders and gastrointestinal problems.

#### **DEVELOPMENT PROGRAMS**

#### Somatuline® Autogel® and Somatuline® Depot®

Ipsen is pursuing the following developments:

- a phase III clinical trial of Somatuline® Autogel® for the treatment of neuroendocrine tumors is in progress in Europe and the US;
- additional phase III clinical trials for the treatment of neuroendocrine tumor symptoms in order to register Somatuline® Depot® (the equivalent of Somatuline® Autogel® in the US) were launched in 2009;
- a phase III clinical trial for Somatuline® Autogel® in acromegaly has been completed, and its results should be published in 2010;
- in Japan, the Group's partner Teijin entered phase III with Somatuline® Autogel® for the treatment of acromegaly in January 2010.

#### BIM 23A760

Ipsen has synthesized a chimeric molecule (which simultaneously exercises several pharmacological activities) combining a somatostatin analog and a dopamine agonist to achieve synergistic therapeutic effects in diseases such as acromegaly and neuroendocrine tumors. Clinical phase I and phase IIa studies in acromegaly have demonstrated encouraging signs of efficacy on bioactivity markers such as the IGF-1 growth hormone and prolactin. BIM 23A760 entered phase IIb in multiple doses as well as phase II in neuroendocrine tumors.

#### Co-administration of rhGH and rhIGF-1

Ipsen is studying the co-administration of rhGH and rhIGF-1; a phase II clinical study will be completed in 2010. In September 2009, Ipsen published encouraging preliminary results evaluating the co-administration of recombinant human growth hormone and recombinant type 1 human insulin growth factor in two separate injections as a potential treatment for children with short stature associated with low levels of IGF-1.

#### Taspoglutide (BIM 51077)

Taspoglutide, currently in phase III, is a peptide hormone GLP-1 analog which is the subject of a partnership agreement with Roche. In Japan, Teijin is conducting a phase II study with this new peptide.

"Regarding the management of short stature in childhood and adolescence, by moving towards a more individualized approach the diagnosis and treatment of growth failure will certainly be influenced positively by the application of pharmacogenomics. Indications for growth hormone (GH) and IGF-1 therapies are already well-established. The challenges faced by clinicians today relate more to diagnosis and prognosis of growth disorders, and to the definition of which short-statured patients should benefit from one specific therapy (GH) or another (IGF-1). What we realize more and more, if we look at patients who are part of a spectrum between these two outliers (GH deficiency versus primary IGF-1 deficiency), is that many patients may not fit one of these two well-defined diagnoses. It is within the group of less well-defined patients, such as milder IGFD patients, 'partial' GH deficient patients, or ISS patients that we need to become better at diagnosing and treatment. For many patients, standard growth hormone therapy alone isn't very successful, or IGF-1 therapy alone does not make strong clinical sense, so there may be a solid case for the consideration of GH/IGF-1 combination therapy. As the company that has access to both growth hormone and IGF-1 treatment modalities, and which invests heavily in pharmacogenomics, Ipsen is in a unique position to improve healthcare for children with growth disorders. Ipsen has an important role to play in exploring potential indications for such combination therapy, whether first or second line."

Philippe F. Backeljauw, MD Professor of Clinical Pediatrics Cincinnati Children's Hospital Medical Center (USA)



## Neurology: State-of-the-Art

lpsen has developed solid expertise in treating neuromuscular disorders. The Group currently markets two products, corresponding to two distinct markets.

The botulinum toxin type A Dysport®, which has been marketed since 1991 and is available in 75 countries, is primarily used in the symptomatic treatment of three illnesses: cervical dystonia, blepharospasm (involuntary contraction of the eyelids) and spasticity (exaggerated muscle tone leading to spasms). Botulinum toxin is also used in esthetic medicine. mainly for treating wrinkles. In this field, lpsen has called on specialist partners to market its toxin, thereby seeking to achieve a consistent level of excellence while remaining focused on its therapeutic use.

In April 2009, US regulatory authorities (FDA) granted marketing authorization for Ipsen's botulinum toxin type A for the treatment of both cervical dystonia and frown lines under a single brand: Dysport®. It is marketed for esthetic indications by Medicis in the US, and by Galderma, under the Azzalure® brand, in Europe. In 2009, Azzalure® was granted marketing authorization in seven countries.

In addition, since 2008, the Group has been marketing Apokyn® in the US. It is the only drug available in the US for the treatment of "off" motor episodes (the unforeseen reemergence of symptoms during treatment) in patients with advanced Parkinson's disease. Apokyn® is an excellent promotional companion for Dysport<sup>®</sup>.

growth in neurology sales in 2009 (excluding foreign exchange impacts)

Finally, Ipsen has entered into a partnership with Pharnext to explore a new therapeutic technology, pleotherapy (a technology based on combining several molecules with a synergistic effect), for treating Charcot-Marie-Tooth disease (a severe chronic neuromuscular disease mainly affecting peripheral nerves).

"The presence of another leading pharmaceutical company involved in dystonia and other movement disorders in the US is very good news. The launch of another botulinum toxin A should significantly contribute to increased knowledge and better education, for both patients and physicians, about movement disorders. It should also allow us to reach more patients and more areas in the US that have yet to be reached by this effective therapy."

Kapil D. Sethi MD FRCP, Professor of Neurology Director Movement Disorders Program Medical College of Georgia (USA)

#### Dysport®

The active substance in Dysport® is a botulinum neurotoxin type A complex which acts by inhibiting acetylcholine secretion, thereby reducing muscular spasm. It was initially developed to treat motor disorders and various forms of muscular spasticity, including cervical dystonia (or spasmodic torticollis, a chronic condition in which the neck is twisted or deviated), spasticity of the lower part of the lower limbs (heel) in children with cerebral palsy, blepharospasm (involuntary contraction of the eyelids) and hemifacial spasm (a movement disorder characterized by contraction of the muscles located on one side of the face that can lead to disfigurement). Dysport® was later developed for the treatment of a wide variety of neuromuscular disorders, as well as for use in esthetic medicine.

Dysport® was initially launched in the United Kingdom in 1991. At end 2009, Dysport® had been registered in over 75 countries. In 2009, 35.7% of Dysport® sales were generated in the major western European countries.

#### Apokyn®

Apokyn® is used to treat Parkinson's disease as an add-on to conventional oral therapies, and is injected by the patient to treat "off" episodes.

It is the only therapy available in the US for treating advanced Parkinson's disease patients who experience severe on/off fluctuations in motor function (acute re-emergence of Parkinson's disease symptoms) and are unresponsive to other oral Parkinson's disease therapies.

Apokyn®, an apomorphine hydrochloride injection, is a substitute for dopamine, which is deficient in Parkinson's disease patients.

Parkinson's disease is a condition that results from selective degeneration of an area of the brain called the substantia nigra, located at the base of the brain in the basal ganglia. Normally, these nerve cells release dopamine, a chemical that transmits signals between nerve cells (called neurotransmitters). This central signaling pathway is essential for controlling movement and posture, and a deficiency results in the symptoms of Parkinson's disease, namely tremor, rigidity, slow movements and postural instability. Muscle rigidity can become so severe that patients become immobile and are incapable of making the slightest movement.





#### **RESEARCH PROGRAMS**

The Ipsen group's research programs are focused on developing new formulations and studying the mechanism by which botulinum toxin acts.

In the field of neurodegenerative illnesses, the Group has synthesized several original families of chimeric molecules (molecules capable of exerting multiple pharmacological activities). Some of these molecules are intended to protect the mitochondria (intracellular organelles responsible for energy function), the dysfunction of which plays a major part in neurodegenerative diseases such as Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

#### **DEVELOPMENT PROGRAMS**

#### **BOTULINUM TOXIN TYPE A**

#### Medical use

In April 2009, US regulatory authorities approved an application for marketing authorization for the biological product (Biologics License Application or BLA) for Dysport® (abobotulinumtoxin A) for the treatment of cervical dystonia to reduce the severity of abnormal head position and cervical pain. Ipsen markets Dysport® in the US in its therapeutic indication (cervical dystonia). Moreover, the unique name "abobotulinumtoxin A" differentiates Dysport® from other botulinum toxin-based products on the market.

#### Esthetic medicine

#### Dysport®

In April 2009, US regulatory authorities also approved an application for marketing authorization for the biological product for Dysport® (abobotulinumtoxin A) for its esthetic indication – the temporary correction of moderate to severe frown lines in adults aged under 65. Medicis markets Dysport® in the US in this indication.

#### Azzalure®

The Group has granted Galderma the exclusive rights to develop, promote and distribute its botulinum toxin type A product for esthetic indications in Europe and certain other territories. Galderma markets this product under its own Azzalure® brand.

