

Annual report 2005 • • • • • • •



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More than **20**products marketed in over **100** countries



Nearly €170 M of Research and Development expenditure in 2005



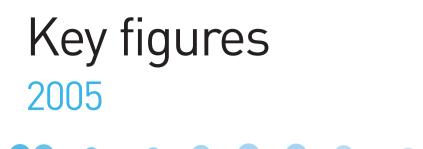
3 targeted therapeutic areas

- oncology
- endocrinology
- neuromuscular disorders

IPSEN is a European pharmaceutical group with over 20 products on the market and a total worldwide staff of nearly 4,000. The Company's development strategy is based on a combination of products in targeted therapeutic areas (oncology, endocrinology and neuromuscular disorders), which are growth drivers and primary care products which contribute significantly to its research financing. This strategy is also supported by an active policy of partnerships. The location of its four R&D centres (Paris, Boston, Barcelona, London) gives the Group a competitive edge in gaining access to leading university research teams and highly qualified personnel. In 2005, Research and Development expenditure reached €169 million, i.e. 20.9% of consolidated sales, which amounted to €807.1 million in the Group's pro forma accounts set up according to the IFRS. Nearly 700 people in R&D are dedicated to the discovery and development of innovative drugs for patient care.

Nearly 4,000 employees More than **20** R&D programmes

All product names listed in this document are either licensed to the Ipsen Group or are registered trademarks of the Ipsen Group or its partners.



CONSOLIDATED SALES (€ million)



The increase of consolidated sales was fuelled by the growth in sales of products in targeted therapeutic areas and strong sales momentum in international markets.

RESEARCH AND DEVELOPMENT EXPENDITURE (€ million)



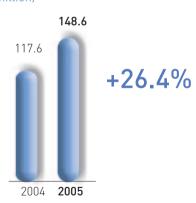
Research and Development expenditure represented 20.9% of sales in 2005, compared with 19.1% of sales in 2004.

OPERATING PROFIT (€ million)



The operating margin (% of sales) improved to 23.0%, compared with 20.8% on a comparable structure basis in 2004.

NET PROFIT GROUP SHARE (€ million)



Consolidated net profit Group share strongly increased, especially thanks to the progression of the operating profit and to the improved effective rate of taxes.

NET SALES OF GROUP'S LEADING PRODUCTS (€ million)

			Variation
	2005	2004	2005/2004
		on a comparable structure basis	on a comparable structure basis
Decapeptyl®	210.6	198.6	6.1%
Tanakan®	121.0	116.3	4.0%
Dysport [®]	92.5	82.3	12.4%
Somatuline®	81.8	72.1	13.4%
Smecta®	67.5	64.6	4.5%
Ginkor Fort®	61.2	59.0	3.7%
Forlax®	42.8	39.4	8.6%
Nisis [®] and Nisisco [®]	41.5	37.1	11.8%
NutropinAq®	5.7	0.8	596.4%

NB: 2004 and 2005 figures are pro forma and prepared in accordance with IFRS. The pro forma consolidated financial statements treat the Group's business activity as if the Group's legal restructuring had taken place on 1 January 2002, instead of 30 June 2005. The statutory auditors have prepared a report on the pro forma financial statements.

In October 2005, the Group sold its primary care business in Spain (with the exception of Tanakan®, namely Tanakene® in Spain) and presented the activity as "discontinued operations" retrospectively in the consolidated financial statements as of 1 January 2005. As a result, 2005 operating profit does not include items relating to that business, including 2005 sales of €16.7 million. In contrast, sales from the business were included in 2004 operating profit for €16.3 million.

2005 SALES

by geographical area

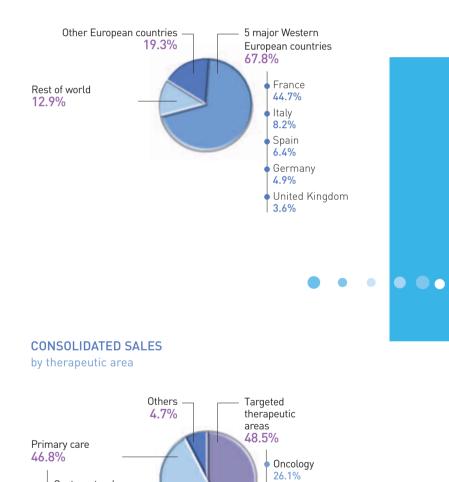
Gastroenterology

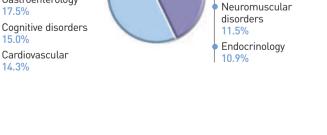
Cardiovascular

17.5%

15.0%

14.3%







Jean-Luc BÉLINGARD Chairman and CEO of the Insen Group

> n December 2005, the Company's shares were listed on the Eurolist by Euronext market. The enthusiastic reception they received from investors illustrates the confidence placed in Ipsen, an international specialty pharmaceutical group focused on innovation.

A strategy of international expansion, especially in the United States

International expansion represents one of our major growth drivers. Ipsen is one of the few pharmaceutical groups set to file four applications for marketing approval in the United States over the next few years. In 2006, we are preparing to make submissions to the FDA concerning Somatuline® Autogel® for the treatment of acromegaly. Two marketing applications are planned in 2007 for our botulinum toxin - one for the treatment of cervical dystonia (Dysport®) and the other for aesthetic medical indications (Reloxin®). Lastly, OBI-1, a recombinant product currently in phase II trials and indicated in the emergency treatment of congenital and acquired haemophilia refractory to human factor VIII, is set to enhance this product portfolio, once its development has been completed. To this end, we are also preparing the ground for our future marketing strategy for these products in the United States. Against this backdrop, the development and distribution agreement signed recently with Medicis, a specialist in dermatology and aesthetic medicine, will provide a very sound platform for Reloxin®.

Once it secures marketing approval, our product will be promoted to dermatologists and plastic surgeons by one of the most effective sales forces in this segment of the US market. Reloxin® will be marketed by our partner to capitalise to the full on synergies with Restylane®, a leading dermal filler. This major alliance, under which Ipsen is expected to receive over US\$190 million in milestone payments, followed by royalties on sales, puts us in a very favourable position to establish ourselves in the US market. We are also working to seal other types of partnerships to market Somatuline® Autogel® in North America.

A specialised group with a robust balance sheet

Our consolidated sales came to €807.1 million during the 2005 financial year, representing an increase of 7.4%, compared with 2004. This growth was driven by the dynamism of our three specialised therapeutic areas (oncology, endocrinology and neuromuscular disorders) and brisk growth in our international sales.

Given the tighter economic regulation of pharmaceutical pricing and reimbursement, a drive to boost efficiency was launched in order to consolidate our earnings performance.

The strong growth in our net profit (Group share) to €148.6 million representing an increase of 26.4% on a comparable structure basis compared with 2004, demonstrates our Company's ability to expand while maintaining a robust financial position.

"Our Group is developing projects with a great future"

The quality of our results and our successful IPO have given us a robust balance sheet, providing us with the financial flexibility we need to meet our development goals in terms of acquisition-led growth and thus to step up the pace of our international expansion. The stock market flotation. which raised the Group's profile to a level commensurate with its future ambitions, was made possible by the support and commitment shown by our longstanding shareholders. In addition, I wish to welcome the new French and international investors who, by joining us for this important next stage in our development, have demonstrated their confidence in our future prospects.

Close to 21% of sales devoted to Research and Development

We have opted to focus the Group's Research and Development efforts on treating hormone-dependent pathologies in both oncology and endocrinology. This decision is predicated on the medical expertise shown by our teams in pathophysiological pathways in these fields, coupled with their expertise in converging technology platforms, notably including peptide and protein engineering. As a result, we have been able to discover and develop compounds suitable for the formulation of sustained-release injectable drugs employing our patented technologies. Thanks to these efforts, we can offer patients innovation, quality of life and efficacy, while providing medical professionals with genuine therapeutic solutions to unmet medical needs.

During 2005, our Research and Development spending rose by 18% to €169 million or 20.9% of sales.

The Group's four research centres, located in Paris, Boston, London and Barcelona, all lie close to centres of academic excellence. The quality of our research is evident from our rich product pipeline, which consists of over 20 programmes. For instance, in endocrinology, we are developing a GLP-1 (Glucagon Like Peptide-1) analogue, which holds promise for the treatment of type II diabetes, under a partnership with Roche. In oncology, we are developing a sustained-release formulation of Decapeptyl[®] as well as a new chemical entity, a sulphatase enzyme inhibitor, the first in its class to be used for the treatment of post-menopausal breast cancer.

The vitality of our research is also sustained by an active policy of partnerships with leading universities and international pharmaceutical groups. For instance, the Group signed major Research and Development agreements during 2005 with Genentech, Pfizer and French public research institutes Inserm and CEA. Ipsen's unique positioning represents a major source of differentiation, which is recognized by the financial markets.

With a balanced product portfolio generating strong growth in our specialised therapeutic areas, eight phase III clinical development programmes, a proven capacity to forge partnerships and the potential to expand sales of its compounds in the United States, Ipsen can look to the future in the highly competitive pharmaceutical industry with confidence.

Accordingly, I wish to express my heartfelt thanks to Ipsen's teams and to everybody who has placed their trust in the Group, enabling it to perform its public health mission by providing both doctors and patients with innovative, effective and well-tolerated drugs. 

Executive committee

Alain HAUT Executive Vice-President, Human Resources Claire GIRAUT Executive Vice-President, Chief Financial Officer Christophe JEAN Executive Vice-President, Chief Operating Officer Peter WILSON Executive Vice-President, Manufacturing and Supply Organisation

Jacques-Pierre MOREAU Executive Vice-President, Chief Scientific Officer Jean-Luc BÉLINGARD Chairman and Chief Executive Officer Alistair STOKES Executive Vice-President, Corporate Development



CORPORATE GOVERNANCE

Ipsen complies with the internal control legislation and its policy abides by principles of good corporate governance.

