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OFFICE OF INTERNATIONAL  
CORPORATE FINANCE

12g-3-2(b) Exemption  
File N° 82-34953

28<sup>th</sup> June 2010



10015961

Dear Sir or Madam,

**SUPL**

Enclosed is information Ipsen:

- made or is required to make public under French law;
- filed or is required to file with and which is made public by Euronext Paris; or
- distributed or is required to distribute to its shareholders.


This information is being furnished under Paragraph (b)(1)(i) of Rule 12g-3-2 of the Securities Exchange Act of 1934; as amended (the **Exchange Act**), with the understanding that such information and documents will not be deemed "filed" with the U.S. Securities and Exchange Commission or otherwise subject to the liabilities of Section 18 of the Exchange Act, and that neither this letter or the furnishing of such documents and information shall constitute an admission for any purpose that Ipsen is subject to the Exchange Act.

Yours sincerely,



**P/10** Claire Giraut  
Executive Vice President,  
Chief Financial Officer

*llw 7/2*





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Press release

## Launch by Menarini and Ipsen of ADENURIC® (febuxostat) in France for the treatment of chronic hyperuricemia in gout

- First therapeutic alternative in gout for decades
- France is the first country to launch ADENURIC® in Europe

**Paris (France), 5 March 2010** - Ipsen (Euronext: FR0010259150; IPN), a global biotechnology specialty care group and Menarini, the first Italian pharmaceutical Group in the world with a significant pan-European presence, today announced the launch of ADENURIC® (febuxostat) in France where they will co-promote the drug. Other launches by Menarini are planned shortly, notably in United Kingdom, Germany and Ireland.

**Thierry Poiraud, MD, General Manager, Menarini France** said: *"We are proud to be the first country in Europe to launch this very promising drug with Ipsen. In collaboration with rheumatologists and general practitioners I hope we can significantly improve the chronic management of this painful and frequent disease, which may lead to serious complications with a major impact on quality of life."*

**Etienne de Blois, Deputy General Manager, Ipsen France Operations**, Ipsen said: *"The launch of ADENURIC® will provide patients and physicians with a new treatment alternative in a condition with high unmet medical needs. It also strengthens Ipsen's primary care franchise in France, the first country to launch the drug in Europe. Ipsen is proud to work with Menarini to make that achievement possible."*

### About ADENURIC® (febuxostat)

ADENURIC® (febuxostat), an oral, once-daily medication, is a novel non-purine, selective inhibitor of xanthine oxidase studied for its effects on lowering levels of serum uric acid (sUA) in patients with gout.

ADENURIC® received marketing authorisation in the European Union on 21<sup>st</sup> April 2008. Its 80 mg and 120 mg tablets are indicated for the treatment of chronic hyperuricemia in conditions where urate deposition has already occurred (including a history, or presence of, tophus and/or gouty arthritis). In its evaluation<sup>1</sup>, the French *Haute Autorité de Santé* indicates that ADENURIC® has demonstrated superiority over allopurinol in decreasing and maintaining uricaemia below the therapeutic objective of 360 µmol/l (6 mg/dl) as defined, in 2006, by EULAR guidelines in the chronic management of gout. Additionally, ADENURIC® can be prescribed without dose adjustment to patients suffering from mild to moderate renal impairment and might be an alternative option for patients that are intolerant to allopurinol. Treatment with febuxostat in patients with ischaemic heart disease or congestive heart failure is not recommended.

In 2003, Teijin Pharma Limited, Tokyo, the core company of Teijin Group's pharmaceutical and home healthcare business, who discovered febuxostat, had granted Ipsen the exclusive

<sup>1</sup> Avis de la commission de transparence M04AA03 - ADENURIC - CT-6315  
Adenuric® is a registered trademark of Teijin Pharma Limited, Tokyo, Japan.



development and marketing rights to ADENURIC® (febuxostat) in Europe. On 20 October 2009, Ipsen has granted Menarini exclusive licence rights to ADENURIC® in the European Union, Russia and countries west of Russia for a total of 41 countries.

### **About gout**

Gout, a particularly painful type of arthritis, is the most frequent arthritis in men. It is caused by elevated levels of uric acid in the body : hyperuricemia. In this condition, crystals of monosodium urate (MSU) are deposited on the articular cartilage of joints, tendons, and surrounding tissues. It is marked by transient painful attacks of acute arthritis initiated by crystallization of urates within and about the joints and can eventually lead to chronic gouty arthritis and the deposition of masses of urates in joints and other sites, sometimes creating tophi. In the absence of treatment, symptomatic chronic hyperuricemia may lead to a handicap and / or a noticeable degradation of quality of life, linked to articular and/or renal (lithiasis, nephropathy) impairment<sup>1</sup>.

In 2006, European League Against Rheumatism (EULAR)<sup>2</sup> established the following principles:

- Optimal management requires both non-pharmacological and pharmacological treatment and needs to be tailored to the individual.
- Urate lowering therapy to promote crystal dissolution and prevent crystal formation is achieved by maintaining the serum uric acid below the saturation point for monosodium urate (360 µmol/l or 6 mg/dl).

Epidemiology data on gout is scarce<sup>3</sup>. However, a 1999 study<sup>4</sup> estimated that prevalence of gout in the U.K. reached 1.4% with rates approaching 7% in men over the age of 65. This prevalence was confirmed by a another study<sup>5</sup> conducted from 2000 to 2005, in the U.K. and Germany. An observational study<sup>6</sup> took place in France in 1981 on 4,663 men employed by a Parisian public organisation, showed prevalence of 1.2% (0.4% in men aged 20-34; 1.1% on men aged 35-39; 2% on men aged 40-44).

### **About Menarini**

Menarini is the first Italian Pharmaceutical Group in the world. Menarini employs nearly 13,000 people, with a strong presence throughout Europe, CIS, Africa and in South and Central America. The company has expertise in successfully developing, registering and delivering medical information for drug products in a broad range of therapeutic areas. including drug products generated by its Research and Development activities located in Florence, Rome, Pisa, Barcelona and Berlin. The Group's total revenue exceeds euro 2.6 billion.

### **About Ipsen**

Ipsen is a global biotechnology specialty care group with total sales in excess of 1 billion euros in 2009, and total worldwide staff of more than 4,400. Its strategy is based on fast growing

<sup>1</sup> Avis de la commission de transparence M04AA03 - ADENURIC - CT-6315

<sup>2</sup> W. Zhang et al. EULAR evidence-based recommendations for gout. Part II: management. Report of a task force of the Eular Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann of Rheum Dis 2006; 65:1312-1324

<sup>3</sup> Avis de la commission de transparence M04AA03 - ADENURIC - CT-6315

<sup>4</sup> Mikuls TR, Farrar JT, Bilker WB, et al. Gout epidemiology: results from the UK General Practice Research Database, 1990-1999. Ann Rheum Dis 2005;64:267-72.

<sup>5</sup> Annemans L et al. Gout in the UK and Germany: prevalence, comorbidities and management in clinical practice. Ann Rheum Dis 2008;67:960-966

<sup>6</sup> Zalokar J, Lellouch J, Claude JR. Goutte et uricémie dans une population de 4663 hommes jeunes actifs. Sem. Hôp. 1981 ;57 : 664-670



specialty care drugs in oncology, endocrinology, neurology and hematology, and primary care drugs, which significantly contribute to research financing. This strategy is also supported by an active policy of partnerships. Ipsen's specific Research & Development (R&D) centers and peptide & protein engineering platform give the Group a competitive edge. Almost 900 people are dedicated to the discovery and development of innovative drugs for patient care. In 2009, R&D spend reached close to €200 million, representing more than 19% of total Group sales. Ipsen's shares are traded on *Segment A* of Euronext Paris (stock code: IPN, ISIN code: FR0010259150). Ipsen's shares are eligible to the "Service de Règlement Différé" ("SRD") and the Group is part of the SBF 120 index. For more information on Ipsen, visit our website at [www.ipсен.com](http://www.ipсен.com).

### **Ipsen Forward Looking Statement**

The forward-looking statements, objectives and targets contained herein are based on the Group's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by the Group. These targets depend on conditions or facts likely to happen in the future, and not exclusively on historical data. Notably, future currency fluctuations may negatively impact the profitability of the Group and its ability to reach its objectives. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties. The Group does not commit nor gives any guarantee that it will meet the targets mentioned above. Furthermore, the Research and Development process involves several stages each of which involve the substantial risk that the Group may fail to achieve its objectives and be forced to abandon its efforts with regards to a product in which it has invested significant sums. Therefore, the Group cannot be certain that favourable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. The Group also depends on third parties to develop and market some of its products which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to the Group's activities and financial results. The Group expressly disclaims any obligation or undertaking to update or revise any forward looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. The Group's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers.



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Press release

## Ipsen Grants Rhythm Exclusive Worldwide License for Two Programs in the Field of Metabolic Disorders

**Paris (France) and Boston (USA), - March 12, 2010** - Ipsen (Euronext: FR0010259150; IPN), a global biotechnology specialty care group, and Rhythm Pharmaceuticals (Rhythm), a biotechnology company developing peptide therapeutics for metabolic diseases, announced today that they have concluded a license agreement for Ipsen's proprietary peptide therapeutics targeting obesity, metabolic diseases, and gastrointestinal disorders. Under the terms of the agreement, Ipsen has granted Rhythm an exclusive worldwide license for research, development, and commercialization of its melanocortin and ghrelin programs originating from Ipsen research.

*"The agreement with Rhythm is a clear catalyst for the development of proprietary molecules from Ipsen in promising indications within the area of metabolic diseases, which are outside of our core strategic focus,"* said **Stéphane Thiroloix, Executive Vice President, Corporate Development, Ipsen**. *"Given Rhythm's complete focus on metabolic diseases, this transaction will leverage our combined expertise and resources to rapidly transform these important discoveries into valuable medical treatments."*

*"Rhythm has a great opportunity to develop significant new peptide therapeutics to improve the health of people with obesity, diabetes, and other intractable metabolic diseases,"* said **Bart Henderson, President of Rhythm**. *"We are extremely fortunate to have access to Ipsen's peptide discoveries and expertise in peptide formulations to help us achieve this vision."*

### **About the Agreement**

The license granted to Rhythm includes Ipsen's compounds and intellectual property related to analogs of the peptide hormones, ghrelin and MSH, which regulate food intake, energy homeostasis, and gastrointestinal function.

- Ghrelin agonists—in particular, the lead compound, BIM-28131—are potential treatments for gastrointestinal motility disorders such as postoperative ileus and diabetic gastroparesis and for cachexia resulting from multiple causes, including cancer.
- Melanocyte-stimulating hormone (MSH) agonists—in particular, the lead compound, BIM-22493—which specifically target the melanocortin-4 (MC4) receptor, are potential treatments for obesity, diabetes, and related metabolic disorders.

Under the terms of the license agreement, Ipsen will receive progressive payments of up to U.S. \$80 million upon the achievement of certain development and commercial milestones and royalties on future sales of the products. Rhythm will also continue to use Ipsen's recognized formulation expertise to develop innovative delivery systems for the peptide programs. Ipsen will also acquire 17% equity in Rhythm and is granted one seat on Rhythm's Board of Directors.



**About Rhythm** ([www.rhythmtx.com](http://www.rhythmtx.com))

Rhythm is a biotechnology company developing peptide therapeutics that address unmet needs in metabolic diseases. Rhythm investors include MPM Capital and New Enterprise Associates. The company is based in Boston, Massachusetts.

**About Ipsen**

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OFFICE OF INTERNATIONAL  
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Press release

**Initiation of two phase II studies with Ipsen's proprietary BIM 23A760 first-in-class chimeric compound in the treatment of acromegaly and carcinoid syndrome due to neuroendocrine tumors**

**Paris (France), 15 March 2010** - Ipsen (Euronext: FR0010259150; IPN) announced today the initiation of dosing in two phase II clinical studies to evaluate efficacy and safety of BIM 23A760 in two groups of patients, one suffering from carcinoid syndrome due to neuroendocrine tumors, the other from acromegaly.

*"After the encouraging signs of efficacy observed in the first clinical studies in healthy as well as acromegalic volunteers, we look forward to further investigating BIM 23A760 efficacy and safety in patients with neuroendocrine tumors or acromegaly. This very promising compound is core to Ipsen's strategy to enhance its fast-growing and competitive endocrinology franchise, featuring among other drugs Somatuline<sup>®</sup>, a somatostatin analogue developed and marketed on a global scale"* said **Stéphane Thiroloix, Executive Vice-President, Corporate Development, Ipsen.**

**About BIM 23A760**

BIM 23A760 has been designed and developed by Ipsen's research team using its validated peptide engineering platform. This first-in-class innovative chimeric compound bears within a single molecule two pharmacological moieties, i.e. a somatostatin analog and a dopamine agonist which act synergistically following activation of those receptors in disorders such as acromegaly and neuroendocrine tumors. The design of BIM 23A760 is based on a novel concept in molecular biology regarding the amplification of intracellular signalling when engaging simultaneously two receptors with their respective ligands. The molecule targets two patho-physiological pathways among the most commonly associated with pituitary tumors: Growth hormone and prolactin. Aside from the symptomatic treatment of acromegaly and carcinoid syndrome due to neuroendocrine tumors, BIM 23A760 might potentially also reduce the tumor size, thereby eliminating some of the shortcomings of the treatments currently available. Ipsen is currently studying this molecule whose spectrum of activity is wider than that of currently marketed somatostatin analogues.