On February 2, 2009, Azzalure® was granted a collective green light by health authorities in 15 European countries (via a decentralized procedure) to proceed with the issuance of national marketing authorizations. The evaluation was based on clinical studies performed on more than 2,600 patients, accrediting the product's tolerance profile and effectiveness. At end 2009, this treatment was marketed in seven European countries.



# Hematology: a Promising Outlook

Hemophilia is an hereditary genetic disease characterized by reduced blood clotting. Hemophilia A is caused by a deficiency of factor VIII, while hemophilia B is caused by a deficiency of factor IX. Approximately 60% of hemophilia subjects suffer from severe illness entailing frequent spontaneous episodes of hemorrhage in addition to abundant bleeding after injury. Hemophilia affects around 400,000 people worldwide.

For several years, Ipsen has been rising to the challenge of this complex indication, in particular through its OBI-1 program. OBI-1 is a recombinant porcine factor VIII intended for patients presenting inhibitors of natural factor VIII.

In January 2010, Ipsen and Inspiration Biopharmaceuticals entered into a partnership to create a world-leading hemophilia franchise. The partnership is designed to leverage combined expertise and resources to advance a broad portfolio of recombinant proteins. These molecules target major types of hemophilia in a unique way, and are based on two largely unsatisfied medical needs: widened access to treatments based on coagulation factors, and the treatment of complications associated with the development of inhibitors.

The two lead product candidates are scheduled to move into phase III clinical testing in 2010, including Ipsen's recombinant porcine factor VIII, OBI-1 (for the treatment of patients with acquired hemophilia or hemophilia A who have developed an inhibitory immune reaction to human forms of factor VIII) and Inspiration's recombinant factor IX product, IB1001 (for the acute and preventive treatment of bleeding in patients with hemophilia B).

a robust portfolio of

molecules in development

Combined with Inspiration's novel proprietary technology and an early stage pipeline of other coagulation factors, this broad and unique portfolio could increase the range of available treatments and fulfill unmet needs in patients suffering from coagulation disorders.

"Providing wider access to treatment with coagulation factors, and improving treatment for inhibitor complication are two significant unmet needs for the hemophilia community. The combination of OBI-1 (the recombinant factor VIII with low cross-reactivity based on porcine amino acid sequence), IB1001 (recombinant factor IX under clinical trial) and recombinant factors VIIa and VIII developed by Inspiration create a portfolio of therapies which address these needs, and represent a significant addition to the treatment arsenal available to hemophilia treatment centers worldwide. I am pleased to see these two teams joining forces to improve hemophilia care."

Professor Claude Négrier, Head of Hematology and Head of the Hemophilia Treatment Center at the Edouard-Herriot Hospital in Lyon (France)

#### **DEVELOPMENT PROGRAMS** LICENSED TO PARTNERS

#### OBI-1

Ipsen has longstanding expertise in the field of homostasis (blood coagulation). Its research has enabled it to enter into partnerships with Emory University (US) and Octagen to develop a recombinant version of porcine factor VIII using the Group's protein engineering platform.

OBI-1 is manufactured by the Group at its biotechnology unit in Boston. This product is intended for the treatment of congenital and acquired hemophilia refractory to human factor VIII. The Group has conducted phase I and II clinical studies with OBI-1 in the US.

In January 2010, Ipsen and Inspiration Biopharmaceuticals entered into a partnership to create a world-leading hemophilia franchise.

This agreement reflects Ipsen's long-term strategy of creating a global franchise of innovative treatments for the benefit of patients. This new alliance gives birth to a franchise with a thriving portfolio of four complementary molecules including OBI-1, Ipsen's recombinant porcine factor VIII intended to treat patients presenting hemophilia with inhibitors, and IB1001, an intravenously administered recombinant factor IX for treating hemorrhaging disorders associated with hemophilia.

#### STRUCTURE OF THE AGREEMENT

- Ipsen paid \$85 million for a 20% stake in Inspiration and a seat on the company's **Board of Directors.**
- Ipsen granted Inspiration exclusive rights to develop and market OBI-1 in exchange for \$50 million payable in the form of convertible bonds and a 27.5% royalty on future sales.
- Ipsen will gradually take up additional convertible bonds issued by Inspiration Biopharmaceuticals to fund the
- development of the four molecules in the combined pipeline, subject to phased success criteria for OBI-1 and IB1001. At the end of these phases, Ipsen is expected to own around 47% of Inspiration Biopharmaceuticals.
- Ipsen will have the right to acquire the remaining shares of Inspiration Biopharmaceuticals.





The complementary nature of OBI-1 and Inspiration's three molecules makes it possible to create a global multi-product franchise that will drive Ipsen's growth in hematology. The new extended portfolio of recombinant proteins targets all major types of hemophilia disorders in a unique way.

Under the terms of the agreement with Inspiration, Ipsen continues to produce OBI-1 at its Boston and Wrexham sites.



Ipsen's bioproduction center in Boston, USA.

#### **PRODUCT PIPELINE**

- IB1001 is an intravenously administered recombinant factor IX intended to treat the acute crisis stage and prevent hemophilia B. IB1001 is in the process of being assessed in a pivotal clinical study conducted in the US and Europe.
- OBI-1 is a recombinant porcine factor VIII (pFVIII) for which a phase III program will begin in early 2010 involving patients with an acquired factor VIII inhibitor (acquired hemophilia).
- Recombinant factor VIIa is used in the treatment of a rare but serious form of hemophilia known as Alexander's disease.
- Recombinant factor VIII is currently the most common treatment for severe hemophilia.



## A Presence in Primary Care

In primary care, Ipsen endeavors to offer treatments for neurological aging diseases as well as treatments in the fields of gastroenterology, cardiology and rheumatology. Over the past few years, the Group has considerably strengthened its primary care franchise outside France.

Ipsen markets Tanakan®, an oral formulation of EGb 761®, extracted from the leaves of the ginkgo biloba tree using a standardized and patented process and used primarily for the treatment of cognitive disorders associated with aging, in over 60 countries. In neurological terms, cerebral aging is characterized by a gradual reduction in both cerebral reserve, i.e. neuronal mass (the number of synapses and neurons), and cognitive reserve, i.e. the quality of cerebral activity.

In the field of gastroenterology, Ipsen markets three main products: Smecta<sup>®</sup>, indicated for the treatment of acute and chronic diarrhea, Forlax®, for the treatment of constipation, and Fortrans®, intended for washing the bowels ahead of a colonoscopy.

In cardiology, the product range has been extended: in France, a co-promotion agreement has been entered into with Novartis relating to anti-hypertensive medication Exforge®, thus complementing the existing portfolio of anti-hypertensives Nisis® and Nisisco®, which Ipsen has been jointly marketing with Novartis since 2003.

Finally, in the field of rheumatology, Ipsen is promoting Adrovance®, indicated for the treatment of osteoporosis, under a joint marketing agreement with MSD.

increase in sales of primary care outside France in 2009 (excluding foreign exchange impacts)

In March 2010, Ipsen and Menarini launched Adenuric® in France for the treatment of chronic hyperuricemia in gout patients. Adenuric® is the first pharmacological innovation in over 40 years for the treatment of gout. Ipsen and Menarini jointly promote Adenuric® in France. Ipsen has granted Menarini exclusive licence rights to Adenuric in 41 countries.

"Therapeutic options for the treatment of gout are currently limited. The most commonly used drug, allopurinol, sometimes causes cutaneous eruptions and cannot be used in high doses in patients presenting renal failure. In comparison, Adenuric® is a drug that can be used in cases of allopurinol intolerance and mild to moderate renal failure. Furthermore, it acts effectively on hyperuricemia, even when severe."

Prof Gérard Chalès, Head of Rheumatology, Rennes University Hospital (France)

Hyperuricemia: excessive levels of uric acid in the blood, a śign of gout.



Smecta® is an oral formulation of pharmaceutical clay created and developed by Ipsen. It is used in the treatment of both chronic and acute diarrhea in adults and children and in the symptomatic treatment of pain associated with esophageal, gastric, duodenal, and colonic disorders. A new flavor was launched in 2008, and new formulations are being researched.

At end 2009, Smecta® had been granted marketing authorizations in over 70 countries. In 2009, approximately two thirds of Smecta® sales were split equally between France and China, the product's main markets.

#### Forlax<sup>®</sup>

Forlax®, an oral laxative created and developed by Ipsen, is a macrogol of high molecular weight. It is used in the treatment of constipation in both adults and children.

At end 2009, Forlax® had been granted marketing authorizations in over 60 countries. In 2009, over 67% of Forlax® sales were generated in France.