Board of Directors

Chairman and Chief Executive Officer Jean-Luc BÉLINGARD

Members

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

Committees of the Board of Directors

The Board has created four permanent committees: strategic committee, audit committee, nomination committee and compensation committee.

Strategic committee

Chairman Jean-Luc BÉLINGARD

Members

Anne BEAUFOUR Henri BEAUFOUR Hervé COUFFIN Antoine FLOCHEL Klaus-Peter SCHWABE

Audit committee

Chairman Yves RAMBAUD

Members Alain BÉGUIN Pierre MARTINET

Nomination committee

Chairman Anne BEAUFOUR

Members Alain BÉGUIN Hervé COUFFIN

Compensation committee

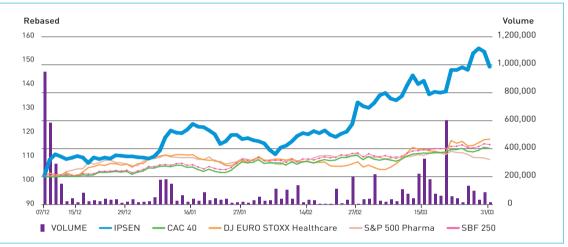
Chairman Antoine FLOCHEL

Members Gérard HAUSER Yves RAMBAUD **IPSEN'S IPO**

Share price evolution

+49% from 6 December 2005 to 31 March 2006 On 24 February 2006, the Ipsen share was added to the SBF 250 and CAC Mid100 indices.

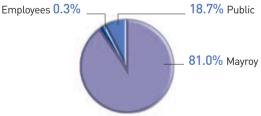
SHARE PRICE EVOLUTION



Source: Bloomberg

FACT SHEETListed on: Segment A of Eurolist by Euronext™ISIN Code: FR0010259150Mnemonic: IPNNominal value: €1First trading: 7 December 2005Number of outstanding sharesas of 31 March 2006: 84,024,683	SHARE PRICE IPO price (6 December 2005): €22.20 Share price as of 31 March 2006: €33.09 Average number of shares traded daily: 84,662
2005 DIVIDEND: €0.60	2005 NET EARNINGS PER SHARE: €2.20
(subject to Ipsen shareholders' meeting approval	(based on the average number of outstanding shares
on 2 June 2006)	during 2005)

SHAREHOLDING STRUCTURE at 31 December 2005



FINANCIAL CALENDAR 2006

1 February:	2005 – full year sales
17 March:	2005 results
2 May:	sales – first quarter 2006
2 June:	general shareholders' meeting and payment of 2005 dividend
1 August:	sales – first half of 2006
6 September:	results – first half of 2006
30 October:	sales – first 9 months of 2006

INVESTOR RELATIONS

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KEY EVENTS

A year full of events, marked by the success of the IPO

MARCH 2006

Ipsen signed an agreement with Medicis, whereby it grants to Medicis, rights to develop, distribute and market Ipsen's botulinum toxin product in the United States, Canada and Japan for aesthetic use by physicians.



Medicis and Ipsen celebrate their agreement and ring the opening bell at the New York Stock Exchange on 22 March 2006.

DECEMBER 2005

Ipsen's IPO on Eurolist by Euronext[™] was a great success with French and international investors. **The offer price is set at 22.20 euros per share.** Trading of Ipsen's shares started on Eurolist by Euronext[™] (Segment A) on 7 December 2005 at 9.00 CET.



NOVEMBER 2005

Ipsen and Pfizer announce the signature of an agreement according to which Pfizer transfers promoting rights for its Artotec[®] product to Ipsen in France as of 1 January 2006. Artotec[®] is a nonsteroidal anti-inflammatory drug which is a diclofenacand misoprostol-based product (protective gastric agent). It achieved sales of over €9 million in France in 2004 (source: Gers Officine 2004) and is indicated for the symptomatic treatment of rheumatic disorders. The agreement has been signed for an initial period of two years.

OCTOBER 2005

Ipsen and Recordati announce the signature of an agreement by which Ipsen grants to Recordati the exclusive marketing and selling rights in France of Tenstaten[®] (cicletanine), a diuretic indicated for the treatment of hypertension developed by Ipsen. The drug is currently marketed in France by Ipsen with sales of over €12 million in 2004.

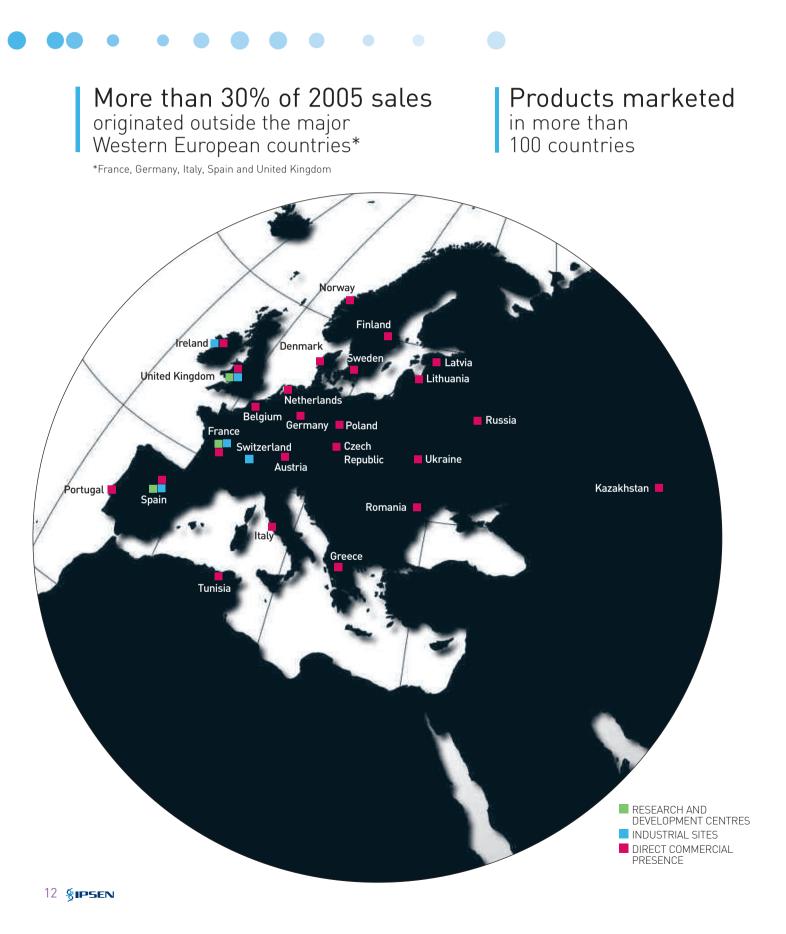
The Ipsen Group announces that its Spanish subsidiary has signed an agreement with Faes Pharma SA. This agreement concerns the transfer of assets belonging to Ipsen's subsidiary relating to the marketing and sales of primary care products – analgesics and generics under the Lasa brand. It does not cover Tanakene® (product marketed as Tanakan® in France), which remains in the Group's product portfolio. These products were previously marketed by Ipsen in Spain only, and represented a turnover of €15.7 million for the financial year ending on 31 December 2004, and €8.2 million for the half-year ending on 30 June 2005.

SEPTEMBER 2005

Ipsen enters into a licensing agreement with Radius, through which Radius acquires the exclusive worldwide rights to develop, manufacture and distribute the molecule BA058 [formerly known as BIM 44058] and its analogues, along with rights to several novel formulation technologies. The license is on a worldwide basis with the exception of Japan, where Ipsen previously granted an exclusive license for BA058 to the Japanese group, Teijin. Developed by Ipsen, BA058 is an analogue of PTHrP and is currently in phase I clinical trials for the treatment of osteoporosis.



A worldwide mission with more than 75 years of operations



An international development strategy focused on the United States



Industrial activi

P production sites in France, United Kinge

FRANCE

Dreux

High-volume oral formulations, 967 million sachets, 746 million tablets, 429 million dry powder capsules, 68.5 million packs for sale, more than 10,000 tonnes distributed. Analytical development and production of medicinal products

for clinical trials. Signes

Sustained-release peptide formulations for injection.

L'Isle-sur-la-Sorgue

API plant, manufacturing more than 2,500 tonnes of therapeutic clay per year, used for gastroenterology products.

Captieux

Plantation and leaf-drying facility (50% share).

Saint-Jean-d'Illac Plantation and leaf-drying facility

(50% share).

UNITED KINGDOM

Wrexham

Preparation of bulk active substances (BAS), purification and formulation of protein-based biological products.

IRELAND

Dublin

API plant, soli synthesis.

Standardised (Ginkgo biloba

CHINA

Tianjin

Local market : The site opera with local part Lu Yuan

Leaf-drying fa operated in co partners.

Zhong Da

Leaf-drying fa conjunction wi

SPAIN

Barcelona

Manufacturing of oral dosage Products man mainly supply (subcontracted WORLDWIDE PRESENCE

ties

dom, Ireland, Spain, Switzerland and China

d phase peptide

olant extract from leaves (50% share).

supply for China. tes as a joint venture mers.

cility set up in 1996, njunction with local

cility operated in th local partners.

and packaging forms. ufactured at this site the Spanish market d activity).

SWITZERLAND

Locarno

Extracts from natural plant sources (including Ginkgo biloba) and related synthetic chemistry for the pharmaceutical and cosmetic industries (50% share).

UNITED STATES

Garnay

Plantation and leaf-drying facility (50% share).

EUROPE

Ipsen is strongly established in five European countries (France, Spain, Italy, Germany and the United Kingdom), which represent its core market, and also in most of the other European countries.

ASIA

The Group directly markets its products in a number of countries in South-East Asia. It manufactures and markets Smecta® in China. In July 2003, Ipsen entered into a partnership agreement with Teijin to develop and market four Ipsen products, including Somatuline® Autogel®, in Japan.

