

Ipsen announces a first set of results on positive phase III clinical study of Dysport® in the treatment of adults suffering from Upper Limb Spasticity at the 8th World Congress for NeuroRehabilitation in Istanbul

- **In adults with upper limb spasticity, treatment with Dysport® demonstrated improvement in muscle tone, clinical benefit and passive function**
- **Safety profile consistent with the known safety profile of Dysport®**

Paris (France), 12 April 2014 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that a first set of results on phase III clinical study of Dysport® in the treatment of adults suffering from Upper Limb Spasticity was presented on Saturday, April 12th, at the 8th World Congress for NeuroRehabilitation in Istanbul (Turkey).

Claude Bertrand, Executive Vice-President Research & Development and Chief Scientific Officer of Ipsen, commented: *“We are pleased that the first robust set of results from the phase III clinical study was presented by the Principal Investigator of the study (Pr JM Gracies) at this major congress. We look forward to sharing with the scientific community some additional data at coming international congresses.”*

Four weeks after Dysport® injection, the Phase III clinical study results demonstrated that:

- Patients treated with Dysport® showed a statistically significantly ($p < 0.0001$) higher proportion of responders in muscle tone improvement versus placebo (i.e. exhibiting ≥ 1 point improvement as measured by the Modified Ashworth Scale, MAS). At week 4, patients treated with Dysport® 500 units and 1000 units showed responding rates of 73.8% and 78.5%, respectively, compared to 22.8% in the placebo arm;
- Patients treated with Dysport® showed a statistically significant ($p < 0.0001$) higher clinical benefit versus placebo, as measured by the Physician Global Assessment (PGA). At week 4, the mean PGA score for patients treated with Dysport® 500 units and 1000 units were 1.4 and 1.8, respectively, compared to 0.6 in the placebo arm.

Additionally, patients treated with Dysport® showed a higher proportion of responders from baseline in improved passive function versus placebo (exhibiting ≥ 1 grade decrease as measured by the disability assessment scale). At week 4, patients treated with Dysport® 1000 units showed



a statistically significant response rate of 62%. Patients treated with Dysport® 500 units showed a clinically relevant response rate of 50%. Placebo arm showed a 39% response rate.

The safety profile observed in the study was consistent with the known safety profile of Dysport®.

Further results from this double-blind study will be disclosed in the next few months at major international congresses.

For more detailed information about the 8th World Congress for NeuroRehabilitation, please see <http://www.wcnr2014.org>

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.

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 phase III 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). In addition, Dysport®'s efficacy was assessed on passive function as measured by the Disability Assessment Scale (DAS).

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 the Disability Assessment Scale (DAS)

The Disability Assessment Scale evaluates upper limb functional disability in patients with spasticity. It ranges from 0 (=no disability) to 3 (=severe disability).



About Dysport®

Dysport® is an injectable form of botulinum toxin type A (BoNT-A), which is isolated and purified from Clostridium BoNT-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.

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Important Safety Information about Dysport®

CONTRAINDICATIONS

Dysport® (abobotulinumToxinA) is contraindicated in individuals with known hypersensitivity to any of its components.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Adverse effects resulting from the distribution of the effects of the toxin to sites remote from the site of administration have been reported. Patients treated with therapeutic doses may present with excessive muscle weakness. The risk of occurrence of such undesirable effects may be reduced by using the lowest effective dose possible and by not exceeding the maximum recommended dose.

Very rare cases of death, occasionally in the context of dysphagia, pneumopathy and/or in patients with significant asthenia have been reported following treatment with botulinum toxin A or B.

Patients with disorders resulting in defective neuromuscular transmission, difficulty in swallowing or breathing are more at risk of experiencing these effects. In these patients, treatment must be administered under the control of a specialist and only if the benefit of treatment outweighs the risk.

Dysport® should be administered with caution to patients with pre-existing swallowing or breathing problems as these can worsen following the distribution of the effect of toxin into the relevant muscles. Aspiration has occurred in rare cases and is a risk when treating patients who have a chronic respiratory disorder.

Dysport® should only be used with caution and under close medical supervision in patients with clinical or sub-clinical evidence of marked defective neuro-muscular transmission (e.g. myasthenia gravis). Such patients may have an increased sensitivity to agents such as Dysport®, which may result in excessive muscle weakness.

The recommended posology and frequency of administration for Dysport® must not be exceeded.

Patients and their care-givers must be warned of the necessity to seek immediate medical treatment in case of problems with swallowing, speech or respiratory problems.

For the treatment of spasticity associated with cerebral palsy in children, Dysport® should only be used in children 2 years of age or over.

As with any intramuscular injection, Dysport® should only be used where strictly necessary in patients with prolonged bleeding times, or infection/inflammation at the proposed site(s) of injection.

It is essential to study the patient's facial anatomy prior to administering Dysport® for the correction of glabellar lines. Facial asymmetry, ptosis, excessive dermatochalasis, scarring, and any alterations to this anatomy as a result of previous surgical interventions should be taken into consideration.



Dysport® should only be used to treat a single patient, during a single session. Any unused product remaining should be disposed of in accordance with Special Precautions for Disposal and Handling. Specific precautions must be taken during the preparation and administration of the product and the inactivation and disposal of any unused reconstituted solution.

This product contains a small amount of human albumin. The risk of transmission of viral infection cannot be excluded with absolute certainty following the use of human blood or blood products.

Antibody formation to botulinum toxin has been noted rarely in patients receiving Dysport®. Clinically, neutralizing antibodies might be suspected by a substantial deterioration in response to therapy and / or the need for consistent use of increased doses.

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.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.

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