#### Tanakan®

Tanakan® is an oral formulation of EGb 761®, extracted from the leaves of the ginkgo biloba tree using a standardized and patented process that ensures a consistent, accurate mixture of the various pharmacologically active substances. It was initially developed for the treatment of various neurological disorders, including, in particular, age-related cognitive impairment, neurosensorial disorders - namely ear,

nose and throat - and visual disorders such as vertigo, tinnitus, acute or chronic hearing difficulties, and certain retinal disorders. At end 2009, Tanakan® had been approved for use in over 60 countries, mainly in Europe and Asia. It is indicated and reimbursed in Belgium in the symptomatic treatment of mild to moderate forms of Alzheimer's-type dementia accompanied by memory disorders and cognitive disorders.

#### Nisis® and Nisisco®

In 2003, the Group added Nisis® and Nisisco®, two anti-hypertensive products, to its portfolio by entering into an agreement with Novartis to market the products in France, Andorra and Monaco. Nisis® is an oral formulation containing valsartan, while Nisisco® contains valsartan and hydrochlorothiazide. The products are used in the treatment of arterial hypertension.

#### **Exforge®**

Exforge® combines two widely studied molecules, which are among the most prescribed worldwide, in a single tablet: valsartan and amlodipine, a sartan and a calcium channel blocker respectively. The fixed valsartan/amlodipine combination can be used to treat patients whose blood pressure is not adequately controlled by amlodipine or valsartan in monotherapy.

In 2009, Novartis Pharma and Ipsen announced that they had signed an agreement to jointly promote Exforge® in France. Under this agreement, Ipsen promotes Exforge® mainly to cardiologists and general practitioners.



#### Adrovance®

On January 30, 2007, MSD granted Ipsen the French marketing rights to Adrovance®, indicated for the treatment of postmenopausal osteoporosis in patients at risk of vitamin D deficiency. Osteoporosis is a diffuse disease of the skeleton whose main characteristic is low bone mass and deterioration of bone tissue. The resulting bone fragility increases susceptibility to fractures.

#### Adenuric®

Adenuric® is indicated for the treatment of gout, a particularly painful form of arthritis that generally occurs in men. It is caused by hyperuricemia, a high level of uric acid in the body.

Adenuric® is the first major therapeutic alternative for chronic hyperuricemia made available to patients suffering from gout since 1964. Adenuric® 80mg and 120mg (tablets) are indicated in the treatment of chronic hyperuricemia for conditions in which urate deposition exists or has occurred (including a history or presence of tophus and/or gouty arthritis). The therapeutic objective is to reduce the rate of serum uric acid and keep it below 360µmol/l (6mg/dl). On October 20, 2009, the Group granted exclusive rights to Adenuric® in 41 countries to the Menarini Group. Ipsen has been jointly promoting Adenuric® in France since the first quarter of 2010.

#### **DEVELOPMENT PROGRAMS**

The GuidAge study was set up to evaluate the effectiveness of EGb 761® in preventing Alzheimer's disease in patients aged over 70 spontaneously expressing memory complaints to their general practitioners. Recruitment of 2,800 patients was completed in November 2004 and those patients were treated over a five year period; the results of the study should be available in 2010.

Another study evaluating the effect of EGb 761® on the cerebral metabolism of glucose (by neuroimaging) on three patient groups is also in progress: patients suffering from memory complaints both with and without objective cognitive disorders and patients with Alzheimer's disease.

A further study evaluating the effects of EGb 761® on mitochondrial metabolic functions in children with a rare genetic disorder, Friedreich's ataxia, is also being carried out.





## An ongoing commitment

Ipsen's commitment is reflected in a range of initiatives intended to promote ethics, equal opportunity and the adoption of best practices by Group employees.

Ipsen's commitment also encompasses environmental protection, corporate citizenship and sponsorship.

### Human Resources

Our short- and medium-term priorities with regard to human resources are focused on three main areas: clarifying the roles and responsibilities of each person within the organization, promoting the development of human resources, and fostering employee commitment throughout the Group.

In 2009, Ipsen's Human Resources department continued its actions aimed at creating the required conditions for:

- improving individual and group performance;
- developing staff, in particular through access to training and mobility;
- promoting a culture of management excellence;
- obtaining commitment from all staff, in particular by ensuring that remuneration policy is both fair and competitive.

#### IMPROVING INDIVIDUAL AND GROUP PERFORMANCE

Ipsen's success is the result of both individual and collective success. This is why the annual performance appraisal is a key management process. Performance is monitored throughout the year, with two important meetings at mid-year and year-end providing managers and their staff with the opportunity to discuss and agree on the expected level of performance. This framework enables managers to reiterate and clarify overall Group strategy, and translate it into ambitious but achievable individual targets. It also defines the competencies and resources required to achieve those targets. In order to ensure that this dialog is of high quality, the Human Resources department has organized training sessions for all Group managers and staff to reiterate key principles and success factors.

#### TWO NEW TRAINING THEMES

Ipsen wishes to constantly provide its employees with opportunities for high-quality training and development appropriate to the needs of the Group and the specific characteristics of each business area. These opportunities fall into two categories: at the Group level, training programs are organized to promote the development

of management skills and Group cohesion, while at a local level, technical training is delivered in connection with the areas of expertise needed by each business area. This represented an investment of 173,108 hours of training in 2009.

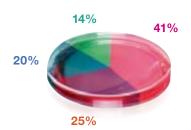
Ipsen has defined four key training themes. Two new programs have been developed in addition to existing programs covering ethics and information security. The first, an English language learning program based on the level of English required for each role, has been designed to facilitate team work and use of a common language. The second, which focuses on developing management skills, is in progress.

#### **CREATION OF** A MOBILITY COMMITTEE

As its employees are one of the major drivers of Ipsen's development, it is essential that the Group promote internal mobility so as to enhance performance by diversifying both experiences and skills. It is for this reason that the principle of giving priority to internal candidates for all recruitment activity was reaffirmed in 2009. To this end, and with the aim of efficiently coordinating internal mobility. an eponymous committee was formed to identify potential candidates and opportunities for positions within the Group. All aspects of internal mobility must be promoted: mobility within roles, as well as hierarchical, functional and geographical mobility. Employees are regularly made aware of job opportunities through the jobs forum, which can be accessed via the Group's intranet. In 2010, a mobility charter will set out the detailed principles and responsibilities of all staff, and will be communicated to all Ipsen employees.



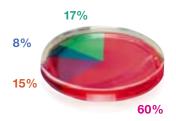
#### Breakdown of headcount by job category



Sales: 41% Manufacturing and Supply Organization: 21% Research and Development: 20% Administration and other: 14%

Total: 4,428

#### Breakdown of headcount by geographical area



Major Western European countries: 60% Rest of Europe: 15% North America: 8% Rest of World: 17% Total: 4,428

#### **A DESIRE** FOR TRANSPARENCY

Ipsen's Human Resources department has continued its policy of transparency throughout the year. In 2009, this was particularly reflected in a communication to Group managers explaining the three principles on which Ipsen's remuneration policy is built: internal fairness based on levels of responsibility within each business area, the recognition of external competitiveness in order to attract and retain talent, and the recognition of performance through an annual appraisal.

#### **FOUR KEY** TRAINING THEMES

The "Ethics" program, which was launched in 2007, aims to ensure that all staff understand, put into practice, and comply with Ipsen's ethical principles, as set out in the Business **Ethics Code of Conduct.** 

Information security is the subject of an entertaining online training program, launched in 2008 and designed for all Group employees.

The English language skills policy, launched in 2009, aims at developing employees' English language skills in line with the requirements of their roles.

The management development program - Management Excellence will be launched in the second half of 2010. The aim of this program is to further develop the range of professional and personal skills of Ipsen's managers.

# Ethics and Corpora Citizenship

Ipsen's commitment to ethics as well as its corporate citizenship policy demonstrate the Group's humane approach. Ipsen's various initiatives encourage all of its employees on a daily basis to innovate for patient care.

#### **ETHICS**

lpsen endeavors to apply the highest ethical standards. To this end, a Business Ethics Code of Conduct was implemented at each Group subsidiary by local management in 2005. An ethics and compliance program was launched in 2007 addressing the full range of principles covered by the Code, and over 80% of target employees followed the various training activities throughout 2009. These rules of conduct apply to all Group employees, irrespective of seniority and role.

The ethics and compliance program is built on four fundamental principles: providing better care, protecting innovation, fair competition and integrity.

Patient care: the Ipsen group's primary objective is to meet unsatisfied medical needs and to use its knowledge, expertise, and technology to provide effective therapeutic solutions that cater to patient needs.

Protection of innovation: innovation is at the heart of Ipsen's business. Intellectual property rights are a major issue for the Group, which seeks to protect its innovations, brands and copyrights. In addition, in order to protect its innovations, the Group has developed an information security policy that applies to all Group entities and staff.