NORTH AMERICA

The Group's presence in the United States is mainly based on its research activities, located near to Boston: a new biotechnology unit has been operational at this site since March 2005. The Group's partnership policy and Research and Development activities should enable, in the future, to expand its presence in this region, which is the leading pharmaceutical market worldwide. Three products are currently under clinical development in the US: two are in phase III (Dysport[®]/Reloxin[®] and Somatuline[®] Autogel[®]) and one in phase II (OBI-1).



A well-balanced and diversified product portfolio, in 3 targeted therapeutic areas and in primary care



Targeted therapeutic areas, key drivers for the future

<u>ONCOLOGY</u>

Decapeptyl®

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

ACTIVE SUBSTANCE

The active substance in Decapeptyl® is triptorelin, a decapeptide analogue of GnRH, a hormone secreted by the hypothalamus, which, in a pulsatile way, initially stimulates the release of pituitary gonadotrophins (hormones produced by the pituitary gland), which in turn control hormonal secretions by the testes and ovaries.

Analogues of GnRH, administered continuously, paradoxically act as castration agents; it is the reason why they are used as therapeutics in diseases induced by sexual hormones.

INDICATIONS

Prostate cancer, uterin fibroids, endometriosis, early-onset puberty and female infertility (*in vitro* fertilisation).

RESEARCH AND DEVELOPMENT

Under the aegis of the International Breast Cancer Study Group, Ipsen is participating in a study of the treatment of pre-menopausal breast cancer comparing the standard treatment regimen with a hormone therapy combining Decapeptyl[®] with oestrogen-suppressing agents, such as Aromasin[®], which is marketed by Pfizer. Hormone therapy for cancer offers a better tolerated option than traditional chemotherapy and is particularly suitable for long-term treatment.

Moreover, the Group is developing sustained-release formulations for a minimal period of four months.





Marketing

Decapeptyl[®] was initially launched in France during 1986. At 31 December 2005, Decapeptyl[®] had marketing authorisations in over 60 countries, including 25 in Europe. Decapeptyl[®] was launched in Great Britain in 2003 (quarterly formulation) and in Germany during 2004 (under the Pamorelin[®] brand). In 2005, 67.1% of Decapeptyl[®] sales derived from the major Western European countries.

<u>ENDOCRINOLOGY</u>



Somatuline[®]

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

Somatuline[®] Autogel[®] releases the active substance with no excipient other than water over a period of at least twenty-eight days, thus requiring just one injection per month compared with the two or three injections previously necessary. This product is presented in a pre-filled syringe for easier administration.

ACTIVE SUBSTANCE

The active substance in Somatuline[®] and Somatuline[®] Autogel[®] is lanreotide, which inhibits the growth and secretion of several endocrine, exocrine and paracrine hormones. It is particularly effective in inhibiting the secretion of growth and certain digestive hormones.

INDICATIONS

Acromegaly and neuroendocrine tumours

RESEARCH AND DEVELOPMENT

An application for marketing authorisation in the United States has been submitted for Somatuline® in the treatment of acromegaly. In response, the Food and Drug Administration (FDA) has issued an approvable letter, subject to the completion of additional studies, including an analysis of its carcinogenic risks. Ipsen is currently finalising its work as part of the preparation of submission for Somatuline® Autogel®, in respect of which an application for marketing authorisation is likely to be made in the United States during 2006 for the treatment of acromegaly.

Furthermore, phase III and IV clinical trials with Somatuline® Autogel® have been planned for the treatment of neuroendocrine tumours in the United States and in Europe.

The Group is also pursuing the development of sustained-release formulations for treatment durations of approximately three months.

In Japan, the Group's partner (Teijin) is on the verge of completing phase I clinical trials of Somatuline® Autogel® in the symptomatic treatment of acromegaly.



Marketing

Somatuline L.P. 120 mg

Somatuline[®] was initially launched in France in 1995. At 31 December 2005, Somatuline[®] and Somatuline[®] Autogel[®] had marketing authorisations in over 50 countries (including 26 in Europe) for the treatment of acromegaly and neuroendocrine tumours and in six countries (including two in Europe) for the treatment of acromegaly alone.

In 2005, 69.7% of the sales generated by Somatuline® and Somatuline® Autogel® derived from the major Western European countries. Somatuline® Autogel® accounted for 81.4% of total sales of this product.

ENDOCRINOLOGY

NutropinAq®

The growth hormone is involved in several physiological processes including growth in stature and bone development.



Marketing

In September 2002, Genentech granted Ipsen exclusive marketing rights for NutropinAq® worldwide, outside North America, Mexico and Japan. Genentech has pioneered the development of growth hormone and is currently one of the leading players in the United States market.

At 31 December 2005, the Group had marketing authorisations for 29 countries (including 27 in Europe). The product was launched in over 20 countries across Europe during 2004 and 2005, and there are plans to introduce it in a further four countries during 2006.

ACTIVE SUBSTANCE

NutropinAq[®] is a liquid formulation of recombinant human growth hormone to be used with the NutropinAq[®] Pen.

INDICATIONS

NutropinAq[®] is prescribed for : - the long-term treatment of children with growth failure owing to inadequate endogenous growth hormone secretion; - the long-term treatment of growth failure associated with Turner's syndrome; - the treatment of prepubertal children with growth failure associated with chronic renal insufficiency ahead of kidney transplantation;

- the treatment of adults with growth hormone deficiency of either childhood or adult-onset.

RESEARCH AND DEVELOPMENT

NutropinAq Pen

Within the framework of its agreement with Genentech signed in September 2002, Ipsen received from Genentech a copy of the registration dossier compiled by Genentech and filed with the FDA in January 2004 with a view to extending the indication for the treatment of idiopathic short stature. The Group is currently evaluating the dossier and is considering filing in 2006 its own application for an extension of this indication with the European medicines agency (EMEA).

Ipsen is also pursuing a phase II study of NutropinAq[®] in children in the prevention of growth failure caused by long-term treatment with high-dose glucocorticoids, in conjunction with the University of Gothenburg (Sweden).

The Group is also pursuing Research and Development projects, within the framework of the agreement signed with Genentech in November 2004, aiming to develop a sustained-release formulation for recombinant growth hormone.

ENDOCRINOLOGY

Testim[®]

Testim® 50 mg Gel is a testosterone gel prescribed as a hormone replacement therapy for patients with primary or secondary hypogonadism. It is commonly recognised that around 20% of men over 60 years old have insufficient testosterone levels: Testim® 50 mg Gel can be used to treat these insufficiencies.



Marketing

Testosterone gels have revolutionised the treatment of testosterone deficiency since they were introduced in the United States in 2000 and in Europe in 2003, gradually replacing the other formulations (oral, injection or patch forms) and thus significantly contributing to market expansion.

In March 2004, the Group acquired exclusive marketing rights to Testim[®] 50 mg Gel worldwide, excluding North America, Mexico and Japan, from US firm Auxilium. Auxilium itself holds the rights to the product from US firm Bentley Pharmaceuticals. Testim[®] 50 mg Gel obtained marketing authorisation from the Food and Drug Administration (FDA) in the United States in March 2003, and marketing authorisation for the United Kingdom in June 2003. Testim[®] 50 mg Gel was launched in the United States market by Auxilium, and is available to urologists, andrologists and endocrinologists. At 31 December 2005, Testim[®] 50 mg Gel was approved in 15 European countries under the mutual recognition procedure. Testim[®] 50 mg Gel was launched in 10 European countries during 2005.



ACTIVE SUBSTANCE

Testim[®] 50 mg Gel is a clear to translucent hydroalcoholic gel containing 1% testosterone (i.e. 50 mg per 5 g tube).

INDICATIONS

Testim[®] 50 mg Gel is indicated as a hormone replacement therapy to restore serum testosterone levels in adult males and improve health problems related to reduced testosterone levels resulting from primary or secondary hypogonadism.

NEUROMUSCULAR DISORDERS

Dysport[®]

Dysport[®], which acts to block acetylcholine release, reduces muscular spasm. It was initially developed for the treatment of motor disorders and various forms of muscular spasticity, including cervical dystonia (a chronic condition in which the neck is twisted or deviated), spasticity of the lower limbs (heel) in children with cerebral palsy, blepharospasm (involuntary eye closure) and hemifacial spasm. It was later developed for the treatment of a wide variety of neuromuscular disorders, as well as in aesthetic indications.





Marketing

Dysport® was originally launched in the United Kingdom in 1991. At 31 December 2005, Dysport® had marketing authorisations in over 70 countries (including 28 in Europe). 17 marketing authorisations had been obtained in aesthetic medicine indications. In 2005, 50.7% of Dysport®'s sales derived from the major Western European countries.

ACTIVE SUBSTANCE

The active substance in Dysport[®] is a botulinum neurotoxin type A complex, which acts at the level of the neuromuscular junction in the targeted muscle.

INDICATIONS

Cervical dystonia, cerebral palsy in children, blepharospasm/hemifacial spasm, hyperhidrosis and glabellar lines.

RESEARCH AND DEVELOPMENT

In August 2005, Ipsen initiated phase III clinical trials of Dysport[®] in the United States in the treatment of cervical dystonia.

Dysport[®] is currently undergoing phase II clinical trials in the treatment of myofascial pain.

Dysport[®] is currently undergoing phase III clinical trials in the United States for aesthetic medicine indications (frown

lines). Provided the outcome of these trials is positive, the Group plans to file regulatory submissions with the FDA during 2007 under a brand name other than Dysport[®], which may be Reloxin[®].

In March 2006, Ipsen entered into a development and distribution agreement with Medicis, whereby Ipsen grants Medicis rights to develop, distribute and commercialize Ipsen's botulinum toxin product in the United States, Canada and Japan for aesthetic use, under a brand name other than Dysport[®], which may be Reloxin[®].

In Europe, the Group has conducted phase III clinical trials of Dysport® and is overseeing the registration procedures for aesthetic medicine indications (frown lines) currently underway in France and Germany. Registration of Dysport® under the mutual recognition procedure is planned for 2006.

