

Ipsen Biopharmaceuticals, Inc. announces FDA approval of Dysport® (abobotulinumtoxinA) for injection in the treatment of upper limb spasticity in adults in the United States

Phase III registration study showed significant improvements on co-primary endpoints evaluating muscle tone and global assessment by physician at Week 4

Clinical improvement may be expected one week after treatment

BASKING RIDGE, N.J., July 16, 2015 – [Ipsen Biopharmaceuticals, Inc.](http://www.ipseven.com), an affiliate of Ipsen (Euronext: IPN; ADR: IPSEY), today announced that the U.S. Food and Drug Administration (FDA) has approved its supplemental Biologics License Application (sBLA) for Dysport® (abobotulinumtoxinA) for the treatment of upper limb spasticity (ULS) in adult patients to decrease the severity of increased muscle tone in elbow flexors, wrist flexors and finger flexors. Clinical improvement may be expected one week after administration of Dysport®. A majority of patients in clinical studies were retreated between 12 and 16 weeks; however, some patients had a duration of response as long as 20 weeks. Dysport® is the first therapy in the past five years that was approved by the FDA for the treatment of adults with upper limb spasticity. The Dysport® Phase III trial was the first registration study to evaluate ULS treatment in adult patients with both stroke and traumatic brain injury. Dysport® was previously approved for the treatment of adults with cervical dystonia (CD) in the United States in April 2009.

“It is estimated that 1.8 million adult Americans may suffer from spasticity¹²³⁴, which in the upper arm can cause muscle stiffness, flexing, spasms, twitching and pain. We are pleased to offer another treatment option for those individuals with upper limb spasticity, a debilitating condition that often comes on the heels of a traumatic health event such as a stroke or brain injury,” said Cynthia Schwalm, Chief Executive Officer, Ipsen Biopharmaceuticals, Inc. “Spasticity can have a profound impact on adult patients and their abilities to perform the most basic daily tasks. Ipsen is committed to providing these patients, their caregivers and physicians with a comprehensive support offering including Dysport®, the IPSEN CARES™ patient assistance program, and the C.L.I.M.B. injector training platform for healthcare providers.”

The approval was based on a rigorous development program that included clinical trials conducted in over 600 patients. In the Phase III pivotal study, 238 adult patients with upper limb spasticity participated in the study for up to one year. The international, multi-center, double-blind, randomized, placebo-controlled study compared the efficacy of Dysport® (n=159) versus placebo (n=79) in hemiparetic patients following stroke or brain trauma. The trial also included patients who were botulinum toxin naïve or previously treated with a botulinum toxin, encompassing a broad patient population. The co-primary endpoints of the study were the improvement of muscle tone in the treated upper limb measured by the Modified Ashworth Scale (MAS) versus placebo and the clinical benefit for patients as assessed by the Physician Global Assessment (PGA) versus placebo at Week 4. The trial was followed by an open-label study wherein patients received Dysport® for up to five treatment cycles to assess the long term safety.

The Phase III pivotal data showed that those treated with Dysport® demonstrated statistically significant improvement in muscle tone measured by the MAS and a significantly higher

physician-rated clinical benefit measured by the PGA versus placebo at Week 4 ($p \leq 0.05$). At Week 4, both doses of Dysport[®] (500 units and 1000 units) significantly reduced muscle tone as measured by MAS in all primary target muscle groups, which included elbow, wrist, and finger muscles, with approximately 3 out of 4 patients* responding to Dysport[®]. The most frequently reported adverse reactions ($\geq 2\%$) are urinary tract infection, nasopharyngitis, muscular weakness, musculoskeletal pain, dizziness, fall and depression. The safety profile observed in the study was consistent with the known safety profile of Dysport[®], and there were no differences in the rate of serious adverse events between the treatment groups: placebo (3.7%), Dysport[®] 500 U (3.7%), Dysport[®] 1000 U (3.7%).

Dysport[®] and all botulinum toxin products have a Boxed Warning which states that the effects of the botulinum toxin may spread from the area of injection to other areas of the body, causing symptoms similar to those of botulism. Those symptoms include swallowing and breathing difficulties that can be life-threatening. Please see below for additional Important Safety Information.