Fair competition: through its medical excellence, the quality of its products, and the quality of the associated information, Ipsen seeks to outperform its competitors through honest, legal means. The Group is careful to ensure that it competes fairly on the market and complies with applicable legal requirements wherever it operates.

Integrity: Ipsen acts with integrity and honor in its dealings with all stakeholders: patients, healthcare professionals, public authorities, public officials, shareholders, and staff.

A new Ethics Committee was formed in 2009: its main duties are to ensure the positive development of the Group's ethical behavior and culture, and to ensure that Ipsen's organizational structure and procedures are consistent with these four fundamental principles and the Code of Ethics.

#### CORPORATE CITIZENSHIP

In France, the Ipsen group is a member of the Tulipe association, which pools medicines donated by pharmaceutical companies to meet urgent needs among populations affected by crises, natural disasters, and conflicts. For example, at the beginning of 2010, Ipsen donated boxes of Smecta® via Tulipe to help the population of Haiti.

Ipsen is also committed to the Fondation de la Deuxième Chance ("Second Chance Foundation") whose goal is to provide human and financial support to people living in unstable conditions. Ipsen's involvement in this mission has been by way of establishing a support site in Dreux with the aim of being as close as possible to the front line

#### **ALZHEIMER'S SCHOLARSHIP**

In liaison with the Fondation de Coopération Scientifique de la Maladie d'Alzheimer (the French foundation for scientific cooperation on Alzheimer's disease), of which it is a member, Ipsen will award a €75,000 scholarship in 2010 to support post-doctoral research carried out by a French scientist. The selected researcher will work for two years alongside internationally recognized researchers at one of the Salk Institute's four laboratories in the US.





so as to better support the winners of the award to whom the association has granted help.

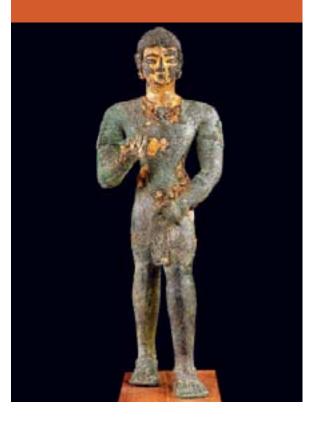
In Mexico, Ipsen set up the Candy Foundation with the aim of helping low-income families with children suffering from cerebral palsy. Since its creation in 2008, the Candy Foundation has opened three centers which have welcomed close to 300 children suffering from cerebral palsy.

#### ASSOCIATIONS, FOUNDATIONS AND UNIVERSITIES: A VARIETY **OF PARTNERSHIPS**

Ipsen is a privileged contact point for learned societies, healthcare and medical institutions, and patient associations. For example, the Group works with associations supporting cancer patients in Italy and associations supporting and assisting acromegaly patients in South Korea. In the United Kingdom, the Ipsen Fund works to promote assistance for sick children. In Australia, the Group supports the Australian Pituitary Foundation, which, since 2006, has been publishing reviews aimed at informing and educating patients. The Group is also keen to work with learned societies and healthcare institutions to support research programs and training for healthcare personnel. In this context, the Group works with university and academic groups, medical centers, and associations to carry out many initiatives throughout the world. Furthermore, as part of a partnership with the Health Chair of the "Sciences Po" (school of political sciences in Paris), the Group takes a strong interest in diversifying educational programs, developing continuing education, and stimulating research in life sciences.

#### **IPSEN** AND THE LOUVRE MUSEUM MEROE, AN EMPIRE ON THE NILE

Ipsen, which has long been committed to cultural sponsorship, has renewed its support for the Louvre museum. After being involved in 2007 in acquiring an Egyptian medical papyrus from the New Empire which was declared a "national treasure", Ipsen is supporting the exhibition, "Meroe, an empire on the Nile". The exhibition, which runs from March 26 to September 6, 2010, is the first one to appear on the subject of Meroe. Over 200 objects illustrate the majesty of this ancient civilization which combines African, Egyptian and Greco-Roman influences.



## Environment, Health and Safety

Preserving health is at the heart of Ipsen's vocation. Its activities have naturally led the Group to implement optimum levels of security in fulfilling its mission, and to set out an environmentally friendly development strategy. This commitment is formalized by way of an overall environment, health and safety (EHS) policy.

A five-year EHS plan covering all Ipsen group sites was implemented in 2008.

The first stage consists of implementing a management system aligned with international standards, as well as identifying and categorizing potential chemical risks associated with the full range of products arising from Ipsen's R&D activities.

The second stage consists in incorporating EHS policy into all Group activities, including operations and offices. As such, in 2009 the Group began taking into account EHS issues through eco-design projects, and incorporated the EHS policy into its purchasing strategies.

The third stage focuses on three priority issues: reducing dependence on personal protective equipment in favor of collective protection, significantly reducing the Group's

environmental footprint, and implementing visible EHS initiatives.

For example, while growth in consolidated sales reached 6.4% in 2009, energy consumption (electricity, gas and fuel oil) attributable to the Group's manufacturing sites rose by only 1% in comparison. Also, as a result of the Group's environmental efforts, the proportion of recycled waste reached 83.6% in 2009.

In order to ensure the health and safety of its employees, each site has rolled out a training program aligned with its specific risks and impacts. As such, all employees receive training in the risks inherent to their roles and the environmental impacts associated with their activities. This ensures that they have a responsible attitude in their day-to-day work.

#### **GREEN CHEMISTRY**

The Group launched an initiative in 2009 to develop ideas that could lead to the use of more environmentally friendly products. Such projects include the following:

- At the Cork site, an ethanol reduction project led to a 37.9 ton reduction in the use of this solvent.
- At the Dublin site, three key actions were introduced to reduce the use of solvents and hazardous substances.
- At the Wrexham site, a policy of gradually replacing hazardous substances with less dangerous ones has been implemented.

A solvent recovery program is also included in this approach. In 2009, of the more than 19,000 tons of solvents across the Group's sites, 93% were recovered.



The design of Ipsen's headquarters in Boulogne-Billancourt complies with the highest environmental





#### **CERTIFICATION**

The Group pursues a voluntary policy of implementing management systems that comply with the OHSAS 18001 health and safety at work standard and the ISO 14001 environmental standard. In 2009, ISO 14001 certification, obtained in 2004, was maintained for the Isle-sur-la-Sorgue site (France) following an audit. The Wrexham plant (UK) secured Green Dragon certification from local environmental authorities in 2008 and 2009, demonstrating the success of its environmental efforts.

In addition, the Cork plant in Ireland, which has been ISO 14001 certified since 2008, is preparing to seek OHSAS 18001 certification. The Signes (France) and Tianjin (China) manufacturing sites are also committed to achieving ISO 14001 certification.

#### **CARBON FOOTPRINT**

In 2009, the Group teamed up with the French association of pharmaceutical companies (Leem) to initiate a process to quantify the sector's greenhouse gas emissions using a common and consistent methodology. The Signes production site and the Dreux and Les Ulis R&D centers have begun the process of assessing their CO2 emissions.

## The "Fondation Ipse

Created in 1983 under the aegis of the "Fondation de France", the Fondation Ipsen's mission is to contribute to the development and dissemination of scientific knowledge.

#### INTERNATIONAL **PUBLICATIONS**

The Fondation Ipsen publishes reference works following its seminars. They are distributed by international publishing companies as part of various English language collections:

- Research and Perspectives in Alzheimer's Disease
- Research and Perspectives in Neurosciences
- Research and Perspectives in Longevity
- Research and Perspectives in Endocrinology
- The "WHO/Fondation Ipsen" Collection
- The "Mind and Brain" collection

It also publishes reports from its "Medicine and Research" seminars devoted to cancer. In addition, since 1986, the Fondation Ipsen publishes "Alzheimer's News", a periodical devoted to Alzheimer's disease (202 issues released).

Focused on the long term, the Fondation Ipsen's activities are aimed at fostering interaction between researchers and clinicians. This type of dialog is essential due to the extreme specialization of the professions in question.

The Fondation Ipsen's ambition is to initiate discussions on the major scientific challenges of the coming years. For each of its initiatives, the Fondation Ipsen brings together partners from international academic and scientific communities to independently set out the major issues upon which it has chosen to focus, and to review the status of current knowledge.