PORTFOLIO - PRIMARY CARE

Primary care a longstanding expertise



GASTROENTEROLOGY

Smecta®

Smecta[®] is an oral formulation devised by the Group. It is used in the treatment of both chronic and acute diarrhoea in adults and children and in the symptomatic treatment of pain associated with oesophageal, gastric, duodenal or colonic disorders.

ACTIVE SUBSTANCE

Smecta®'s active substance is diosmectite, a natural clay processed for therapeutic use.

Marketing

The Group launched Smecta® in France in 1977. At 31 December 2005, it held marketing authorisations for Smecta® in over 70 countries. In 2005, 33.6% and 31.7% of Smecta®'s sales derived respectively from France and China, the main markets for the product.







Forlax®

Forlax[®] is an oral laxative created by the Group. It is used in the treatment of constipation.

ACTIVE SUBSTANCE

Forlax®'s active substance is Macrogol 4000, a linear polyethylene glycol polymer.

Marketing

The Group launched Forlax[®] in France in 1996 and has since obtained marketing authorisations in more than 60 countries. In 2005, 84.2% of Forlax[®]'s sales derived from the major Western European countries.

COGNITIVE DISORDERS

Tanakan®

Tanakan[®] is an oral formulation of EGb 761[®], extracted from the leaves of the Gingko biloba tree (dioecious tree in the Ginkgoaceae family) using a standardised process that ensures a consistent composition of the various pharmacologically active substances. It was initially developed in the treatment of various vascular and neurological disorders, mainly the treatment of age-related cognitive impairment, pathophysiological deficiencies, vertigo, tinnitus, acute or chronic hearing difficulties and retinal disorders (visual impairment).



ACTIVE SUBSTANCE

The active substance in Tanakan®, EGb 761®, is extracted from Ginkgo biloba leaves cultivated under controlled conditions in specially designed plantations. It contains natural substances with antioxidant, neuroprotective and vasoactive properties (i.e. it increases the diameter of capillary vessels and hence improves microcirculation).

INDICATIONS

Age-related cognitive disorders, pathophysiological deficiency, cochleovestibular disorders, retinal deficit.

RESEARCH AND DEVELOPMENT

The Group is currently investigating EGb 761[®], the Ginkgo biloba extract in Tanakan[®], in the treatment of neurodegenerative disorders, such as the symptomatic treatment of Alzheimer's disease. Over 8,000 patients are taking part in these research programmes, and eight clinical trials are currently in progress, some being conducted in the United States by the National Institutes of Health and others in Europe by Ipsen (notably GuidAge study).

Marketing

Tanakan® was initially launched in France in 1975. At 31 December 2005. Tanakan® had been approved for use in over 60 countries, mainly in Europe and Asia. Since 2004, it has been indicated and reimbursed in Belgium in the symptomatic treatment of mild to moderate forms of Alzheimer'stype dementia associated with memory disorders and cognitive disorders. In 2005, 77.7% of Tanakan®'s sales derived from the major Western European countries.



CARDIOVASCULAR

Ginkor Fort®

Ginkor Fort[®] is used in the treatment of vascular conditions, of venous insufficiency of the lower limbs and of acute haemorrhoid episodes.

ACTIVE SUBSTANCE

Ginkor Fort[®] is an oral formulation containing three active substances, namely troxerutin A (a vasoactive rutin analogue, a flavonoid of plant origin), heptaminol chlorhydrate and a standardised Ginkgo biloba extract.

Marketing

This product was initially launched as Ginkor[®] in France in 1972 and subsequently changed its name to Ginkor Fort[®] in France during 1989. Ipsen sells Ginkor Fort[®] chiefly in France from where it derived 94% of the product's sales during 2005. The French government issued a ministerial order on 25 January 2006 in the *Journal officiel*, whereby the reimbursement rate of the veinotonics, class to which Ginkor Fort[®] belongs, will be curbed to 15% from 1 February 2006 to 31 December 2007. It will be withdrawn from the list of reimbursed medicines, as from 1 January 2008.



Nisis[®] and Nisisco[®]

In 2003, the Group added Nisis[®] and Nisisco[®], two antihypertensive products, to its portfolio by signing an agreement with Swiss group Novartis, to market the products in France, Andorra and Monaco.

Marketing

Nisis[®] and Nisisco[®] were initially launched in France by Sanofi-Aventis. Following the contracts entered with Novartis and Sanofi-Aventis in March 2003, Ipsen holds marketing authorisations and has marketed Nisis[®] and Nisisco[®] in France since May 2003. In 2005, these two products generated sales of €41.5 million.

ACTIVE SUBSTANCE

Nisis[®] is an oral formulation containing valsartan, while Nisisco[®] contains valsartan and hydrochlorothiazide. The products are used in the treatment of arterial hypertension. The active substance in Nisis[®] and Nisisco[®] is valsartan, a synthetic angiotensin II antagonist compound.





Nearly €**170**M of R&D expenditure in 2005

From the discovery of new molecules to life cycle management of marketed products





The Group's R&D activities are focused on the discovery and development of new molecules as well as on programmes relating to life cycle management for products already marketed by the Group (development of new formulations or extensions of indications and product registrations in new geographical areas). The Group's significant **Research and Development** effort is complemented by an active partnership policy.

The Group's R&D programmes are based on four integrated technological platforms: peptide engineering, protein engineering, medicinal chemistry and advanced drug delivery systems. This array of technologies is

necessary to meet the Group's objectives:

- fulfilling unmet medical needs,
- optimising the efficacy of active substances,
- providing patients with better quality of life,
- improving administration of these products by healthcare personnel.

integrated technological platforms

Peptide engineering



BOSTON (United States)

focuses on the modification, by synthesis, of naturally occurring neuropeptide hormones. This research is being conducted by the Boston R&D facility (United States).

Protein engineering

aims to improve the therapeutic properties of naturally-occurring proteins through the selective modification of their sequences. This research is being conducted by the Boston R&D facility (United States).



Medicinal chemistry

aims to discover enzyme inhibitors, mitochondrial protective agents, together with non-peptide ligands (molecules that bind preferentially to one or more receptors) for specific hormone receptors. Research in the field of medicinal chemistry is being conducted by the Paris R&D facility (France).



BARCELONA (Spain)

Advanced drug delivery

aims to create and develop sustained-release formulations for new or existing products, using proprietary technologies. It aims to optimise the efficacy of the active substances while improving patient quality of life and facilitating the use of the products by healthcare professionals. This Research is being conducted by the Barcelona R&D facility (Spain).

PARIS, BOSTON, LONDON, BARCELONA

An international network of Research and Development centres

Ipsen has established an international network of Research and Development centres, each located in areas that allow access to major expertise in academic research and to employees skilled in technology and development processes.

PARIS France

The Paris R&D centre, specialising in medicinal chemistry, was opened in 1969. New facilities were built in 1996. A research team (chemists, biologists and pharmacologists) essentially works on discovering new chemical entities, with having access to high-throughput screening and combinatorial chemistry. The key areas of research are molecular and cellular oncology, together with neuromuscular disorders.

The Group also has a clinical development team in Paris that coordinates clinical trials around the world.

Analytical development and production of medicinal products for clinical trials are carried out at the Group site located in Dreux (France).

BOSTON United States

The Boston R&D centre is specialised in protein and peptide research.

The research scientists mainly work on metabolism disorders, endocrine diseases, as well as in hormone-dependent cancers. The Boston centre benefits from an extensive knowledge in hormonedependent mechanisms in which neuropeptides are involved. Ipsen also has a clinical research and development team, dedicated to the coordination of clinical research in North America and regulatory activities involving the US Food and Drug Administration (FDA). In March 2005, Ipsen inaugurated a biotechnology unit which has extended the activities of the Boston centre. The new site houses a team specialising in the development processes specific to genetic engineering, industrial development, analysis and formulation of proteins, production, quality assurance together with quality control. One of the main activities of the site is to modify the structure of endogenous proteins and peptides in order to improve their properties. Replacing certain sequences within a protein may reduce antigenicity (recognition by existing antibodies), toxicity or immunogenicity (development of new antibodies) and increase the duration of action, specificity or compatibility with controlledrelease formulations.

LONDON United Kingdom

Located near London, the corporate clinical development and regulatory affairs departments develop marketing authorisation strategies and implement preclinical and clinical development programmes in line with these strategies.

They coordinate international multicentric clinical trials, collect data, analyse results and file dossiers and registration applications with international regulatory authorities in order to ensure that lpsen obtains the necessary approvals to market its products in the shortest possible time.





The main objective of the clinical development teams is to execute or commission execution of clinical trials complying strictly with the regulatory standards and able to provide high-quality and extensive data about the efficacy and safety of using the Group's products. Successful registration requires the consolidation, on a Group level, of all regulatory data necessary for a dossier.

BARCELONA SPAIN

The Barcelona R&D centre is a research unit specialised in the discovery, design and development of advanced drug delivery systems.

Its main objective is to create innovative formulations, mainly sustained-release formulations using Ipsen's proprietary technologies. Its teams were, for instance, behind the development of the Somatuline[®] Autogel[®] formulation, which releases the active substance, without any excipients other than water, over a period of at least twenty-eight days. Somatuline[®] Autogel[®] is now the Group's 5th leading product, with net sales of €66.6 million in 2005. This research plays a critical role in Ipsen's core strategy: improve the quality of life of patients by providing them with convenient therapeutic regimens and delivery systems that minimise discomfort. The Barcelona centre employs researchers, together with scientists and technicians specialising in drug delivery systems, and is supported by a pharmacokinetics department integrated with the worldwide clinical development group.



Research and Development excellence

ONCOLOGY

RESEARCH PROGRAMMES

Ipsen's technology programmes in peptide and protein engineering and medicinal chemistry enable it to explore and develop new approaches in cancer treatment under hormonal control, such as:

- key enzyme inhibitors in the biosynthesis of steroids;
- growth factors, notably including prolactins, Growth Hormone Releasing Hormone, Mullerian Inhibiting Substance;
- enzymes regulating cell cycles (notably phosphatases).

