

Ipsen demonstrates leadership position in neurotoxin research with strong presence at TOXINS 2019

Paris (France), 11 January 2019 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that abobotulinumtoxinA (Dysport®) and its recombinant botulinum toxins pipeline are the subject of 50 posters at the 2019 TOXINS International Conference. Results are presented from basic science (*in vivo*, *in vitro*, *ex vivo*, *in silico*), to clinical (Phase I to IV) and patients and caregivers surveys. Data highlights include further differentiation of Dysport® in the treatment of spasticity and movement disorders¹, results from the first in-human study of a recombinant neurotoxin (rBoNT-E), real life data (ULIS-III) as well as a survey with insights from patients and caregivers on the burden of spasticity (Carenity).

“Our data at TOXINS 2019 further differentiate Dysport® in the treatment of spasticity and other movement disorders, and demonstrate the headway we are making with our innovative pipeline, including new recombinant botulinum toxins such as our fast-acting rBoNT-E,” said **Alexandre Lebeaut, Executive Vice President, R&D and Chief Scientific Officer, Ipsen.** *“We look forward to many more years of real and significant progress toward our commitment to improving people’s lives through innovative and effective treatments and by transforming the treatment paradigm with tailored approaches.”*

With Dysport® (abobotulinumtoxinA), Ipsen offers a single product to treat a range of therapeutic indications². Injected at approved doses, the amount of active neurotoxin in Dysport® (data³ published in Toxins, in December 2018) may help to explain the long-lasting symptomatic relief observed in clinical studies (based on phase 3 trials^{4,5}) within a well-characterized safety and tolerability profile. With a long duration of response, Dysport® aims at providing an answer to the unmet need of patients and their families.

Alexandre Lebeaut added: *“We are proud and excited to be presenting these new data at TOXINS 2019 as we continue to build on more than 30 years of clinical experience with Dysport®. We will continue investing in this unique product through research and novel programs studies to further explore its potential and address patients’ unmet needs”.*

About TOXINS conference

Held every 2 years, TOXINS is a key event for experts – clinicians and researchers from academia and industry - in the field of neurotoxins and especially Botulinum toxins. The international congress will take place in 16-19 January 2019, in Copenhagen, Denmark. The TOXINS 2019 scientific program will feature presentations on the latest developments in the basic science and clinical applications of neurotoxins.

About spasticity and cervical dystonia

Spasticity is a condition in which there is an abnormal increase in muscle tone or stiffness in one or more muscles, which might interfere with movement. Spasticity is usually caused by damage to nerve pathways in the brain or spinal cord that control muscle movement, and may occur in association with cerebral palsy, spinal cord injury, multiple sclerosis, stroke, and brain or head trauma⁸.

With a prevalence of 4.98/100,000 in Europe, cervical dystonia is the most common adult-onset focal dystonia, a movement disorder characterized by involuntary and sustained muscle spasms⁹. Also known as spasmodic torticollis, cervical dystonia is an idiopathic chronic condition in which the neck is twisted or deviated.

About Dysport®

Dysport® is an injectable form of a botulinum neurotoxin type A product, which is a substance derived from Clostridium bacteria producing BoNT-A that inhibits the effective transmission of nerve impulses and thereby reduces muscular contractions⁶. It is supplied as a lyophilized powder. As of 31 December 2018, Dysport® had marketing authorization in more than 85 countries and more than 30 years of clinical experience⁷.

NOTE: Dysport® labels and approved indications may vary from country to country

INDICATIONS AND IMPORTANT SAFETY INFORMATION

Dysport® is approved for the treatment of adult upper and lower limb spasticity, paediatric lower limb spasticity and cervical dystonia (referred to spasmodic torticollis in some markets) in many international markets. Please refer to national labelling for details of the locally approved prescribing information in each of these indications.

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 (including but not limited to dyspnoea, respiratory failure, respiratory arrest) 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. Caution should be exercised when treating adult patients, especially the elderly, with focal spasticity affecting the lower limbs, who may be at increased risk of fall. In placebo-controlled clinical studies where patients were treated for lower limb spasticity, 6.3% and 3.7% of patients experienced a fall in the Dysport® and placebo groups, respectively. 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 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. 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.”

About Ipsen

Ipsen is a global biopharmaceutical group focused on innovation and specialty care. The group develops and commercializes innovative medicines in three key therapeutic areas - Oncology, Neuroscience and Rare Diseases. Its commitment to Oncology is exemplified through its growing portfolio of key therapies for prostate cancer, neuroendocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen also has a well-established Consumer Healthcare business. With total sales over €1.9 billion in 2017, Ipsen sells more than 20 drugs in over 115 countries, with a direct commercial presence in more than 30 countries. Ipsen's R&D is focused on its innovative and differentiated technological platforms located in the heart of the leading biotechnological and life sciences hubs (Paris-Saclay, France; Oxford, UK; Cambridge, US). The Group has about 5,400 employees worldwide. Ipsen is listed in Paris (Euronext: IPN) and in the United States through a Sponsored Level I American Depository Receipt program (ADR: 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. 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 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. 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. The risks and uncertainties set out are not exhaustive and the reader is advised to refer to the Group's 2017 Registration Document available on its website (www.ipsen.com).