#### **MEDICINE AND RESEARCH SEMINARS**

The Fondation Ipsen also brings together leading experts through its "Medicine and Research" seminars. These annual international meetings are devoted to emerging themes in various fields of medicine and biology:

- Alzheimer's disease: since 1987, this theme has been the subject of 24 seminars. The last was held in Paris on April 6, 2009 on the theme "Diabetes, Insulin and Alzheimer's disease".
- Neuroscience: this series of seminars, which began in 1990, identifies the major emerging themes in this field, from molecular biology to cognitive sciences. The 17th seminar in this series was held in Paris (France) on April 20, 2009 under the title "Macro-roles for microRNAs in the life and death of cells".
- Endocrinology: this series, launched in 2002, aims to study endocrine interactions and their role in body function. The ninth seminar in this series took place on December 4, 2009 on the theme of adipocytes.
- Cancer: this major series, launched in 2005, brings together, each year, the leading specialists from around the world working in such varied fields as inflammation, metastasis, metabolism, molecular targets of therapy, and stem cells.



The 2009 Longevity Prize awarded to Jacques Vallin.

- The vascular tree (2004-2008): this series explored the various stages that lead to the development of the vascular system, its growth in harmony with other organs, its physiology, its degeneration, its death and its potential for regeneration, as well as the relationship between oxygen metabolism and blood vessels.

#### **PRESTIGIOUS PARTNERSHIPS**

The Fondation Ipsen has forged partnerships with international institutions and organizations, bringing together experts from a variety of disciplines, including the World Health Organization (WHO), the French National Gerontology Foundation ("Fondation Nationale de Gérontologie") and Harvard University. In 2007, three new partnerships were initiated:

- The Salk Institute and Nature magazine: this partnership takes the form of a series of annual meetings on biological complexity. In January 2009, a meeting entitled "The aging process" focused on the decoding mechanisms involved in senescence and the onset of diseases and disturbances.
- Cell Press and the Massachusetts General Hospital the "Exciting Biologies" series: the third meeting in this series was held in Buenos Aires (Argentina) in October 2009 and focused on "biological equilibrium".
- Nature magazine: four annual "Emergence and Convergence" meetings cover subjects such as small RNAs in development, immunology and cancer, the evolution of the genome and structural variation, epigenetics and behavior, multiple sclerosis, cellular form and polarity, mitochondrial dysfunction in neurological diseases, and epigenetic dynamics in the immune system.



A meeting, focused on "biological equilibrium", organized by Cell Press, the Massachusetts General Hospital and the Fondation Ipsen brought together approximately 60 scientists in Buenos Aires in October 2009.

#### AWARDS TO ENCOURAGE RESEARCH

The Fondation Ipsen awards prizes to scientists who lead cutting edge work:

- Neuroscience: the 20th Neuronal Plasticity prize was awarded in 2009 by an international panel chaired by Professor Wolf Singer (Max Planck Institute, Frankfurt, Germany) to Alim-Louis Benabid (CEA Minatec LETI, Grenoble, France), Apostolos P. Georgopoulos (University of Minnesota, Minneapolis, USA) and Miguel A. L. Nicolelis (Duke University, Durham, USA), for their work on brain-machine interactions.
- Longevity: the 2009 prize was awarded to Dr. Jacques Vallin (French National Institute of Demographic Studies, Paris, France) for his international study of longevity in relation to hygienic changes.
- Neuropsychology: the 2009 Jean-Louis Signoret prize was awarded to Dr. Pierre Maguet (Cyclotron Research Center, Liège, Belgium) for his research on "sleep and cognition".
- Endocrinology: in 2009, an international panel chaired by Iain Robinson (National Institute for Medical Research, London, UK) selected Professor Gilbert Vassart (Hôpital Erasme, Brussels, Belgium) for his contribution to the understanding of molecular endocrinology diseases and translational medicine.



#### Financial Information

## Strong **performance**

In 2009, the Ipsen group once again demonstrated its ability to achieve its objectives and maintain above-sector growth. In a depressed economic environment, this strong performance illustrates the relevance of Ipsen's products, the Group's research efforts, and the commitment of its employees.

# The Ipsen Share

#### SHARE INFORMATION

Listing: Compartment A of the Euronext™

Eurolist market

ISIN code: FR 0010259150

Ticker symbol: IPN

FTSE classification: 486 - pharmacy ICB industry sector: 4577 - pharmacy

Par value: 1 euro

#### FINANCIAL CALENDAR(1)

May 28: Annual Shareholders' Meeting June 4: Payment of 2009 dividend(2)

August 31: Half-year sales and results for 2010

October 28: 2010 nine month sales

(1) This financial calendar is for indicative purposes only and the Group could change its publication dates should it deem necessary.
(2) Subject to approval by the Annual Shareholders' Meeting on May 28, 2010.

#### IPSEN SHARE PRICE BETWEEN JANUARY 1, 2009 AND FEBRUARY 26, 2010

Average share price	33.51
High	41.72
Low	24.86
% change (between highest price and price at January 1, 2009)	45%
Average daily trading volume per day	112,719

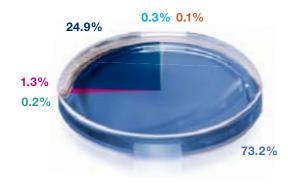
#### BREAKDOWN OF SHARE CAPITAL (AT DECEMBER 31, 2009)

Directors: 0.1% Mayroy: 73.2%

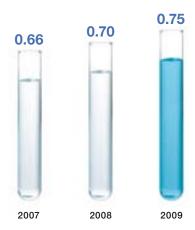
Employee investment fund: 0.2%

Treasury shares: 1.3% Public: 24.9%

Other registered stockholders: 0.3%



#### **DIVIDEND PER SHARE FOR** THE LAST THREE FISCAL YEARS



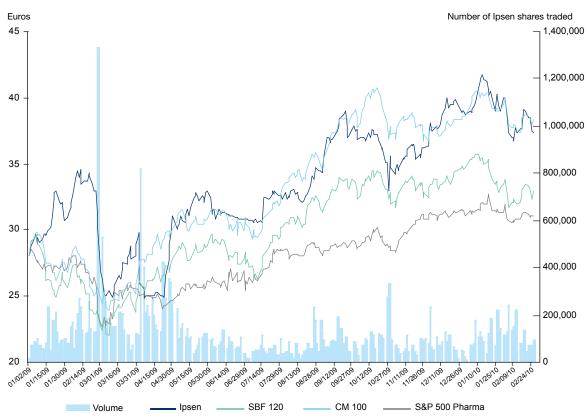
Ipsen's Board of Directors decided to propose to the Annual Shareholders' Meeting, to be held on May 28, 2010, a dividend of €0.75 per share, up 7.1% year on year, representing a payout ratio of approximately 40% of consolidated net income.





#### COMPARISON OF IPSEN SHARE PRICE PERFORMANCE WITH KEY INDICES FROM JANUARY 1, 2009 TO FEBRUARY 26, 2010

(SOURCE: REUTERS, rebased on Ipsen share price at January 1, 2009)



### CONSOLIDATED INCOME STATEMENT

(in thousands of euros)	December 31, 2009	December 31, 2008 <sup>(1)</sup>	December 31, 2007 <sup>(3)</sup>
Sale of goods	1,032,807	971,022	920,475
Other revenues	79,576	67,090	73,282
Revenue	1,112,383	1,038,112	993,757
Cost of goods sold	(237,807)	(220,113)	(198,987)
Research and development expense	(197,293)	(182,843)	(184,650)
Selling expenses	(396,144)	(354,969)	(319,944)
General and administrative expenses	(88,461)	(85,812)	(80,326)
Other operating income and expenses	(9,683)	(8,257)	368
Amortization of intangible assets (2)	(10,525)	(4,321)	(1,338)
Restructuring costs	-	(2,620)	8
Impairment losses	-	-	-
Operating income	172,470	179,177	208,888
Investment income	2,703	21,425	11,541
Financing costs	(4,399)	(4,348)	(1,950)
Net financing costs	(1,696)	17,077	9,591
Other financial income and expense	(3,468)	(5,335)	(2,855)
Income taxes	(10,593)	(32,832)	(54,478)
Share of profit/loss from associated companies	-	(10,847)	(8,764)
Net profit from continuing operations	156,713	147,240	152,382
Net profit from discontinued operations	453	(172)	(1,313)
Consolidated net profit	157,166	147,068	151,069
- Attributable to shareholders of Ipsen	156,584	146,563	150,611
- Minority interests	582	505	458
Basic earnings per share, continuing operations (in € per share)	1.85	1.75	1.81
Diluted earnings per share, continuing operations (in $\in$ per share)	1.85	1.75	1.81
Basic earnings per share, discontinued operations (in € per share)	0.01	0.00	(0.02)
Diluted earnings per share, discontinued operations (in € per share)	0.01	0.00	(0.02)
Basic earnings per share (in € per share)	1.86	1.75	1.80
Diluted earnings per share (in € per share)	1.86	1.74	1.79

<sup>(1)</sup> The information presented above as of December 31, 2008 has been restated to account for the purchase price accounting impact related to the Group's transaction with Tercica Inc. and Vernalis Inc.