These research programmes are conducted internally with assistance from university and industry specialists.

The February 2004 acquisition of Sterix has opened up new opportunities for the Group in the development of medicinal products derived from steroids. Steroid hormones play an essential role in the processes controlling vital functions. Having signed a partnership agreement with the Group, the team from the University of Bath in the United Kingdom discovered a chemical modification which, when applied to steroids and their derivatives, enables the selective inhibition of enzymes that convert precursor steroids into their biologically active form.

The agreement signed with Spirogen in May 2003 has provided the Group with access to a technological platform with the potential to identify the genes involved in serious diseases such as cancer. The Group has exclusive access to this technology for several genes involved in cancers refractory to conventional therapies.

DEVELOPMENT PROGRAMMES

DECAPEPTYL®

Ipsen is developing sustained-release formulations of Decapeptyl[®] for treatment durations longer than three months. A formulation for a minimum treatment duration of four months is currently close to completing its phase II clinical trials.

The Group is also participating in three phase III studies conducted under the auspices of the International Breast Cancer Study Group in the

treatment of breast cancer in premenopausal women, comparing the conventional treatment methods with hormone therapy combining Decapeptyl[®] with oestrogen suppressant agents, such as Aromasin[®], marketed by Pfizer. These trials are due to take place until 2015. Hormone therapy for cancer offers a better tolerated option than traditional chemotherapy and is particularly suitable for long-term treatment.

At last, the Group is conducting several pre-clinical programmes with a view to overcoming iatrogenic effects (hot flushes, bone loss) resulting from chronic use of LHRH agonists, such as Decapeptyl[®] in combination with other products (notably oestrogens and biphosphonates).

BN 83495 (STX 64)

BN 83495 and similar molecules acquired through the acquisition of Sterix, are selective inhibitors of the sulphatase enzyme involved in a key stage of the biosynthesis of oestrogens, one of the principal factors contributing to breast cancer in postmenopausal women. A phase I clinical trial in patients with breast cancer has been completed and the results demonstrate the inhibition of the sulphatase enzyme at the dosages tested in tumour biopsies. The Group is currently developing an oral formulation of this compound. Subject to positive results and the requisite pre-clinical research, the Group will be in a position to initiate phase II trials.

BIM 46187

BIM 46187 is an innovative anti-tumour compound that acts on cellular signals by the receptors attached to Protein G (the most common form of receptors for neuropeptide hormones and neurotransmitters). Preclinical development of this molecule is underway. Phase I trials of this compound in cancer patients are due to start in 2007. BIM 46187 may be used either alone or in combination with other cancer therapies in the treatment of solid tumours, such as lung and prostate cancer.

BN 2629 (SJG-136)

BN 2629, a product originating from Spirogen, is a synthetic molecule that has demonstrated during preclinical studies its ability to block the anarchic cellular proliferation process characteristic of



cancers. This product is being studied in three phase I studies of different administration regimens in patients with metastatic tumours resistant to certain types of chemotherapy conducted by two renowned institutions, namely Cancer Research in the United Kingdom and the National Cancer Institute in the United States. The Group is pursuing *ex vivo* research using this molecule in leukaemia resistant to other treatments.



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

Diflomotecan

Diflomotecan is a cytotoxic agent (cell killer) that inhibits the topoisomerase 1 enzyme. Two phase II clinical trials in lung cancer have been completed, but failed to achieve their safety and efficacy targets in this indication for the dosages tested. During phase I clinical trials, Diflomotecan showed high oral bioavailability, low gastrointestinal toxicity and no cumulative haemotoxicity. Investigations into other indications are due to be carried out.

Elomotecan

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

ENDOCRINOLOGY

RESEARCH PROGRAMMES

In pituitary disorders, Ipsen is involved in several research programmes, chiefly in pituitary adenomas, such as acromegaly.

The Group is also continuing its efforts to identify second-generation somatostatin analogues and growth hormone antagonists. Acromegaly used to be treated by surgical removal of the benign tumour followed by radiotherapy; then, if the tumour did not respond sufficiently, a somatostatin analogue was administered. However, because of the heterogeneity of certain types of these tumours, new therapies are needed. Ipsen is currently investigating molecules with a broader spectrum of activity and hopes that they will not only provide a symptomatic treatment for acromegaly, but also offer the possibility of reducing tumour size, thereby eliminating many of the limitations associated with existing treatments (dopastatin). Ipsen is also exploring the role of certain peptide

hormones (Ghrelin, MSH/MC4) in regulating food intake with the priority objective of treating cachexia (lack of appetite), which is often the cause of functional disorders in the elderly, cancer patients and patients with chronic illnesses. The Group is continuing to pursue the programmes it initiated in 11-ß-HSD enzyme inhibitors with a view to developing a therapy for the related metabolic syndromes associated in obese patients with hyperinsulinemia, which principally manifests itself in the form of greater cardiovascular risks.

In conjunction with Asterion, the Group is also continuing to develop analogues of growth hormone antagonists.

DEVELOPMENT PROGRAMMES

SOMATULINE® AUTOGEL®

The phase III clinical trials in the United States with Somatuline[®] Autogel[®] for the symptomatic treatment of acromegaly have ended. Compilation of the registration dossier is being finalised and it is due to be filed with the FDA during 2006.

Additional phase III and IV clinical trials are planned in the treatment of neuroendocrine tumours in the United States and in Europe.

Ipsen is also pursuing the development of sustainedrelease formulations for treatment durations of approximately three months. Development of this formulation is currently at the pre-clinical stage.

In Japan, the Group's partner (Teijin) has completed clinical phase I trials for the symptomatic treatment of acromegaly. Approval of the development plans by the regulatory authorities is due to take place in 2006, with phase II clinical trials scheduled to follow after validation.

The Group envisages securing additional marketing authorisations for Somatuline® Autogel® shortly, in Turkey, Poland and Russia for the treatment of acromegaly and neuroendocrine tumours, and in France, Germany and Switzerland for the treatment of neuroendocrine tumours.

NUTROPINAq®

Within the framework of its agreement with Genentech signed in September 2002, Ipsen received from Genentech a copy of the registration dossier it compiled and filed with the FDA in January 2004 with a view to extending the indication for the treatment of idiopathic short stature. The Group is currently evaluating the dossier, which is likely to be filed in 2006 with a view to securing an extension of this indication with the European medicines agency (EMEA).

Ipsen is also carrying out a phase II study of NutropinAq[®] in the prevention of growth failure caused by long-term treatment with high-dose glucocorticoids in children, in conjunction with the University of Gothenburg (Sweden).

The Group is pursuing Research and Development projects under the agreement signed with Genentech in November 2004 that aim to develop a sustained-release formulation for recombinant growth hormone.

BIM 51077

BIM 51077 is an analogue of peptide hormone GLP-1 (Glucagon Like Peptide-1), which is covered by an option for a development and distribution licence with Roche. BIM 51077 controls insulin secretion in response to elevated blood glucose levels. This compound is currently in phase II clinical trials for glycaemia control in diabetic patients. The Group is aiming to develop the molecule in sustainedrelease formulations. Thanks to its advanced drug delivery platform, the Group has already identified several sustained-release formulations, which are currently undergoing phase I trials.

In Japan, the Group's Japanese partner (Teijin) has completed phase I trials of BIM 51077 and is preparing to hold further phase I trials with sustainedrelease formulations.

NEUROMUSCULAR DISORDERS

RESEARCH PROGRAMMES

The Group's research programmes in neuromuscular disorders mainly focus on the identification of new botulinum toxin formulations.

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

DEVELOPMENT PROGRAMMES

DYSPORT®

In August 2005, the Group initiated phase III clinical trials of Dysport[®] in the United States in the treatment of cervical dystonia. Subject to positive results, the Group envisages filing a registration dossier with the FDA in 2007.

Dysport[®] is currently undergoing phase II clinical trials in the treatment of myofascial pain.

Ipsen's botulinum toxin product (Reloxin®) is currently undergoing phase III clinical trials in the United States for aesthetic medicine indications (frown lines). The Group plans to file regulatory submissions with the FDA during 2007 under a brand name other than Dysport®, which may be Reloxin®.

In Europe, the Group has conducted phase III clinical trials of Dysport[®] and the registration procedures for aesthetic medicine indications (frown lines) are currently underway in France and Germany under the Group's responsibility. Registration in Europe under the mutual recognition procedure is scheduled to take place in 2006. This product may be marketed in Europe once it has been registered under a brand name other than Dysport[®], which may be Reloxin[®].

OTHER PROGRAMMES

COGNITIVE DISORDERS

The Group is endeavouring to validate the clinical benefits of Tanakan[®] in the treatment of agerelated cognitive impairment and behavioural disorders. The Group is thus involved in the assessment of EGb 761[®], the extract of Ginkgo biloba present in Tanakan[®], for the treatment of neurodegenerative disorders such as Alzheimer's disease. More than 8,000 patients are enrolled in these research programmes, and eight clinical studies are currently underway:

The National Institutes of Health (United States) are currently sponsoring four clinical trials:

- a study on the prevention of mild cognitive impairment (MCI) in patients aged over 85;
- a study ("GEM") on the primary prevention of Alzheimer's disease in "healthy" patients aged over 75. The 3,000 patients for this study have now been recruited, and they will be treated at least until 2008;
- two pilot studies on the cognitive disorders caused by cancer treatments (chemotherapy or radiation therapy).

The Group is the sponsor of four other studies in Europe, including:

- the GuidAge study assessing the effectiveness of EGb 761[®] in the prevention of Alzheimer's disease in patients of more than 70 years of age presenting with a spontaneous memory complaint; the 2,800 patients were recruited by September 2004 and their treatment will continue for five years. The results of this study are likely to be available in 2010;
- a study evaluating the efficacy of EGb 761[®] in cognitive disorders in patients with Alzheimer's disease and related behavioural and psychological disorders (Behavioural and Psychological Symptoms in Dementia);
- two pilot studies aiming to study the efficacy of EGb 761[®] in cognitive impairment related to various disorders, such as multiple sclerosis and the consequences following a stroke.

