

Ipsen announces publication in *The Lancet Neurology* of the results of the phase III randomized study (NCT01313299) showing efficacy and safety of Dysport[®] (abobotulinumtoxinA) in adult patients with upper limb spasticity (ULS)

Global regulatory submissions had been filed resulting in the US approval of Dysport[®] in the treatment of Adult patients with ULS and submission of variations in EU and Rest of the World countries

Paris (France), 31 August 2015 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that *The Lancet Neurology* has published online at <http://www.thelancet.com/neurology> the detailed results from the Ipsen sponsored phase III randomized study (NCT01313299) showing the efficacy and safety of Dysport[®] in post-stroke or traumatic brain injury patients with upper limb spasticity. This international phase III registration study led to the approval of Dysport[®] for the treatment of ULS in the US by the FDA on July 16, 2015. In Europe, the upper limb spasticity elements of the Dysport[®] SmPC have already been modified in some countries to include key medical data. Regulatory procedures are still ongoing in different European and Rest of World countries.

This new study met the primary endpoint (Modified Ashworth Scale, MAS) and the first secondary endpoint of Physician Global Assessment (PGA) in patients injected in different upper limb muscle groups (fingers, wrist, elbow or/and shoulder) according to patient disease presentation as Dysport[®] shows muscle tone reduction and clinical benefit. In addition, efficacy on active movements, spasticity, passive function and ease of applying splints was demonstrated in a statistically and clinically significant manner as compared to placebo. Efficacy was observed as early as one week post-injection and lasted up to 20 weeks in some patients.

Claude Bertrand, Executive Vice President R&D and Chief Scientific Officer, Ipsen stated: *“The publication of these data in *The Lancet Neurology* illustrates the high quality of our study and Ipsen’s commitment to continue to improve the treatment of patients with spasticity helping them gain autonomy. It confirms the therapeutic value of Dysport[®] in this debilitating condition.”*

Professor Jean-Michel Gracies, Neurorehabilitation, Neurology & Neurophysiology, Chairman of the Department of Physical Medicine & Rehabilitation, Groupe Hospitalier Albert CHENEVIER - Henri MONDOR (Créteil, France) stated: *“The publication of this study is great news for the field of neurorehabilitation and botulinum toxin use. This is the first study that demonstrates substantial improvements in active range of motion against the injected muscles in the paretic upper limb, together with expected improvements in tone, spasticity per se, and both*



patient-rated and physician-rated clinical improvement after one injection only. In itself, this study both confirms the therapeutic value of abobotulinum toxin and shows the practicality and value of new assessment methods that should be used as primary outcome in future studies on the product.”

About the Double Blind Phase 3 Study conducted in Adult Upper Limb spasticity with Dysport®

The Phase III study (NCT01313299) was multi-center, prospective, double blind, randomized, and placebo-controlled. It was conducted in the U.S., France, Italy, Belgium, the Czech Republic, Poland, Slovakia, Russia and Hungary.

A total of 243 patients from 34 centers were randomized to treatment with Dysport® 500U (n=80), Dysport® 1000U (n=79) or placebo (n=79). The purpose of this study was to assess the efficacy of Dysport® compared to placebo in improving Upper Limb Spasticity in hemiparetic patients following a stroke or brain trauma. The new study results published in The Lancet Neurology showed improvements on muscle tone (MAS) with mean change in MAS score from baseline at week 4 in the Primary Targeted Muscle Group was -0.3 (SD 0.6) in the placebo group, -1.2 (1.0) in the Dysport® 500 U group ($p < 0.0001$ vs placebo), and -1.4 (1.1) in the Dysport® 1000 U group ($p < 0.0001$ vs placebo). On the Physician Global Assessment score, the mean change from baseline at week 4 was 0.6 (SD 1.0) in the placebo group, 1.4 (1.1) in the Dysport® 500 U group ($p = 0.0003$ vs placebo), and 1.8 (1.1) in the Dysport® 1000 U group ($p < 0.0001$ vs placebo). The efficacy of Dysport® was observed as early as week 1 and persisted up to 20 weeks in some patients.

The mean change from baseline at week 4 in Disability Assessment Scale (DAS) (passive function) for the principal target of treatment was -0.5 (0.7) in the placebo group (n=79), -0.7 (0.8) in the Dysport® 500 U group ($p = 0.2560$ vs placebo), and -0.7 (0.7) in the Dysport® 1000 U group ($p = 0.0772$ vs placebo). Significantly more patients receiving Dysport® 1000 U achieved reductions of 1 point or greater in the DAS for the principal target of treatment at weeks 4 and 12 than in the placebo group. These benefits persisted at week 12 ($p = 0.0002$). In addition, this is the first large study of botulinum toxin A with a stepwise evaluation of spastic paresis, including active movements opposing targeted antagonists and spasticity measured by the Tardieu Scale. Tardieu Scale angles of catch (XV3) improved in finger, wrist and elbow flexors at week 4; the other Tardieu parameters (range of passive slow movement (XV1), spasticity angle (X) and spasticity grade (Y)) improved in some but not all cases at week 4. Active range of motion improved for movements opposing finger, wrist, and elbow flexors in the Dysport® 1000 U group and in finger flexors in the 500 U group. All those improvements in spasticity and function were accompanied by an improvement in the ease of applying splints by the patient after 4 weeks in the Dysport® groups compared with the placebo group. Dysport® was well tolerated at the two doses tested. After the completion of this double blind study, patients were offered the option to continue in an open label long-term study where they would receive additional treatment with Dysport® for a total of 15 months.

About Ipsen

Ipsen is a global specialty-driven biotechnological group with total sales exceeding €1.2 billion in 2014. Ipsen sells more than 20 drugs in more than 115 countries, with a direct commercial presence in 30 countries. Ipsen's ambition is to become a leader in specialty healthcare solutions for targeted debilitating diseases. Its development strategy is supported by 3 franchises: neurology, endocrinology and urology-oncology. Ipsen's commitment to oncology is exemplified through its growing portfolio of key therapies



improving the care of patients suffering from prostate cancer, bladder cancer or neuroendocrine tumors. Ipsen also has a significant presence in primary care. Moreover, the Group has an active policy of partnerships. Ipsen's R&D is focused on its innovative and differentiated technological platforms, peptides and toxins, located in the heart of the leading biotechnological and life sciences hubs (Les Ulis, France; Slough/Oxford, UK; Cambridge, US). In 2014, R&D expenditure totaled close to €187 million, representing about 15% of Group sales. The Group has more than 4,500 employees worldwide. Ipsen's shares are traded on segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150) and eligible to the "Service de Règlement Différé" ("SRD"). 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 www.ipsen.com.

Ipsen 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. All of the above risks could affect the Group's future ability to achieve its financial targets, which were set assuming reasonable macroeconomic conditions based on the information available today. Use of the words "believes," "anticipates" and "expects" and similar expressions are intended to identify forward-looking statements, including the Group's expectations regarding future events, including regulatory filings and determinations. 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. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties, notably the fact that a promising product in early development phase or clinical trial may end up never being launched on the market or reaching its commercial targets, notably for regulatory or competition reasons. The Group must face or might face competition from generic products that might translate into a loss of market share. Furthermore, the Research and Development process involves several stages each of which involves 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. There can be no guarantees a product will receive the necessary regulatory approvals or that the product will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Other risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the Group's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the Group's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or



regulatory actions. 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 cannot be certain that its partners will fulfil their obligations. It might be unable to obtain any benefit from those agreements. A default by any of the Group's partners could generate lower revenues than expected. Such situations could have a negative impact on the Group's business, financial position or performance. 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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