<sup>(2)</sup> Excludes software.

<sup>(3)</sup> The consolidated income statement shown for the period 2007 differs from the one previously reported, the Group having detailed amortization of intangible assets excluding software in a separate line as of 2009.

### CONSOLIDATED BALANCE SHEET - BEFORE ALLOCATION OF NET PROFIT

(in thousands of euros)	December 31, 2009	December 31, 2008 <sup>(1)</sup>	December 31, 2007 <sup>(2)</sup>
ASSETS		222.242	100.010
Goodwill	290,236	290,816	189,013
Other intangible assets	236,967	232,935	89,169
Property, plant & equipment	251,778	237,860	221,891
Equity investments	3,410	2,650	1,457
Investments in associated companies	-	-	40,948
Non-current financial assets	3,384	3,810	25,883
Other non-current assets	17,778	8,039	55,632
Deferred tax assets	120,953	98,343	61,393
Total non-current assets	924,506	874,454	685,386
Inventories	102,970	115,782	87,111
Trade receivables	223,105	217,845	216,214
Current tax assets	55,966	49,509	26,569
Other current assets	50,575	63,383	53,753
Current financial assets	1,162	2,528	96
Securities held for sale	-	-	6,000
Cash and cash equivalents	218,584	239,584	247,068
Total current assets	652,362	688,631	636,811
Assets of discontinued operations	4 570 000	1,333	725
TOTAL ASSETS	1,576,868	1,564,418	1,322,922
EQUITY & HORWITES			
EQUITY & LIABILITIES	04.400	0.4.000	04044
Share capital	84,128	84,060	84,044
Additional paid-in capital and consolidated reserves	784,449	698,976	582,557
Net profit for the period	156,584	146,563	150,611
Foreign exchange differences	(42,537)	(44,567)	(17,350)
Equity – attributable to shareholders of Ipsen	982,624	885,032	799,862
Attributable to minority interests	1,724	1,580	1,247
Total shareholders' equity	984,348	886,612	801,109
Retirement benefit obligation	13,989	11,530	10,038
Long-term provisions	37,425	34,739	14,981
Bank loans	-	148,941	4,379
Other financial liabilities	12,190	13,803	16,449
Deferred tax liabilities	7,093	5,296	3,932
Other non-current liabilities	211,771	142,560	192,043
Total non-current liabilities	282,468	356,870	241,822
Short-term provisions	2,621	8,952	6,598
Bank loans	4,000	4,000	5,375
Financial liabilities	4,188	4,346	3,831
Trade payables	122,647	103,835	104,181
Current tax liabilities	4,030	36,315	12,327
Other current liabilities	157,338	156,345	136,234
Bank overdrafts	13,183	2,259	6,161
Total current liabilities	308,007	316,052	274,707
Liabilities of discontinued operations	2,045	4,884	5,284
TOTAL EQUITY & LIABILITIES	1,576,868	1,564,418	1,322,922

<sup>(1)</sup> The information presented above as of December 31, 2008 has been restated to account for the purchase price accounting impact related to the Group's transaction with Tercica Inc. and Vernalis Inc.

<sup>(2)</sup> The consolidated income statement shown for the period 2007 differs from the one previously reported, the Group having detailed amortization of intangible assets excluding software in a separate line as of 2009.