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Abstracts list

I. Dysport® differentiation

ORAL:

1. **Thursday January 17th 2019, 17:30 - 18:00**

[Poster n° 9.26] AbobotulinumtoxinA and rehabilitation vs rehabilitation alone in post-stroke spasticity: an Italian cost-utility analysis (Italy); Lazzaro et al.

Presenting author: Alessio Baricich (Italy)

POSTERS:

1. [Poster n° 1.16] AbobotulinumtoxinA, onabotulinumtoxinA and incobotulinumtoxinA neurotoxin content and activity: potential implications for duration of efficacy in patients; Field et al.
2. [Poster n° 1.22] AbobotulinumtoxinA (Dysport®) shows higher efficacy and longer duration of action in rats with spinal cord injury-mediated spasticity than in healthy controls; Kalinichev et al.
3. [Poster n° 3.3] The patients' perspective on botulinum neurotoxin A treatment: results of a multinational survey for patients with spasticity; Bahroo et al.
4. [Poster n° 3.9] Assessment of upper limb active movement facilitation and neuromuscular plasticity induced by abobotulinumtoxinA in chronic post-stroke; Chalard et al.
5. [Poster n° 3.11] Botulinum neurotoxins are used at low doses in the treatment of spasticity in clinical practice: Results from market research analysis; de Sainte-Marie et al.
6. [Poster n° 3.16] AbobotulinumtoxinA (Dysport®) improves functional outcomes after single and repeat dosing in adults and children with spasticity; Esquenazi et al.
7. [Poster n° 3.22] AbobotulinumtoxinA (Dysport®), a long-acting botulinum neurotoxin; Foster et al.
8. [Poster n° 3.51] Management of upper limb spasticity with botulinum toxin A: Baseline data from the Italian cohort of the upper limb international spasticity (ULIS)-III Study (Italy); Cosma et al.
9. [Poster n° 3.65] Efficacy of abobotulinumtoxinA for the treatment of hemiparetic adult patients with lower limb spasticity previously treated with botulinum toxins; Boyer et al.
10. [Poster n° 3.66] Time to retreatment with botulinum toxin a in upper limb spasticity management: upper limb international spasticity (ULIS)-III study interim analysis; Turner-Stokes et al.
11. [Poster n° 3.68] Fewer injections of botulinum toxin type A for treatment of spasticity are perceived as beneficial by both patients and caregivers; Wein et al.
12. [Poster n° 3.72] First results from the EARLY-BIRD study, a prospective, non-interventional study to assess effectiveness of abobotulinumtoxinA (Dysport®) in post-stroke upper limb spasticity in relation to timing of treatment (Germany); Wissel et al.
13. [Poster n° 8.1] Economic benefits of AUL spasticity treatment with Dysport® compared to Botox® or Xeomin®: Analysis of a real-life setting in France; Schnitzler et al.
14. [Poster n° 9.10] AbobotulinumtoxinA time to retreatment across indications; Gracies et al.

II. Leadership in Neurotoxins

ORAL:

1. **Thursday January 17th 2019, 15:30 – 16:00**

[Poster n° 1.14] Botulinum neurotoxin B engineered for increased receptor affinity has improved clinical potential; Elliott et al.

Presenting author: Johannes Krupp (UK)

2. **Thursday January 17th 2019, 15:30 – 16:00**

[Poster n° 1.60] Chimeras of anthrax toxin and botulinum neurotoxin as novel analgesic proteins; Yang et al.

Presenting author: Nicole Yang (USA)

3. **Thursday January 17th 2019, 17:00 – 17:30**

[Poster n° 1.7] Mutations in light chains of botulinum neurotoxin A enable cleavage of human SPAP-23; Binz et al.

Presenting author: Thomas Binz (Germany)

4. **Friday January 18th 2019, 15:30 – 16:00**

[Poster n° 1.30] Exploring the effect of various BoNT serotypes in a model of autonomic nervous system hyperactivity from rodents and humans: paving the way to better targeting therapeutics in autonomic disorders? Maignel et al.

Presenting author: Jacque Maignel (France)

5. **Friday January 18th 2019, 18:00 – 18:30**

[Poster n° 1.42] Development of an in vitro human neuromuscular junction; Nicoleau et al.

