

## **Ipsen Biopharmaceuticals, Inc. Announces FDA Acceptance of Filing for Dysport® (abobotulinumtoxinA) in the Treatment of Upper Limb Spasticity in Adult Patients**

*Over half a million Americans may suffer from painful and debilitating spasticity, which in upper arm is marked by rotated shoulders, fixed elbows and wrists and clenched wrists*

**BASKING RIDGE, N.J., December 1, 2014** – Ipsen Biopharmaceuticals, Inc., an affiliate of Ipsen (Euronext: IPN; ADR: IPSEY), today announced that the U.S. Food and Drug Administration (FDA) has accepted for review its supplemental Biologics License Application (sBLA) for Dysport® (abobotulinumtoxinA) for the treatment of upper limb spasticity in adult patients.

The regulatory filing was based on a Phase III study involving nearly 250 adult patients with upper limb spasticity. The international, multi-center, double-blind, randomized, placebo-controlled trial compared the efficacy of Dysport® versus placebo in hemiparetic patients following stroke or brain trauma. The data showed that those treated with Dysport® demonstrated a statistically significant improvement in muscle tone ( $p < 0.0001$ ), and a higher clinical benefit versus placebo. The safety profile observed in the study was consistent with the known safety profile of Dysport®.

*“There is more than 20 years of clinical experience worldwide with Dysport® in a variety of neurologic conditions,”* said **Cynthia Schwalm, Chief Executive Officer, Ipsen Biopharmaceuticals**. *“We are excited at the prospect of being able to bring adult patients who suffer from upper limb spasticity a new treatment option upon an anticipated FDA approval.”*

Dysport® is approved for the treatment of upper limb spasticity in many international markets, but not in the United States (U.S.).

Dysport®'s only approved therapeutic indication in the U.S. is for the treatment of adults with cervical dystonia (referred to as spasmodic torticollis in other markets). As such, data from the Phase III study in adults with upper limb spasticity are with respect to an investigational use of Dysport® in the U.S.

### **About Upper Limb Spasticity**

Over half a million Americans may suffer from spasticity, which in the upper arm can cause muscle stiffness, flexing, spasms and twitching. While not life threatening, upper limb spasticity is painful and can make everyday tasks, such as bathing and dressing, difficult. The condition most commonly occurs after a stroke, but can also result from a spinal cord or traumatic brain injury or in adults with multiple sclerosis (MS) or cerebral palsy. Symptoms may not appear until weeks, months or even years after the stroke or injury but can include rotated shoulders, bent elbows or wrists and hands clenched into fists.

### **About the study**

This phase III research study included 243 patients and was multicenter, prospective, double blind, randomized, and placebo-controlled. It was conducted in the USA, France, Italy, Belgium, Czech Republic, Poland, Slovakia, Russia and Hungary.



The purpose of this study was to assess the efficacy of Dysport<sup>®</sup> compared to placebo in improving upper limb spasticity in hemiparetic patients following a stroke or a brain trauma. The study 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). In addition, Dysport<sup>®</sup>'s efficacy was assessed on passive function as measured by the Disability Assessment Scale (DAS).

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

### **About Dysport**

Dysport<sup>®</sup> is an injectable form of botulinum toxin type A (BoNT-A), which is isolated and purified from Clostridium BoNT-A bacteria. It is supplied as a lyophilized powder. Dysport<sup>®</sup> 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 (ST) (previously referred to as cervical dystonia), pediatric lower limb spasticity due to cerebral palsy (CP), axillary hyperhidrosis, and glabellar lines.

### **About abobotulinumtoxinA (Dysport<sup>®</sup>) in the United States**

Dysport<sup>®</sup> is an injectable form of botulinum toxin type A (BoNT-A), which is isolated and purified from Clostridium BoNT-A bacteria. It is supplied as a lyophilized powder.

Dysport<sup>®</sup>'s approved therapeutic indication is for the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain in both toxin-naïve and previously treated patients.

### **Important Safety Information about Dysport<sup>®</sup> for Healthcare Professionals**

#### **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 spasticity in children and adults, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.**

#### **Contraindications**

Dysport is contraindicated in patients with hypersensitivity to any botulinum toxin product or its excipients, including human albumin, lactose, and cow's milk protein, or who have an infection at the proposed injection site.

#### **Lack of interchangeability between botulinum toxin products**

The potency Units of Dysport 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. Recommended dose and frequency of administration should not be exceeded.

