

## **Ipsen announces positive initial results from the international double-blind clinical phase III study of Dysport<sup>®</sup> in the treatment of Adults suffering from Upper Limb Spasticity**

- **Treatment with Dysport<sup>®</sup> demonstrated statistically significant improved muscle tone and clinical benefit in adults with upper limb spasticity**
- **Safety profile consistent with the known safety profile of Dysport<sup>®</sup> in this indication**

**Paris (France), 17 December 2013** – Ipsen (Euronext: IPN; ADR: IPSEY) today announced positive initial results from the double-blind phase III study of Dysport<sup>®</sup> (abobotulinumtoxinA) in Adult Upper Limb spasticity. Regarding the primary endpoints, treatment with Dysport<sup>®</sup> showed statistically significant response versus placebo in the improvement of muscle tone, as measured by the Modified Ashworth Scale (MAS). In addition, a statistically significant clinical benefit for the patients treated with Dysport<sup>®</sup> was demonstrated versus placebo, as measured by the Physician Global Assessment (PGA). The safety profile observed in the study was consistent with the known safety profile of Dysport<sup>®</sup> in this indication. Comprehensive results from this double-blind study will be disclosed in the next few months at major international congresses.

**Marc de Garidel, Chairman and CEO of Ipsen** stated: *“These clinical results are an important step in our ambition to become a global leader in the treatment of targeted debilitating diseases. Expanding our scope of indications for Dysport<sup>®</sup> would help us further develop the neurology franchise, notably in the USA.”*

**Claude Bertrand, Executive Vice-President Research & Development and Chief Scientific Officer of Ipsen** commented: *“Ipsen is very pleased with the initial results of the Dysport<sup>®</sup> study in Adult Upper Limb spasticity. We believe it should meet the expectations of physicians by potentially providing a new alternative for treating patients suffering from this debilitating condition. We are grateful to the clinicians, caregivers, patients and their families who were involved in this study.”*

**Prof. Jean-Michel Gracies (Global Principal Investigator of the study) and Prof. Allison Brashear (US Principal Investigator)** stated: *“This global double-blind phase III study provides robust evidence that Dysport<sup>®</sup> markedly improves muscle tone and demonstrates significant*



*clinical benefit in adults with stroke or traumatic brain injury causing upper limb spasticity. This study also reveals that it was possible to achieve highly productive collaboration with a large number of investigators from several countries and health systems. In addition, it is important to stress 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 study**

This phase III research study included 243 patients and was multicentric, prospective, double blind, randomised, 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 of Dysport® compared to placebo in improving upper limb spasticity in hemiparetic patients following a stroke or a brain trauma. The study co-primary endpoints were the improvement of muscle tone in the treated upper limb measured by the Modified Ashworth Scale (MAS) and the clinical benefit for the patients assessed by the Physician Global Assessment (PGA).

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 a well-known tool used by clinicians to assess the overall clinical benefit for their patients. 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 more than 75 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 in many international markets, 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 this study in adults with upper limb spasticity are with respect to an investigational use of Dysport® in the USA.

#### **Important Safety Information about Dysport®**

Postmarketing reports indicate that the effects of Dysport® and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria,



urinary incontinence, and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening, and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity, but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and adults, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.

#### Contraindications

Dysport® is contraindicated in patients with hypersensitivity to any botulinum toxin product or its excipients, including human albumin, lactose, and cow's milk protein, or who have an infection at the proposed injection site.

#### Lack of interchangeability between botulinum toxin products

The potency Units of Dysport® are not interchangeable with other preparations of botulinum toxin products and, therefore, Units of biological activity of Dysport® cannot be compared to or converted into Units of any other botulinum toxin products. Recommended dose and frequency of administration should not be exceeded.

#### Dysphagia and breathing difficulties

Immediate medical attention may be required in cases of respiratory, speech, or swallowing difficulties. Dysphagia may persist for several weeks, and require use of a feeding tube to maintain adequate nutrition and hydration. Aspiration may result from severe dysphagia and is a particular risk when treating patients in whom swallowing or respiratory function is already compromised. Concomitant neuromuscular disorder may exacerbate clinical effects of treatment.

#### Pre-existing neuromuscular disorders

Patients with neuromuscular disorders should be monitored particularly closely when given botulinum toxin as they may be at increased risk of clinically significant effects, including severe dysphagia and respiratory compromise from typical doses.

#### Human albumin

Dysport® contains human albumin. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases or Creutzfeldt-Jakob disease (CJD). No cases of transmission of viral diseases or CJD have ever been identified for albumin.

#### Immune reaction

The possibility of an immune reaction when injected intradermally is unknown. The safety of Dysport® for the treatment of hyperhidrosis has not been established.

#### Drug interactions

Patients receiving concomitant treatment of Dysport® and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like agents), or muscle relaxants, should be observed closely because the effect of botulinum toxin may be potentiated. Use of anticholinergic drugs may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxins during the course of treatment with Dysport® is unknown.



### Special populations

Based on animal data, may cause fetal harm. Dysport® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Care should be exercised when administering Dysport® to elderly patients, reflecting the greater frequency of concomitant disease and other drug therapy.

### Adverse reactions

The most commonly observed adverse reactions (>5% of patients) with Dysport® for the treatment of cervical dystonia are muscular weakness, dysphagia, dry mouth, injection site discomfort, fatigue, headache, neck pain, musculoskeletal pain, dysphonia, injection site pain, and eye disorders.

### About Ipsen

Ipsen is a global specialty-driven pharmaceutical company with total sales exceeding €1.2 billion in 2012. 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 2012, R&D expenditure totalled close to €250 million, representing more than 20% of Group sales. The Group has close to 4,900 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.ipсен.com](http://www.ipсен.com).

### 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. 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.

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 Generics 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. 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.

**For further information:**

**Media**

**Didier Véron**

Senior Vice-Président, Public Affairs  
and Communication

Tel.: +33 (0)1 58 33 51 16

Fax: +33 (0)1 58 33 50 58

E-mail: [didier.veron@ipsen.com](mailto:didier.veron@ipsen.com)

**Brigitte Le Guennec**

Media and Public Relations Officer

Tel.: +33 (0)1 58 33 51 17

Fax: +33 (0)1 58 33 50 58

E-mail : [brigitte.le.guennec@ipsen.com](mailto:brigitte.le.guennec@ipsen.com)

**Financial Community**

**Pierre Kemula**

Vice President, Corporate Finance, Treasury and  
Financial Markets

Tel.: +33 (0)1 58 33 60 08

Fax: +33 (0)1 58 33 50 63

E-mail: [pierre.kemula@ipsen.com](mailto:pierre.kemula@ipsen.com)

**Stéphane Durant des Aulnois**

Investor Relations Officer

Tel.: +33 (0)1 58 33 60 09

Fax: +33 (0)1 58 33 50 63

E-mail: [stephane.durant.des.aulnois@ipsen.com](mailto:stephane.durant.des.aulnois@ipsen.com)

**Thomas Peny-Coblentz**

Investor Relations Manager

Tel.: +33 (0)1 58 33 56 36

Fax: +33 (0)1 58 33 50 63

E-mail: [thomas.peny-coblentz@ipsen.com](mailto:thomas.peny-coblentz@ipsen.com)