**About the phase II trial in acromegaly**

The clinical trial is a phase II open, randomized, parallel group, non comparative multicenter study to assess the efficacy and safety of repeated subcutaneous (s.c.) administration of different doses of BIM 23A760 on growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels in patients with acromegaly after 6 months of treatment.

This clinical trial follows phase I and IIa trials. In the phase I, BIM 23A760 administration in healthy volunteers potently suppressed prolactin levels and statistically significant reductions in IGF-1 levels were observed. In the phase IIa study, the exposure to BIM 23A760 in acromegalic patients, exhibited a 66–74% mean maximum reduction in growth hormone (GH) levels. A dose dependent tendency for a more pronounced and longer GH inhibition was also observed. Additionally, a reduction in IGF-1 levels was seen in both dosage (1 mg and 4 mg). BIM 23A760 was well tolerated at both dosages.



### About acromegaly

Acromegaly is a disorder caused by the over production of growth hormone due to a benign tumor of the anterior pituitary gland. This relatively rare disorder occurs in approximately 90 out of every one million people (90/1,000,000). Both men and women are affected. Approximately 50% of the diagnosed patients receive a drug therapy.

### **About the phase II trial in neuroendocrine tumors**

The clinical trial is a phase II, open, adaptive, dose escalating, multicentre titration study to assess the efficacy and safety of repeated s.c. administration of different doses of BIM 23A760 for the treatment of carcinoid syndrome in patients affected with neuroendocrine tumors on patient's overall satisfaction in terms of symptom relief after 6 months of treatment.

### About Carcinoid tumors

Carcinoid tumors are rare diseases affecting about 2.5 to 5 out of 100 000 people. Most of them develop in the gastrointestinal tract. The hypersecretion of substances by the tumor, in particular serotonin, results in symptoms, mainly diarrhea and flushing. The treatment includes symptomatic control as well as tumor reduction.

### **About Ipsen**

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Press release

## GTx and Ipsen expand partnership

**Paris (France) and Memphis (USA), 23 March 2010** – Ipsen (Euronext: FR0010259150; IPN) and GTx, Inc. (Nasdaq: GTXI) today announced the expansion of their partnership for the development and commercialization of toremifene 80 mg for the reduction of fractures in men with advanced prostate cancer on androgen deprivation therapy (ADT) and toremifene 20 mg for the prevention of prostate cancer in high risk patients with High Grade Prostatic Intraepithelial Neoplasia lesions (HGPIN).

Under the terms of the amended collaboration agreement, Ipsen will pay GTx up to €42 million (approximately \$58 million, based on current exchange rates) in milestone payments upon the initiation, enrollment and progression of the second toremifene 80 mg Phase III clinical trial. In return, GTx has granted Ipsen:

- The right to co-promote toremifene 80 mg in the United States or, in lieu of co-promoting in the US, the right to a double digit royalty stream on net sales of toremifene 80 mg in the U.S.
- An expansion of Ipsen's licensed territory for marketing toremifene products beyond Europe, including Australia and certain countries in North Africa, the Middle East, and Asia (excluding Japan).
- Relief from Ipsen's previous contractual obligations, notably to pay GTx potential remaining milestones related to the European approval of toremifene 80 mg.
- Royalties on Ipsen's net sales of toremifene 80 mg set at a fixed low teens rate compared to a variable rate previously.
- A first right of negotiation under certain conditions for rights to GTx-758, currently in Phase II clinical trial for the first-line treatment of men with advanced prostate cancer, in Ipsen's licensed toremifene territories.

*"Once the agreement is reached with the FDA on a final study protocol required for marketing approval, we will initiate the second phase III clinical trial later this year with toremifene 80 mg to reduce fractures in men with prostate cancer on androgen deprivation therapy" said **Mitchell S. Steiner, MD, Chief Executive Officer of GTx.** "We are excited to expand our toremifene clinical and commercial partnership with Ipsen."*

**Stéphane Thiroloix, Executive Vice President, Corporate Development, Ipsen** said: *"This new agreement with GTx gives us expanded market reach and rights for toremifene, in what we view as significant unmet medical needs for patients suffering from prostate cancer. It will strengthen Ipsen's franchise in hormone-dependent cancers and broaden our drug range in the oncology area."*

### **About toremifene**

Toremifene is a selective estrogen receptor modulator, or SERM, developed by GTx as a daily tablet for the treatment of the multiple estrogen related side effects of androgen deprivation therapy for advanced prostate cancer and for the prevention of prostate cancer in high risk



patients with High Grade Prostatic Intraepithelial Neoplasia lesions (HGPIN). Toremifene was designed to bind to and selectively modulate estrogen receptors depending on the tissue type.

#### About the second toremifene 80 mg phase III clinical trial

In 2008, based upon the successful results of a first Phase III clinical trial, GTx submitted a New Drug Application to the United States Food and Drug Administration (FDA) for toremifene 80 mg for the reduction of fractures in men with prostate cancer on ADT. In October 2009, GTx received a Complete Response Letter from the FDA requesting a second Phase III clinical trial.

In the second half of 2010, GTx plans to initiate the second international, randomized, double-blind, placebo-controlled phase III clinical trial evaluating toremifene 80 mg in men with advanced prostate cancer on androgen deprivation therapy (ADT) who are at increased risk of fractures. The primary endpoint will be the incidence of new vertebral fractures. Additional efficacy data on bone mineral density (BMD), hot flushes and breast tenderness/pain will also be collected as well as toremifene safety/tolerance data.

#### **About GTx**

GTx, Inc., headquartered in Memphis, Tenn., is a biopharmaceutical company dedicated to the discovery, development, and commercialization of small molecules that selectively target hormone pathways to prevent and treat cancer, fractures and bone loss, muscle loss and other serious medical conditions. For more information on GTx, visit our website, [www.gtxic.com](http://www.gtxic.com).

#### ***Forward-Looking Information is Subject to Risk and Uncertainty***

This press release contains forward-looking statements based upon GTx's current expectations. Forward-looking statements include, but are not limited to, statements relating to GTx's plans to continue to pursue the development of and marketing approval for, and the potential commercialization of, toremifene 80 mg, and the continued development and potential commercialization of GTx's other product candidates. Forward-looking statements involve risks and uncertainties. GTx's actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, the risks (i) that GTx and its collaboration partner will not be able to commercialize their product candidates if clinical trials do not demonstrate safety and efficacy in humans, including in any additional clinical trials that GTx may conduct in connection with the NDA for toremifene 80 mg to reduce fractures in men with prostate cancer on ADT; (ii) that GTx may not be able to obtain required regulatory approvals to commercialize its product candidates, including toremifene 80 mg to reduce fractures in men with prostate cancer on ADT or toremifene 20 mg for the prevention of prostate cancer in high risk men with high grade prostatic intraepithelial neoplasia, in a timely manner or at all; (iii) that clinical trials being conducted or planned to be conducted by GTx and its collaboration partner may not be initiated or completed on schedule, or at all, or may otherwise be suspended or terminated; (iv) related to GTx's dependence on its collaboration partner for product candidate development and commercialization efforts; (v) related to GTx's reliance on third parties to manufacture its product candidates and to conduct its clinical trials; and (vi) that GTx could utilize its available cash resources sooner than it currently expects and may be unable to raise capital when needed, which would force GTx to delay, reduce or eliminate its product candidate development programs or commercialization efforts. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this press release. GTx's annual report on Form 10-K filed with the SEC on March 15, 2010 contains under the heading, "Risk Factors," a more comprehensive description of these and other risks to which GTx is subject. GTx expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

**About Ipsen**

Ipsen is a global biotechnology specialty care group with total sales in excess of 1 billion euros in 2009, and total worldwide staff of more than 4,400. Its strategy is based on fast growing specialty care drugs in oncology, endocrinology, neurology and hematology, and primary care drugs, which significantly contribute to research financing. This strategy is also supported by an active policy of partnerships. Ipsen's specific Research & Development (R&D) centers and peptide & protein engineering platform give the Group a competitive edge. Almost 900 people are dedicated to the discovery and development of innovative drugs for patient care. In 2009, R&D spend reached close to €200 million, representing more than 19% of total Group sales. Ipsen's shares are traded on Segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150). Ipsen's shares are eligible to the "Service de Règlement Différé" ("SRD") and the Group is part of the SBF 120 index. For more information on Ipsen, visit our website at [www.ipsen.com](http://www.ipsen.com).

**Forward-looking statements**

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OFFICE OF INTERNATIONAL  
CORPORATE FINANCE

Press release

## Update on Ipsen's share capital structure

**Paris (France), 24 March 2010** – Ipsen (Euronext: IPN) announced today that it has been informed that its controlling shareholder Mayroy completed an institutional private placement of 4,029,979 shares representing approximately 4.8% of Ipsen's share capital, at a price of 34.50 euros per share.

Ipsen has also been informed that the proceeds of this sale will be used to finance the repurchase by Mayroy of the entire stake held in the company by one of its minority shareholders, BMH2. BMH2 is a Luxembourg-registered company held by a trust whose beneficiaries are Mrs Véronique Beaufour and her descendants, and which today holds approximately 6.7% of Mayroy's share capital. BMH2 and its stakeholders do not sit on the Board of Directors of Ipsen and play no active role in the management of the Group.

As a result of this transaction, Ipsen's free-float increased to 31.7% from approximately 26.9% and Mayroy's stake in Ipsen's share capital and voting rights now amounts to 68.3% and 81.5% respectively. The indirect stake currently held by Beech Tree (controlling shareholder of Mayroy) in Ipsen remains unchanged.

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Press release

## **Dicerna Pharmaceuticals and Ipsen enter into an exclusive research collaboration for the development of new therapeutic agents in endocrinology and oncology**

- **Ipsen's expertise in peptide engineering will be combined with Dicerna's exclusive Dicer Substrate Technology to develop innovative molecules as potential therapeutic agents**

**PARIS (France) and WATERTOWN, Mass. (USA), 30 March 2010** – Dicerna Pharmaceuticals, Inc., (Dicerna) a second generation RNA interference (RNAi) company, and Ipsen (Euronext: FR0010259150; IPN), a global biotechnology specialty care group, announced today that the two companies have entered into an exclusive research collaboration agreement to leverage their expertise in Dicer Substrate siRNA (DsiRNA) research and peptide engineering. The companies will develop novel conjugates of Dicerna's DsiRNA molecules and Ipsen's peptide targeting vectors in the therapeutic areas of oncology and endocrinology.

RNAi is a key cellular mechanism regulating gene expression in both normal and disease processes. Based on gene sequence rather than protein structure, RNAi therapeutics have the potential to silence disease-causing genes using small synthetic RNA molecules, which may enable the development of new therapies for many acute and chronic diseases. The resulting target gene knockdown reduces gene expression in a way that is highly selective and specific.

"We are very excited to partner with Ipsen on this exclusive research collaboration. This agreement further advances our discovery efforts and provides us with the opportunity to develop Dicer Substrate siRNA therapies and targeted drug delivery systems while working with a partner who brings a unique peptide technology platform to the collaboration," said **James C. Jenson, Ph.D., chief executive officer and co-founder of Dicerna**. "This is the second significant partnership with a major biopharmaceutical company that we have entered into in 2010, further validating our next generation Dicer Substrate Technology and our unique ability to generate a greater number of more potent gene silencing molecules."

"Combining Dicerna's Dicer Substrate Technology with Ipsen's innovative peptide technology that can target specific cell types of interest and mediate intracellular delivery of DsiRNA, will enable us to jointly explore a number of therapeutic programs in the areas of oncology and endocrinology," said **Claude Bertrand, Executive Vice-President, Chief Scientific Officer, Ipsen Group**. "We believe that this collaboration brings together two leading companies with unique and complementary technology platforms which could potentially lead to the discovery of breakthrough DsiRNA-based therapies."

### **About the collaboration**

By combining Dicerna's proprietary Dicer Substrate Technology and DsiRNAs to silence disease-causing genes with Ipsen's peptide technology platform to allow cell-specific, intracellular delivery, the companies will conduct collaborative research aimed at identification of



new DsiRNA-based therapies with targeted delivery, superior potency and extended duration of action. Both companies will contribute their break-through technologies to the joint research collaboration. Dicerna and Ipsen may collaborate further to move the programs discovered under this partnership into development and eventual commercialization.

#### **About Dicer Substrate RNAi**

Dicer is a critical enzyme involved in the RNAi gene silencing cascade and acts earlier in the pathway, preparing double-stranded RNA for processing. Dicer then hands off these small RNA molecules to the mature gene silencing complex (RISC). Dicerna's synthetic Dicer Substrate siRNA (DsiRNA) molecules are 25 or more base pairs in length and take advantage of this natural and early entry point.

#### **About Ipsen**

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#### **About Dicerna**

Dicerna Pharmaceuticals is a private, venture-backed RNAi-focused biopharmaceutical company developing novel therapeutic agents and related drug delivery systems in multiple disease areas based on its proprietary Dicer Substrate Technology platform and Dicer Substrate siRNA (DsiRNA). The company is developing second generation DsiRNA-based therapies that engage the enzyme Dicer within cells, an early step in the gene silencing process, to exploit a natural initiation point for the RNAi cascade.

