

Ipsen announces *The Lancet Neurology* publishes Dysport® Phase III registration trial results in adult patients with upper limb spasticity (ULS)

- *Dysport showed significant improvements in muscle tone and in physician global assessment at Week 4*
- *Clinical improvement was observed at one week post-injection and lasted 12 to 16 weeks in most, and up to 20 weeks in some patients*
- *Phase III registration trial was part of FDA submission which led to U.S. FDA approval of Dysport® for the treatment of ULS in adults on July 15, 2015*

BASKING RIDGE, N.J., August 31, 2015 – The U.S. affiliate of Ipsen (Euronext: IPN; ADR: IPSEY) today announced that *The Lancet Neurology* has published clinical trial results showing the efficacy and safety of Dysport® (abobotulinumtoxinA) in post-stroke or traumatic brain injury patients with upper limb spasticity. It is estimated that 1.8 million adult Americans may suffer from spasticity¹⁻⁴, which in the upper arm can cause muscle stiffness, flexing, spasms, twitching and pain.

The international Phase III randomized, double-blind, placebo-controlled study of the efficacy and safety of Dysport® was conducted in 34 neurology/rehabilitation clinics in nine countries. The article titled “Safety and efficacy of abobotulinumtoxinA for hemiparesis in adults with upper limb spasticity after stroke or traumatic brain injury: a double-blind, randomised, controlled trial” is published online at <http://www.thelancet.com/neurology> and will be published in an upcoming print edition. The phase III registration trial was part of submission which led to U.S. FDA approval of Dysport® for the treatment of ULS in adults on July 15, 2015. Dysport® is the first therapy in the past five years approved by the FDA for the treatment of adults with upper limb spasticity.

A total of 243 patients were randomized to treatment with Dysport® 500U (n=80), Dysport® 1000U (n=79) or placebo (n=79). The data gathered from 161 Dysport-treated patients showed statically significant changes in the severity of increased muscle tone measured by the mean change in Modified Ashworth Scale (MAS), the study’s primary endpoint, from baseline at week 4 in the primary target muscle group (PTMG) versus placebo ($p \leq 0.05$). Improvements in muscle tone were reported at 1 week after injection and additional improvements in MAS score seemed to be maintained in the Dysport groups compared with placebo at weeks 16 and 20. The elbow flexors, wrist flexors and extrinsic finger flexors were selected as the PTMG in most patients. Significant changes in overall treatment response as measured by the Physician Global Assessment (PGA), the study’s first secondary endpoint, were also observed in week 4 for both Dysport treatment groups (500 units and 1000 units) compared to placebo ($p \leq 0.05$). Treatment-related adverse events were reported in 2% of patients in the placebo group, 7% of patients in the Dysport 500 U group and in 9% of patients in the Dysport 1000 U group. The most common treatment-emergent adverse event was nasopharyngitis and the most common treatment-related adverse events were muscular weakness, asthenia and injection site erythema.

Dysport® and all botulinum toxin products have a Boxed Warning which states that the effects of the botulinum toxin may spread from the area of injection to other areas of the body, causing symptoms similar to those of botulism. Those symptoms include swallowing and breathing difficulties that can be life-threatening. Please see below for additional Important Safety Information.

“This is the first registration study to evaluate ULS treatment in adult patients with both stroke and traumatic brain injury,” said Allison Brashear, M.D., Professor and Chair of Neurology, Wake Forest Baptist Medical Center and the U.S. principal investigator of the Phase III trial.

“The publication of the Dysport® data in *The Lancet Neurology* marks another important milestone in the path to improving the lives of patients with upper limb spasticity and supports the role of Dysport in the treatment of this debilitating condition,” said Cynthia Schwalm, Chief Executive Officer, Ipsen Biopharmaceuticals, Inc. “Ipsen is committed to the continued clinical development of Dysport in partnership with clinicians to support the improvement of patient care in the treatment of spasticity.”

About the Phase III Pivotal Study

The Phase III study was multi-center, prospective, double blind, randomized, and placebo-controlled (ClinicalTrials.gov NCT01313299). 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 ULS in hemiparetic patients following a stroke or brain trauma. The study’s primary endpoint was the improvement of muscle tone in the treated upper limb measured by the Modified Ashworth Scale (MAS) and the secondary endpoint was the overall treatment response for the patients assessed by the Physician Global Assessment (PGA). 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 Upper Limb Spasticity

It is estimated that 1.8 million adult Americans may suffer from spasticity, which in the upper arm can cause muscle stiffness, flexing, spasms, twitching and pain. Upper limb spasticity (ULS) can make every day simple tasks, such as washing your hands, difficult. The condition most commonly occurs in adults after a stroke, but can also result from other injuries to the central nervous system, such as a spinal cord injury or traumatic brain injury (TBI), multiple sclerosis (MS) or adult cerebral palsy (CP). Symptoms may not appear for months or even years after the stroke or injury, but may include bent elbows or wrists, and hands clenched into fists.

About Dysport® (abobotulinumtoxinA)

Dysport® is an injectable form of botulinum toxin type A (BoNT-A), which is isolated and purified from *Clostridium* bacteria producing BoNT-A. It is supplied as a lyophilized powder. Dysport® has approved therapeutic indications in the United States for the treatment of adults with Cervical Dystonia (CD), and now for the treatment of Upper Limb Spasticity (ULS) in adult patients, to decrease the severity of increased muscle tone in elbow flexors, wrist flexors and finger flexors. The medicine was first registered in the United Kingdom in 1990 for other uses

and is licensed in more than 80 countries in eight different indications, with over 1,300 peer-reviewed publications.

