

Ipsen announces publication in *Pediatrics* of the results of the phase III randomized study showing the efficacy and safety of Dysport[®] (abobotulinumtoxinA) in children with dynamic equinus foot deformity due to cerebral palsy

- **Single injections of both Dysport[®] (abobotulinumtoxinA) doses (10U/kg/leg and 15U/kg/leg) significantly reduce muscle hypertonia and spasticity translating into clinical and functional benefits**

Paris (France), 26 January 2016 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the scientific journal *Pediatrics* published¹ the detailed results of the phase III randomized study (NCT01249417) showing both the efficacy and the safety of Dysport[®] in the treatment of dynamic equinus foot deformity (also known as pediatric lower limb spasticity), a condition associated with cerebral palsy in children.

The study met the primary endpoint (Modified Ashworth Scale, MAS) and the first secondary endpoint (Physician Global Assessment, PGA) in children with dynamic equinus foot deformity who received injections of Dysport[®] in the gastrocnemius and soleus calf muscles. Dysport[®] showed statistically significant improvement in muscle tone, resulting in an improved overall clinical benefit at week 4 at the two dose levels tested (10 and 15U/kg for unilateral injection or 20 and 30U/kg for bilateral injections). In addition, improvement of spasticity and attainment of overall treatment goals were demonstrated in a statistically and clinically significant manner as compared to placebo at week 4 after injection. Both doses of Dysport[®] were well tolerated and there was no evidence of a dose relationship for adverse events. The most frequent treatment emergent adverse events were common childhood infections (upper respiratory tract infections).

Claude Bertrand, Executive Vice President R&D and Chief Scientific Officer, Ipsen stated: *“The peer-reviewed publication of these Phase 3 results in the journal *Pediatrics* confirms the favorable efficacy and safety profile of Dysport[®] in the treatment of lower limb spasticity in children with cerebral palsy and demonstrates improvement in functional benefit after a single*

¹ online at <http://pediatrics.aappublications.org/content/early/2016/01/24/peds.2015-2830>



injection of Dysport[®]. The study results confirm the therapeutic value of Dysport[®] in this debilitating condition, the most common cause of chronic motor disability in childhood^{2;3;4}.”

Professor Mauricio Delgado, Director of the Pediatric Neurology Department at Texas Scottish Rite Hospital for Children and Professor of Neurology and Neurotherapeutics at the University of Texas Southwestern Medical Center) and Principal Investigator of the study stated: “The publication of this study in *Pediatrics* is important news for the field of pediatric neurorehabilitation and for the treatment of children with equinus foot deformity due to cerebral palsy. This is the first international study that demonstrates substantial improvements in muscle tone and spasticity translating into clinical and functional benefits after a single injection in this patient population. This study both highlights the potential therapeutic value of Dysport[®] (abobotulinum toxin) in children with cerebral palsy and shows the potential value of new assessment methods that could have practical clinical application.”

About the Double Blind Phase 3 Study in cerebral palsy (hemiplegic and diplegic) children with lower limb spasticity

The Phase III study (NCT01249417) was multi-center, prospective, double blind, randomized, and placebo-controlled. It was conducted in the U.S., Mexico, Chile, Turkey, France and Poland.

A total of 241 patients from 27 centers were randomized to treatment with Dysport[®] 10U/kg/leg (n=80), Dysport[®] 15U/kg/leg (n=80) or placebo (n=81). The purpose of this study was to assess the efficacy of Dysport[®] compared to placebo in the treatment of Lower Limb Spasticity in children with cerebral palsy. Muscle tone and spasticity were assessed using the MAS and the Tardieu Scale; patient functionality was assessed using the Physician’s Global Assessment (PGA) and goal attainment scaling (GAS).

Study results showed a significant improvement versus placebo on muscle tone at both doses at week 4 post-injection (Primary endpoint – Assessment scale: Modified Ashworth Scale) with abobotulinumtoxinA; mean [95%CI] treatment differences vs. placebo were: -0.49 [-0.75, -0.23] (p=0.0002) for 15U/kg/leg and -0.38 [-0.64, -0.13] (p=0.003) for 10U/kg/leg.

A significant improvement was also observed on the overall clinical improvement (first secondary endpoint - Physician Global Assessment) with mean treatment differences vs. placebo of 0.77 [0.45, 1.10] for 15U/kg/leg and 0.82 [0.50, 1.14] for 10U/kg/leg (both p<0.0001).

In addition, significant improvement in spasticity (tertiary endpoint - using the Tardieu scale) was observed at Week 4. Both doses improved the Tardieu scale spasticity grade Y at 4 Weeks (p<0.001). For the 15U/kg/leg dose, Week 4 improvements were also accompanied by significant improvements in the angle of catch X_{V3} (p=0.0003) and angle of arrest X_{V1} (p=0.01).

² Delgado MR, Albright AL. Movement disorders in children: definitions, classifications, and grading systems. *J Child Neurol*. 2003;18 Suppl 1:S1-8.

³ Aisen ML, Kerkovich D, Mast J, et al. Cerebral palsy: clinical care and neurological rehabilitation. *Lancet Neurol*. 2011;10(9):844-852.

⁴ Yeargin-Allsopp M, Van Naarden Braun K, Doernberg NS, Benedict RE, Kirby RS, Durkin MS. Prevalence of cerebral palsy in 8-year-old children in three areas of the United States in 2002: a multisite collaboration. *Pediatrics*. 2008;121(3):547-554.



The use of Goal Attainment Scale clearly demonstrates that improvements in tone and spasticity allow the patients to achieve their overall functional goals, namely those related to walking and gait pattern at both doses tested at Week 4.

Both doses of Dysport[®] were well tolerated and there was no evidence of a dose relationship for adverse events (AEs). The most frequent TEAEs (treatment emergent adverse events) were common childhood infections (upper respiratory tract infections). Five patients in the abobotulinumtoxinA groups had an AE of epilepsy recorded versus none in the placebo group, however none was considered related to study treatment and there was an over-representation of epilepsy in the treatment groups.

After the completion of this double blind study, patients were offered the option to continue in an open label long-term study where they would receive additional treatment with Dysport[®].

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. It is licensed in 82 countries for various indications including blepharospasm, upper and lower limb spasticity in adults, hemifacial spasm, spasmodic torticollis (also referred to as cervical dystonia), lower limb spasticity due to cerebral palsy in children, axillary hyperhidrosis and glabellar lines.

Dysport[®] is approved for the treatment of lower limb spasticity in children in many European and international markets, but not in the United States (USA). As such, data from studies of Dysport[®] in children with lower limb spasticity are investigational in the USA.

About Ipsen

Ipsen is a global specialty-driven biotechnological group with total sales exceeding €1.2 billion in 2014. Ipsen sells more than 20 drugs in more than 115 countries, with a direct commercial presence in 30 countries. 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 urology-oncology. Ipsen's commitment to oncology is exemplified through its growing portfolio of key therapies improving the care of patients suffering from prostate cancer, bladder cancer or neuroendocrine tumors. Ipsen also has a significant presence in primary care. 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, located in the heart of the leading biotechnological and life sciences hubs (Les Ulis, France; Slough/Oxford, UK; Cambridge, US). In 2014, R&D expenditure totaled close to €187 million, representing about 15% of Group sales. The Group has more than 4,500 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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