DsiRNA takes advantage of this distinct biological pathway, resulting in greater potency, longer duration of action and enhanced delivery potential, differentiating it from other RNAi approaches. Dicerna believes that its Dicer Substrate Technology is based on intellectual property that is both broadly enabling and distinct from other IP in the field. Dicerna has exclusive, worldwide rights to the Dicer Substrate Technology and has the sole right to grant sublicenses to the full portfolio of Dicer Substrate intellectual property. Dicerna has a major alliance with Kyowa Hakko Kirin for DsiRNA pharmaceuticals and drug delivery systems, initially focused on oncology, and a collaboration with Archemix to research novel conjugates of DsiRNA and aptamers for targeted delivery. Dicerna is based in Watertown, Massachusetts. For more information, please visit [www.dicerna.com](http://www.dicerna.com).

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Press Release

**Ipsen and Invida Enter into a Partnership for the Commercialization of Ipsen's Specialty Care Drugs in South-East Asia**

- **New Geographical Footprint for Ipsen's Specialty Care Portfolio in Oncology and Endocrinology**
- **Diphereline<sup>®1</sup>, Somatuline<sup>®</sup> Autogel<sup>®</sup> and Increlex<sup>®</sup> to be Commercialized by Invida in Certain Asian Countries**

**Paris (France) and Singapore, [27] April 2010** – Ipsen (Euronext: FR0010259150; IPN), a global biopharmaceutical group, and Invida Group, the leading healthcare commercialization solutions partner in the Asia Pacific region, announced today an agreement for the exclusive distribution and promotion by Invida of Ipsen's drugs Diphereline<sup>®</sup> 3.75mg & 11.25mg, Somatuline<sup>®</sup> Autogel<sup>®</sup> and Increlex<sup>®</sup> in selected countries in South-East Asia. Invida will be in charge of filing and commercialising the drugs in the different countries. The agreement is for an initial period of five years renewable for an additional period of five years, and covers Singapore, Malaysia, Philippines, Indonesia, Thailand and India, with the exception of Diphereline<sup>®</sup> for Thailand. In the context of the agreement, Ipsen will receive payments upon achievement by Invida of certain commercial milestones.

**Christophe Jean, Executive Vice President, Chief Operating Officer, Ipsen** said, *"We are very pleased to partner with Invida, a well-established healthcare group in Asia, that will optimize time-to-market in the region while allowing us to work with a single, trusted partner. This agreement contributes to expand the geographical reach of Ipsen's specialty care portfolio in the Asia Pacific region and give physicians and patients access to innovative treatments in severe conditions in oncology and endocrinology."*

**John Graham, Invida Group CEO**, said, *"This partnership is an excellent opportunity for Invida to expand its specialty care offerings in the region, a segment which we feel possesses immense potential for Invida as the demand grows throughout Asia. We are thrilled to partner with Ipsen, as both our companies are strongly focused on bringing innovative products to market. We feel that by introducing Ipsen's drugs into these countries, we will be able to improve the lives of patients while advancing the standard of care for these important indications. This partnership will allow Ipsen to leverage Invida's local expertise, proven methodology, and market insights to commercialize these products to a wide audience throughout Asia."*

**About Diphereline<sup>®</sup>/Decapeptyl<sup>®</sup>**

The active substance in Diphereline<sup>®</sup>/Decapeptyl<sup>®</sup> is triptorelin, a decapeptide analogue of GnRH (Gonadotrophin Releasing Hormone), a hormone secreted by the hypothalamus, which initially stimulates the release of pituitary gonadotrophins (hormones produced by the pituitary gland), which in turn control

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<sup>1</sup> Depending on the countries, Decapeptyl<sup>®</sup> is marketed under different brand names (Diphereline<sup>®</sup>, Pamorelin<sup>®</sup>, Arvekap<sup>®</sup>) - triptorelin embonate (INN) = triptorelin pamoate (USAN)



hormonal secretions by the testes and ovaries. Debiopharm, which holds the patent to the pamoate formulations of Decapeptyl<sup>®</sup>, granted Ipsen an exclusive licence to market Decapeptyl<sup>®</sup> within the European Union and in certain other countries. Decapeptyl<sup>®</sup> contains a formulation that was initially developed and continues to be used mainly in the treatment of advanced metastatic prostate cancer. Additional indications have been subsequently developed (uterine fibroids, endometriosis, in vitro fertilisation, precocious puberty) in some countries. Decapeptyl<sup>®</sup> is available in monthly or quarterly sustained-release formulations, as well as a daily formulation. Decapeptyl<sup>®</sup>'s sales in 2009 amounted to more than € 250 million.

#### **About Somatuline<sup>®</sup> Autogel<sup>®</sup>**

The active substance in Somatuline<sup>®</sup> and Somatuline<sup>®</sup> Autogel<sup>®</sup> is lanreotide, a somastatin analogue that inhibits the secretion of several endocrine, exocrine and paracrine functions. It is particularly effective in inhibiting the secretion of growth hormones and certain hormones secreted by the digestive system. Somatuline<sup>®</sup> and Somatuline<sup>®</sup> Autogel<sup>®</sup> are sustained-release formulations for injection containing lanreotide. As far as Ipsen is aware, this is the first semi-solid formulation for injection without any excipient, since the active substance itself controls the sustained release. Somatuline<sup>®</sup> was initially developed and continues to be used for the treatment of acromegaly and was subsequently developed for the treatment of symptoms associated with neuroendocrine tumours (particularly of a carcinoid type). Somatuline<sup>®</sup> was initially launched in France in 1995. At 31 December 2009, sales of Somatuline<sup>®</sup> and Somatuline<sup>®</sup> Autogel<sup>®</sup> amounted to almost € 140 million and the drugs were marketed in over 45 countries (including 26 in Europe) for the treatment of acromegaly and neuroendocrine tumours.

#### **About Increlex<sup>®</sup>**

The active substance in Increlex<sup>®</sup> is a recombinant insulin-like growth factor of human origin (IGF-1). IGF-1 is the direct hormonal mediator of stature and bone growth and must be present for normal growth of bones and cartilage in children. In severe primary IGF-1 deficiency, children's serum IGF-1 levels are low despite the presence of normal or elevated GH levels. If the IGF-1 is not present in sufficient quantities, the child will not reach a normal stature. In October 2006, Tercica Inc. granted Ipsen the rights to develop and market Increlex<sup>®</sup> worldwide, with the exception of the United States, Japan, Canada, the Middle East and Taiwan. Ipsen's acquisition of Tercica in 2008 gave it full access to this molecule (IGF-1). The only indication filed for Increlex<sup>®</sup> is the treatment of severe primary IGF-1 deficiency in children and adolescents. Increlex<sup>®</sup> has been marketed in the United States since the beginning of 2006. It was granted orphan drug status by the EMEA on 5 April 2006 and marketing authorisation in the European Union on 9 August 2007. Increlex<sup>®</sup> is currently marketed by Ipsen in most European countries. Increlex<sup>®</sup>'s sales in 2009 were close to € 21 million.

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### **About Invida**

Invida improves the lives of patients in Asia by commercializing differentiated pharmaceutical products of superior quality - the result of which will allow all our stakeholders to prosper. We do this through our proven brand marketing and sales know-how, strong expertise across a number of key therapeutic categories and deep experience in all critical Asian markets. Comprehensive functional capabilities provide rapid market access delivered by our passionate team of professionals.

With more than 4,000 employees in 13 markets in Asia Pacific, Invida operates across the commercial value chain from regulatory approval and product launch to lifecycle management. We manage a portfolio of proprietary healthcare brands as well as licensed products from small biotech firms and large multinational companies. Partnering is a critical component of Invida's business model. We collaborate closely with our partners in developing effective strategies and put our extensive experience behind maximizing the potential of the assets entrusted to us.

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## **Ipsen's partner Roche announces that Taspoglutide meets its primary endpoint in a key phase III clinical trial**

**Taspoglutide demonstrates superiority in HbA1c change versus placebo as add-on to metformin and pioglitazone**

**Paris (France), 29 April 2010** - Ipsen (Euronext: FR0010259150; IPN), a global biopharmaceutical group, today announced that its partner Roche has disclosed results of the phase III T-emerge 3 study in patients with diabetes with taspoglutide, the first once weekly glucagon-like peptide-1 (GLP-1) analogue based on a human sequence. Taspoglutide originating from Ipsen's research is developed by Roche.

The results of T-emerge 3 showed that taspoglutide demonstrated superiority in HbA1c change versus placebo following 24 weeks of treatment. The study analysis included 326 patients, randomized into three arms (taspoglutide 10 mg once weekly, taspoglutide 20 mg once weekly and placebo).

In this study taspoglutide was generally well tolerated and the most frequently reported adverse events among taspoglutide treated patients were nausea and vomiting.

In addition to the already released T-emerge 1, T-emerge 2, T-emerge 4, T-emerge 5 and T-emerge 7 studies, data from T-emerge 3 will be submitted for presentation at upcoming international scientific meetings. A further two T-emerge Phase III trials exploring taspoglutide in patients with diabetes are ongoing.

### **About T-emerge 3**

T-emerge 3 is a combination therapy (add on to metformin and pioglitazone), double blind, placebo controlled, 24 week core study, to demonstrate superiority versus placebo, involving 326 patients equally randomised into three arms (taspoglutide at doses of 10 mg and 20 mg once weekly, and placebo). All patients continue into the 28-week long-term extension on taspoglutide.

### **About the T-emerge Program**

Roche's T-emerge Phase III clinical trials are designed as multicenter, multi-country, randomized, controlled (active or placebo), double-blind and open studies. Over 6,000 patients will be enrolled in the eight studies that comprise the T-emerge program. Studies include two parallel taspoglutide arms including 10 mg once weekly and 10 mg once weekly titrated up to 20 mg once weekly after 4 weeks. Four of the eight studies have active comparators, including exenatide, sitagliptin, insulin glargine and pioglitazone.



### **About Taspoglutide (R1583)**

Taspoglutide was selected from a family of human once-weekly long-acting glucagon-like peptide-1 (GLP-1) analogues with structural modifications which confer intrinsic controlled release properties. Ipsen is the originator of the concept of matrix free sustained release formulation applied to therapeutic peptides and proteins. Taspoglutide is being developed, by Roche, as a novel and innovative treatment for patients with type 2 diabetes mellitus, the fourth leading cause of death in most developed countries. The structure of the molecule is similar to that of the natural human hormone GLP-1, and has the potential for intervals of up to two weeks in between administration without the use of a matrix.

### **About Diabetes**

Diabetes is a disease characterized by excess blood glucose due to a deficiency in insulin availability and/or resistance to its action. Type 2 diabetes accounts for 90% to 95% of all diabetes cases worldwide and occurs almost entirely in adults. Complications from diabetes, such as coronary artery and peripheral vascular disease, stroke, diabetic neuropathy, amputations, renal failure and blindness, are resulting in increasing disability, reduced life expectancy and enormous health cost for virtually every society. According to current estimates by the World Health Organization, the number of people with diabetes is set to more than double in the next 20 years to over 300 million by the year 2025.

### **About the agreement**

Roche exercised its licensing option for taspoglutide from Ipsen in 2006 and acquired exclusive worldwide rights to develop and market taspoglutide, except in Japan where these rights are shared with Teijin and in France where Ipsen has elected to retain co-marketing rights.

### **About Ipsen**

Ipsen is a global biopharmaceutical group with total sales in excess of 1 billion euros in 2009, and total worldwide staff of more than 4,400. Its strategy is based on fast growing specialty care drugs in oncology, endocrinology, neurology and hematology, and primary care drugs, which significantly contribute to research financing. This strategy is also supported by an active policy of partnerships. Ipsen's specific Research & Development (R&D) centers and peptide & protein engineering platform give the Group a competitive edge. Almost 900 people are dedicated to the discovery and development





of innovative drugs for patient care. In 2009, R&D spend reached close to €200 million, representing more than 19% of total Group sales. Ipsen's shares are traded on Segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150). Ipsen's shares are eligible to the "Service de Règlement Différé" ("SRD") and the Group is part of the SBF 120 index. For more information on Ipsen, visit our website at [www.ipsen.com](http://www.ipsen.com).

### **Ipsen Forward Looking Statement**

The forward-looking statements, objectives and targets contained herein are based on the Group's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by the Group. These targets depend on conditions or facts likely to happen in the future, and not exclusively on historical data. Notably, future currency fluctuations may negatively impact the profitability of the Group and its ability to reach its objectives. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties. The Group does not commit nor gives any guarantee that it will meet the targets mentioned above. Furthermore, the Research and Development process involves several stages each of which involve the substantial risk that the Group may fail to achieve its objectives and be forced to abandon its efforts with regards to a product in which it has invested significant sums. Therefore, the Group cannot be certain that favourable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. The Group also depends on third parties to develop and market some of its products which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to the Group's activities and financial results. The Group expressly disclaims any obligation or undertaking to update or revise any forward looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. The Group's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers.

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Press release

## Ipsen's first quarter 2010 sales

- Drug sales up 6.2% year on year at constant currency
  - Strong sales growth of Specialty care products:
    - +16.4% year-on-year at constant currency
      - All Specialty care products growing double-digit
      - Weight of Specialty Care nears two thirds of Ipsen's total drug sales
- Dynamic growth in North America: + 35.3% year-on-year in local currency
  - Sustained growth outside the major Western European countries:
    - +12.9% year-on-year at constant currency
  - Full-year 2010 sales objectives confirmed

Paris (France), 3 May 2010 - Ipsen (Euronext: IPN) reported today its sales for the first quarter 2010.