“The FDA approval of Dysport[®] provides a new therapeutic option to help adults living with spasticity,” said Allison Brashear, M.D., Professor and Chair of Neurology, Wake Forest Baptist Medical Center and the U.S. principal investigator of the Phase III trial. “This approval is based on strong data which showed that Dysport[®] improved muscle tone in the upper limb – essential for active use of the hand and arm. It is important to realize that early identification is critical for patients with upper limb spasticity, given that when left untreated, spasticity can result in increased muscle tone.”

About Upper Limb Spasticity

It is estimated that 1.8 million adult Americans may suffer from spasticity¹²³⁴, which in the upper arm can cause muscle stiffness, flexing, spasms, twitching and pain. Upper limb spasticity (ULS) can make everyday simple tasks, such as washing your hands, difficult. The condition most commonly occurs in adults after a stroke, but can also result from other injuries to the central nervous system, such as a spinal cord injury or traumatic brain injury (TBI), multiple sclerosis (MS) or cerebral palsy (CP). Symptoms may not appear for months or even years after the stroke or injury, but may include bent elbows or wrists, and hands clenched into fists.

About the Phase III Pivotal Study

The Phase III research study sponsored by Ipsen included 238 patients and was multi-center, prospective, double blind, randomized, and placebo-controlled. It was conducted in the U.S., France, Italy, Belgium, the Czech Republic, Poland, Slovakia, Russia and Hungary.

The purpose of this study was to assess the efficacy of Dysport[®] compared to placebo in improving ULS in hemiparetic patients following a stroke or brain trauma. The study's 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).

Patients were offered the option to continue in an open label long-term study where they would receive additional treatment with Dysport[®] for a total of 15 months.

About Dysport[®] (abobotulinumtoxinA)

Dysport[®] is an injectable form of botulinum toxin type A (BoNT-A), which is isolated and purified from Clostridium bacteria producing BoNT-A. It is supplied as a lyophilized powder. Dysport[®] has approved therapeutic indications in the United States for the treatment of adults with

Cervical Dystonia (CD), and now for the treatment of Upper Limb Spasticity (ULS) in adult patients, to decrease the severity of increased muscle tone in elbow flexors, wrist flexors and finger flexors. The medicine was first registered in the United Kingdom in 1990 for other uses and is licensed in more than 80 countries in eight different indications, with over 1,300 peer-reviewed publications.

The C.L.I.M.B. (Continuum of Learning to Improve Management With Botulinum Toxin; <http://www.climb-training.com/>) injector training platform is a multi-tiered learning continuum designed to educate physicians with every level of experience with botulinum toxin therapy. C.L.I.M.B. can help physicians improve their clinical skills involving the appropriate use of Dysport[®].

About IPSEN CARES™

IPSEN CARES™ (Coverage, Access, Reimbursement, & Education Support) is dedicated to ensuring patients, providers and caregivers have the resources needed to help access the Ipsen medications that are critical to managing their conditions. IPSEN CARES™ is staffed Monday to Friday by experts who can assist with a broad range of medical, educational, logistical and coverage information regarding Ipsen medicines, including Dysport[®] (abobotulinumtoxinA), Increlex[®] (mecasermin) and Somatuline Depot[®] (lanreotide). Involving the entire treatment team that surrounds patients on a daily basis, IPSEN CARES™ can provide benefits verification (research of a patient's medical or pharmacy benefit insurance coverage); prior authorization information; a patient assistance program (free medications for uninsured patients); co-pay assistance programs; billing and coding support; coordination with specialty pharmacies. Additional information is also available by visiting (<http://www.ipsencares.com>).

What is Dysport[®]?

Dysport[®] is a prescription medicine that is injected into muscles and used to treat:

- increased muscle stiffness in elbow, wrist, and finger muscles in adults with upper limb spasticity
- cervical dystonia (CD) in adults

It is not known whether Dysport[®] is safe or effective in children under 18 years old or for the treatment of other types of muscle spasms.