HAEMATOLOGY

Ipsen also boasts longstanding expertise in haemostasis (blood coagulation). The Group's research has enabled it to establish partnerships with Emory University and Octagen, in order to





develop a recombinant version of porcine factor VIII using its protein engineering platform. This product (OBI-1) is intended for the treatment of congenital and acquired haemophilia resistant to human factor VIII. OBI-1 has secured FDA approval for the initiation of phase II clinical trials in the United States. OBI-1 is produced at the new biotechnology unit in Boston inaugurated in March 2005.

RHEUMATOLOGY

Within the framework of the partnership established in July 2003 with Japanese group Teijin in endocrinology, Ipsen signed a specific agreement to develop in Europe febuxostat, a drug intended for the treatment of symptomatic hyperuricaemia, currently in the process of being registered by TAP Pharmaceuticals (joint venture Abbott and Takeda) in the United States. The FDA issued an approvable letter in October 2005. With a view towards possibly launching the compound in Europe, the Group is assessing the submissions filed by TAP Pharmaceuticals with the FDA in February 2006 in response to this approvable letter, to decide on the suitability of its submission in Europe. Ipsen is expected to reach a decision during 2006.



A Research and Development portfolio with more than 20 programmes, including 7 new chemical entities

DEVELOPMENT PIPELINE	INDICATIONS		ST	AGE	
		PRE-CLINICAL	PHASE I	PHASE II	PHASE III
Decapeptyl®	Combined hormone therapy for premenopausal breast cancer				
Decapeptyl®	Combination therapy to address the side effects of GnRH analogues	•			
Decapeptyl®	Prostate cancer (new formulation: 4 months)			•	
BN 83495 (STX 64)	Post-menopausal breast cancer expressing oestrogen receptors		•		
BIM 46187	Cytostatic drug, solid tumours				
BN 2629 (SJG-136)	Advanced metastatic cancer refractory to chemotherapy		•		
Diflomotecan	Advanced metastatic cancer: colon, breast and prostate			•	
Elomotecan	Metastatic tumours		•		
Somatuline [®] Autogel [®]	Acromegaly				
Somatuline [®] Autogel [®]	Neuroendocrine tumours				•
Somatuline [®] Autogel [®]	Acromegaly (new formulation: 3 months)	•			
BIM 51077	Type II diabetes			•	
NutropinAq®	Idiopathic short stature				•
NutropinAq®	Prevention of the long-term effects of glucocorticoid treatment			•	
Human sustained-release growth hormone	Long-term treatment of growth failure in children or adults	•			
Dysport [®]	Cervical dystonia				
Dysport®/Reloxin®	Aesthetic medicine				•
Dysport®	Myofascial pain			•	
Tanakan®	Mild cognitive impairment related to age				•
OBI-1	Haemophilia				
Febuxostat (TMX-67)	Symptoms related to hyperuricemia				•

As of 31 March 2006.





Auxilium Bayer Health Protection Agency (HPA) Debiopharm Expansia Genentech Imperial College London Asterion

An active policy of alliances and partnerships at the core of lpsen's strategy

Indena Novartis Octagen and Emory University Pfizer	Cancer Research UK National Cancer Institute Spirogen	Roche Bath University Cambridge University Teijin	CEA Medicis Schwabe Thomas Jefferson University	CNRS Inserm Tulane University Radius Recordati
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ONCOLOGY

INSERM Paris, France

In October 2005, Ipsen signed a partnership agreement with Inserm (French national health and medical research institute) to conduct a R&D programme in the treatment of breast and prostate cancer.

SPIROGEN London, United Kingdom

In May 2003, Ipsen signed a partnership agreement with Spirogen, a UK biotechnology company. This partnership comprises, on the one hand, an agreement covering the development and marketing by the Group of a patented anti-cancer drug, namely SJG-136 (BN 2629) and, on the other hand, a research agreement for other anti-cancer compounds through implementation of a gene targeting technology patented by Spirogen.

ENDOCRINOLOGY

AUXILIUM Philadelphia, United States

In March 2004, the Group entered into a licensing agreement with Auxilium to distribute Testim[®] 50 mg Gel worldwide, except for the United States, Mexico, Canada and Japan. This product was developed by Auxilium using patents belonging to Bentley Pharmaceuticals.

GENENTECH San Francisco, United States

The exclusive distribution agreement entered into in September 2002 by the Group with Genentech covers NutropinAq®, a liquid formulation of human growth hormone produced using recombinant DNA technology. Under this agreement, the Group has the exclusive right to market worldwide (with the exception of North America, Mexico and Japan) NutropinAq® and the NutropinAq® Pen Cartridge (i.e. the configuration used for the daily administration of the liquid formulation of NutropinAq®) and any improvement made to these products. Ipsen signed with Genentech a R&D agreement in November 2004 covering the development of sustained-release formulations of recombinant growth hormones using the technology platforms of Genentech, Ipsen and third parties.

ROCHE Basel, Switzerland

In October 2003, Ipsen signed an agreement under which it granted Roche an option on an exclusive licence to the rights to develop and market worldwide (with the exception of Japan and France) a class of anti-diabetic GLP-1 drugs discovered by the Group's research activities and notably including the BIM 51077 compound.

TEIJIN Tokyo, Japan

In July 2003, Ipsen entered into a R&D partnership with Teijin. This partnership covers, on the one hand, the development of four of Ipsen's products, including Somatuline® Autogel® and BIM 51077; and, on the other hand, the marketing of the products from the development programme, notably febuxostat.

NEUROMUSCULAR DISORDERS

MEDICIS Scottsdale, United States

In March 2006, the Group entered into a development and distribution agreement with Medicis, covering certain botulinum toxin formulations for aesthetic medicine in the United States, Canada and Japan under a brand name other than Dysport[®], which may be Reloxin[®].

PARTNERSHIPS



OTHER DOMAINS

CEA Paris, France

In October 2005, Ipsen signed a letter of intent with the French atomic energy commission, CEA, to carry out research programmes related to the treatment of Parkinson's and Alzheimer's diseases.

NOVARTIS Basel, Switzerland

In March 2003, Ipsen signed a series of agreements with Novartis, including a trademark transfer agreement and a distribution agreement in France for two antihypertensive agents, Nisis[®] and Nisisco[®], which were previously marketed and distributed by Sanofi-Aventis. The Marketing Authorisations were transferred to Ipsen at that date.

PFIZER New York, United States

In November 2005, the Pfizer group entrusted Ipsen with promoting its Artotec[®] product in France from 1 January 2006. Artotec[®] is a non-steroidal anti-inflammatory drug based on diclofenac (NSAI) and misoprostol (gastric protective agent).

RADIUS Cambridge, United States

In September 2005, Ipsen signed a licensing agreement with Radius under the terms of which the Group granted Radius the exclusive right to develop, manufacture and distribute a compound belonging to the Group known as BIM 44058 (as well as its analogues) using the sustained-release formulation technology developed by the Group for the development of a drug in the treatment of osteoporosis.

RECORDATI Milan, Italy

In October 2005, Ipsen sold the exclusive rights to market and sell Tenstaten[®] in France to Recordati for an initial period of seven years beginning 1 January 2006. The Group, which developed and marketed the product in France until that date, posted sales of Tenstaten[®] of €12.6 million in 2004 and €11.4 million in 2005.







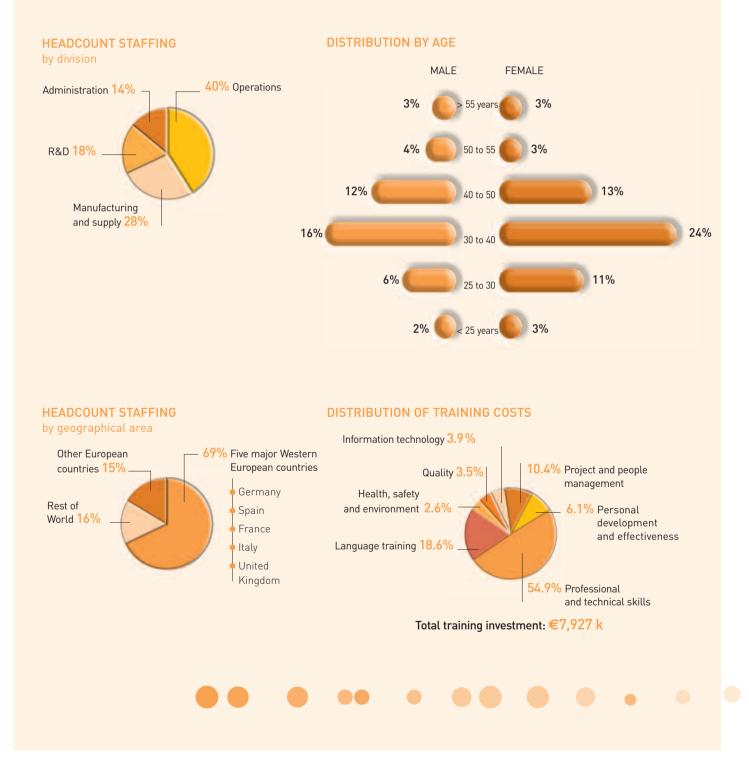
HUMAN RESOURCES SUSTAINABLE DEVELOPMENT LA FONDATION IPSEN

A strategy respectful of working conditions, environment and dissemination of knowledge

Nearly **4,000** employees
More than
700 recruitments
in 2005
Almost **€8**M
devoted to
training in 2005
4 prizes
to encourage
research



NEARLY 4,000 EMPLOYEES WORLDWIDE IN 2005



Create environment and working conditions

favourable to motivation, development and skill valuation

Ipsen has structured its human resources strategy around four lines of expertise: training and development, compensation and benefits, recruitment and selection, social relations. According to a functional and matricial structure, which makes it possible to support the whole of activities of the Group in all the countries where it is established, the teams of human resources support the employees within the framework of this policy and the respect of the principles of equity and merit.