### First quarter 2010 unaudited IFRS consolidated sales

(in million euros)	2010	2009	% Change	% Change at constant currency
<b>SALES BY REGION</b>				
Major Western European countries	138.3	138.7	(0.2)%	(0.4)%
Other European countries	65.6	50.8	29.1%	28.2%
North America	9.9	7.8	26.6%	35.3%
Rest of the world	52.3	54.5	(3.9)%	(4.4)%
<b>Group Sales</b>	<b>266.2</b>	<b>251.8</b>	<b>5.7%</b>	<b>5.6%</b>
<b>SALES BY THERAPEUTIC AREA</b>				
Specialty Care	168.5	143.8	17.1%	16.4%
Primary care	89.5	98.9	(9.5)%	(9.0)%
<b>Total Drug Sales</b>	<b>258.0</b>	<b>242.8</b>	<b>6.3%</b>	<b>6.2%</b>
<b>Drug-related Sales<sup>1</sup></b>	<b>8.2</b>	<b>9.0</b>	<b>(9.0)%</b>	<b>(9.5)%</b>
<b>Group Sales</b>	<b>266.2</b>	<b>251.8</b>	<b>5.7%</b>	<b>5.6%</b>

Commenting on the first quarter performance, **Jean-Luc Bélingard, Chairman and Chief Executive Officer of Ipsen** said: "Ipsen's specialty care franchise is more than ever confirming its high growth potential and has passed a landmark, as it now represents nearly two thirds of Ipsen's total drug sales. Our three therapeutic areas have grown double-digit this quarter, with oncology, endocrinology and neurology up 11.4%, 23.3% and 16.0% at constant currency respectively. In that context, the launch of the new Decapeptyl<sup>®</sup> 6-month formulation in France and soon throughout Europe, and our entry in the US, epitomized by the recent launch of Dysport<sup>®</sup> in this country are key milestones that will allow the

<sup>1</sup> Drug related sales correspond to sales of active ingredients and raw materials (eg Ginkgo Biloba extract, EGb 761<sup>®</sup>) and are subject to a high volatility from one quarter to another, making comparisons more difficult.



Group to continue to grow Specialty Care very dynamically in the years to come.” Jean-Luc Bélingard added: “In parallel, over the same period, Ipsen has significantly leveraged its R&D pipeline, notably through several key partnerships with Inspiration in hematology, Rhythm in metabolic disorders, GTx in oncology and Dicerna in cutting edge siRNA technologies.” Jean-Luc Bélingard concluded: “In the near future, capitalizing on these positive developments, Ipsen will continue to progress its rich R&D pipeline, optimize the contribution of its presence in primary care and strengthen its R&D organization.”

### **First quarter 2010 sales highlights**

**Consolidated Group sales** reached €266.2 million, up 5.7% year-on-year.

**Drug sales** reached €258.0 million, up 6.3% year-on-year or 6.2% excluding foreign exchange impacts. This performance was driven by strong **Specialty Care sales**, with all products growing double digit: oncology, endocrinology and neurology grew 11.4%, 23.3% and 16.0% excluding foreign exchange impacts respectively over the period. Specialty care sales reached €168.5 million up 17.1% year-on-year, and its relative weight in total drug sales grew sharply to 65.3% from 59.3% a year earlier. **Primary Care sales** reached €89.5 million, down 9.5% year-on-year, impacted by slower sales in France notably.

Sales in **Major Western European countries** amounted to €138.3 million, slightly down 0.2% year-on-year. Despite a tougher competitive environment, notably in the French primary care landscape, sales were driven by the Group's dynamic speciality care products. Sales in this region represented 52.0% of total sales compared with 55.1% a year earlier.

Sales generated in the **Other European countries** reached €65.6 million, up 29.1% year-on-year from a low first quarter 2009. Growth was fuelled notably by Nordic countries, and by Russia and other Eastern European countries recovering from their low performance in the first quarter 2009. The relative weight of the sales in this region was up sharply to 24.7% of total consolidated Group sales, from 20.2% a year earlier.

Sales generated in **North America** reached €9.9 million, up 26.6% year-on-year or up 35.3% excluding foreign exchange impacts. This reflected a sustained and dynamic growth of all products and notably Somatuline<sup>®</sup>, up 51.9% year-on-year excluding foreign exchange impacts. Dysport<sup>®</sup>, which was launched in the US in late 2009, achieved its first commercial sales over the period after a successful sampling campaign.

Sales generated in countries in the **Rest of the World** reached €52.3 million, down 4.4% year-on-year excluding foreign exchange impacts. This region was negatively impacted by a change in importation regulations in Algeria at the end of 2009 which affected the timing of local sales, while in Brazil, for technical reasons the first quarter 2009 represented a high baseline. In addition the region was also affected by slower sales in China, notably as a result of the progressive implementation of the Essential Drug List, affecting the volume as well as the seasonality of the sales of Smecta<sup>®</sup>, which for the time being does not participate in this programme. Sales in the Rest of the World represented 19.7% of total consolidated Group sales, against 21.6% a year earlier.



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## APPENDICES

### Risk factors

The Group carries out business in an environment which is undergoing rapid change and exposes its operations to a number of risks, some of which are outside its control. The risks and uncertainties set out below are not exhaustive and the reader is advised to refer to the Group's 2009 Registration Document available on its website ([www.ipsen.com](http://www.ipsen.com)).

- The Group is dependent on the setting of prices for medicines and is vulnerable to the possible lowering of the reimbursement rate of certain of its products or to their possible withdrawal from the list of reimbursable products by public or private payers in the countries where it does business. In general terms, the Group is faced with uncertainty in relation to the prices set for all its products, in so far as medication prices have come under severe pressure over the last few years as a result of various factors, including the tendency for governments and private medical insurance organisations to lower prices or reimbursement rates for certain drugs marketed by the Group in the countries in which it operates, or even to remove those drugs from lists of reimbursable drugs.
- The Group depends on third parties to develop and market some of its products, which generates substantial royalties for the Group, but these third parties could behave in ways which cause damage to the Group's business. The Group cannot be certain that its partners will fulfil their obligations and it might be unable to obtain any benefit from those agreements. A default by any of the Group's partners could result in some of the Group's products generating lower revenues than expected. Such situations could have a negative impact on the business of the Group, its financial situation or its results.
- Actual results may depart significantly from the objectives set by the management given that a new product can appear to be promising at a development stage or after clinical trials but never be launched on the market or be launched on the market but fail to sell notably for regulatory or competitive reasons.
- The Group's competitors could infringe its patents or circumvent them through design innovations. In order to prevent infringements, the Group could engage in patent litigation which is costly and time-consuming. It is difficult to monitor the unauthorised use of the Group's intellectual property rights and it could find itself unable to prevent the unlawful appropriation of its intellectual property rights.
- The Group must deal with or may have to deal with competition (i) from generic products in particular for some of the Group's products that do not benefit from any patent protection, such as Forlax<sup>®</sup> or Smecta<sup>®</sup> for example (ii) products which, although they are not strictly identical to the Group's products or which have not demonstrated their bioequivalence, may obtain a marketing authorisation for indications similar to those of the Group's products pursuant to the bibliographic reference regulatory procedure (well established medicinal use) before the patents protecting its products expire, in particular Tanakan<sup>®</sup>. To try to avoid such situations or reduce their impact, the Group could, where possible, bring legal actions against the counterfeiters in order to protect its rights. However, such a situation could result in the Group losing market share which could affect its current level of growth in sales or profitability.
- Third parties might claim the benefit of intellectual property rights in respect to the Group's inventions. The Group collaborates with various third parties (including universities and other public or private entities), and exchanges in this context information and data in various forms relating to the research, development, manufacture and marketing of its products with these third parties. Despite the precautions taken by the Group with regard to these third parties, in particular of a contractual nature, they (or certain of their members or affiliates) could claim ownership of intellectual property rights arising from the work carried out by their employees or any other intellectual property right relating to the Group's products or to compounds in developments.
- The Group's strategy includes acquiring companies or assets which may enable or facilitate access to new markets, research projects or geographical regions or enable it to realise synergies with its existing businesses. Should the growth prospects or earnings potential of such assets as well as a change in valuation assumptions change materially at any point in time and significantly depart from initial assumptions, the Group might be under the obligation to adjust the values of these assets in its balance sheet, thereby negatively impacting its earnings and financial situation.

- In certain countries exposed to significant public deficits, and where it sells its drugs notably to public hospitals, the Group could be experience discounts or lengthened payment terms or difficulties in recovering its receivables in full. In Greece notably, which represented in 2009 approximately 2.0% of its consolidated sales, and where payment terms from public hospitals are particularly long, the Group is closely monitoring the current situation. More generally, the Group may also be unable to purchase sufficient credit insurance to protect itself adequately against the risk of payment default from certain customers worldwide. Such situations could negatively impact the Group's activities, financial situation and earnings.
- In the normal course of business, the Group is or may be involved in legal or administrative proceedings. Financial claims are or may be brought against the Group in connection with some of these proceedings. The main legal disputes in which the Group is involved include a dispute initiated in Louisiana (USA) by Tulane University (New Orleans, USA) and a member of its faculty (hereinafter collectively referred to as "Tulane") against Biomeasure, a subsidiary of the Ipsen Group (based in Milford, MA, USA), for breach of contract and violation of certain patent rights relative to Taspoglitide, the rights to which had been granted under licence to Roche in July 2006. The Group is reviewing its response to these proceedings with its lawyers. If Tulane were to prevail in spite of Ipsen's arguments in its defence against these allegations, Ipsen could be forced to pay Tulane royalties and/or other amounts corresponding to intellectual property rights.

### Major developments

During the first quarter 2010, major developments included:

- On January 21, 2010 – Ipsen and Inspiration Biopharmaceuticals announced that they had entered into a partnership to create a world leading hemophilia franchise.
- Since February 2010, the 6-month formulation of Decapeptyl<sup>®</sup>, 22.5 mg triptorelin, is marketed in France having received the green light in November 2009 by European regulators in the framework of a decentralised procedure in nine countries for the treatment of locally advanced or metastatic prostate cancer.
- On 5 March 2010, Ipsen and Menarini announced the launch of Adenuric<sup>®</sup> (febuxostat) in France where they will co-promote the drug. Other launches by Menarini are expected shortly, notably in the United Kingdom, Germany and Ireland.
- On 12 March 2010, Ipsen and Rhythm, a biotechnology company developing peptide therapeutics for metabolic diseases, concluded a licensing agreement for peptide therapeutics targeting obesity, metabolic disorders and gastrointestinal disorders. Under the terms of the agreement, Ipsen has granted Rhythm an exclusive worldwide license for research, development and commercialisation of its melanocortin and ghrelin programmes originating from Ipsen research.
- On 15 March 2010, Ipsen announced the start of two international phase II clinical studies to evaluate the efficacy and safety of BIM 23A760 in two groups of patients, one suffering from carcinoid syndrome due to neuroendocrine tumours, the other from acromegaly.
- On 23 March 2010, Ipsen and GTx Inc. announced the expansion of their partnership for the development and commercialization of toremifene 80 mg for the reduction of fractures in men with advanced prostate cancer on androgen deprivation therapy (ADT) and toremifene 20 mg for the prevention of prostate cancer in high risk patients with High Grade Prostatic Intraepithelial Neoplasia lesions (HGPIN).
- On 24 March 2010, Ipsen announced that it has been informed that its controlling shareholder Mayroy completed an institutional private placement of 4,029,979 shares representing approximately 4.8% of Ipsen's share capital.
- On 29 March 2010, Ipsen announced that it filed with the *Autorité des Marchés Financiers* (AMF) its *Document de Référence 2009*.
- On 30 March 2010, Ipsen and Dicerna Pharmaceuticals, Inc. (Dicerna) announced that the two companies have entered into an exclusive research collaboration agreement to leverage their expertise in Dicer Substrate siRNA (DsiRNA) research and peptide engineering. The companies will develop novel conjugates of Dicerna's DsiRNA molecules and Ipsen's peptide targeting vectors in the therapeutic areas of oncology and endocrinology.

European governments have decided various measures to reduce public healthcare spending growth. In this context, 2010 sees the acceleration of new measures taken by governments that may affect the Group's sales and earnings in 2010 and beyond.

Countries most affected by the crisis such as Romania, Czech Republic and Greece have announced new drastic price cuts through international reference pricing to lowest prices in Europe. Romania has implemented an additional 8% sales tax while Czech Republic and Greece have announced their intentions to limit the reimbursement amount by therapeutic class. Other Western European countries, less affected by the crisis, have also announced drastic measures such as Netherlands reference pricing leading to price cuts ranging from 20 to 45% for Ipsen products, Introduction of a 4% sales tax in Ireland, Germany increase of their sales tax from 6 to 16% and Spain looking for a 10% cut in the drugs bill mainly through the implementation of a 30% price cut on products for which a generic or a biosimilar is available in at least one country in Europe. In France, the reimbursement rate of certain medicines, including Tanakan<sup>®</sup>, whose rendered medical service were assessed as "low" or "insufficient" by the *Haute Autorité de Santé* were cut to 15% from 35%, on April 16, 2010.

