

Ipsen announces topline results of two double-blind phase III studies of Dysport[®] in lower limb spasticity in children and in adults

- **Treatment with Dysport[®] at the doses of 10U/kg/leg and 15U/kg/leg statistically significantly improved muscle tone (primary endpoint) in hemiplegic and diplegic cerebral palsy children with lower limb spasticity**
- **Treatment with Dysport[®] at the dose of 1500U statistically significantly improved muscle tone (primary endpoint) in adult patients with lower limb spasticity**
 - **Safety profile consistent with known safety profile of Dysport[®] in these indications**

Paris (France), 26 January 2015 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced topline results for two double-blind phase III studies of Dysport[®] (abobotulinumtoxinA) in Pediatric Lower Limb (PLL) spasticity in children with cerebral palsy and in Adult Lower Limb (ALL) spasticity in patients who had experienced a stroke or traumatic brain injury.

In the PLL phase III study, conducted in children with hemiparetic or diplegic cerebral palsy, treatment with Dysport[®] showed a statistically significant response versus placebo in the improvement of muscle tone, as measured by the Modified Ashworth Scale (MAS; primary endpoint), and a statistically significant overall benefit versus placebo, as measured by the Physician Global Assessment (PGA; first secondary endpoint).

In the ALL phase III study, conducted in hemiparetic patients who had experienced a stroke or traumatic brain injury, treatment with Dysport[®] at the dose of 1500U showed a statistically significant response versus placebo in the improvement of muscle tone, as measured by the Modified Ashworth Scale (MAS; primary endpoint). An overall benefit (measured by the Physician Global Assessment (PGA); first secondary endpoint) versus placebo was observed but did not reach statistical significance according to the pre-specified statistical analysis.



Other spasticity and functional outcome results are currently being analyzed. The safety profile observed in the studies was consistent with the known safety profile of Dysport® in these indications.

Comprehensive results from these double-blind studies will be disclosed in the next few months at major international congresses. Ipsen will share these results with key regulatory agencies this year.

Claude Bertrand, Executive Vice-President Research & Development and Chief Scientific Officer of Ipsen commented: *“We believe these results should meet the expectations of physicians by potentially providing a new alternative for treating adults and children suffering from lower limb spasticity. This unique data is a testimony to Ipsen’s growing scientific leadership in the field of toxins. We are grateful to the clinicians, caregivers, patients and their families who were involved in this study.”*

Pr. Mauricio Delgado, Principal Investigator of the PLL study stated: *“This is the largest pediatric double-blind placebo controlled study demonstrating that Dysport® is an effective and safe treatment for spasticity in children with Cerebral Palsy. Unlike previous studies, this study was designed to demonstrate efficacy through a variety of outcome measures that are of direct relevance to the patient and their family. The study brought together an international and multidisciplinary group of investigators including pediatric neurologists, physiatrists, orthopedic surgeons and physical therapists who got the benefit of using standardized clinical assessments having a positive impact on their clinical practice.”*

Pr. Jean Michel Gracies, Principal Investigator of the ALL study stated: *“This global double-blind phase III study provides evidence that Dysport® demonstrates high benefit in adults with stroke or traumatic brain injury causing lower limb spasticity. This study also reveals that it was possible to achieve highly productive collaboration with a very large number of investigators from several countries and health systems. In addition, it must be stressed that this study involved multidisciplinary teams including physical and occupational therapists, particularly involved in patient assessment. These important results reinforce the positioning of Dysport® as an excellent treatment for patients with spastic paresis.”*

About the studies

The Phase III study conducted in children with cerebral palsy included 235 patients and was multicentric, prospective, double blind, randomized, and placebo-controlled. It was conducted in the USA, France, Turkey, Poland, Mexico and Chile. The purpose of this study in children was to assess the efficacy and safety of Dysport® compared to placebo in improving lower limb spasticity in hemiparetic or diplegic cerebral palsy patients.

The phase III study in adults suffering from lower limb spasticity included 388 patients and was international, multicentric, prospective, double blind, randomized and placebo-controlled. It was conducted in the USA, France, Italy, Belgium, Czech Republic, Poland, Slovakia, Russia and Hungary. The purpose of



this study was to assess the efficacy and safety of Dysport[®] compared to placebo in improving lower limb spasticity in hemiparetic adult patients who had experienced a stroke or a traumatic brain injury.

The primary endpoint for both studies was the improvement of muscle tone in the treated lower limb measured by the Modified Ashworth Scale (MAS). Patients were offered to continue in an open label long-term study wherein they will be receiving additional Dysport[®] treatment cycles within a total of 15 months.

About the Modified Ashworth Scale (MAS)

The MAS is the reference clinical scale to assess muscle tone in clinical trials in patients with spasticity. It allows categorizing the severity of spasticity by evaluating resistance to passive movement. It ranges from 0 (=no increase in tone) to 4 (=affected limb rigid in flexion or extension).

About the Physician Global Assessment (PGA)

The PGA is an outcome measure used to assess the overall clinical benefit for the patient. It is a 9-point scale that ranges from -4 (markedly worse) to +4 (markedly better).

About Dysport[®]

Dysport[®] is an injectable form of botulinum toxin type A (BTX-A), which is isolated and purified from Clostridium BTX-A bacteria. It is supplied as a lyophilized powder.

Dysport[®] was first registered for the treatment of blepharospasm and hemifacial spasm in the United Kingdom in 1990, and is licensed in 82 countries for various indications including: blepharospasm, adult upper and lower limb spasticity, hemifacial spasm, spasmodic torticollis (ST) (previously referred to as cervical dystonia), pediatric lower limb spasticity due to cerebral palsy (CP), axillary hyperhidrosis, and glabellar lines.

Dysport[®] is approved for the treatment of upper limb spasticity and pediatric lower limb spasticity in many international markets, but not in the United States (US). Dysport[®] is also approved for the treatment of adult lower limb spasticity in some European countries, but not in the United States (US). Dysport[®]'s only approved therapeutic indication in the United States (US) is for the treatment of adults with cervical dystonia (referred to as spasmodic torticollis in other markets). As such, data from studies in adults and children with lower limb spasticity are of an investigational use of Dysport[®] in the USA.

About Ipsen

Ipsen is a global specialty-driven pharmaceutical company with total sales exceeding €1.2 billion in 2013. 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 uro-oncology. 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. In 2013, R&D expenditure totaled close to €260 million, representing more than 21% of Group sales. Moreover, Ipsen also has a significant presence in primary care. The Group has close to 4,600 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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