### CONSOLIDATED STATEMENT OF CASH FLOWS

Share of profic/loss from associated companies   10,847   156,871   158,087   151,144     Net profit from continuing operations before share from associated companies   156,713   158,087   151,144     Poperciation, amortization, provisions and impairment losses   44,938   51,514   41,226     Change in fair value of financial derivatives   3,712   24,749   (252)     Net gains and losses on disposals of non-current assets   3,712   24,749   (252)     Share of government grants released to profit and loss   393   (47,49   (252)     Share of government grants released to profit and loss   339   (47,49	(in thousands of euros)	December 31, 2009	December 31, 2008 <sup>(1)</sup>	December 31, 2007
Net profit from discontinued operations   459   172   1.318	CONSOLIDATED NET PROFIT	157,166	147,068	151.069
Share of profit/loss from associated companies   10,047   156,718   158,087   151,146   Non-cash and non-operating items   - Depreciation, amortization, provisions and impairment losses   44,935   51,514   41,226   Change in fair value of financial derivatives   (1,429)   5,829   (1,929)   Net gains and losses on disposals of non-current assets   3,712   (24,744)   (25,25)   Net gains and losses on disposals of non-current assets   3,712   (24,744)   (25,25)   Net gains and losses on disposals of non-current assets   3,712   (24,744)   (25,25)   Net gains and losses on disposals of non-current assets   3,712   (24,744)   (25,25)   Net gains and losses on disposals of non-current assets   3,739   (17)   3,905   (17)   3,905   (17)   4,905   (17)				1,313
Net profit from continuing operations before share from associated companies         156,713         158,087         161,146           Non-cash and non-operating items         - Despreciation, amortization, provisions and impairment losses         44,935         51,514         41,228           - Change in fiar value of financial derivatives         (1,429)         5,829         (1,929)           - Net gains and losses on disposals of non-current assets         3,712         (24,744)         (252)           - Share of government grants released to profit and loss         (93)         (94)         (97)           - Foreign exchange differences         3,79         (1,71)         3,905           - Change in deferred taxes         (20,724)         450         394           - Share-based payment expense         8,016         6,586         7,624         545           - Char non-cash items         704         (605)         1,754           - Cother non-cash items         1704         (605)         1,754           - Char non-cash items         182,330         (1,204)         1,902           - (Increase)/decrease in in ventronies         12,232         (12,333)         (9,026)           - (Increase)/decrease in in ventronies         18,330         1,176         5,087           - (Increase)/decrease in inve		-	10.847	
Non-cash and non-operating items		156.713		<u> </u>
Depreciation, amortization, provisions and impairment losses			,	,
-Change in fair value of financial derivatives - Net gains and losses on disposals of non-current assets - Share of government grants released to profit and loss - Share of government grants released to profit and loss - Good government grants released to profit and loss - Good government grants released to profit and loss - Good government grants released to profit and loss - Good government grants released to profit and loss - Good government grants released to profit and loss - Foreign exchange differences - Good government grants released to profit and loss - Change in deferred taxes - Change in deferred taxes - Change in deferred taxes - Share-based payment expense - Gain or loss on sales of treasury shares - Cesh four from operating activities before changes in working capital - Change in more proteing activities before changes in working capital - Change in more proteing activities before changes in working capital - Increases/decrease in intrade receivables - (Increases/decrease) in trade payables - Increases/decrease) - Increases/decrease in intrade receivables - Net change in other operating assets and liabilities - Net change in other operating assets and liabilities - Net change in other operating activities - Change in working capital related to operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Net change in other operating activities - Good - Good - Net control of the c		44,935	51,514	41,226
Net gains and losses on disposals of non-current assets   9,712   (24,744)   (252)		(1.429)		
Share of government grants released to profit and loss   339   (94)   (97)     Foreign exchange differences   379   (17)   3,905     Change in deferred taxes   (20,724)   (46)   394     Share-based payment expense   8,016   6,885   7,562     Share-based payment expense   528   (724)   545     Cash flow from operating activities before changes in working capital   704   (605)   1,754     Cash flow from operating activities before changes in working capital   792,741   796,291   214,254     (Increase)/decrease in inventories   12,232   (12,353)   (9,026)     (Increase)/decrease in inventories   12,232   (12,353)   (12,053)     (Increase)/decrease in inventories   12,232   (12,353)   (12,053)     (Increase)/decrease in inventories   13,390   (1,176   5,097     (Increase)/decrease) in intrade payables   76,286   24,119   29,506     (Increase)/decrease) in income tax liability   (38,487)   (1,261)   (38,456)     (Increase)/decrease)   (38,487)   (1,261)   (38,456)   (38,457)   (1,261)   (38,456)   (38,457)   (38,248)   (38,457)   (38,		( , ,		
-Foreign exchange differences (20,724) 460 394 - Share-based payment expense 8,016 6,655 7,562 - Gain or loss on sales of treasury shares 528 (724) 545 - Chen non-cash items 704 (605) 1,754 - Cother non-cash items 8704 (605) 1,754 - Cother non-cash items 9704 (605) 1,754 - Coth flow from operating activities 9704 (605) 1,754 - Coth flow from operating activities 9704 (605) 1,754 - Cother non-cash items 9704 (605) 1,754 - Cother non-cash 1,754 - Cother non				
-Change in deferred taxes -Share-based payment expense -Sian or loss on sales of treasury shares -Som or loss on sales of treasury shares -Som or loss on sales of treasury shares -Cother non-cash items -Cother non-cash items -Increase/decrease in inventories -Increase/decrease in inventories -Increase/decrease in inventories -Increase/decrease in trade receivables -(Increase)/decrease in trade receivables -(Increase)/decrease) in trade payables -Increase/decrease) in trade payables -Increase/dec		` ,	( /	
-Share-based payment expense	<u> </u>	(20,724)	. ,	· · · · · · · · · · · · · · · · · · ·
Gain or loss on sales of treasury shares   528   (724)   545			6.585	7.562
Cosh flow from operating activities before changes in working capital   192,741   196,297   214,254   (Increase)/decrease in inventories   12,232   (12,363)   (9,026)   (Increase)/decrease in inventories   12,232   (12,363)   (9,026)   (Increase)/decrease) in trade receivables   (3,539)   (4,294)   (25,395)   (1,026)   (Increase)/decrease) in trade receivables   (3,539)   (4,294)   (25,395)   (1,026)				,
Cash flow from operating activities before changes in working capital   192,741   196,291   214,254   - (Increase)/decrease in inventories   12,232   (12,353)   (9,026)   - (Increase)/decreases in tade receivables   (3,539)   (4,294)   (25,395)   - Increase/(decrease) in trade payables   18,390   1,176   5,087   - Net change in income tax liability   (38,487)   (1,261)   (38,485)   - Net change in other operating assets and liabilities   76,286   24,119   29,506   Change in working capital related to operating activities   64,882   7,387   (38,284)   NET CASH PROVIDED BY OPERATING ACTIVITIES   257,623   203,678   175,970   Acquisition of property, plant & equipment   (40,319)   (61,447)   (58,672)   (68,483)   (7,297)   (7,272   1,160   Acquisition of intangible assets and property, plant & equipment   1,729   27,272   1,160   Acquisition of shares in non-consolidated companies   (24,744)   (33,762)   (26,483)   Acquisition of shares in non-consolidated companies   (20,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (44,386)   Acquisitions of shares in associated companies   (2,000)   - (2,000)   - (2,000)   - (2,000)   - (2,000)   - (2,000)   - (2,000)   - (2,000)   - (2,000)   - (2,000)   - (2,000)	· · · · · · · · · · · · · · · · · · ·	704	<u> </u>	
- (Increase)/decrease in inventories	Cash flow from operating activities before changes in working capital	192,741		
- (Increase)/decrease in trade receivables (3,539) (4,294) (25,395) - Increase/(decrease) in trade payables 18,390 1,176 5,087 - Net change in income tax liability (38,487) (1,261) (38,486) - Net change in other operating assets and liabilities 76,286 24,119 29,506 Change in working capital related to operating activities 64,882 7,387 (38,284) NET CASH PROVIDED BY OPERATING ACTIVITIES 25,7652 20,3678 175,970 Acquisition of property, plant & equipment (40,319) (61,447) (58,672) Acquisition of property, plant & equipment (40,319) (61,447) (58,672) Acquisition of intangible assets (24,744) (33,762) (26,483) Proceeds from disposal of intangible assets and property, plant & equipment 1,729 27,272 1,180 Acquisition of shares in non-consolidated companies (420) (3,224) (698) Acquisitions of shares in associated companies (420) (3,224) (698) Acquisitions of shares in associated companies (2,000) - (44,386) Proceeds from sales of investment securities (2,000) - (44,386) Proceeds from sales of investment securities (2,000) - (44,389) Broceeds from sales of investment securities (2,365) (1,904) (5,026) Impact of changes in the consolidation scope - (214,939) 8 Broceeds from sales of investment activities (6,770) - (44,801) Advances on other investment securities (6,770) - (44,601) Advances on other investment activities (2,476) 1,660 (8,000) Advances on other investment activities (4,426) (5,145) 7,433 (1,012) (4,601) Acquisitions paid to investment activities (4,246) (5,145) (7,436) (285,486) (140,278) NET CASH USED BY INVESTMENT ACTIVITIES (71,336) (285,486) (140,278) Dividends paid by subsidiaries to minority interests (391) (215) (631) (2,170) Net change in short-term borrowings (5,118) (9,284) (24,758) Dividends paid by subsidiaries to minority interests (391) (215) (631) (2,170) Net Change in working capital related to financing activities (943) (2,264) 814 NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES (14,768) (14,768) (14,768) (14,768) (14,768) (14,768) (14,768) (14,768) (14,768) (14,768) (14,768) (14,768) (14,			<u> </u>	
- Increase/(decrease) in trade payables			( , ,	
- Net change in income tax liability - Net change in other operating assets and liabilities - Net change in other operating assets and liabilities - Robert Change in working capital related to operating activities - 64,882 - 7,387 - 843,8284 - RET CASH PROVIDED BY OPERATING ACTIVITIES - 257,623 - 203,678 - 175,970 - Requisition of property, plant & equipment - (40,319) - (61,447) - (58,672) - (64,483) - Requisition of property, plant & equipment - (40,319) - (61,447) - (68,672) - (24,744) - (33,762) - (26,483) - Requisition of intangible assets - (24,744) - (33,762) - (26,483) - Requisition of shares in non-consolidated companies - (420) - (3,224) - (898) - Requisitions of shares in non-consolidated companies - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (44,386) - (2,000) - (2,000) - (44,386) - (2,000) - (2,000) - (4,				, ,
Net change in other operating assets and liabilities				,
Change in working capital related to operating activities         64,882         7,387         (38,284)           NET CASH PROVIDED BY OPERATING ACTIVITIES         257,623         203,678         175,970           Acquisition of property, plant & equipment         (40,319)         (61,447)         (58,672)           Acquisition of intangible assets         (24,744)         (33,762)         (26,843)           Proceeds from disposal of intangible assets and property, plant & equipment         1,729         27,272         1,160           Acquisition of shares in non-consolidated companies         (420)         (3,224)         (698)           Acquisitions of shares in associated companies         -         -         (2,129)           Convertible note subscriptions         (2,000)         -         (44,386)           Proceeds from sales of investment securities         -         1,410         -           Payments to post-employment benefit plans         (2,235)         (1,904)         (5,026)           Impact of changes in the consolidation scope         -         (214,939)         8           Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities <td></td> <td> ,</td> <td> ,</td> <td>( , ,</td>		,	,	( , ,
NET CASH PROVIDED BY OPERATING ACTIVITIES         257,623         203,678         175,970           Acquisition of property, plant & equipment         (40,319)         (61,447)         (58,672)           Acquisition of intangible assets         (24,744)         (33,762)         (26,483)           Proceeds from disposal of intangible assets and property, plant & equipment         1,729         27,272         1,160           Acquisition of shares in non-consolidated companies         (420)         (3,224)         (698)           Acquisitions of shares in associated companies         -         -         (2,129)           Convertible note subscriptions         (2,000)         -         (44,386)           Proceeds from sales of investment securities         -         1,410         -           Proceeds from sales of investment securities         (2,235)         (1,904)         (5,026)           Impact of changes in the consolidation scope         -         (214,939)         8           Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012		,		