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## Comparison of consolidated sales for the first quarter 2010 and 2009

### Sales by geographical area

Group sales by geographical area for the first quarter 2010 and 2009 were as follows:

(in million euros)	2010	2009	% Change	% Change at constant currency
France	75.8	78.2	(3.2)%	(3.2)%
Spain	15.8	15.2	3.7%	3.7%
Italy	20.2	18.8	7.4%	7.4%
Germany	16.5	16.5	(0.2)%	(0.2)%
United Kingdom	10.1	9.9	2.3%	0.1%
<b>Major Western European countries</b>	<b>138.3</b>	<b>138.7</b>	<b>(0.2)%</b>	<b>(0.4)%</b>
<b>Other European countries</b>	<b>65.6</b>	<b>50.8</b>	<b>29.1%</b>	<b>28.2%</b>
<b>North America</b>	<b>9.9</b>	<b>7.8</b>	<b>26.6%</b>	<b>35.3%</b>
Asia	27.7	28.7	(3.6)%	(2.3)%
Other countries in the rest of the world	24.6	25.7	(4.3)%	(6.6)%
<b>Rest of the world</b>	<b>52.3</b>	<b>54.5</b>	<b>(3.9)%</b>	<b>(4.4)%</b>
<b>Group Sales</b>	<b>266.2</b>	<b>251.8</b>	<b>5.7%</b>	<b>5.6%</b>
of which : Drug sales	258.0	242.8	6.3%	6.2%
Drug-related Sales	8.2	9.0	(9.0)%	(9.5)%

For the first quarter 2010, sales generated in the **Major Western European countries** amounted to €138.3 million, slightly down 0.2% year-on-year (first quarter 2009, €138.7 million). Dynamic sales growth of specialty care products in France, Italy, Germany and Spain were more than offset by the consequences of a tougher competitive environment, notably in the French primary care landscape. As a result, sales in this region at the end of the first quarter 2010 represented 52.0% of total sales, compared with 55.1% at the same period a year earlier.

**France** – For the first quarter 2010, sales reached €75.8 million, down 3.2% year-on-year (first quarter 2009, €78.2 million), despite the good performances of Somatuline<sup>®</sup>, NutropinAq<sup>®</sup> and, most importantly, Decapeptyl<sup>®</sup>, following the launch of a new 6-month formulation in February. This performance was more than offset by a decrease in sales of Primary Care products, with the launch of a generic competitor in March 2009 negatively impacting the sales of Forlax<sup>®</sup>, a lower level of pathology impacting the sales of Smecta<sup>®</sup> and the announcement of the decrease of the reimbursement rate (to 15% from 35% for the entire therapeutic class) impacting the sales of Tanakan<sup>®</sup>. The relative weight of France in the Group's consolidated sales thus continued to decline at the end of the first quarter 2010, representing 28.5% of total Group sales against 31.1% a year earlier.

**Spain** – For the first quarter 2010, sales reached €15.8 million, up 3.7% year-on-year (first quarter 2009, €15.2 million) fuelled by a double digit growth of Somatuline<sup>®</sup> and Increlex<sup>®</sup>, partly offset by a slowdown of Decapeptyl<sup>®</sup>, pending the launch of Ipsen's new 6-month formulation. Sales in Spain represented 5.9% of total group sales, against 6.0% a year earlier.

**Italy** – For the first quarter 2010, sales reached €20.2 million, up 7.4% year-on-year (first quarter 2009, €18.8 million), driven by the good performances of Somatuline<sup>®</sup>, Decapeptyl<sup>®</sup> and

Increlex<sup>®</sup>. The weight of Italy in the Group's consolidated sales was stable at 7.6% of total Group sales at the end of the first quarter 2010, against 7.5% a year earlier.

**Germany** – For the first quarter 2010, sales reached €16.5 million, down 0.2% year-on-year (first quarter 2009, €16.5 million). Solid drug sales growth with strong performances of Decapeptyl<sup>®</sup>, Nutropin<sup>®</sup>, Somatuline<sup>®</sup> and Increlex<sup>®</sup> was offset by a decrease in Dysport<sup>®</sup> sales, mainly due to the transfer of sales in aesthetic use to the Group's partner Galderma, in the context of the launch of Azzalure<sup>®</sup> in this country. In the first quarter 2010, sales in Germany represented 6.2% of total Group sales against 6.6% a year earlier.

**United Kingdom** – For the first quarter 2010, sales reached €10.1 million, up 2.3% year-on-year (first quarter 2009, €9.9 million) or up 0.1% excluding foreign exchange, impacted by the transfer of sales in aesthetic use to the Group's partner Galderma, in the context of the launch of Azzalure<sup>®</sup> in this country. Over the first quarter 2010, United Kingdom represented 3.8% of total Group sales against 3.9% in 2009.

For the first quarter 2010, sales generated in the **Other European countries** reached €65.6 million, up 29.1% year-on-year (up 28.2% year-on-year excluding foreign exchange impacts), fuelled by sustained growth, notably in Nordic countries while the situation in certain Eastern European countries and in Russia was sharply up compared to a low first quarter 2009. Hence, over the first quarter 2010, sales in this region showed strong growth, representing 24.7% of total consolidated Group sales, against 20.2% a year earlier.

For the first quarter 2010, sales generated in **North America** reached €9.9 million, up 26.6% a year earlier or up 35.3% excluding foreign exchange impacts, reflecting a sustained and dynamic growth of all products. Somatuline grew 51.9% excluding foreign exchange impacts over the period. Dysport<sup>®</sup>, launched in late 2009 in cervical dystonia, still had limited sales over the period following a successful sampling campaign, leading to higher than expected sample requests, reflecting physicians' interest for the product. Sales in North America represented 3.7% of total consolidated Group sales, against 3.1% a year earlier.

Sales generated in countries in the **Rest of the World** reached €52.3 million, down 4.4% year-on-year excluding foreign exchange impacts. This region was negatively impacted by a change in importation regulations in Algeria at the end of 2009 which affected the timing of local sales, while in Brazil, for technical reasons the first quarter 2009 represented a high baseline. In addition the region was also affected by slower sales in China, notably as a result of the progressive implementation of the Essential Drug List, affecting the volume as well as the seasonality of the sales of Smecta<sup>®</sup>, which for the time being does not participate in this programme. Sales in the Rest of the World represented 19.7% of total consolidated Group sales, against 21.6% a year earlier.

### Sales by therapeutic area and by products

The following table shows sales by products for the first quarter and 2010 and 2009:

(in million euros)	2010	2009	% Change	% Change at constant currency
Oncology	68.4	61.4	11.5%	11.4%
of which Decapeptyl®	68.4	61.4	11.5%	11.4%
Endocrinology	57.9	46.8	23.8%	23.3%
of which Somatuline®	40.7	32.4	25.7%	24.5%
NutropinAq®	11.4	9.3	21.5%	20.2%
Increlex®	5.8	4.7	24.2%	31.2%
Neurology	42.1	35.7	18.2%	16.0%
of which Dysport®	40.8	34.6	17.9%	15.5%
Apokyn®	1.3	1.1	26.8%	35.6%
<b>Specialty Care</b>	<b>168.5</b>	<b>143.8</b>	<b>17.1%</b>	<b>16.4%</b>
Gastroenterology	43.9	52.0	(15.7)%	(14.7)%
of which Smecta®	25.2	29.5	(14.9)%	(13.0)%
Forlax®	9.3	12.8	(27.3)%	(27.4)%
Cognitive disorders	23.5	25.7	(8.6)%	(8.6)%
of which Tanakan®	23.5	25.7	(8.6)%	(8.6)%
Cardiovascular	18.1	18.1	0.0%	0.0%
of which Nisis® and Nisisco®	13.7	12.6	8.9%	8.9%
Ginkor Fort®	3.2	3.8	(15.8)%	(15.8)%
Other Primary Care products	4.0	3.1	30.0%	30.0%
of which Adrovanse™	3.2	2.2	47.9%	47.9%
<b>Primary Care</b>	<b>89.5</b>	<b>98.9</b>	<b>(9.5)%</b>	<b>(9.0)%</b>
<b>Total Drug sales</b>	<b>258.0</b>	<b>242.8</b>	<b>6.3%</b>	<b>6.2%</b>
<b>Drug-related sales</b>	<b>8.2</b>	<b>9.0</b>	<b>(9.0)%</b>	<b>(9.5)%</b>
<b>Group Sales</b>	<b>266.2</b>	<b>251.8</b>	<b>5.7%</b>	<b>5.6%</b>

For the first quarter 2010, sales of **Specialty Care products** reached €168.5 million, up 17.1% year-on-year (first quarter 2009, €143.8 million) or up 16.4% excluding foreign exchange impacts. Oncology, endocrinology and neurology grew 11.4%, 23.3% and 16.0% respectively over the period and at constant currency. The relative weight of Specialty Care products in total Group sales grew sharply to 63.3%, from 57.1% a year earlier.

**In the oncology franchise**, sales of **Decapeptyl®** reached €68.4 million for the first quarter 2010, up 11.5% year-on-year, fuelled by solid growth in France - following the launch of a new 6 month formulation - Germany and China due to a lower first quarter 2009. This first quarter 2010 performance is compared with a low first quarter 2009, notably in Russia and Poland, which were impacted by strong currency movements and subsequent supply chain disruptions in the context of the financial crisis. For the first quarter 2010, sales in oncology represented 25.7% of total Group sales, against 24.4% a year earlier.

**In the endocrinology franchise**, sales reached €57.9 million for the first quarter 2010, up 23.8% year-on-year (first quarter 2009, €46.8 million), or up 23.3% excluding foreign exchange impacts, reflecting a

good performance of all products. For the first quarter 2010, sales in endocrinology represented 21.8% of total Group sales, against 18.6% a year earlier.

**Somatuline<sup>®</sup>** – For the first quarter 2010, sales reached €40.7 million, up 25.7% year-on-year (first quarter 2009, €32.4 million), or up 24.5% excluding foreign exchange impacts, fuelled by strong volume growth in France and Poland. In the US, Somatuline<sup>®</sup> continued to perform well, growing 41.1% year-on-year or 50.8% excluding foreign exchange impacts achieving a market share above 20% during the quarter<sup>1</sup>.

**NutropinAq<sup>®</sup>** – For the first quarter 2010, sales reached €11.4 million, up 21.5% year-on-year (first quarter 2009, €9.3 million), or up 20.2% excluding foreign exchange impacts, driven by strong performances in Germany, France and Austria, where the drug is promoted alongside Increlex<sup>®</sup>.

**Increlex<sup>®</sup>** – For the first quarter 2010, sales reached €5.8 million, up 24.2% year-on-year (first quarter 2009, €4.7 million), or up 31.2% excluding foreign exchange impacts. In the US, Increlex<sup>®</sup> growth continues to be driven by patient intake, which can be estimated to 890 in February 2010 versus 753 in February 2009.

**In the neurology franchise**, sales reached €42.1 million for the first quarter 2010, up 18.2% year-on-year (first quarter 2009, €35.7 million), or up 16.0% excluding foreign exchange impacts. Sales in neurology represented 15.8% of total Group sales, against 14.2% a year earlier.

**Dysport<sup>®</sup>** – For the first quarter 2010, sales reached €40.8 million, up 17.9% year-on-year (first quarter 2009, €34.6 million), or up 15.5% excluding foreign exchange impacts, fuelled notably by strong growth in Russia, Turkey, Poland and Australia, slightly offset by the consequences of the launch of Azzalure in Germany, France and the UK for aesthetic use by Galderma, while in Brazil, the first quarter 2009 had benefited from a positive technical stocking effect. Dysport<sup>®</sup>, launched in late 2009 in cervical dystonia, still had limited sales over the period following a successful sampling campaign, leading to higher than expected sample requests, reflecting physicians' interest for the product.

**Apokyn<sup>®</sup>** – For the first quarter 2010, sales reached €1.3 million in the United States, up 26.8% compared with the same period in 2009, or up 35.6% excluding foreign exchange impacts.

In the first quarter 2010, sales of **Primary Care products** amounted to €89.5 million, down 9.5% year-on-year (first quarter 2009, €98.9 million), or down 9.0% excluding foreign exchange impacts, mainly due to decreasing sales in France. French Primary care sales represented 52.7% of total Primary Care sales in the first quarter 2010 compared with 54.8% a year earlier while at the same time total Primary Care sales represented 33.6% of the Group's consolidated sales over the period, sharply down from 39.3% a year before.

**In gastroenterology**, sales reached €43.9 million in the first quarter 2010, down 15.7% year-on-year (first quarter 2009, €52.0 million), or down 14.7% excluding foreign exchange impacts.

**Smecta<sup>®</sup>** – For the first quarter 2010, sales reached €25.2 million, down 14.9% year-on-year (first quarter 2009, €29.5 million), or down 13.0% excluding foreign exchange impacts, due to lower sales in France, subsequent to a lower level of seasonal pathology during the first quarter this year. In China, the progressive implementation of the Essential Drug List, affecting the sales of Smecta<sup>®</sup>, which for the time being does not participate in this programme. In Algeria, technical importation regulation changes and in Russia, seasonal stocking effects, both impacted sales. Sales of Smecta outside France represented 74.2% of total Smecta sales in the first quarter 2010 compared with 69.5% a year earlier.

**Forlax<sup>®</sup>** – For the first quarter 2010, sales reached €9.3 million, down 27.3% year-on-year (first quarter 2009, €12.8 million), following the launch of a generic competitor in France in March 2009. During the first quarter 2010, France represented 59.8% of the overall sales of the product, sharply down from 77.8% a year ago.

