

Press release

## **Results of Phase I and Phase IIa clinical studies confirm the inhibitory effect of proprietary Ipsen's BIM23A760 first-in-class "chimeric" compound on growth hormone, IGF-1 and prolactin levels<sup>1</sup>**

**Paris (France), 16 July 2009** - Ipsen (Euronext: FR0010259150; IPN) today announced the results of phase I and Phase IIa clinical studies for its BIM23A760 designed and developed by Ipsen's research team using its validated peptide engineering platform. BIM23A760 is a first-in-class innovative "chimeric" compound that bears within a single molecule two pharmacological moieties, i.e. a somatostatin analog and a dopamine agonist. This molecule targets two of the most commonly patho-physiological pathways associated with pituitary tumours: growth hormone and prolactin. The design of BIM23A760 is based on a novel concept in molecular biology regarding the amplification of intracellular signalling when engaging simultaneously two receptors with their respective ligands.

In the phase I trial, the exposure to BIM23A760 in healthy volunteers showed a pharmacokinetic profile consistent with sustained release compatible with a once-weekly dosing. BIM23A760 treatment potently suppressed prolactin levels at all tested doses after single dosing, with a decrease in prolactin sustained for at least 4 weeks after repeated dosing. In addition, statistically significant reductions in IGF-1 levels were observed after repeated dosing.

In the Phase IIa study, the exposure to BIM23A760 in acromegalic patients, exhibited a pharmacological activity as evidenced by a 66–74% mean maximum reduction in growth hormone (GH) levels compared to baseline. 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). The pharmacokinetic profile of BIM23A760 among patients with acromegaly was similar to the profile observed among healthy participants in the phase I study. BIM 23A760 was well tolerated at both dosages.

**Jacques-Pierre Moreau**, Executive Vice-President, Chief Scientific Officer said :*"The Phase I and Phase IIa results for BIM23A760 show encouraging signs of efficacy with the markers of bioactivity pointing in the right direction. BIM23A760's original design might represent a true advance in the therapy of pituitary adenomas. This compound is at the very heart of Ipsen's endocrinology focus and expertise on homeostasis, namely restoring the hormonal imbalance induced by pituitary disorders."*

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<sup>1</sup> Posters presented at the Endocrine Society's 91st Annual Meeting in Washington, DC, USA

- Safety, Pharmacokinetics and Pharmacodynamics after Subcutaneous Administration of BIM 23A760, a Chimeric Compound Combining Dopaminergic Agonist and Somatostatin Analog, in Healthy Male Volunteers
- A Phase 2 Exploratory Study of BIM 23A760 in Acromegalic Patients: Preliminary Results of Safety and Efficacy after a Single-dose Administration



### **About BIM23A760**

BIM23A760 is a new chimeric compound that contains structural elements of both somatostatin analogues and dopamine agonists and acts synergistically by inducing an interaction between these receptors in disorders such as acromegaly and neuroendocrine tumours. Ipsen is currently studying this molecule whose spectrum of activity is wider than that of currently marketed somatostatin analogues. Aside from the symptomatic treatment of acromegaly and neuroendocrine tumours, BIM23A760 might also reduce the tumour size, thereby eliminating some of the shortcomings of the treatments currently available.

### **About the trials**

The Phase I investigated the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of single and multiple ascending doses of BIM23A760 administered by subcutaneous injection. This double-blind, randomized, placebo-controlled, escalating-dose study was conducted at two investigational sites in France with a total of 64 healthy males volunteers. The PK profile was evaluated over several weeks. Serum levels were determined by a validated LC-MS/MS method. PD variables were GH, IGF-1, and prolactin levels.

The phase IIa, ascending dose, multinational, open-label study aimed to investigate the pharmacodynamics, pharmacokinetics, and safety of single doses of BIM23A760 in 11 patients with acromegaly. The duration of exposure increased from approximately 2 weeks at the 1 mg dose and for 2 to 3 weeks at the 4 mg dose. The primary endpoint was the maximum observed percentage of GH inhibition over 29 days (1-mg cohort) or 43 days (4-mg cohort). Secondary endpoints included serum levels of IGF-1, prolactin, pharmacokinetics, and safety.

### **About Acromegaly**

Acromegaly is a disorder caused by the over-production of growth hormone or prolactin due to a benign tumour of the anterior pituitary gland. This relatively rare disorder occurs in approximately 60 out of every one million people (60/1,000,000). Both men and women are affected. Approximately 50% of the patients receive a drug therapy.

### **About Ipsen**

Ipsen is an innovation-driven international specialty pharmaceutical group with over 20 products on the market and a total worldwide staff of nearly 4,200. Its development strategy is based on a combination of specialty products, which are growth drivers, in targeted therapeutic areas (oncology, endocrinology and neurology), and primary care products which contribute significantly to its research financing. The location of its four Research & Development centres (Paris, Boston, Barcelona, London) and its peptide and protein engineering platform give the Group a competitive edge in gaining access to leading university research teams and highly qualified personnel. More than 800 people in R&D are dedicated to the discovery and development of innovative drugs for patient care. This strategy is also supported by an active policy of partnerships. In 2008, Research and Development expenditure was about €183 million, close to 19% of consolidated sales, which amounted to €971 million while total revenues exceeded €1 billion. 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).

### **Forward Looking Statements**

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 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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