Ipsen Biopharmaceuticals, Inc. announces FDA approval of Dysport® (abobotulinumtoxinA) for the treatment of lower limb spasticity in pediatric patients aged two and older

First and only FDA-approved botulinum toxin for the treatment of pediatric lower limb spasticity and studied in patients with cerebral palsy

Pivotal study in cerebral palsy patients with lower limb spasticity aged 2 to 17 showed significant improvements in co-primary efficacy endpoints at Week 4 that evaluated Modified Ashworth Scale in ankle plantar flexor muscle tone and Physician’s Global Assessment response to treatment score

BASKING RIDGE, N.J., August 01, 2016 – Ipsen Biopharmaceuticals, Inc., a subsidiary of Ipsen SA (Euronext: IPN; ADR: IPSEY) (Ipsen), today announced that the U.S. Food and Drug Administration (FDA) has approved its supplemental Biologics License Application (sBLA) for Dysport® (abobotulinumtoxinA) for injection for the treatment of lower limb spasticity in pediatric patients two years of age and older. Dysport® is the first and only FDA-approved botulinum toxin for the treatment of pediatric lower limb spasticity. Those treated with Dysport® showed statistically significant improvement in co-primary efficacy assessments: mean change from baseline in Modified Ashworth scale (MAS) in ankle plantar flexor muscle tone and mean Physician’s Global Assessment (PGA) response to treatment score at Week 4 and Week 12. A majority of patients in the clinical study were eligible for retreatment between 16 and 22 weeks; however, some had a longer duration of response. This approval is based on a randomized, multicenter, double-blind, placebo-controlled, international Phase III pivotal study in 235 pediatric patients (158 received Dysport® and 77 received placebo) aged 2 to 17 years with lower limb spasticity due to cerebral palsy causing dynamic equinus foot deformity.

“Pediatric lower limb spasticity is a neurological condition that is commonly seen in children with cerebral palsy, which affects the communication between the brain and the muscles, resulting in movement and posture problems,” said Cynthia Schwalm, Chief Executive Officer, Ipsen Biopharmaceuticals, Inc. “Dysport® is the first and only FDA-approved botulinum toxin for the treatment of pediatric lower limb spasticity. Ipsen is committed to providing patients, their caregivers and their 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.”

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. 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. 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. Please see below for additional Important Safety Information.
“This approval means that, for the first time, physicians have a FDA-approved botulinum toxin with recommended dosing guidance for the treatment of children two years of age and older with lower limb spasticity based on a large registrational study,” said Ann Tilton M.D., Professor of Clinical Neurology, Chief, Section of Child Neurology, Louisiana State University School of Medicine.

“United Cerebral Palsy (UCP) is honored to work with responsible companies, like Ipsen, to help meet the needs of people with challenging conditions such as cerebral palsy,” said Gloria Johnson-Cusack, Board Chair, United Cerebral Palsy. “Lower limb spasticity in pediatric patients with cerebral palsy represents a significant unmet treatment need, as there have been no FDA-approved botulinum toxin treatment options available until now. It is our hope that the work of Ipsen in this area will benefit many individual pediatric patients who struggle with lower limb spasticity.”

About Pediatric Lower Limb 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. Lower limb spasticity commonly involves spasticity in the gastrocnemius and soleus muscle complex located in the calf. These calf muscles, during walking, work to raise the heel from the ground.

Symptoms of spasticity may include increased muscle tone, rapid muscle contractions, exaggerated deep tendon reflexes, and/or muscle spasms. The degree of spasticity can vary from mild muscle stiffness to severe, painful, and uncontrollable muscle spasms.

About the Phase III Pivotal Study
The Phase III registrational study sponsored by Ipsen included 235 pediatric patients (158 received Dysport® and 77 received placebo; intent to treat population) and was multicenter, double-blind, prospective, randomized, and placebo-controlled. It was conducted in the U.S., Mexico, Poland, Turkey and France.

Patients were randomized (1:1:1) to Dysport® 10 Units/kg/leg, Dysport® 15 Units/kg/leg or placebo injected into the gastrocnemius-soleus muscle complex located in the calf. The trial included patients who were botulinum toxin naïve or previously treated with a botulinum toxin more than six months before study entry.