<sup>1</sup> Source : Wolters Kluwer

**In the cognitive disorders area**, sales of **Tanakan®** for the first quarter 2010 reached €23.5 million, down 8.6% year-on-year (first quarter 2009, €25.7 million), negatively impacted by slower sales in Russia and in France, where distributors anticipated the decrease in reimbursement rate, finally implemented in April 2010. In China, sales were also affected by a technical destocking following a change in the Group's distribution model from local distributor to direct sales, and in Algeria, importation regulations changes impacted the sales dynamics. Sales of **Tanakan®** in France over the first quarter 2010 represented 54.6% of total product sales compared with 53.4% a year earlier.

**In the cardiovascular area**, sales in the first quarter 2010 amounted to €18.1 million, flat year-on-year, with sales of **Nisis®** and **Nisisco®** up 8.9% year-on-year, amounting to €13.7 million.

**Other primary care products** sales reached €4.0 million for the first quarter 2010, against €3.1 million a year earlier, with sales of **Adrovance®** contributing to €3.2 million, up 47.9% year-on-year.

For the first quarter 2010, **drug-related sales (active ingredients and raw materials)** reached €8.2 million, down 9.0% mainly due to a slowdown of sales of Ginkgo biloba extract (**EGb 761®**) in Germany.

Press Release

**Combined Shareholders' Meeting of Ipsen S.A.**  
**held on 28 May 2010**

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**Adoption of all resolutions submitted to the Shareholders' vote**

**Paris (France), 28 May 2010** – Ipsen's (Euronext: IPN) Combined Shareholders' Meeting was held today, chaired by Jean-Luc Bélingard, Chairman of the Board and Chief Executive Officer, in the presence of the Board of Directors and the Group's management.

All resolutions submitted to the Shareholders' Meeting were approved, including the distribution of a €0.75 dividend per share to be paid on June 4, 2010 (ex-dividend date June 1, 2010).

During the meeting, Jean-Luc Bélingard and Claire Giraut, Executive Vice-President, Chief Financial Officer, presented Ipsen's strategy, financial results and major events for 2009 as well as 2010 first quarter sales and outlook.

**About Ipsen**

Ipsen is a global biopharmaceutical group with total sales in excess of 1 billion euros in 2009, and total worldwide staff of more than 4,400. Its strategy is based on fast growing specialty care drugs in oncology, endocrinology, neurology and hematology, and primary care drugs, which significantly contribute to research financing. This strategy is also supported by an active policy of partnerships. Ipsen's specific Research & Development (R&D) centers and peptide & protein engineering platform give the Group a competitive edge. Almost 900 people are dedicated to the discovery and development of innovative drugs for patient care. In 2009, R&D spend reached close to €200 million, representing more than 19% of total Group sales. Ipsen's shares are traded on Segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150). Ipsen's shares are eligible to the "Service de Règlement Différé" ("SRD") and the Group is part of the SBF 120 index. For more information on Ipsen, visit our website at [www.ipsen.com](http://www.ipsen.com).

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OFFICE OF INTERNATIONAL  
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Press release

**Implementation of a Sponsored Level I  
American Depositary Receipt (ADR) program:  
A new step in Ipsen's development in the United States**

**Paris (France), 9 June 2010** – Ipsen (Euronext : FR0010259150; IPN) announced today that it has implemented a Sponsored Level I American Depositary Receipt (ADR) program initiated with Deutsche Bank, the Group's appointed depository bank for the program. ADRs will trade on the over-the-counter market in the United States under the symbol IPSEY. Each ADR represents one quarter of one ordinary share. The company's ordinary shares are listed on Compartment A on Euronext Paris under the symbol IPN.

In line with its ongoing strategy to grow and globalize its specialty care business, the Group entered the US pharmaceutical market in 2008 and now markets four field-proven products and benefits from a full US clinical development platform. More recently, further expanding the Group's global specialty care footprint, Ipsen and Inspiration Biopharmaceuticals, a US Biotech, announced a partnership to create a world leading hemophilia franchise. With endocrinology, neurology and potentially hemophilia, the Group is set to globalize three of its four specialty care franchises.

**Claire Giraut, Executive Vice-President, Chief Financial Officer of Ipsen** said: *"Since its initial public offering in December 2005, Ipsen has been highly committed to its strategy to become a leading global biopharmaceutical company, notably through a direct US specialty care presence. The Company now seeks to improve the visibility of its stock in the US, the largest pharmaceutical market in the world. We believe the addition of this sponsored level I ADR program to its existing Euronext listing in Paris will facilitate investor's access to the Company."*

**About Sponsored Level I ADR program**

ADRs are U.S. dollar-denominated negotiable instruments issued by a depository bank. They can represent a fraction of a share, a single share, or multiple shares of the foreign stock. The price of an ADR often tracks the price of the foreign stock in its home market, adjusted for the ratio of ADRs to foreign company shares, but may vary according to other factors. Level I depository receipts are the first level of sponsored ADRs that can be issued and may only be traded on the OTC market. When a company establishes a sponsored ADR, it appoints a depository bank who also acts as its US transfer agent. The majority of sponsored ADR programs currently trading are Level I programs.



## **About Ipsen**

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## **Forward Looking Statement**

The forward-looking statements, objectives and targets contained herein are based on the Group's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by the Group. These targets depend on conditions or facts likely to happen in the future, and not exclusively on historical data. Notably, future currency fluctuations may negatively impact the profitability of the Group and its ability to reach its objectives. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties. The Group does not commit nor gives any guarantee that it will meet the targets mentioned above. Furthermore, the Research and Development process involves several stages each of which involve the substantial risk that the Group may fail to achieve its objectives and be forced to abandon its efforts with regards to a product in which it has invested significant sums. Therefore, the Group cannot be certain that favourable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. The Group also depends on third parties to develop and market some of its products which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to the Group's activities and financial results. The Group expressly disclaims any obligation or undertaking to update or revise any forward looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. The Group's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers.

## **About Deutsche Bank**

Deutsche Bank is a leading global investment bank with a strong and profitable private clients franchise. A leader in Germany and Europe, the bank is continuously growing in North America, Asia and key emerging markets. With 77,053 employees in 72 countries, Deutsche Bank offers unparalleled financial services throughout the world. The bank competes to be the leading global provider of financial solutions for demanding clients creating exceptional value for its shareholders and people. [www.db.com](http://www.db.com)





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## **OBI-1 developed by Ipsen and Inspiration has obtained a positive opinion for the orphan drug status in Europe**

**Paris (France) and Laguna Niguel (CA, USA), 17 June 2010** – Ipsen (Euronext: FR0010259150; IPN) and Inspiration Biopharmaceuticals, Inc. (Inspiration) announced today that the Committee for Orphan Medicinal Products of the European Medicines Agency has issued a positive opinion on the granting of orphan drug status for OBI-1 for the treatment of hemophilia. Final adoption of the opinion is expected from the European Commission later this year and subject to it being finally granted, the orphan drug status would trigger a 10-year market exclusivity to OBI-1 in the European Union after its marketing approval. The FDA also issued an Orphan Drug Designation for OBI-1 in March 2004.

**Jean-Luc Bélingard, Chairman and Chief Executive Officer of Ipsen** said: *“Our transaction with Inspiration in late January of this year expresses Ipsen’s long term strategy to create a world leading hemophilia franchise. We are honored that the Committee for Orphan Medicinal Products of the European Medicines Agency shares our view of the medical benefit provided by OBI-1 to the hemophilia community.”*

**John Taylor, Co-Founder and Chairman of Inspiration** added: *“We are pleased with the continued progress of OBI-1 as a new, innovative therapy in the treatment of unmet medical needs in hemophilia.”*

### **About Hemophilia**

Hemophilia, congenital or acquired, is a bleeding disorder caused by low levels or absence of a protein called a coagulation factor, essential for blood clotting. The two most common forms of hemophilia are types A and B. Hemophilia A is caused by a factor VIII deficiency and occurs in ~1 out of every 5,000 male births. Hemophilia B is caused by factor IX deficiency and occurs in ~1 out of every 30,000 male births. Approximately 60% of persons with hemophilia have a severe condition, which results in frequent spontaneous bleeding episodes in addition to serious bleeding after injuries. The market for hemophilia treatment is 7.5 billion dollars annually.

### **About OBI-1**

About a third of patients with congenital hemophilia A and patients with acquired hemophilia develop an immune reaction to human forms of FVIII (hFVIII) and can no longer respond to human Factor VIII. Since OBI-1 possesses low cross reactivity to anti-hFVIII antibodies, it is expected that OBI-1 can provide therapeutic benefits to patients who are not able to use hFVIII.

OBI-1, a recombinant B-domain deleted FVIII bioengineered for low cross reactivity to anti-human FVIII inhibitors based on the porcine amino acid sequence, has recently been tested in a Phase II trial. OBI-1 was administered to patients with congenital hemophilia A complicated by the presence of human FVIII inhibitors experiencing a non-life/non-limb threatening bleed. A total of 25 bleeding episodes in 9 patients were treated with OBI-1, and all were successfully controlled. One subject had a mild infusion reaction and when re-treated for a subsequent bleed the subject did not report any adverse event. Eight out of nine (89%) subjects developed anti-pFVIII antibodies following exposure to OBI-1 and in subjects receiving repeated OBI-1 treatment higher anti-pFVIII titres did not affect efficacy or safety. The study demonstrated that OBI-1 is well-tolerated and can be given as a short infusion. OBI-1 is expected to enter phase III in 2010.

### **About Ipsen**

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### **About Inspiration Biopharmaceuticals**

Inspiration Biopharmaceuticals was founded in 2004 with the mission to revolutionize treatments for hemophilia. The Company is focused on developing products that have the potential to broaden patient access to therapy, including prophylactic use. Greater access and more frequent prophylactic therapy have been shown to reduce complications of the disease and enhance patients' long-term health and quality of life. Underlying the Company's programs is a novel, proprietary manufacturing technology that allows a greater yield of high-quality protein. Inspirations' lead product candidate, IB1001 is an intravenous recombinant factor IX product for the acute and preventative treatment of bleeding in patients with hemophilia B. The development of Inspiration's lead product, IB1001 for the treatment of Hemophilia B and its earlier stage coagulation factor product candidates have been partially funded to date by Celtic Pharma, a global private equity and drug development firm.

Inspiration is utilizing its proprietary technology to develop a broad portfolio of hemophilia and bleeding disorder products that address a \$7.5 billion market worldwide, which has grown historically at a 12% CAGR. With over 130 years of combined management experience in commercializing hemophilia products at firms such as Baxter and Bayer, Inspiration has been able to rapidly and efficiently develop protein therapeutics for hemophilia.

### **Ipsen's Forward Looking Statement**

The forward-looking statements, objectives and targets contained herein are based on the Group's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by the Group. These targets depend on conditions or facts likely to happen in the future, and not exclusively on historical data. Notably, future currency fluctuations may negatively impact the profitability of the Group and its ability to reach its objectives. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties. The Group does not commit nor gives any guarantee that it will meet the targets mentioned above. Furthermore, the Research and Development process involves several stages each of which involve the substantial risk that the Group may fail to achieve its objectives and be forced to abandon its efforts with regards to a product in which it has invested significant sums. Therefore, the Group cannot be certain that favourable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. The Group also depends on third parties to develop and market some of its products which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to the Group's activities and financial results. The Group expressly disclaims any obligation or undertaking to update or revise any forward looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or



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circumstances on which any such statements are based, unless so required by applicable law. The Group's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers.

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Press release

## **Ipsen's partner Roche announces amendment of the trial protocols for the taspoglutide phase III programme**

**Paris (France), 18 June 2010** - Ipsen (Euronext: IPN – ADR: IPSEY), a global biopharmaceutical group, today announced that its partner Roche today announced the implementation of a risk mitigation plan in the taspoglutide Phase III programme. Taspoglutide, the first once weekly glucagon-like peptide-1 (GLP-1) analogue based on a human sequence, originating from Ipsen's research is developed by Roche. This compound is similar to the natural hormone GLP-1 which has a key role in blood sugar regulation.

In the Phase III studies, the incidence of hypersensitivity reactions reported as related to taspoglutide is higher than expected for the study population, although it remains uncommon (i.e. incidence < 1%). The most frequently reported symptoms in patients who developed hypersensitivity reactions were skin reactions and gastrointestinal symptoms, while cardiovascular and respiratory symptoms were less frequent. All patients recovered without complications.

Roche has identified a potential association between hypersensitivity reactions and anti-drug antibodies (ADAs). In consultation with the Food and Drug Administration (FDA), Roche has decided to implement a risk mitigation plan, which has been communicated to Health Authorities globally. The plan is designed to identify patients at potential risk of these reactions. As such, ADA levels will be routinely monitored and patients that develop pre-specified ADA levels will discontinue treatment and continue to be monitored in the trials. The continued safety of patients in the clinical development programmes remains the highest priority for Roche. Roche is committed to working with Health Authorities globally to continue the development of taspoglutide to meet the needs of patients with type 2 diabetes. Roche is investigating the cause of the hypersensitivity reactions and testing specific means to resolve this issue. The impact of this plan on the project and in particular on the timelines for regulatory filing are currently being assessed, however, a minimum of 12 to 18 months delay is anticipated.

Roche looks forward to sharing with the medical community at the forthcoming American Diabetes Association, data from five phase III trials demonstrating that taspoglutide delivered combined benefits of consistent robust glycemic control, across a wide spectrum of patients versus exenatide, sitagliptin and even the highest dose of insulin glargine used in a development program. In addition, taspoglutide was associated with a low risk of hypoglycaemia and clinically important weight loss. Over the next few weeks, Roche also expects to get the headline data on the 52-week extended trials.

