

Ipsen announces clinical results of Dysport[®] Next Generation (DNG) and its intent to file the first ready-to-use liquid toxin A in Europe and ROW¹

- DNG efficacious at single and repeated dose
- In cervical dystonia Phase III study, DNG significantly superior to placebo. Non-inferiority versus Dysport[®] at week 4 not demonstrated
 - In glabellar lines Phase II study, DNG superior to placebo and comparable to Dysport[®]
- DNG safety profile consistent with known profile of Dysport[®]

Paris (France), 5 February 2014 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced the results of the international Phase III clinical trial of Dysport[®] Next Generation (DNG) in cervical dystonia and the results of the European Phase II clinical trial of DNG in glabellar lines. In the light of these results, Ipsen announces its intention to file the first ready-to-use liquid toxin A in Europe and in the Rest of the World¹ (ROW).

Pr. Werner Poewe (International Principal Investigator of the study) said: *“This is the very first international Phase III trial to show that a liquid toxin A is safe and efficacious. Although the statistical non-inferiority criterion between DNG and Dysport[®] was not formally met in the Double Blind Phase of the trial, this is unlikely to reflect clinical meaningful differences between the two formulations. In addition, the Open Label Long Term data show sustained and robust efficacy of DNG with a good safety profile. These important results will help the medical community to assess the place of a ready-to-use liquid toxin A in the treatment options for patients suffering from cervical dystonia.”*

Claude Bertrand, Executive Vice-President Research & Development and Chief Scientific Officer of Ipsen commented: *“With these studies, we confirm our role of pioneer in the field of toxins and our leadership in developing innovative therapeutic solutions. Ipsen’s ambition is to become the first company to file a ready-to-use liquid toxin A, which should meet the expectations of physicians by potentially providing a new treatment option for patients.”*

DNG was clinically and statistically superior to placebo in the cervical dystonia Phase III study at the dose of 500 units at week 4 after single dose (adjusted mean reduction of 12.5 with DNG

¹ Latin America, Middle East and Asia (ex Japan and China)



versus 3.9 with placebo as assessed by the Toronto Western Spasmodic Torticollis Rating Scale, or TWSTRS, total score).

When compared to Dysport[®], DNG did not demonstrate the statistical non-inferiority in efficacy at week 4 (adjusted mean reduction of 12.5 with DNG versus 14.0 with Dysport[®] in TWSTRS total score). This efficacy difference is unlikely to be of clinical relevance.

After repeated dose, DNG showed comparable efficacy to that of Dysport[®] as observed in former Phase III studies¹.

DNG was clinically and statistically superior to placebo and comparable to Dysport[®] in the glabellar lines Phase II study at the dose of 50 units after single dose.

Across the studies, DNG showed safety profiles consistent with the known safety profile of Dysport[®].

Regarding DNG stability, analysis is still ongoing. The stability data trends are positive, providing confidence of achieving a commercially viable product. Ipsen is continuing stability testing to establish maximum shelf life across full product range.

On the basis of these results and feedback from the Principal Investigator of the Phase III study, Ipsen intends to initiate a dialog with key agencies on the regulatory approach to file the first ready-to-use liquid toxin A in Europe and ROW².

About Dysport[®]

Dysport[®] is an injectable form of botulinum toxin type A (BoNT-A), which is isolated and purified from Clostridium BTX-A bacteria. The product is supplied as a lyophilised 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 (previously referred to as cervical dystonia), paediatric spasticity due to cerebral palsy, axillary hyperhidrosis, and glabellar lines.

About Dysport[®] Next Generation

Dysport[®] Next Generation is a ready-to-use liquid botulinum toxin A solution. This product offers the advantage to simplify the preparation of the drug to be injected, help physicians focus on patient care and potentially increase safety by reducing the risk of preparation errors.

About the clinical studies

The Randomised, Double-blind and Open Label Phase, Active and Placebo Controlled phase III trial in Cervical Dystonia included 369 patients.

It included BoNT-A naïve or non-naïve patients suffering from this disease for at least 18 months. In the double blind part of the study, patients were randomly assigned to treatment with DNG, Dysport[®] or

¹ Truong D. et al. *Mov. Disord.*, 2005; 20 (7) 783-791; Truong et al., *Parkinsonism Relat Disord.* 2010 Jun;16(5):316-23

² Latin America, Middle East and Asia (ex Japan and China)



placebo injections into the neck muscles. The patients then entered into an open label part of the study wherein they could receive up to 5 injections of DNG.

The primary endpoint of the study was the assessment of DNG efficacy and safety, as compared to placebo and Dysport[®], in the treatment of patients with cervical dystonia.

There was a statistically significant decrease in TWSTRS (Toronto Western Spasmodic Torticollis Rating Scale) score and an increase in proportion of patients responding to Dysport[®] and DNG vs. placebo ($p < 0.001$) at the dose of 500 units after single dose at Week 4. DNG was clinically and statistically superior to placebo with an adjusted mean reduction of 12.5 (versus 3.9 with placebo) in TWSTRS total score at week 4. When compared to Dysport[®], DNG did not demonstrate the non-inferiority with an adjusted mean reduction of 12.5 (versus 14.0 with Dysport[®]) in TWSTRS total score at week 4.

Patients receiving DNG and Dysport[®] also reported an improvement in quality of life after single dose as compared to placebo. In the open label part of the study, the efficacy and quality of life improvement was maintained in patients receiving DNG. The safety profile of DNG after single and repeated dose was excellent and consistent with the known safety profile of Dysport[®].

The Double Blind, Randomised, Placebo and Active Comparator Controlled Phase II trial in glabellar lines included 176 patients.

The primary endpoint of the study was the assessment of DNG efficacy and safety, as compared to placebo and Dysport[®], in the treatment of patients with moderate to severe glabellar lines. DNG was clinically and statistically superior to placebo and comparable to Dysport[®] at the dose of 50 units after single dose at week 4, as assessed by a co-primary endpoint composed of the “investigator live assessment” and “the subject self-assessment”. Based upon “the investigator live assessment”, the responder rate was 91% for DNG and 77% for Dysport[®], respectively. Based upon the “patient self-assessment”, the responder rate was 86% for DNG and 83% for Dysport[®], respectively. The responder rate corresponds to the number of patients who had an improvement of their wrinkles from “severe/moderate wrinkles” to “mild/no wrinkle” on any scale.

The safety profile observed of DNG after unique and repeated dose was excellent and consistent with the known safety profile of Dysport[®].



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 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.

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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