

Ipsen announces eight oral presentations from its Neurosciences portfolio at the 10th World Congress for Neurorehabilitation (WCNR)

Paris (France), 7 February 2018 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that results from its Neurosciences portfolio are the subject of eight oral presentations at the World Congress for Neurorehabilitation (WCNR 2018). The presentations focus on improvements in care for patients with spasticity and spasticity management with abobotulinumtoxinA (Dysport®). The meeting takes place in Mumbai, India, February 7-10, 2018.

“Ipsen has a very strong presence at WCNR 2018 with eight abstracts accepted as oral presentations, and we look forward to reporting these important data on spasticity management with Dysport®. We are notably pleased to present the first milestone in one of the largest patient-centred spasticity management observational studies, ULIS-III which has enrolled over 1,000 patients to be followed up for two years. These presentations demonstrate the commitment of Ipsen to improving the lives of patients with spasticity.” said **Alexandre Lebeaut, MD, Executive Vice-President R&D and Chief Scientific Officer, Ipsen.**

Since its inception, the Upper Limb International Spasticity (ULIS) programme has involved more than 2,400 patients living with upper limb spasticity in 31 countries. The objective of the ULIS program is to develop a comprehensive and patient-centred approach to spasticity management to be implemented internationally.

“Since the start of the program ten years ago, we have participated in significant training and standardisation efforts, developed and refined methods of outcomes assessment and learned a lot about how we use botulinum toxins in routine clinical practice.” said **Professor Lynne Turner-Stokes, DM FRCP MBE, Northwick Park Professor of Rehabilitation Medicine, King’s College London, and Director, Regional Hyper-acute Rehabilitation Unit, Northwick Park Hospital and Coordinating investigator of the ULIS program.**

“Ipsen’s long-lasting partnership with the WFNR confirms Ipsen’s commitment to both neurorehabilitation research and the daily care of patients with spasticity. WFNR, in collaboration with Ipsen, conducted the first International survey related to “Patients living with Spasticity”, which was published in Disability and Rehabilitation in 2016. This survey gave our patients the opportunity to let clinicians hear their voice.”* said **Professor Mike Barnes, Founding President of the WFNR, Honorary Professor of Neurological rehabilitation at Newcastle University.**

At WCNR 2018 in Mumbai, abstracts on the following topics will be presented from Thursday 8th February 2018 to Saturday 10th February:

* Barnes M. et al, An international survey of patients living with spasticity. Disability and Rehabilitation. 2016; Volume 39, 2017 -issue 14

The Upper Limb International Spasticity (ULIS) programme:

- *Title:* Time to retreatment with botulinum toxin A in upper limb spasticity management: initial data from the Upper Limb International Spasticity (ULIS)-III study

Presenter: Lynne Turner-Stokes, UK
Thursday 8th February, 14:00 - 14:08; Hall D

- *Title:* Relief of spasticity-related pain with Botulinum neurotoxin-A (BoNT-A) in real life practice. Post-hoc analysis from a large international cohort series

Presenter: Lynne Turner-Stokes, UK
Thursday 8th February, 15:12 - 15:20; Hall F

- *Title:* Botulinum Toxin A in Upper Limb Spasticity Management: Baseline Data from the Upper Limb International Spasticity (ULIS)-III Study

Presenter: Lynne Turner-Stokes, UK
Friday 9th February, 14:36 - 14:44; Hall A

The ONTIME Pilot study:

- *Title:* Effect of early use of abobotulinumtoxinA (Dysport®) on time to post-stroke spasticity progression: Results of the ONTIME pilot study

Presenter: Raymond L Rosales, Philippines
Thursday 8th February, 15:03 - 15:11; Hall A

The ENGAGE study:

- *Title:* Effect on voluntary movements of simultaneous upper and lower limb abobotulinumtoxinA injections in conjunction with Guided Self-rehabilitation Contracts in adults with spastic hemiparesis: methodology of the ENGAGE study

Presenter: Jean-Michel Gracies, France
Saturday 10th February, 14:09 - 14:17; Hall A

The Adult Upper Limb Spasticity, Adult Lower Limb Spasticity, and ULIS-2 studies:

- *Title:* AbobotulinumtoxinA injections in shoulder muscles: results from a real world and phase 3 studies

Presenter: Thierry Lejeune, Belgium
Thursday 8th February, 15:12 - 15:20; Hall D



- *Title:* AbobotulinumtoxinA injections in the upper and lower limb in patients with spastic paresis and impaired function following stroke or traumatic brain injury

Presenter: Jean-Michel Gracies, France
Friday 9th February, 14:18 - 14:26; Hall A

- *Title:* Continuous Improvement in Composite Active Range of Motion Across Repeated Injections with AbobotulinumtoxinA (Dysport®) for Upper and Lower Limb Spasticity

Presenter: Jean-Michel Gracies, France
Saturday 10th February, 14:00 - 14:08; Hall A

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 contractions. It is supplied as a lyophilized powder. As of 31 December 2017, Dysport® had marketing authorization in more than 85 countries.