### **About the T-emerge Programme**

The T-emerge Phase III clinical trial programme is designed as multicenter, multi-country, randomized, controlled (active or placebo), double-blind and open studies. Over 6,000 patients have been enrolled in the eight studies that comprise the T-emerge programme. Studies include two parallel taspoglutide arms including 10 mg once weekly and 10 mg once weekly titrated up to 20 mg once weekly after four weeks. Four of the eight studies have active comparators, including exenatide, sitagliptin, insulin glargine and pioglitazone.



### **About Taspoglutide (R1583)**

Taspoglutide was selected from a family of human once-weekly long-acting glucagon-like peptide-1 (GLP-1) analogues with structural modifications which confer intrinsic controlled release properties. Ipsen is the originator of the concept of matrix free sustained release formulation applied to therapeutic peptides and proteins. Taspoglutide is being developed, by Roche, as a novel and innovative treatment for patients with type 2 diabetes mellitus, the fourth leading cause of death in most developed countries. The structure of the molecule is similar to that of the natural human hormone GLP-1, and has the potential for intervals of up to two weeks in between administration without the use of a matrix.

### **About the agreement**

Roche exercised its licensing option for taspoglutide from Ipsen in 2006 and acquired exclusive worldwide rights to develop and market taspoglutide, except in Japan where these rights are shared with Teijin and in France where Ipsen has elected to retain co-marketing rights.

### **About Ipsen**

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### **Ipsen's Forward Looking Statement**

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filed with the French Autorité des Marchés Financiers.

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Press release

## **Encouraging results of GuidAge<sup>®</sup>, large scale European trial conducted in the prevention of Alzheimer's Dementia**

- **Primary efficacy objective (to delay conversion to Alzheimer's Dementia):**
  - Unmet in overall study population
  - Met in patients treated for a duration of at least 4 years
- **The GuidAge<sup>®</sup> study marks a milestone for future research on Alzheimer's Disease and for prevention strategies**
- **Ipsen intends to transfer a unique biobank to French Academic research**

**Paris (France), 22 June 2010** - Ipsen (Euronext: IPN; ADR: IPSEY) today announced top line results of GuidAge<sup>®</sup>, the longest (5 years) and largest (2,854 subjects) European study in the prevention of Alzheimer's Dementia (AD). This trial was conducted according to the most stringent international standards. The aim of this study was to assess the efficacy of a 5-year treatment with EGb 761<sup>®</sup> in the prevention of Alzheimer's Dementia in a population of elderly aged 70 or more, with memory complaint spontaneously expressed to their family physician and who lived at home at the inclusion in the study.

- 1. Primary efficacy objective (to delay conversion to Alzheimer's Dementia): significant difference not statistically observed in the overall study population:** during the study, 134 individuals developed Alzheimer's Dementia, including 61 patients (4.3%) in the EGb 761<sup>®</sup> group and 73 patients (5.2%) in the placebo group ( $p=0.31$ ). **However, a statistically significant difference between EGb 761<sup>®</sup> and placebo was observed in patients treated for a least 4 years:** pre-specified planned statistical analyses suggest a difference in favour of EGb 761<sup>®</sup> versus placebo on the conversion to Alzheimer's Dementia in patients treated for at least 4 years: 15 out of 947 patients (1.6%) in the EGb 761<sup>®</sup> group with treatment duration of at least 4 years converted to Alzheimer's dementia versus 29 out of 966 (3.0%) in the placebo group (statistically significant at  $p=0.03$ ).

These analyses suggest as well a statistically significant difference in favour of EGb 761<sup>®</sup> in males: 14 out of 480 males (2.9%) in the EGb 761<sup>®</sup> group converted to AD versus 32 out of 460 (7.0%) in the placebo group (statistically significant at  $p=0.007$ ).

Complementary analyses will enable to further investigate these differences.

**EGb 761<sup>®</sup>'s favourable long-term safety profile was monitored and confirmed.**

- 2. GuidAge<sup>®</sup> study marks a milestone for future research on Alzheimer's Disease and for prevention strategies**

Beyond clinical results, this major trial, which involved a total population of 2,854 patients at risk of developing Alzheimer's Disease, will provide large opportunities for further investigation by the scientific and medical communities. In particular, new perspectives were opened by the study:

- Forthcoming analyses of GuidAge<sup>®</sup> results to identify the transition from subjective memory complaint to cognitive decline and dementia up to 5 years.





- Leverage of Alzheimer's disease research through the transfer from Ipsen to French academic research of a biobank constituted along the GuidAge® trial and containing blood samples and DNA extraction from 2,107 patients.

GuidAge® is therefore one of the main scientific contribution to neurodegenerative research in line with the French Government's strategy of fostering research and prevention in Alzheimer's dementia.

**Pr. Bruno Vellas, Principal Investigator of the study, INSERM U558, Gérontopôle (Toulouse, France),** said: *"The specific characteristics of GuidAge® study are on the one hand the target population (subjects aged of at least 70 with memory complaint spontaneously expressed to their family physician), and on the second hand, the cooperation between memory clinics and a network of 658 family physicians trained in clinical research, probably responsible for the noticeable compliance in 93 % of the intention-to-treat population. The results of this clinical trial, which will have to be investigated in further studies, are encouraging and open new perspectives."*

**Dr. Patrick Mérat, Senior Vice-President, Drug Development and Chief Medical Officer, Ipsen,** said: *"Ipsen is proud to have carried out the largest and longest European study in the prevention of Alzheimer's Dementia, thus contributing to a public health priority. We would like to express our gratitude to the renowned scientific and independent data monitoring committees as well as to the investigators and patients involved in the study. Ipsen is determined to pursue its long term commitment with academic investigators to advance knowledge in Alzheimer's disease by its intent to transfer GuidAge® remarkable biological bank to French academic research. This biobank will represent a valuable source of knowledge in the Alzheimer's Disease area. Within the context of these results, it is Ipsen's intention to assess all the potential strategies so as to carry these findings further. "*

#### **About EGb 761®**

EGb 761®, which is the active substance of Tanakan®, is a unique standardized extract of Ginkgo biloba. This compound features antioxidant and neuroprotective property as well as an action on  $\beta$ -amyloid protein in experimental models. Its consistent composition in pharmacologically active substances is achieved through specially designed plantations of Ginkgo biloba (dioecious tree in the Ginkgoaceae family) that are cultivated under controlled conditions and a standardised extraction and purification process. EGb 761® is indicated and registered in many countries for the treatment of cognitive disorders in the elderly as well as neurosensory disorders.

#### **About GuidAge®**

The aim of the GuidAge® study was to assess the efficacy of EGb 761® at a dose of 240 mg daily in the prevention of Alzheimer's Dementia (AD) in a population of subjects aged 70 or more with a memory complaint spontaneously expressed to their family physician and living at home at the inclusion. GuidAge® is the longest and largest European study in this disease and has been conducted in full compliance with the most stringent international standards.

GuidAge® was a 5-year double-blind randomized trial versus placebo conducted in France by a network of family physicians and memory clinics. The primary endpoint was the incidence of AD during a 5-year follow-up period. A total of 2,854 subjects were enrolled between March 2002 and November 2004. At entry, the mean age of the study population was 76.3 ( $\pm$  4.4), with mean MMSE (Mini Mental State Evaluation) at entry of 27.6 ( $\pm$  1.9). Last patient last treatment date was November 2009.

The outcomes of the study pointed out that 134 individuals developed dementia of Alzheimer's type, including 61 patients (4.3%) in the EGb 761® group and 73 patients (5.2%)



in the placebo group; this difference was not significant ( $p=0.31$ ). Global conversion rate found in the placebo group (5.2%) was 50% lower than usually reported in the general French population. In planned pre-specified analysis, results were in favour of EGb 761<sup>®</sup> in patients treated for at least 4 years (1.6% versus 3.0% in the placebo group,  $p=0.03$ ) and in males (2.9% versus 7.0% in the placebo group,  $p=0.007$ ).

Both the dose and indication in the GuidAge<sup>®</sup> study are not approved by regulatory authorities.

#### **About Ipsen's involvement in neurology**

Ipsen has developed specialized expertise in the treatment of neuromuscular disorders and neurodegenerative diseases. The Group currently market Dysport<sup>®</sup> which is mainly used in the symptomatic treatment of spasticity, cervical dystonia and blepharospasm, as well as Apokyn<sup>®</sup> for the treatment of "off" episodes (re-emergence of Parkinson's disease symptoms) associated with advanced Parkinson's disease in the United States. Whereas Ipsen's research in neurology mainly focus on the development of new botulinum toxin formulations, Ipsen has synthesized several classes of chimeric compounds in neurodegenerative conditions such as Parkinson's and Huntington's diseases or amyotrophic lateral sclerosis.

#### **About Ipsen**

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Press release

## **Ipsen's partner Roche confirms the promising efficacy profile of Taspoglutide**

- **Taspoglutide, when used alone or added to metformin significantly reduced HbA1c and body weight with low risk of hypoglycemia**
- **Taspoglutide shows comparable or greater reduction in HbA1c levels with a low risk of hypoglycemia versus exenatide, sitagliptin and insulin glargine**

**Paris (France), 26 June 2010** - Ipsen (Euronext: IPN; ADR: IPSEY) a global biopharmaceutical group, today announced that its partner Roche disclosed results of five Phase III 24-week studies for taspoglutide for type 2 diabetes at the American Diabetes Association's (ADA) 70<sup>th</sup> Annual Scientific Sessions. Taspoglutide, the first once weekly glucagon-like peptide-1 (GLP-1) analogue based on a human sequence, originating from Ipsen's research is developed by Roche. This compound is similar to the natural hormone GLP-1 which has a key role in blood sugar regulation.

Three head-to-head comparisons against exenatide, sitagliptin and insulin glargine found that treatment with taspoglutide showed comparable or greater reductions in HbA1c levels with a low risk of hypoglycemia, resulted in more patients reaching the ADA target for HbA1c of <7.0%, and produced clinically meaningful weight loss.

Two additional Phase III studies showed that taspoglutide, when used alone or added to metformin (the most common first-line treatment for type 2 diabetes), significantly reduced HbA1c and body weight with low risk of hypoglycemia. Further studies suggest that taspoglutide may help restore a normal insulin response as well as potentially preserving insulin-producing beta cells and subsequently protect them from cell death.

In the studies, taspoglutide was administered once a week with a pre-filled, disposable syringe with a small-gauge needle.

The most common adverse events seen with taspoglutide based on the 24-week data are related to gastrointestinal tolerability and injection site reactions. Nausea and vomiting were of mild to moderate intensity, generally occurred early in treatment on the day of injection and predominantly as a single episode. Roche also recently announced the implementation of a risk mitigation plan in the Phase III programme designed to identify patients at potential risk of hypersensitivity reactions. While the occurrence of hypersensitivity reactions reported as related to taspoglutide is higher than expected for the study population in the Phase III trials, the incidence remains uncommon (< 1%).

**Jean-Luc Bélingard, Chairman and Chief Executive Officer of the Ipsen Group, stated:** *"These 5 phase III clinical trials have clearly demonstrated the marked and reproducible efficacy profile of taspoglutide in blood glucose control and body weight loss. The T-emerge programme provides the medical community with extensive data on the competitive positioning of this promising compound in the treatment of type 2 diabetes. We are confident that the ongoing clinical programme will further establish taspoglutide as a potential best-in-class with the added convenience of a once-a-week injection."*

### About the T-emerge Programme

The T-emerge Phase III clinical trial programme is designed as multicenter, multi-country, randomized, controlled (active or placebo), double-blind and open studies. Over 6,000 patients have been enrolled in the eight studies that comprise the T-emerge programme. Studies include two parallel taspoglutide arms including 10 mg once weekly and 10 mg once weekly titrated up to 20 mg once weekly after four weeks. Four of the eight studies have active comparators, including exenatide, sitagliptin, insulin glargine and pioglitazone.

Unless noted in the tables below, the T-emerge studies presented at ADA included two parallel taspoglutide arms with 10 mg and 20 mg doses (starting at 10 mg and titrated up after four weeks). Pre-specified analyses were conducted after 24 weeks of treatment. Measures refer to changes from baseline. All T-emerge Phase III studies continue for at least 52 weeks and some for up to three years.

### Results of five Phase III 24-week T-Emerge studies presented at ADA

#### T-emerge 1

Number: **399-PP**: "Taspoglutide, a Once-Weekly Human GLP-1 Analog, as Monotherapy Significantly Lowers A1c and Body Weight in Patients with Type 2 Diabetes (T2D)"

This study evaluated the efficacy and safety profile of once-weekly taspoglutide used alone in treatment-naïve patients whose diabetes was uncontrolled after diet and exercise. 373 patients with HbA1c  $\geq 6.5$  and  $\leq 10.0\%$  were randomized into three groups and given either taspoglutide 10 mg, taspoglutide 20 mg, or placebo.