The co-primary efficacy endpoints showed a statistically significant improvement in mean change from baseline in MAS in ankle plantar flexor muscle tone at both doses of Dysport® vs. placebo at Week 4 [LS mean treatment difference vs. placebo were: -0.5 for placebo, -0.9 for Dysport® 10 Units/kg/leg, and -1.0 for Dysport® 15 Units/kg/leg (p<0.05)]. Data at Week 12 as measured by the MAS was also statistically significant [LS mean treatment difference vs. placebo were: -0.5 for placebo, -0.8 for Dysport® 10 Units/kg/leg, and -1.0 for Dysport® 15 Units/kg/leg (p<0.05)]. The most common adverse reactions (≥10% of patients in any group and greater than placebo) in pediatric patients with lower limb spasticity for Dysport® 10 Units/kg, 15 Units/kg, 20 Units/kg, or 30 Units/kg; and placebo, respectively, were: nasopharyngitis (9%, 12%, 16%, 10%, 5%), upper respiratory tract infection (9%, 20%, 5%, 10%, 13%), influenza (0%, 5%,...
10%, 14%, 3%, 8%) and pharyngitis (5%, 0%, 11%, 3%, 8%), cough (7%, 6%, 14%, 10%, 6%), and pyrexia (7%, 12%, 8%, 7%, 5%).

A statistically significant improvement was also observed on the mean PGA response to treatment score at Week 4 [LS mean treatment difference of 0.7 for placebo, 1.5 for Dysport® 10 Units/kg/leg, and 1.5 for Dysport® 15 Units/kg/leg (p<0.05)]. Data at Week 12 as measured by the mean PGA response to treatment score was also statistically significant [LS mean treatment difference vs. placebo were: 0.4 for placebo, 0.8 for Dysport® 10 Units/kg/leg, and 1.0 for Dysport® 15 Units/kg/leg (p<0.05)].

A majority of patients in the clinical study were eligible for retreatment between 16 and 22 weeks; however, some had a longer duration of response. The degree and pattern of muscle spasticity and overall clinical benefit at the time of re-injection may necessitate alterations in the dose of Dysport® and muscles to be injected.

**About Dysport® (abobotulinumtoxinA) for Injection**

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 indications in the United States for the treatment of adults with Cervical Dystonia (CD) and 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 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 CARESTM**

IPSEN CARESTM (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 CARESTM is staffed Monday to Friday by experts who can assist with a broad range of medical, educational, logistical and coverage information regarding Ipsen medicines. Involving the entire treatment team that surrounds patients on a daily basis, IPSEN CARESTM 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 for eligible patients; 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
- increased muscle stiffness in calf muscles in children 2 years of age and older with lower limb spasticity

It is not known whether Dysport® is safe or effective in children under 2 years old for the treatment of lower limb spasticity.
It is not known whether Dysport® is safe or effective for the treatment of other types of muscle spasms.

It is not known whether Dysport® is safe or effective for the treatment cervical dystonia or upper limb spasticity in children under 18 years of age.

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®. Death can happen as a complication if you have severe problems with swallowing or breathing after treatment with 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, operate machinery, 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, muscle pain, problems speaking, eye problems, difficulty swallowing, injection site pain, and headache.

Most common side effects of Dysport® in children (2 to 17 years of age) with lower limb spasticity include: upper respiratory infection, stuffy or runny nose and sore throat, flu, cough, and fever.

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 www.fda.gov/medwatch or call 1-800-FDA-1088.

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

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

About Ipsen
Ipsen SA is a global specialty-driven biotechnological group with total sales exceeding €1.4 billion in 2015. Ipsen sells more than 20 drugs in more than 115 countries, with a direct commercial presence in more than 30 countries. One of the leading affiliates is Ipsen Biopharmaceuticals, Inc., the North American arm of Ipsen, headquartered in Basking Ridge, NJ. Ipsen’s ambition is to become a leader in specialty healthcare solutions for targeted debilitating diseases. Its fields of expertise cover oncology, neurosciences and endocrinology (adult & pediatric). 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 and neuro-endocrine 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/Paris-Saclay, France; Slough/Oxford, UK; Cambridge, US). In 2015, R&D expenditure totaled close to €193 million. The Group has more than 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 on Ipsen, 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 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 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.

For further information:

Media
Rob Kloppenburg  
Vice President, North America, Communications  
Tel.: 908-275-6388  
E-mail: robert.kloppenburg@ipsen.com
Erinn White  
Centron PR  
Tel: 917-769-2785  
Email: ewhite@centronpr.com

Didier Véron  
Senior Vice-President, Public Affairs and Communication  
Tel.: +33 (0)1 58 33 51 16  
Fax: +33 (0)1 58 33 50 58  
E-mail: didier.veron@ipsen.com
Brigitte Le Guennec  
Corporate External Communication Manager  
Tel.: +33 (0)1 58 33 51 17  
Fax: +33 (0)1 58 33 50 58  
E-mail: brigitte.le.guennec@ipsen.com

Financial Community
Eugenia Litz  
Vice President – Investor Relations  
Tel.: +44 () 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

References


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