The C.L.I.M.B. (Continuum of Learning to Improve Management With Botulinum Toxin; <http://www.climb-training.com/>) injector training platform is a multi-tiered learning continuum designed to educate physicians with every level of experience with botulinum toxin therapy. C.L.I.M.B. can help physicians improve their clinical skills involving the appropriate use of Dysport®.

IPSEN CARES™ (Coverage, Access, Reimbursement, & Education Support) is dedicated to ensuring patients, providers and caregivers have the resources needed to help access the Ipsen medications that are critical to managing their conditions. Additional information is available by visiting (<http://www.ipsencares.com>).

Indication

Dysport® (abobotulinumtoxinA) for injection is indicated for the treatment of adults with:

- upper limb spasticity, to decrease the severity of increased muscle tone in elbow flexors, wrist flexors, and finger flexors
- cervical dystonia

It is not known whether Dysport® is safe or effective in patients under 18 years old.

Important Safety Information

Warning: Distant Spread of Toxin Effect

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 in approved indications, cases of spread of effect have been reported at doses comparable to lower than the maximum recommended dose.

Contraindications

Dysport® is contraindicated in patients with known hypersensitivity to any botulinum toxin preparation or to any of the components; or in the presence of infection at the proposed injection site(s). Patients known to be allergic to cow's milk protein should not be treated with Dysport® as the product may contain trace amounts of this protein.

Warnings and Precautions

Lack of interchangeability between botulinum toxin products

The potency Units of Dysport® are specific to the preparation and assay method utilized. They 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 assessed with any other specific assay method.

Dysphagia and Breathing Difficulties

Treatment with Dysport® and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or swallowing. When distant side effects occur, additional respiratory muscles may be involved (see Boxed Warning). Deaths as a complication of severe dysphagia have reported after treatment with botulinum toxin. 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. These reactions can occur within hours to weeks after injection with botulinum toxin.

Pre-existing Neuromuscular Disorders

Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of Dysport®.

Human Albumin

This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been reported for albumin.

Intradermal 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. Dysport® is approved only for intramuscular injection.

Adverse reactions

Most common adverse reactions ($\geq 2\%$ and greater than placebo in either Dysport® group) in adults with upper limb spasticity for Dysport® 500 Units, Dysport® 1000 Units, and Placebo, respectively, were: nasopharyngitis (4%, 1%, 1%), urinary tract infection (3%, 1%, 2%), muscular weakness (2%, 4%, 1%), musculoskeletal pain (3%, 2%, 2%), dizziness (3%, 1%, 1%), fall (2%, 3%, 2%), and depression (2%, 3%, 1%).

Most common adverse reactions ($>5\%$ and greater than placebo) in adults with cervical dystonia for Dysport® 500 Units and Placebo, respectively, were: muscular weakness (16%, 4%), dysphagia (15%, 4%), dry mouth (13%, 7%), injection site discomfort (13%, 8%), fatigue

(12%, 10%), headache (11%, 9%), musculoskeletal pain (7%, 3%), dysphonia (6%, 2%), injection site pain (5%, 4%), and eye disorders (7%, 2%).

Drug interactions

Co-administration 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 after administration of Dysport® may potentiate systemic anticholinergic effects such as blurred vision. The effect of administering different botulinum neurotoxins at the same time or within several months of each other is unknown. Excessive weakness may be exacerbated by another administration of botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of Dysport®.

Use in Pregnancy

Based on animal data Dysport® may cause fetal harm. There are no adequate and well-controlled studies in pregnant women. Dysport should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Geriatric Use

In general, elderly patients should be observed to evaluate their tolerability of Dysport, due to the greater frequency of concomitant disease and other drug therapy.

To report SUSPECTED ADVERSE REACTIONS or product complaints, contact Ipsen at 1-855-463-5127. You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the Dysport® Medication Guide for patients available [here](#).

Please see full Prescribing Information for Dysport® available [here](#).

About Ipsen

Ipsen is a global specialty-driven pharmaceutical company with total sales exceeding EUR1.2 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 EUR260 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, visit www.ipsen.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. 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 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 favorable 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 fulfill 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:

References:

1. "Stroke Facts." Centers for Disease Control and Prevention. Web. 10 June 2015. <http://www.cdc.gov/stroke/facts.htm> 24 March 2015.

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2. Opheim A, et al. (2014). Upper-Limb Spasticity During the First Year After Stroke. Stroke Arm Longitudinal Study at the University of Gothenburg. *American Journal of Physical Medicine & Rehabilitation*, 93: 884:896.
3. "Traumatic Brain Injury in the United States: Fact Sheet." Centers for Disease Control and Prevention. 6 June 2015. http://www.cdc.gov/traumaticbraininjury/get_the_facts.html, 24 February 2014.
4. Ganish S, et al. (2013). Medical Comorbidities in Disorders of Consciousness Patients and Their Association with Functional Outcomes. *Archives of Physical Medicine and Rehabilitation*, 94: 1899-907.

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