<b>Efficacy summary at 24-weeks</b>	<b>Taspoglutide 10 mg (N=112)</b>	<b>Taspoglutide 20 mg (N=127)</b>	<b>Placebo (N=115)</b>
Baseline HbA1c	7.5%	7.7%	7.6%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-1.01%	-1.18%	-0.09%
% of patients who met target HbA1c of <7%*	65%	71%	20%
Baseline weight (kg)	88 kg	85 kg	87 kg
Average body weight change from baseline (p<0.05)	-1.5 kg	-2.3 kg	-1.2 kg

<b>Most common adverse events at 24-weeks</b>	<b>Taspoglutide 10 mg (N=116)</b>	<b>Taspoglutide 20 mg (N=129)</b>	<b>Placebo (N=123)</b>
Nausea	25.9% (30)	31% (40)	4.1% (5)
Vomiting	17.2% (20)	17.8% (23)	-
Injection site reactions	28.5% (33)	27.1% (35)	1.6% (2)
Hypoglycemia Reported	5.2% (6)	3.9% (5)	0.8% (1)

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=116)	Taspoglutide 20 mg (N=129)	Placebo (N=123)
Confirmed (<55 mg/dL)	-	0.8% (1)	-
% discontinuation due to GI adverse events	3.4% (4)	4.7% (6)	-

\*excluding patients who entered the study with HbA1c <7.0% at baseline

### **T-emerge 2**

Number: **62-OR**: "Superior Glycemic Control with Taspoglutide, a Once-Weekly Human GLP-1 Analog, Compared With Twice Daily Exenatide in Type 2 Diabetes (T2DM) Inadequately Controlled on Oral Agents: The T-emerge 2 Trial" Saturday, June 26, 8:00 am EST

The study compared the efficacy and safety profile of once-weekly taspoglutide to twice-daily exenatide (10 mcg) in patients inadequately controlled on metformin +/- thiazolidinedione. 1,189 patients with HbA1c  $\geq$  7.0% and  $\leq$ 10% were randomized into three groups and given taspoglutide 10 mg, taspoglutide 20 mg, or exenatide, in addition to their current regimens.

Efficacy summary at 24-weeks	Taspoglutide 10 mg + metformin +/- thiazolidinedione (N=399)	Taspoglutide 20 mg + metformin +/- thiazolidinedione (N=398)	Exenatide 10 mcg + metformin +/- thiazolidinedione (N=392)
Baseline HbA1c	8.1%	8.1%	8.1%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-1.24%	-1.31%	-0.98%
% of patients who met target HbA1c of <7%*	62%	63%	46%
Baseline weight (kg)	95 kg	93 kg	95 kg
Average body weight change from baseline (p<0.05)	-1.6 kg	-2.3 kg	-2.3 kg

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=394)	Taspoglutide 20 mg (N=394)	Exenatide 10 mcg (N=385)
Nausea	40.1% (158)	47.2% (186)	29.9% (115)
Vomiting	20.8% (82)	23.6% (93)	10.9% (42)
Injection site reactions	24.7% (97)	31.7% (125)	1.4% (5)
Hypoglycemia Reported Confirmed (<55 mg/dL)	8.6% (34) 0.5% (3)	9.9% (39) 2.3% (5)	9.9% (38) 1.8% (3)
% discontinuation due to GI adverse events (p<0.001)	4.1% (16)	7.6% (30)	6.5% (25)



T-emerge 2 subset analysis, number: **719-P**: A meal tolerance test was conducted in a subset of 148 patients, randomized into three groups and given either taspoglutide 10 mg, taspoglutide 20 mg or exenatide. Post-meal glucagon and post-meal glucose were measured at baseline and week 24. Patients in all three groups experienced a similar average reduction in post-meal glucagon (-4.5 for taspoglutide 10 mg, -5.0 for taspoglutide 20 mg, -4.3 for exenatide) and similar improvement in post-meal glucose (-32.1, -35.3, -31.7, respectively). Significantly increased insulin was observed in patients who received taspoglutide 10 mg (23.1) and taspoglutide 20 mg (7.3), while increase in insulin was not significant for exenatide (-10.1). Results reflect 95% confidence interval.

**T-emerge 2: 52 week data**

Data from the 52-weeks trials from T-emerge 2 and other T-emerge studies are expected soon and will be published at a future scientific congress. Roche believes that these 52-week data will help us better inform the safety and efficacy profile of taspoglutide in diabetes.

**T-emerge 4**

Number: **58-OR**: "Once-weekly Taspoglutide, a Human GLP-1 Analog, is Superior to Sitagliptin in Improving Glycemic Control and Weight Loss in Patients with Type 2 Diabetes (T2D): Results from the T-emerge 4 Trial," Saturday, June 26, 8:00 am EST

This study compared the efficacy and safety profile of once-weekly taspoglutide to daily oral sitagliptin in patients whose diabetes was inadequately controlled on metformin. 666 patients with HbA1c  $\geq 7.0\%$  and  $\leq 10\%$  were randomized into four groups and given either taspoglutide 10mg, taspoglutide 20mg, sitagliptin, or placebo, in addition to their current regimens.

<b>Efficacy summary at 24-weeks</b>	<b>Taspoglutide 10 mg + metformin (N=182)</b>	<b>Taspoglutide 20 mg + metformin (N=187)</b>	<b>Sitagliptin 100 mg + metformin (N=177)</b>	<b>Placebo (N=90)</b>
Baseline HbA1c	8.0%	8.0%	7.9%	8.0%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-1.23%	-1.30%	-0.89%	-0.10%
% of patients who met target HbA1c < 7% (p<.001)	64%	65%	50%	14%
Baseline weight (kg)	94 kg	92 kg	93 kg	91 kg
Average body weight change from baseline	-1.8 kg (p<0.01 vs. placebo) (p<0.05 vs. sitagliptin)	-2.6 kg (p<0.001 vs. placebo and vs. sitagliptin)	-0.9 kg	-0.5 kg

<b>Most common adverse events at 24-weeks</b>	<b>Taspoglutide 10 mg (N=187)</b>	<b>Taspoglutide 20 mg (N=192)</b>	<b>Sitagliptin 100 mg (N=184)</b>	<b>Placebo (N=93)</b>
Nausea	43.9% (82)	42.2% (81)	10.3% (19)	8.6% (8)

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=187)	Taspoglutide 20 mg (N=192)	Sitagliptin 100 mg (N=184)	Placebo (N=93)
Vomiting	21.4% (40)	28.1% (54)	4.3% (8)	1.1% (1)
Injection site reactions	21.9% (41)	50.4% (77)	9.2% (17)	7.7% (7)
Hypoglycemia Reported Confirmed ( $<55$ mg/dL)	7% (13) -	4.7% (9) 0.5% (1)	5.4% (10) 1.1% (2)	1.1% (1) -
% discontinuation due to GI adverse events ( $p<0.001$ )	12.3% (23)	8.3% (16)	0.5% (1)	-

### **T-emerge 5**

Number: **60-OR**: "Taspoglutide, a Once-Weekly Human GLP-1 Analog, Provides Comparable Glycemic Control to Insulin Glargine, with Superior Weight Loss and Less Hypoglycemia in Type 2 Diabetes (T2D): A Phase III, Open-Label Trial," Saturday, June 26, 8:00 am EST

The study compared the efficacy and safety profile of once-weekly taspoglutide to daily insulin glargine in patients whose diabetes was inadequately controlled on metformin + sulfonylurea. 1,049 patients with HbA1c  $\geq 7.0\%$  and  $\leq 10.0\%$  were randomized into three groups and given either taspoglutide 10 mg, taspoglutide 20 mg, or insulin glargine in addition to their current regimens. Sulfonylurea was withdrawn five days prior to randomization.

Efficacy summary at 24-weeks	Taspoglutide 10 mg + metformin (N=361)	Taspoglutide 20 mg + metformin (N=348)	Insulin glargine + metformin (N=319)
Baseline HbA1c	8.2%	8.3%	8.3%
Primary endpoint: Average HbA1c change from baseline ( $p<0.001$ )	-0.77%	-0.98%	-0.84%
% of patients who met target HbA1c of $< 7\%$	34%	41%	28%
Baseline weight (kg)	90 kg	91 kg	91 kg
Average body weight change from baseline ( $p<0.001$ )	-3.3 kg	-4.1 kg	-0.4 kg

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=364)	Taspoglutide 20 mg (N=351)	Insulin glargine (N=322)
Nausea	39.3% (143)	45.3% (159)	1.9% (6)
Vomiting	19.8% (72)	22.8% (80)	1.2% (4)
Injection site reactions	17.8% (65)	20.5% (72)	0.3% (1)
Hypoglycemia Reported Confirmed	4.9% (18) 0.3% (1)	6.0% (21) 0.9% (3)	17.4% (56) 3.1% (10)





Most common adverse events at 24-weeks ( $<55$ mg/dL)	Taspoglutide 10 mg (N=364)	Taspoglutide 20 mg (N=351)	Insulin glargine (N=322)
% discontinuation due to GI adverse events	4.4% (16)	6.6% (23)	-

### **T-emerge 7**

Number: **585-P**: "Once-Weekly Taspoglutide, a Human GLP-1 Analog, is Superior to Placebo in Improving Glycemic Control and Body Weight Loss in Obese Patients with Type 2 Diabetes (T2D) Inadequately Controlled with Metformin Monotherapy"

This study evaluated efficacy and safety profile of once-weekly 20 mg taspoglutide used alone in obese patients whose diabetes was uncontrolled on metformin alone. 305 obese patients with HbA1c  $\geq 6.5\%$  and  $\leq 9.5\%$  were randomized into two groups and given taspoglutide 20 mg or placebo in addition to their current regimens.

Efficacy summary at 24-weeks	Taspoglutide 20mg + metformin (N=149)	Placebo + metformin (N=143)
Baseline HbA1c	7.5%	7.5%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-0.81%	-0.09%
% of patients who met target HbA1c of $< 7\%$ *	53%	21%
Baseline weight (kg)	104 kg	101 kg
Average body weight change from baseline (p <0.01)	-3.2 kg	-1.9 kg

Most common adverse events at 24-weeks	Taspoglutide 20mg + metformin (N=154)	Placebo + metformin (N=150)
Nausea	35.1% (54)	5.3% (8)
Vomiting	24% (37)	3.3% (5)
Injection site AEs	50.6% (78)	8.1% (12)
Hypoglycemia Confirmed ( $\leq 55$ mg/dL)	9.7% (15)	2.7% (4)
% discontinuation due to GI adverse events	3.9% (6)	-

\*excluding patients who entered the study with HbA1c  $< 7.0\%$  at baseline

Full efficacy and safety data for each study will be presented at ADA.

### **Additional taspoglutide posters to be presented at the meeting:**

"Effect of Taspoglutide, a Human GLP-1 Analog, on Insulin Secretion in Patients with Type 2 Diabetes (T2D)," Poster, Monday, June 28 12 noon, number: **588-P**

"Taspoglutide, a Novel Human Once-Weekly GLP-1 Analog, Improves B-Cell Survival In ZDF Rats," Poster, Monday, June 28 12 noon, number **544-P**

### **About Taspoglutide (R1583)**



Taspoglutide was selected from a family of human once-weekly long-acting glucagon-like peptide-1 (GLP-1) analogues with structural modifications which confer intrinsic controlled release properties. Ipsen is the originator of the concept of matrix free sustained release formulation applied to therapeutic peptides and proteins. Taspoglutide is being developed, by Roche, as a novel and innovative treatment for patients with type 2 diabetes mellitus, the fourth leading cause of death in most developed countries. The structure of the molecule is similar to that of the natural human hormone GLP-1, and has the potential for intervals of up to two weeks in between administration without the use of a matrix.

#### **About the agreement**

Roche exercised its licensing option for taspoglutide from Ipsen in 2006 and acquired exclusive worldwide rights to develop and market taspoglutide, except in Japan where these rights are shared with Teijin and in France where Ipsen has elected to retain co-marketing rights.

#### **About Ipsen**

Ipsen is a global biopharmaceutical group with total sales in excess of 1 billion euros in 2009, and total worldwide staff of more than 4,400. Its strategy is based on fast growing specialty care drugs in oncology, endocrinology, neurology and hematology, and primary care drugs, which significantly contribute to research financing. This strategy is also supported by an active policy of partnerships. Ipsen's specific Research & Development (R&D) centers and peptide & protein engineering platform give the Group a competitive edge. Nearly 900 people are dedicated to the discovery and development of innovative drugs for patient care. Nearly 900 people are dedicated to the discovery and development of innovative drugs for patient care. In 2009, R&D spend reached close to €200 million, representing more than 19% of total Group sales. Ipsen's shares are traded on Segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150). Ipsen's shares are eligible to the "Service de Règlement Différé" ("SRD") and the Group is part of the SBF 120 index. Ipsen has implemented a Sponsored Level I American Depositary Receipt (ADR) program, which trade on the over-the-counter market in the United States under the symbol IPSEY. For more information on Ipsen, visit our website at [www.ipsen.com](http://www.ipsen.com).

#### **Ipsen's Forward Looking Statement**

The forward-looking statements, objectives and targets contained herein are based on the Group's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by the Group. These targets depend on conditions or facts likely to happen in the future, and not exclusively on historical data. Notably, future currency fluctuations may negatively impact the profitability of the Group and its ability to reach its objectives. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties. The Group does not commit nor gives any guarantee that it will meet the targets mentioned above. Furthermore, the Research and Development process involves several stages each of which involve the substantial risk that the Group may fail to achieve its objectives and be forced to abandon its efforts with regards to a product in which it has invested significant sums. Therefore, the Group cannot be certain that favourable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. The Group also depends on third parties to develop and market some of its products which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to the Group's activities and financial results. The Group expressly disclaims any obligation or undertaking to update or revise any forward looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. The Group's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers.

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