TRAINING AND DEVELOPMENT

Ipsen consistently aims to provide its employees with high-quality training tailored to the specific features of each profession. At corporate level, training programmes are organised to promote the development of managerial expertise and the cohesion of the Group, and, at local level, technical training is provided linked to business expertise.

A new Group-wide framework (IDEA: Ipsen Development and Education Academy) was implemented during 2005 to facilitate the development of training and development initiatives.

IDEA is oriented toward six principal goals:

- core competencies, to facilitate the development and advancement of a corporate culture,
- integration of new employees, using a common standard implemented at local level, by plant and by geographical region. It will be complemented

by e-integration via the Intranet site and a specific programme for managers,

- young professionals college, which aims to attract, secure the loyalty and accelerate the development of high-potential graduates who will be involved in key roles within the Group's various divisions,
- the managers college, which aims to raise the performance of supervisors and managers to a high level guaranteeing the consistency of management practices within the Group,
- the leaders college, which aims to hone the leadership skills of senior executives in long-term strategic areas,
- the Group's image, to bolster the Group's credentials as an employer of choice in the current market through its image and clear communication of the Group's human resources practices and management initiatives.

To optimise continuous investment in the training and development initiatives, a network of collaborators specifically trained to deliver Ipsen programmes will be rolled out during 2006.



COMPENSATION AND BENEFITS

Ipsen's compensation and benefits policy is based on a global approach, which endeavours to value all functions, as well as measure the performance of its employees.

It is based on four main principles: an assessment of the positions using a model applicable to all Group's entities; competitiveness at regional, national and international level; equal internal opportunities; and performance-based compensation.

These principles are applied in countries where the Group operates, and the way they are implemented is adapted to the local socio-economic and legal environment.

Annual pay increases are implemented using a common framework and identical schedule for the entire Group. This organisation makes it possible for example to analyse the achievement of individual objectives, to perform the annual review of individual performance under a more logical schedule, as well as to obtain more precise information about trends in the salaries market.

Employees performing a management role are eligible to a bonus system. The proportion of variable compensation has been increased with efforts by the Group to foster a performance-based culture.

RECRUITMENT AND INTERNAL PROMOTION

Group's employment policy aims at attracting and maintaining a suitably qualified, well trained and highly motivated workforce to perform, as efficiently as possible, the various tasks and roles inherent to the Group's business activities.

A specific attention is paid to the recruitment and promotion policy which are made in the respect of the Group's values. Thus, in 2005, 746 new employees have joined Ipsen, including 576 for permanent jobs.

Internal promotion is one of the key ways to motivate employees and their supervisors. Accordingly, opportunities to change jobs, switch functions and to move to new locations are regularly offered to Group's employees on the job forum of the Group's Intranet site. In 2005, 182 employees were promoted, which represents 5% of Ipsen's total workfoce.

SOCIAL RELATIONSHIPS

Ipsen gives a huge attention to the quality of the social relations and dialogue within the various entities of the Group. Employees are represented in accordance with the applicable local legislation. The frequency of meetings between management and employee representatives also depends on the applicable local legislation.

Ipsen ensures that the rights and freedoms of employee representatives are strictly observed and that they enjoy the same promotion and training opportunities as other employees.

Where there are relevant local regulations, the Group applies collective bargaining agreements or industry agreements for the pharmaceutical sector. In addition, companies negotiate specific agreements according to their individual characteristics. Certain agreements, which give rise to employee benefits, have been negotiated on a centralised basis, particularly supplementary pension plans and a "time bank", in France. In connection with the recognition of Group-wide agreements embodied by the recent legislative reform of labour-management dialogue in France, negotiations on issues such as employee profit-sharing and

health insurance are now conducted on a centralised

basis





Work in secured sites, respectful of environment

Ipsen regularly devotes a significant budget to environmental protection. In addition, the Group pursued awareness-raising campaigns concerning energy consumption at most of its manufacturing facilities during 2005. Furthermore, all energy-consuming investments now undergo an assessment and an energy review by the manufacturing and supply organisation. Responsibility for environmental protection at each plant is assigned to named individual. In 2005, 17 members of staff were involved in this organisation across the Group as a whole. It is managed by the head of the Health-Safety-Environment function for the whole of the Group's manufacturing and supply organisation.

ENERGY CONSUMPTION FURTHER EFFORTS TO ACHIEVE GREATER ENERGY EFFICIENCY

The Group's energy consumption increased by 8.3% in 2005. This increase was attributable to the strong rise in production volumes. Consumption trends at individual plants mirrored trends in production volumes, albeit with a generally favourable and significant differential. This improved energy efficiency was the result of deliberate efforts to reduce consumption at most plants.

WATER CONSUMPTION

WATER CONSUMPTION TIGHTLY CONTROLLED IN SPITE OF GROWTH OF PRODUCTION VOLUMES

The Group's water consumption increased by 4.6% in 2005, which was smaller than the increase in production volumes over the same period. This increase was tightly controlled through initiatives taken to recycle manufacturing and washing process water.

SOLID AND LIQUID WASTE ACTIONS TAKEN TO REUSE WASTE

The Group increased its waste by 4.8% in 2005, a slower rate of growth than that seen in production volumes over the same period. The proportion of recycling is thus steadily increasing, while incineration and landfill volumes are moving in the opposite direction. Significant efforts are underway and/or being developed by the majority of facilities to reuse a larger proportion of their waste. For instance, more and more organic waste is being composted in Cork (Ireland), paper and cardboard recycling is being developed in Tianjin (China), and dichloromethane recycling was rolled out at the Signes (France) plant during 2005.

DISCHARGE INTO THE AIR IMPROVEMENT IN QUALITY OF WASTE

The Group has made ongoing efforts over the past few years in this area, particularly through the substantial decrease in fuel oil consumption (it declined by 7% in 2005, after a 10%-fall in 2004), with the scrapping of this energy source in Dublin at year-end 2003 and at Dreux from early 2005.



EFFLUENTS ENCOURAGING TREND IN THE EFFLUENT TO SALES RATIO

Group-wide effluent volumes increased of 6% in 2005, a smaller rate of increase than that seen in product volumes over the same period. All the plants recorded lower effluent volumes thanks to specific reprocessing measures and/or efforts to curb inputs.

NOISE LIMITED NOISE POLLUTION

No particular noise issues were reported at the vicinity of the Group's manufacturing facilities.



SOIL POLLUTION INTENSE SCRUTINY

Ipsen attaches a very high level of importance to the issue of the impact of its operations on the soil in and around its plants. No instances of soil pollution were recorded at the Group's facilities in 2005.



Contribute to the development and dissemination of knowledge

Created in 1983 under the patronage of *La Fondation de France, La Fondation Ipsen*'s mission is to contribute to the development and dissemination of scientific knowledge. *La Fondation Ipsen* promotes sustainable interactions between research scientists and clinicians. These exchanges are critical today due to the acute specialisation of these professions. The goal of *La Fondation Ipsen* is not to provide definitive knowledge but to trigger discussions on the major scientific challenges for the years to come. In all its activities, *La Fondation Ipsen* works closely with international partners from the academic and scientific community to throw independent light upon the major issues upon which it has chosen to focus, and to provide updated information on the current state of knowledge.

MEDICINE AND RESEARCH SEMINARS

La Fondation Ipsen has developed a strong international network of scientific experts who meet regularly during meetings known as Medicine and Research Seminars. These international meetings bring together leading specialists who present the latest findings and research programmes. Grouped into series, these seminars are organised according to themes where research is particularly active:

ALZHEIMER'S DISEASE

Since 1987, this theme has been the subject of annual events which have followed or anticipated developments in the field of Alzheimer's disease.

NEUROSCIENCES

Initiated in 1990, this series of seminars gives an overview of the major themes emerging in this field, from molecular biology to cognitive sciences. The seminar held on 24 April 2006 was about "Memories: molecules and circuits".

LONGEVITY

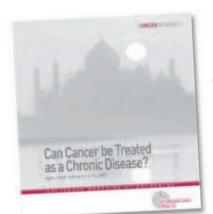
Launched in 1996, this series debates the issues and contradictions in medical approaches focusing not only on disease but on better resistance to harmful attacks that weaken the body systems.

ENDOCRINOLOGY

This series, initiated in 2002, explores interactions within the endocrine system, one of the major components involved in integrating all the body's functions.

THE VASCULAR TREE

This series, launched in 2004, aims to analyse the different stages which lead to the development of the vascular system, to its corresponding growth in relation to that of different organs, to its degeneration, to its death and its regeneration capabilities.



CANCER

The first conference (2005) was entitled "Can Cancer be Treated as a Chronic Disease?". Another challenging subject was discussed this year in Cape Town (Republic of South Africa) "Are Inflammation and Cancer Linked?". Inflammation has since long been thought to have a critical role in cancer develop-

ment, long before the oncogene theory of cancer was promulgated in the 1970s. But only very recent studies accumulated evidence that inflammation can be associated with increased cancer risk. Beyond these data, precise aspects of biological responses involved have been elucidated, including free radicals, growth factors and transcription factors like NFkB, cytokines and chemokines. These discoveries will pave the way for new therapies. Besides Prof. David Baltimore (Pasadena), Nobel Prize of Medicine in 1975, the leading experts invited to present their works were: Sebastian Amigorena (Paris), Frances Balkwill (London), Yinon Ben Neriah (Jerusalem), Hans Clevers (Utrecht), Ron Evans (La Jolla), Richard Flavell (New Heaven), Rudolf Jaenisch (Cambridge, United States), Michael Karin (La Jolla), Alberto Mantovani (Milan), Anthony Segal (London), Tadatsugu Taniguchi (Tokyo), Thomas Tursz (Villejuif), Inder Verma (La Jolla), Timothy C. Wang (New York), Robert Weinberg (United States).