### **Dysphagia and breathing difficulties**

Immediate medical attention may be required in cases of respiratory, speech, or swallowing difficulties. 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. Concomitant neuromuscular disorder may exacerbate clinical effects of treatment.

### **Pre-existing neuromuscular disorders**

Patients with neuromuscular disorders should be monitored particularly closely when given botulinum toxin as they may be at increased risk of clinically significant effects, including severe dysphagia and respiratory compromise from typical doses.

### **Human albumin**

Dysport contains human albumin. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases or Creutzfeldt-Jakob disease (CJD). No cases of transmission of viral diseases or CJD have ever been identified for albumin.

### **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.

### **Drug interactions**

Patients receiving concomitant treatment 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 may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxins during the course of treatment with Dysport is unknown.

### **Special populations**

Based on animal data, may cause fetal harm. Dysport should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Care should be exercised when administering Dysport to elderly patients, reflecting the greater frequency of concomitant disease and other drug therapy.

### **Adverse reactions**

The most commonly observed adverse reactions (>5% of patients) with Dysport for the treatment of cervical dystonia are muscular weakness, dysphagia, dry mouth, injection site discomfort, fatigue, headache, neck pain, musculoskeletal pain, dysphonia, injection site pain, and eye disorders.

To report SUSPECTED ADVERSE REACTIONS or product complaints, contact Ipsen at 1-877-397-7671.

You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Please see the full Prescribing Information for Dysport available at [http://www.dysport.com/hcp/PDFs/Dysport\\_Patients\\_PI\\_Sept2013.pdf](http://www.dysport.com/hcp/PDFs/Dysport_Patients_PI_Sept2013.pdf)



## **Important Safety Information about Dysport® for Patients**

**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. Deaths due to these problems have occurred. 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.** This is usually because the muscles used to breathe and swallow can become weak after the injection. Death can happen if you have severe problems with swallowing or breathing after treatment with Dysport. People who already have problems with swallowing or breathing 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 (dysphonia), trouble speaking (dysarthria), 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.

Dysport contains albumin, which is naturally found in human blood. An extremely remote risk for spreading viral diseases or Creutzfeldt-Jakob disease (CJD) does exist. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

It is not known whether Dysport is safe or effective in children under 18 years of age.

It is not known whether Dysport is safe or effective for the treatment of other types of muscle spasms.

### **What is Dysport?**

Dysport is a prescription medicine that is injected into muscles and used to treat the abnormal head position and neck pain that happens with cervical dystonia (CD) in adults.

**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.

**Tell your doctor about all your medical conditions**, such as diseases that affect 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 severe dysphagia (difficulty swallowing) and respiratory problems (difficulty breathing) from normal doses of Dysport.



**Tell your doctor if you have or have had any of the following:** allergies to any botulinum toxin product, side effect(s) from any botulinum toxin product in the past, breathing problems (such as asthma or emphysema), swallowing problems, bleeding problems, diabetes, slow heartbeat, or other problems with your heart rate or rhythm.

**Tell your doctor if you have plans to have surgery,** head 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, such as Myobloc<sup>®</sup>, Botox<sup>®</sup>, or Xeomin<sup>®</sup>, in the past; have recently received an antibiotic by injection; take muscle relaxants; take an allergy or cold medicine; or take a sleep medicine. Be sure your doctor knows exactly which product you received.

**The dose of Dysport is not the same** as the dose of any other botulinum toxin product.

**Other side effects** of Dysport include dry mouth, injection site discomfort or pain, tiredness, headache, neck pain, muscle pain, and eye problems, such as double vision, blurred vision, decreased eyesight, problems with focusing the eyes (accommodation), drooping eyelids, and swelling of the eyelids.

**Symptoms of an allergic reaction** to Dysport may include itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint. Tell your doctor or get medical help right away if you get wheezing or asthma symptoms, or if you get dizzy or faint.

**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.

**Call your doctor** for medical advice about side effects. You may report side effects to the FDA at 1–800–FDA–1088.

**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 at [http://www.dysport.com/ps/PDFs/Dysport%20Medication%20Guide\\_Mar2012.pdf](http://www.dysport.com/ps/PDFs/Dysport%20Medication%20Guide_Mar2012.pdf).

The full Prescribing Information for Dysport is available at [http://www.dysport.com/hcp/PDFs/Dysport\\_Patients\\_PI\\_Sept2013.pdf](http://www.dysport.com/hcp/PDFs/Dysport_Patients_PI_Sept2013.pdf)

### **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.ipсен.com](http://www.ipсен.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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