Presenting author: Camille Nicoleau (France)

POSTERS:

1. [Poster n° 1.2] Building the landscape: Stability profile of botulinum neurotoxins; Barata et al.
2. [Poster n° 1.3] Computational tools for the design, characterisation and optimisation of recombinant botulinum neurotoxins for therapeutic applications; Barata & Bunting.
3. [Poster n° 1.4] Recombinant expression and characterisation of a botulinum neurotoxin serotype X chimera; Beard et al.
4. [Poster n° 1.8] New modified recombinant botulinum neurotoxin type F with enhanced potency; Burgina et al.
5. [Poster n° 1.10] Pharmacodynamic characterisation of a new recombinant serotype E botulinum toxin using electromyography in the monkey; Cornet et al.
6. [Poster n° 1.12] Potency comparison in vitro, ex vivo and in vivo assays of commercially available botulinum neurotoxin serotypes A1, B1 and F1; Donald et al.
7. [Poster n° 1.17] Development of a cell-based assay to replace LD50 for botulinum neurotoxin A1; Fonfria et al.
8. [Poster n° 1.18] Phage assisted continuous evolution of botulinum neurotoxin light chains generates novel light chains with modified SNARE cleavage specificity; Foster et al.
9. [Poster n° 1.27] Engineering fluorescently-labelled botulinum neurotoxins and derivatives to image their trafficking in neuronal and non-neuronal cells; Loss and Elliott.
10. [Poster n° 1.33] How to safely manufacture nature's most potent toxins; Marks.
11. [Poster n° 1.34] Distribution of botulinum toxin receptors and targets in different rat tissues; Martin et al.
12. [Poster n° 1.35] Evaluation of the fate of different fragments of SNAP25 in the injected muscle with BoNT/A or BoNT/E over a 30-day or a 75-day period in the rat; Martin et al.
13. [Poster n° 1.41] Assessment of multiple hiPSC-derived models for botulinum neurotoxin testing; Nicoleau et al.
14. [Poster n° 1.43] Translational Value of hiSPC-Derived Models for Botulinum Neurotoxin Research; Nicoleau et al.
15. [Poster n° 1.47] Outcomes of the first-in-human study with a recombinant botulinum toxin E (rBoNT-E): safety and pharmacodynamic profile of rBoNT-E compared with abobotulinumtoxinA (Dysport®); Pons et al.
16. [Poster n° 1.53] Comparative Botulinum Neurotoxin Type-A Activity in the EndoPep Assay – Formulation Effects; van der Schans et al.
17. [Poster n° 1.61] Genome-wide siRNA screen identification of genes in regulation of BoNT/A trafficking in a sensitized human neuronal stem cell line; Yeo et al.
18. [Poster n° 9.13] Predictive models using fusion methods to estimate pharmacodynamic properties of a recombinant botulinum toxin E in humans; Laugerotte et al.

III. Commitment to patients

POSTERS:

1. [Poster n° 1.6] Results from the INPUT survey: Training impact on usage of botulinum neurotoxin-A for cervical dystonia and spastic paresis management; Bhidayasiri et al.
2. [Poster n° 1.15] AbobotulinumtoxinA (Dysport®) shows efficacy in a model of MRMT-1-induced cancer pain in the rat; Favre-Guilmard et al [Poster n° 2.6] How satisfied are cervical dystonia patients after 3 years of botulinum toxin treatment? Colosimo et al.
3. [Poster n° 2.7] AbobotulinumtoxinA using 2mL dilution maintains durable functional improvements across multiple treatment cycles (US); Dashtipour et al.
4. [Poster n° 2.25] Factors predicting Long-term patient satisfaction with botulinum toxin treatment in cervical dystonia; Misra et al.
5. [Poster n° 3.55] Burden of spasticity among patients and caregivers: results of a multinational survey; Patel et al.
6. [Poster n° 5.2] Rationale and design for a phase II trial of abobotulinumtoxinA (Dysport®) in the management of vulvodinia; Goldstein et al.
7. [Poster n° 6.3] Systematic literature review examining the efficacy of abobotulinumtoxinA in aesthetic indications; Cohen et al.
8. [Poster n° 6.5] Dosing of abobotulinumtoxinA for long-term treatment of glabellar lines: Injection practices from the APPEAL non-interventional study; Gubanova et al.
9. [Poster n° 6.14] Systematic literature review examining patient and investigator satisfaction with abobotulinumtoxinA treatment in aesthetic indications; Redaelli et al.
10. [Poster n° 9.3] Rationale and design for a Phase II trial of abobotulinumtoxinA (Dysport®) in the management of hallux valgus; Armstrong et al.
11. [Poster n° 9.11] Improvement of Cervical Dystonia and Spastic Paresis Management: Assessment of 5 Years of the Innovative International Educational Program Ixcellence Network; Jacinto et al.