OTHER INTERNATIONAL MEETINGS

La Fondation Ipsen organises international meetings in partnership with several national and international scientific bodies. Since 1989, several meetings have been organised jointly with the World Health Organisation (WHO) on the topic of human genetics, and have addressed some of the most hotly debated

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subjects in this area. *La Fondation Ipsen* is also a partner in seminars organised by the French National Gerontology Foundation (La Fondation Nationale de Gérontologie) on the topics of dementia and cognitive ageing. With Harvard University, it instigated an international event relative to perspectives in cognitive sciences, the report of which was published by Harvard University Press under the title The Languages of the Brain (A. Galaburda, S. Kosslyn, Y. Christen, eds.). Lastly, in the field of neuropsychology, it created the Behavioural Neurology Circle (Le Cercle de Neurologie Comportementale) which has been meeting twice a year since 1994 for high-level discussions on the topic of cognition. Furthermore, since 1991, La Fondation Ipsen has been co-organising the annual Jean-Louis Signoret Neuropsychology Days.

INTERNATIONAL PUBLICATIONS

Some of the findings from *La Fondation Ipsen*'s meetings have been released by international publishers as part of different collections edited in English by *La Fondation Ipsen*:

- Research and Perspectives in Alzheimer's disease
- Research and Perspectives in Neurosciences
- Research and Perspectives in Longevity
- Research and Perspectives in Endocrinology
- WHO/Fondation Ipsen collection
- Mind and Brain collection
- Cellular and Molecular Biology

Furthermore, since 1986, *La Fondation Ipsen* has published a periodical dedicated to Alzheimer's disease: *Alzheimer Actualités* (184 editions published), and various brochures for use by practitioners and patients' families. It offers a French translation of the Geriatric's Review Syllabus published by the American Geriatrics Society. Scientific films have played a major role in providing training for the medical profession, some of which have won awards at specialist festivals.

L'Arbre

vasculaire

Neurobiology of Human Values

cognition sociale



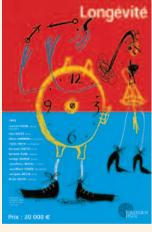
Prizes to encourage research

La Fondation Ipsen awards prizes to scientists for work that is deemed to be of particular importance and relevance by prestigious juries. Some scientists, such as Eric Kandel, have subsequently been awarded the Nobel Prize for Medicine.

Through these awards, the aim of *La Fondation lpsen* is to encourage research on a long-term basis. There are currently four prizes:

- the Jean-Louis Signoret neuropsychology prize, awarded in 2005 to Marc Jeannerod (Harvard Medical School, Boston, US) for his work on the meaning of dreams and mental simulation;
- the Longevity prize given in 2006 to Cynthia Kenyon (UCSF Hillblom Center for the Biology of Aging, San Francisco, US);
- the Neuronal Plasticity prize awarded to three researchers in 2005: Mary Kennedy (Caltech, Pasadena, US), Morgan Sheng (Harvard University, Cambridge, US) and Eckart Gundelfinger (Leibniz Institute for Neurobiology, Magdeburg, Germany) for their work in neuronal plasticity on the pre- and post-synaptic protein complex;
- **the Endocrinology prize** was awarded in 2005 to Tomas Hökfelt (Karolinska Institute, Stockholm) for his work on determining the structure and defining the role of neuropeptides.







2005 Pro forma* consolidated financial statements

- Consolidated income statement
- Consolidated balance sheet
- Consolidated statement of cash flows



* The pro forma financial information present the Group's accounts as if the legal reorganisation (that ended in late June 2005), took place on 1 January 2002

Pro forma consolidated income statement

	31 December 2005	31 December 2004 ⁽¹⁾
(In thousands of euros) Sales		
	807,114	751,539
Other revenue	80,738	63,287
Total revenue	887,852	814,826
Cost of goods sold	(171,042)	(165,658)
Research and development expenses	(169,025)	(143,227)
Selling, general and administrative expenses	(364,135)	(330,390)
Other operating income and expenses	1,169	2,123
Restructuring costs	530	(10,436)
Impairment losses	-	(10,757)
Operating income	185,349	156,481
Investment revenue	1,952	2,184
Cost of financing	(7,870)	(11,004)
Net finance cost	(5,918)	(8,820)
Other financial income and expense	(632)	(466)
Income taxes	(34,208)	(42,039)
Net profit from continuing operations	144,591	105,156
Discontinued operations	4,416	12,748
Net profit for the period	149,007	117,904
- attributable to equity holders of the parent	148,638	117,638
- attributable to minority interests	369	266
Basic earnings per share, continuing operations (in euros)	2.14	1.79
Diluted earnings per share, continuing operations (in euros)	2.14	1.79
Basic earnings per share, discontinued operations (in euros)	0.06	0.22
Diluted earnings per share, discontinued operations (in euros)	0.06	0.22
Basic earnings per share (in euros)	2.20	2.01
Diluted earnings per share (in euros)	2.20	2.01

(1) In accordance with IFRS 5, the 2004 income statement has been restated to provide comparable data for the periods presented.

Pro forma consolidated balance sheet*

(In thousands of euros)	31 December 2005	31 December 2004
ASSETS		
Goodwill	188,836	188,836
Intangible assets, net	39,800	35,221
Property, plant & equipment, at cost	440,703	415,248
Depreciation, amortisation and impairment losses	(252,934)	(237,436)
Property, plant & equipment, net	187,769	177,812
Equity investments	2,656	3,003
Other non-current financial assets	2,671	2,292
Non-current financial assets	5,327	5,295
Deferred tax assets	13,096	8,235
Total non-current assets	434,828	415,399
Inventories	74,390	71,464
Trade receivables	164,681	160,137
Current tax assets	10,951	2,245
Other current assets	42,966	32,783
Cash and cash equivalents	202,034	94,321
Total current assets	495,022	360,950
Assets of discontinued operations	12,659	-
TOTAL ASSETS	942,509	776,349
EQUITY & LIABILITIES		
Share capital	84,025	571,391
Share premiums and consolidated reserves	420,591	(367,885)
Net profit for the year	119,230	117,638
Cumulative translation reserve	(4,080)	(7,346)
Equity attributable to equity holders of the parent	619,766	313,798
Minority interests	1,334	1,188
Total equity	621,100	314,986
Retirement benefit obligation	8,032	7,594
Long-term provisions	8,266	10,330
Bank loans	37,751	215,010
Other financial liabilities	15,508	12,455
Deferred tax liabilities	1,358	862
Total non-current liabilities	70,915	246,251
Short-term provisions	3,309	4,240
Bank loans	7,074	10,171
Financial liabilities	1,760	892
Trade payables	107,045	99,332
Current tax liabilities	2,223	8,910
Other current liabilities	113,525	90,009
Bank overdrafts	1,470	1,558
Total current liabilities	236,406	215,112
Liabilities of discontinued operations	14,088	-
TOTAL EQUITY AND LIABILITIES	942,509	776,349
	,	

(*) Pro forma balance sheet figures at 31 December 2005 have not been provided as the only difference compared with the published figures is the breakdown of equity.

Pro forma consolidated statement of cash flows*

(In thousands of euros)	31 December 2005	31 December 2004
Net profit for the period	149,007	117,904
Net profit from discontinued operations	(4,416)	-
Net profit from continuing operations	144,591	-
Non-cash and non-operating items:		
- Depreciation, amortisation and impairment losses	30,603	27,477
- Change in fair value of derivative financial instruments	276	-
- Impairment of goodwill	-	10,757
- Net gains or losses on disposal of non-current assets	232	(12,171)
- Share of government grant released to profit and loss	(135)	(127)
- Exchange differences	(1,238)	525
- Change in deferred taxes	(4,717)	(920)
- Share-based payment expense	3,355	2,247
Cash flow from operating activities before changes in working capital	172,967	145,692
- (Increase)/decrease in inventories	(5,315)	(257)
- (Increase)/decrease in trade receivables	(6,755)	(24,780)
- (Decrease)/increase in trade payables	9,192	12,900
- Net change in income tax liability	(15,110)	[4,967]
- Net change in other operating assets and liabilities	21,875	(3,905)
Change in working capital related to operating activities	3,887	(21,009)
NET CASH PROVIDED BY OPERATING ACTIVITIES	176,854	124,683
Acquisition of property, plant & equipment	(36,479)	(40,884)
Acquisition of intangible assets	(7,944)	(22,524)
Payments to post-employment benefit plans	(1,400)	-
Proceeds from disposal of intangible assets and property, plant & equipment	1,124	1,104
Acquisition of investments in non-consolidated companies	-	(1,250)
Impact of changes in the scope of consolidation	-	[47,449]
Other cash flows related to investing activities	(426)	76
Change in working capital related to investing activities	(7,624)	8,450
NET CASH USED BY INVESTING ACTIVITIES	(52,749)	(102,477)
Additional long-term borrowings	13,052	126,350
Repayment of long-term borrowings	(189,969)	(47,051)
Net change in short-term borrowings	(3,095)	(322)
Ipsen S.A. capital increase.	9,088	-
Increase in share premiums or transfer premium	182,731	-
Capital reductions made by subsidiaries	-	442
Dividends paid by Ipsen S.A.	(29,303)	(91,900)
Dividends paid by subsidiaries to minority interests	(300)	(119)
Change in working capital related to financing activities	(1,154)	655
NET CASH USED BY FINANCING ACTIVITIES	(18,950)	(11,945)
Impact of operations due to be sold or discontinued	12,001	-
Reported change in cash and cash equivalents	117,156	10,261
Impact of pro forma restatements	(10,150)	(15,227)
CHANGE IN CASH AND CASH EQUIVALENTS	107,006	[4,966]
Opening cash and cash equivalents	92,763	99,725
Impact of exchange rate fluctuations	795	(1,996)
Closing cash and cash equivalents	200,564	92,763

(*) As the balance sheet at 31 December 2004 has not been restated for the disposal of the Group's Spanish operation (in accordance with IFRS 5), the cash flow statement has not been restated either.

Administration and Finance Claire Giraut

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