Important Safety Information for Dysport[®]

Dysport[®] (abobotulinumtoxinA) may cause serious side effects that can be life threatening, including problems breathing or swallowing, and spread of toxin effects. These problems can happen within hours, or days to weeks after an injection of Dysport[®]. Call your doctor or get medical help right away if you have any of these problems after treatment with Dysport[®]:

- **Problems swallowing, speaking, or breathing** after an injection of Dysport[®] if the muscles that you use to breathe or swallow become weak. If these problems are severe, death can happen as a complication. People with certain breathing problems may need to use muscles in their necks to help them breathe and may be at greater risk for serious breathing problems with Dysport[®].
- Swallowing problems may last for several weeks; you may need a feeding tube to receive food or water. If swallowing problems are severe, food or liquids may go into

your lungs. People who already have swallowing or breathing problems before receiving Dysport[®] have the highest risk of getting these problems.

Spread of toxin effects. In some cases, the effects of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. The symptoms of botulism include: loss of strength and muscle weakness all over the body, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice, trouble saying words clearly, loss of bladder control, trouble breathing, or trouble swallowing. These problems could make it unsafe for you to drive a car or do other dangerous activities.

Do not take Dysport[®] if you are allergic to Dysport[®] or any of the ingredients in Dysport[®] (See Medication Guide for ingredients), or are allergic to cow's milk protein; had an allergic reaction to any other botulinum toxin product, such as Myobloc[®] (rimabotulinumtoxinB), Botox[®] (onabotulinumtoxinA), or Xeomin[®] (incobotulinumtoxinA); or have a skin infection at the planned injection site.

Before you take Dysport[®], tell your doctor about all your medical conditions, including if you have a disease that affects your muscles and nerves (such as amyotrophic lateral sclerosis [ALS or Lou Gehrig's disease], myasthenia gravis, or Lambert-Eaton syndrome), as you may be at increased risk of serious side effects, including difficulty swallowing or breathing.

Before you take Dysport[®], tell your doctor if you have or have had any of the following: a side effect from any botulinum toxin in the past; breathing problems such as asthma or emphysema; swallowing problems; bleeding problems; diabetes; and slow heartbeat, or other problems with your heart rate or rhythm.

Tell your doctor if you have plans to have surgery, had surgery on your face, have weakness of your forehead muscles (such as trouble raising your eyebrows), have drooping eyelids, or have any other change in the way your face normally looks.

Tell your doctor if you are pregnant, plan to become pregnant, or are breast-feeding or planning to breast-feed. It is not known if Dysport[®] can harm your unborn baby. It is not known if Dysport[®] passes into breast milk.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal products. Using Dysport[®] with certain other medicines may cause serious side effects. **Do not start any new medicines until you have told your doctor that you have received Dysport[®] in the past.**

Especially tell your doctor if you have received injections of botulinum toxin in the last four months or in the past. Be sure your doctor knows exactly which product you received such as Myobloc[®] (rimabotulinumtoxinB), Botox[®] (onabotulinumtoxinA), or Xeomin[®] (incobotulinumtoxinA); have recently received an antibiotic by injection; take muscle relaxants; take an allergy or cold medicine; or take a sleep medicine.

Most common side effects of Dysport[®] in people with upper limb spasticity include: urinary tract infection, muscle weakness, musculoskeletal pain, fall, depression, stuffy or runny nose and sore throat, and dizziness.

Most common side effects of Dysport® in people with cervical dystonia include: muscle weakness, dry mouth, feeling of tiredness, neck pain or muscle pain, problems speaking, eye problems, difficulty swallowing, injection site pain, and headache.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of Dysport®. For more information, ask your doctor or pharmacist.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit <http://www.fda.gov/medwatch> or call 1-800-FDA-1088.

Please see Dysport® Full Prescribing Information including **Boxed Warning** and Medication Guide.

The Medication Guide summarizes the most important information about Dysport®. If you would like more information, talk with your doctor. Full Product Information, including Boxed Warning, and Medication Guide, has been provided to your doctor.

Please see the Dysport® Medication Guide for patients available [here](#).

Please see full Prescribing Information for Dysport® available [here](#).

About Ipsen

Ipsen is a global specialty-driven pharmaceutical company with total sales exceeding EUR1.2 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 EUR260 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, visit www.ipsen.com.

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 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 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. 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 fulfill 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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Botox[®], Xeomin[®] and Myobloc[®] are registered trademarks of their respective owners.

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*MAS responders week 4: 74% to Dysport[®] 500 units, 79% to Dysport[®] 1000 units and 23% to placebo

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