About Spasticity

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 trauma.³ In adults, approximately one in three stroke patients, one in three patients with spinal cord injury, one in six patients with traumatic brain injury, and two in three patients with MS will develop lower limb spasticity.^{1,2}

INDICATIONS AND IMPORTANT SAFETY INFORMATION for the United States

INDICATIONS

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

- Adults with cervical dystonia
- Spasticity in adult patients
- Lower limb spasticity in pediatric patients 2 years of age and older

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 upper limb spasticity in children, and in approved

indications, cases of spread of effect have been reported at doses comparable to or lower than the maximum recommended total 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); or in patients known to be allergic to cow's milk protein. Hypersensitivity reactions including anaphylaxis have been reported.

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. Deaths as a complication of severe dysphagia have been 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. Patients treated with botulinum toxin may require immediate medical attention should they develop problems with swallowing, speech, or respiratory disorders. 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 (e.g., 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 and Transmission of Viral Diseases

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 and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

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.

Most Common Adverse Reactions



Adults with upper limb spasticity ($\geq 2\%$ and greater than placebo): nasopharyngitis, urinary tract infection, muscular weakness, musculoskeletal pain, dizziness, fall, and depression.

Adults with lower limb spasticity ($\geq 5\%$ and greater than placebo): falls, muscular weakness, and pain in extremity.

Adults with cervical dystonia ($\geq 5\%$ and greater than placebo): muscular weakness, dysphagia, dry mouth, injection site discomfort, fatigue, headache, musculoskeletal pain, dysphonia, injection site pain, and eye disorders.

Pediatric patients with lower limb spasticity ($\geq 10\%$ and greater than placebo): upper respiratory tract infection, nasopharyngitis, influenza, pharyngitis, cough, and pyrexia.

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.

Pediatric Use

Based on animal data Dysport® may cause atrophy of injected and adjacent muscles; decreased bone growth, length, and mineral content; delayed sexual maturation; and decreased fertility.

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. Subjects aged 65 years and over who were treated with Dysport® for lower limb spasticity reported a greater percentage of fall and asthenia as compared to those younger (10% vs. 6% and 4% vs. 2%, respectively).

To report SUSPECTED ADVERSE REACTIONS or product complaints in the United States, 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 [Full Prescribing Information](#), including **Boxed Warning** and [Medication Guide](#).

About Ipsen

Ipsen is a global specialty-driven biopharmaceutical group focused on innovation and specialty care. The group develops and commercializes innovative medicines in three key therapeutic areas - Oncology, Neurosciences 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 close to €1.6 billion in 2016, 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 5,100 employees worldwide. Ipsen is listed in Paris (Euronext: IPN) and in the United States through a Sponsored Level I American Depositary Receipt program (ADR: IPSEY). For more information on Ipsen, visit www.ipсен.com.

Ipsen 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 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.

The risks and uncertainties set out are not exhaustive and the reader is advised to refer to the Group's 2016 Registration Document available on its website (www.ipсен.com).



References:

1. Martin A, et al. Epidemiological, humanistic, and economic burden of illness of lower limb spasticity in adults: a systematic review. *Neuropsychiatric Disease and Treatment*. 2014; 10 (111-122)
2. Sköld A, et al. Spasticity after traumatic spinal cord injury: nature, severity, and location. *Archives of Physical Medicine and Rehabilitation*. 1999; 80 (1548-57)
3. National Institute of Neurological Disorders and Stroke. Spasticity Information Page. <https://www.ninds.nih.gov/Disorders/All-Disorders/Spasticity-Information-Page> Accessed May 16, 2017.

For further information:

Media

Ian Weatherhead

Vice President, Corporate External Communications
Tel.: +44 (0) 1753 627733
E-mail: ian.weatherhead@ipsen.com

Brigitte Le Guennec

Senior Manager, Global External Communications
Tel.: +33 (0)1 58 33 51 17
E-mail : brigitte.le.guennec@ipsen.com

Financial Community

Eugenia Litz

Vice-President Investor Relations
Tel.: +44 (0) 1753 627721
E-mail: eugenia.litz@ipsen.com

Côme de La Tour du Pin

Investor Relations Executive
Tel.: +33 (0)1 58 33 53 31
E-mail: come.de.la.tour.du.pin@ipsen.com