Requisition of property, plant & equipment				
Acquisition of intangible assets   (24,744)   (33,762)   (26,483)     Proceeds from disposal of intangible assets and property, plant & equipment   1,729   27,272   1,160     Acquisition of shares in non-consolidated companies   (420)   (3,224)   (698)     Acquisitions of shares in associated companies   (2,129)     Convertible note subscriptions   (2,000)   -   (44,386)     Proceeds from sales of investment securities   -   1,410       Payments to post-employment benefit plans   (2,235)   (1,904)   (5,026)     Impact of changes in the consolidation scope   -   (214,939)   8     Change in cash securities held for sale   -   6,000   (6,000)     Advances on other investment securities   (6,770)   -   -   -     Other cash flow related to investment activities   (2,476)   1,265   (944)     Deposits paid   1,473   (1,012)   (4,601)     Changes in working apital related to investment activities   4,426   (5,145)   7,493     NET CASH USED BY INVESTMENT ACTIVITIES   (71,336)   (285,486)   (140,278)     Additional long-term borrowings   (151,340)   (6,521)   (2,170)     Net change in short-term borrowings   (151,340)   (6,521)   (2,170)     Dividends paid by lpsen   (1,056   -   -   -   -   -   -       Treasury shares   (5,118)   (9,284)   (24,758)     Dividends paid by subsidiaries to minority interests   (943)   (2,264   814     NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES   (29,491)   (2,118)   (39,841)     NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES   (29,491)   (2,118)   (39,841)     NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES   (29,491)   (2,118)   (39,841)     NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES   (29,491)   (2,118)   (39,841)     NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES   (29,491)   (2,118)   (39,841)   (39,841)   (39,841)   (39,841)   (39,841)   (39,841				
Proceeds from disposal of intangible assets and property, plant & equipment         1,729         27,272         1,160           Acquisition of shares in non-consolidated companies         (420)         (3,224)         (698)           Acquisitions of shares in associated companies         -         -         (2,129)           Convertible note subscriptions         (2,000)         -         (44,386)           Proceeds from sales of investment securities         -         1,410         -           Payments to post-employment benefit plans         (2,235)         (1,904)         (5,026)           Impact of changes in the consolidation scope         -         (214,939)         8           Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -         -           Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012)         (4,801)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -		,		
Acquisition of shares in non-consolidated companies         (420)         (3,224)         (698)           Acquisitions of shares in associated companies         -         -         (2,129)           Convertible note subscriptions         (2,000)         -         (44,386)           Proceeds from sales of investment securities         -         1,410         -           Payments to post-employment benefit plans         (2,235)         (1,904)         (5,026)           Impact of changes in the consolidation scope         -         (214,939)         8           Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         -         (1,375)         (1,584)				
Acquisitions of shares in associated companies   -   -   (2,129)				
Convertible note subscriptions         (2,000)         -         (44,386)           Proceeds from sales of investment securities         -         1,410         -           Payments to post-employment benefit plans         (2,235)         (1,904)         (5,026)           Impact of changes in the consolidation scope         -         (214,939)         8           Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         71,336         (285,486)         (140,278)           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -           Treasury shares	'	-	-	, ,
Proceeds from sales of investment securities         -         1,410         -           Payments to post-employment benefit plans         (2,235)         (1,904)         (5,026)           Impact of changes in the consolidation scope         -         (214,939)         8           Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         1,056         -         -           Capital increase by Ipsen         (5,118)         (9,284)         (24,758)           Dividends paid by subsidiaries to minority interests         (5,118)         (9,284)         (24,758)	·	(2,000)	-	
Payments to post-employment benefit plans         (2,235)         (1,904)         (5,026)           Impact of changes in the consolidation scope         -         (214,939)         8           Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities         (2,476)         1,265         (9944)           Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends		-	1.410	-
Impact of changes in the consolidation scope   - (214,939)   8     Change in cash securities held for sale   - 6,000   (6,000)     Advances on other investment securities   (6,770)         Other cash flow related to investment activities   (2,476)   1,265   (944)     Deposits paid   1,473   (1,012)   (4,601)     Changes in working capital related to investment activities   4,426   (5,145)   7,493     NET CASH USED BY INVESTMENT ACTIVITIES   (71,336)   (285,486)   (140,278)     Additional long-term borrowings   - 148,941   1,900     Repayment of long-term borrowings   (151,340)   (6,521)   (2,170)     Net change in short-term borrowings   1,056   -   -     Treasury shares   (5,118)   (9,284)   (24,758)     Dividends paid by Ipsen   (58,033)   (55,027)   (50,389)     Dividends paid by subsidiaries to minority interests   (391)   (215)   (631)     Deposits received   1   174   -     Changes in working capital related to financing activities   (943)   2,264   814     NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES   (214,768)   78,957   (76,818)     Impact of businesses to be sold or discontinued   (1,010)   732   1,285     CHANGE IN CASH AND CASH EQUIVALENTS   (29,491)   (2,118)   (39,841)     Opening cash and cash equivalents   (2,433)   (1,464)   (2,995)		(2,235)		(5,026)
Change in cash securities held for sale         -         6,000         (6,000)           Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Repayment of long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)		-	,	
Advances on other investment securities         (6,770)         -         -           Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(		-	, , ,	(6,000)
Other cash flow related to investment activities         (2,476)         1,265         (944)           Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         1,74         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)		(6,770)	-	-
Deposits paid         1,473         (1,012)         (4,601)           Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND	Other cash flow related to investment activities		1,265	(944)
Changes in working capital related to investment activities         4,426         (5,145)         7,493           NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         -         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)				, ,
NET CASH USED BY INVESTMENT ACTIVITIES         (71,336)         (285,486)         (140,278)           Additional long-term borrowings         -         148,941         1,900           Repayment of long-term borrowings         (151,340)         (6,521)         (2,170)           Net change in short-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exch		4,426	(5,145)	7,493
Additional long-term borrowings       - 148,941       1,900         Repayment of long-term borrowings       (151,340)       (6,521)       (2,170)         Net change in short-term borrowings       - (1,375)       (1,584)         Capital increase by Ipsen       1,056       -       -         Treasury shares       (5,118)       (9,284)       (24,758)         Dividends paid by Ipsen       (58,033)       (55,027)       (50,389)         Dividends paid by subsidiaries to minority interests       (391)       (215)       (631)         Deposits received       1       174       -         Changes in working capital related to financing activities       (943)       2,264       814         NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES       (214,768)       78,957       (76,818)         Impact of businesses to be sold or discontinued       (1,010)       732       1,285         CHANGE IN CASH AND CASH EQUIVALENTS       (29,491)       (2,118)       (39,841)         Opening cash and cash equivalents       237,325       240,907       283,743         Impact of exchange rate fluctuations       (2,433)       (1,464)       (2,995)		(71,336)	(285,486)	(140,278)
Repayment of long-term borrowings       (151,340)       (6,521)       (2,170)         Net change in short-term borrowings       -       (1,375)       (1,584)         Capital increase by Ipsen       1,056       -       -         Treasury shares       (5,118)       (9,284)       (24,758)         Dividends paid by Ipsen       (58,033)       (55,027)       (50,389)         Dividends paid by subsidiaries to minority interests       (391)       (215)       (631)         Deposits received       1       174       -         Changes in working capital related to financing activities       (943)       2,264       814         NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES       (214,768)       78,957       (76,818)         Impact of businesses to be sold or discontinued       (1,010)       732       1,285         CHANGE IN CASH AND CASH EQUIVALENTS       (29,491)       (2,118)       (39,841)         Opening cash and cash equivalents       237,325       240,907       283,743         Impact of exchange rate fluctuations       (2,433)       (1,464)       (2,995)		-		1,900
Net change in short-term borrowings         -         (1,375)         (1,584)           Capital increase by Ipsen         1,056         -         -           Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)		(151,340)		
Capital increase by Ipsen       1,056       -       -         Treasury shares       (5,118)       (9,284)       (24,758)         Dividends paid by Ipsen       (58,033)       (55,027)       (50,389)         Dividends paid by subsidiaries to minority interests       (391)       (215)       (631)         Deposits received       1       174       -         Changes in working capital related to financing activities       (943)       2,264       814         NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES       (214,768)       78,957       (76,818)         Impact of businesses to be sold or discontinued       (1,010)       732       1,285         CHANGE IN CASH AND CASH EQUIVALENTS       (29,491)       (2,118)       (39,841)         Opening cash and cash equivalents       237,325       240,907       283,743         Impact of exchange rate fluctuations       (2,433)       (1,464)       (2,995)		-		
Treasury shares         (5,118)         (9,284)         (24,758)           Dividends paid by lpsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)		1,056	=	=
Dividends paid by Ipsen         (58,033)         (55,027)         (50,389)           Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)			(9,284)	(24,758)
Dividends paid by subsidiaries to minority interests         (391)         (215)         (631)           Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)				
Deposits received         1         174         -           Changes in working capital related to financing activities         (943)         2,264         814           NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)	1 7 1			
Changes in working capital related to financing activities       (943)       2,264       814         NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES       (214,768)       78,957       (76,818)         Impact of businesses to be sold or discontinued       (1,010)       732       1,285         CHANGE IN CASH AND CASH EQUIVALENTS       (29,491)       (2,118)       (39,841)         Opening cash and cash equivalents       237,325       240,907       283,743         Impact of exchange rate fluctuations       (2,433)       (1,464)       (2,995)			<u> </u>	-
NET CASH PROVIDED/(USED) BY FINANCING ACTIVITIES         (214,768)         78,957         (76,818)           Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)		(943)		814
Impact of businesses to be sold or discontinued         (1,010)         732         1,285           CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)		, ,	,	(76,818)
CHANGE IN CASH AND CASH EQUIVALENTS         (29,491)         (2,118)         (39,841)           Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)				1,285
Opening cash and cash equivalents         237,325         240,907         283,743           Impact of exchange rate fluctuations         (2,433)         (1,464)         (2,995)				(39,841)
Impact of exchange rate fluctuations (2,433) (1,464) (2,995)				283,743
				(2,995)
	Closing cash and cash equivalents	205,401	237,325	240,907

<sup>(1)</sup> The information presented above as of December 31, 2008 has been restated to account for the purchase price accounting impact related to the Group's transaction with Tercica Inc. and Vernalis Inc.

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